AAOS
American Academy of Orthopaedic Surgeons

Preventing Venous Thromboembolic Disease in Patients Undergoing Elective Hip and Knee Arthroplasty

Evidence-Based Clinical Practice Guideline

Adopted by:
The American Academy of Orthopaedic Surgeons Board of Directors
September 23, 2011

Please cite this Appropriate Use Criteria as: American Academy of Orthopaedic Surgeons Clinical Practice Guideline on Preventing Thromboembolic Disease in Patients Undergoing Elective Hip and Knee Arthroplasty https://www.aaos.org/globalassets/quality-and-practice-resources/vte/vte_full_guideline_10.31.16.pdf Published September 23, 2011

Disclaimer
This clinical guideline was developed by an AAOS physician volunteer Work Group and experts in systematic reviews. It is provided as an educational tool based on an assessment of the current scientific and clinical information and accepted approaches to treatment. The recommendations in this guideline are not intended to be a fixed protocol as some patients may require more or less treatment or different means of diagnosis. Patients seen in clinical practice may not be the same as those found in a clinical trial. Patient care and treatment should always be based on a clinician's independent medical judgment given the individual clinical circumstances.

Disclosure Requirement
In accordance with AAOS policy, all individuals whose names appear as authors or contributors to this clinical practice guideline filed a disclosure statement as part of the submission process. All panel members provided full disclosure of potential conflicts of interest prior to beginning work on the recommendations contained within this clinical practice guideline.

Funding Source
The American Academy of Orthopaedic Surgeons exclusively funded this clinical practice guideline. The Academy received no funding from outside commercial sources to support the development of this document.

FDA Clearance
Some drugs or medical devices referenced or described in this clinical practice guideline may not have been cleared by the Food and Drug Administration (FDA) or may have been cleared for a specific use only. The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or device he or she wishes to use in clinical practice.

Published 2011 by the American Academy of Orthopaedic Surgeons
6300 North River Road
Rosemont, IL 60018
Second Edition

Summary of Recommendations

The following is a summary of the recommendations of the AAOS' clinical practice guideline, Preventing Venous Thromboembolic Disease in Patients Undergoing Elective Hip and Knee Arthroplasty. This summary does not contain rationales that explain how and why these recommendations were developed, nor does it contain the evidence supporting these recommendations. All readers of this summary are strongly urged to consult the full guideline and evidence report for this information. We are confident that those who read the full guideline and evidence report will see that the recommendations were developed using systematic evidence-based processes designed to combat bias, enhance transparency, and promote reproducibility.

This summary of recommendations is not intended to stand alone. Treatment decisions should be made in light of all circumstances presented by the patient. Treatments and procedures applicable to the individual patient rely on mutual communication between patient, physician, and other healthcare practitioners.

1. We recommend against routine post-operative duplex ultrasonography screening of patients who undergo elective hip or knee arthroplasty.

   Grade of Recommendation: Strong

   Description: Evidence is based on two or more "High" strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a strong negative recommendation), and that the strength of the supporting evidence is high.

   Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

2. Patients undergoing elective hip or knee arthroplasty are already at high risk for venous thromboembolism. The practitioner might further assess the risk of venous thromboembolism by determining whether these patients had a previous venous thromboembolism.

   Grade of Recommendation: Limited

   Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

   Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

Current evidence is not clear about whether factors other than a history of previous venous thromboembolism increase the risk of venous thromboembolism in patients undergoing elective hip or knee arthroplasty and, therefore, we cannot recommend for or against routinely assessing these patients for these factors.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

3. Patients undergoing elective hip or knee arthroplasty are at risk for bleeding and bleeding-associated complications. In the absence of reliable evidence, it is the opinion of this work group that patients be assessed for known bleeding disorders like hemophilia and for the presence of active liver disease which further increase the risk for bleeding and bleeding-associated complications.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

Current evidence is not clear about whether factors other than the presence of a known bleeding disorder or active liver disease increase the chance of bleeding in these patients and, therefore, we are unable to recommend for or against using them to assess a patient's risk of bleeding.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

4. We suggest that patients discontinue antiplatelet agents (e.g., aspirin, clopidogrel) before undergoing elective hip or knee arthroplasty.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

5. We suggest the use of pharmacologic agents and/or mechanical compressive devices for the prevention of venous thromboembolism in patients undergoing elective hip or knee arthroplasty, and who are not at elevated risk beyond that of the surgery itself for venous thromboembolism or bleeding.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

Current evidence is unclear about which prophylactic strategy (or strategies) is/are optimal or suboptimal. Therefore, we are unable to recommend for or against specific prophylactics in these patients.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

In the absence of reliable evidence about how long to employ these prophylactic strategies, it is the opinion of this work group that patients and physicians discuss the duration of prophylaxis.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

6. In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who have also had a previous venous thromboembolism, receive pharmacologic prophylaxis and mechanical compressive devices.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

7. In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who also have a known bleeding disorder (e.g., hemophilia) and/or active liver disease, use mechanical compressive devices for preventing venous thromboembolism.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

8. In the absence of reliable evidence, it is the opinion of this work group that patients undergo early mobilization following elective hip and knee arthroplasty. Early mobilization is of low cost, minimal risk to the patient, and consistent with current practice.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

9. We suggest the use of neuraxial (such as intrathecal, epidural, and spinal) anesthesia for patients undergoing elective hip or knee arthroplasty to help limit blood loss, even though evidence suggests that neuraxial anesthesia does not affect the occurrence of venous thromboembolic disease.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

10. Current evidence does not provide clear guidance about whether inferior vena cava (IVC) filters prevent pulmonary embolism in patients undergoing elective hip and knee arthroplasty who also have a contraindication to chemoprophylaxis and/or known residual venous thromboembolic disease. Therefore, we are unable to recommend for or against the use of such filters.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

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Peer Review Organizations

Participation in the AAOS peer review process does not constitute an endorsement of this guideline by the participating organization.

The following organizations participated in peer review of this clinical practice guideline and gave explicit consent to be listed as peer reviewers:

American Academy of Family Physicians
American Association of Hip and Knee Surgeons
American College of Chest Physicians
American Society of Regional Anesthesia and Pain Medicine
American Surgical Association/Society of Surgical Chairs
International Society on Thrombosis and Haemostasis
The Joint Commission on Accreditation of Healthcare Organizations

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AAOS Clinical Guideline on Preventing Venous Thromboembolic Disease in Patients Undergoing Elective Hip and Knee Arthroplasty

Introduction and Methods

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I. INTRODUCTION

OVERVIEW

This clinical practice guideline is based on a systematic review of published studies on preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. In addition to providing practice recommendations, this guideline also highlights gaps in the literature and areas that require future research.

This guideline is intended to be used by all appropriately trained surgeons and all qualified physicians managing the prevention of venous thromboembolic (VTE) disease in patients undergoing elective hip and knee arthroplasty.

GOALS AND RATIONALE

The purpose of this clinical practice guideline is to help improve screening, prevention, and treatment based on the current best evidence. Current evidence-based medicine (EBM) standards demand that physicians use the best available evidence in their clinical decision making. To assist them, this clinical practice guideline consists of a systematic review of the available literature on the prevention of venous thromboembolic disease. The systematic review detailed herein was conducted between March 2010 and April 2011 and demonstrates where there is good evidence, where evidence is lacking, and what topics future research could target to improve the prevention of venous thromboembolic disease among patients undergoing elective hip and knee arthroplasty. AAOS staff methodologists and the physician work group systematically reviewed the available literature and subsequently wrote the following recommendations based on a rigorous, standardized process.

Musculoskeletal care is provided in many different settings by many different providers. We created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

INTENDED USERS

This guideline is intended to be used by orthopaedic surgeons and all qualified clinicians managing the prevention of venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. Typically, orthopaedic surgeons will have completed medical training, a qualified residency in orthopaedic surgery, and some may have completed additional sub-specialty training.

The guideline is intended to both guide clinical practice and to serve as an information resource for medical practitioners. An extensive literature base was considered during the development of this guideline. In general, practicing clinicians do not have the resources necessary for such a large project. The AAOS hopes that this guideline will assist practitioners not only in making clinical decisions about their patients, but also in describing, to patients and others, why the chosen treatment represents the best available course of action.

This guideline is not intended for use as a benefits determination document. Making these determinations involves many factors not considered in the present document, including available resources, business and ethical considerations, and needs.

Evidence for the effectiveness of medical services is not always present. This is true throughout all areas of medicine. Accordingly, all users of this clinical practice guideline are cautioned that an absence of evidence is not evidence of ineffectiveness. An absence means just that; there are no data. It is the AAOS position that rigorously developed clinical practice guidelines should not seek to guide clinical practice when data are absent unless the disease, disorder, or condition in question can result in loss of life or limb. The AAOS incorporates expert opinion into a guideline under these circumstances, and only under these circumstances. Accordingly, when the AAOS states that it cannot recommend for or against a given intervention or service, it is stating that currently available data do not provide clear guidance on which course of action is best, and that it is therefore reluctant to make a recommendation that has potentially national ramifications. Although true in all circumstances, the AAOS believes that when evidence is absent, it is particularly important for the prevention of venous thromboembolic disease to be based on mutual patient and physician communication, with discussion of available treatments and procedures applicable to that patient, and with consideration of the natural history of the disease and the current practice patterns. Once the patient has been informed of available therapies and has discussed these options with his/her physician, an informed decision can be made. Clinician input based on experience with both non-operative management and surgical skills increases the probability of identifying patients who will benefit from specific treatment options.

PATIENT POPULATION

This document addresses the prevention of venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. It is not intended for treatment of patients who present with venous thromboembolic disease.

BURDEN OF DISEASE AND ETIOLOGY

Approximately 200,000 primary total hip arthroplasties and 400,000 primary total knee arthroplasties were performed in the United States in 2003, with a projected increase to 250,000 hip procedures and over 600,000 knee procedures in 2010.[1] During the ninety days following primary arthroplasty surgery, hospitalization due to symptomatic deep vein thrombosis occurs in 0.7% of hip patients and 0.9% of knee patients, while hospitalization due to pulmonary embolism occurs in 0.3% of both hip and knee patients.[2, 3]

POTENTIAL HARMS, BENEFITS, AND CONTRAINDICATIONS

The goal of prophylaxis is prevention of mortality and other serious complications resulting from venous thromboembolic (VTE) disease. Most treatments are associated with some known risks, especially invasive and operative treatments. In addition, contraindications vary widely based on the treatment administered. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and physician, weighing the potential risks and benefits for that patient.

DIFFERENCES BETWEEN THE PRESENT AND THE PREVIOUS AAOS GUIDELINE

The present clinical practice guideline is an update of the AAOS 2007 guideline, "Prevention of Symptomatic Pulmonary Embolism in Patients Undergoing Total Hip or Knee Arthroplasty." As an update, the present guideline supersedes the previous AAOS guideline.

There are numerous and substantial differences between our present and previous guideline. Among them are new processes for preventing bias. These new processes are outlined in the section, "Preventing Bias in an AAOS Clinical Practice Guideline." We also employ a relatively new statistical technique, network meta-analysis, to analyze the data. This technique allows one to gauge how the pharmaceuticals of interest compare to each other, even when published studies do not explicitly make all comparisons. Also, we employ more rigorous methods for evaluating the quality of the published studies, and we employ similarly rigorous methods to evaluate the generalizability of their results.

This update contains information published since we issued our previous guideline in addition to the studies we previously evaluated. There are some differences between the guidelines in the article inclusion criteria. (Please see the "Study Selection Criteria", page 18)

II. **PREVENTING BIAS IN AN AAOS CLINICAL PRACTICE GUIDELINE**

Clinical practice guidelines (CPGs) have come under scrutiny because many of them are not objective. Shaneyfelt and Centor have noted that most current guidelines are not at all like those the Institute of Medicine (IOM) had originally intended, and that they have strayed so far from this original concept that they are mere consensus reports.[4] More recently, the IOM has stated that "the quality of CPG development processes and guideline developer adherence to quality standards have remained unsatisfactory and unreliable for decades."[5] The AAOS understands that only high quality guidelines are credible, and we go to great lengths to ensure the integrity of our guidelines. The purpose of this section is to highlight the processes whereby the AAOS accomplishes this. Additional details about how we combat bias also appear in the Methods section of this guideline.

The AAOS combats bias beginning with the selection of work group members. Applicants for AAOS development work groups who have financial conflicts of interest (COI) related to the guideline topic cannot participate on an AAOS work group if they currently have, or have had a relevant conflict within a year of the start date of guideline development. Applicants also cannot participate if one of their immediate family members has, or has had a relevant conflict of interest.

Financial COI are not the only COI that can influence a guideline. The IOM has noted that income source, long service on government committees or with private insurers, authorship of articles on guideline-related subjects, and biases from personal experience can also cause bias. [6] This suggests that those with the greatest expertise in any given topic area are also those most likely to introduce bias into guideline development. It also suggests that bias can only be counteracted by processes that are in place throughout the entirety of the development, and not just at the beginning.

One manner whereby the AAOS combats bias throughout guideline development is by having a team that is free of all of the above-mentioned COI conduct the literature searches, evaluate the quality of the literature, and sythesize the data (see Appendix I for a list of the work group members and methodologists who participated in the development of this guideline). Hirsh and Guyatt[7] have suggested that using such conflict-free methodologists is critical to developing an unbiased guideline.

Our use of methodologists changes the traditional role of clinicians in guideline development. The clinicians on an AAOS guideline work group serve as content experts. One of the clinicians' tasks is to frame the scope of the guideline by developing preliminary recommendations (these are the questions that will be addressed by the guideline; see below for further information). Another is to develop the article inclusion criteria. After they have done so, the AAOS medical librarian obtains key words from work group members and uses words, the preliminary recommendations, and inclusion criteria to construct literature search strategies. Clinicians are not permitted to suggest specific articles for inclusion at this time inasmuch as those suggestions are often about articles they have authored or that support a particular point of view.

Methodologists then determine which articles should be recalled and whether a recalled article meets the inclusion criteria. After completing this task, the clinician work group is given a list of the recalled articles that are proposed for inclusion and a list of the recalled studies proposed for exclusion. The work group then reviews these lists and suggests modifications. The purpose of this step is to assure the integrity of the guideline's data set. The methodologists are not obligated to take the work group's suggestions, but they are obligated to explain why they did not. Articles included or excluded as a result of this clinician review are handled as all other included articles or excluded studies. The methodologists also appraise the quality and applicability of each included study (we use "quality" as synonymous with "risk of bias." The latter term is preferred by others but, since quality and risk of bias are measured exactly the same way, the difference between the two seems largely semantic. Similarly, we use the terms "applicability" and "generalizability" as synonyms.)

Quality appraisal is a subject worth special mention because it is a necessary step in performing a systematic review and in developing a clinical practice guideline. One evaluates the quality (or risk of bias) of a study to determine how "believable" its results are, the results of high quality studies are more believable than those of low quality studies. This is why, all other things being equal, a recommendation based on high quality evidence will receive a higher grade than recommendations based on lower quality evidence (see Grades of Recommendation for more information). Biases in quality evaluation can cause overestimates of the confidence one should have in available data, and in a guideline recommendation.

Bias in quality evaluation arises when members of a work group view the papers they authored as being more believable than similar research performed by others, view certain studies as more believable simply because they were conducted by thought leaders in a given medical speciality area, and/or view research results that they are "comfortable" with as more believable than results they are not comfortable with.

The problem of biased quality evaluations is aggravated by the fact that no method for qualiy/risk of bias assessment has been empirically validated. Ultimately, therefore, all methods of quality/risk of bias assessment, are based on expert opinion (including those based on expert consensus obtained through formal methods like the Delphi method), and they all require judgements that are arbitrary. The method we use is no exception.

Given that all currently available quality evaluation systems are imperfect, their susceptibility to bias must be a deciding factor about whether to use them in clinical practice guideline development.The AAOS methodology is guided by the thinking that, if guideline developers have the choice between several methodologically imperfect systems, the least biased system is the best.

The burden that falls to readers of clinical practice guidelines is to determine which ones are not. Making this determination requires readers to examine two aspects of quality evaluation; the individual criteria used to evaluate a study, and how those criteria are translated into a final determination of a study's believability.

The criteria used to evaluate a study are often framed as one or more questions about a study's design and/or conduct. At the AAOS, these questions are answered by independent

methodologists. This combats bias by virtually eliminating the intellectual conflicts of interest that can arise when others are providing the answers.

Also preventing bias is the way the quality questions are phrased, and the fact that there are specific criteria (described in almost 300 pages of documentation) for answering each question. The simplest example, the AAOS question "Was there >80% follow-up" illustrates the point. The question is answered "Yes,", "No", or "Unclear." To determine whether a "Yes" or "No" answer is unclear, the methodologist merely looks at the number of patients present at the follow-up time of interest, the number of patients present at the start of the study, and expresses the former as a percentage of the latter. If the article does not report the information required to compute this percentage (or does not directly report the percentage), an "Unclear" answer is supplied. In answering this or any other question in the AAOS quality assessment scheme, the analyst is merely checking to see if the article provides specific data or makes specific statements. If it does, a "Yes" or "No" answer is supplied. If it does not, an "Unclear" answer is given. This lack of ambiguity in the criteria required to answer each question makes answering each question an almost completely objective exercise.

This stands in sharp contrast to the use of Levels of Evidence systems (also called evidence hierarchies), which are probably the most commonly used way of evaluating study quality in clinical practice guideline development. The vagueness of these systems opens the opportunity for bias. For example, these systems often hold that Level I evidence (i.e., the highest quality evidence) is from a well-designed randomized controlled trial, without ever specifying what "well-designed" means. This lack of specific instructions creates the possibility for bias in grading articles because it allows for an *ad hoc* appraisal of study quality. Furthermore, there are over 50 such systems, individuals do not consistently apply any given system in the same way, many are not sensible to methodologists,[8] and Level I studies, those of the highest level of evidence, do not necessarily report that they used adequate safeguards to prevent bias.[9]

Obviously, simply answering a series of questions about a study does not complete the quality evaluation. All clinical practice guideline developers then use that information to arrive at a final characterization of a study's quality. This can be accomplished in two (and only two) ways, by allowing those who are performing this final characterization to use their judgement, or by not letting them do so. Bias is possible when judgement is allowed. Bias is not possible in the AAOS system because the final rating is accomplished entirely by a computer that uses a pre-determined algorithm.

This aspect of the AAOS system contrasts with the GRADE system,[10] which places the final determination about whether a study has "no", "serious" or "very serious" limitations in the hands of the reviewer. Furthermore, the GRADE system allows the investigator to specify "other sources of bias" (i.e. sources of bias that were not specified *a priori*) and, although this is a theoretically sound way to approach quality evaluation, in practice it too, could allow for *ad hoc* criticisms of a study, and to criticisms that are not evenly applied across all studies. We recognize that we may miss some uncommon study flaws in our evaluation. While this means that our quality evaluation system is not perfectly comprenensive, it does not mean that it is biased. This is yet another example of how the AAOS, faced with a choice among imperfect quality/risk of bias systems, chooses the least biased approach. Given the above-mentioned history of guideline development, the AAOS emphasis on elimination of bias seems prudent.

The AAOS system, unlike the GRADE system, also specifically addresses the issue of statistical power (i.e., number of patients enrolled) of a trial. Low statistical power is a common problem in the medical literature,[11] and low power studies can lead reviewers to incorrectly conclude that a statistically non-significant result means that a given treatment does not work or, perhaps more serious, to reach positive conclusions about an intervention based on the putative "trends" reported in such studies. We regard low power studies as uninformative, and do not consider them when formulating a final recommendation. (We do, however, include low power studies in meta-analyses, inasmuch as one purpose of a meta-analysis is to overcome the low power of individual studies.)

Like the GRADE system, the AAOS guidelines will include observational studies. However, we do not always do so. Rather, we perform "best evidence" syntheses in AAOS guidelines in which we examine the best available (as opposed to the best possible) evidence. We use the best evidence because it is more believable than other evidence. The results of studies that are more believable should not be modified by results that are less believable.

When an AAOS guideline includes uncontrolled studies (e.g., case series) it only includes prospective case series that meet a number of other quality-related criteria. We do not include retrospective case series under any circumstances. Such studies lack virtually every component of a scientific study. There is no specific prohibition against using such studies in the GRADE system. We suggest that all guideline developers who are attempting to produce unbiased guidelines employ similar *a priori* criteria to specify the point at which they consider evidence to be too unreliable to consider.

Also unlike the GRADE system, the AAOS guidelines make provisions for making recommendations based on expert opinion. This recognizes the reality of medicine, wherein certain necessary and routine services (e.g., a history and physical) should be provided even though they are backed by little or no experimental evidence, and wherein certain diseases, disorders, or conditions are so grave that issuing a recommendation in the absence of evidence is more beneficial to patients than not issuing one. To prevent the bias that can result when recommendations based on expert opinion proliferate, we have (as further discussed below) specific rules for when opinion-based recommendations can be issued and, perhaps more importantly, for when they cannot be issued. The AAOS will only issue an opinion-based recommendation when the service in question has virtually no associated harms and is of low cost (e.g., a history and physical) or when the consequences of doing (or not doing) something are so catastrophic that they will result in loss of life or limb

Clinical practice guidelines have not met quality standards for a long time. In recognition of this, the IOM has developed two checklists, one for systematic reviews[12] and another for clinical practice guidelines.[5] Meeting the items on these checklists should assure readers of a guideline that it is unbiased. Table 1 and Table 2 show the performance of the present AAOS guideline on these standards.

Table 1. IOM Clinical Practice Guidelines Standards

IOM Standard	AAOS Guideline Meets Standard
1. Establishing transparency	Yes

2. Management of Conflict of Interest	Yes
3. Guideline development group composition	No – do not involve patient representative
4. Clinical practice guideline – systematic review intersection	Yes
5. Establishing evidence foundations for and rating strength of recommendations	Yes
6. Articulation of recommendations	Yes
7. External review	Yes
8. Updating	Yes

Table 2. IOM Systematic Review Standards

IOM Systematic Review Standard	AAOS Systematic Reviews Meet Standard
2.1. Establish a team with appropriate expertise and experience to conduct the systematic review	Yes
2.2. Manage bias and conflict of interest (COI) of the team conducting the systematic review	Yes
2.3. Ensure user and stakeholder input as the review is designed and conducted	Yes
2.4. Manage bias and COI for individuals providing input into the systematic review	Yes
2.5. Formulate the topic for the systematic review	Yes
2.6. Develop a systematic review protocol	Yes
2.7. Submit the protocol for peer review	No – do not have peer review of protocol
2.8. Make the final protocol publicly available, and add any amendments to the protocol in a timely fashion	Yes
3.1. Conduct a comprehensive systematic search for evidence	Yes
3.2. Take action to address potentially biased reporting of research results	No – do not search for unpublished information
3.3. Screen and select studies	Partially – do not use two independent researchers to screen studies (one screener and all work group members audit results)
3.4. Document the search	Yes
3.5. Manage data collection	Partially - do not use two independent researchers to extract data
3.6. Critically appraise each study	Yes
4.1. Use a prespecified method to evaluate the body of evidence	Yes
4.2. Conduct a qualitative synthesis	Yes
4.3. Decide if, in addition to a qualitative analysis, the systematic review will include a quantitative analysis (meta-analysis)	Yes
4.4. If conducting a meta-analysis, then do the following:	Yes
5.1. Prepare final report using a structured format	Partially - no lay public summary
5.2. Peer review the draft report	Partially - do not use independent third party to manage peer review process
5.3. Publish the final report in a manner that ensures free public access	Yes

III. METHODS

To develop this guideline, the work group held an introductory meeting on March 27, 2010 to establish the scope of the guideline and the systematic reviews. Upon completing the systematic reviews, the work group participated in a two-day recommendation meeting on April 2 and 3, 2011 at which time the final recommendations and rationales were edited, written, and voted on.

FORMULATING PRELIMINARY RECOMMENDATIONS

The work group determined the scope of the guideline by constructing a set of preliminary recommendations. These recommendations specify [what] should be done in [whom], [when], [where], and [how often or how long]. This is similar to the PICO (patients, interventions, comparisons, and outcomes) format used when the scope of a guideline is framed using key questions instead of preliminary recommendations. The preliminary recommendations function as questions for the systematic reviews that underpin each preliminary recommendation, not as final recommendations or conclusions. To avoid "wordsmithing" discussions at the initial work group meeting, the preliminary recommendations are always worded as recommending for something.

Once established, these preliminary recommendations cannot be modified until the final work group meeting. At this time, they can only be modified in accordance with the available evidence and only in accordance with the AAOS rules for how the wording of a recommendation depends on the grade of recommendation (see below for information about this wording). No modifications of the preliminary recommendations can require new literature searches and, at the final work group meeting, no recommendations can be added that require the use of expert opinion.

FULL DISCLOSURE INFORMATION

All of the work group's preliminary recommendations are represented in this guideline. This ensures full disclosure of the information that the AAOS work group examined, and assures readers that they are seeing *all* the information, and not just a selected portion of it.

STUDY SELECTION CRITERIA

We developed *a priori* article inclusion criteria for the systematic reviews for each preliminary recommendation. These criteria are our "rules of evidence." Articles that did not meet them are, for the purposes of this guideline, not evidence.

To be included in our systematic reviews (and hence, in this guideline) an article had to be a report of a study that:

- Investigated elective hip and knee arthroplasty patients
- Was a full article report of a clinical study
- Was not a retrospective case series
- Was not a medical records review, meeting abstract, historical article, editorial, letter, or a commentary
- If a prospective case series, reported baseline values
- Case series studies that have non-consecutive enrollment of patients are excluded
- Appeared in a peer-reviewed publication or a registry report

- Enrolled 100 or more patients per arm for studying deep vein thrombosis or pulmonary embolism, and more than 10 patients per arm per intervention (20 total) for all other outcomes
- Was of humans
- Was published in or after 1966
- Quantitatively presented results
- Was not be an *in vitro* study
- Was not be a biomechanical study
- Was not performed on cadavers
- Was published in English

The restriction on English language papers is unlikely to influence the recommendations in the present clinical practice guideline. An umbrella review of systematic reviews on language restriction found that none of the systematic reviews provided empirical evidence that excluding non-English language studies resulted in biased estimates of an intervention's effectiveness.[13]

We did not include systematic reviews or meta-analyses conducted by others, or guidelines developed by others. These documents are developed using different inclusion criteria than those specified by the AAOS work group. Therefore, they may include studies that do not meet our inclusion criteria. We recalled these documents if their abstract suggested that they might address one of our recommendations, and we searched their bibliographies for additional studies.

LITERATURE SEARCHES

We searched for articles published from January 1966 to February 24, 2011. We searched four electronic databases; PubMed, EMBASE, CINAHL, and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by the AAOS Medical Librarian using previously published search strategies to identify relevant studies.[14-19]

We supplemented searches of electronic databases with manual screening of the bibliographies of all retrieved publications. We also searched the bibliographies of recent systematic reviews and other review articles for potentially relevant citations. All articles identified were subject to the study selection criteria listed above. As noted above, the guideline work group also examined lists of included and excluded studies for errors and omissions.

We went to these lengths to obtain a complete set of relevant articles. Having a complete set ensures that our guideline is not based on a biased subset of articles.

The study attrition diagram in Appendix IV provides details about the inclusion and exclusion of the studies considered for this guideline. The search strategies used to identify these studies are provided in Appendix V.

BEST EVIDENCE SYNTHESIS

We included only the best available evidence for any given outcome addressing a recommendation. Accordingly, we first included the highest quality evidence for any given outcome if it was available. In the absence of two or more studies that reported an outcome at this quality, we considered studies of the next lowest quality until at least two or more

occurrences of an outcome had been acquired. For example, if there were two "Moderate" quality studies that reported an outcome, we did not include "Low" quality studies that also reported this outcome, but if there was only one "Moderate" quality study that reported an outcome, we also included "Low" quality studies.

APPRAISING EVIDENCE QUALITY AND APPLICABILITY

STUDIES OF INTERVENTIONS

QUALITY

As noted earlier, we judged quality using questions specified before this guideline topic was selected, and a computer program determined the final quality rating. Accordingly, it is highly unlikely that bias affected our determinations of quality.

We separately evaluated the quality of evidence for each outcome reported by each study. This follows the suggestion of the GRADE working group and others.[10, 20] We evaluated quality using a domain-based approach. Such an approach is used by the Cochrane Collaboration.[21] Unlike the Cochrane Collaboration's scheme (which is for studies with parallel control groups), our scheme allows for evaluation of studies of all designs. The domains we used are whether:

- The study was prospective (with prospective studies, it is possible to have an *a priori* hypothesis to test; this is not possible with retrospective studies.)
- The study was of low statistical power
- The assignment of patients to groups was unbiased
- There was blinding to mitigate against a placebo effect
- The patient groups were comparable at the beginning of the study
- The intervention was delivered in such a way that any observed effects could reasonably be attributed to that intervention
- Whether the instruments used to measure outcomes were valid
- Whether there was evidence of investigator bias

Each quality domain is addressed by one or more questions that are answered "Yes," "No," or "Unclear." These questions and the domains that each addresses are shown in Appendix VI.

To arrive at the quality of the evidence for a given outcome, all domains except the "Statistical Power" domain are termed as "flawed" if one or more questions addressing any given domain are answered "No" for a given outcome, or if there are two or more "Unclear" answers to the questions addressing that domain. The "Statistical Power" domain is considered flawed if a given study did not enroll enough patients to detect a standardized difference between means of 0.2.

Domain flaws lead to corresponding reductions in the quality of the evidence. The manner in which we conducted these reductions is shown in the table below (Table 1). For example, the evidence reported in a randomized controlled trial (RCT) for any given outcome is rated as "High" quality if zero or one domain is flawed. If two or three domains are flawed for the evidence addressing this outcome, the quality of evidence is reduced to "Moderate," and if four or five domains are flawed, the quality of evidence is reduced to "Low." The quality of evidence is reduced to "Very Low" if six or more domains are flawed.

Some flaws are so serious that we automatically term the evidence as being of "Very Low" quality, regardless of a study's domain scores. These serious design flaws are:

- Non-consecutive enrollment of patients in a case series
- Case series that gave patients the treatment of interest AND another treatment
- Measuring the outcome of interest one way in some patients and measuring it in another way in other patients
- Low statistical power

Table 3 Relationship between Quality and Domain Scores for Interventions

Number of Flawed Domains	Strength of Evidence
0-1	High
2-3	Moderate
4-5	Low
>5	Very Low

Although we mention levels of evidence in this guideline, we do so only to provide some very general information about study quality to those readers familiar with the levels of evidence system of *The Journal of Bone and Joint Surgery - American*. However, for the reasons noted above, we do not use levels of evidence as when we speak of "quality" in this document, and levels of evidence play no role in our determination of the grade of the final recommendations.

APPLICABILITY

We rated the applicability (also called "generalizability" or "external validity") of the evidence for each outcome reported by each study. As with quality, applicability ratings were determined by a computer program that used predetermined questions about specific applicability domains. We rated applicability as either "High", "Moderate", or "Low" depending on how many domains are flawed. As with quality, a domain is "flawed" if one or more questions addressing that domain is answered "No: or if two or more are answered "Unclear." We characterized a domain as "flawed" if one or more questions addressing any given domain are answered "No" for a given outcome, or if there are two or more "Unclear" answers to the questions addressing that domain (see Appendix VI for the specific applicability questions we employed and the domains that each question addresses).

Our questions and domains about applicability are those of the PRECIS instrument.[22] The instrument was originally designed to evaluate the applicability of randomized controlled trials, but it can also be used for studies of other design. The questions in this instrument fall into four domains. These domains and their corresponding questions are shown in Appendix VI. As shown in Table 4, the applicability of a study is rated as "High" if it has no flawed domains, as "Low" if all domains are flawed, and as "Moderate" in all other cases.

Table 4 Relationship between Applicability and Domain Scores for Interventions

Number of Flawed Domains	Applicability
0	High
1, 2, 3	Moderate
4	Low

STUDIES OF SCREENING AND DIAGNOSTIC TESTS

QUALITY

As with our appraisal of the quality of studies of intervention, our appraisal of studies of screening and diagnostic tests is a domain-based approach conducted using *a priori* questions (please see Appendix VI for the questions we used and the domains to which they apply), and scored by a computer program. The questions we used are those of the QUADAS instrument,[23, 24] and the six domains we employed are listed below:

1. Participants (whether the spectrum of disease among the participants enrolled in the study is the same as the spectrum of disease seen in actual clinical practice)
2. Reference Test (whether the reference test , often a "gold standard," and the way it was employed in the study ensures correct and unbiased categorization of patients as having or not having disease)
3. Index Test (whether interpretation of the results of the test under study, often called the "index test", was unbiased)
4. Study Design (whether the design of the study allowed for unbiased interpretation of test results)
5. Information (whether the same clinical data were available when test results were interpreted as would be available when the test is used in practice)
6. Reporting (whether the patients, tests, and study protocol were described well enough to permit its replication)

We characterized a study that has no flaws in any of its domains as being of "High" quality, a study that has one flawed domain as being of "Moderate" quality, a study with two flawed domains as being of "Low" quality, and a study with three or more flawed domains as being of "Very Low" quality (Table 5).We characterized a domain as "flawed" if one or more questions addressing any given domain are answered "No" for a given screening/diagnostic/test, or if there are two or more "Unclear" answers to the questions addressing that domain.
We considered some design flaws as so serious that their presence automatically guarantees that a study is characterized as being of "Very Low" quality regardless of its domain scores. These flaws are:

- The presence of spectrum bias (occurs when a study does not enroll the full spectrum of patients who are seen in clinical practice. For example, a diagnostic case control study enrolls only those known to be sick and those known to be well, a patient population quite different from that seen in practice. Because diagnostic case control studies enroll only the easy to diagnose patients, these kinds of studies typically overestimate the abilities of a diagnostic test.)
- Failure to give all patients the reference standard regardless of the index test results
- Non-independence of the reference test and the index text

Table 5. Relationship between Domain Scores and Quality of Screening/Diagnostic Tests

Number of Flawed Domains	Quality
0	High
1	Moderate
2	Low
≥3	Very Low

APPLICABILITY

We judged the applicability of evidence pertinent to screening and diagnostic tests using a modified version of the PRECIS instrument, implying that the questions are determined *a priori*. As before, scoring was accomplished by a computer. The applicability domains we employed for screening and diagnostic tests were:

1. Patients (i.e., whether the patients in the study are like those seen in actual clinical practice)
2. Index Test (i.e., whether the test under study could be used in actual clinical practice and whether it was administered in a way that reflects its use in actual practice)
3. Directness (i.e., whether the study demonstrated that patient health is affected by use of the diagnostic test under study)
4. Analysis (i.e., whether the data analysis reported in the study was based on a large enough percentage of enrolled patients to ensure that the analysis was not conducted on "unique" or "unusual" patients)

The specific questions we used, and the domains to which they pertain are provided in Appendix VI.

We characterized a domain as "flawed" if one or more questions addressing any given domain are answered "No" for a given screening/diagnostic/test, or if there are two or more "Unclear" answers to the questions addressing that domain. We characterized the applicability of a screening/diagnostic test as "High" if none of its domains are flawed, "Low" if all of its domains are flawed, and "Moderate" in all other cases (Table 6).

Table 6. Relationship between Domain Scores and Applicability for Studies of Prognostics

Number of Flawed Domains	Applicability
0	High
1,2, 3	Moderate
4	Low

STUDIES OF PROGNOSTICS

QUALITY

Our appraisal of studies of prognostics is a domain-based approach conducted using *a priori* questions, and scored by a computer program (please see Appendix VI for the questions we used and the domains to which they apply). The six domains we employed are:

1. Prospective (A variable is specified as a potential prognostic variable *a priori*. This is not possible with retrospective studies.)
2. Power (Whether the study had sufficient statistical power to detect a prognostic variable as statistically significant)
3. Analysis (Whether the statistical analyses used to determine that a variable was rigorous to provide sound results)
4. Model (Whether the final statistical model used to evaluate a prognostic variable accounted for enough variance to be statistically significant)
5. Whether there was evidence of investigator bias

We separately determined a quality score for each prognostic reported by a study. We characterized the evidence relevant to that prognostic variable as being of "High" quality if there are no flaws in any of the relevant domains, as being of "Moderate" quality if one of the relevant domains is flawed, as "Low" quality if there are two flawed domains, and as "Very Low" quality if three or more relevant domains are flawed (Table 7). We characterized a domain as "flawed" if one or more questions addressing any given domain are answered "No" for a given prognostic variable, or if there are two or more "Unclear" answers to the questions addressing that domain.

Table 7. Relationship between Quality and Domain Scores for Studies of Prognostics

Number of Flawed Domains	Quality
0	High
1	Moderate
2	Low
≥3	Very Low

APPLICABILITY

We separately evaluated the applicability of each prognostic variable reported in a study, and did so using a domain-based approach (please see in Appendix VI for the relevant questions and the domains they address) that involves predetermined questions and computer scoring. The domains we used for the applicability of prognostics are:

1. Patients (i.e. whether the patients in the study and in the analysis were like those seen in actual clinical practice)
2. Analysis (i.e., whether the analysis was not conducted in a way that was likely to describe variation among patients that might be unique to the dataset the authors used)
3. Outcome (i.e., whether the prognostic was a predictor of a clinically meaningful outcome)

We characterized the evidence relevant to that prognostic as being of "High" applicability if there are no flaws in any of the relevant domains, as being of "Low" applicability if all three domains are flawed, and as of "Moderate" applicability in all other cases (Table 8). We characterized a domain as "flawed" if one or more questions addressing any given domain are answered "No" for a given prognostic variable, or if there are two or more "Unclear" answers to the questions addressing that domain.

Table 8. Relationship between Domain Scores and Applicability for Studies of Prognostics

Number of Flawed Domains	Applicability
0	High
1,2	Moderate
3	Low

OTHER BIASES IN THE PUBLISHED LITERATURE

Despite our efforts to rigorously evaluate the quality of the studies we included, there remains the possibility that some of the articles considered in this guideline are biased. A 2007 umbrella review found that 20 of 23 previous systematic reviews found a positive relationship between pharmaceutical industry support and pro-industry findings,[25] leading the author to conclude that

"it is unequivocally the case that sponsorship influences published results." The relationship also seems to exist in orthopaedics, where authors of industry-funded studies of hip and knee arthroplasty come to positive conclusions more often that authors of studies not funded by industry,[26] and where the association between trial outcome and funding source exists across subspecialty societies.[27]

These apparent biases may not be related to the article's quality[25] and, therefore, may not be detected by our evaluations or the quality/risk of bias evaluations performed by others. Accordingly, we follow the suggestion of Montori et al.[28] and do not use the conclusions of the authors of any article. Rather, we use only the information provided in an article's Methods section and in its Results section. Furthermore, we perform our analysis using network meta-analysis, an analytical technique that considers the full range of alternatives rather than just those comparisons selected by industry.[29]

GRADES OF RECOMMENDATION

A grade of recommendation expresses the degree of confidence one can have in each of the final recommendations. Grades express how likely it is that a recommendation will be overturned by future evidence, and are termed "Strong," "Moderate," or "Limited."

We used the above-discussed quality and applicability ratings in conjunction with consistency, whether the studies reported outcomes that the work group deemed "critical," and the potential for catastrophic harm to determine the final grade of recommendation. More specifically, we began by setting the grade as equal to the quality of the available evidence. In other words, high quality evidence is preliminarily taken as a "Strong" grade, moderate quality as a "Moderate" grade, and low quality as a "Limited" grade. (As noted above, very low quality evidence is not included in AAOS guidelines. Accordingly, the final versions of preliminary recommendations that are based on such evidence will either state that the AAOS cannot recommend for or against a given medical service or, assuming that the requirements for a recommendation based on expert opinion are met, it will be a consensus-based recommendation. We then adjusted the grade down one step if the evidence is of "Low" applicability, is inconsistent (defined as studies that report qualitatively different effects, a heterogeneous meta-analysis, or a network meta-analysis with statistically significant inconsistency), if there is only one study that addresses a given recommendation, or if a majority of the outcomes deemed "critical" are not reported in the literature. Preliminary grades were adjusted upwards if the evidence is of "High" applicability or if providing the intervention decreases the potential for catastrophic harm (loss of life or limb). Preliminary grades were adjusted downward if the evidence is of "Low" applicability or if the medical service in question is accompanied with catastrophic harm. In the present guideline, catastrophic harm did not occur frequently enough to allow for increasing or decreasing the preliminary grade.

For a recommendation of a "Strong" grade, a minimum of two high quality studes are needed. A minimum of two moderate quality studies are required for a "Moderate" grade, and a minimum of two low quality studies are needed for a "Limited" grade. Recommendations addressed by only very low quality studies are consensus-based.

WORDING OF THE FINAL RECOMMENDATIONS

To prevent biased nuances in the way recommendations are worded, the AAOS uses predetermined, specific language for its recommendations. The exact wording is governed by the final grade of the recommendation. This wording, and the corresponding grade, is shown in Table 9.

Table 9 AAOS guideline language

Guideline Language	Grade of Recommendation
We ***recommend***	Strong
We ***suggest***	Moderate
The Practitioner ***might***	Limited
We are ***unable to recommend for or against***	Inconclusive
In the absence of reliable evidence, the ***opinion*** of this work group is*	Consensus*

*Consensus based recommendations are made only if specific criteria are met (see below).

Recommendation Strengths, Descriptions and Clinical Implications

Evidence Rating	Description of Evidence Strength	Implication for Practice
Strong	Evidence is based on two or more "High" strength studies with consistent findings in support of recommending for or against the intervention. A **Strong** (positive) recommendation means that the benefits of the recommended approach clearly exceed the potential harm, and/or that the strength of the supporting evidence is high. A **Strong** (negative) recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.	Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate	Evidence from two or more "Moderate" strength studies with consistent results, or evidence from a single "High" strength study recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.	Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.
Limited	Evidence from two or more "Low" strength studies with consistent results, or evidence from a single Moderate strength study recommending for or against the intervention. A **Limited** recommendation means that the strength of the supporting evidence is unconvincing, or that well-conducted studies show little clear advantage to one approach over another.	Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.
Inconclusive	Evidence from a single low strength study or otherwise conflicting evidence that does not allow a recommendation to be made for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.	Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.
Consensus	The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria in the systematic review.	Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

CONSENSUS RECOMMENDATIONS

Consensus recommendations are recommendations based on expert opinion. As noted above, there are times when it is prudent to make such recommendations. However, liberal use of them can allow for bias. Accordingly, we allow consensus-based recommendations using the procedures described by the United States Preventative Services Task Force (USPSTF).[30] In effect, this means that the AAOS will only issue a consensus-based recommendation under two circumstances. The first is for low cost procedures that have virtually no associated harms, are of relatively low cost, and that reflect current, routine clinical practice. The second is when providing (or not providing) a service could result in loss of life or limb. Because they are based on expert opinion, consensus recommendations are the weakest type of recommendation.

In making such recommendations, the AAOS instructs its clinician work group members to address:

- The potential preventable burden of disease (if the burden is low, a consensus-based recommendation cannot be issued)
- Potential harms (if there are serious harms that result from providing a medical service, a consensus-based recommendation cannot be issued)
- Current practice (a consensus-based recommendation cannot be issued if a service is not currently widely used)
- Why, if warranted, a more costly service is being recommended over a less costly one

The AAOS employs additional rules to combat the bias that may affect such recommendations. The rationale for the recommendation cannot contain references to studies that were not included in the systematic reviews that underpin a guideline. Excluded articles are, in effect, not evidence, and they may not be cited. Also, the final recommendation must use the language shown in Table 7. The rationale cannot contain the language "we recommend," "we suggest," or "the practitioner might" inasmuch as this wording could be confused with the evidence-based recommendations in a guideline. In addition, the rationale must address apparent discrepancies in logic with other recommendations in the guideline. For example, if a guideline does not come to a recommendation is some instances but, in the instance in question, the work group has issued a consensus-based recommendation, the rationale must explain the reason for this difference.

One consequence of these restrictions is that the AAOS does not typically recommend new medical devices, drugs, or procedures. These procedures are usually supported by little research, and the AAOS is reluctant to make recommendations that could have a national impact based on small amounts of data.

When it is not possible to issue a recommendation (i.e., when the recommendation reads that "we are unable to recommend for or against," the explanation for why a recommendation cannot be given cannot contain an implied recommendation. For example, in the case of a new device, drug, or procedure, the work group may not write a recommendation like "Although treatment X *appears to be promising*, there is currently insufficient evidence to recommend for or against its use." The italicized phrase implies that treatment X is effective, whereas not being able to recommend "for or against" something implies that effectiveness is currently indeterminate.

VOTING ON THE RECOMMENDATIONS

The recommendations and their strength were voted on using a structured voting technique known as the nominal group technique.[31] We present details of this technique in Appendix VIII. Voting on guideline recommendations is conducted using a secret ballot and work group members are blinded to the responses of other members. If disagreement between work group members is significant, there is further discussion to see whether the disagreement(s) can be resolved. Up to three rounds of voting are held to attempt to resolve disagreements. If disagreements are not resolved following three voting rounds, no recommendation is adopted. Lack of agreement is a reason that the grade of some recommendations can be labeled "Inconclusive."

Formal votes on all recommendations that are evidence-based or that read "we are unable to recommend for or against" are only on the recommendations. The rationales require only approval of the work group chair and the methodologists unless the recommendation is consensus-based. Both the recommendation and the rationale of a consensus –based recommendation are the subject of formal votes.

OUTCOMES CONSIDERED

In considering the outcomes discussed in this guideline, it is important to distinguish between patient-oriented and surrogate outcomes. Patient-oriented outcomes measure how a patient feels, functions, or survives.[32] A patient-oriented outcome "tells clinicians, directly and without the need for extrapolation, that a diagnostic, therapeutic or preventive procedure helps patients live longer or live better."[33] Patient-oriented outcomes include pain relief, death, and fractures. Surrogate outcomes are laboratory measurements or physical signs used as substitutes for patient-oriented outcomes. Surrogate outcomes include outcomes like blood cholesterol levels, laboratory and imaging results, and bone mineral densities.

Surrogate outcomes are problematic. An intervention that improves a surrogate outcome does not necessarily improve a patient-oriented outcome. The opposite can be true. Using a surrogate outcome as a study endpoint can make a harmful treatment look beneficial. For example, although the surrogate outcome cardiac sinus rhythm improves when quinidine is given after conversion, mortality is tripled. Similarly, sodium fluoride increases bone mineral density, but it also increases the rate of non-vertebral fractures.[33, 34] This leads to an important (and often overlooked) aspect about surrogate outcomes. To be useful, a surrogate outcome must not only correlate with the patient-oriented outcome of interest, but also the surrogate must predict (capture) the effects of an intervention on that outcome.[32, 34, 35] Many surrogates correlate with an outcome, but few predict the effects of an intervention. A systematic review on this issue has concluded that it is not currently possible to reach a conclusion about how well deep vein thrombosis (DVT) captures the effect of thromboprophylaxis from the available data. [36]

For these reasons, the AAOS rarely uses surrogate outcomes as endpoints in its clinical practice guidelines. We make an exception in this guideline for DVT, because it is a surrogate outcome that has received considerable attention.

When thinking about DVT as an outcome, the clinical issue is that patients and physicians would ideally like to be reassured that if they do not have a DVT, they will not have a pulmonary embolism (PE) and, therefore, can avoid the risks that may be associated with thromboembolic

prophylaxis. They also want to know that patients who have a DVT are at a risk that is high enough to warrant thromboembolic prophylaxis. Balancing these two considerations is complicated because it is not only certain that some patients who develop a PE have also had a DVT, it is also certain that some patients who have had a PE have never had a detectable DVT. In other words, both true positives (a patient who had a DVT also had a PE) and false negatives (a patient who had a PE did not have a detectable DVT) occur.

One way to address the issue of how reliably a DVT predicts a future PE is by thinking of DVT as a diagnostic test for a PE. To accomplish this, we define true positives and false negatives as just stated, and also define true negatives as patients who had neither a DVT nor a PE, and false positives as patients who had a DVT but not a PE.

We can now consider the three studies that published relevant information in patients who received a total hip or total knee arthroplasty. (These studies were of patients not given DVT prophylaxis. We do not consider studies wherein DVT prophylaxis was given because prophylaxis could affect the relationship between DVT and PE.) These are the studies by Barrellier et al., Della Valle et al., and Kalebo et al.[37-39] The former two studies diagnosed DVT using ultrasound, and the latter by venography. Barrellier et al. looked for asymptomatic distal DVT, and Della Valle et al. looked for proximal DVT. Della Valle et al. enrolled only patients suspected of having a PE. Barrellier et al. enrolled only patients who received a total knee arthroplasty, Kalebo et al. enrolled only those who received a total hip arthroplasty, and Della Valle et al. enrolled both types of patients. When evaluated as studies of diagnostics, two of the studies are Moderate", and one is "High" quality. All are of "Moderate" applicability (Table 10).

Table 10. Quality and Applicability of Studies on the Relationship between DVT and PE

●: Domain free of flaws

○: Domain flaws present

Study	Reporting (Penalty)	Index Test	Reference Test	Participants	Information	Study Design	*Quality*	Participants	Index Test	Directness of Results	Analysis	*Applicability*
Kalebo 1990	○	●	●	●	●	●	High	●	○	●	●	Moderate
Barrellier 2010	○	●	●	●	●	○	Moderate	○	○	●	●	Moderate
Della Valle 2003	○	●	●	●	●	●	High	●	○	●	●	Moderate

The 2 x 2 "truth tables" for each of these studies are shown below:

Barrellier et al.:[37]

		DVT +	DVT –
PE	+	1	140
	–	1	279

Della Valle et al.:[38]

		DVT +	DVT –
PE	+	2	4
	–	33	96

Kalebo et al.:[39]

		DVT +	DVT –
PE	+	3	42
	–	0	77

We can now translate these data into likelihood ratios. In the present case, a positive likelihood ratio expresses how good of a "rule in" predictor DVT is. A positive likelihood ratio greater than 10 means that a patient with a DVT is very likely to have a PE. A negative likelihood ratio expresses how good of a "rule out" test DVT is. A negative likelihood ratio of less than 0.1 means that a patient without a DVT is very unlikely to have a PE.[40, 41] The positive and negative likelihood ratios for each of these studies are shown in Table 11. For a number of reasons related to the methodology of these three studies, we stress that our results are not definitive. Regardless, none of the positive likelihood ratios are more than 10 (in fact, their confidence intervals do not even contain 10), and none of the negative likelihood ratios are less than 0.1 (although one of the confidence intervals does contain this number). These results illustrate that the presence of a DVT may not reliably predict PE, and that the absence of a DVT does not seem to assure physicians and patients that the patient will not have a PE.

Table 11 Positive and Negative Likelihood Ratios for DVT as a Predictor of PE

Study	LR^{+*}	LR^{-*}
Barrellier et al.[37]	1.49 (0.48-4.7)**	0.75 (0.24-2.34)
Della Valle et al.[38]	1.43 (0.27-7.46)	0.98 (0.90-1.08)
Kalebo et al.[39]	2.47 (1.59- 3.84)	0.19 (0.01-2.60)

*LR^+ refers to the positive likelihood ratio, and LR^- to the negative likelihood ratio.
** Figures in parentheses are the 95% confidence intervals.

DVT is not the only outcome we consider. We also consider PE. That PE is a patient-oriented outcome does not imply it is a perfect outcome. Many of the trials we include in this guideline withdrew patients and gave them more aggressive treatment if they experienced a DVT. From the perspective of an explanatory trial (one that attempts to determine cause and effect relationships), this likely causes an underestimate of the effectiveness of treatment. However, this practice may mirror actual clinical practice so, from the point of view of a pragmatic trial (a trial that attempts to determine how well something works in routine clinical practice), this is likely a sound procedure. The requirements of an explanatory trial are captured in our ratings of quality, and those of a pragmatic trial are captured in our ratings of applicability (see above for how we arrive at these ratings). The trade-off that occurs between these two sets of requirements is captured in our grades of recommendation (see below).

We also consider major bleeding, all-cause mortality, symptomatic DVT, and proximal DVT. We consider these outcomes because they are the outcomes addressed in the literature, not because they are the most critical clinical outcomes. For the purposes of this guideline, we define a critical outcome as an outcome the work group deemed necessary to determine whether a medical device, drug, or procedure is effective.

We used a modified Delphi approach to determine the critical clinical outcomes. In this approach, work group members individually listed the outcomes they thought were critical. To combat bias, they did so before the literature searches were conducted. The group ranked the importance of these outcomes on a scale of 1-9, where rankings of 7-9 indicated that an outcome was "critical." We conducted three rounds of Delphi rankings,

and used the average of the final round (please see Appendix III for further description of our processes for determining critical outcomes).

The outcomes the work group deemed critical for evaluating the effectiveness of thromboprophylaxis were:

- All cause mortality
- Death from bleeding
- Death from PE
- Periprosthetic joint infection
- Reoperation due to bleeding
- Reoperation for any reason within 90 days of surgery
- Symptomatic PE

STATISTICAL METHODS

We performed network meta-analyses (also known as a mixed treatment comparisons analyses) to ascertain the comparative effectiveness of strategies for preventing venous thromboembolism. All of the trials entered into our analyses were randomized controlled trials (most, but not all, were of "High" quality; additional details on their quality are presented in the sections of this guideline that present our results of the appraisal of these studies). Some of the trials that met our original inclusion criteria did not observe any events in any of their groups. In accordance with suggestions of the Cochrane collaboration,[42] we excluded them from our analyses.

We compare the treatments of interest to both placebo (or no treatment) and enoxaparin. Although the comparisons to placebo are easier to interpret, more of the published comparisons are to enoxaparin than any other treatment. This means that the comparisons to enoxaparin have greater precision than the comparisons to placebo. None of the studies that report all-cause mortality in our final model used a placebo comparator. Therefore, we only present the comparisons to enoxaparin.

Analyses were preformed as described by Lu and Ades[43] using Winbugs v 1.4.3. This method preserves the randomization of the original trials. The Markov chains in our model were said to have converged if plots of the Gelman-Rubin statistics indicated that widths of pooled runs and individual runs stabilized around the same value and their ratio was approximately one.[44] In general, we performed 100,000 iterations, the first 50,000 of which were discarded as "burn in" iterations for each of the network models we describe. The one exception was our initial analysis of major bleeding, in which we used a burn in of 150,000 iterations. We specified vague priors for the trial baselines and the basic parameters (normal distribution with mean 0 and variance 10,000) and for the random effects standard deviation (uniform distribution: U(0,2)). We use $p < 0.05$ to define statistical significance.

To assess the adequacy of our models, we checked their overall fit by comparing the posterior mean deviance to the number of data points in any given model. These two figures are approximately equal for models that fit the data well. We also checked the statistical consistency of the models using a "back-calculation" method for networks with direct evidence from multi-arm trials.[45] This method requires point estimates and

dispersions of the trial data being entered into the network meta-analysis. When there were two or more trials comparing two of the same treatments, we obtained these latter two quantities from meta-analytic models computed using the Peto odds ratio as the test statistic. This statistic is the optimal way to compute the odds ratio when events are sparse.[46] All traditional meta-analyses were performed using STATA 10.0.

We adopted the following criteria to determine whether a model was satisfactory:

1. A satisfactory model must exhibit statistical consistency for all of the outcomes of interest. This reflects our view that if a set of studies causes inconsistency in even one of the five outcomes of interest, then this is *prima facie* evidence that there is something different about this set of studies that could influence the analyses all of the other outcomes. Accordingly, differences in the structure of our initial, revised, and final models are due solely to differences in the outcomes that were reported in different trials.

2. Use of a continuity correction should not alter the statistical consistency of a model. The events of interest are rare. This is illustrated by Table 12, which shows the rates of several of the outcomes we considered in the placebo/untreated control groups of the trials that we included in our analysis on the effectiveness of thromboembolic prophylaxis. These low event rates pose statistical challenges because no events were observed in many groups in the included studies.

3. **Table 12. Event Rates in Placebo/Untreated Control Groups**

Outcome	Number of Studies	Rate in Placebo/None Groups
PE	4	<0.88%
Major Bleeding	10	<1.96%
All-Cause Mortality	0	---
Symptomatic DVT	2	<1.12%
DVT	3	37%

We included trials that observed no events in some groups, but this necessitated use of a continuity correction.[42] Because such corrections can have undesirable influences on results, [47] we performed additional analyses. We accomplished this by conducting network meta-analyses from which all studies that required a continuity correction were omitted, and we did so despite the fact that the initial, continuity-corrected models were statistically consistent for all outcomes. This latter analysis yielded statistically significant inconsistency on two outcomes (pulmonary embolism and major bleeding), and the results suggested that we exclude trials of heparin (which were also the oldest trials we examined). The results of a model excluding the trials of heparin were also inconsistent, this time due to the presence of studies that had more than two arms (the inconsistency again occurred for pulmonary embolism and major bleeding, and seemed to arise

in these multi-arm trials that observed no events in at least two groups. Accordingly, we omitted these trials (along with the trials of heparin) and arrived at a final model that did not incorporate studies requiring a continuity correction, and that was consistent for all outcomes.

4. The point estimates of the differences between models that incorporated continuity-corrected studies and those that did not should not be significantly different from each other.

5. None of the point estimates from models with data from both hip and knee patients should significantly differ from the point estimates derived from models containing only data from patients who received a hip arthroplasty or models that contained only data from patients who received a knee arthroplasty. This criterion tests whether it is appropriate to combine data from such patients.

6. The qualitative conclusions (derived from a deliberately strict interpretation of p-values) of the models must remain logically consistent when the analysis comparator (i.e., the "anchor") is changed. For example, our initial models suggested that enoxaparin was more effective than heparin (there were significantly fewer pulmonary emboli with enoxaparin than with heparin), and that enoxaparin was not different from placebo. Taken together, these findings imply that heparin is less effective than placebo. However, our models did not yield this result. Accordingly, we termed these models as logically inconsistent.

   The primary reason that the results of our models using placebo as a comparator may qualitatively differ from models using the enoxaparin comparator is that the fewer trials had a placebo group. This causes the precision of these models to be lower than that of the models using enoxaparin as a comparator. This criterion serves as a warning that the precision of the model using placebo comparisons may be too low.

These five criteria gave rise to that analytical sequence depicted in Figure 1.

Figure 1. Analytical Sequence for Network Meta-Analyses

We performed these analyses for each of the six outcomes (PE, major bleeding, all-cause mortality, symptomatic DVT, proximal DVT, and DVT) of interest. This resulted in a total of 41 network meta-analyses (Table 10, unshaded cells) and 40 consistency checks (Table 10, shaded cells).

Table 13. Network Meta-Analysis Models and Consistency Checks

Pulmonary Embolism	Major Bleeding	All-Cause Mortality	Symptomatic DVT	Proximal DVT	DVT
Initial Model (patients with hip and patients with knee replacement and with continuity-corrected data, using placebo as a comparator)	***Initial Model*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Initial Model*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Initial Model*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Initial Model*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Initial Model*** (patients with hip and patients with knee replacement and with continuity-corrected data)
Logical Consistency Check (patients with hip and patients with knee replacement and with continuity-corrected data)	***Logical Consistency Check*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Logical Consistency Check*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Logical Consistency Check*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Logical Consistency Check*** (patients with hip and patients with knee replacement and with continuity-corrected data)	***Logical Consistency Check*** (patients with hip and patients with knee replacement and with continuity-corrected data)
" Hip Combinability" Check (hip replacement only, continuity-corrected data	***" Hip Combinability" Check*** (hip replacement only, continuity-corrected data)	***" Hip Combinability" Check*** (hip replacement only, continuity-corrected data)	***" Hip Combinability" Check*** (hip replacement only, continuity-corrected data)	***" Hip Combinability" Check*** (hip replacement only, continuity-corrected data)	***" Hip Combinability" Check*** (hip replacement only, continuity-corrected data)
" Knee Combinability" Check (knee replacement only, continuity-corrected data)	***" Knee Combinability" Check*** (knee replacement only, continuity-corrected	***" Knee Combinability" Check*** (knee replacement only, continuity-corrected	***" Knee Combinability" Check*** (knee replacement only, continuity-corrected	***" Knee Combinability" Check*** (knee replacement only, continuity-corrected	***" Knee Combinability" Check*** (knee replacement only, continuity-corrected

Pulmonary Embolism	Major Bleeding	All-Cause Mortality	Symptomatic DVT	Proximal DVT	DVT
	data)	data)	data)	data	data)
Statistical Consistency Check #1on Initial Model (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Initial Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Initial Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Initial Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Initial Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Initial Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)
Statistical Consistency Check #2 (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2*** *Not Performed. Results from other outcomes show this model does not meet our criteria*	***Statistical Consistency Check #2*** (patients with hip and patients with knee replacement, without continuity-corrected data)
Revised Model (patients with hip and patients with knee replacements, no trials of heparin, no continuity-corrected studies)	***Revised Model*** (patients with hip and patients with knee replacements, no trials of heparin, no continuity-corrected studies)	***Revised Model*** (patients with hip and patients with knee replacements, no trials of heparin, no continuity-corrected studies)	***Revised Model*** (patients with hip and patients with knee replacements, no trials of heparin, no continuity-corrected studies)	***Revised Model*** *Not Performed. Results from other outcomes show this model does not meet our criteria*	***Revised Model*** (patients with hip and patients with knee replacements, no trials of heparin, no continuity-corrected studies)
Statistical Consistency Check on Revised Model (patients with hip and patients with knee replacements, without	***Statistical Consistency Check on Revised Model*** (patients with hip and patients with knee	***Statistical Consistency Check on Revised Model*** (patients with hip and patients with knee	***Statistical Consistency Check on Revised Model*** (patients with hip and patients with knee	***Statistical Consistency Check on Revised Model*** *Not Performed. Results from other*	***Statistical Consistency Check on Revised Model*** (patients with hip and patients with knee

Pulmonary Embolism	Major Bleeding	All-Cause Mortality	Symptomatic DVT	Proximal DVT	DVT
trials of heparin, and without continuity-corrected studies)	replacements, without trials of heparin, and without continuity-corrected studies))	replacements, without trials of heparin, and without continuity-corrected studies)	replacements, without trials of heparin, and without continuity-corrected studies)	*outcomes show this model does not meet our criteria*	replacements, without trials of heparin, and without continuity-corrected studies)
Final Model (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms, placebo comparator)	***Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms, placebo comparator)	***Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms)	***Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms)	***Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms)	***Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, without trials of heparin, and without trials with >2 arms)
Logical Consistency Check on Final Model (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)	***Logical Consistency Check on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)	***Logical Consistency Check on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)	***Logical Consistency Check on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)	***Logical Consistency Check on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)	***Logical Consistency Check on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data, enoxaparin comparator)
" Hip Combinability" Check on Final Model (hip replacement only, continuity-corrected data, without trials of heparin, without trials with >2	***" Hip Combinability" Check on Final Model*** (hip replacement only, continuity-corrected data, without trials of heparin, without trials	***" Hip Combinability" Check on Final Model*** (hip replacement only, continuity-corrected data, without trials of heparin, without trials	***" Hip Combinability" Check on Final Model*** (hip replacement only, continuity-corrected data, without trials of heparin, without trials	***" Hip Combinability" Check on Final Model*** (hip replacement only, continuity-corrected data, without trials of heparin, without trials	***" Hip Combinability" Check on Final Model*** (hip replacement only, continuity-corrected data, without trials of heparin, without trials

Pulmonary Embolism	Major Bleeding	All-Cause Mortality	Symptomatic DVT	Proximal DVT	DVT
arms)	with >2 arms)	with >2 arms)	with >2 arms)	with >2 arms)	with >2 arms)
"Knee Combinability" Check on Final Model (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)	***"Knee Combinability" Check on Final Model*** (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)	***"Knee Combinability" Check on Final Model*** (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)	***"Knee Combinability" Check on Final Model*** (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)	***"Knee Combinability" Check on Final Model*** (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)	***"Knee Combinability" Check on Final Model*** (knee replacement only, continuity-corrected data, without trials of heparin, without trials with >2 arms)
Statistical Consistency Check #1on Final Model (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)	***Statistical Consistency Check #1on Final Model*** (patients with hip and patients with knee replacement, with continuity-corrected data)
Statistical Consistency Check #2 on Final Model (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2 on Final Model*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2 on Final Model*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2 on Final Model*** (patients with hip and patients with knee replacement, without continuity-corrected data)	***Statistical Consistency Check #2 on Final Model*** (patients with hip and patients with knee replacement, without continuity-corrected data	***Statistical Consistency Check #2 on Final Model*** (patients with hip and patients with knee replacement, without continuity-corrected data)

PEER REVIEW

A draft of the present guideline was peer reviewed. Peer review was performed using a structured peer review form (see Appendix IX). This form requires all peer reviewers to declare their conflicts of interest.

To determine who would serve as peer reviewers, the work group nominated external specialty societies before work on the guideline began. By having work groups specify *organizations* for review (as opposed to individuals), we are attempting to prevent overly favorable reviews that could arise should work group members choose reviewers whom they had personal or professional relationships. We also blind peer reviewers to the identities of the work group members when they peer review the draft.

The outside specialty societies were nominated at the beginning of the process and solicited for names of peer reviewers approximately six weeks before the final recommendation meeting for a guideline. The physician members of the AAOS Guidelines Oversight Committee and the Evidence Based Practice Committee review all draft AAOS clinical practice guidelines.

On occasion, some specialty societies (both orthopaedic and non-orthopaedic) ask their evidence-based practice (EBP) committee to provide peer review of our guidelines. The specialty society is responsible for compiling this type of review into one document before it is returned to us. We ask that the Chairs of these external EBP committees declare their conflicts of interest and manage the conflicts of interest of their committee members. Some specialty societies ask to post the guideline on their website for review by all of their interested members. Again, the AAOS asks that these reviews be collated into a single response by the specialty society, and that the person responsible for submitting this document to the AAOS disclose his or her financial conflicts of interest. We also ask that this posting be to the "members" only portion of the specialty societies' website because our drafted document represents a "work in progress" and is subject to change as a direct result of the review process. In addition, the draft has not been formally approved by the AAOS Board of Directors. This is not an attempt to restrict input on the draft. Nor do we consider it as a method to imply that outside specialty societies who provide review of the document necessarily agree with the stated recommendations. Hence, the reason all peer review comments and our responses are made publicly available.

The clinical practice guidelines manager drafted initial responses to comments about methodology. These responses were then reviewed by the work group chair and vice-chair, who also responds to questions concerning clinical practice and techniques, and the AAOS Director of Research and Scientific Affairs. All changes to a recommendation as a result of peer review input were voted on and accepted by a majority of the work group members via teleconference. All changes to any guideline recommendation must be based on the evidence. Final changes to the guideline are incorporated, detailed in a summary sheet and forwarded with the document through the rest of the review and approval process.

The AAOS believes that it is important for guideline developers to demonstrate that they are responsive to peer review. Accordingly, after the AAOS Board of Directors approves a guideline, the AAOS posts all peer reviewer comments on its website (see http://www.aaos.org/research/guidelines/guide.asp to access these documents) with a point-by-point description of how the AAOS responded to each non-editorial comment made by each reviewer. Reviewers who wish to remain anonymous can notify the AAOS, and their names will be redacted; their comments, our responses and their conflicts of interest will however still be posted for review.

Twenty-six outside organizations were solicited to provide peer reviewers for this document. The draft of this guideline was sent to 25 review organizations who responded to the solicitation and a total of 33 peer reviewers received the document not including the AAOS Evidence-based Practice Committee and Guidelines Oversight Committee members. Twelve of these reviewers returned comments (see Appendix IX). The disposition of all non-editorial peer review comments was documented and accompanied this guideline through the public commentary and the AAOS guideline approval process.

PUBLIC COMMENTARY

After modifying the draft in response to peer review, the guideline was sent for a thirty day period of "Public Commentary." Public Commentators are blinded to the identities of the work group members. Commentators consist of members of the AAOS Board of Directors (BOD), members of the Council on Research and Quality (CORQ), members of the Board of Councilors (BOC), and members of the Board of Specialty Societies (BOS). AAOS guidelines are automatically forwarded to the AAOS BOD and CORQ for commentary. Members of the BOC and BOS are solicited for interest. If they ask to see the document, it is forwarded to them. For this guideline, 20 members not including the CORQ and the AAOS BOD, received the draft for comment.

The draft guideline is, if warranted, modified in response to public commentary by the AAOS Clinical Practice Guidelines Unit and the work group members. If changes are made as a result of public comment, these changes are summarized, and those who provided commentary are notified that their input resulted in a change in the guideline. Changes as a result of public commentary must be based on evidence. All changes are detailed in a summary sheet that accompanies the document through the approval process.

Over 200 commentators have had the opportunity to provide input into this guideline. Of these, 66 members received the document and returned comments (see Appendix X).

THE AAOS GUIDELINE APPROVAL PROCESS

This final guideline draft was approved by the AAOS Evidence Based Practice Committee, the AAOS Guidelines Oversight Committee, the AAOS Council on Research and Quality, and the AAOS Board of Directors. Descriptions of these bodies are provided in Appendix II. These reviewing bodies do not have the option to modify the draft guideline during the approval process. They can only vote to approve it or reject it. Accordingly, no changes were made to this guideline during the approval process.

REVISION PLANS

This guideline represents a cross-sectional view of current treatment and may become outdated as new evidence becomes available. This guideline will be revised in accordance with new evidence, changing practice, rapidly emerging treatment options, and new technology. This guideline will be updated or withdrawn in five years in accordance with the standards of the National Guideline Clearinghouse.

GUIDELINE DISSEMINATION PLANS

The primary purpose of the present document is to provide interested readers with full documentation about not only our recommendations, but also about how we arrived at those recommendations. This document is also posted on the AAOS website at http://www.aaos.org/research/guidelines/guide.asp.

Shorter versions of the guideline are available in other venues. Publication of most guidelines is announced by an Academy press release, articles authored by the work group and published in the Journal of the American Academy of Orthopaedic Surgeons, and articles published in AAOS *Now*. Most guidelines are also distributed at the AAOS Annual Meeting in various venues such as on Academy Row and at Committee Scientific Exhibits.

Selected guidelines are disseminated by webinar, an Online Module for the Orthopaedic Knowledge Online website, Radio Media Tours, Media Briefings, and by distributing them at relevant Continuing Medical Education (CME) courses and at the AAOS Resource Center.

Other dissemination efforts outside of the AAOS will include submitting the guideline to the National Guideline Clearinghouse and distributing the guideline at other medical specialty societies' meetings.

Recommendations

RECOMMENDATION 1

We recommend against routine post-operative duplex ultrasonography screening of patients who undergo elective hip or knee arthroplasty.

Grade of Recommendation: Strong

Description: Evidence is based on two or more "High" strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a strong negative recommendation), and that the strength of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

RATIONALE

We cannot recommend the routine use of ultrasound for the screening of patients after knee or hip arthroplasty for VTED. The best available evidence comes from two randomized controlled studies, both of high quality and moderate applicability (see Table 14 for a summary of the results of these studies, Table 15 through Table 18 for a detailed presentation of results, and Table 47 in Appendix XIII for our appraisal of their quality and applicability), that compared routine ultrasound screening to not screening. The control group was prolonged prophylaxis in one study, and a sham ultrasound in the other. In the ultrasound groups, treatment of asymptomatic DVTs was based on the ultrasound findings. Neither study found a statistically significant difference in symptomatic PE rates (Table 15) between the ultrasound-screened and unscreened patients, despite the fact that they had adequate statistical power.

Similar results are found when screening is accomplished using venography (Table 14 summarizes the results of the studies that evaluated the effects of ultrasound and venographic screening on patient outcomes). Two retrospective comparative studies of low quality and moderate applicability (see Table 47 in Appendix XIII) compared results of patients who were screened for DVT by venography against results of patients who were not screened (Table 16). Treatment of asymptomatic DVT varied according to venographic results. Rates of readmission for PE and DVT did not significantly differ between those who received screening venography and those who did not.

The available evidence also suggests that D-dimer is not a useful screening test for DVT after arthroplasty. Three studies, one of high quality and two of moderate quality and all of moderate applicability (Table 48 in Appendix XIII), evaluated the screening performance of D-dimer. Two used ultrasound as the reference standard, while one used venography.

One study of high quality and moderate applicability evaluated the screening performance of magnetic resonance (MR) venography as compared to standard

venography. These data indicated that MR venography may be a good "rule in" test but not a good "rule out" test.

Given the lack of utility of ultrasound for diagnosis of unsuspected DVT's and the lack of any commonly available alternative screening test with greater utility, we do not recommend routine screening for DVT in the hip and knee arthroplasty postoperative patient population.

The reasons we excluded some studies initially considered for this recommendation appears in Appendix XIV, Table 57.

FINDINGS

Table 14. DVT Screening Summary Table

Outcome	Ultrasound vs. Prolonged Prophylaxis	Ultrasound (proximal) vs. Sham Ultrasound	Venography vs. No Venography
Fatal PE	○	○	○
Symptomatic PE	○	○	
Symptomatic DVT	○		
Symptomatic Proximal DVT	○	○	
Symptomatic Distal DVT	○	○	
DVT	○		
Proximal DVT	○		
Distal DVT	○		
Major Bleeding		○	
Readmission for PE			○
Readmission for DVT			○

○: no statistically significant difference. ●: statistically significant in favor of screening

QUALITY AND APPLICABILITY

Two high quality randomized trials addressed ultrasound screening. Two low quality comparative studies addressed venography screening. One high quality and two moderate quality diagnostic studies addressed D-dimer screening, and one high quality diagnostic study addressed MR venography. Each of these studies was of moderate applicability. For details, see Table 47 and Table 48 in Appendix XIII.

RESULTS

Table 15. Ultrasound Screening vs. No Screening - Results

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 % (event/n)	Group2 % (event/n)	Results
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	High	Fatal PE	0% (0/174)	0.6% (1/172)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	High	Symptomatic PE	0.6% (1/174)	1.2% (2/172)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	High	Symptomatic DVT	1.1% (2/174)	1.7% (3/172)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	High	Symptomatic Proximal DVT	1.1% (2/174)	1.2% (2/172)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	High	Symptomatic Distal DVT	0% (0/174)	0.6% (1/172)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	Moderate	Asymptomatic DVT (at day 35)	4.1% (7/172)	6.8% (11/162)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	Moderate	Asymptomatic Proximal DVT (at day 35)	1.7% (3/172)	1.9% (3/162)	Not Significant
Schimdt et al. 2003	346	Both	Ultrasound Screening	Prolonged Prophylaxis	Moderate	Asymptomatic Distal DVT (at day 35)	2.3% (4/172)	4.9% (8/162)	Not Significant

Table 15. Ultrasound Screening vs. No Screening - Results

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 % (event/n)	Group2 % (event/n)	Results
Robinson et al. 1997	1024	Both	Ultrasound Screening (proximal)	Sham Ultrasound	High	Symptomatic Proximal DVT	0.8% (4/518)	0.6% (3/506)	Not Significant
Robinson et al. 1997	1024	Both	Ultrasound Screening (proximal)	Sham Ultrasound	High	Symptomatic PE	0% (0/518)	0.4% (2/506)	Not Significant
Robinson et al. 1997	1024	Both	Ultrasound Screening (proximal)	Sham Ultrasound	High	Fatal PE	0% (0/518)	0% (0/506)	Not Significant
Robinson et al. 1997	1024	Both	Ultrasound Screening (proximal)	Sham Ultrasound	High	Major Bleeding	0.2% (1/518)	0% (0/506)	Not Significant

Table 16. Venography Screening vs. No Screening - Results

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 % (event/n)	Group2 % (event/n)	Results
Pellegrini et al. 2006 (Rochester data)	559	Knee	Venogram	No venogram	Low	Readmission for PE	0% (0/199)	0% (0/360)	Not Significant
Pellegrini et al. 2006 (Penn State data)	707	Knee	Venogram	No venogram	Low	Readmission for PE	0.5% (3/611)	0% (0/96)	Not Significant
Pellegrini et al. 2006 (Rochester data)	559	Knee	Venogram	No venogram	Low	Fatal PE	0% (0/199)	0% (0/360)	Not Significant
Pellegrini et al. 2006 (Penn State data)	707	Knee	Venogram	No venogram	Low	Fatal PE	0.2% (1/611)	0% (0/96)	Not Significant
Pellegrini et al. 2006 (Rochester data)	559	Knee	Venogram	No venogram	Low	Readmission for DVT	0.5% (1/199)	0.6% (2/360)	Not Significant
Pellegrini et al. 2006 (Penn State data)	707	Knee	Venogram	No venogram	Low	Readmission for DVT	0.3% (2/611)	0% (0/96)	Not Significant
Pellegrini et al. 2005 (Rochester data)	1079	Hip	Venogram	No venogram	Low	Readmission for PE	1.4% (5/347)	0.4% (3/732)	Not Significant
Pellegrini et al. 2005 (Penn State data)	824	Hip	Venogram	No venogram	Low	Readmission for PE	0.9% (6/685)	0% (0/139)	Not Significant
Pellegrini et al. 2005 (Rochester data)	1079	Hip	Venogram	No venogram	Low	Fatal PE	0.6% (2/347)	0% (0/732)	Not Significant
Pellegrini et al. 2005 (Penn State data)	824	Hip	Venogram	No venogram	Low	Fatal PE	0.1% (1/685)	0% (0/139)	Not Significant
Pellegrini et al. 2005 (Rochester data)	1079	Hip	Venogram	No venogram	Low	Readmission for DVT	0.6% (2/347)	1.2% (9/732)	Not Significant
Pellegrini et al. 2005 (Penn State data)	824	Hip	Venogram	No venogram	Low	Readmission for DVT	1.0% (7/685)	0% (0/139)	Not Significant

Table 17. D-dimer - Diagnostic Performance

Author	N	Test	Joint	Reference Standard	Outcome	Positive LR	Negative LR	Sensitivity	Specificity
Abraham et al. 1999	168	D-dimer, day 1, cut-off 2.808 µg/ml	Both	Ultrasound	Total DVT	2.67 (1.2, 5.95)	0.85 (0.74, 0.99)	0.21 (0.12, 0.34)	0.92 (0.85, 0.96)
Niimi et al. 2010	207	D-dimer, day 1, cut-off 4.88 µg/ml	Both	Ultrasound	Total DVT	1.28 (1.12, 1.47)	0.27 (0.13, 0.57)	0.92 (0.85, 0.97)	0.28 (0.2, 0.38)
Niimi et al. 2010	207	D-dimer, day 1, cut-off 9.78 µg/ml	Both	Ultrasound	Total DVT	1.67 (1.27, 2.19)	0.56 (0.41, 0.76)	0.66 (0.56, 0.75)	0.6 (0.5, 0.7)
Niimi et al. 2010	207	D-dimer, day 7, cut-off 5.35 µg/ml	Both	Ultrasound	Total DVT	1.18 (1.04, 1.33)	0.41 (0.21, 0.82)	0.9 (0.83, 0.95)	0.23 (0.16, 0.33)
Niimi et al. 2010	207	D-dimer, postop day 7, cut-off 8.26 µg/ml	Both	Ultrasound	Total DVT	1.64 (1.28, 2.09)	0.49 (0.34, 0.7)	0.73 (0.63, 0.81)	0.55 (0.45, 0.65)
Bounameaux et al. 1998	119	D-dimer, day 3, cut-off 1µg/ml	Knee	Venography	Total DVT	1.06 (0.99, 1.13)	0.15 (0.01, 2.68)	1 (0.93, 1)	0.06 (0.02, 0.14)
Bounameaux et al. 1998	119	D-dimer, day 3, cut-off 2µg/ml	Knee	Venography	Total DVT	1.15 (0.9, 1.47)	0.75 (0.43, 1.29)	0.73 (0.58, 0.84)	0.37 (0.25, 0.49)
Bounameaux et al. 1998	119	D-dimer, day 3, cut-off 3µg/ml	Knee	Venography	Total DVT	2.22 (1.41, 3.51)	0.56 (0.39, 0.8)	0.59 (0.44, 0.72)	0.74 (0.61, 0.83)
Bounameaux et al. 1998	119	D-dimer, day 3, cut-off 4µg/ml	Knee	Venography	Total DVT	2.67 (1.24, 5.74)	0.78 (0.63, 0.95)	0.31 (0.19, 0.46)	0.88 (0.78, 0.95)
Bounameaux et al. 1998	119	D-dimer, day 3, cut-off 5µg/ml	Knee	Venography	Total DVT	2.93 (1.09, 7.92)	0.85 (0.72, 0.99)	0.22 (0.11, 0.35)	0.93 (0.84, 0.98)

Table 18. MR Venography - Diagnostic Performance

Author	N	Test	Joint	Reference Standard	Outcome	Positive LR	Negative LR	Sensitivity	Specificity
Larcom et al. 1996	191[a]	MR venography	Both	Venography	Proximal DVT	44.55 (9.7, 204.3)	0.55 (0.32, 0.95)	0.45 (0.17, 0.77)	0.99 (0.96, 1)

[a]207 extremities in 191 patients

RECOMMENDATION 2

Patients undergoing elective hip or knee arthroplasty are already at high risk for venous thromboembolism. The practitioner might further assess the risk of venous thromboembolism by determining whether these patients had a previous venous thromboembolism.

Grade of Recommendation: Limited

Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

Current evidence is not clear about whether factors other than a history of previous venous thromboembolism increase the risk of venous thromboembolism in patients undergoing elective hip or knee arthroplasty and, therefore, we are unable to recommend for or against routinely assessing these patients for these factors.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

Patients undergoing elective hip or knee arthroplasty are at high risk for venous thromboembolic disease (VTED). Only one risk factor, previous history of VTED, has sufficient evidence indicating that some of these patients may be at even higher risk.

The relevant evidence comes from two studies that evaluated patients with a personal history of VTED – one of medium and one of low strength. The Pedersen study of over 68,000 patients found a relative risk of 8.1, and the Warwick study of over 14,000 patients found a hazard ratio of 4.92 for post-operative VTED in patients with a previous history of VTED (see Table 20 for a summary of the results of these studies).

Twenty-nine studies addressed whether patients with one or more potential risk factors, other than previous VTED, have higher rates of VTED. The list of potential VTED risk factors for which we sought evidence is listed in Table 19. The studies were all of low or very low quality (see Table 49 in Appendix XIII for a summary of our appraisal of the quality and applicability of these studies). A statistically significant increase in VTED

resulting from these other risk factors that confer an increased risk of VTED in surgeries other than primary hip or knee arthroplasty was not found in studies of hip or knee arthroplasty patients. This might be because these other VTED risk factors confer a lower overall risk than primary hip or knee arthroplasty surgery itself. Therefore, their effects may not be seen against the relatively high background risk already being experienced by patients receiving elective hip or knee arthroplasty. Therefore, we are unable to recommend further risk stratification based on these factors.

No data specific to hip or knee arthroplasty were found addressing many potential risk factors, and in many instances where it was found, it was of very low quality and it was contradictory (see Table 19 for a summary of the results of these studies and Table 21 for a detailed presentation of their results). Data from patients undergoing surgical procedures other than primary hip and knee arthroplasty were found also of very low quality (Table 23) and therefore were unreliable. We excluded some of the studies we retrieved to address this recommendation. These studies, and the reasons for their exclusion are listed in Appendix XIV, Table 58.

FINDINGS

Table 19. VTED Risk Factors Summary Table

Risk Factor	Symptomatic VTE	Symp. PE	Symp. DVT	VTE	PE	DVT
Personal history of VTE	●●			○		
Age	○○			●○●○		●
Cancer	○			○○●○		
Personal/family history of blood clotting disorders				○		●
Birth control or hormone replacement therapy	○			○	○	○
Varicose Veins				○●		○
Venous Stasis Disease	○					○
Obesity	●			○○●○		●
Chronic Lung Disease				○●○		
Current bed rest or restricted mobility				○		●
Diabetes	○			○○		○
Stable hypertension		○○	○	○○		
Stable cardiovascular disease	●○			○○○		
Smoking				○○○○		○○
Ethnicity/race				○●●	○○●●	
Duration of surgery				○●		○
Peripheral vascular disease				○	○	
Recent pelvic or lower extremity surgery				○		
Screening instruments (Caprini)				♦♦		
Central venous access				♦		
Inflammatory bowel disease				◊		
Immobilization of limb for last month						
Recent confinement to bed rest for 72 hours (3 months)						
Lymphedema						

○: no statistically significant difference; ●: statistically significant risk factor; ♦: statistically significant risk factor among non-arthroplasty patients; ◊: no statistically significant difference among non-arthroplasty patients

Note: Each circle or diamond represents a separate study.

QUALITY AND APPLICABILITY

Three low quality studies addressed the history of VTED as arisk factor for VTED. One study was of high applicability, raising its overall strength to moderate. The other two studies were of moderate applicability. For details, see Table 49 in Appendix XIII.

We included eight low quality and twenty-one very low quality studies addressing other potential risk factors for VTED. One low quality study had high applicability, raising its strength to moderate, while another low quality study had low applicability, lowering its strength to very low. Five very low quality studies had low applicability. All other studies were of moderate applicability. For details, see Table 49 in Appendix XIII.

RESULTS

Table 20. History of VTE as a Risk Factor for VTE

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Pedersen	68,155	Moderate	VTE hospitalization	Hip	History of VTE	RR: 8.1 (6.1, 10.8)
Warwick	14,802	Low	Symptomatic VTE	Both	History of VTE	HR: 4.92 (3.15, 7.67)
Joseph	569	Low	VTE	Both	History of VTE	NS

Table 21. Risk Factors for VTE among Hip and Knee Arthroplasty Patients

Author	N	Strength	Outcome	Joint	Personal or Family History of VTE	Age	Cancer	Recent Pelvic or Lower Extremity Surgery	History of Blood Clotting Disorders	Birth Control or Hormone Replacement Therapy	Varicose Veins	Venous Stasis Disease	Obesity	Chronic Lung Disease	Diabetes	Hypertension	Stable Cardiovascular Disease	Peripheral Vascular Disease	Smoking	Ethnicity/Race	Duration of Surgery	Restricted Mobility
Pedersen	68,155	Moderate	VTE hospitalization	Hip	●	○	○	x	x	x	x	x	x	x	○	x	●	x	x	x	x	x
Fujita	302	Low	DVT (venogram)	Both	x	●	x	x	x	x	x	x	●	x	○	x	x	x	○	x	○	x
Joseph	569	Low	VTE	Both	○	●	○[a]	○[b]	○	x	x	x	○	x	x	x	x	x	x	x	○	○
Warwick	14,802	Low	Symptomatic VTE	Both	●	○	x	x	x	x	x	○	●	x	x	x	○	x	x	x	x	x
Leizorovicz	386	Low	VTE	Both	x	○	○	x	x	x	○	x	○	○	x	x	○	x	○	x	●	x
Guijarro (hip)	31,769	Low	VTE	Hip	x	●	○	x	x	x	x	x	○	○	○	○	○	x	x	x	x	x
Guijarro (knee)	58,037	Low	VTE	Knee	x	○	●	x	x	x	x	x	●	●	○	○	○	x	x	x	x	x
Eriksson	135	V. Low	VTE	Hip	●	○	x	x	x	x	●	x	x	x	○	x	x	x	○	x	○	x
Beksac	1,986	V. Low	VTE	Hip	●	○	●	x	x	x	x	x	●	x	x	x	x	x	○	x	x	x
Lowe	374	V. Low	DVT (venogram)	Hip	x	●	x	x	●[c]	x	○	x	●	x	x	x	x	x	○	x	x	x
Won	1,608	V. Low	VTE	Both	x	○	○[a]	x	x	x	x	x	○	x	○	x	x	x	○	x	○	x

Gandhi	1,460	V. Low	Symptomatic DVT	Knee	x	○	x	x	x	x	x	x	○ [d]	x	○ [d]	○ [d]	x	x	x	x	x	x
Mahomed 2003	55,975 / 12,233†	V. Low	PE	Hip	x	○/ ●	x	x	x	x	x	x	x	x	x	x	x	x	x	○	x	x
Mahomed 2005	124,986/ 11,726†	V. Low	PE	Knee	x	●/ ○	x	x	x	x	x	x	x	x	x	x	x	x	x	○	x	x
Memtsoudis	6,901,324	V. Low	PE	Both	x	* [e]	x	x	x	x	x	x	●	○	*	x	*	x	x	●	x	x
Pearse	223	V. Low	DVT (ultrasound)	Knee	○	○	x	x	x	○	x	○	○	x	x	x	x	x	x	x	x	x
Ryu	338	V. Low	Symptomatic PE	Knee	x	○	x	x	x	x	x	x	○	○	○	○	x	x	○	x	○	x
SooHoo 2006	222,684	V. Low	PE	Knee	x	●	x	x	x	x	x	x	x	x	x	x	x	x	x	●	x	x
Mraovic	7,389	V. Low	Symptomatic PE	Both	x	●	○	x	x	x	x	x	●	○	○ [f]	○	○	x	x	x	○	x
Keeney	705	V. Low	VTE	Hip	●	●	x	x	x	x	x	x	○	x	x	x	x	x	x	○	○	x
White 1998	77,629	V. Low	VTE	Hip	x	□	x	x	x	x	x	x	x	x	x	x	x	x	x	●	x	x
SooHoo 2010	138,399	V. Low	VTE	Hip	x	●	x	x	x	x	x	x	x	x	○	x	x	○	x	●	x	x
White 2000	889	Low	VTE hospitalization	Hip	●	●	○	x	x	○	x	x	●	x	x	x	x	x	x	○	○	x
Hurbanek	318	V. Low	VTE	Both	□	□	□	x	x	○	x	x	□	□	□	□	□	x	□	x	x	x
Lemos	240	V. Low	PE	Both	○	●	○	x	x	○	○	x	x	○	○	○	*	○	○	x	○	x
Nathan	137	V. Low	Proximal DVT (ultrasound)	Knee	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	●

●= statistically significant risk factor; ○= not statistically significant risk factor; x=not included in regression model;*= significantly lower risk; □= used as covariate in model, multivariate results not reported

[a] History of cancer; [b]Recent surgery; [c]APC Resistance p=.02 ,Factor V Leiden p=0.08; [d] individual variable not significant but included in model with metabolic syndrome, which was significant and included the individual variables; [e] lower risk at <44 years and at >85 years; [f] diabetes not significant, but elevated blood glucose was significant in same model; †primary / revision

Table 22. Risk Factors for VTE among Hip and Knee Arthroplasty Patients - Results

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Fujita	302	Low	DVT (venogram)	Both	Age	OR: 1.036/yr.
Warwick	14,802	Low	Symptomatic VTE	Both	Age	NS
Joseph	569	Low	VTE	Both	Age	Significant
Leizorovicz	386	Low	VTE	Both	Age	NS
Guijarro	31,769	Low	VTE	Hip	Age	Age >70 OR: 1.5 (1.1, 1.9)
Guijarro	58,037	Low	VTE	Knee	Age	NS
Pedersen	68,155	Moderate	VTE hospitalization	Hip	Age	<50 yrs = reference 50-59: RR = 0.81 (0.54, 1.22) 60-69: 0.92 (0.64, 1.32) 70-79: 0.92 (0.59, 1.44) 80+: 0.88 (0.59, 1.32)
Leizorovicz	386	Low	VTE	Both	Cancer	NS
Guijarro	31,769	Low	VTE	Hip	Cancer	NS
Guijarro	58,037	Low	VTE	Knee	Cancer	OR: 2.2 (1.03, 4.6)
Pedersen	68,155	Moderate	VTE hospitalization	Hip	Cancer	RR: 0.93 (0.68, 1.28)
Warwick	14,802	Low	Symptomatic VTE	Both	Cardiovascular Disease	NS
Leizorovicz	386	Low	VTE	Both	Cardiovascular Disease	NS
Guijarro	31,769	Low	VTE	Hip	Cardiovascular Disease	NS
Guijarro	58,037	Low	VTE	Knee	Cardiovascular Disease	NS
Pedersen	68,155	Moderate	VTE hospitalization	Hip	Cardiovascular Disease	RR: 1.4 (1.15, 1.7)

Table 22. Risk Factors for VTE among Hip and Knee Arthroplasty Patients - Results

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Leizorovicz	386	Low	VTE	Both	Chronic Lung Disease	NS
Guijarro	31,769	Low	VTE	Hip	Chronic Lung Disease	NS
Guijarro	58,037	Low	VTE	Knee	Chronic Lung Disease	OR: 1.5 (1.02, 2.1)
Guijarro	31,769	Low	VTE	Hip	Diabetes	NS
Guijarro	58,037	Low	VTE	Knee	Diabetes	NS
Pedersen	68,155	Moderate	VTE hospitalization	Hip	Diabetes	RR: 1.13 (0.76, 1.69)
Joseph	569	Low	VTE	Both	Duration of Surgery	NS
Leizorovicz	386	Low	VTE	Both	Duration of Surgery	OR: 1.47/hr. (1.08, 2.01)
Joseph	569	Low	VTE	Both	History of VTE	NS
Lowe	374	V. Low	DVT (venogram)	Hip	History of Blood Clotting Disorders	APC Resistance OR: 3.13 (1.2, 8.17) Factor V Leiden OR: 3.21 (0.88, 11.69)
Joseph	569	Low	VTE	Both	History of Blood Clotting Disorders	NS
Joseph	569	Low	VTE	Both	History of Cancer	NS
Warwick	14,802	Low	Symptomatic VTE	Both	History of VTE	HR: 4.92 (3.15, 7.67)
Pedersen	68,155	Moderate	VTE hospitalization	Hip	History of VTE	RR: 8.1 (6.1, 10.8)
Pearse	223	V. Low	DVT (ultrasound)	Knee	Hormone Replacement Therapy	OR: 0.69 (0.15, 3.1)
Lemos	240	V. Low	PE	Both	Hormone Replacement Therapy	NS

Table 22. Risk Factors for VTE among Hip and Knee Arthroplasty Patients - Results

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Hurbanek	318	V. Low	VTE	Both	Hormone Replacement Therapy	OR: 0.68 (0.3, 1.2) (95% CI estimated from graph)
White 2000	889	Low	VTE Hospitalization	Hip	Hormone Replacement Therapy	NS
Gandhi	1,460	V. Low	Symptomatic DVT	Knee	Hypertension	OR: 2.3 (0.6, 32.2); also metabolic syndrome OR: 3.0 (1.1, 12.4)
Ryu	338	V. Low	Symptomatic PE	Knee	Hypertension	NS
Mraovic	7,389	V. Low	Symptomatic PE	Both	Hypertension	OR: 0.86 (0.56, 1.32)
Guijarro	31,769	Low	VTE	Hip	Hypertension	NS
Guijarro	58,037	Low	VTE	Knee	Hypertension	NS
Fujita	302	Low	DVT (venogram)	Both	Obesity	OR: 1.122/unit BMI
Warwick	14,802	Low	Symptomatic VTE	Both	Obesity	BMI >30: HR: 1.68 (1.25, 2.26)
Joseph	569	Low	VTE	Both	Obesity	NS
Leizorovicz	386	Low	VTE	Both	Obesity	NS
Guijarro	31,769	Low	VTE	Hip	Obesity	NS
Guijarro	58,037	Low	VTE	Knee	Obesity	OR: 1.7 (1.2, 2.3)
Lemos	240	V. Low	PE	Both	Peripheral Vascular Disease	NS
SooHoo 2010	138,399	V. Low	VTE	Hip	Peripheral Vascular Disease	OR: 1.10 (0.69, 1.77)
Mahomed 2003	55,975 (primary)	V. Low	PE	Hip	Race	African American vs. White OR: 1.07 (0.69, 1.65)
Mahomed 2003	12,233 (revision)	V. Low	PE	Hip	Race	African American vs. White OR: 1.24 (0.53, 2.92)
Mahomed 2005	124,986 (primary)	V. Low	PE	Knee	Race	African American vs. White RR: 1.0 (0.8, 1.3)

Table 22. Risk Factors for VTE among Hip and Knee Arthroplasty Patients - Results

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Mahomed 2005	11,726 (revision)	V. Low	PE	Knee	Race	African American vs. White OR: 1.4 (0.6, 3.5)
Memtsoudis	6,901,324	V. Low	PE	Both	Race	White = reference African American: OR:1.45 (1.38, 1.53) Not Stated: OR: 1.32 (1.28,1.36) Other: OR: 0.82 (0.72, 0.93)
SooHoo 2006	222,684	V. Low	PE	Knee	Race	White = reference African American: OR: 1.74 (1.36, 2.23) Hispanic: OR: 0.84 (0.65, 1.09)
Keeney	705	V. Low	VTE	Hip	Race	NS (African American vs. White)
White 1998	77,629	V. Low	VTE	Hip	Race	White = reference Asian African American Hispanic
SooHoo 2010	138,399	V. Low	VTE	Hip	Race	White = reference African American: OR: 1.89 (1.44, 2.47) Asian: OR: 1.17 (0.75, 1.83) Hispanic: 0.73 (0.53, 1.01)
Joseph	569	Low	VTE	Both	Recent Surgery	NS
Nathan	137	V. Low	Proximal DVT (ultrasound)	Knee	Restricted Mobility	Significant - univariate (9.5% of homebound patients vs. 4.8% of ambulant <1 km vs. 0% of ambulant >1 km)
Joseph	569	Low	VTE	Both	Restricted Mobility	NS
Lowe	374	V. Low	DVT (venogram)	Hip	Smoking	NS

Table 22. Risk Factors for VTE among Hip and Knee Arthroplasty Patients - Results

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Leizorovicz	386	Low	VTE	Both	Smoking	NS
Eriksson	135	V. Low	VTE	Hip	Smoking	NS
Beksac	1,986	V. Low	VTE	Hip	Smoking	NS
Won	1,608	V. Low	VTE	Both	Smoking	NS
Lowe	374	V. Low	DVT (venogram)	Hip	Varicose Veins	NS
Leizorovicz	386	Low	VTE	Both	Varicose Veins	NS
Eriksson	135	V. Low	VTE	Hip	Varicose Veins	Significant
Pearse	223	V. Low	DVT (ultrasound)	Knee	Venous Stasis Disease	OR: 2.7 (0.95, 7.6)
Warwick	14,802	Low	Symptomatic VTE	Both	Venous Stasis Disease	NS

HR= Hazard Ratio; OR= Odds Ratio; RR= Relative Risk; NS= Not Significant in multivariate analysis

Note: If 95% Confidence Intervals are not listed in the above table, they were not reported by the study authors

Table 23. Risk Factors for VTE - Data from Non--Arthroplasty Patients

Author	N	Strength	Outcome	Type(s) of Surgery	Risk Factor	Results
Kosir	108	V. Low	DVT	General, lasting at least 1 hour	Prognostic indicator (risk score based on age, BMI, Hemoglobin level, and colorectal patients)	No DVTs in any of 108 patients in study
Hatef	360	V. Low	VTE	Excisional Body Contouring	4-level risk score based on Davison-Caprini model	Significant risk factor; no adjustment for other variables
Bahl	8216	V. Low	VTE	General, Vascular, and Urologic	4-level risk score based on Caprini model	Significant risk factor after adjustment for year and length of inpatient stay
Bahl	8216	V. Low	VTE	General, Vascular, and Urologic	Inflammatory Bowel Disease	Not significant risk factor
Bahl	8216	V. Low	VTE	General, Vascular, and Urologic	Central venous access	Significant risk factor after adjustment for other factors in Caprini model
Frizzelli	810	V. Low (case series)	DVT	Cardiac	Central venous catheter	48% of patients had DVT

RECOMMENDATION 3

Patients undergoing elective hip or knee arthroplasty are at risk for bleeding and bleeding-associated complications. In the absence of reliable evidence, it is the opinion of this work group that patients be assessed for known bleeding disorders like hemophilia and for the presence of active liver disease which further increase the risk for bleeding and bleeding-associated complications.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

Current evidence is not clear about whether factors other than the presence of a known bleeding disorder or active liver disease increase the chance of bleeding in these patients and, therefore, we are unable to recommend for or against using them to assess a patient's risk of bleeding.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

Bleeding complications related to the soft tissue envelope around the surgical site and the effects of bleeding on functional outcomes are an important concern. A hematoma can lead to joint stiffness and a compromised functional outcome or to a periprosthetic joint infection (with its associated morbidity). Although these potential risks have historically not been addressed in other guidelines on this topic, given the seriousness of these concerns, this work group believed it necessary to address them.

We found very little data that addressed risk factors for bleeding in patients undergoing elective hip or knee replacement surgery (see Table 24 for the list of risk factors for which we sought evidence and for a summary of these results. Two studies of very low quality (see Table 50 in Appendix XIII) addressed patients with hemophilia, with the

only comparative study finding it to be a significant predictor of hemarthrosis. One comparative study of very low quality addressed cirrhosis of the liver and found it to be a significant predictor of perioperative blood loss (Table 25).

Therefore, patients with a known bleeding disorder or active liver disease may have an increased risk for bleeding. Evaluating patients for these factors has minimal cost and low risk to the patient; we believe that these actions are consistent with the current practice of most orthopaedic surgeons. Recommendation 7 discusses the recommended thromboprophylaxis strategy for these patients.

Evidence about whether factors other than the presence of a known bleeding disorder or active liver disease affect the risk for bleeding in patients undergoing primary hip and knee arthroplasty is unclear. Six low quality studies among non-arthroplasty surgical patients did not find convincing evidence that preoperative coagulation screening predicts postoperative bleeding (Table 50 in Appendix XIII summarizes our evaluation of the quality and applicability of these studies).

- bleeding time predicted blood loss in one of three studies
- fibrinogen predicted blood loss in one of three studies
- platelet count predicted blood loss in one of six studies
- prothrombin time predicted blood loss in one of six studies (Table 27).

In other very low quality (and, therefore, unreliable) studies of non-arthroplasty surgical patients (Table 26):

- thrombocytopenia was a significant predictor of postoperative intracranial hematoma among intracranial surgery patients,
- a history of gastrointestinal (GI) bleed was not a significant predictor of postoperative upper GI bleeding among non-ulcer surgery patients,
- a history of bleeding with previous surgery did predict excessive bleeding among cardiac bypass patients, while
- epistaxis and a history of bleeding with dental extraction each did not predict major bleeding among Type 1 von Willebrand disease patients undergoing surgery.

No data were found addressing the other risk factors (see Table 24 for the list of risk factors for which we sought evidence).

The data on hemorrhage-related complications are also sparse. Three low quality and fourteen very low quality studies addressed whether patients with one or more potential risk factors have higher rates of hemorrhage-associated complications. (The results of these studies are summarized in Table 28, Table 29 and Table 30, which provide a

detailed description of these studies' results. Our evaluation of their quality and applicability is shown in Appendix XIII, Table 51) Low hemoglobin levels and more complex revision procedures did predict a higher risk of transfusion, but none of the factors studied could be directly tied to hemorrhage-associated complications such as deep periprosthetic joint infection.

Due to the inconclusive evidence regarding other risk factors for bleeding or hemorrhage-associated complications among elective hip and knee arthroplasty patients, we are unable to recommend for or against further risk stratification.

The clinician should be aware of established contraindications against the use of individual anticoagulant agents.

We excluded some of the studies we retrieved to address this recommendation. These studies, and the reasons for their exclusion are listed in Appendix XIV, Table 59- Table 60.

FINDINGS

QUALITY AND APPLICABILITY

The two studies addressing hemophilia and the study addressing cirrhosis of the liver were of very low quality. The six studies addressing coagulation screening were all of low quality. The five included studies addressing other potential risk factors for bleeding were all of very low quality. All included studies for this recommendation were of moderate applicability. For details, see Table 50 in Appendix XIII.

We included three low quality and fourteen very low quality studies addressing potential risk factors for hemorrhage-associated complications. All included studies were of moderate applicability. For details, see Table 51 in Appendix XIII.

RESULTS

Table 24. Risk Factors for Bleeding Summary Table

Risk Factor	Hemar-throsis	Peri-operative Blood Loss	Intra-operative Blood Loss	Post-operative Blood Loss	Intra-cranial Hematoma	Reoperation due to Bleeding	Major Bleeding	Excessive Bleeding	Upper GI Bleeding
History of GI Bleeding									◊
History of Bleeding with Previous Surgery								♦	
Bleeding Disorder	●								
History of Bleeding After Dental Extractions							◊		
History of Hemorrhagic Stroke									
History of Retroperitoneal Bleeding									
Liver Disease		●							
Thrombocytopenia					♦				
Easy Bruising									
Epistaxis							◊		
History of DIC									
Abnormal Coagulation Screening:									
aPTT		◊◊◊◊	◊					◊	
Bleeding Time		◊◊	♦					◊	
Fibrinogen		♦	◊		◊				
Platelet Count		◊◊◊◊	♦		◊			◊	
Prothrombin Time		◊◊◊◊	♦		◊			◊	
Relevant bleeding in the past 6 months									

○: no statistically significant difference; ●: statistically significant risk factor; ♦: statistically significant risk factor among non-arthroplasty patients; ◊: no statistically significant difference among non-arthroplasty patients Note: Each circle or diamond represents a separate study.

Table 25. Risk Factors for Bleeding - Data among Arthroplasty Patients

Author	Risk Factor	N	Strength	Joint	Outcome	Results
Sikkema 2010	Hemophilia	81	V. Low	Both	Hemarthrosis	52% in hemophilia patients vs. 7% in control patients (p<.001)
Innocenti 2007	Hemophilia	20	V. Low (Case Series)	Knee	Perioperative Blood Loss Hemarthrosis	1100 mL (range: 300-1200) 1 (5%)
Shih 2004	Cirrhosis of the Liver	84	V. Low	Knee	Perioperative Blood Loss	470 mL more in cirrhosis patients (1370 vs. 900: p <.001)
Kim 2000	Aplastic Anemia	19	V.Low (Case Series)	Hip	Postoperative Blood Loss	656 mL (range: 252-1274)

Table 26. Risk Factors for Bleeding - Data among Non-Arthroplasty Patients

Author	Risk Factor	N	Strength	Patient Type	Outcome	Results
Woods 2008	Epistaxis	311	V. Low	Type 1 von Willebrand and possible Type 1 von Willebrand disease patients undergoing any surgical procedure	Major bleeding	Not significant in multivariate analysis
Woods 2008	History of Bleeding with Dental Extractions	311	V. Low	Type 1 von Willebrand and possible Type 1 von Willebrand disease patients undergoing any surgical procedure	Major bleeding	Not significant in multivariate analysis
Nuttall 2006	History of Bleeding with Previous Surgery	174	V. Low	Cardiac Surgery with Cardiopulmonary Bypass	Excessive Bleeding (chest tube drainage over 24 hours of 750mL)	Significant Adjusted OR: 2.42 (1.1, 5.29)
Della Ratta 1993	History of GI Bleed	180	V. Low	Nonulcer Surgery	Postoperative Upper Grastrointestinal Tract Bleeding	NS OR: 1.31 (0.36, 4.36)
Chan 1989	Thrombocytopenia (platelet count < 150,000/µl)	1582	V. Low	Intracranial Surgery	Postoperative Intracranial Hematoma	Significant OR: 41 (17, 94)

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Table 27. Coagulation Screening among Non-Arthroplasty Patients - Results

Author	Coagulation Screening Test	Test Range	N	Strength	Patient Type	Outcome	Results from Multivariate Analysis
Gravlee 1994	Activated Partial Thromboplastin Time	Not Reported	897	Low	Cardiac Surgery with Cardiopulmonary Bypass	Mediastinal Drainage (16 hours)	NS
Dorman 1993	Activated Partial Thromboplastin Time	17.8-40 (s)	60	Low	Coronary Artery Bypass Surgery	Intraoperative Blood Loss	NS
Despotis 1996	Activated Partial Thromboplastin Time	Not Reported	487	Low	Cardiac Surgery with Cardiopulmonary Bypass	Cumulative (24 hours) Chest Tube Drainage (CTD) and Excessive CTD	NS
ElMalik 2000	Activated Partial Thromboplastin Time	80-153 (Pt/control %)	121	Low	Transurethral Prostatectomy	Total Blood Loss (24 hours)	NS
Karlsson 2008	Activated Partial Thromboplastin Time	All in normal range	170	Low	Coronary Artery Bypass Grafting Surgery	Chest Tube Drainage (12 hours)	NS
Gerlach 2002	Partial Thromboplastin Time	Not Reported	876	Low	Intracranial Surgery	Intracranial Hematoma	NS
Dorman 1993	Bleeding Time	1.5-12 (min)	60	Low	Coronary Artery Bypass Surgery	Intraoperative Blood Loss	P<.05
Despotis 1996	Bleeding Time	Not Reported	487	Low	Cardiac Surgery with Cardiopulmonary Bypass	Cumulative (24 hours) Chest Tube Drainage (CTD) and Excessive CTD	NS

Table 27. Coagulation Screening among Non-Arthroplasty Patients - Results

Author	Coagulation Screening Test	Test Range	N	Strength	Patient Type	Outcome	Results from Multivariate Analysis
Gravlee 1994	Earlobe Bleeding Time	Not Reported	897	Low	Cardiac Surgery with Cardiopulmonary Bypass	Mediastinal Drainage (16 hours)	NS
Dorman 1993	Fibrinogen	201-812 (mg/dL)	60	Low	Coronary Artery Bypass Surgery	Intraoperative Blood Loss	NS
Gerlach 2002	Fibrinogen	Not Reported	876	Low	Intracranial Surgery	Intracranial Hematoma	NS
Karlsson 2008	Fibrinogen	2.4-8.1 g/L	170	Low	Coronary Artery Bypass Grafting Surgery	Chest Tube Drainage (12 hours)	r=-0.53, P<.001
Gravlee 1994	Platelet Count	Not Reported	897	Low	Cardiac Surgery with Cardiopulmonary Bypass	Mediastinal Drainage (16 hours)	NS
Dorman 1993	Platelet Count	140-440 ($x10^3/mm^3$)	60	Low	Coronary Artery Bypass Surgery	Intraoperative Blood Loss	P<.05
Despotis 1996	Platelet Count	Not Reported	487	Low	Cardiac Surgery with Cardiopulmonary Bypass	Cumulative (24 hours) Chest Tube Drainage (CTD) and Excessive CTD	NS
ElMalik 2000	Platelet Count	101-525 (x $x10^3/\mu L$)	121	Low	Transurethral Prostatectomy	Total Blood Loss (24 hours)	NS
Gerlach 2002	Platelet Count	Not Reported	876	Low	Intracranial Surgery	Intracranial Hematoma	NS
Karlsson 2008	Platelet Count	All in normal range	170	Low	Coronary Artery Bypass Grafting Surgery	Chest Tube Drainage (12 hours)	NS

Table 27. Coagulation Screening among Non-Arthroplasty Patients - Results

Author	Coagulation Screening Test	Test Range	N	Strength	Patient Type	Outcome	Results from Multivariate Analysis
Gravlee 1994	Prothrombin Time	Not Reported	897	Low	Cardiac Surgery with Cardiopulmonary Bypass	Mediastinal Drainage (16 hours)	NS
Dorman 1993	Prothrombin Time	10.7-13.2 (s)	60	Low	Coronary Artery Bypass Surgery	Intraoperative Blood Loss	P<.05
Despotis 1996	Prothrombin Time	Not Reported	487	Low	Cardiac Surgery with Cardiopulmonary Bypass	Cumulative (24 hours) Chest Tube Drainage (CTD) and Excessive CTD	NS
ElMalik 2000	Prothrombin Time	91-125 (Pt/control %)	121	Low	Transurethral Prostatectomy	Total Blood Loss (24 hours)	NS
Gerlach 2002	Prothrombin Time	Not Reported	876	Low	Intracranial Surgery	Intracranial Hematoma	NS
Karlsson 2008	Prothrombin Time	6 patients had elevated INR (1.3-1.9)	170	Low	Coronary Artery Bypass Grafting Surgery	Chest Tube Drainage (12 hours)	NS

Table 28. Summary Table for Hemorrhage-Associated Complications Risk Factors

Risk Factor	Infection	Transfusion	Dehiscence	Hemarthrosis Requiring Operation
Patient unwilling to accept transfusion				
Obesity	○○●	○○		
Low Hemoglobin		●●●●		
Immunocompromised State	●●	○●		○
Inflammatory Arthritis	○●	○○	●	
Connective Tissue Disease				
Previous surgery or revision arthroplasty		●●●○○		
Spinal or epidural anesthesia for which >2 attempts at placement were made, or the placement was traumatic				
Planned indwelling intrathecal or epidural catheter >6 hours post-surgery				

○: no statistically significant difference. ●: statistically significant risk factor

Table 29. Risk Factors for Hemorrhage-Associated Complications - Multivariate Results

Author	N	Strength	Anticoagulation Used	Outcome	Joint	Immuno-compromised	Inflammatory Arthritis	Low Hemoglobin	Obesity	Revision Arthroplasty
Guerin	162	Low	Yes	Transfusion	Both	x	x	●	x	x
Aderinto	1016	Low	Yes	Transfusion	Hip	x	x	●	○	x
Borghi	2884	Low	Not Reported	Allogenic Transfusion	Both	x	x	●	x	●
Mesa-Ramos	121	V. Low	Yes	Transfusion	Knee	○	x	●	○	x
Moran	759	V. Low	Not Reported	Superficial Wound Infection	Hip	x	x	x	○	x
Amin	76	V. Low	Yes	Superficial Wound Infection	Knee	x	□	x	●	x
Chee	106	V. Low	Yes	Superficial Wound Infection	Hip	x	x	x	○	x
Rashiq	918	V. Low	Not Reported	Allogenic Transfusion	Hip	x	x	●	x	○
Rashiq	957	V. Low	Not Reported	Allogenic Transfusion	Knee	x	x	●	x	○
Bong	1194	V. Low	Yes	Any Transfusion/Allogenic Transfusion	Knee	x	○/●	●	○	x
Walsh	1035	V. Low	Yes	Any Transfusion/Allogenic Transfusion	Hip	x	○	●/○	○	x
Sikkema	81	V. Low	N/Y†	Hemarthrosis requiring reoperation	Both	○	x	x	x	x
SooHoo	138,399	V. Low	Not Reported	Infection	Hip	●	○	x	x	x
Marchant	1,032,039	V. Low	Not Reported	Infection/Transfusion/Other Wound Complications	Both	●*/●/○	x	x	x	x
Larocque	599	V. Low	Not Reported	Transfusion	Both	x	x	●	x	●
Saleh	1142	V. Low	Not Reported	Transfusion	Both	x	x	●	x	●
Marx	354	V. Low	Not Reported	Transfusion	Hip	x	○	●	x	○
White	9580	V. Low	Not Reported	Wound infection/dehiscence	Hip	x	●	x	x	x

●= statistically significant risk factor; ○= not statistically significant risk factor; x=not included in regression model; □= used as covariate in model, multivariate results not reported; *Infection is significant only for uncontrolled diabetes, not controlled diabetes; †Hemophilia patients did not receive antithrombotic prophylaxis but control patients did

Table 30. Risk Factors for Hemorrhage-Associated Complications – Results Details

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Sikkema	81	V. Low	Hemarthrosis requiring reoperation	Both	Hemophilia	11.1% vs. 1.9% (not significant)
Bong	1194	V. Low	Allogenic Transfusion	Knee	Inflammatory Arthritis	RR: 2.36 (significant)
Walsh	1035	V. Low	Allogenic Transfusion	Hip	Inflammatory Arthritis	RR: 1.51 (not significant)
Bong	1194	V. Low	Any Transfusion	Knee	Inflammatory Arthritis	RR: 1.41 (not significant)
Walsh	1035	V. Low	Any Transfusion	Hip	Inflammatory Arthritis	RR: 1.27 (not significant)
SooHoo	138,399	V. Low	Infection	Hip	Inflammatory Arthritis	OR: 1.47 (0.90, 2.41)
Marx	354	V. Low	Transfusion	Hip	Inflammatory Arthritis	Not Significant
White	9580	V. Low	Wound Dehiscence	Hip	Inflammatory Arthritis	0.6% vs 0.1% (age-adjusted p<0.001)
White	9580	V. Low	Wound Infection	Hip	Inflammatory Arthritis	1.7% vs. 0.8% (age-adjusted p=.01)
Guerin	162	Low	Transfusion	Both	Low Hemoglobin (continuous)	Significant; <13 g/dL vs. 13-15 g/dL: RR=1.5; vs. 15+: RR=4
Borghi	2884	Low	Allogenic Transfusion	Both	Low Hemoglobin (<10 g/dL)	OR: 8.8 (6.5, 16.8)
Aderinto	1016	Low	Transfusion	Hip	Low Hemoglobin (continuous)	Significant
Moran	759	V. Low	Superficial Wound Infection	Hip	Obesity	Not Significant
Amin	76	V. Low	Superficial Wound Infection	Knee	Obesity	17.1% among morbidly obese vs. 0% among non-obese (significant)
Chee	106	V. Low	Superficial Wound Infection	Hip	Obesity	9.1% among morbidly obese vs. 3.6% among non-obese (not significant)

Table 30. Risk Factors for Hemorrhage-Associated Complications – Results Details

Author	N	Strength	Outcome	Joint	Risk Factor	Results
Aderinto	1016	Low	Transfusion	Hip	Obesity	Not Significant
Mesa-Ramos	121	V. Low	Transfusion	Knee	Obesity	Not Significant
Borghi	2884	Low	Allogenic Transfusion	Both	Revision Arthroplasty	OR of hip revision vs. primary hip or knee: 5.8 (3.9,8.5)
Rashiq	918	V. Low	Allogenic Transfusion	Hip	Revision Arthroplasty	OR: 1.07 (0.61, 1.89);
Rashiq	957	V. Low	Allogenic Transfusion	Knee	Revision Arthroplasty	OR: 1.08 (0.63, 1.85)
Larocque	599	V. Low	Transfusion	Both	Revision Arthroplasty	OR: 4.5 (1.36, 14.6)
Saleh	1142	V. Low	Transfusion	Both	Revision Arthroplasty	Reference: Primary knee Revision knee OR: 1.88 (0.62, 5.22) Primary hip: OR: 4.6 (3.01, 6.83) Revision hip: OR: 17.8 (9.6, 33)
Marx	354	V. Low	Transfusion	Hip	Revision Arthroplasty	Not Significant
Marchant	1,032,039	V. Low	Infection	Both	Uncontrolled Diabetes	OR: 2.310 (1.424,3.747)
Marchant	1,032,039	V. Low	Infection	Both	Controlled Diabetes	OR: 0.998 (0.843, 1.066)
SooHoo	138,399	V. Low	Infection	Hip	Uncomplicated diabetes	OR: 1.72 (1.48, 2.08)
SooHoo	138,399	V. Low	Infection	Hip	Complicated diabetes	OR: 3.7 (2.39, 5.74)
Marchant	1,032,039	V. Low	Other Wound Complications	Both	Uncontrolled Diabetes	OR: 2.587 (0.637, 10.510)
Marchant	1,032,039	V. Low	Other Wound Complications	Both	Controlled Diabetes	OR: 1.062 (0.620, 1.819)
Marchant	1,032,039	V. Low	Transfusion	Both	Uncontrolled Diabetes	OR: 1.29 (1.133,1.468)
Marchant	1,032,039	V. Low	Transfusion	Both	Controlled Diabetes	OR: 1.092 (1.058, 1.126)
Mesa-Ramos	121	V. Low	Transfusion	Knee	Diabetes	Not Significant

RECOMMENDATION 4

We suggest that patients discontinue antiplatelet agents (e.g., aspirin, clopidogrel) before undergoing elective hip or knee arthroplasty.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a Moderate recommendation but remain alert to new information and be sensitive to patient preferences.

RATIONALE

Among non-arthroplasty surgical patients, preoperative antiplatelet use predicted higher perioperative blood loss in three studies of moderate to high quality. Reoperation rates due to bleeding only varied in one of the three studies (see Table 26 for a detailed presentation of these results, and Table 52 in Appendix XIII for our appraisal of the quality and applicability of these studies).

Although this evidence is not specific to elective hip or knee arthroplasty patients, the work group believed the evidence is still applicable to these patients who are at risk for bleeding and bleeding-associated complications.

We excluded some of the studies we retrieved to address this recommendation. These studies and the reasons for their exclusion are listed in Appendix XIV, Table 61.

FINDINGS

QUALITY AND APPLICABILITY

Of the three studies addressing preoperative antiplatelet use, one was of high quality and two were of moderate quality. All three were of moderate applicability. For details, see Table 52 in Appendix XIII.

RESULTS

Table 31. Preoperative Antiplatelet Use - Data among Non-Arthroplasty Patients

Author	Risk Factor	N	Strength	Patient Type	Outcome	Results
Kallis 1994	Antiplatelet Use (aspirin vs. placebo for 2 weeks before surgery)	100	High	Coronary Artery Bypass Grafting	Intraoperative Blood Loss	Significantly more blood lost in the aspirin group (454 vs. 372 ml, p=.05)
Firanescu 2009	Antiplatelet Use (stopping clopidogrel 5 days vs. 3 days vs. 0 days before surgery)	118	Moderate	Coronary Artery Bypass Grafting	Intraoperative Blood Loss	NS
Kallis 1994	Antiplatelet Use (aspirin vs. placebo for 2 weeks before surgery)	100	High	Coronary Artery Bypass Grafting	Postoperative Blood Loss	Significantly more blood lost in the aspirin group (1185 vs. 791 ml, p=.001)
Ghaffarinejad 2007	Antiplatelet Use (preoperative aspirin use vs. no aspirin for at least 7 days before surgery)	200	Moderate	Coronary Artery Bypass Grafting	Postoperative Blood Loss	Significantly more blood lost in the aspirin group (608 vs. 483 ml, p=.005)
Firanescu 2009	Antiplatelet Use (stopping clopidogrel 5 days vs. 3 days vs. 0 days before surgery)	118	Moderate	Coronary Artery Bypass Grafting	Postoperative Blood Loss	Significantly more blood lost in patients stopping clopidogrel the day of surgery (p=.022)
Kallis 1994	Antiplatelet Use (aspirin vs. placebo for 2 weeks before surgery)	100	High	Coronary Artery Bypass Grafting	Reoperation due to Bleeding	Higher reoperation rate in aspirin group (8% vs 0%, p=.04)

Table 31. Preoperative Antiplatelet Use - Data among Non-Arthroplasty Patients

Author	Risk Factor	N	Strength	Patient Type	Outcome	Results
Ghaffarinejad 2007	Antiplatelet Use (preoperative aspirin use vs. no aspirin for at least 7 days before surgery)	200	Moderate	Coronary Artery Bypass Grafting	Reoperation due to Bleeding	No significant difference (3% in each group)
Firanescu 2009	Antiplatelet Use (stopping clopidogrel 5 days vs. 3 days vs. 0 days before surgery)	118	Moderate	Coronary Artery Bypass Grafting	Reoperation due to Bleeding	NS

RECOMMENDATION 5

We suggest the use of pharmacologic agents and/or mechanical compressive devices for the prevention of venous thromboembolic disease in patients undergoing elective hip or knee arthroplasty, and who are not at elevated risk beyond that of the surgery itself for venous thromboembolism or bleeding.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

Current evidence is unclear about which prophylactic strategy (or strategies) is/are optimal or suboptimal. Therefore, we are unable to recommend for or against specific prophylactics in these patients.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

In the absence of reliable evidence about how long to employ these prophylactic strategies, it is the opinion of this work group that patients and physicians discuss the duration of prophylaxis.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

RATIONALE

We recognize the diversity of opinion concerning the clinical importance of DVT as an isolated event or as a surrogate outcome for PE or post-thrombotic syndrome, (for further discussion, please see the Methods section), and understand that for clinical, and sometimes for even medico-legal reasons, DVT prevention may be the clinician's immediate concern. There is moderate evidence to suggest that pharmacological agents and/or mechanical compression devices reduce DVT rates in patients undergoing elective knee or hip arthroplasty. This is why we are suggesting prophylaxis. Readers of this guideline should recognize, however, that the available, published evidence does not establish whether these prophylactic strategies affect rates of all-cause mortality, fatal PE, symptomatic PE, or symptomatic DVT in patients undergoing elective hip or knee arthroplasty.

We also note that the present recommendation for prophylaxis is of a "Moderate" (rather than "Strong") grade partly because it is based on a surrogate outcome we do not consider "critical" (we considered major bleeding, pulmonary emboli, and all cause mortality as "critical," and symptomatic DVT, any DVT, and proximal DVT as not critical). The "critical" outcomes are all patient-oriented. The non-critical outcomes are not.

The inability to recommend a specific prophylactic strategy is a direct result of the network meta-analyses we performed. We performed numerous such analyses with sensitivity analyses that included separately analyzing data from patients who underwent hip and knee arthroplasty, analyzing these data combined, evaluating the impact of study quality on the results, and by comparing the results of each prophylactic strategy to placebo (or no treatment) and, when placebo/no treatment data were not available, comparing the results of each strategy to results obtained with enoxaparin (as discussed in the Methods section, this use of two comparators allows us to check the logical consistency of our models). The results of these analyses did not consistently suggest that any one strategy is preferable to another (please see Figure 38 - Figure 55 and Table 32 - Table 34; and, for the results of our sensitivity analyses, see Appendix XV).

We also analyzed data on other outcomes but, due to lack of data, network meta-analysis was not possible for them. In total, then, our analyses of the different prophylactic strategies is comprised of 112 high-or medium quality randomized controlled studies that enrolled patients undergoing elective hip and/or knee arthroplasty (see Appendix XIII, Table 53). As with the network meta-analyses, the data did not suggest that any specific prophylactic strategy was superior or inferior.

Part of the reason that current data do not permit a conclusion about specific prophylactic strageties is that, in our final network meta-analyses, no pharmacological agents showed a statistically significant effect in preventing all-cause mortality, symptomatic pulmonary emboli, symptomatic DVT, and major bleeding, when data from hip and knee studies were analyzed separately or when they were combined. This may be because these events are rare. In addition, infection rates and re-operations (for any reason) were not reported. Reoperations due to bleeding were reported, but were often part of the study authors' definition of major bleeding.

Many of the commonly used agents such as sodium warfarin and various low molecular weight heparinoids did not show efficacy for preventing VTED. This may be partially explained by the lack of comparison studies with placebo controls and by the rarity of the events of interest. In the final model with PE as the outcome, there were 181 events among 42,390 patients across 25 trials, and only 3 of these trials had a placebo or no prophylaxis arm.

There were a limited number of studies that evaluated mechanical compression devices. In one study on total hip arthroplasties,[48] there was a lower risk of major bleeding in the mechanical group. However, this study was only of moderate quality, partially because only 37% of the compression group had this device alone, with the remainder of the patients receiving low dose aspirin (81 mg/day) as well. There were also difficulties with the comparability of the control and intervention groups (that some of the studies we examined were not of high quality is another reason why the present recommendation is of "Moderate" strength).

In some analyses of mechanical compression device studies, less bleeding was found in comparison to no treatment. This may not appear intuitively logical, but might be occurring because of problems with randomization and the patient populations which may not be generalizable to the standard population of patients typically undergoing total hip and knee arthroplasties. The effect may also be occurring for some presently unknown physiological reasons. Other potentially confounding factors with these studies are enumerated below.

Conclusions about specific prophylactic strategies are also difficult because, in addition to the above-mentioned challenges posed by the rarity of the events of interest and the lack of reporting of critical outcomes, the available studies:

- Enrolled a select group of patients and did not necessarily include patients who had a high risk for VTED or bleeding and may not be representative of a typical patient population
- Used different drug doses (e.g. Enoxaparin at 30 mg bid vs. 40 mg per day).
- Used different timing of administration of agents (short-term vs. longer-term dosing)
- Used different routes of administration

Comparing different prophylactic strategies is difficult because there is a paucity of placebo-controlled trials because of early acceptance of prophylaxis being the standard of care.

Also, we are unable to recommend specific pharmacologic agents and/or mechanical devices because the results of our analyses with DVT as the outcome were not robust on sensitivity analyses. Due to the rarity of the critical outcomes of interest and the limited number of placebo-controlled trials, we had to rely on the analysis of DVT (i.e., any DVT), a surrogate measure, to evaluate the relative efficacy of the prophylactic strategies. However, the results of these analyses depend on the structure of the model

used, as agents shown to significantly reduce the occurrence of DVT in one model are often not statistically significant in an alternate model (see Table 97 in Appendix XV).

Some clinical practice guidelines make recommendations about the duration of pharmacologic prophylaxis. The available evidence is partially from manufacturer-funded trials, and is of only one agent. The latter is particularly problematic because the potential differences in the risks and benefits of various pharmacological agents may become more prominent as the duration of prophylaxis increases. We are, therefore, reluctant to make such a recommendation until more is known about the relative risk/benefit profiles of these different agents. Rather, the work group recommends that patients and physicians discuss the appropriate duration of prophylaxis for each individual situation. This physician-patient discussion is low cost and consistent with current practice.

As of April 1, 2011, several of the analyzed agents are not approved for marketing or the treatment of any medical condition in the United States. The United States Food and Drug Administration's (FDA) current policy regarding disclosure of marketing applications can be found in "Current Disclosure Policies for Marketing Applications" on the FDA website.

We excluded some studies we retrieved for this recommendation. The reasons for doing so are shown in Appendix XIV, Table 62).

FINDINGS

QUALITY AND APPLICABILITY

Of the 112 included studies for this recommendation, 87 were of high quality and 25 were of moderate quality. All but two studies were of moderate applicability; the other two were of low applicability. For details, see Table 53 in Appendix XIII.

RESULTS

SUMMARY OF DIRECT COMPARISONS

The figures below summarize the results of direct comparisons made for the six outcomes addressed by the network meta-analysis. If a single study addressed a given comparison of two treatments, that is the result presented. If multiple studies addressed a given comparison, results of the corresponding meta-analysis are presented. More information on these direct comparisons can be found in Appendix XV (Table 67 through Table 84). Studies with no events in any arm are not included in this analysis.

Note: For all figures and tables in this recommendation, the outcome Deep Vein Thrombosis (DVT) refers to any DVT: symptomatic or asymptomatic.

Figure 2. Pulmonary Embolism Direct Comparisons among Hip and Knee Patients

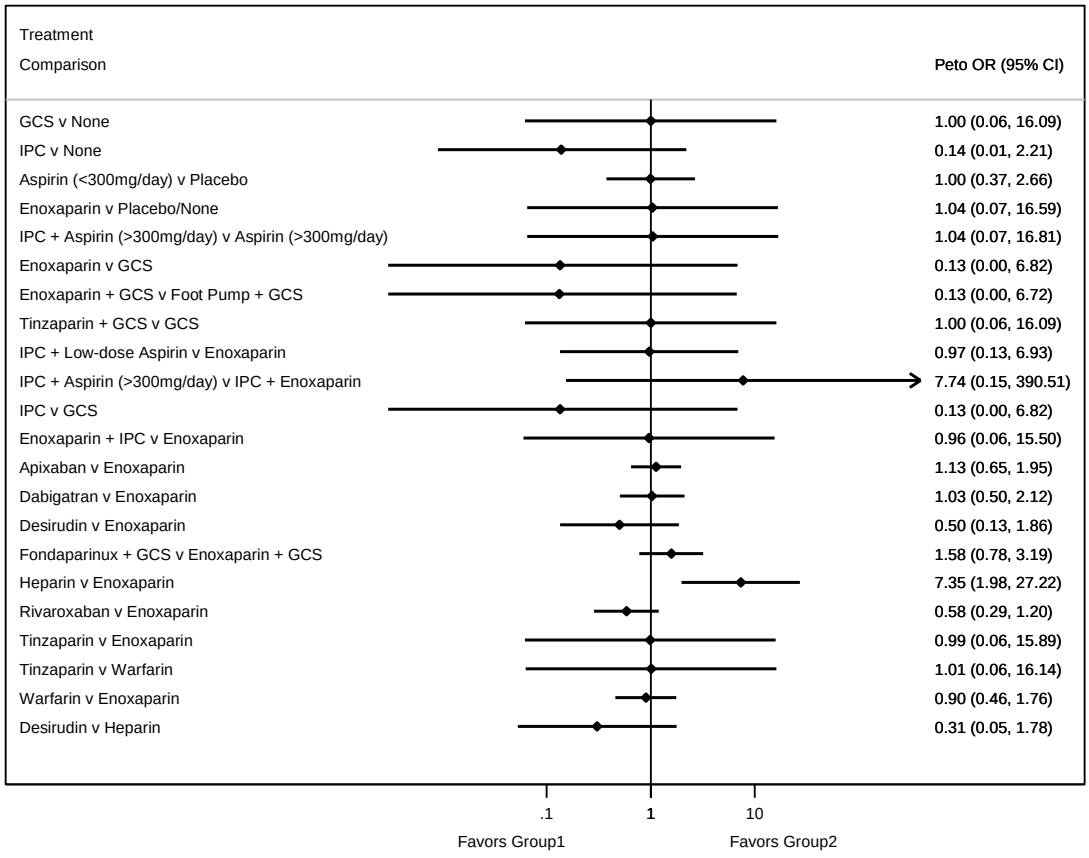


Figure 3. Pulmonary Embolism Direct Comparisons among Hip Patients

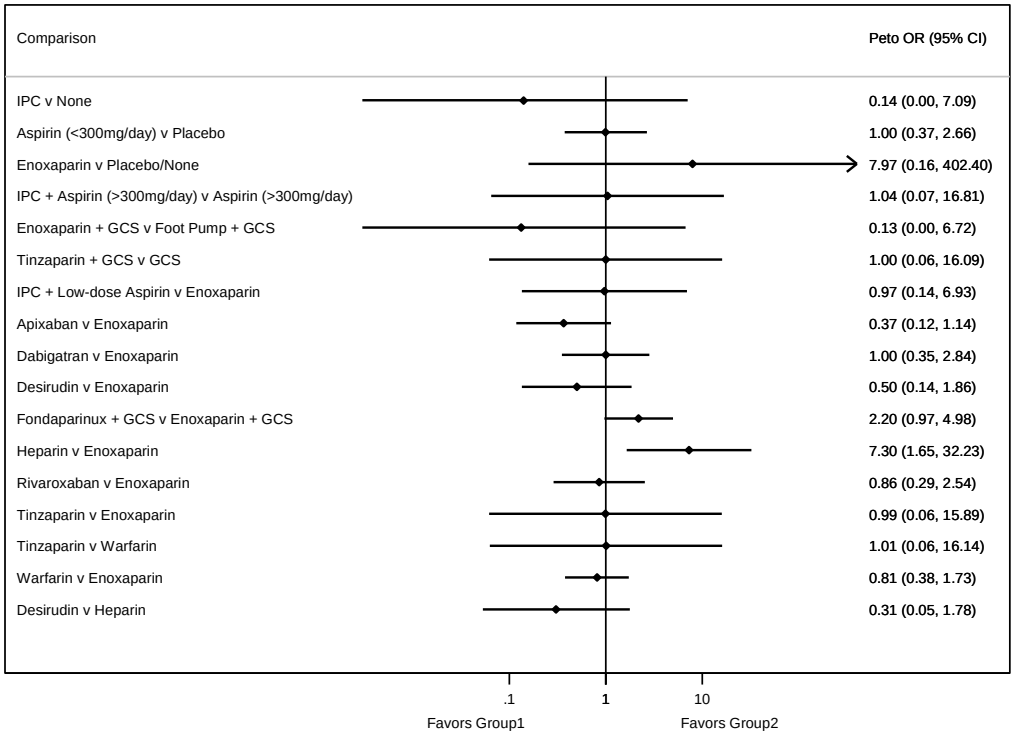


Figure 4. Pulmonary Embolism Direct Comparisons among Knee Patients

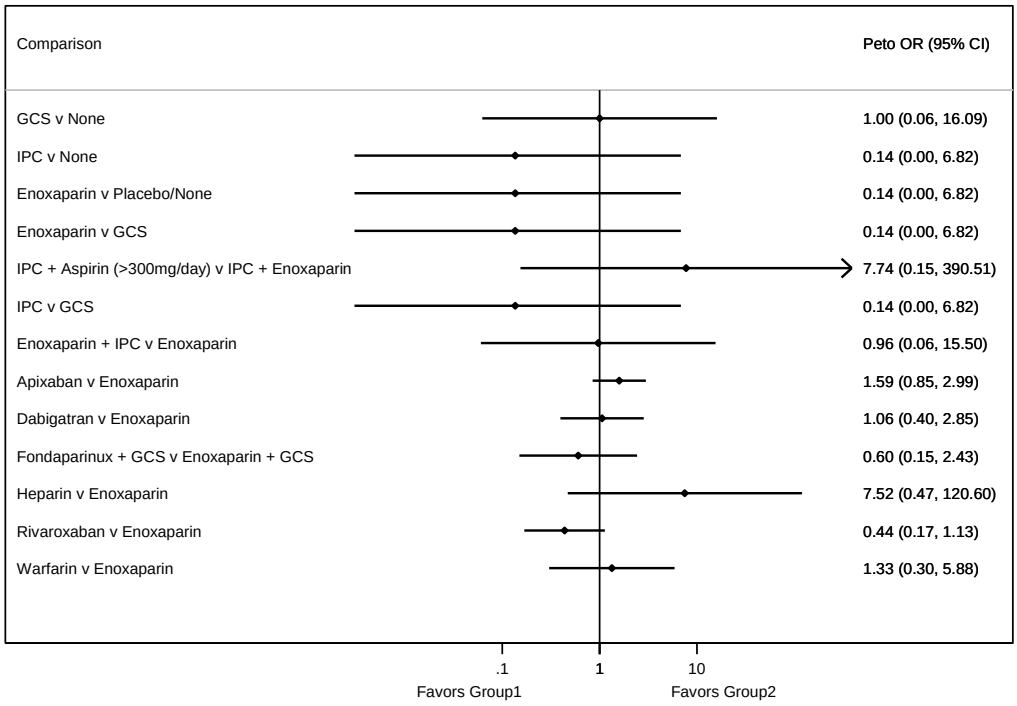


Figure 5. Major Bleeding Direct Comparisons among Hip and Knee Patients

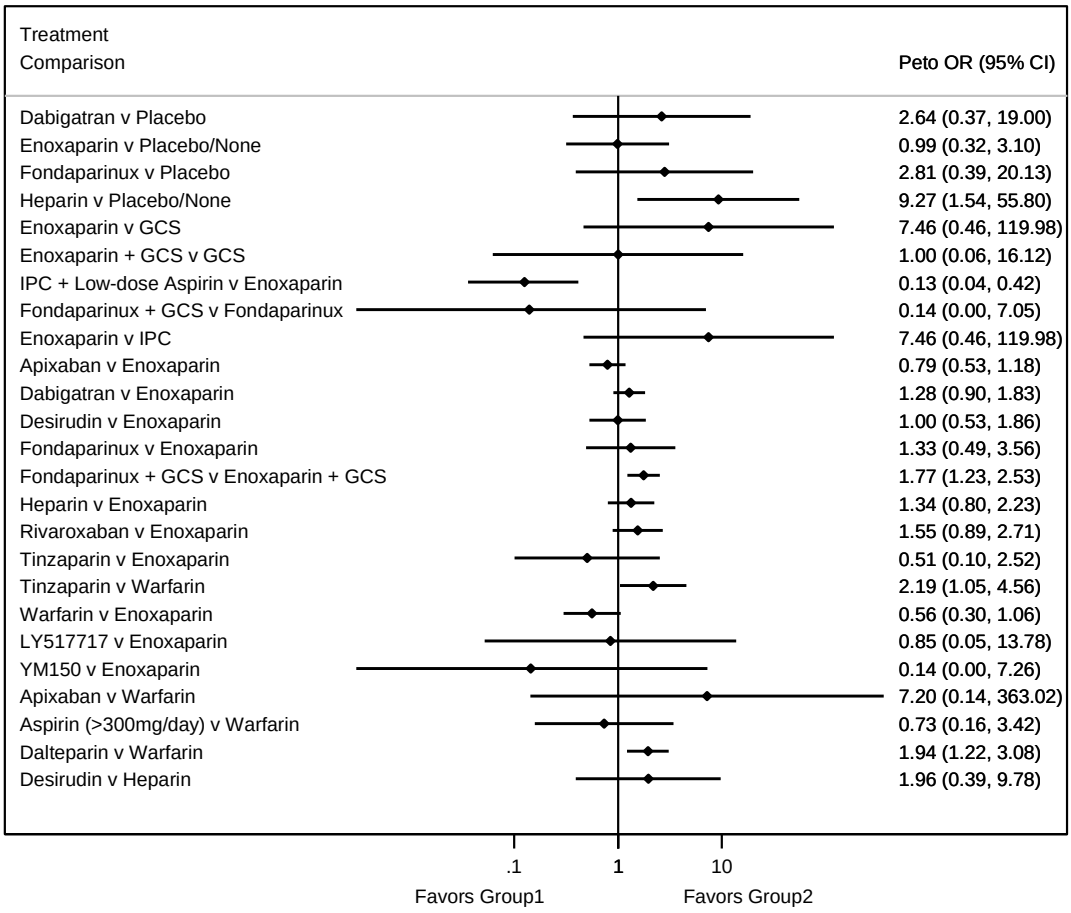


Figure 6. Major Bleeding Direct Comparisons among Hip Patients

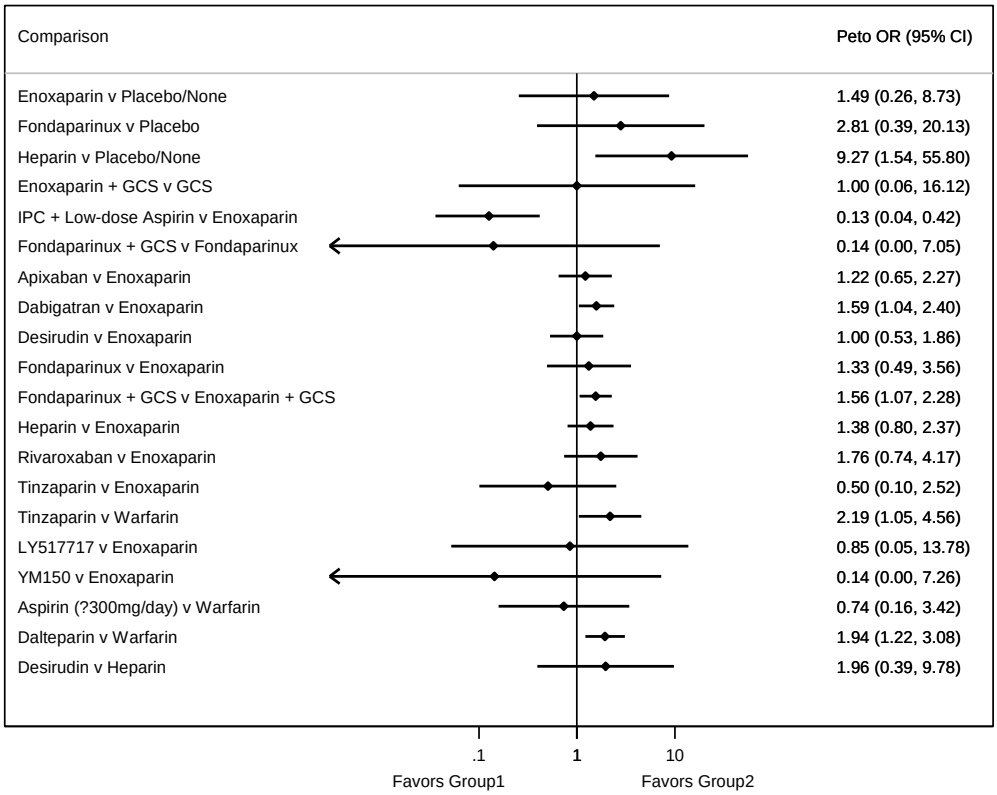


Figure 7. Major Bleeding Direct Comparisons among Knee Patients

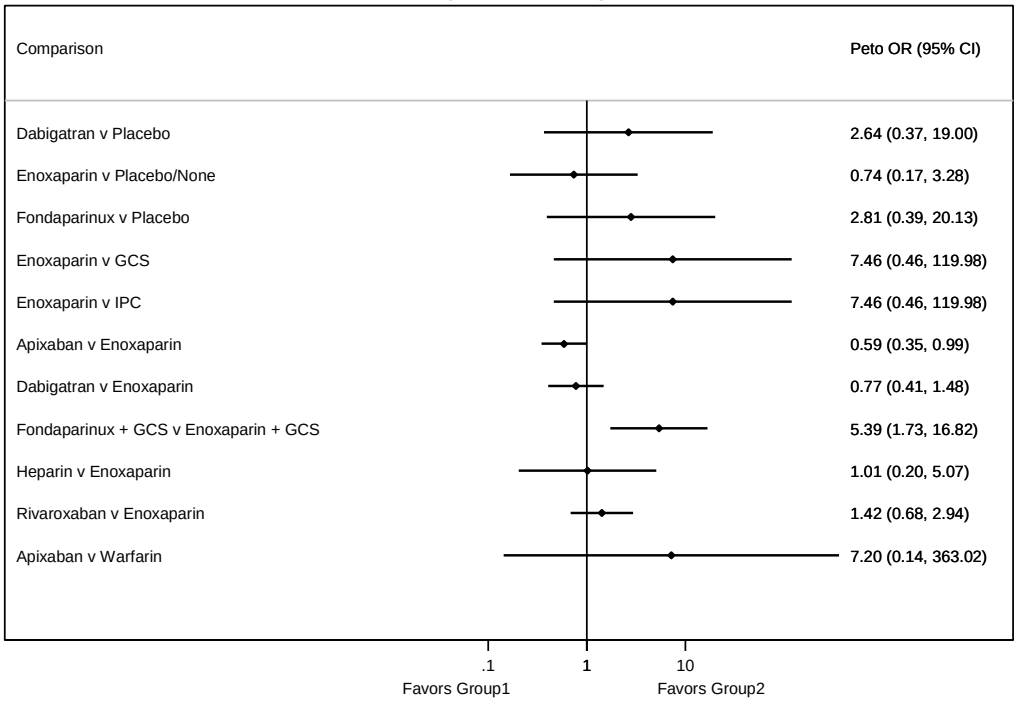


Figure 8. All Cause Mortality Direct Comparisons among Hip and Knee Patients

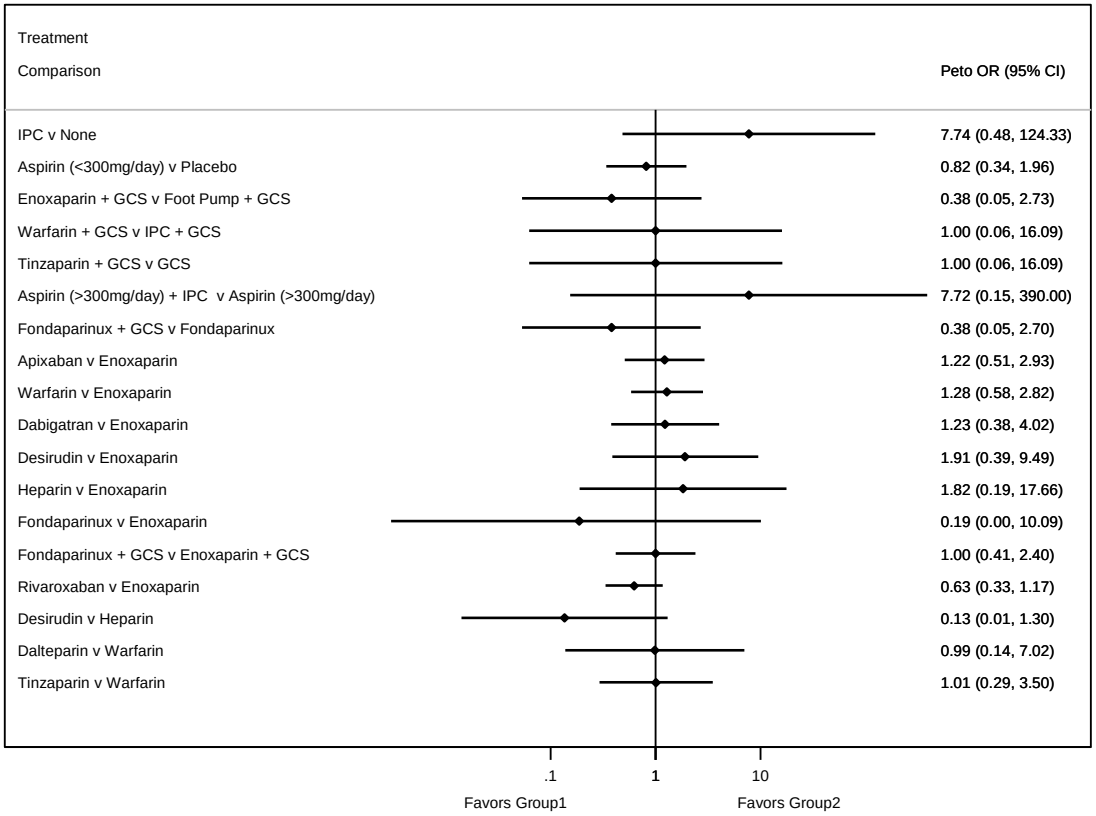


Figure 9. All Cause Mortality Direct Comparisons among Hip Patients

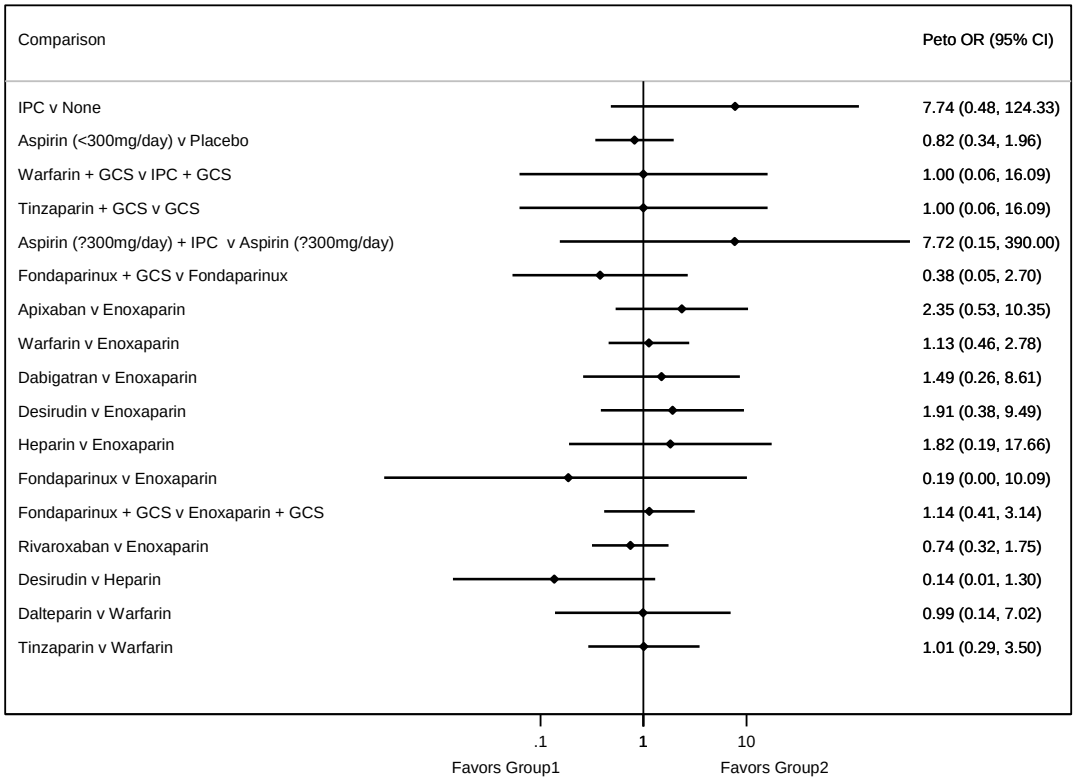


Figure 10. All Cause Mortality Direct Comparisons among Knee Patients

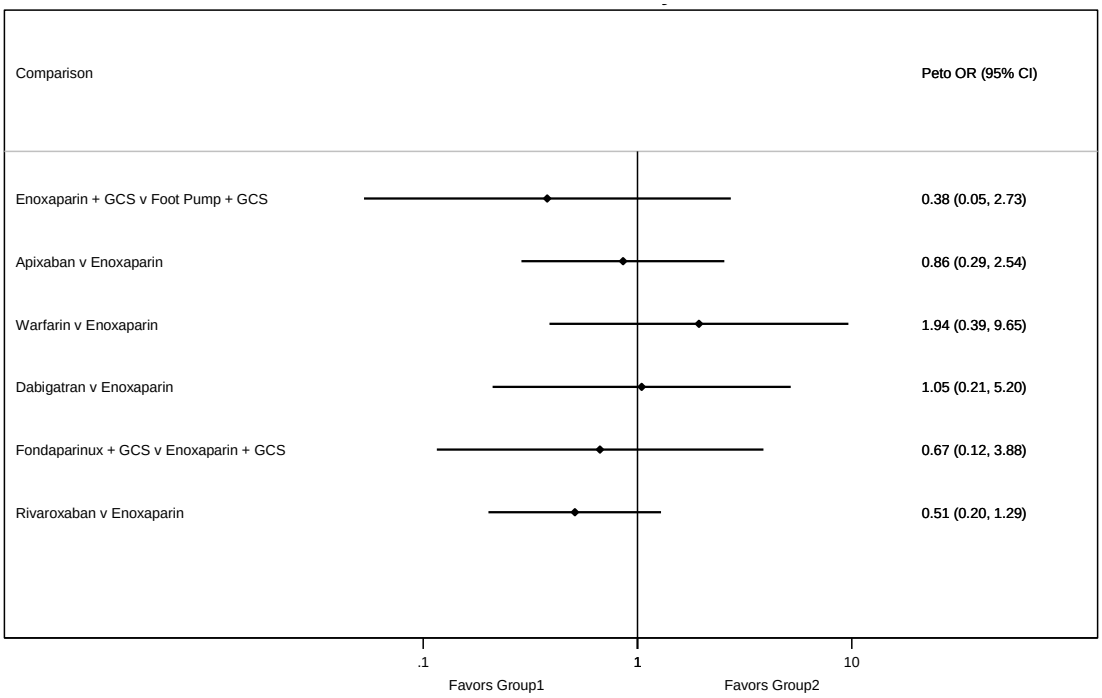


Figure 11. Symptomatic Deep Vein Thrombosis Direct Comparisons among Hip and Knee Patients

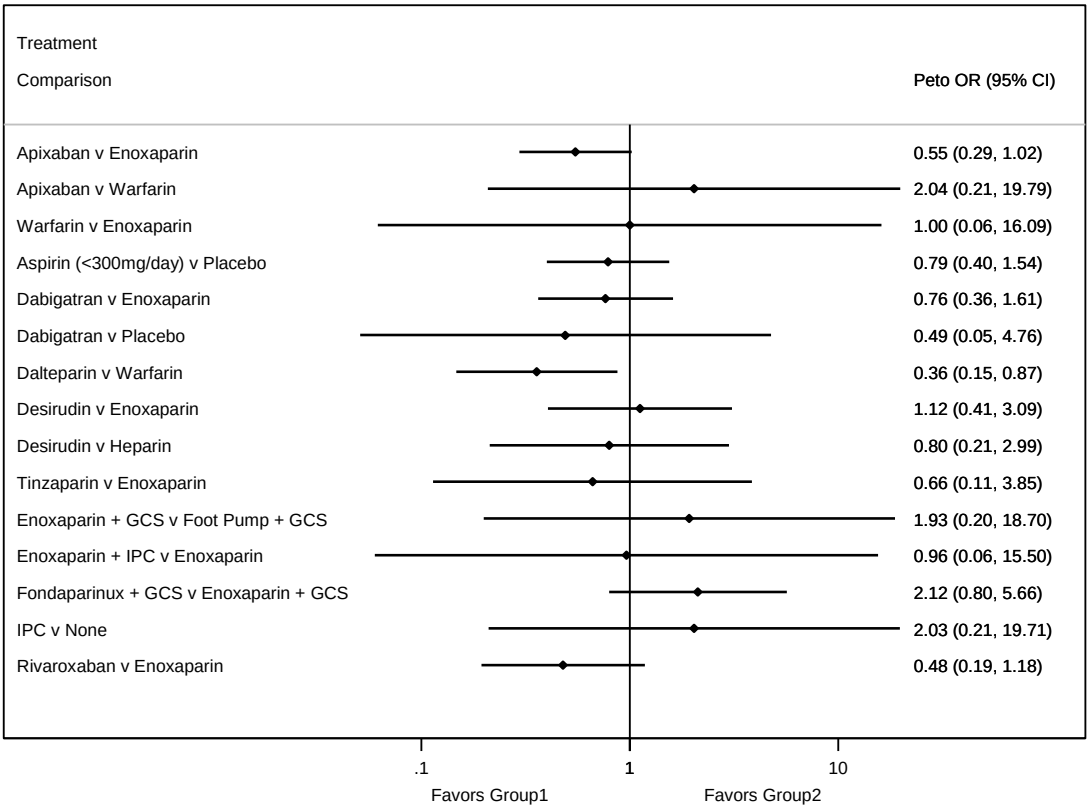


Figure 12. Symptomatic Deep Vein Thrombosis Direct Comparisons among Hip Patients

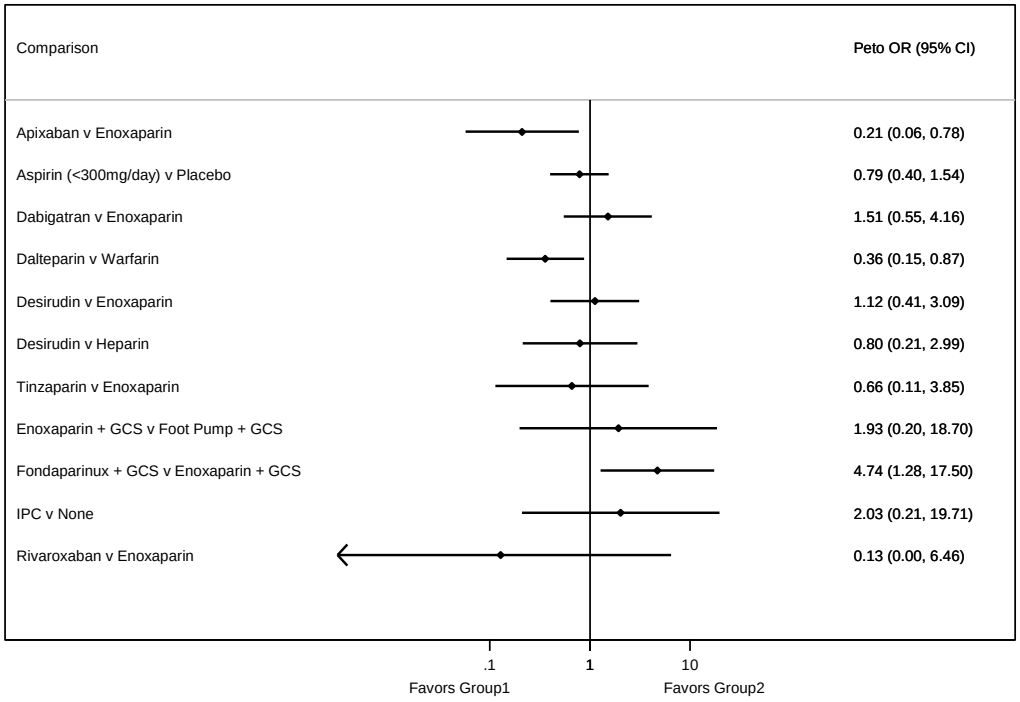


Figure 13. Symptomatic Deep Vein Thrombosis Direct Comparisons among Knee Patients

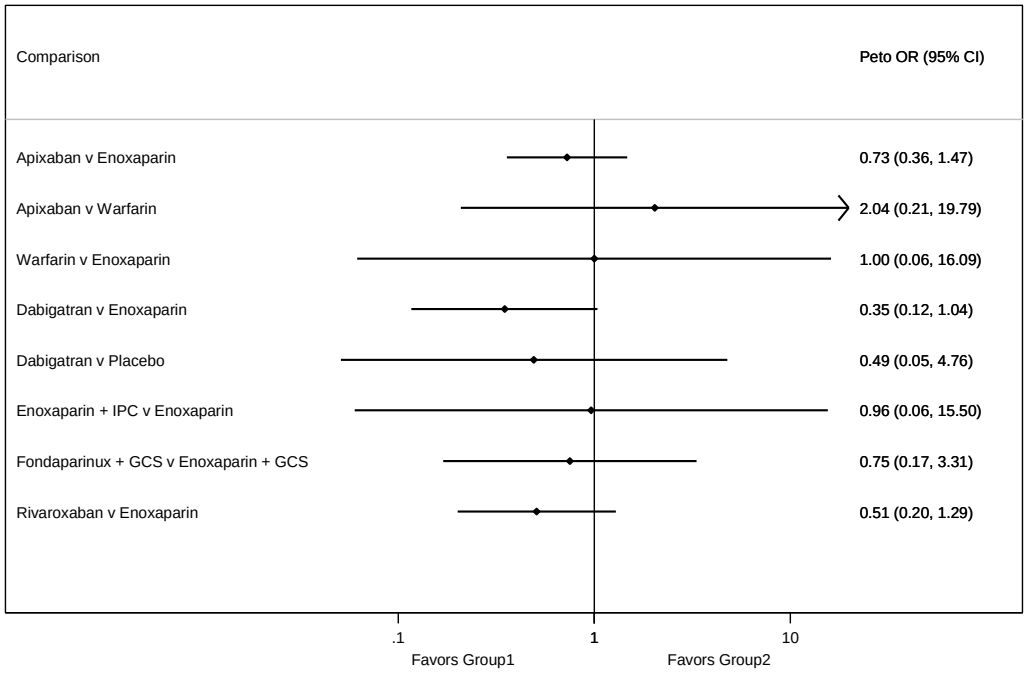
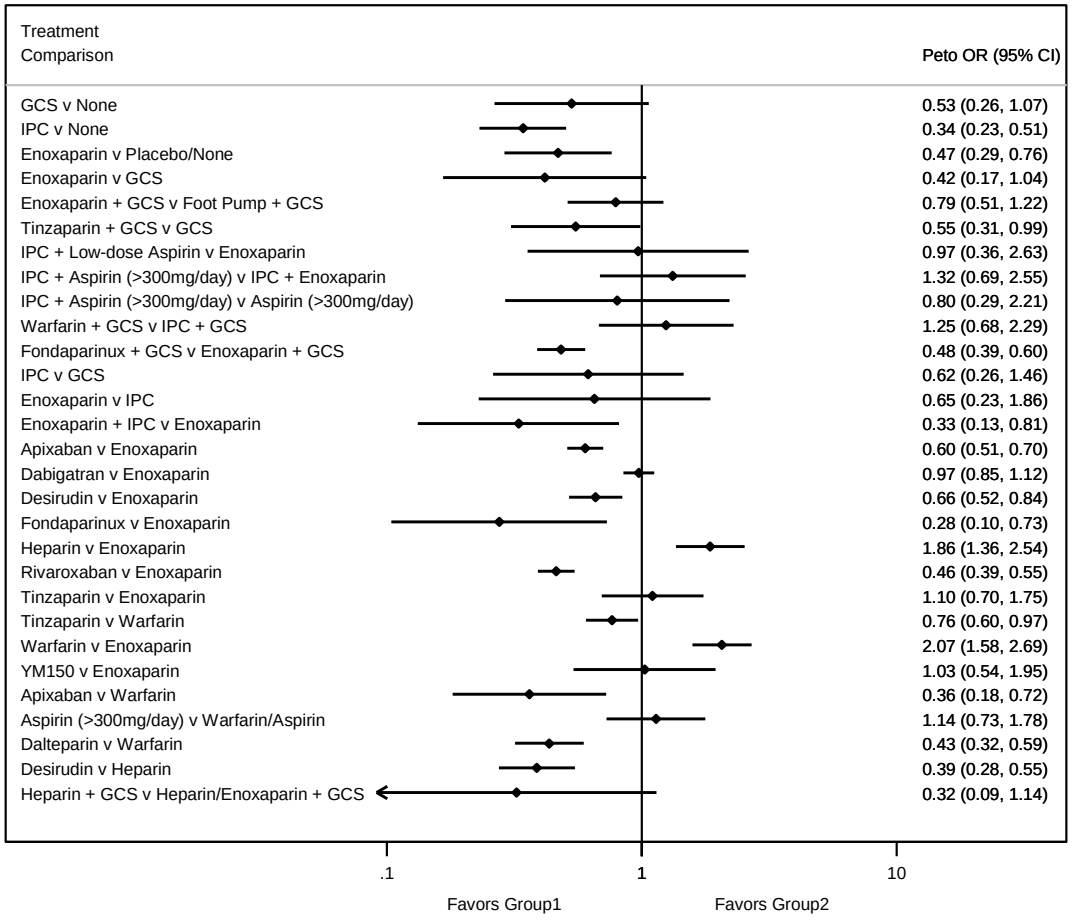


Figure 14. Deep Vein Thrombosis Direct Comparisons among Hip and Knee Patients



Note: For all figures and tables in this recommendation, the outcome Deep Vein Thrombosis (DVT) refers to any DVT: symptomatic or asymptomatic.

Figure 15. Deep Vein Thrombosis Direct Comparisons among Hip Patients

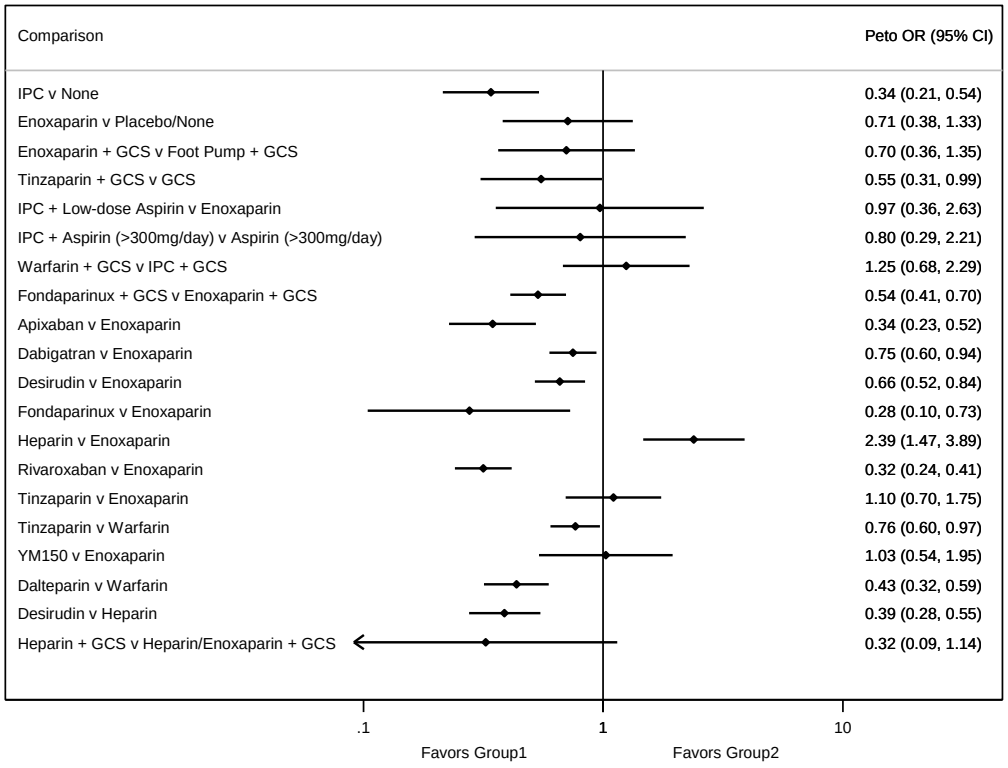


Figure 16. Deep Vein Thrombosis Direct Comparisons among Knee Patients

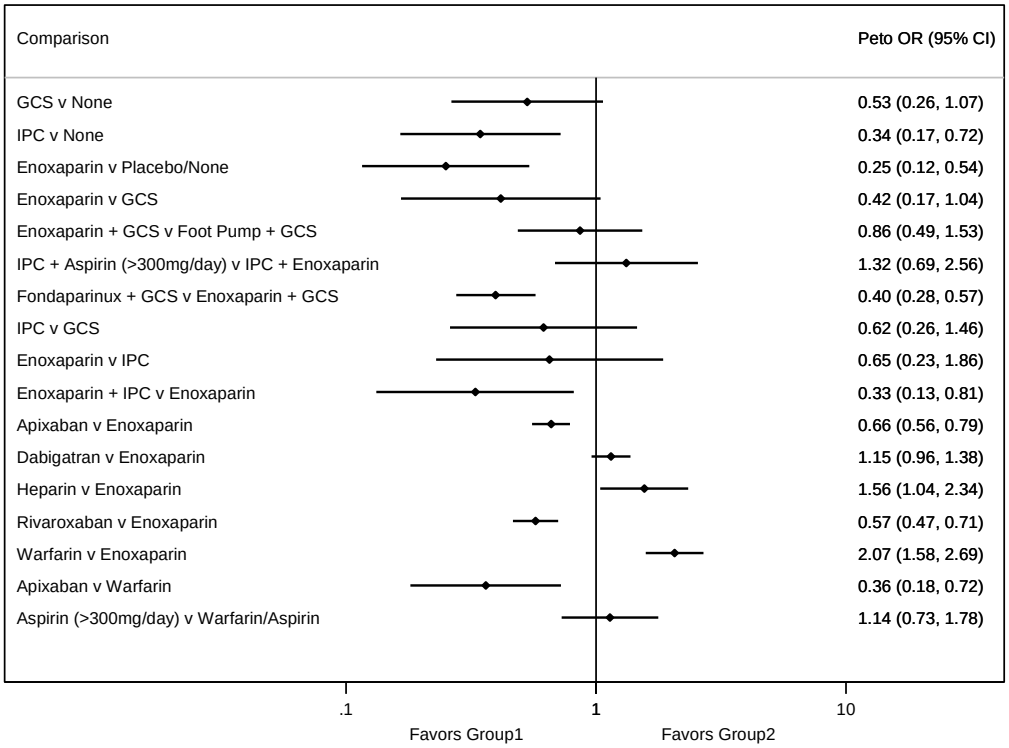


Figure 17. Proximal DVT Direct Comparisons among Hip and Knee Patients

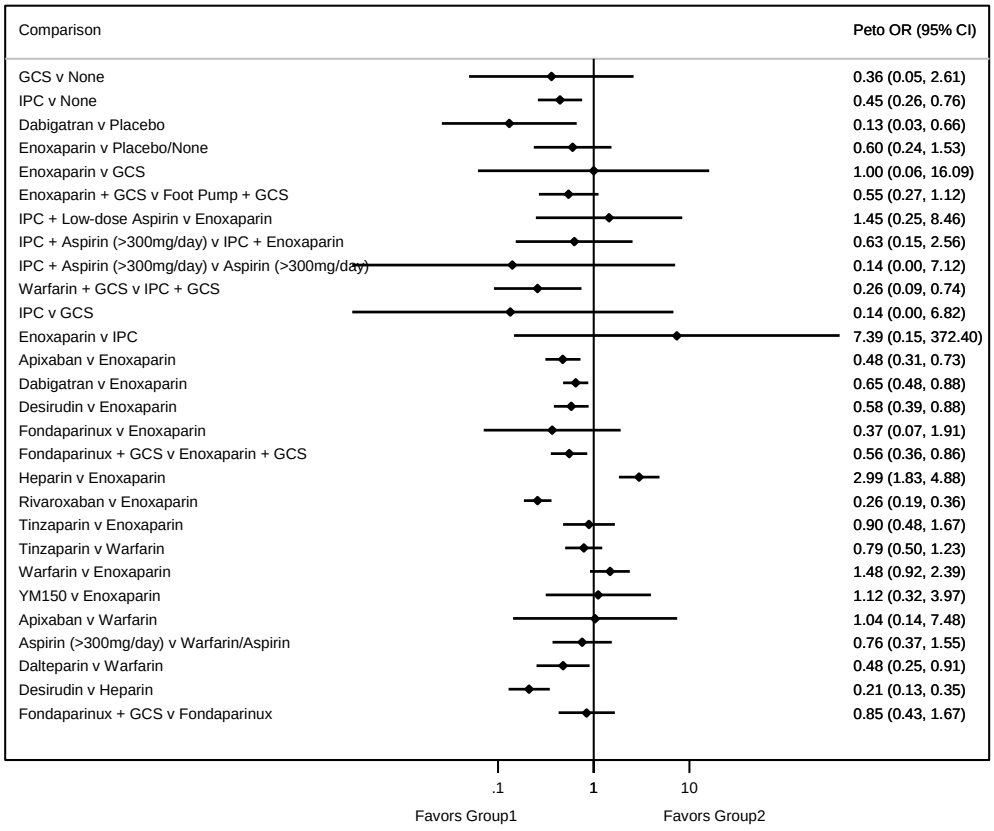


Figure 18. Proximal DVT Direct Comparisons among Hip Patients

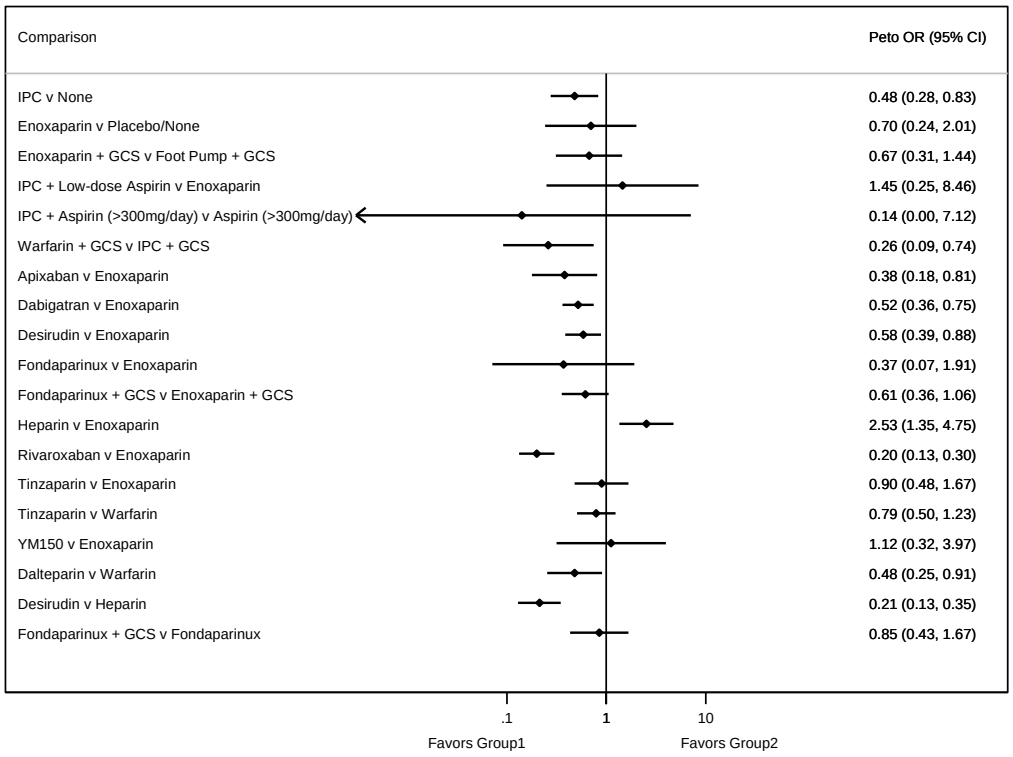
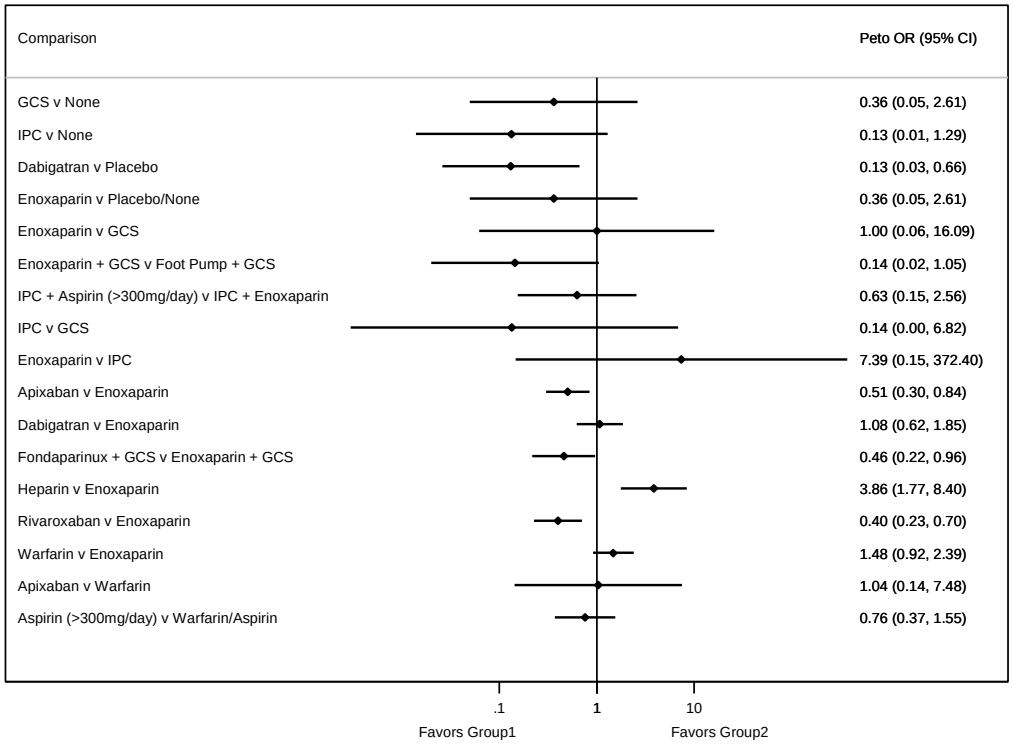


Figure 19. Proximal DVT Direct Comparisons among Knee Patients

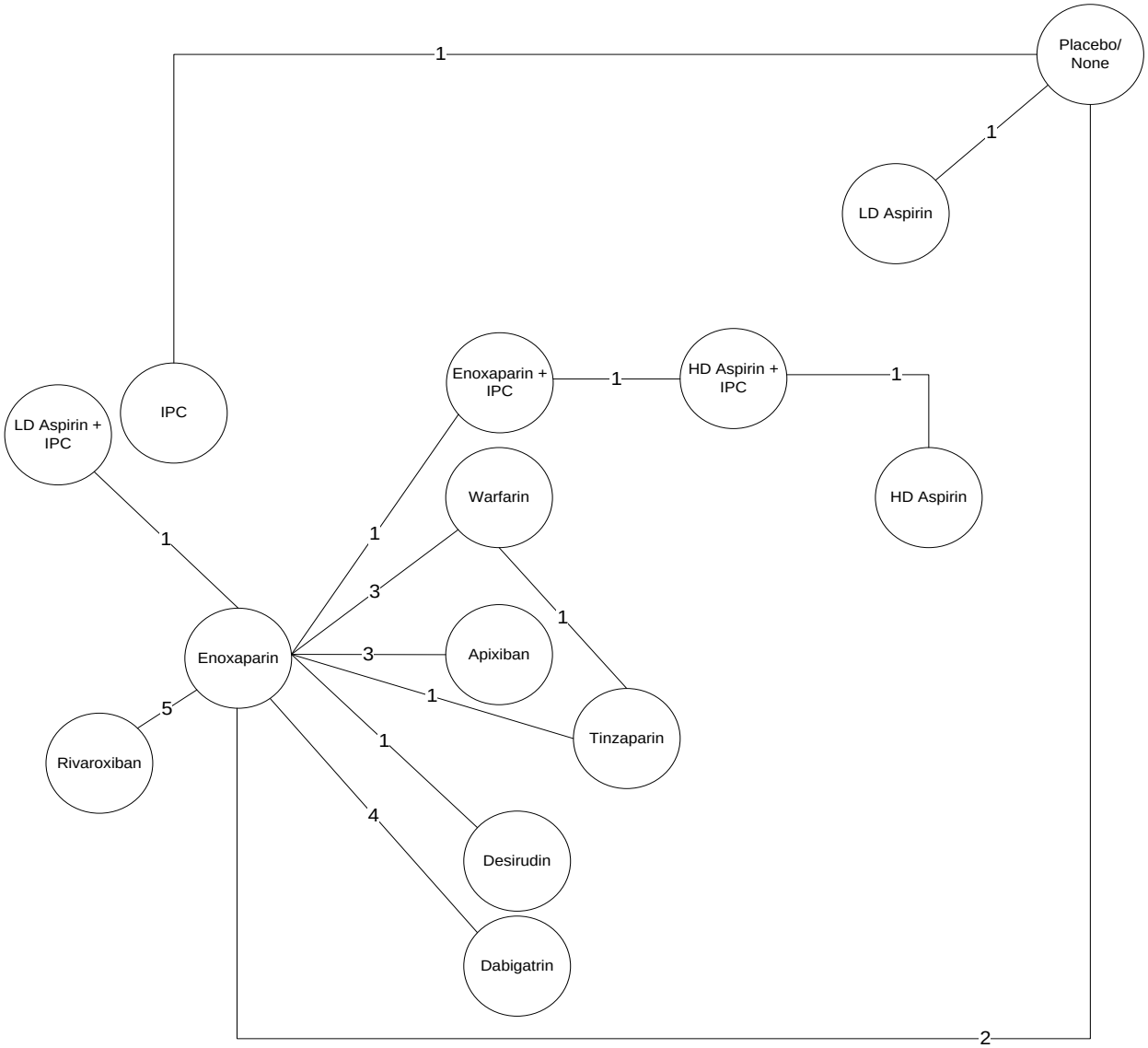


NETWORK META-ANALYSES

MODELS

This section depicts our final models. Please see Appendix XV for the models depicting our sensitivity analyses.

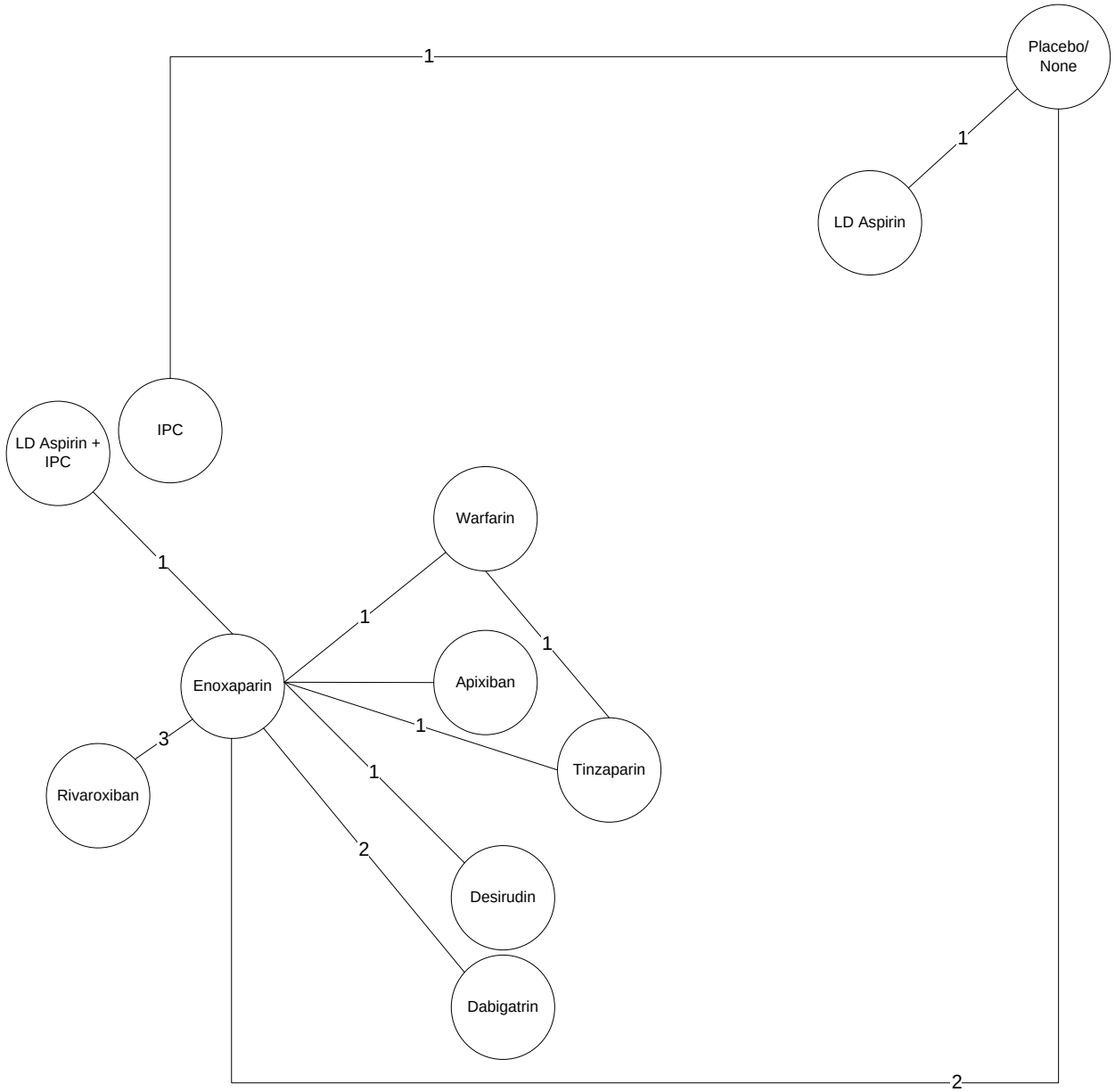
Figure 20. Final Pulmonary Embolism Model (with continuity correction, without heparin or multi-arm trials)



The model depicted in the figure is the final model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip arthroplasty and those who received a total knee arthroplasty. It does not include trials of heparin and trials with > 2 arms. Circles denote the treatments studied. Lines between circles denote treatment

comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

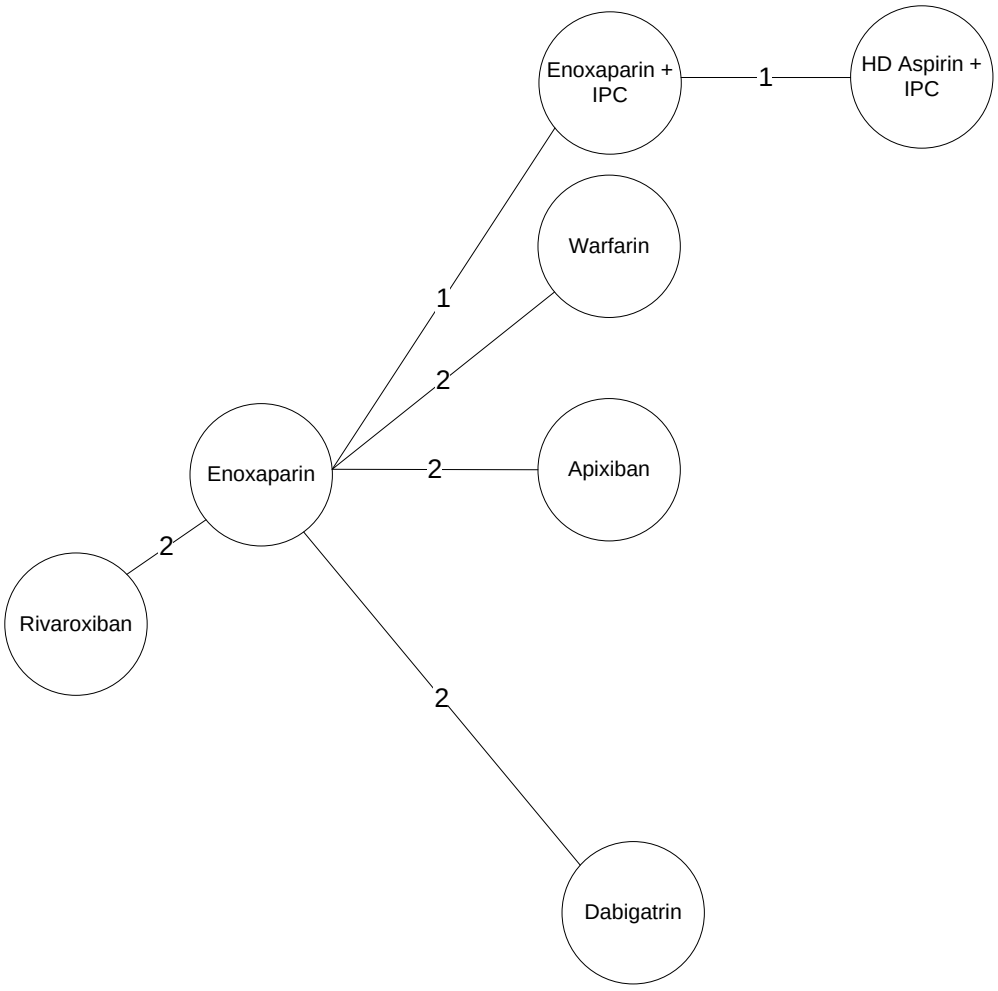
Figure 21. Final Pulmonary Embolism Model (with continuity correction, without heparin, or multi-arm trials, H**ip patients only**



The model depicted in the figure is a model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers

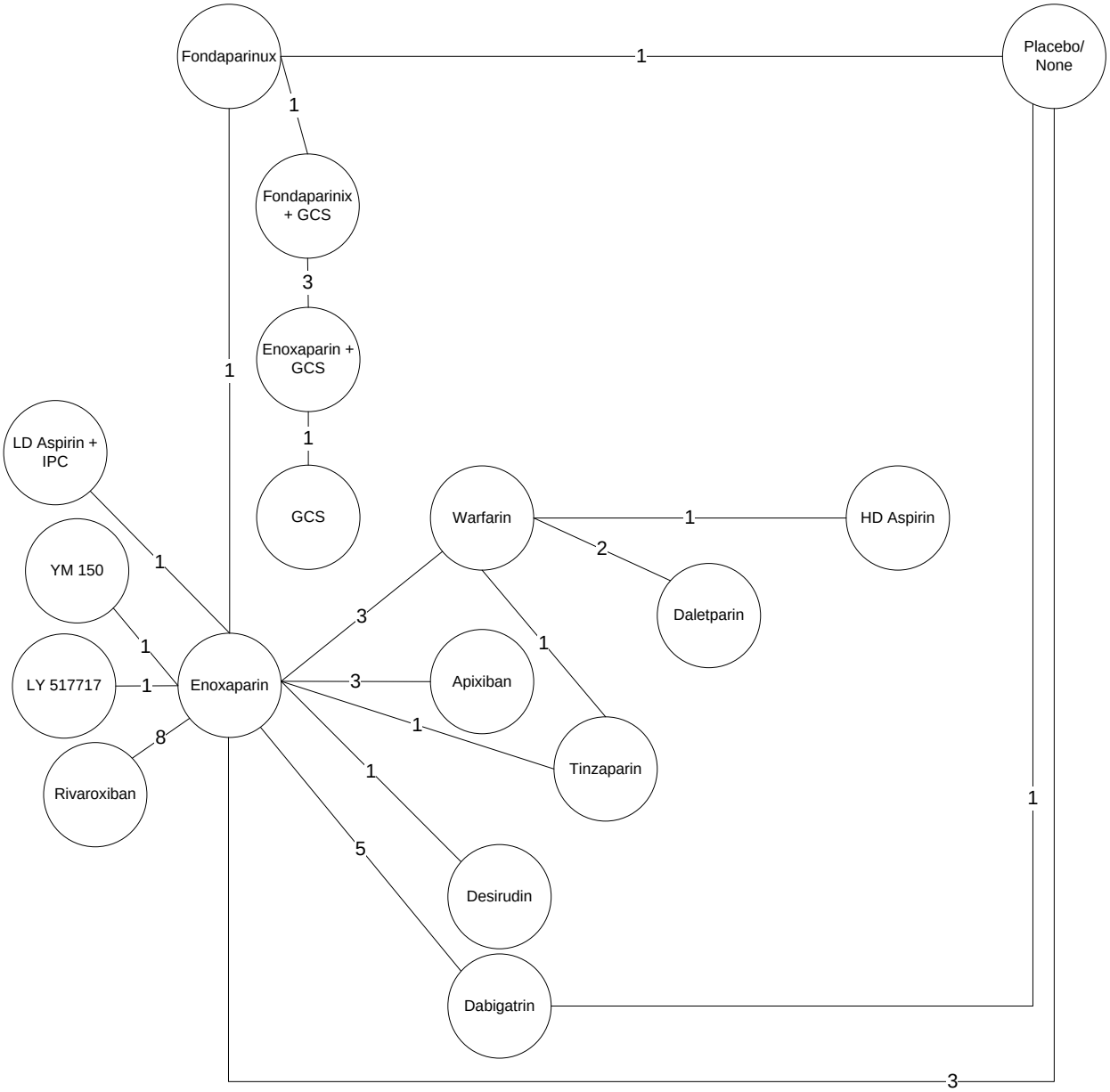
on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 22. Final Pulmonary Embolism Model (with continuity correction, without heparin, or multi-arm trials, Knee patients only



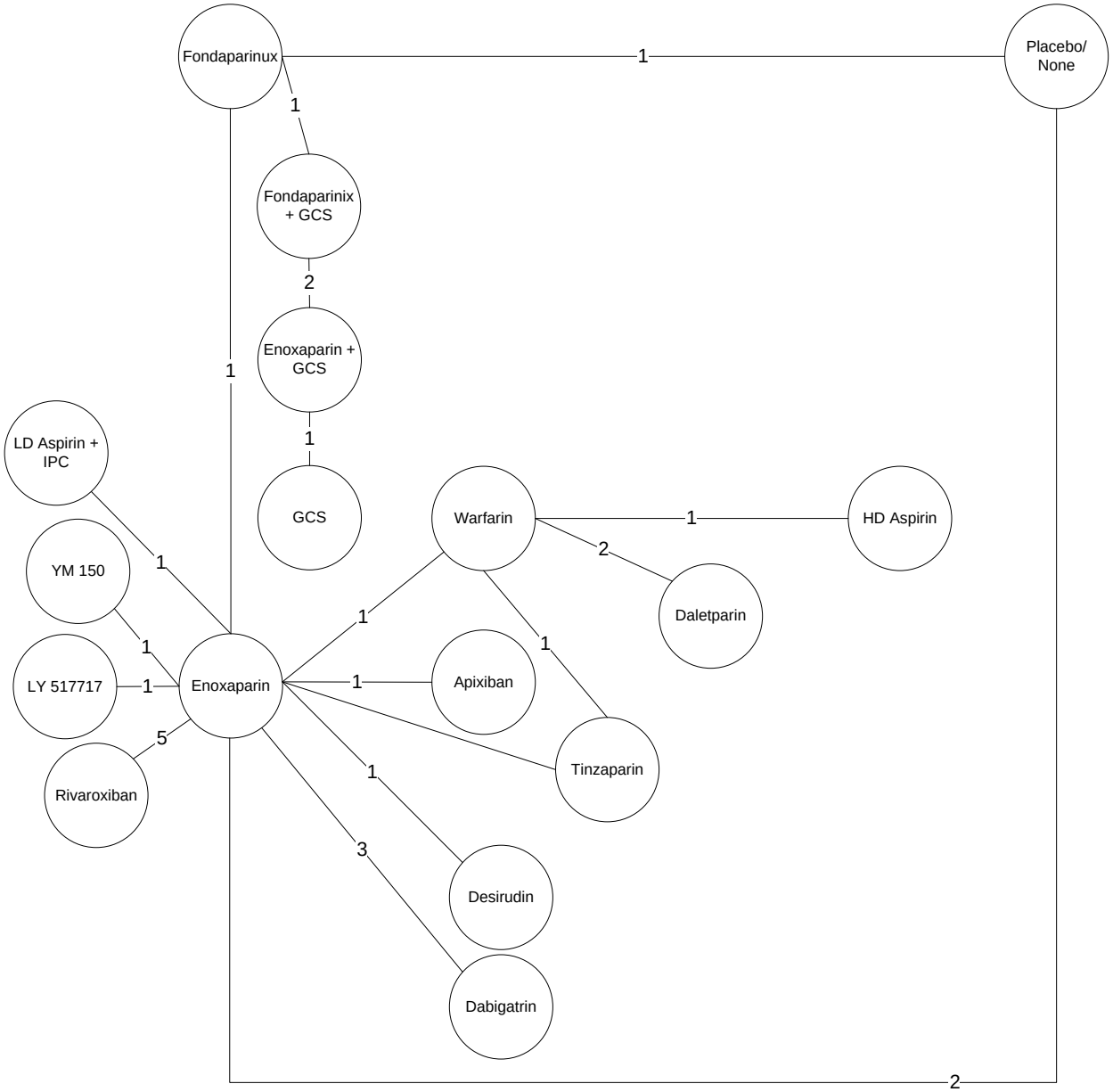
The model depicted in the figure is a model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 23. Final Major Bleeding Model (with continuity correction, without heparin or multi-arm trials)



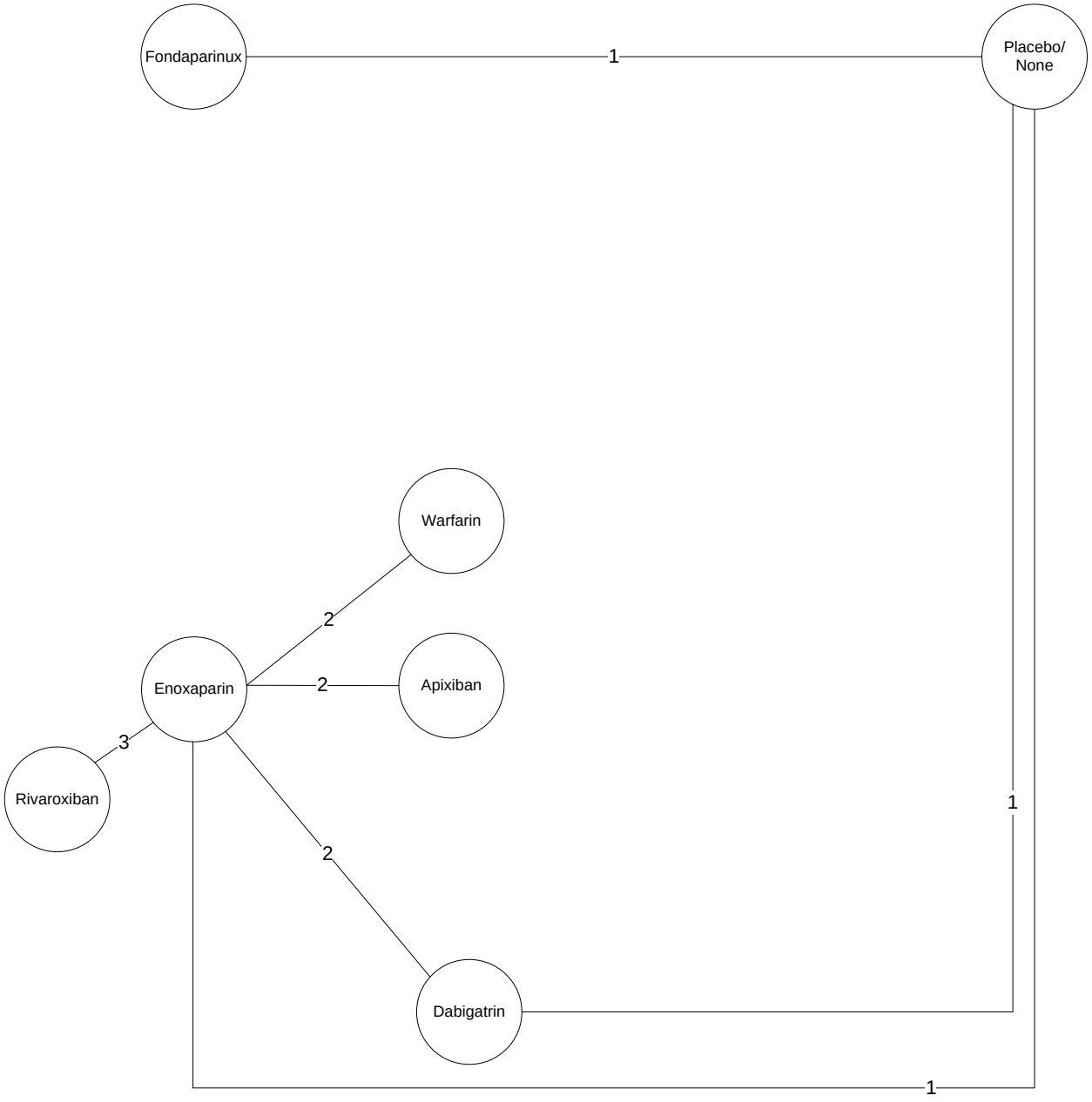
The model depicted in the figure is the final model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip arthroplasty and those who received a total knee arthroplasty. It does not include trials of heparin and trials with > 2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 24. Final Major Bleeding Model (with continuity correction, without heparin, or multi-arm trials, Hip patients only



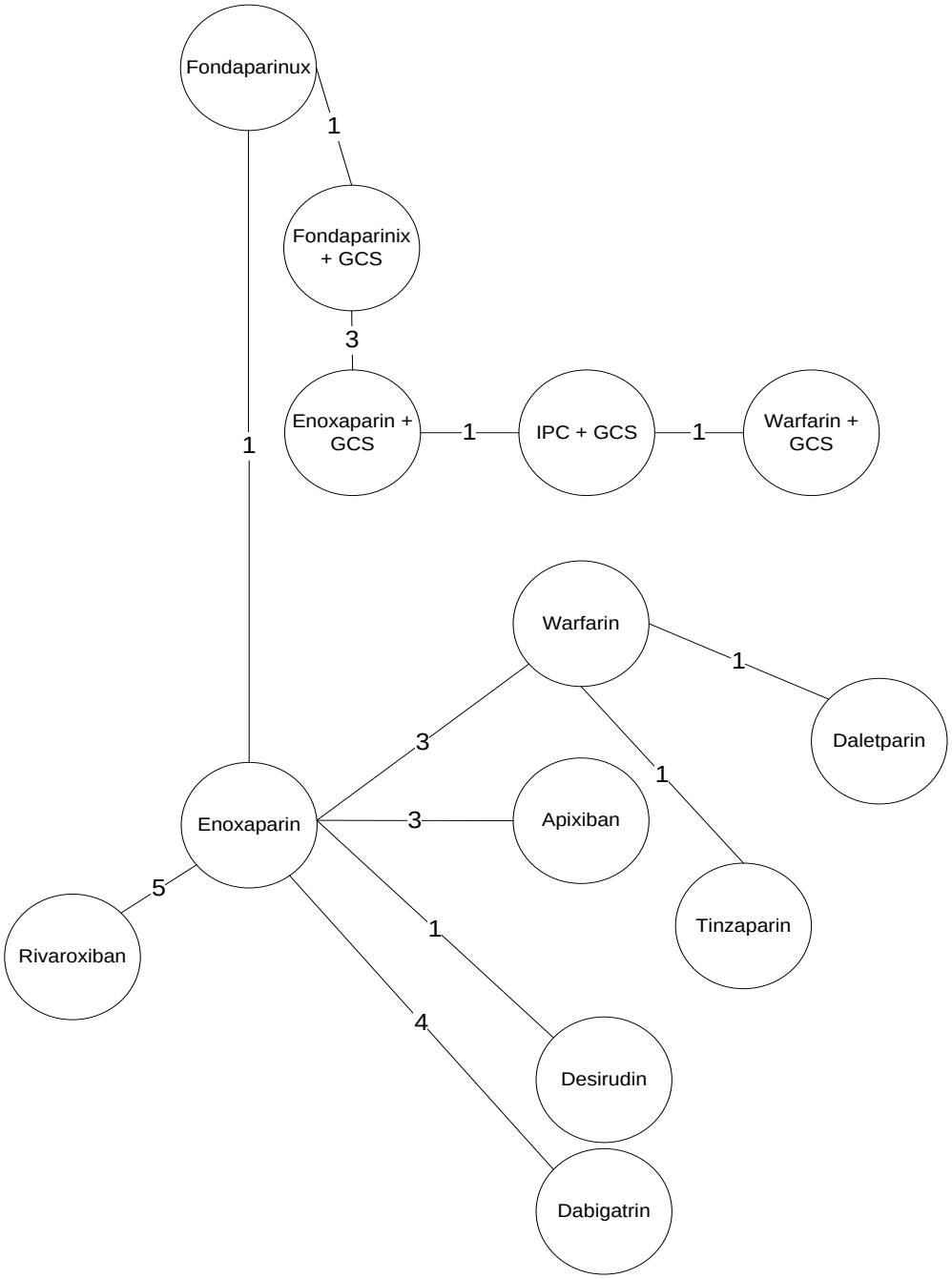
The model depicted in the figure is a model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 25. Final Major Bleeding Model (with continuity correction, without heparin, or multi-arm trials, Knee patients only



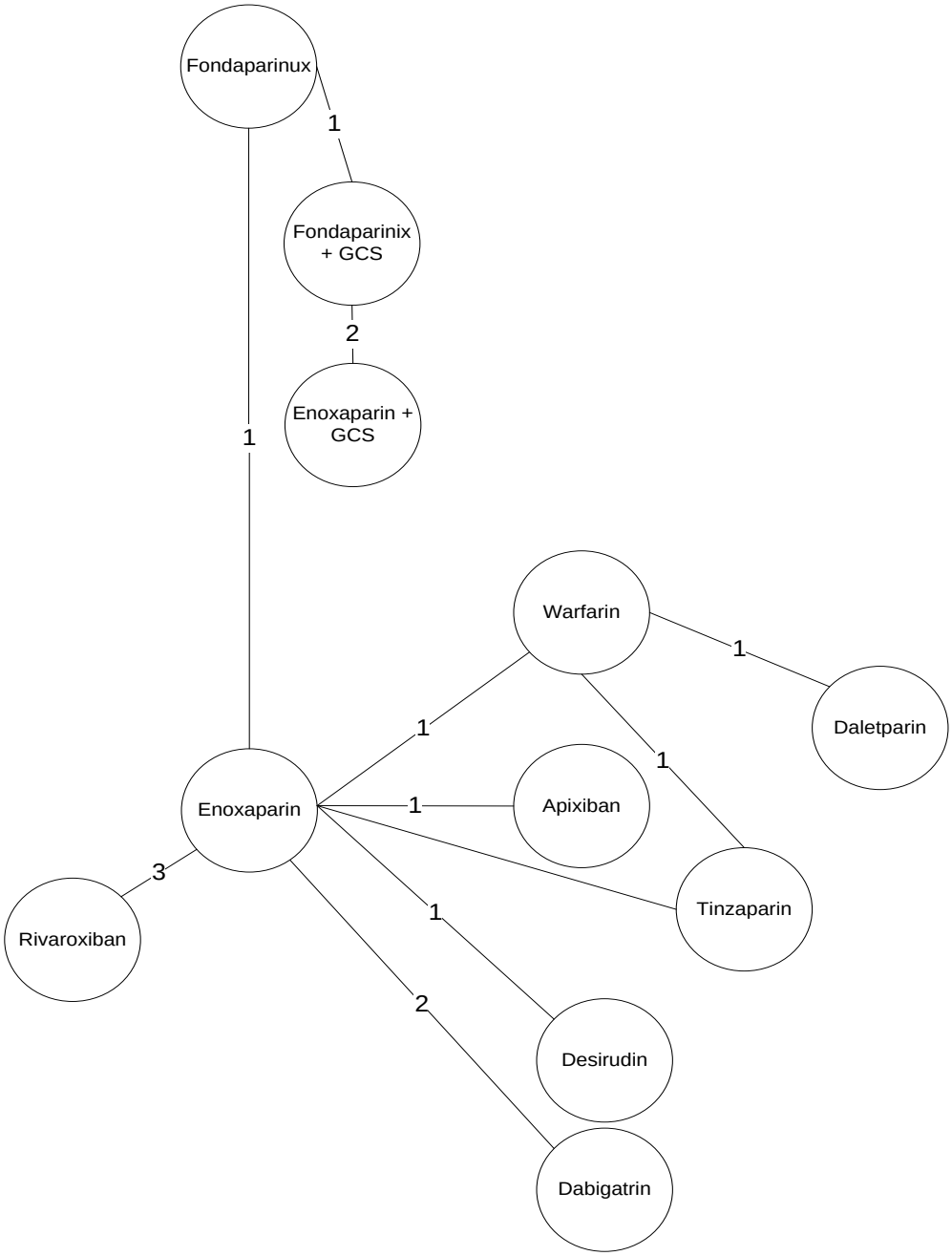
The model depicted in the figure is a model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 26. Final All Cause Mortality Model (with continuity correction, without heparin or multi-arm trials)



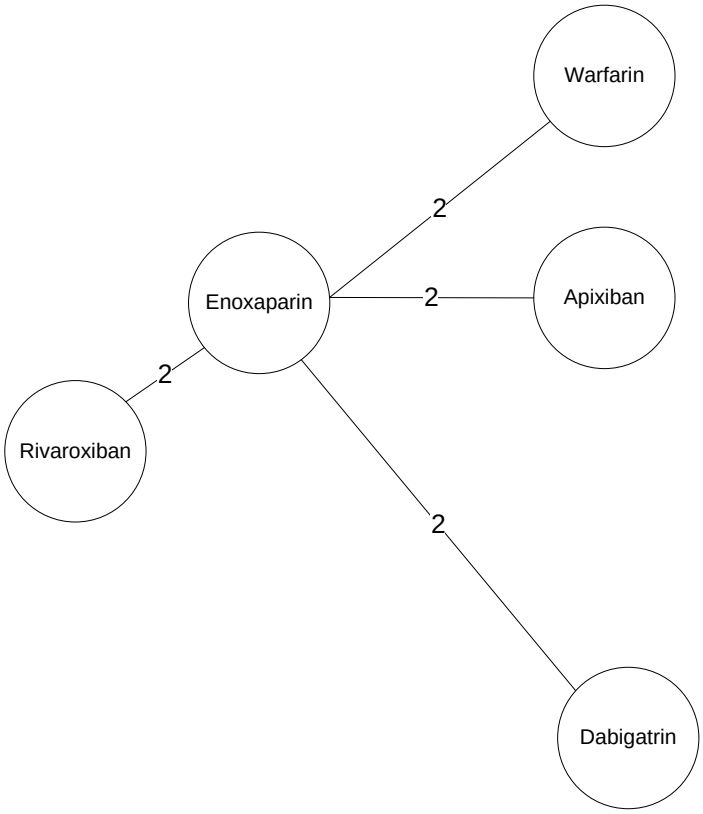
The model depicted in the figure is the final model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip arthroplasty and those who received a total knee arthroplasty. It does not include trials of heparin and trials with > 2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 27. Final All Cause Mortality Model (with continuity correction, without heparin, or multi-arm trials, Hip patients only



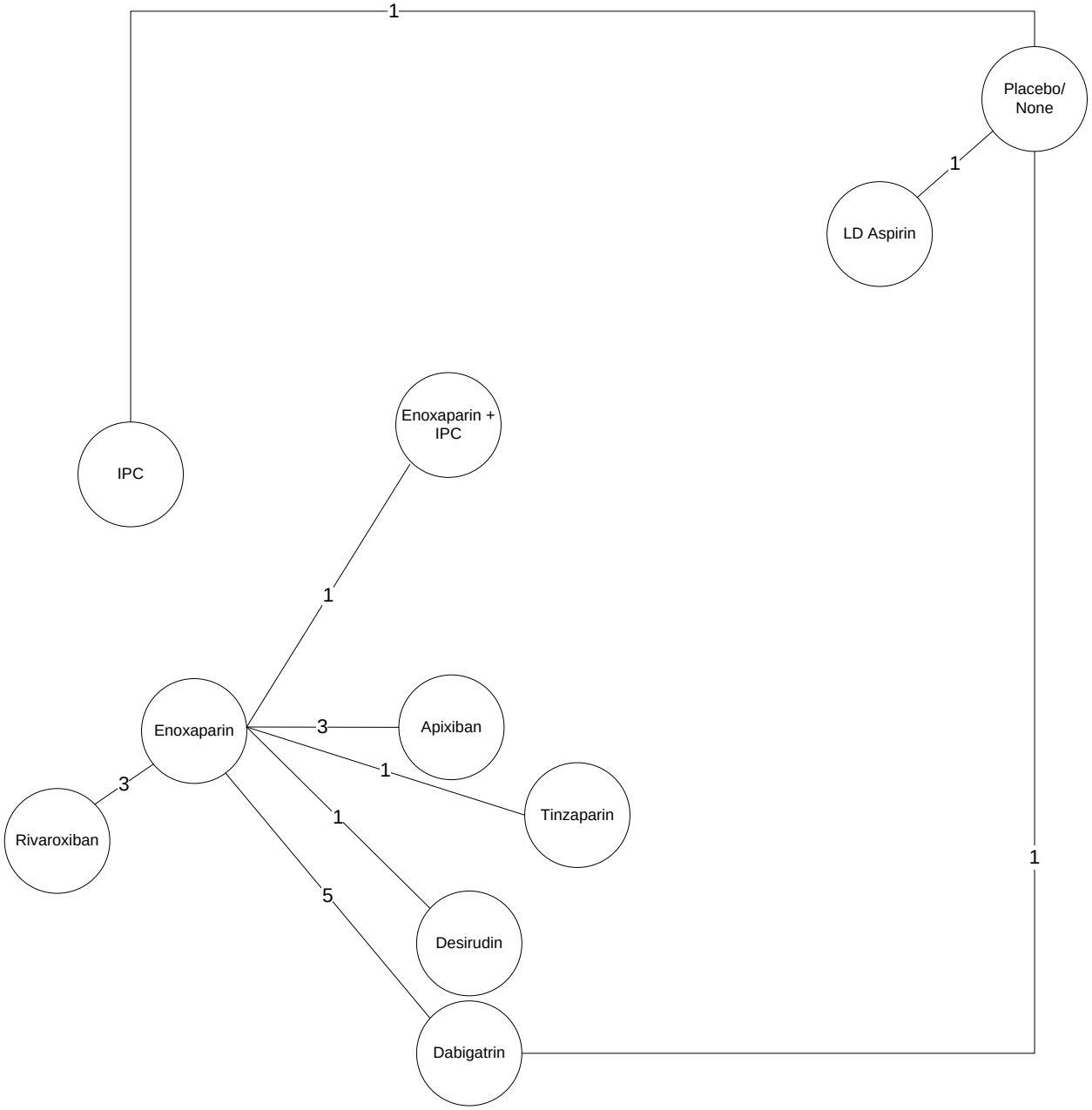
The model depicted in the figure is a model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 28. Final All Cause Mortality Model (with continuity correction, without heparin, or multi-arm trials, Knee patients only



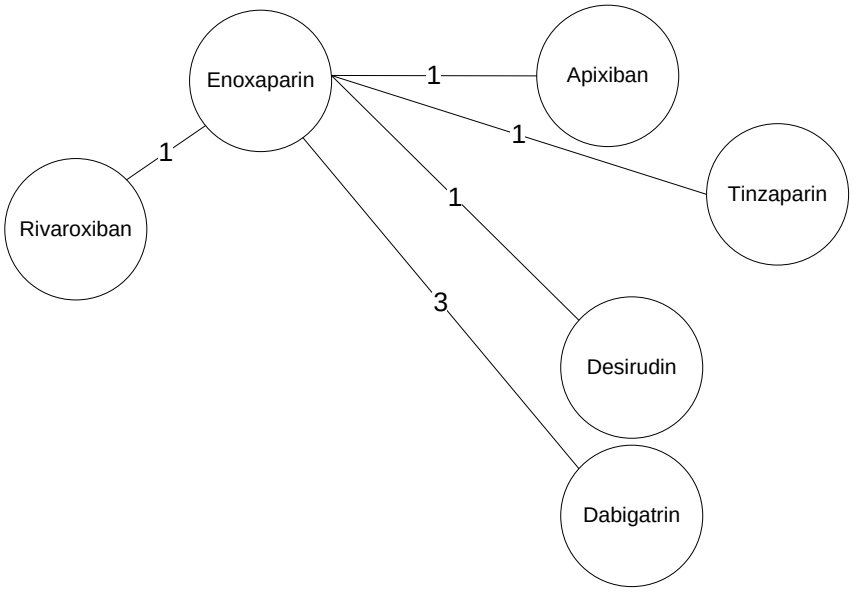
The model depicted in the figure is a model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 29. Final Symptomatic DVT Model (with continuity correction, without heparin, or multi-arm trials.



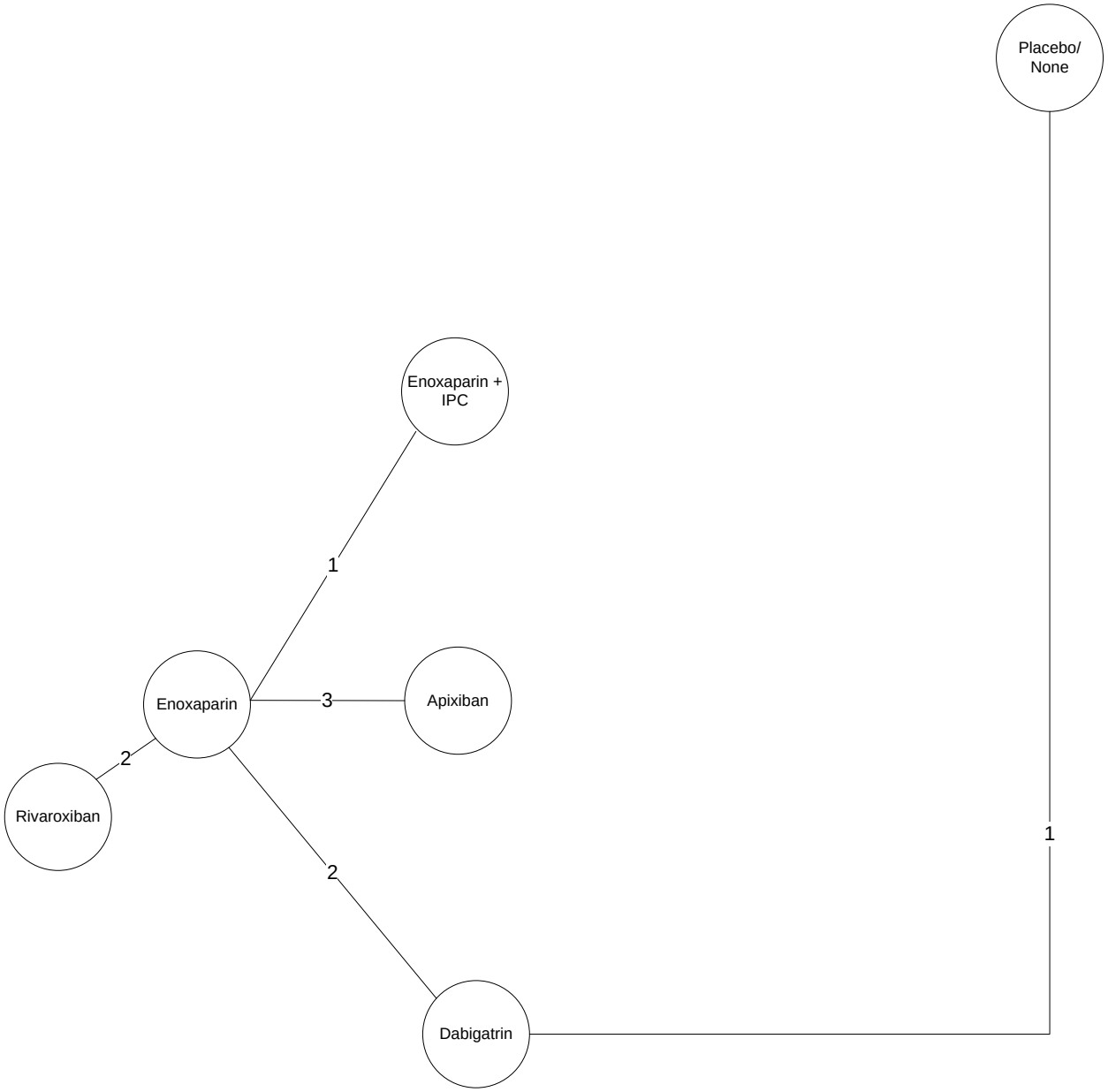
The model depicted in the figure is the final model for symptomatic DVT that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip arthroplasty and those who received a total knee arthroplasty. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles. None of the included studies required a continuity correction, so this is the same model as for the model without continuity corrected studies.

Figure 30. Final Symptomatic DVT Model (with continuity correction, without heparin, or multi-arm trials, Hip patients only



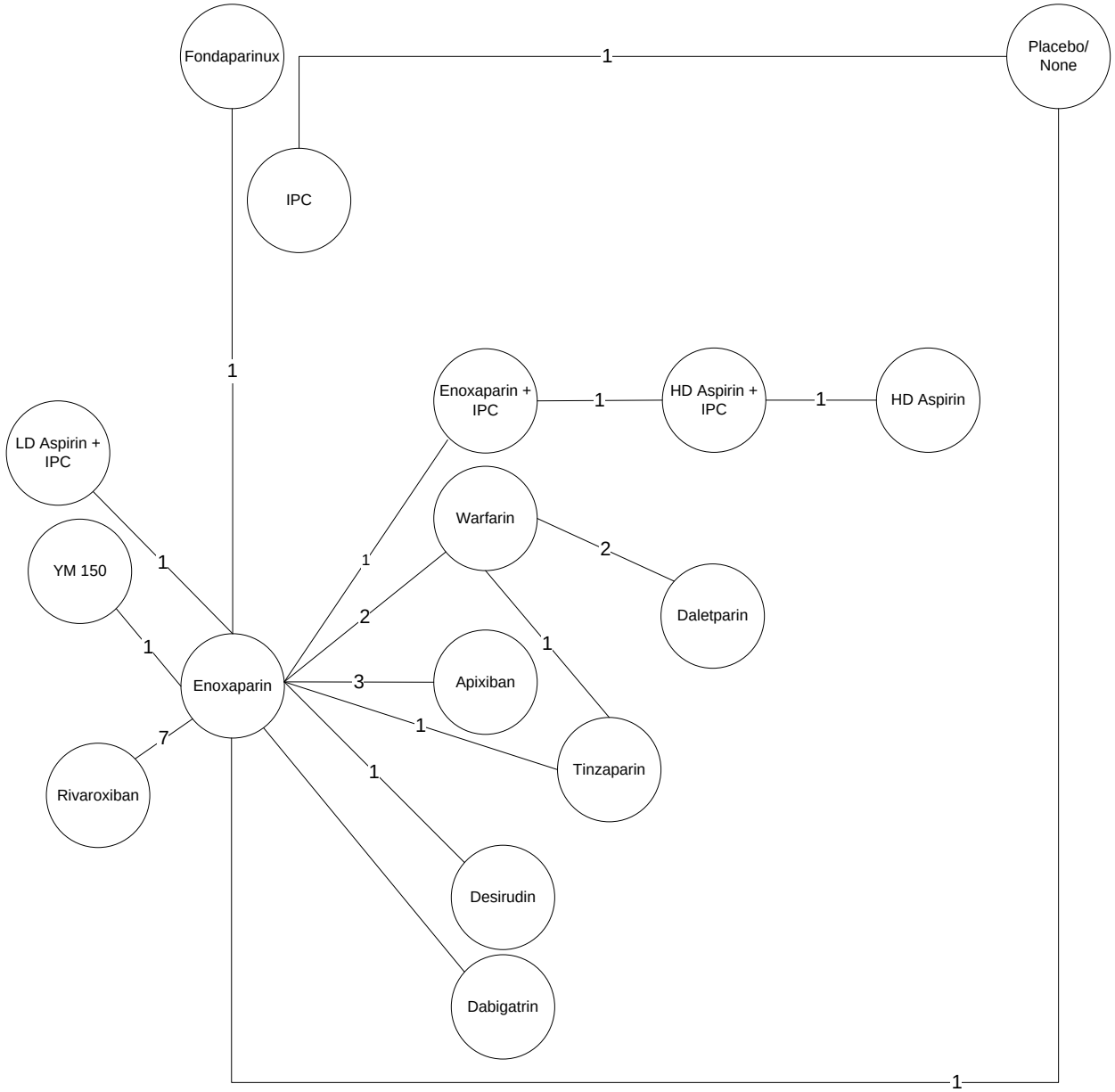
The model depicted in the figure is a model for symptomatic DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 31. Final Symptomatic DVT Model (with continuity correction, without heparin, or multi-arm trials, Knee patients only



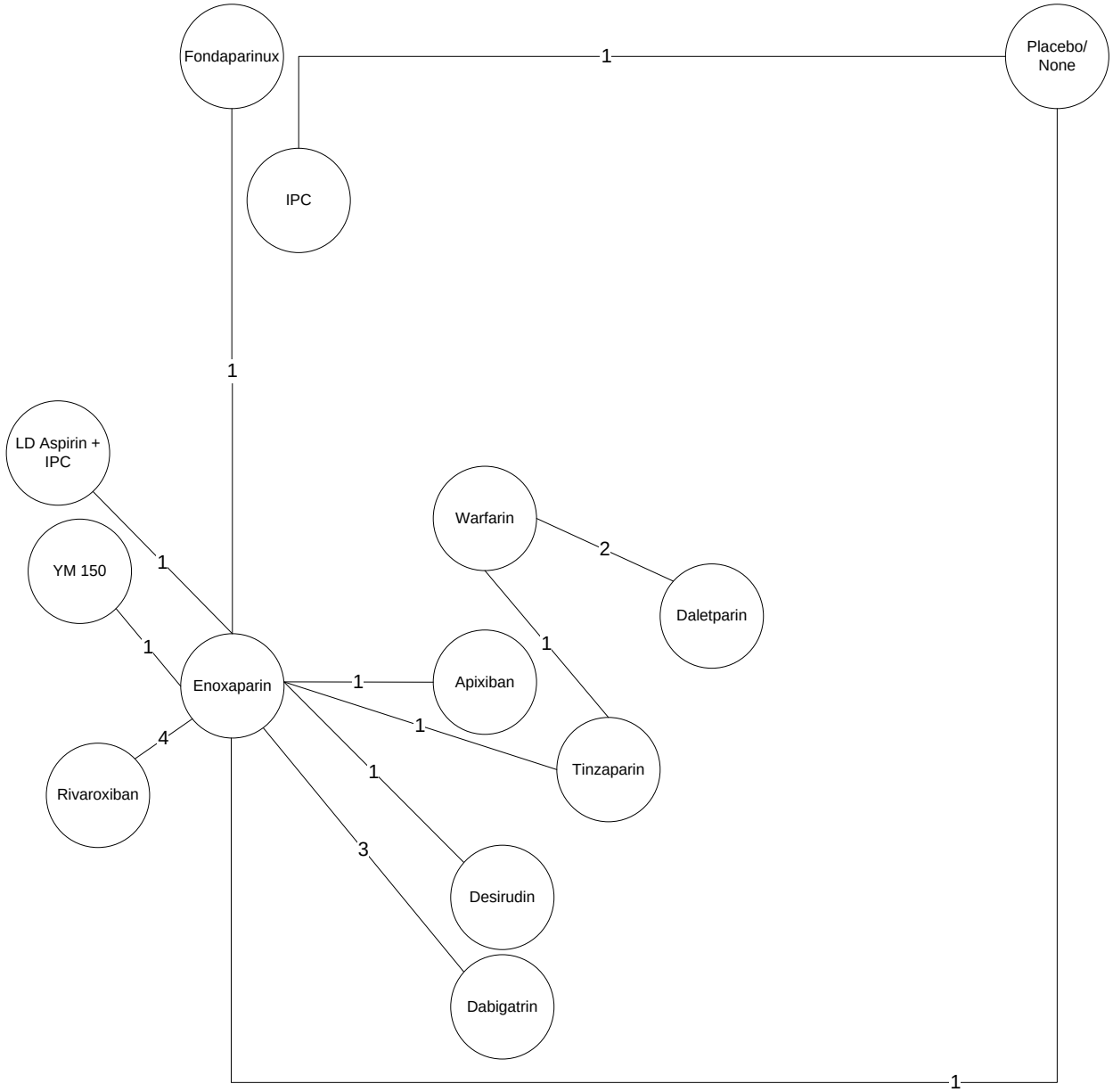
The model depicted in the figure is a model for symptomatic DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 32. Final DVT Model (with continuity correction, without heparin or multi-arm trials)



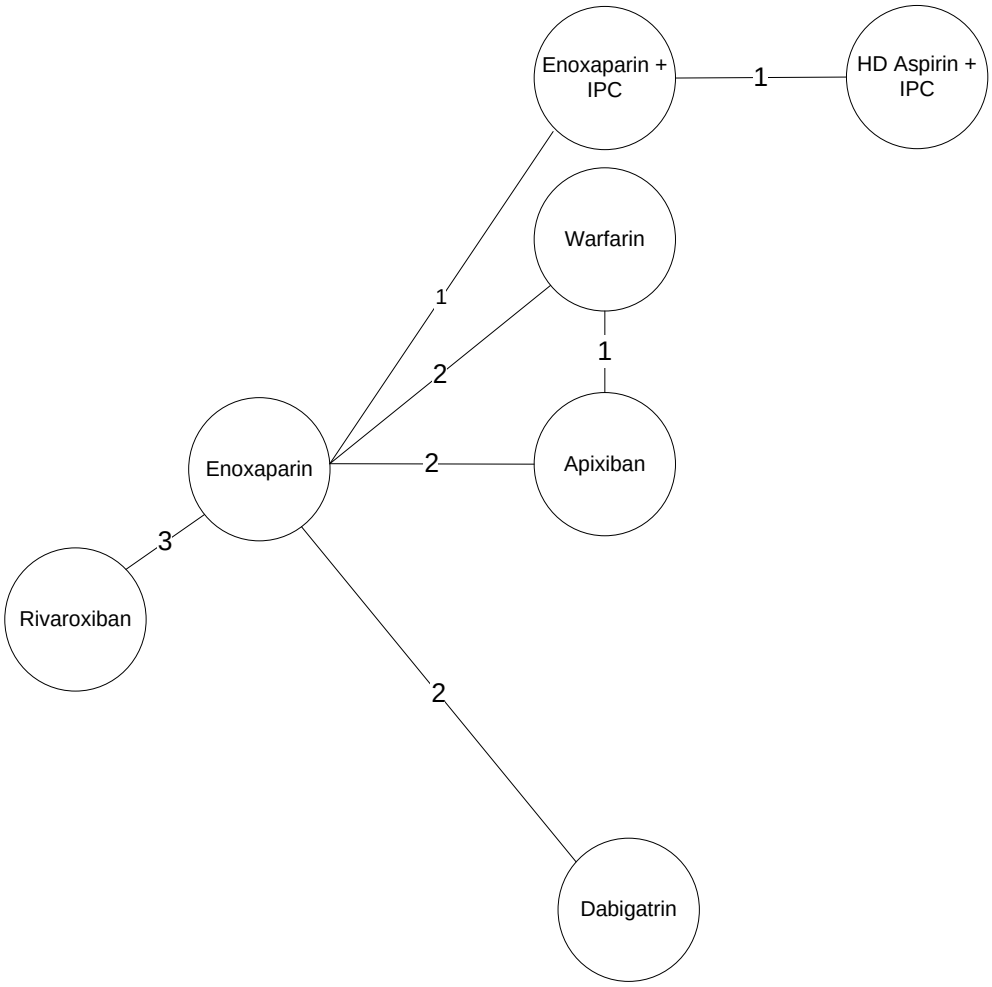
The model depicted in the figure is the final model for DVT that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip arthroplasty and those who received a total knee arthroplasty. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles. None of the included studies required a continuity correction, so this is the same model as for the model without continuity corrected studies.

Figure 33. Final DVT Model (with continuity correction, without heparin or multi-arm trials), Hip patients only



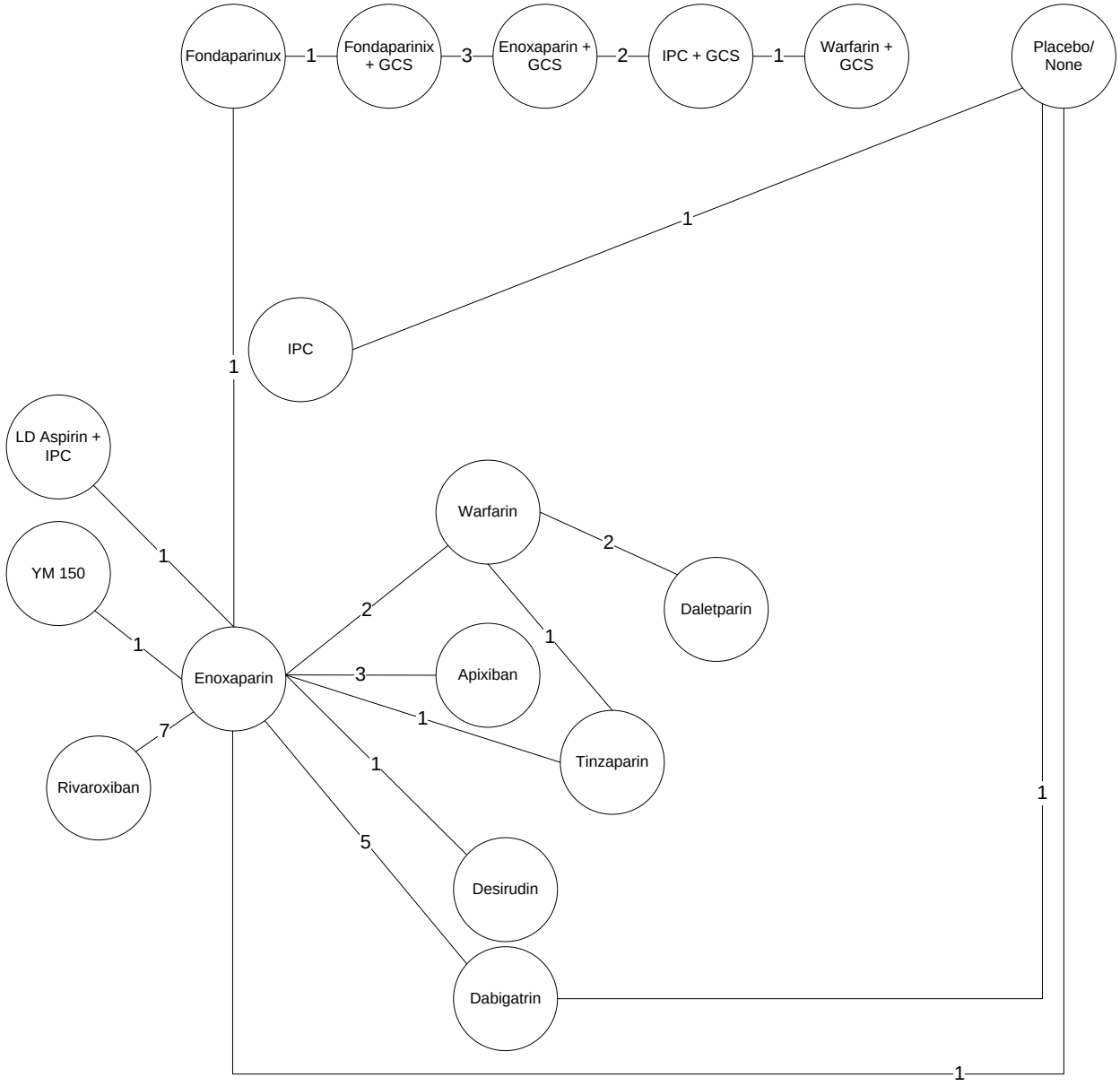
The model depicted in the figure is a model for DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 34. Final DVT Model (with continuity correction, without heparin or multi-arm trials), Knee patients only



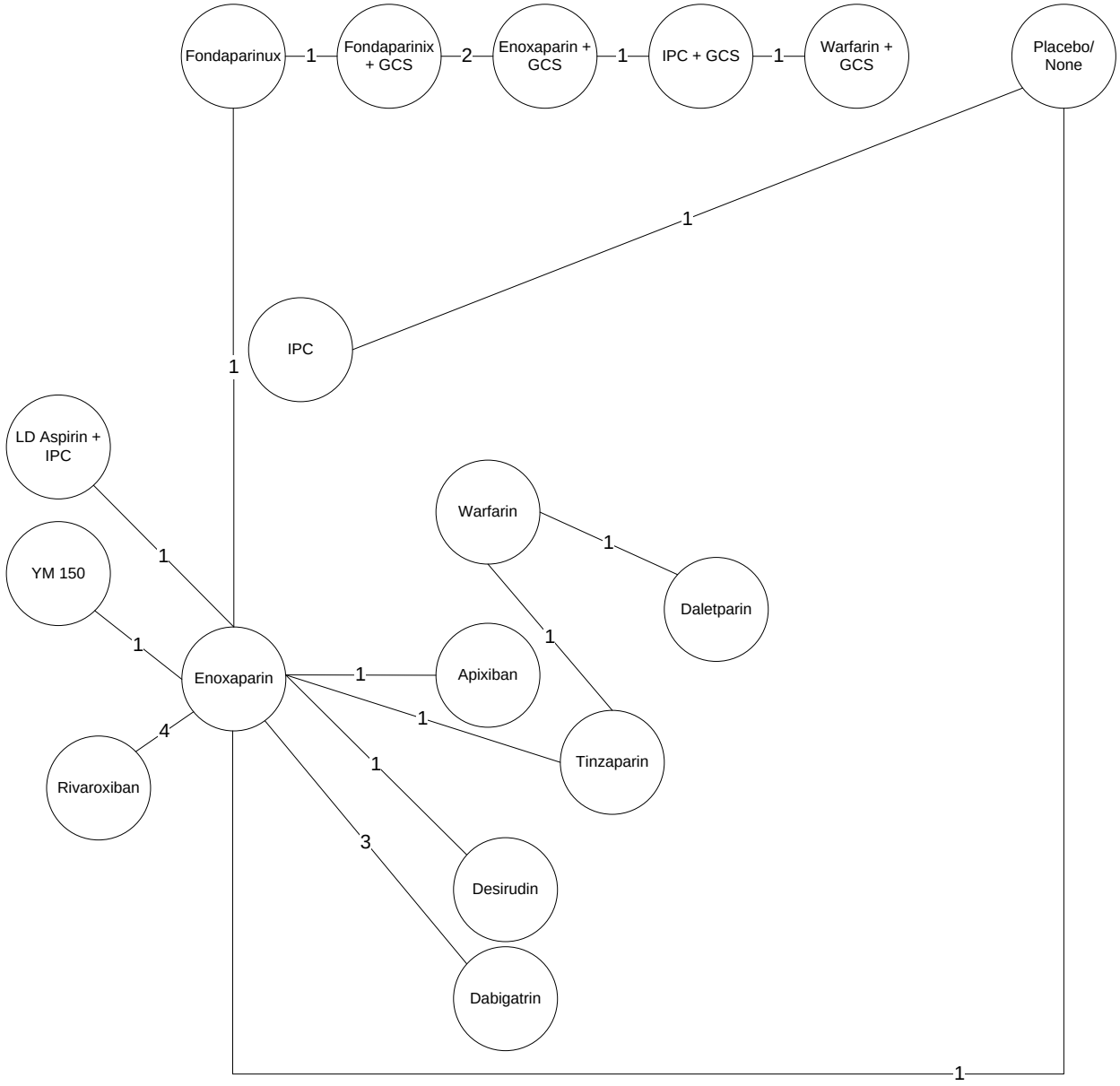
The model depicted in the figure is a model for DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. It does not include trials of heparin or trials with >2 arms. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 35. Final Proximal DVT Model (with continuity correction, without heparin or multi-arm trials)



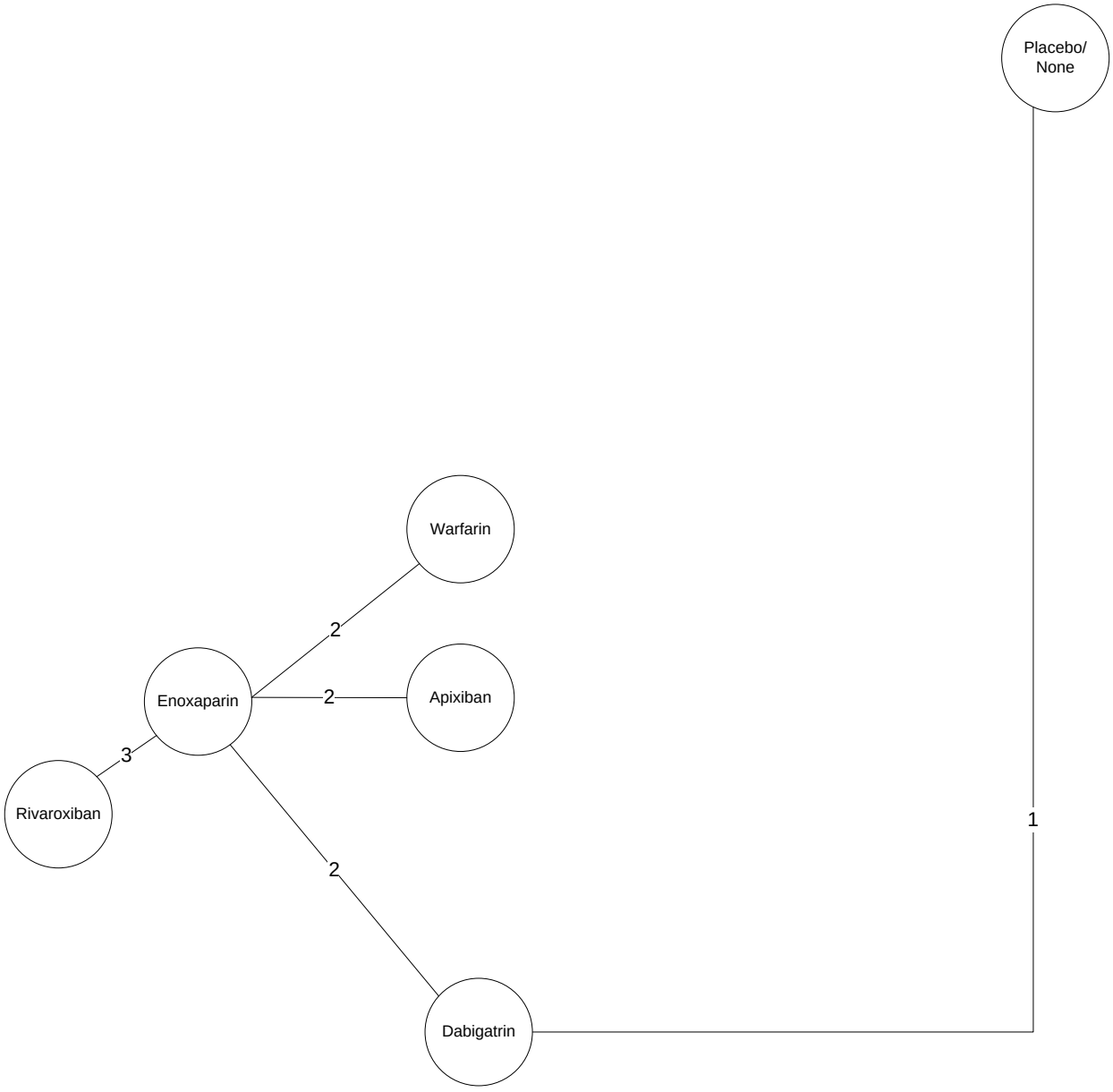
The model depicted in the figure a model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip arthroplasty and those who received a knee arthroplasty. Trials of heparin and trials with >2 arms are not included. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 36. Final Proximal DVT Model (with continuity correction, without heparin or multi-arm trials), Hip patients only



The model depicted in the figure a model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip arthroplasty. Trials of heparin and trials with >2 arms are not included. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 37. Final Proximal DVT Model (with continuity correction, without heparin or multi-arm trials), Knee patients only



The model depicted in the figure a model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee arthroplasty. Trials of heparin and trials with >2 arms are not included. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

NETWORK META-ANALYSIS RESULTS

The results of the network meta-analyses for each of the six outcomes are shown in the figures below. Here, we present our final models, which exclude trials with > 2 arms (multi-arm trials) and heparin trials. It includes patients who received a total hip arthroplasty and patients who received a total knee arthroplasty. The two multi-arm trials each had zero events in at least two study arms for major bleeding and pulmonary embolism. In this analysis, we added a continuity correction factor to studies with zero events in one arm of the trial.

In addition to the results presented in the figures below, Appendix XV presents the results of the final model for each outcome with each treatment in the model ranked relative to each other.

Appendix XV presents the results of our sensitivity analyses, first by excluding trials with zero events in one arm of a trial, making the use of the continuity correction unneccesary. Then we excluded trials of heparin and, finally, we also excluded multi-arm trials. The results of these sensitivity analyses were not significantly different than the results of our final model.

The results of our consistency checks appear in Appendix XV. Our final models were consistent.

Goodness-of-fit statistics are also presented in Appendix XV. These results suggest that our model fits the available data.

Results are presented in terms of the odds ratio of each treatment as compared to no treatment. However, for all-cause mortality, results are presented as compared to enoxaparin because there are no trials compared to no treatment for this outcome. In Appendix XV, results are presented as compared to enoxaparin for all models; in addition, results are presented as compared to no treatment for the models using the continuity correction when the data allow.

PULMONARY EMBOLISM

Figure 38. Pumonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

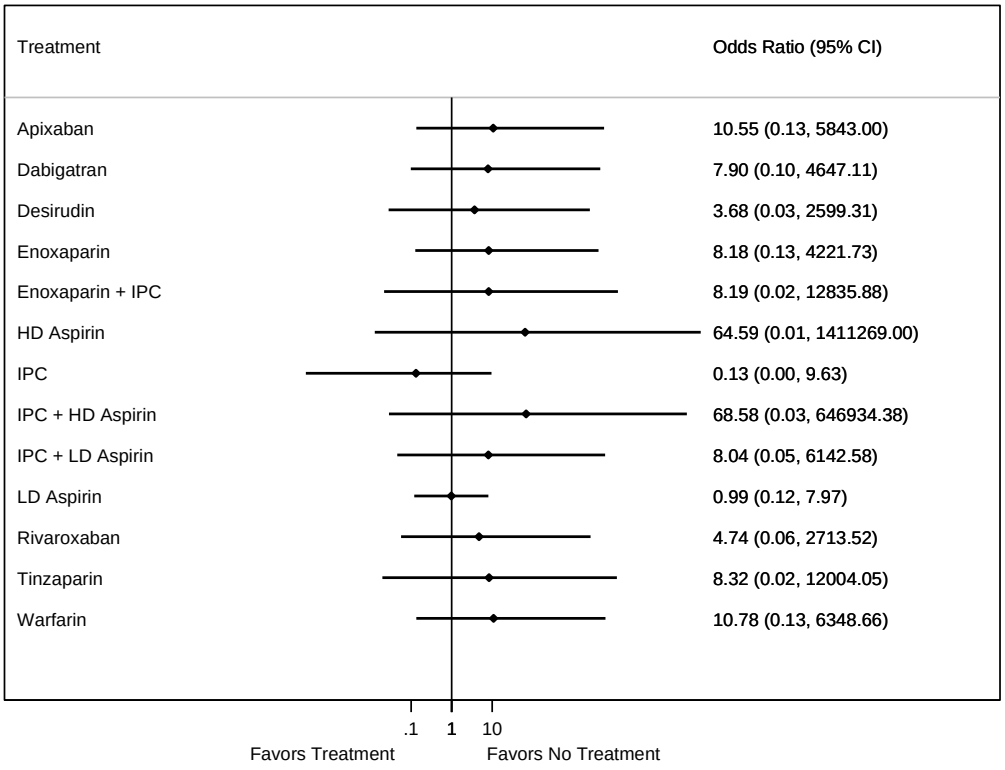


Figure 39. Pumonary Embolism among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

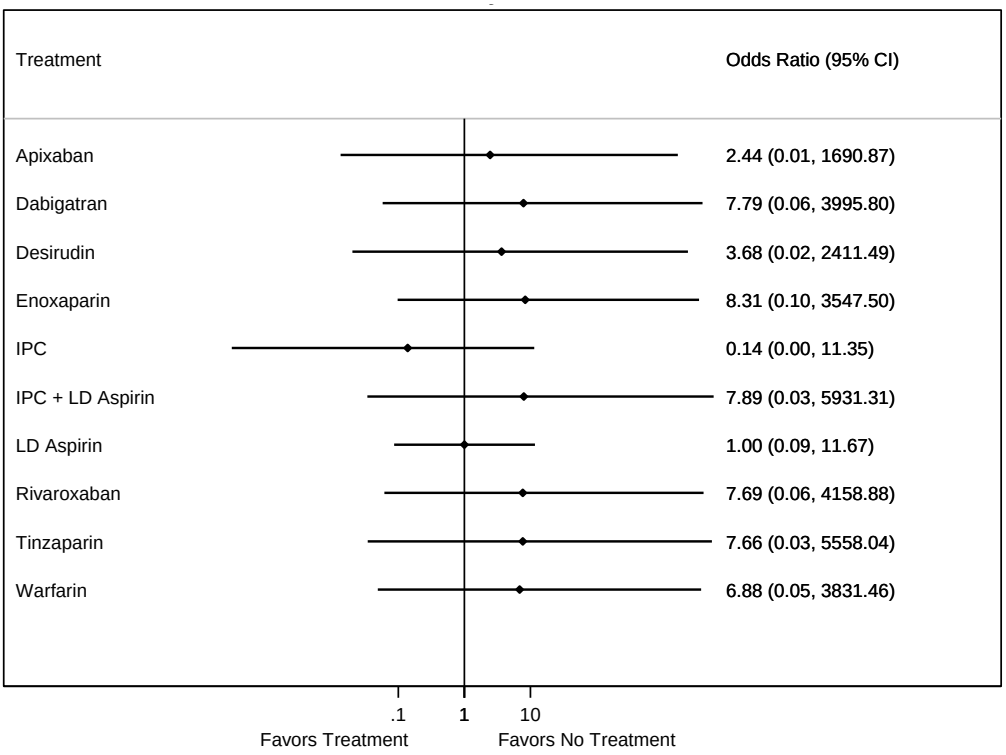


Figure 40. Pumonary Embolism among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

No studies in the model with no treatment as a comparator

MAJOR BLEEDING

Figure 41. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

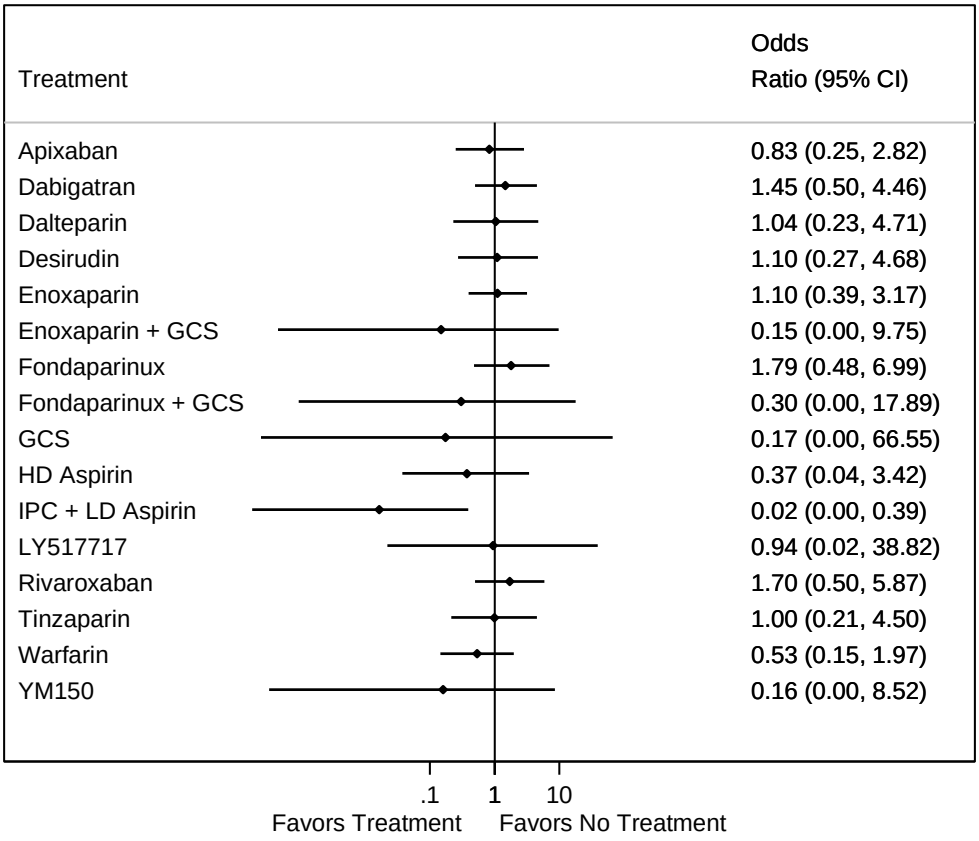


Figure 42. Major Bleeding among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

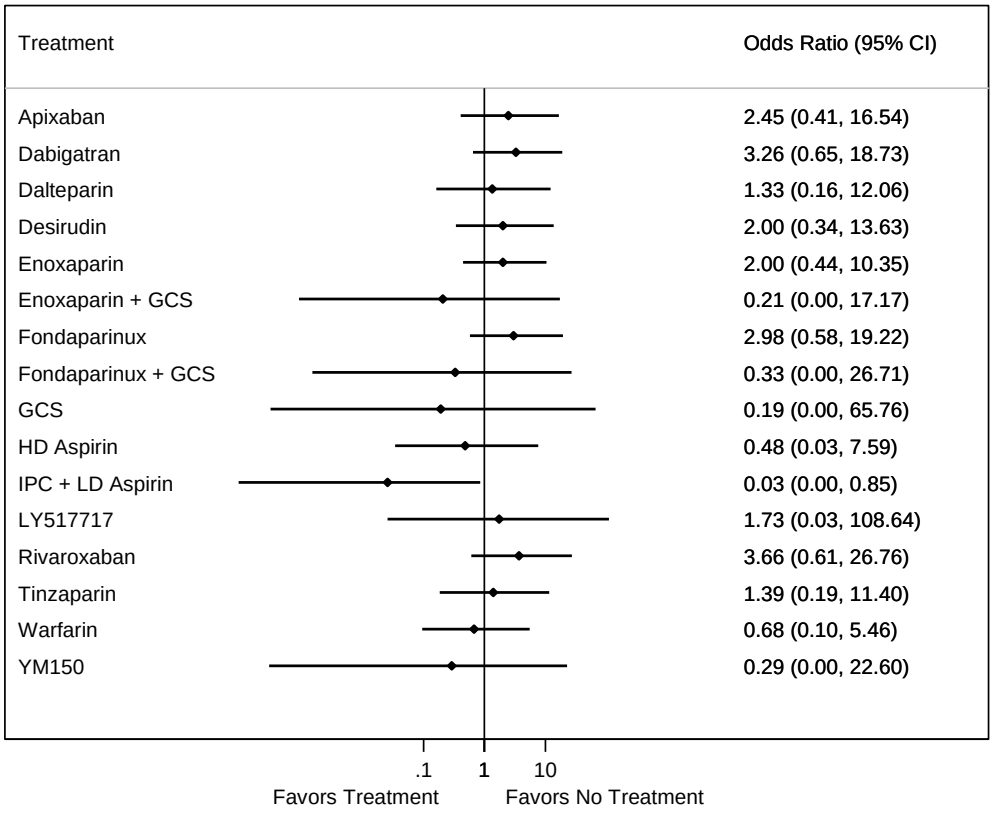
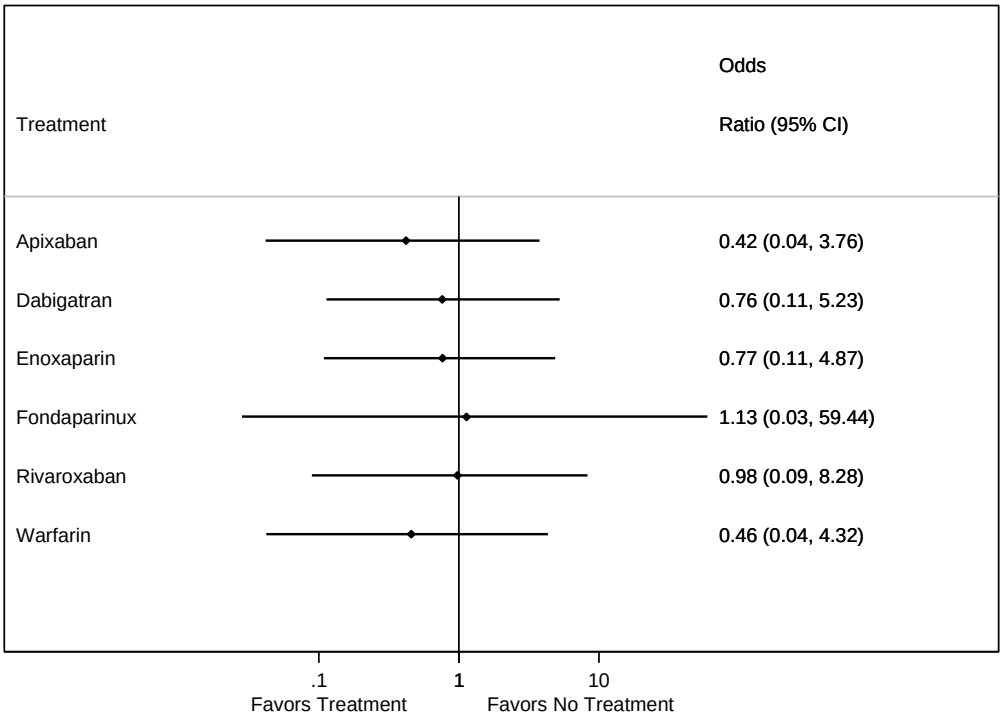


Figure 43. Major Bleeding among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)



ALL CAUSE MORTALITY

Note: For this outcome, results are only presented compared to enoxaparin because there are no trials with a no treatment arm.

Figure 44. All Cause Mortality among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

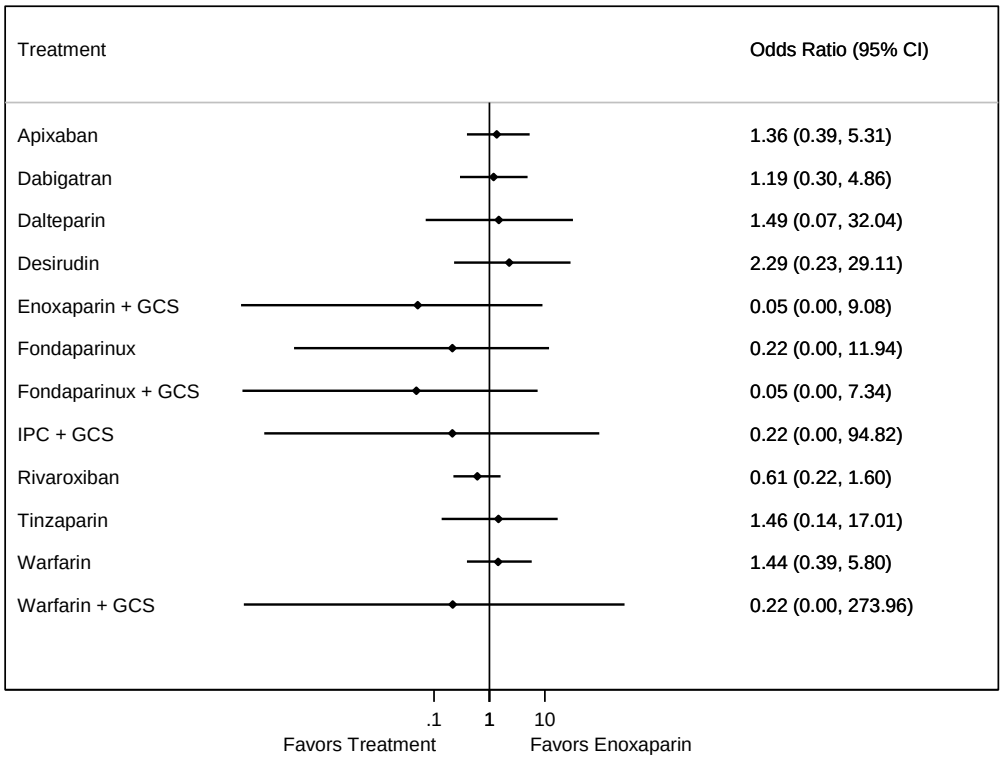


Figure 45. All Cause Mortality among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

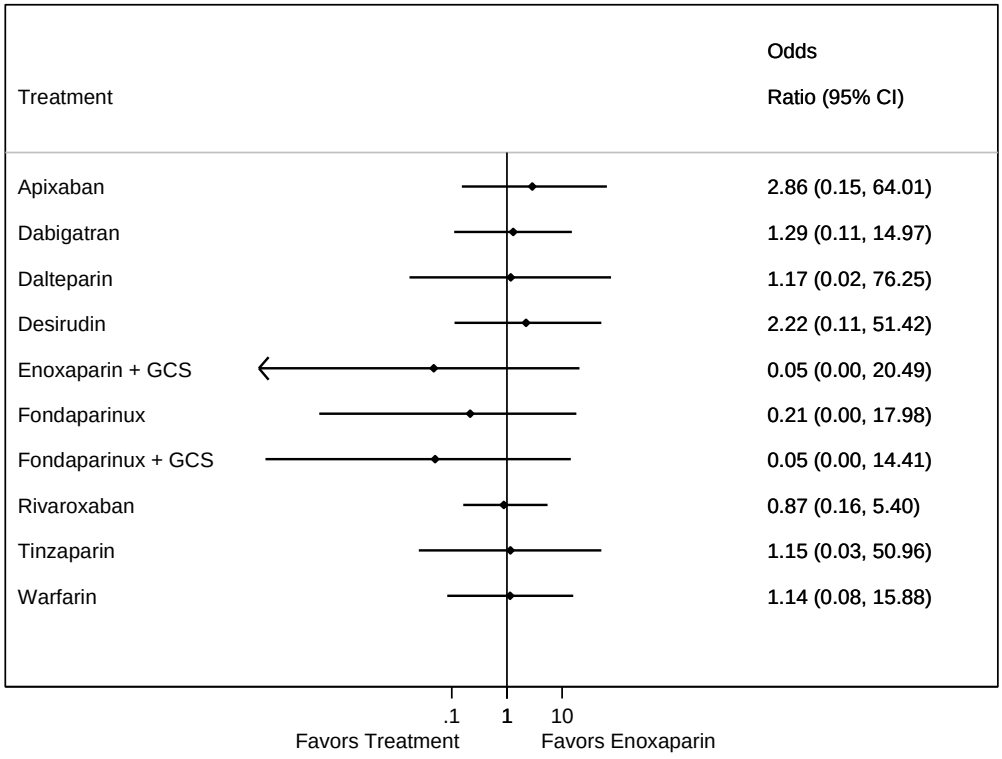
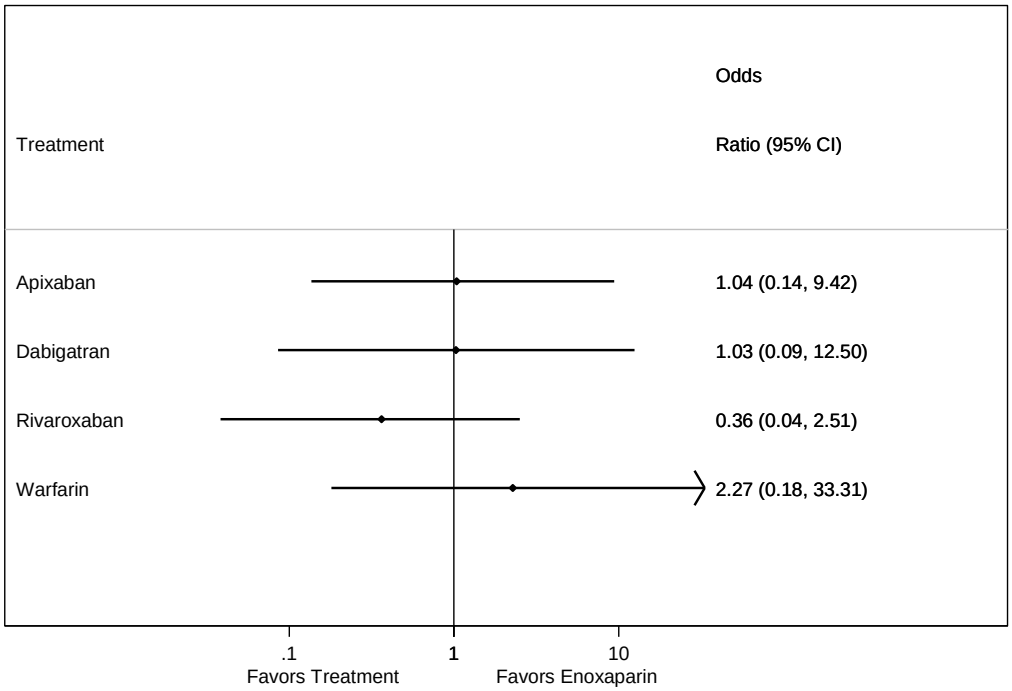


Figure 46. All Cause Mortality among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



SYMPTOMATIC DEEP VEIN THROMBOSIS

Figure 47. Symptomatic DVT among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

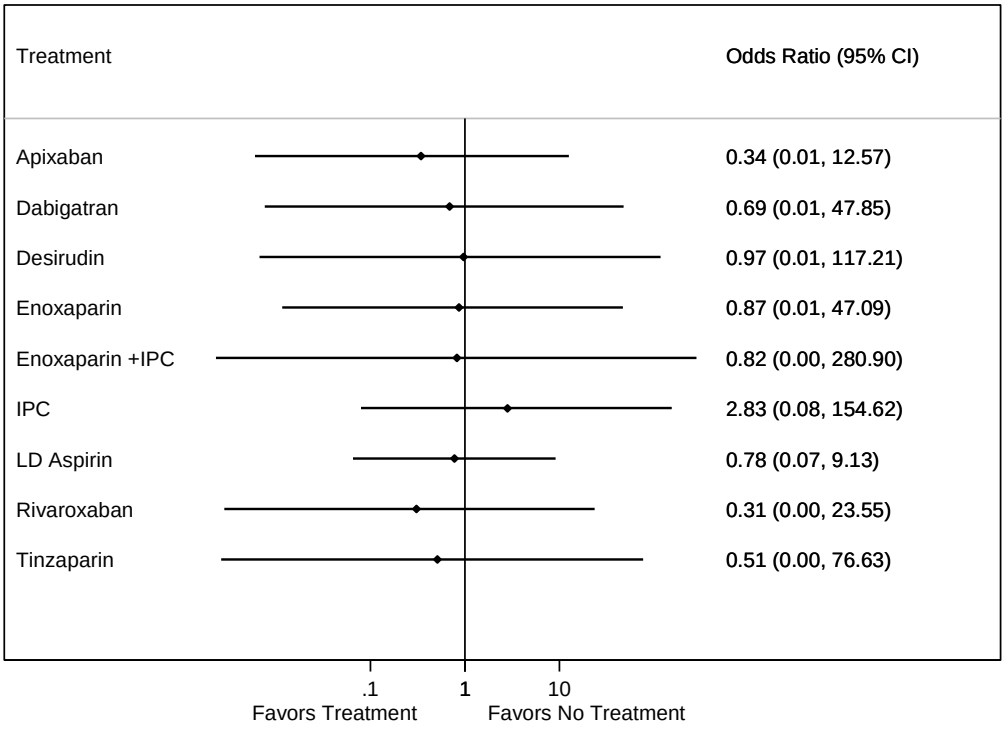
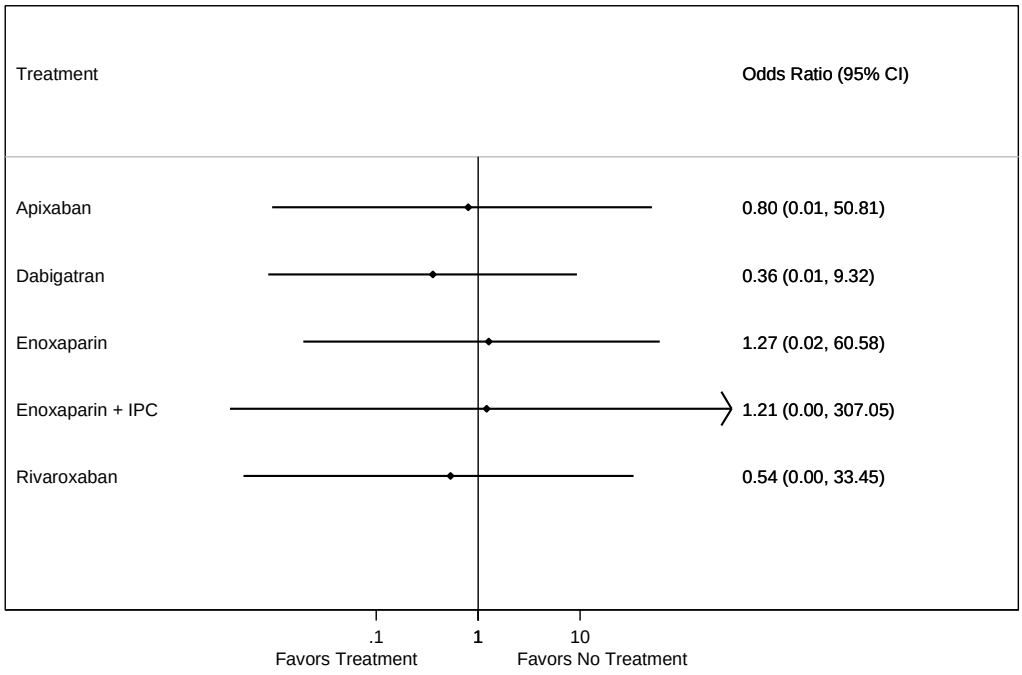


Figure 48. Symptomatic DVT among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

No studies in the model with no treatment as a comparator

Figure 49. Symptomatic DVT among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)



DEEP VEIN THROMBOSIS

Figure 50. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

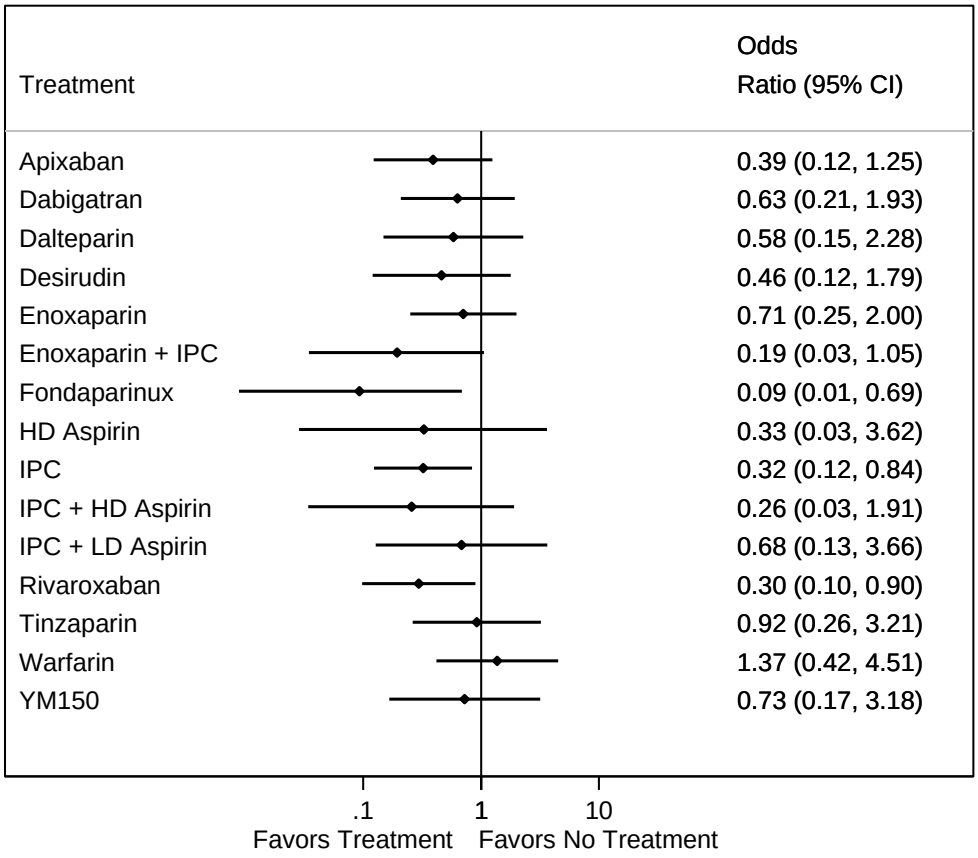


Figure 51. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

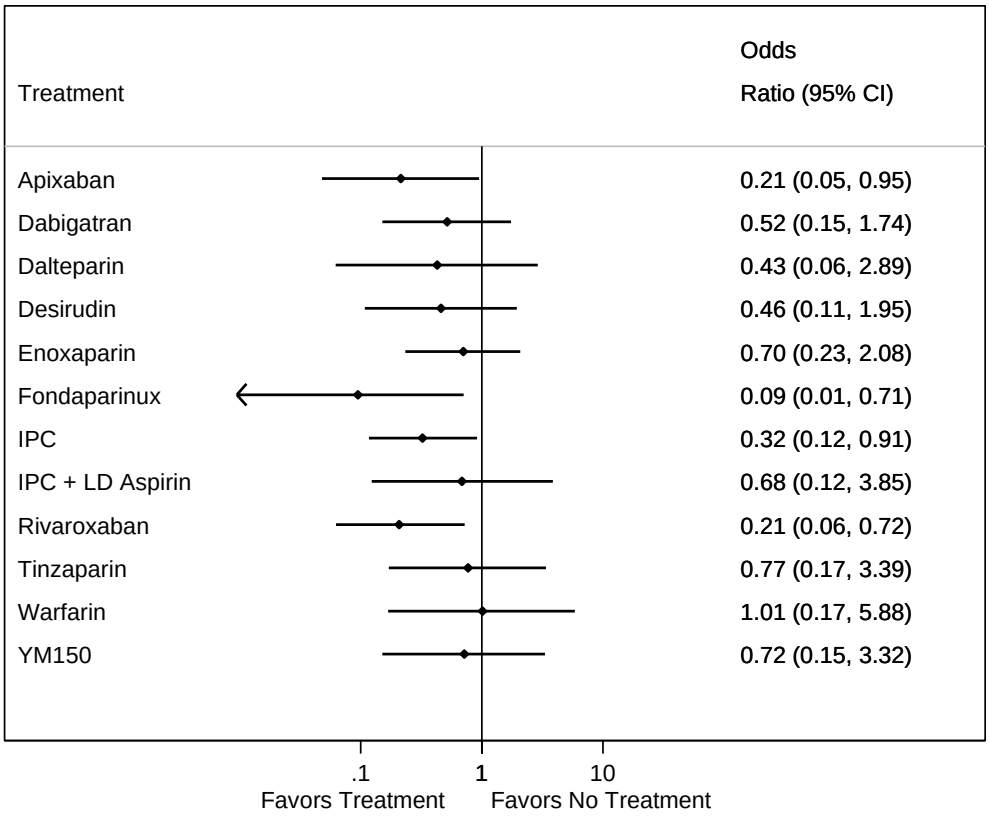


Figure 52. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

No studies in the model with no treatment as a comparator

PROXIMAL DEEP VEIN THROMBOSIS

Figure 53. Proximal Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

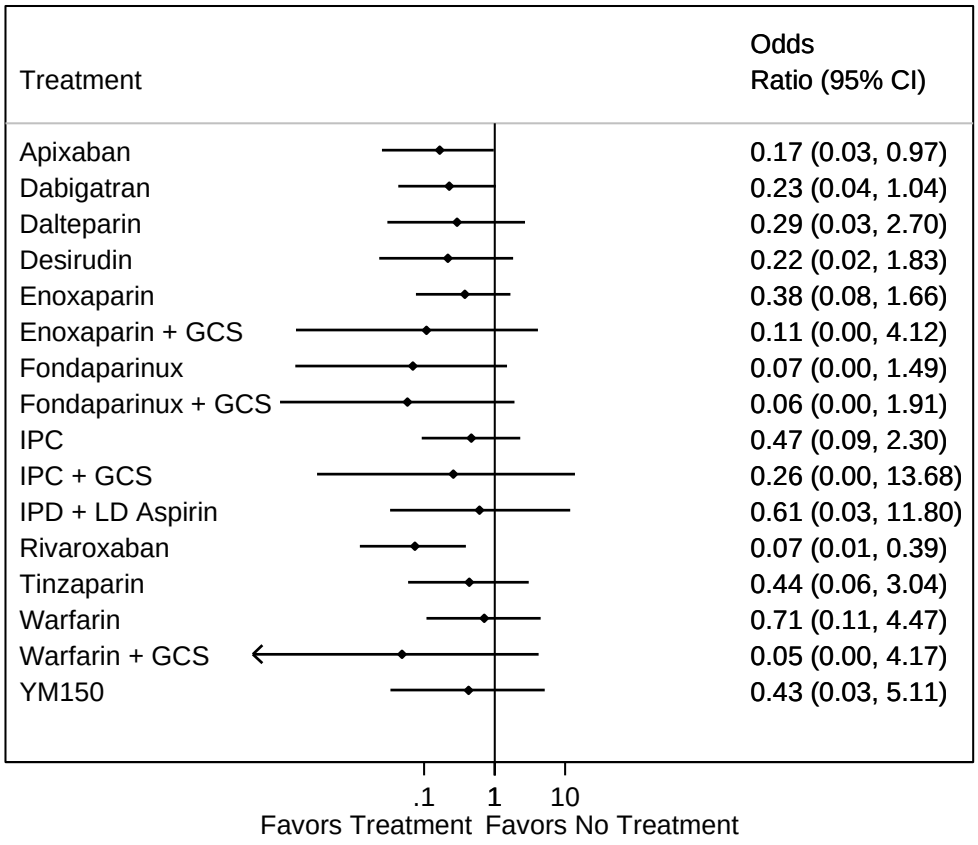


Figure 54. Proximal Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)

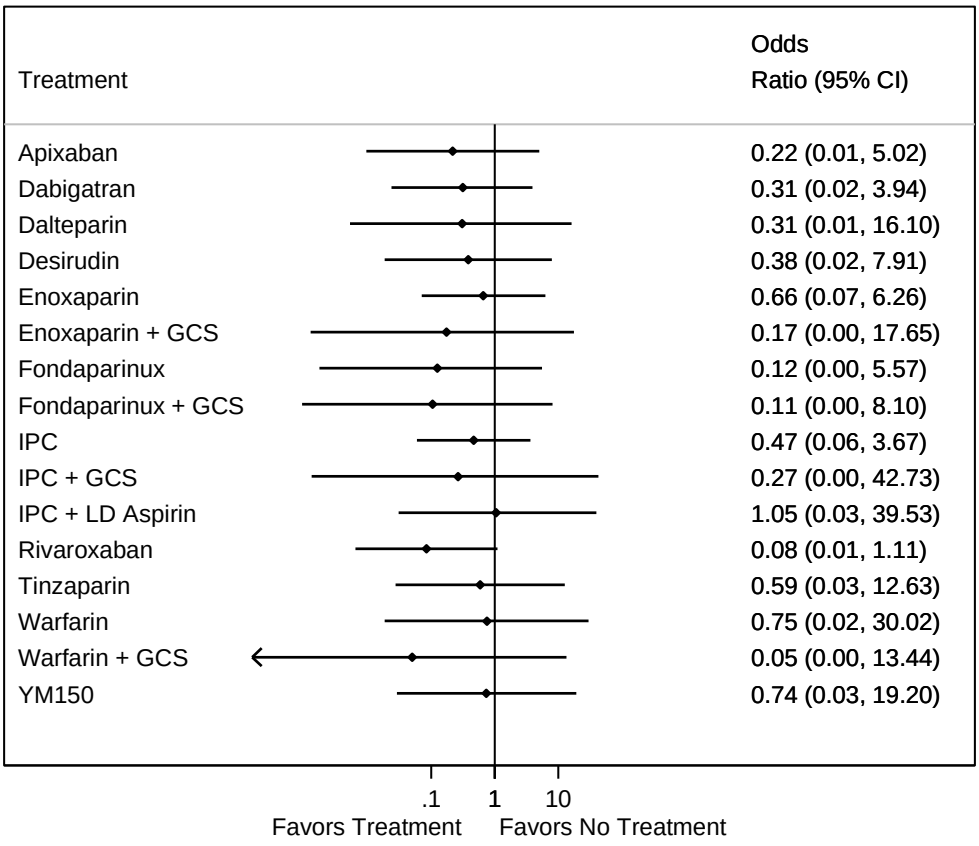
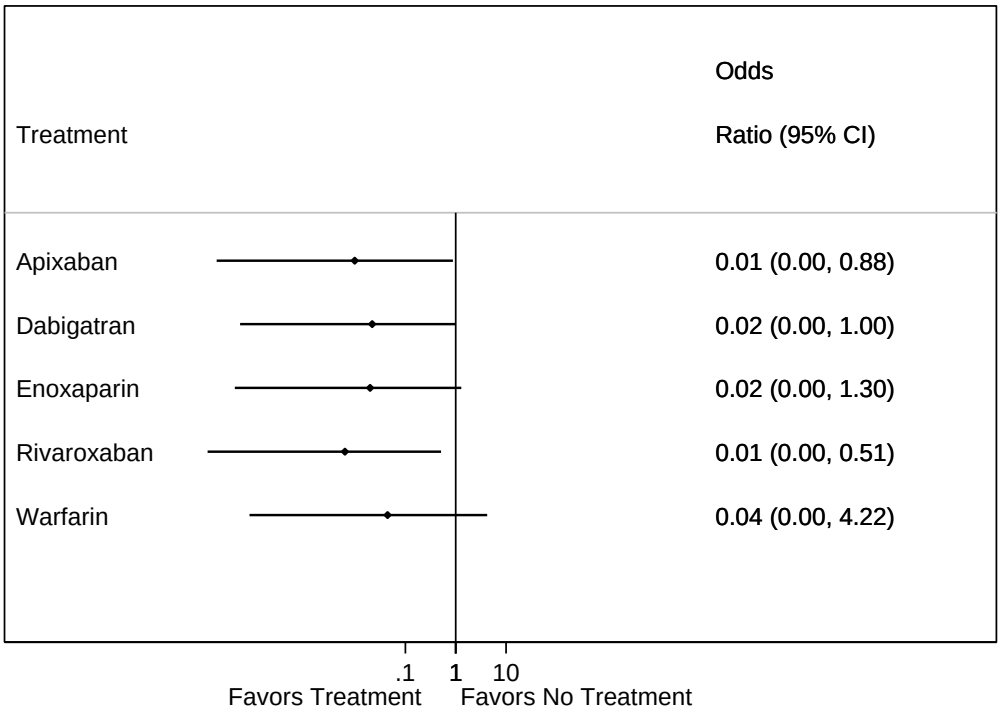


Figure 55. Proximal Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. No Treatment)



NETWORK META-ANALYSIS PAIRWISE COMPARISONS

All significant pairwise comparisons from the final network meta-analysis are listed in the tables below. There were no significant comparisons for pulmonary embolism, symptomatic DVT, or all cause mortality. All pairwise comparisons from all network meta-analyis models are presented in Appendix XV.

Table 32. Major Bleeding Significant Pairwise Comparisons - Final Model

Comparison	Patient Populations with Significant Comparison
Enoxaparin + GCS favored over Fondaparinux + GCS	Hip and Knee
IPC + LD Aspirin favored over Apixaban	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Dabigatran	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Dalteparin	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Desirudin	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Enoxaparin	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Fondaparinux	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over No Treatment	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Rivaroxaban	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Tinzaparin	Hip and Knee, and Hip Only
IPC + LD Aspirin favored over Warfarin	Hip and Knee
Warfarin favored over Dabigatran	Hip and Knee, and Hip Only
Warfarin favored over Rivaroxaban	Hip and Knee, and Hip Only

Table 33. DVT Significant Pairwise Comparisons - Final Model

Comparison	Patient Populations with Significant Comparison
Apixaban favored over Enoxaparin	Hip and Knee, and Hip Only
Apixaban favored over No Treatment	Hip Only
Apixaban favored over Warfarin	Hip and Knee, and Knee Only
Dabigatran favored over Warfarin	Hip and Knee
Dalteparin favored over Warfarin	Hip and Knee, and Hip Only
Desirudin favored over Warfarin	Hip and Knee
Enoxaparin + IPC favored over Dabigatran	Knee Only
Enoxaparin + IPC favored over Enoxaparin	Knee Only
Enoxaparin + IPC favored over Tinzaparin	Hip and Knee
Enoxaparin + IPC favored over Warfarin	Hip and Knee, and Knee Only
Enoxaparin favored over Warfarin	Hip and Knee, and Knee Only
Fondaparinux favored over Dabigatran	Hip and Knee
Fondaparinux favored over Enoxaparin	Hip and Knee, and Hip Only
Fondaparinux favored over No Treatment	Hip and Knee, and Hip Only
Fondaparinux favored over Tinzaparin	Hip and Knee, and Hip Only
Fondaparinux favored over Warfarin	Hip and Knee, and Hip Only
Fondaparinux favored over YM150	Hip and Knee, and Hip Only
HD Aspirin + IPC favored over Warfarin	Knee Only
IPC favored over No Treatment	Hip and Knee, and Hip Only
Rivaroxaban favored over Dabigatran	Hip and Knee, and Hip Only
Rivaroxaban favored over Enoxaparin	Hip and Knee, Hip Only, and Knee Only
Rivaroxaban favored over No Treatment	Hip and Knee, and Hip Only
Rivaroxaban favored over Tinzaparin	Hip and Knee, and Hip Only
Rivaroxaban favored over Warfarin	Hip and Knee, Hip Only, and Knee Only

Table 34. Proximal DVT Significant Pairwise Comparisons - Final Model

Comparison	Patient Populations with Significant Comparison
Apixaban favored over No Treatment	Hip and Knee, and Knee Only
Apixaban favored over Warfarin	Hip and Knee
Rivaroxaban favored over Dabigatran	Hip and Knee
Rivaroxaban favored over Enoxaparin	Hip and Knee, and Hip Only
Rivaroxaban favored over No Treatment	Hip and Knee, and Knee Only
Rivaroxaban favored over Tinzaparin	Hip and Knee
Rivaroxaban favored over Warfarin	Hip and Knee

INDIVIDUAL STUDY RESULTS

Individual study results for each of the six outcomes analyzed in a network meta-analysis, as well as for other outcomes reported by the included studies, can be found in Appendix XV. Details of each study can also be found in Appendix XV.

RECOMMENDATION 6

In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who have also had a previous venous thromboembolism, receive pharmacologic prophylaxis and mechanical compressive devices.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

RATIONALE

Given that patients who are receiving a hip or knee arthroplasty are already at high risk for VTED, a further risk increase in these patients is of concern. Although none of the studies we located enrolled such patients, the work group deemed that an even greater risk of VTED in these patients justified issuing a consensus-based recommendation for these patients. The consensus of the work group is that both pharmacologic prophylaxis and mechanical compressive devices are appropriate for these patients, assuming that their risk of VTED is greater than their risk of bleeding. Since patients undergoing hip or knee arthroplasty will be receiving some form of prophylaxis anyway, the added costs of using both pharmacologic and mechanical compressive devices will not always be large. Furthermore, the approach in this recommendation is consistent with current practice.

RECOMMENDATION 7

In the absence of reliable evidence, it is the opinion of this work group that patients undergoing elective hip or knee arthroplasty, and who also have a known bleeding disorder (e.g., hemophilia) and/or active liver disease, use mechanical compressive devices for preventing venous thromboembolism.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

RATIONALE

As discussed in Recommendation 3, patients who have a known bleeding disorder or active liver disease are at elevated risk for bleeding. Due to the serious complications that can occur in these patients, the work group deemed it appropriate to issue a consensus-based recommendation in spite of a lack of relevant, published data. It is the consensus of the work group that mechanical compressive devices are appropriate for these patients, as pharmacologic prophylaxis may exacerbate the risk of bleeding. Using mechanical compressive devices is of low risk and consistent with current practice. Consultation with a hematologist or other specialist may be warranted in some cases, especially when a patient is both at an elevated risk of bleeding and at an elevated risk of VTED.

RECOMMENDATION 8

In the absence of reliable evidence, it is the opinion of this work group that patients undergo early mobilization following elective hip and knee arthroplasty. Early mobilization is of low cost, minimal risk to the patient, and consistent with current practice.

Grade of Recommendation: Consensus

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

RATIONALE

VTED is a potentially catastrophic complication faced by all patients who undergo elective hip and knee arthroplasty. Risk factors that predispose to VTED are embodied by "Virchow's Triad" – hypercoagulability, endothelial injury, and stasis. Early mobilization following hip or knee arthroplasty addresses the stasis limb of Virchow's triad; movement of the operated limb promotes regional blood flow. Mobilization should begin as soon postoperatively as possible. Practices should be in place to ensure that appropriate support are provided throughout the hospital stay to minimize the risk of falls during transfer and ambulation.

Although one moderate quality study and five low quality studies compared VTED rates based on timing of mobilization, their results are conflicting (these results are summarized in Table 35, our evaluation of their quality and applicability is shown in Table 54, and a more detailed presentation of their results is in Table 36). One study of moderate quality suggests patients mobilizing within 2-4 hours of surgery do not have lower VTED readmission rates vs. patients mobilizing the afternoon or evening of surgery. Three low quality studies suggest that there is no difference in VTED due to timing of mobilization, while two other low quality studies did find lower rates of PE or VTED readmission among patients who mobilized earlier. Based on the fact that early mobilization has minimal cost, low risk to the patient, and is consistent with current clinical practice, issuing a consensus based consensus-based recommendation is warranted.

Table 63 in Appendix XIV summarizes the reasons for excluding some of the studies we initially considered for this recommendation.

FINDINGS

Table 35. Early Mobilization Summary Table

Outcome	2-4 hours vs. 6-12 hours	0-1 day vs. 2+ days	0-2 days vs. 2+ days	2 days vs. 3+ days
All-Cause Mortality	○			
DVT		○		
DVT Readmission	○			
Fatal PE				○
PE		○		●
PE Readmission	○			
Symptomatic VTE			○	
VTE		○		
VTE Readmission		●		
Minor Wound Problems		♦		
Wound Dehiscence		○		

○: no statistically significant difference. ●: statistically significant in favor of earlier mobilization. ♦: statistically significant in favor of mobilization on the 2nd post operative day as opposed to within the first 24 hours.

QUALITY AND APPLICABILITY

Of the included studies addressing VTED-related outcomes, one was of moderate quality and five were of low quality. One additional moderate quality study addressed wound problems. All seven included studies were of moderate applicability. For details, see Table 54 in Appendix XIII.

RESULTS

Table 36. Early Mobilization Results

Author	N	Joint	Group 1	Group2	Strength	Outcome (Duration)	% Group1	% Group2	Results
Johnson	7846	Hip	Mobilization starting day 2	Grp2: Day 3-6 Grp3: Day 7-10 Grp4:Day 11-14 Grp5:Day 15-19 Grp6:Day 20+	Low	Fatal PE	1.1%	Grp2: 0.9% Grp3: 1.3% Grp4: 0.9% Grp5: 2.4% Grp6: 0.7%	No significant difference
Husted	1977	Both	Mobilized within 2-4h	Mobilized afternoon or evening of surgery	Moderate	All-Cause Mortality (3 months)	0	0.3%	No significant difference
Husted	1977	Both	Mobilized within 2-4h	Mobilized afternoon or evening of surgery	Moderate	PE readmission (3 months)	0.1%	0.4%	No significant difference OR: 0.3 (.01, 2.4)
Johnson	7846	Hip	Mobilization starting day 2	Grp2: Day 3-6 Grp3: Day 7-10 Grp4:Day 11-14 Grp5:Day 15-19 Grp6:Day 20+	Low	PE	7.4%	Grp2: 10.5% Grp3: 11.9% Grp4: 6.1% Grp5: 9.6% Grp6: 6.1%	Favors Group1 (vs. all other groups combined) OR: 0.8 (0.6, 0.97)
Kelsey	1035	Hip	1 day in bed	Grp2: 2-3 days in bed Grp3: 4+ days in bed	Low	PE	7.8%	Grp2: 9.1% Grp3: 10.9%	No significant difference OR: 0.8 (0.4, 1.3)

Author	N	Joint	Group 1	Group2	Strength	Outcome (Duration)	% Group1	% Group2	Results
Husted	1977	Both	Mobilized within 2-4h	Mobilized afternoon or evening of surgery	Moderate	DVT readmission (3 months)	0.5%	0.6%	No significant difference OR: 0.8 (0.2, 3.0)
Kelsey	1035	Hip	1 day in bed	Grp2: 2-3 days in bed Grp3: 4+ days in bed	Low	DVT	12.8%	Grp2: 8.6% Grp3:14.5%	No significant difference OR: 1.1 (0.7, 1.7)
White	886	Hip	Mobilization on day 0 or 1	Mobilization on day 2 or later	Low	VTE readmission (3 months)	44%	61%	Favors Group1 Adjusted OR*: 0.7 (0.5, 0.9)
Samama	1062	Both	Weight-bearing within 48h	No weight-bearing within 48h	Low	Symptomatic VTE (3 months)	Not Reported	Not Reported	No significant difference OR: 0.4 (0.1, 1.4)
Kelsey	1035	Hip	1 day in bed	Grp2: 2-3 days in bed Grp3: 4+ days in bed	Low	VTE	17.1%	Grp2:15.1% Grp3:22.3%	No significant difference† OR: 0.9 (0.6, 1.3)
Leizorovicz	386	Both	Duration of immobilization – continuous variable	Not Applicable	Low	VTE or sudden death (hospital discharge)	Median: 4 days (range 1-87)	NA	No significant difference
Pearse	195	Knee	Walk independently within 24h	Walk on 2nd post-operative day	Moderate	Minor Wound Problems - ooze and erythema	23.7%	11.2%	Favors Group2 OR: 2.5 (1.1, 6.0)
Pearse	195	Knee	Walk independently within 24h	Walk on 2nd post-operative day	Moderate	Wound dehiscence	0	0	No difference

*Adjusted for Age, sex, race, history of thromboembolism, rheumatoid arthritis, BMI, thromboprophylaxis;† no significant differences comparing grp 1 vs any group, OR presented is grp1 vs grp2+3

RECOMMENDATION 9

We suggest the use of neuraxial (such as intrathecal, epidural, and spinal) anesthesia for patients undergoing elective hip or knee arthroplasty to help limit blood loss, even though evidence suggests that neuraxial anesthesia does not affect the occurrence of venous thromboembolic disesase.

Grade of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

RATIONALE

There is one high quality study and two moderate quality studies that addressed neuraxial anesthesia and VTE disease (Table 37 summarizes their results, Table 38 through Table 44 present a detailed description of their results, and Table 55 in Appendix XIII summarizes the results of our quality and applicability evaluations). None of these studies found a statistically significant difference in outcomes between regional (epidural or spinal) and general anesthesia.

Fifteen randomized controlled trials of high quality and moderate applicability compared peri-operative blood loss among patients receiving general, epidural, or a combination of general and epidural, or a combination of general anesthesia and lumbar plexus block. There were eight high quality studies comparing epidural and general anesthesia. Epidural anesthesia resulted in lower intra-operative blood loss. The combination of epidural and general anesthesia resulted in lower intra-operative blood loss compared to general anesthesia alone in two high quality studies. The combination of lumbar plexus block and general anesthesia resulted in lower intra- and post-operative blood loss compared to general anesthesia alone in two high quality studies. Hypotensive epidural anesthesia resulted in lower post-operative blood loss compared to spinal anesthesia in two high quality studies.

Table 64 in Appendix XIV summarizes the reasons for excluding some of the studies we initially considered for this recommendation.

FINDINGS

Table 37. Neuraxial Anesthesia Summary Table

Outcome	Epidural vs. General	Spinal vs. General	General + Epidural vs. General	General + Lumbar Plexus Block vs. General	Epidural vs. Spinal	Epidural vs. General + Epidural	Epidural + Spinal vs. General
All-Cause Mortality	○						
Symptomatic VTE	○	○○			○		
New Perfusion Defects	○						
Intraoperative Blood Loss	●○●●○●○		●○●●	●●	♦●	○○	○
Postoperative Blood Loss	♦○○●○●		♦○○●	○●	●●	●○	○
Total Blood Loss	○○		○●●	●	●○	○	
Wound Hematoma	○						
Wound Infection	○						○
Transfusion	○○		○●	○		○	

○: no statistically significant difference; ●: statistically significant in favor of group 1 (listed first)
♦: statistically significant in favor of group 2

QUALITY AND APPLICABILITY

Of the three included studies addressing VTED-related outcomes, one was of high quality and two were of moderate quality. All three were of moderate applicability. Fifteen included studies addressing blood loss were all of high quality and moderate applicability. For details, see Table 55 in Appendix XIII.

RESULTS

Table 38. Regional vs. General Anesthesia - VTED-related Outcomes

Author	N	Joint	Group 1	Group2	Strength	Outcome	% Group1	% Group2	Results
Williams-Russo et al. 1996	262	Knee	Epidural	General	High	All-Cause Mortality (2 months)	0.7%	0.8%	No significant difference OR:0.95 (.01, 75.5)
Williams-Russo et al. 1996	178	Knee	Epidural	General	Moderate	Proximal DVT (day 5)	0	0	No events
Williams-Russo et al. 1996	153	Knee	Epidural	General	Moderate	New Perfusion Defects (day 5)	11.6%	9.0%	No significant difference OR: 1.3 (0.4, 4.7)
Warwick et al. 2007	15903	Both	Any spinal	Grp2: Any general Grp3: Epidural Grp4: Lumbar plexus block	Moderate	Symptomatic VTE	2.2%	Grp2: 1.2% Grp3: 1.0% Grp4:1.9%	No significant difference in multivariate analysis
Maurer et al. 2007	606	Hip	Spinal	General	Moderate	Symptomatic VTE	1.6%	1.7%	No significant difference OR:0.9 (0.2, 4.6)

Figure 56. Epidural vs. General Anesthesia - Intraoperative Blood Loss

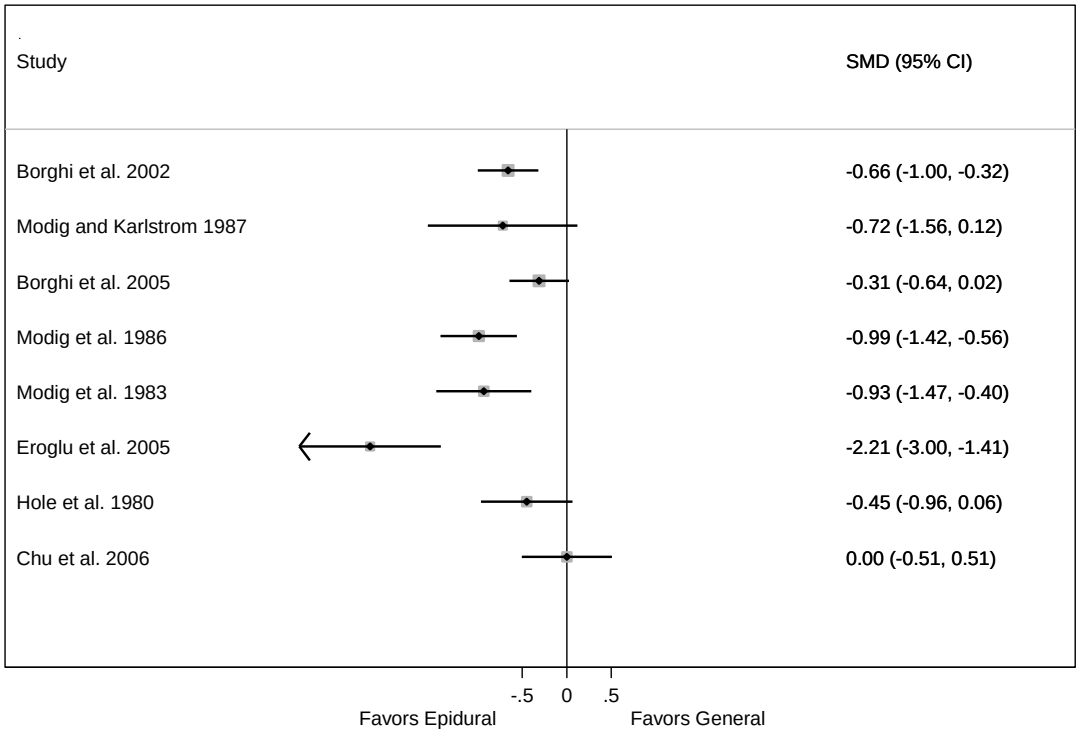


Figure 57. Epidural vs. General Anesthesia - Postoperative Blood Loss

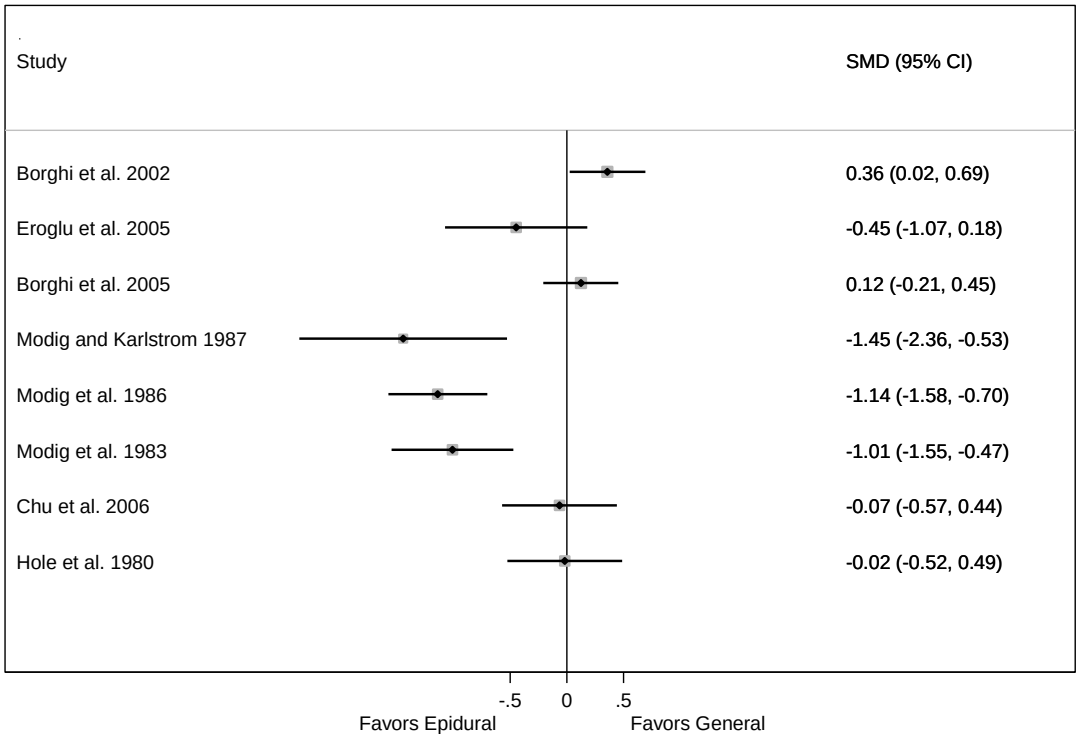


Figure 58. Epidural + General vs. General Anesthesia - Intraoperative Blood Loss

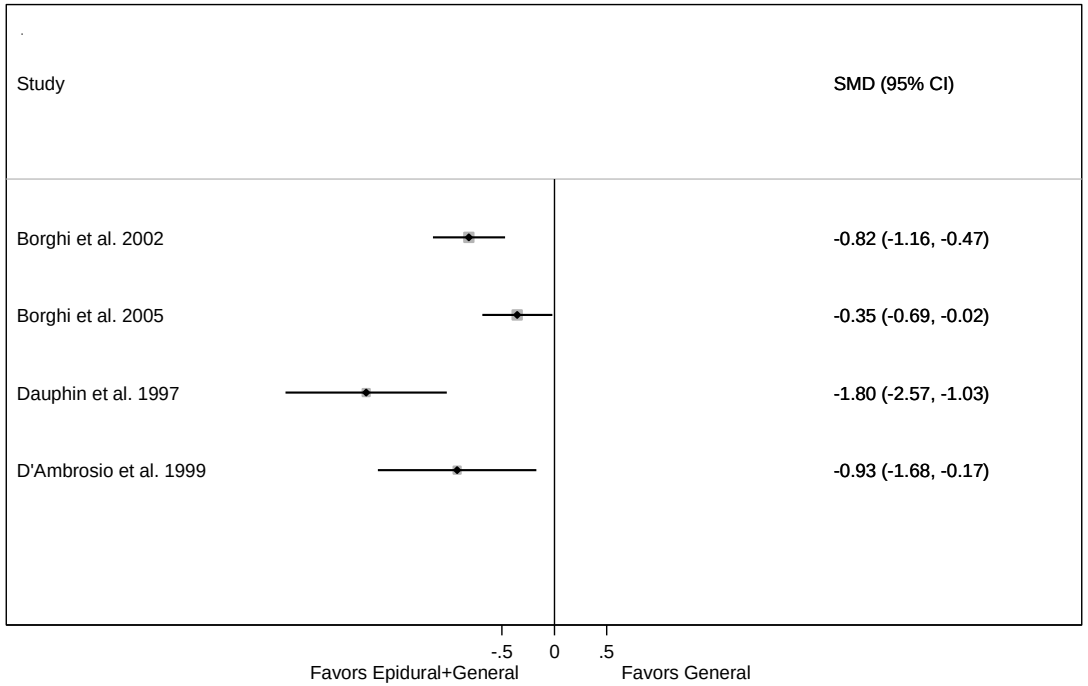


Figure 59. Epidural + General vs. General Anesthesia - Postoperative Blood Loss

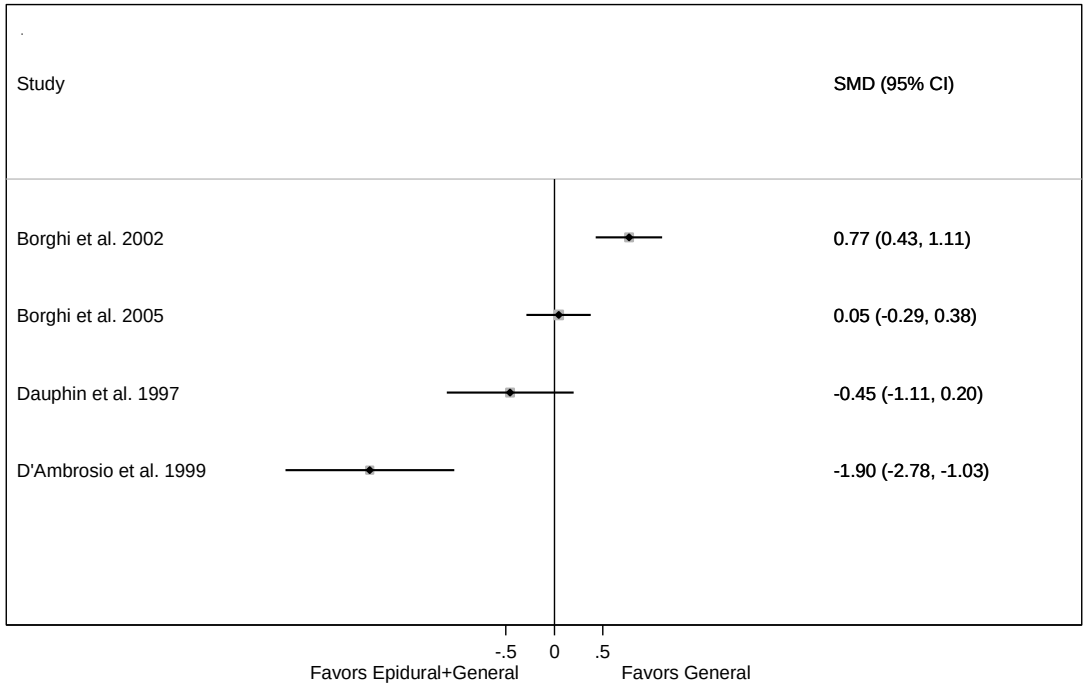


Table 39. Epidural vs. General Anesthesia - Intraoperative Blood Loss

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range)	Group2 Mean (SD) o r Median (range)	Results
Eroglu et al. 2005	40	Hip	Hypotensive Epidural	Hypotensive Total IV	High	Intraoperative Blood Loss	305 (210-550)	515 (380-780)	Favors Hypotensive Epidural
Hole et al. 1980	60	Hip	Epidural	General	High	Intraoperative blood loss	1274 (598)	1567 (696)	No Difference
Modig et al. 1983	60	Hip	Epidural	General	High	Intraoperative Blood Loss	1148 (446)	1548 (410)	Favors Epidural
Modig et al. 1986	94	Hip	Epidural	General	High	Intraoperative Blood Loss	1210 (490)	1680 (460)	Favors Epidural
Modig and Karlstrom 1987	38	Hip	Epidural	Grp2:General Grp3: General (IPPV)	High	Intraoperative Blood Loss	950 (300)	Grp2:1140 (200) Grp3:1540 (340)	Favors Epidural and General vs. General (IPPV); no difference in Epidural vs. General
Borghi et al. 2002	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Intraoperative Blood Loss	479 (107)	Grp2:547 (99) Grp3:465 (102)	Favors Epidural vs. General and Epidural-General vs. General; no difference in Epidural vs. Epidural-General
Borghi et al. 2005	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Intraoperative Blood Loss	449 (207)	Grp2:515 (219) Grp3:435 (233)	No Difference
Chu et al. 2006	60	Knee	Spinal-Epidural	General	High	Intraoperative Blood Loss	200 (5-300)	200 (100-212.5)	No Difference

IPPV: Intermittent Positive Pressure Ventilation

Table 40. Epidural vs. General Anesthesia - Postoperative Blood Loss

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range)	Group2 Mean (SD) o r Median (range)	Results
Hole et al. 1980	60	Hip	Epidural	General	High	Postoperative Blood Loss	552 (232)	556 (206)	No Difference
Eroglu et al. 2005	40	Hip	Hypotensive Epidural	Hypotensive Total IV	High	Postoperative Blood Loss	645 (380-960)	682 (520-980)	No Difference
Modig et al. 1983	60	Hip	Epidural	General	High	Postoperative Blood Loss	294 (64)	427 (175)	Favors Epidural
Borghi et al. 2002	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Postoperative Blood Loss	545 (110)	Grp2:502 (129) Grp3:593 (106)	Favors General vs. Epidural and vs. Epidural-General; Favors Epidural vs. Epidural-General
Borghi et al. 2005	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Postoperative Blood Loss	541 (402)	Grp2:495 (342) Grp3:510 (322)	No Difference
Modig et al. 1986	94	Hip	Epidural	General	High	Postoperative Blood Loss	412 (70)	518 (112)	Favors Epidural
Modig and Karlstrom 1987	38	Hip	Epidural	Grp2:General Grp3: General (IPPV)	High	Postoperative Blood Loss	370 (80)	Grp2:480 (70) Grp3:500 (110)	Favors Epidural vs. both forms of General
Chu et al. 2006	60	Knee	Spinal-Epidural	General	High	Postoperative Blood Loss	385 (275-560)	400 (197.5-530)	No Difference

IPPV: Intermittent Positive Pressure Ventilation

Table 41. Epidural vs. General Anesthesia - Other Outcomes

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range) or %	Group2 Mean (SD) o r Median (range) or %	Results
Jorgensen et al. 1991	39	Knee	Extradural	General	High	Total Drain Volume	650 (340-1845)	950 (195-3275)	No Difference
Borghi et al. 2005	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Total Blood Loss	972 (470)	Grp2:1003 (431) Grp3:917 (399)	No Difference
Hole et al. 1980	60	Hip	Epidural	General	High	Wound Hematoma	3%	10%	No Difference
Hole et al. 1980	60	Hip	Epidural	General	High	Wound Infection	3%	10%	No Difference
Hole et al. 1980	60	Hip	Epidural	General	High	Transfusion	24%	26%	No Difference
Borghi et al. 2002	210	Hip	Epidural	Grp2: General Grp3: Epidural-General	High	Homologous Blood Transfusion	23%	Grp2: 13% Grp3: 19%	No Difference
Chu et al. 2006	60	Knee	Spinal-Epidural	General	High	Wound Infection	3%	3%	No Difference

Table 42. General + Epidural vs. General Anesthesia - Results

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range) or %	Group2 Mean (SD) o r Median (range) or %	Results
Dauphin et al. 1997	37	Hip	General	Epidural-General	High	Intraoperative Blood Loss	1259.2 (366)	663.8 (299)	Favors Epidural-General
D'Ambrosio et al. 1999	60	Hip	Epidural-General-Aprotinin	Grp2: Epidural-General Grp3: General-Aprotinin Grp4: General	High	Intraoperative Blood Loss	252.1 (108)	Grp2: 246.5 (127) Grp3:273.5 (84) Grp4:355.5 (107)	Favors all 3 groups vs. General (Grp4); all other comparisons not significant
Dauphin et al. 1997	37	Hip	General	Epidural-General	High	Postoperative Blood Loss	600.8 (390.8)	444 (300.8)	No Difference
D'Ambrosio et al. 1999	60	Hip	Epidural-General-Aprotinin	Grp2: Epidural-General Grp3: General-Aprotinin Grp4: General	High	Postoperative Blood Loss	330.8 (210)	Grp2: 486.2 (185) Grp3:574.6 (146) Grp4:862.9 (210)	Favors Grp1 vs. each of other 3 groups; Favors all 3 groups vs. General (Grp4)
Dauphin et al. 1997	37	Hip	General	Epidural-General	High	Total Blood Loss	1860 (616.6)	1107.8 (378.6)	Favors Epidural-General
D'Ambrosio et al. 1999	60	Hip	Epidural-General-Aprotinin	Grp2: Epidural-General Grp3: General-Aprotinin Grp4: General	High	Total Blood Loss	583 (300)	Grp2: 732.7 (262) Grp3:848.2 (169) Grp4:1198 (280)	Favors all 3 groups vs. General (Grp4); Favors Grp1 vs. Grp3
Dauphin et al. 1997	37	Hip	General	Epidural-General	High	Homologous Blood Transfusion	88%	35%	Favors Epidural-General

Table 43. General + Lumbar Plexus Block vs. General Anesthesia - Results

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range) or %	Group2 Mean (SD) o r Median (range) or %	Results
Twyman et al. 1990	20	Hip	General-Lumbar Plexus Block	General	High	Intraoperative Blood Loss	310 (81)	617 (230)	Favors General-Lumbar Plexus Block
Stevens et al. 2000	60	Hip	General-Lumbar Plexus Block	General	High	Intraoperative Blood Loss	420 (187)	538 (254)	Favors General-Lumbar Plexus Block
Twyman et al. 1990	20	Hip	General-Lumbar Plexus Block	General	High	Postoperative Blood Loss	402 (185)	457 (111)	No Difference
Stevens et al. 2000	60	Hip	General-Lumbar Plexus Block	General	High	Postoperative Blood Loss	170 (125)	310 (204)	Favors General-Lumbar Plexus Block
Twyman et al. 1990	20	Hip	General-Lumbar Plexus Block	General	High	Total Blood Loss	712 (199)	1074 (250)	Favors General-Lumbar Plexus Block
Stevens et al. 2000	60	Hip	General-Lumbar Plexus Block	General	High	Autologous Blood Transfusion	13%	13%	No Difference

Table 44. Epidural vs. Spinal Anesthesia - Blood Loss

Author	N	Joint	Group 1	Group2	Strength	Outcome	Group1 Mean (SD) o r Median (range)	Group2 Mean (SD) o r Median (range)	Results
Juelsgaard et al. 2001	30	Knee	Hypotensive Epidural	Spinal	High	Intraoperative Blood Loss	146 (100)	13 (27)	Favors Spinal
Niemi et al. 2000	30	Hip	Hypotensive Epidural	Spinal	High	Intraoperative Blood Loss	400 (163-575)	900 (663-1100)	Favors Hypotensive Epidural
Juelsgaard et al. 2001	30	Knee	Hypotensive Epidural	Spinal	High	Postoperative Blood Loss at 3hours	499 (171)	1036 (595)	Favors Hypotensive Epidural
Juelsgaard et al. 2001	30	Knee	Hypotensive Epidural	Spinal	High	Postoperative Blood Loss at 24 hours	816 (271)	1461 (612)	Favors Hypotensive Epidural
Juelsgaard et al. 2001	30	Knee	Hypotensive Epidural	Spinal	High	Total Blood Loss	1056 (272)	1826 (765)	Favors Hypotensive Epidural
Niemi et al. 2000	30	Hip	Hypotensive Epidural	Spinal	High	Total Blood Loss at 3 hours	600 (300-775)	1100 (763-1338)	Favors Hypotensive Epidural
Niemi et al. 2000	30	Hip	Hypotensive Epidural	Spinal	High	Total Blood Loss at 24 hours	850 (500-1350)	1500 (1025-1838)	No Difference

RECOMMENDATION 10

Current evidence does not provide clear guidance about whether inferior vena cava (IVC) filters prevent pulmonary embolism in patients undergoing elective hip and knee arthroplasty who also have a contraindication to chemoprophylaxis and/or known residual venous thromboembolic disease. Therefore, we are unable to recommend for or against the use of such filters.

Grade of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

RATIONALE

No studies met the inclusion criteria for VTED-related outcomes in arthroplasty patients. Two studies of non-arthroplasty patients compared PE and death rates between patients who received IVC filters and those who did not (see Table 45 for a summary of the results of these studies, Table 46 for a detailed presentation of the results of these studies, and Table 56 in Appendix XIII for our evaluations of their quality and applicability). One was a low quality study of bariatric surgery patients, which found no differences in VTED outcomes between patients with and without IVC filters. The other was a low quality study of trauma patients which reported lower rates of PE and fatal PE in patients who received IVC filters. The work group did not make a consensus recommendation for or against the use of inferior vena cava filters because these filters require surgery to place in the patient. Surgery adds cost and potential harms to the patient, and consensus recommendations are only allowed for low cost and low risk interventions. Therefore, based on the limited and conflicting data regarding the benefits of IVC filters in preventing pulmonary embolism, and the fact that none of the studies included arthroplasty patients, we are unable to recommend for or against their use in hip and knee arthroplasty patients (the reasons we excluded some studies that were initially considered for this recommendation are provided in Appendix XIV, Table 65).

FINDINGS

Table 45. IVC Filter Summary Table

Outcome	Arthroplasty Patients	Bariatric Surgery Patients	Trauma Surgery Patients
All-Cause Mortality	No data	○	○
PE		○	●
PE-Related Death			●
DVT		○	

○: no statistically significant difference ●: statistically significant in favor of filter

QUALITY AND APPLICABILITY

The two included studies for this recommendation were both of low quality and moderate applicability. For details, see Table 56 in Appendix XIII.

RESULTS

Table 46. IVC Filter Results

Author	N	Patient Population	Study Design	Strength	Outcome	Results
Obeid	2099	Bariatric surgery patients	Retro Comparative	Low	All-Cause Mortality	No significant difference OR: 3.8 (0.3, 26.3)
Obeid	2099	Bariatric surgery patients	Retro Comparative	Low	PE	No significant difference OR: 1.4 (0.1, 6.3)
Obeid	2099	Bariatric surgery patients	Retro Comparative	V. Low	DVT	No significant difference OR: 1.9 (0.3, 7.0)
Khan-sarinia	324	Trauma patients	Historically-matched controls	Low	All-Cause Mortality	No significant difference OR: 0.7 (0.4, 1.4)
Khan-sarinia	324	Trauma patients	Historically-matched controls	Low	PE-related Death	Favors filter patients OR: 0 (0, 0.8)
Khan-sarinia	324	Trauma patients	Historically-matched controls	Low	PE	Favors filter patients OR: 0 (0, 0.6)

FUTURE RESEARCH

The inability of the available data to distinguish between prophylaxis and no prophylaxis as well as between different prophylactic regimens with regard to the critical outcomes (reoperation due to bleeding, death from bleeding, symptomatic PE, death from PE, peri-prosthetic joint infection, all cause mortality, reoperation for any reason within 90 days of surgery) in addition to the uncertainty concerning the value of surrogate outcomes (such as the incidence of deep vein thrombosis), suggests that the approach to conducting clinical trials on thrombo-prophylactic agents needs to be re-examined. Studies need to be sufficiently powered to detect relatively rare events; the use of registries may help in addressing this requirement. In addition, clinical trials need to report the critical outcomes noted above. Specific areas that the work group targeted for further research include:

1. Characterization of risk factors for VTED and bleeding in hip and knee arthroplasty patients;
2. Evaluation of multi-modal treatment regimens which combine pharmaco-prophylaxis, mechanical prophylaxis, and other modalities (e.g. early mobilization and regional anesthesia);
3. Utilization of administrative data sets to obtain the necessary sample size. This would be facilitated by creating codes for the different drugs and mechanical devices used during hospitalization;
4. Utilization of placebo controls in patients at standard risk of VTED in future clinical trials;
5. Utilization of advanced imaging studies (such as Magnetic Resonance Venography) to establish the presence of DVT in patients with definitive evidence of PE, as prior studies that have evaluated the prevalence of DVT in this population with ultrasonography have found a prevalence similar to routine screening;
6. Performance of a meta-analysis of the studies that have attempted to correlate DVT and PE;
7. Performance of studies evaluating the optimal timing and duration of administration of prophylactic agents and/or mechanical compression devices;
8. Performance of focused studies enrolling patients at high risk of VTED or bleeding;
9. Performance of clinical trials in revision hip and knee arthroplasty procedures; and
10. Clarification of the role of IVC filters in prophylaxis of high-risk patients.

Appendices

APPENDIX I

Work Group Roster

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APPENDIX II
AAOS BODIES THAT APPROVED THIS CLINICAL PRACTICE GUIDELINE

Guidelines Oversight Committee

The AAOS Guidelines Oversight Committee (GOC) consists of sixteen AAOS members. The overall purpose of this Committee is to oversee the development of the clinical practice guidelines, performance measures, health technology assessments and utilization guidelines.

Evidence Based Practice Committee

The AAOS Evidence Based Practice Committee (EBPC) consists of ten AAOS members. This Committee provides review, planning and oversight for all activities related to quality improvement in orthopaedic practice, including, but not limited to evidence-based guidelines.

Council on Research, Quality Assessment, and Technology

To enhance the mission of the AAOS, the Council on Research and Quality promotes the most ethically and scientifically sound basic, clinical, and translational research possible to ensure the future care for patients with musculoskeletal disorders. The Council also serves as the primary resource to educate its members, the public, and public policy makers regarding evidenced-based medical practice, orthopaedic devices and biologics, regulatory pathways and standards development, patient safety, occupational health, technology assessment, and other related areas of importance.

The Council is comprised of the chairs of the AAOS Biological Implants, Biomedical Engineering, Evidence Based Practice, Guidelines Oversight, Occupational Health and Workers' Compensation, Patient Safety, Research Development, and US Bone and Joint Decade committees. Also on the Council are the AAOS second vice-president, representatives of the Diversity Advisory Board, the Women's Health Issues Advisory Board, the Board of Specialty Societies (BOS), the Board of Councilors (BOC), the Communications Cabinet, the Orthopaedic Research Society (ORS), the Orthopedic Research and Education Foundation (OREF), and three members at large.

Board of Directors

The 17 member AAOS Board of Directors manages the affairs of the AAOS, sets policy, and determines and continually reassesses the Strategic Plan.

DOCUMENTATION OF APPROVAL

AAOS Work Group Draft Completed	April 22, 2011
Peer Review Completed	May 22, 2011
Public Commentary Completed	August 26, 2011
AAOS Guidelines Oversight Committee	September 7, 2011
AAOS Evidence-Based Practice Committee	September 7, 2011
AAOS Council on Research and Quality	September 13, 2011
AAOS Board of Directors	September 23, 2011

A minimum of **63** professionals reviewed and were provided the opportunity to vote on the contents of this document during the approval process.

APPENDIX III
DETERMINING CRITICAL OUTCOMES
WORK GROUP PARTICIPATION

The first task of the work group is to determine what outcomes are critical to addressing the recommendations in the guideline. This is accomplished by asking the work group to construct a preliminary list of important outcomes prior to attending the introductory meeting. Following the introductory meeting, the work group will be asked to participate in three Delphi rounds, completing the "Critical Outcomes Form" shown below.

CRITICAL OUTCOMES FORM

DETERMINING OUTCOMES

The first task as a guideline work group is to determine what outcomes the guideline should address. We accomplish this by listing the outcomes you think are relevant, by determining how important each outcome is, by focusing on patient-oriented outcomes, and by looking at benefits and harms.

Criticality

Some outcomes are more important than others. The outcomes that are *most* important are critical outcomes. Critical outcomes are vital to determining whether you should offer a treatment or diagnostic test to a patient. Without knowing what the critical outcomes are and how that treatment or test affects them, you cannot determine whether the treatment or test is worth giving.

For example, you couldn't decide whether to give a patient a knee replacement if you knew nothing about whether it would relieve that patient's pain or nothing about the severity and frequency of adverse surgical-related events like the frequency of pulmonary emboli. Pain relief and pulmonary embolisms are critical outcomes, If you knew absolutely nothing about how knee replacement affected them, the formal possibility that knee replacement surgery did not relieve pain but did cause pulmonary emboli would exist. As physicians, your goal is just the opposite; to relive suffering and to first do no harm.

Patient-Oriented Outcomes

In general, good medicine and good evidence-based medicine gives priority to patient-oriented outcomes. These are the outcomes patients care about. Patient oriented outcomes:

- Help the patient live longer or better
- Are typically something the patient feels
- Are often the patient's diagnostic or treatment goal(s)
- Do not require extrapolation or interpolation to determine their importance to the patient

Examples of patient-oriented outcomes are:

- Survival/mortality
- Pain relief
- Fracture prevention
- Functional Status
- Quality of Life

Surrogate Outcomes
Patient-oriented outcomes contrast with surrogate outcomes. Surrogate outcomes:

- Substitute measures for patient-oriented outcomes
- Are typically not felt by the patient
- Are typically not the reason the patient goes to a physician and, therefore, not typically the patient's goal for the treatment.
- Require extrapolation or interpolation to determine their relationship to (or effect on) patient-oriented outcomes

Examples of surrogate outcomes are:

- Blood cholesterol (a surrogate for survival)
- Bone mineral density (a surrogate for fractures)
- All imaging results (imaging results are often surrogates for pain or functional status, but they can be surrogates for other patient-oriented outcomes, too)

Benefits and Harms
As physicians, you are interested in benefits and harms. Benefits are patient-oriented outcomes the patient wants and harms are patient-oriented outcomes they don't want. Avoiding something (e.g. fractures or death) can be a benefit.

Words of Warning
To determine which outcomes to examine and their importance, you need to think not only like a physician, but like a patient. Ask yourself, "What do patients want?" "How will they judge whether the treatment is a success or failure?"

If you only spend about 15 minutes on specifying critical outcomes:

- You haven't done your job

- The strength of the recommendation you can make on a given topic will be adversely affected. It may even be the case that a guideline cannot make a recommendation about a very important treatment or diagnostic

- You will be unhappy the final guideline

Rating Outcomes
In addition to asking you to identify important outcomes, we are also asking you to specify how important each outcome is. To do this, please rate them on a scale of 1-9. The meaning of these ratings is shown in the table below:

Rating	***Importance***
9	
8	**Critical**
7	
6	
5	**Important**
4	
3	
2	**Not Important**
1	

Please also note that:

1. **Unless you are interested in measures of diagnostic test performance (e.g., sensitivity and specificity), no surrogate outcome may be rated as "Critical" (i.e., rated 7-9)**

2. **If you rate every outcome as important in an effort to include every outcome in the guideline, we will have to discard your input. The outcomes you list and the ratings you provide will not be considered.**

Final Determinations
We expect that the work group input will differ. Some of you will list outcomes that are not listed by others and your ratings of the importance of outcomes will also differ from those of other members of your work group. We will use the Delphi method to determine which outcomes to include, and which outcomes are critical and which are not. We will limit the method to three rounds.

PLEASE RETURN THIS PAGE WITH YOUR INPUT

On this page, please list up to 10 outcomes that this guideline should address, and rate them on a scale from 1-9. PLEASE DO NOT CONSULT WITH OTHER MEMBERS OF THE WORK GROUP WHEN LISTING OUTCOMES OR MAKING YOUR RATINGS.

Outcome Number	Outcome	Rating
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

Please use the table below to assist you in assigning ratings to the importance of each of the outcomes you listed:

Rating	*Importance*
9	
8	**Critical**
7	
6	
5	**Important**
4	
3	
2	**Not Important**
1	

Please also note that:

1. Unless you are interested in measures of diagnostic test performance (e.g., sensitivity and specificity), no surrogate outcome may be rated as "Critical" (i.e., rated as 7-9).

2. If you rate every outcome as critical (i.e., as 7, 8, or 9) in an effort to include every outcome in the guideline, we will discard your input. The outcomes you list and the ratings you provide will be discarded.

3. ***This form will be forwarded <u>three times.</u> We will use the Delphi method to determine which outcomes to include, and which outcomes are critical and which are not. We will limit the method to three rounds. Thank you in advance for your cooperation.***

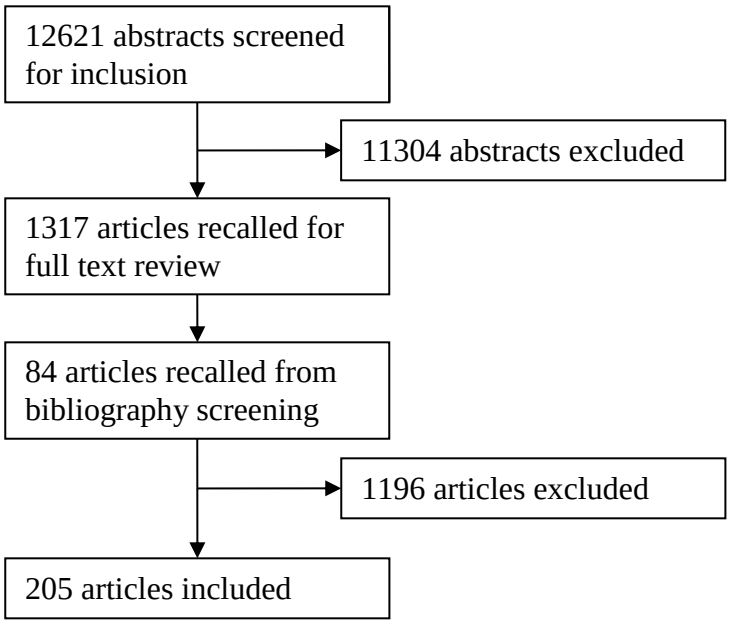
Using this Delphi process, the work group identified seven critical outcomes for this guideline: all cause mortality, death from bleeding, death from pulmonary embolism, periprosthetic joint infection, reoperation due to bleeding, reoperation for any reason within 90 days of surgery, and symptomatic pulmonary embolism.

The work group identified the following outcomes as important: asymptomatic PE, bleeding (any site), cellulitis/minor wound hematoma, disability from PE, disability from vein occlusion, duration of hospitalization, ease of use of prophylactic regimen, function, infection (all sites), long-term anticoagulation due to symptomatic PE, long-term anticoagulation for proximal DVT, major post-phlebitic syndrome, non-surgical site bleeding, pain, post-op bleeding/hematoma, post-phlebitic syndrome, quality of life, readmission, symptomatic DVT, thigh DVT, and vena caval filter for recalcitrant/recurrent DVT.

The work group identified the following outcomes as not important: asymptomatic DVT, calf DVT, duration of anti-coagulation, long-term anticoagulation for distal DVT, and looks better.

APPENDIX IV

INCLUDED AND EXCLUDED ARTICLES FLOWCHART



[(12,621-11,304) + 84] – 1,196 = 205

APPENDIX V
LITERATURE SEARCHES
SEARCH STRATEGY TIER 1 (HIP AND KNEE ARTHROPLASTY)
MEDLINE

#1 "arthroplasty, replacement, hip"[mh] OR "arthroplasty, replacement, knee"[mh] OR "hip prosthesis"[mh] OR "knee prosthesis"[mh] OR (("Joint Prosthesis"[mh:noexp] OR "Prostheses and Implants"[mh:noexp] OR "arthroplasty"[mh:noexp] OR "arthroplasty, replacement"[mh:noexp]) AND (hip OR hips OR knee OR knees OR joint* OR "lower limb"))

#2 "total knee" OR "total hip" OR ((THR OR TKR OR THA OR TKA OR prosthesis OR prostheses OR replacement* OR arthroplast*) AND (hip OR hips OR knees OR knee OR joint* OR "lower limb"))

#3 #1 OR #2

#4 "Venous Thrombosis"[mh:noexp] OR Thrombophlebitis[mh] OR "Venous Thromboembolism"[mh] OR dvt OR vte OR thrombos* OR thrombophleb* OR thromboembol* OR thromboprophyla* OR "Pulmonary embolism"[mh] OR ((pulmonary OR lung OR lungs) AND (infarct* OR embol* OR clot OR clots OR bloodclot*))

#5 chemoprophyla*[tiab] OR Anticoagulants[mh] OR anticoagulants[pa] OR anticoagul*[tiab] OR "fibrinolytic agents"[mh] OR "fibrinolytic agents"[pa] OR antithrombo*[tiab] OR thrombolytic*[tiab] OR thromboprophyla*[tiab] OR antiplatelet*[tiab] OR anti-platelet*[tiab] OR "platelet aggregation inhibitors"[mh] OR heparin[mh] OR heparin*[tiab] OR enoxaparin[tiab] OR lovenox[tiab] OR plavix[tiab] OR coumadin[tiab] OR clopidogrel[nm] OR warfarin[mh] OR warfarin*[tiab] OR fragmin[tiab] OR dalteparin[tiab] OR innohep[tiab] OR tinzaparin[nm] OR arixtra[tiab] OR fondaparinux[nm] OR "factor Xa inhibitor"[tiab] OR angiomax[tiab] OR bivalirudin[nm] OR refludan[tiab] OR aspirin[mh] OR aspirin[tiab] OR lepirudin[nm] OR iprivask[tiab] OR desirudin[nm] OR pradaxa[tiab] OR dabigatran[tiab] OR "dabigatran etexilate"[nm] OR xarelto[tiab] OR rivaroxaban[nm] OR YM150 OR LY517717 OR apixaban[tw]

#6 "Vena cava filters"[mh] OR ("Vena cava, inferior"[mh] AND "Filtration/instrumentation"[mh] AND 1972:1990[mhda]) OR (("vena cava"[tiab] OR ivc[tiab] OR Greenfield[tiab]) AND (filter*[tiab] OR filtration[tiab]))

#7 "stockings, compression"[mh] OR (compression[tiab] AND (sequential[tiab] OR stocking*[tiab] OR device*[tiab] OR (bandages[mh] AND 1970:2006[mhda]))) OR "Intermittent Pneumatic Compression Devices"[mh] OR (foot[tiab] AND (pump[tiab] OR pumps[tiab])) OR ((pneumatic[tiab] OR leg[tiab] OR calf[tiab]) AND compression[tiab]) OR (mechanical[tiab] AND prophyla*[tiab])

#8 #4 OR #5 OR #6 OR #7

#9 "1966"[PDat]:"2011"[PDat] AND English[lang]

#10 (animal[mh] NOT human[mh]) OR cadaver[mh] OR cadaver*[titl] OR ((comment[pt] OR editorial[pt] OR letter[pt] OR "historical article"[pt]) NOT "Study Characteristics"[pt]) OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR "case report"[titl]

#11 #3 AND #8 AND #9 NOT #10

#12 #1 OR (#2 NOT medline[sb])

#13 bleed*[tiab] OR blood*[tiab] OR hemorrhag*[tiab] OR "Hemorrhage"[mh] OR "Blood Loss, Surgical"[mh] OR "Blood transfusion"[mh] OR transfus*[tiab] OR hematoma* OR haematoma*

#14 #12 AND #13 AND #9 NOT #10

#15 #11 OR #14

EMBASE

#1 Arthroplasty/de OR 'hip arthroplasty'/exp OR 'knee arthroplasty'/exp

#2 (hip OR hips OR knee OR knees OR joint* OR 'lower limb') NEAR/5 (prosthe* OR replacement* OR arthroplast*)

#3 #1 OR #2

#4 'Vein thrombosis'/de OR thrombophlebitis/de OR 'venous thromboembolism'/exp OR 'deep vein thrombosis' OR dvt OR vte OR thrombos* OR thrombophelb* OR thromboembol* OR ((pulmonary OR lung OR lungs) AND (infarct* OR embolism* OR clot OR clots OR bloodclot*))

#5 chemoprophyla* OR 'anticoagulant agent'/exp OR 'thrombin inhibitor'/exp OR 'blood clotting inhibitor'/exp OR antithromb* OR thrombolytic* OR thromboprophyla* OR 'factor Xa inhibitor' OR antiplatelet* OR anti-platelet OR lovenox OR enoxaparin OR plavix OR Coumadin OR clopidogrel/de OR warfarin/de OR warfarin OR fragmin OR dalteparin OR 'heparin derivative'/exp OR innohep OR tinzaparin/de OR arixtra OR fondaparinux/de OR angiomax OR hirulog/de OR refludan OR lepirudin/de OR aspirin OR 'acetylsalicylic acid'/de OR heparin/exp OR argatroban OR argatroban/de OR iprivask OR desulfatohirudin/de OR pradaxa OR 'dabigatran etexilate'/de OR dabigatran/de OR xarelto OR rivaroxaban/de OR YM150 OR LY517717 OR apixaban

#6 'vena cava filter'/de OR (('vena cava' OR ivc OR Greenfield:ti,ab) AND (filter*:ti,ab OR filtration:ti,ab))

#7 'compression garment'/de OR (compression AND (sequential OR stocking* OR device*)) OR 'intermittent pneumatic compression device'/de OR 'foot pumps' OR

((pneumatic OR calf) NEAR/3 compression) OR (mechanical AND prophyla*) OR mobilization OR mobilisation

#8 bleed*:ti,ab OR blood*:ti,ab OR hemorrhag*:ti,ab OR bleeding/exp OR 'Blood transfusion'/de OR transfus* OR hematoma* OR haematoma*

#9 #4 OR #5 OR #6 OR #7 OR #8

#10 #3 AND #9

#11 English:la AND [humans]/lim AND [embase]/lim

#12 cadaver/de OR 'in vitro study'/exp OR 'abstract report'/de OR book/de OR editorial/de OR note/de OR (letter/de NOT 'types of study'/exp) OR 'case report':ti

#13 #10 AND #11 NOT #12

COCHRANE LIBRARY

((hip OR hips OR knee OR knees OR joint* OR "lower limb") AND (arthroplast* OR prosthe*)):ti,ab
AND
(thrombos* OR thrombophleb* OR thromboembol* OR thromboprophyla* OR "pulmonary embolism" OR dvt OR vte OR chemoprophyla* OR anticoagulant OR antithromb* OR thrombolytic* OR thromboprophyla* OR "factor Xa inhibitor" OR antiplatelet* OR lovenox OR plavix OR Coumadin OR clopidogrel OR warfarin OR fragmin OR heparin OR enoxaparin OR dalteparin OR innohep OR tinzaparin OR arixtra OR fondaparinux OR angiomax OR hirulog OR refludan OR lepirudin OR aspirin OR argatroban O OR iprivask OR desulfatohirudin OR pradaxa OR dabigatran OR xarelto OR rivaroxaban OR YM150 OR LY517717 OR apixaban OR "vena cava filter" OR "Greenfield filter" OR "foot pumps" OR ((pneumatic OR calf OR stocking*) AND compression) OR (mechanical AND prophyla*) OR mobilization OR mobilization):ti,ab

SEARCH STRATEGY TIER 2 (EXPAND TO ALL SURGICAL PATIENTS)

For potential risk factors for VTED and bleeding with no evidence from hip or knee arthroplasty patients, we conducted a supplementary search in August, 2010, which expanded the search paramaters to include any surgical patients. We also expanded the search to include any surgical patients for IVC filters due to the lack of evidence specific to hip or knee arthroplasty patients.

RISK OF VTE IN SUBPOPULATIONS

Search strategy PubMed/MEDLINE

#1 "Surgical Procedures, Operative"[mh] OR surgery[tw] OR surgical[tw] OR invasive[tw] OR procedure*[tw]

#2 "Venous Thrombosis"[majr:noexp] OR "Venous Thromboembolism"[majr] OR "Pulmonary embolism"[majr] OR ((dvt[titl] OR vte[titl] OR thrombos*[titl] OR thromboembol*[titl] OR ((pulmonary[titl] OR lung[titl] OR lungs[titl]) AND (infarct*[titl] OR embol*[titl] OR clot[titl] OR clots[titl] OR bloodclot*[titl]))) NOT medline[sb])

#3 "risk factors"[titl] OR "risk assessment"[titl] OR "risk stratification"[titl] OR epidemiolog*[titl]

#4 "pelvic bones/surgery"[mh] OR "Bones of Lower Extremity/surgery"[mh] OR knee/surgery[mh] OR "Bed rest"[mh] OR "bed rest" OR confinement[tiab] OR immobilization[tiab] OR mobility[tiab] OR "casts, surgical"[mh] OR "Catheterization, Central Venous"[mh] OR "Inflammatory Bowel Diseases"[mh] OR "Peripheral Vascular Diseases"[mh] OR Lymphedema[mh] OR screening[tiab] OR caprini[tiab]

#5 risk[tw] OR predict*[tw] OR incidence[tw]

#6 #1 AND #2 AND (#3 OR (#4 AND #5))

#7 "1966"[PDat]:"2010"[PDat] AND English[lang]

#8 (animal[mh] NOT human[mh]) OR cadaver[mh] OR cadaver*[titl] OR ((comment[pt] OR editorial[pt] OR letter[pt] OR "historical article"[pt]) NOT "Study Characteristics"[pt]) OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR "case report"[titl] OR pmcbook

#9 #6 AND #7 NOT #8

Search Strategy EMBASE

#1 Surgery/exp/mj OR surgery:ti OR surgical:ti OR invasive:ti OR procedure*:ti

#2 ‘deep vein thrombosis’/mj OR ‘leg thrombosis’/mj OR ‘venous thromboembolism’/exp/mj

#3 Risk/mj OR “risk stratification”:ti OR epidemiolog*:ti

#4 ‘bones of the leg and foot’/exp/dm_su OR leg/exp/dm_su OR ‘bed rest’/de OR confinement:ti,ab OR immobilization/de OR ‘plaster cast’/de OR ‘restricted mobility’ OR ‘limited mobility’ ‘central venous catheterization’/de OR ‘enteritis’/de OR ‘ulcerative colitis’/de OR ‘colon Crohn disease’/de OR ‘Crohn disease’/de OR ‘peripheral vascular disease’/exp OR lymphedema/exp OR ‘screening test’/de OR screening/de OR caprini:ti,ab

#5 Risk/exp OR predict*:ti,ab OR incidence/de

#6 #1 AND #2 AND (#3 OR (#4 AND #5))

#7 English:la AND [humans]/lim AND [embase]/lim

#8 cadaver/de OR 'in vitro study'/exp OR 'abstract report'/de OR book/de OR editorial/de OR note/de OR (letter/de NOT 'types of study'/exp) OR 'case report':ti

#9 #6 AND #7 NOT #8

RISK OF HEMORRHAGE IN SELECTED SUBPOPULATIONS

Search strategy PubMed/MEDLINE

#1 "Postoperative Hemorrhage"[majr] OR (Hemorrhage[majr] AND "postoperative complications"[majr] AND 1966[mhda]:1995[mhda]) OR "Blood Loss, Surgical"[majr] OR (bleeding[titl] AND ("intraoperative complications"[mh] OR "Postoperative Hemorrhage"[mh] OR "Blood Loss, Surgical"[mh] OR (hemorrhage[mh] AND 1966[mhda]:1995[mhda] AND "Surgical procedures, operative"[mh])))

#2 "risk factors"[tw] OR "risk assessment"[tw] OR "risk stratification"[tw] OR epidemiolog*[tw]

#3 "Peptic Ulcer"[mh] OR "Coagulation Protein Disorders"[mh] OR "Intracranial Hemorrhages"[mh] OR "Intracranial Aneurysm"[mh] OR aneurysm*[tiab] OR "Brain Neoplasms"[mh] OR "Liver Diseases"[mh] OR "Tooth Extraction"[mh] OR "Platelet Aggregation Inhibitors"[mh] OR Contusions[mh] OR bruising[tiab] OR epistaxis[tw] OR "Disseminated Intravascular Coagulation"[mh] OR "Blood Coagulation Tests"[mh] OR "Platelet Count"[mh] OR "Platelet Function Tests"[mh] OR "Blood Coagulation Tests"[mh] OR retroperitoneal[tiab] OR "Medical History Taking"[mh] OR ((history[tiab] OR previous[tiab]) AND bleeding[tiab])

#4 risk[tw] OR predict*[tw] OR incidence[tw]

#5 #1 AND (#2 OR (#3 AND #4))

#6 "1966"[PDat]:"2010"[PDat] AND English[lang]

#7 (animal[mh] NOT human[mh]) OR cadaver[mh] OR cadaver*[titl] OR ((comment[pt] OR editorial[pt] OR letter[pt] OR "historical article"[pt]) NOT "Study Characteristics"[pt]) OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR "case report"[titl] OR pmcbook

#8 #5 AND #6 NOT #7

Search Strategy EMBASE

#1 bleeding/mj OR ‘wound hemorrhage’/mj OR ‘postoperative hemorrhage’/mj

#2 Risk/exp OR “risk stratification” OR epidemiolog*

#3 ‘gastrointestinal hemorrhage’/de OR ‘bleeding tendency’/de OR ‘bleeding disorder’/de OR ‘blood clotting factor deficiency’/exp OR ‘dental surgery’/de OR ‘tooth extraction’/de OR ‘brain hemorrhage’/exp OR ‘brain tumor’/exp OR ‘intracranial aneurysm’/exp OR ‘retroperitoneal hemorrhage’/de OR ‘liver disease’/exp OR ‘antithrombocytic agent’/exp OR thrombocytopenia/exp OR ‘skin bruising’/de OR ‘epistaxis’/de OR ‘disseminated intravascular clotting’/de OR ‘blood clotting test’/exp OR ‘blood clotting parameters’/exp OR ‘medical history’/de

#4 English:la AND [humans]/lim AND [embase]/lim

#5 cadaver/de OR 'in vitro study'/exp OR 'abstract report'/de OR book/de OR editorial/de OR note/de OR (letter/de NOT 'types of study'/exp) OR 'case report':ti

#6 #1 AND #2 AND #3 AND #4 NOT #5

IVC IN PATIENTS CONTRAINDICATED FOR CHEMOPROPHYLAXIS

Search strategyPubMed/MEDLINE

#1 "Surgical Procedures, Operative"[mh] OR surgery[titl] OR surgical[titl] OR invasive[titl] OR procedure*[titl]

#2 "Vena cava filters"[mh] OR ("Vena cava, inferior"[mh] AND "Filtration/instrumentation"[mh] AND 1972:1990[mhda]) OR (("vena cava"[tiab] OR ivc[tiab] OR Greenfield[tiab]) AND (filter*[tiab] OR filtration[tiab]) NOT medline[sb]) OR "stockings, compression"[mh] OR (compression[tiab] AND (sequential[tiab] OR stocking*[tiab] OR device*[tiab] OR (bandages[mh] AND 1970:2006[mhda]))) OR "Intermittent Pneumatic Compression Devices"[mh] OR (foot[tiab] AND (pump[tiab] OR pumps[tiab])) OR ((pneumatic[tiab] OR leg[tiab] OR calf[tiab]) AND compression[tiab]) OR (mechanical[tiab] AND prophyla*[tiab])

#3 contraindicat*[tw] OR recurr*[tiab] OR "high risk" OR residual[tiab] OR hemorrhag*[tiab] OR bleeding[tiab] OR chemoprophyla*[tiab] OR anticoagulants[pa] OR "fibrinolytic agents"[pa]

#4 "Venous Thrombosis"[mh:noexp] OR Thrombophlebitis[mh] OR "Venous Thromboembolism"[mh] OR "Pulmonary embolism"[mh] OR thromboprophyla*[tiab] OR ((thrombos* OR thrombophleb* OR thromboembol* OR ((pulmonary OR lung OR lungs) AND (infarct* OR embol* OR clot OR clots OR bloodclot*))) NOT medline[sb])

#5 #1 AND #2 AND #3 AND #4

#6 "1966"[PDat]:"2010"[PDat] AND English[lang]

#7 (animal[mh] NOT human[mh]) OR cadaver[mh] OR cadaver*[titl] OR ((comment[pt] OR editorial[pt] OR letter[pt] OR "historical article"[pt]) NOT "Study Characteristics"[pt]) OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR "case report"[titl] OR pmcbook

#8 #5 AND #6 NOT #7

Search Strategy EMBASE

#1 Surgery/exp OR surgery:ti OR surgical:ti OR invasive:ti OR procedure*:ti

#2 ‘vena cava filter’/mj OR ‘intermittent pneumatic compression devices’/mj OR ‘compression garment’/mj OR ‘foot pump’ OR ‘foot pumps’ OR ‘mechanical prophylaxis’

#3 Contraindicat* OR recur* OR ‘high risk’ OR ‘high risk patient’/de OR (residual AND (‘deep vein thrombosis’/de OR ‘leg thrombosis’/de)) OR ‘chemoprophylaxis’/de

#4 English:la AND [humans]/lim AND [embase]/lim

#5 cadaver/de OR 'in vitro study'/exp OR 'abstract report'/de OR book/de OR editorial/de OR note/de OR (letter/de NOT 'types of study'/exp) OR 'case report':ti

#6 #1 AND #2 AND #3 AND #4 NOT #5

APPENDIX VI
QUALITY AND APPLICABILITY QUESTIONS
STUDIES OF INTERVENTIONS
QUALITY

Quality questions are separately asked for every outcome reported in a study. The quality questions that are asked vary according to the study's design. Different questions are asked when a study is a controlled study with a contemporary control group, a crossover study, a historically controlled study, or a case series. A total of 20 questions are asked for each design. The questions asked for each design, the domain that each question addresses, and the answers that give rise to the highest possible strength of evidence within each design are shown in the table below.

Quality Questions and Domains for Four Designs of Studies of Interventions

Domain	Question:	Parallel, Contemporary Controls	Crossover Trials	Historical Controls	Case Series
Group Assignment	Stochastic	Yes	Yes	No	No
Group Assignment	Quasi-random Assignment	No	No	No	na*
Group Assignment	Matched Groups	No	No	Yes	No
Group Assignment	Consecutive Enrollment	na	na	na	Yes
Prospective	Prospective	Yes	Yes	Yes	Yes
Blinding	Blinded Patients	Yes	Yes	No	No
Blinding	Blinded Assessors	Yes	Yes	No	No
Blinding	Blinding Verified	Yes	Yes	No	No
Group Comparability	Allocation Concealment	Yes	Yes	No	No
Group Comparability	>80% Follow-up	Yes	Yes	No	Yes
Group Comparability	<20% Completion Difference	Yes	Yes	No	No
Group Comparability	Similar Baseline Outcome Values	Yes	na	Yes	No
Group Comparability	Comparable Pt. Characteristics	Yes	na	Yes	No
Group Comparability	Same Control Group Results	na	Yes	na	na
Group Comparability	Same Experimental Group Results	na	Yes	na	na
Treatment Integrity	Same Centers	Yes	Yes	Yes	No
Treatment Integrity	Same Treatment Duration in and across All Groups	Yes	Yes	Yes	No
Treatment Integrity	Same Concomitant Treatment to All Groups (controlled studies only)	Yes	Yes	Yes	na
Treatment Integrity	No Confounding Treatment (case series only)	na	na	na	Yes
Measurement	Same Instruments	Yes	Yes	Yes	Yes
Measurement	Valid Instrument	Yes	Yes	Yes	Yes
Bias	Article & Abstract Agree	Yes	Yes	Yes	Yes

Domain	Question:	Parallel, Contemporary Controls	Crossover Trials	Historical Controls	Case Series
Bias	All Outcomes Reported	Yes	Yes	Yes	Yes
Bias	A Priori Analysis	Yes	Yes	Yes	Yes
Statistical Power	Statistically Significant	High	High	High	High
Statistical Power	Number of patients in analysis	See below for further information			

*"na" means "not asked"

The statistical power domain is assessed differently from the other domains. We characterize this domain as free from flaws if any one of the following is true:

- The results of a statistical test on the outcome of interest were statistically significant (it is obvious that the study must have had enough power if it found statistically significant results).
- The results of a statistical test of the outcome of interest were not statistically significant (or it was unclear whether the results were statistically significant), and the study was either an uncontrolled study in which data from 34 or more patients were included in the statistical analysis of the outcome of interest OR a controlled study in which data from 128 or more patients were included in the analysis of the outcome of interest.
- The study's results for the outcome of interest are used in a meta-analysis. We make this assumption because one reason for performing a meta-analysis is to compensate for the low statistical power of individual studies. Implicit in this assumption is a second assumption; that the power of the meta-analysis will be sufficient to detect an effect as statistically significant.

We term the power domain as flawed if all of the following are true:

- The results of a statistical test on the outcome of interest were either not statistically significant or it was unclear whether the results of statistical test on the outcome of interest were statistically significant.
- The study was an uncontrolled study in which data from fewer than 15 patients were included in the analysis of the outcome of interest OR the study was a controlled study in which data from fewer than 52 patients were included in the analysis of the outcome of interest.
- The results on the outcome of interest will not be used in a meta-analysis.

The numbers of used to determine whether a study is of sufficient power are based on Cohen's[49] definitions of small, medium, and large effects. To compute the number of patients needed for an uncontrolled study that uses a pretest/posttest design, we assume a paired, 2-tailed t-test on the pre- and post-treatment results. We then determine whether the number of patients in the study was sufficient to detect large effect (defined as a standardized mean difference of ≥ 0.8) while assuming and an alpha of 0.05 as the

significance level, and 80% power. If a study does not have the ability to detect even a large effect as statistically significant, we characterize it as underpowered, and term the power domain as flawed.

To compute the number of patients needed for a controlled study, we assume a 2-tailed t-test of independent groups that contained an equal number of patients, and then determine whether the number of patients in the study was a large effect, again assuming an alpha of 0.05 and 80% power. As above, we term a study as underpowered and the Power domain as flawed if the study did not enroll enough patients to detect a large effect size, and adequately powered if it enrolled enough patients to detect a small effect.

APPLICABILITY

We determine the applicability of a study using the PRECIS instrument.[22] This instrument consists of 10 questions. The domains to each question applies is shown in the table below.

Applicability Questions and the Domains for Studies of Interventions

Question	Domain
All Types of Patients Enrolled	Participants
Flexible Instructions to Practitioners	Interventions and Expertise
Full Range of Expt'l Practitioners	Interventions and Expertise
Usual Practice Control	Interventions and Expertise
Full Range of Control Practitioners	Interventions and Expertise
No Formal Follow-up	Interventions and Expertise
Usual and Meaningful Outcome	Interventions and Expertise
Compliance Not Measured	Compliance and Adherence
No Measure of Practitioner Adherence	Compliance and Adherence
All Patients in Analysis	Analysis

SCREENING AND DIAGNOSTIC TESTS

QUALITY

We evaluate the quality of screening and diagnostic tests using the QUADAS instrument.[23] The 14 QUADAS questions and the quality domains addressed by each are shown in the table below.

QUADAS Questions and Domains

QUADAS Question:	Domain
Full Patient Spectrum	Participants
Patient Selection Criteria Described	Reporting
Ref. Std. Classifies Condition	Reference Test
Disease Progression Absent	Study Design
Partial Verification Avoided	Study Design
Differential Verification Avoided	Study Design
Independent Ref. Std. and Index Test	Reference Test
Index Test Execution Described	Reporting
Reference Std. Execution Described	Reporting
Index Test Interpreted without Ref. Std. Results	Index Test
Ref. Test Interpreted without Index Test Results	Reference Test
Usual Clinical Data Available	Information
Uninterpretable /Indeterminate Results Reported	Reporting
Withdrawals Explained	Reporting

Nine of the QUADAS instrument questions address quality and five address reporting. Quality and reporting are distinct. Quality addresses whether a study's results are "believable" whereas reporting addresses the how well the design, conduct, and analysis of a study were described in a published article. The questions about reporting are:

- Patient Selection Criteria Described
- Index Test Execution Described
- Reference Std. Execution Described
- Uninterruptable/Indeterminate Results Reported
- Withdrawals Explained

The remaining QUADAS questions address quality. Some flaws in quality flaws are so serious that they have a major effect on the quality of a study. These serious flaws are:

- Spectrum bias (Spectrum bias occurs when a study does not enroll the full spectrum of patients who are seen in clinical practice. For example, a diagnostic case control study enrolls only those known to be sick and those known to be well, a patient population quite different from that seen in practice. Because diagnostic case control studies enroll only the easy to diagnose patients, these kinds of studies typically overestimate the abilities of a diagnostic test.)
- Failure to give all patients the reference standard regardless of the index test results

- Non-independence of the reference test and the index text

Because the QUADAS instrument contains reporting questions, quality questions, and questions about whether a study flaw was serious, we arrive at quality ratings in a stepwise answer. First, we determine if one or more serious flaw is present. First, we determine whether any serious flaws are present. If so the quality of evidence is automatically set to "Very Low". "Serious flaws" are present only if the relevant QUADAS question is answered "No". We do not use "Unclear" answers to indicate the presence of a serious flaw.

If no serious flaws are present, we then determine a quality rating using all domains *except* the reporting domain. A domain is considered flawed if there are one or more "No" answer or two or more "Unclear" to the questions that address that domain. The relationship between the five quality domains and the reporting domain are shown in the table below:

Relationship between Quality and Domain Scores for Screening/Diagnostic Tests

Number of Flawed Domains	Strength of Evidence
0	High
1	Moderate
2	Low
≥3	Very Low

Finally, we use the reporting domain to modify the quality determined in the second step. If one or two of the five QUADAS reporting questions are answered "No", the quality rating is not changed. If three questions are answered "No" the quality is reduced by one category (e.g., from "High" to "Moderate), if four reporting questions are "No", the quality is reduced by two categories (e.g., from "High" to "Low"), and if all five reporting questions are answered "No" the quality is reduced by three categories. (e.g., from "High" to "Very Low"). Two "Unclear" answers are counted as equivalent to one "No" answer in the reporting domain. We also set "floor" so that no study can ever have less than "Very Low" quality. For example, evidence classed as "Low" quality at the second step of our quality appraisal cannot be reduced below "Very Low" even if all of the reporting questions are answered "No."

APPLICABILITY

We evaluate the evidence about screening and diagnostic tests using seven questions that fall into four domains. Some of these questions are from the PRECIS instrument. However, because the PRECIS instrument was designed to evaluate studies of interventions, some of the original questions have been deleted and others have been added. The applicability questions that APPRAISE uses for screening and diagnostics, and the domains to which they relate are shown in the table below. For instructions on how to answer these questions, click on the "Help" button shown on the form that displays these questions.

Applicability Questions and Domains for Screening and Diagnostic Tests

Question	Domain
All Types of Patients Enrolled	Participants
Flexible Instructions about Index Test Methods to Practitioners	Index Test
Full Range of Practitioners & Settings	Index Test
Full Range of Index Text Readers	Index Test
Index Test Usable in Routine Practice	Index Test
Patient's Outcomes Measured	Directness
All Patients in Analysis	Analysis

STUDIES OF PROGNOSTICS

QUALITY

We ask one or more questions to evaluate each of the five domains for the quality of the evidence on a prognostic. Most questions about prognostics are from Bagley and Golomb[50] and Concato et al.[51] All questions on prognostics are answered "Yes" or "No."

Quality questions are separately asked for every prognostic variable reported in a study. A minimum of nine questions are asked. When a prognostic variable is one that predicts a dichotomous outcome an additional question is asked, and when the prognostic is one that attempts to predict response to a treatment yet another question is asked. The questions asked, and the domain that each question addresses, are shown in the table below:

Quality Questions and Domains for Studies of Prognostics

Question	Domain
Prospective	Prospective
At Least 10 Patients per Important Variable	Power
At Least 10 Events*	Power
All Important Variables Screened for Entry Into Model	Analysis
Interactions Tested	Analysis
Collinearity Absent	Analysis
Primary Analysis (not subgroup or post hoc)	Analysis
Statistically Significant Fit	Model
Article and Abstract Agree	Investigator Bias
Results Reported for All Variables Studies	Investigator Bias
Blinded Data Analysts**	Investigator Bias

*Asked only if the variable predicted by the prognostic is dichotomous.
**Asked only if the prognostic variable is derived from a study that attempts to predict which patients respond best to a treatment.

APPLICABILITY

We evaluate the applicability of evidence about prognostics using six questions that fall into three domains. We separately evaluate applicability for each prognostic a study reports. All of questions about the applicability of evidence on prognostics are answered "Yes" or "No". The six questions and the domains they address are shown in the table below.

Applicability Questions and Domains for Studies of Prognostics

Question	Domain
Full Spectrum of Patients	Patients
All Patients in Analysis	Patients
No Stepwise Analysis	Analysis
Unambiguous Coding Scheme	Analysis
Model Validated	Analysis
Clinically Meaningful Outcome	Outcome

APPENDIX VII
FORM FOR ASSIGNING GRADE OF RECOMMENDATION

GUIDELINE RECOMMENDATION_____

PRELIMINARY GRADE OF RECOMMENDATION: _____

STEP 1: LIST BENEFITS AND HARMS

Please list the benefits (as demonstrated by the systematic review) of the intervention.

Please list the harms (as demonstrated by the systematic review) of the intervention.

Please list the benefits for which the systematic review is not definitive.

Please list the harms for which the systematic review is not definitive.

STEP 2: IDENTIFY CRITICAL OUTCOMES

Please circle the above outcomes that are critical for determining whether the intervention is beneficial and whether it is harmful.

Are data about critical outcomes lacking to such a degree that you would lower the preliminary strength of the recommendation?

What is the resulting strength of recommendation?

STEP 3: EVALUATE APPLICABILITY OF THE EVIDENCE

Is the applicability of the evidence for any of the critical outcomes so low that substantially worse results are likely to be obtained in actual clinical practice?

Please list the critical outcomes backed by evidence of doubtful applicability.

Should the strength of recommendation be lowered because of low applicability?

What is the resulting strength of recommendation?

STEP 4: BALANCE BENEFITS AND HARMS

Are there trade-offs between benefits and harms that alter the strength of recommendation obtained in STEP 3?

What is the resulting strength of recommendation?

STEP 5 CONSIDER STRENGTH OF EVIDENCE

Does the strength of the existing evidence alter the strength of recommendation obtained in STEP 4?

What is the resulting strength of recommendation?

NOTE: Because we are not performing a formal cost analyses, you should only consider costs if their impact is substantial.

APPENDIX VIII
RULES FOR MAKING OPINION BASED RECOMMENDATIONS

A guideline can contain recommendations that are backed by little or no data. Under such circumstances, work groups often issue opinion-based recommendations. Although doing so is sometimes acceptable in an evidence-based guideline (expert opinion is a form of evidence), it is also important to avoid constructing a guideline that liberally uses expert opinion; research shows that expert opinion is often incorrect.

Opinion-based recommendations are developed only if they address a vitally important aspect of patient care. For example, constructing an opinion-based recommendation in favor of taking a history and physical is warranted. Constructing an opinion-based recommendation in favor of a specific modification of a surgical technique is seldom warranted. To ensure that an opinion-based recommendation is absolutely necessary, the AAOS has adopted rules to guide the content of the rationales that underpin such recommendations. These rules are based on those outlined by the US Preventive Services Task Force (USPSTF).[30] Specifically, rationales based on expert opinion must:

- Not contain references to or citations from articles not included in the systematic review that underpins the recommendation.

- Not contain the AAOS guideline language "We Recommend", "We suggest" or "The practitioner might".

- Contain an explanation of the potential preventable burden of disease. This involves considering both the incidence and/or prevalence of the disease, disorder, or condition and considering the associated burden of suffering. To paraphrase the USPSTF, when evidence is insufficient, provision of a treatment (or diagnostic) for a serious condition might be viewed more favorably than provision of a treatment (or diagnostic) for a condition that does not cause as much suffering. The AAOS (like the USPSTF) understand that evaluating the "burden of suffering" is subjective and involves judgment. This evaluation should be informed by patient values and concerns. The considerations outlined in this bullet make it difficult to recommend new technologies. It is not appropriate for a guideline to recommend widespread use of a technology backed by little data and for which there is limited experience. Such technologies are addressed in the AAOS' Technology Overviews.

- Address potential harms. In general, "When the evidence is insufficient, an intervention with a large potential for harm (such as major surgery) might be viewed less favorably than an intervention with a small potential for harm (such as advice to watch less television)."[30]

- Address apparent discrepancies in the logic of different recommendations. Accordingly, if there are no relevant data for several recommendations and the work group chooses to issue an opinion-based recommendation in some cases but chooses not to make a recommendation in other cases, the rationales for the opinion-based recommendations must explain why this difference exists. Information garnered from the previous bullet points will be helpful in this regard.

- Consider current practice. The USPSTF specifically states that clinicians justifiably fear that not doing something that is done on a widespread basis will lead to litigation.[30]The consequences of not providing a service that is neither widely available nor widely used are less serious than the consequences of not providing a treatment accepted by the medical profession and thus expected by patients. Discussions of available treatments and procedures rely on mutual communication between the patient's guardian and physician, and on weighing the potential risks and benefits for a given patient. The patient's "expectation of treatment" must be tempered by the treating physician's guidance about the reasonable outcomes that the patient can expect.

- Justify, why a more costly device, drug, or procedure is being recommended over a less costly one whenever such an opinion-based recommendation is made.

Work group members write the rationales for opinion based recommendations on the first day of the final work group meeting. When the work group re-convenes on the second day of its meeting, it will vote on the rationales. The typical voting rules will apply. If the work group cannot adopt a rationale after three votes, the rationale and the opinion-based recommendation will be withdrawn, and a "recommendation" stating that the group can neither recommend for or against the recommendation in question will appear in the guideline.

Discussions of opinion-based rationales may cause some members to change their minds about whether to issue an opinion-based recommendation. Accordingly, at any time during the discussion of the rationale for an opinion-based recommendation, any member of the work group can make a motion to withdraw that recommendation and have the guideline state that the work group can neither recommend for or against the recommendation in question.

CHECKLIST FOR VOTING ON OPINION BASED RECOMMENDATIONS

When voting on the rationale, please consider the following:

1. Does the recommendation affect a substantial number of patients or address treatment (or diagnosis) of a condition that causes death and/or considerable suffering?

2. Does the recommendation address the potential harms that will be incurred if it is implemented and, if these harms are serious, does the recommendation justify;

    a. why the potential benefits outweigh the potential harms and/or

    b. why an alternative course of treatment (or diagnostic workup) that involves less serious or fewer harms is not being recommended?

3. Does the rationale explain why the work group chose to make a recommendation in the face of minimal evidence while, in other instances, it chose to make no recommendation in the face of a similar amount of evidence?

4. Does the rationale explain that the recommendation is consistent with current practice?

5. If relevant, does the rationale justify why a more costly device, drug, or procedure is being recommended over a less costly one?

VOTING BY THE NOMINAL GROUP TECHNIQUE

Voting on guideline recommendations will be conducted using a modification of the nominal group technique (NGT), a method previously used in guideline development. [31] Briefly each member of the guideline Work Group ranks his or her agreement with a guideline recommendation or performance measure on a scale ranging from 1 to 9 (where 1 is "extremely inappropriate" and 9 is "extremely appropriate"). Consensus is obtained if the number of individuals who do not rate a measure as 7, 8, or 9 is statistically non-significant (as determined using the binomial distribution). Because the number of Work Group members who are allowed to dissent with the recommendation depends on statistical significance, the number of permissible dissenters varies with the size of the work group. The number of permissible dissenters for several work group sizes is given in the table below:

Work Group Size	Number of Permissible Dissenters
≤3	Not allowed. Statistical significance cannot be obtained
4-5	0
6-8	1
9	1 or 2

The NGT is conducted by first having members vote on a given recommendation/performance measure without discussion. If the number of dissenters is "permissible", the recommendation/measure is adopted without further discussion. If the number of dissenters not permissible, there is further discussion to see whether the disagreement(s) can be resolved. Three rounds of voting are held to attempt to resolve disagreements. If disagreements are not resolved after three voting rounds, no recommendation/measure is adopted.

APPENDIX IX
STRUCTURED PEER REVIEW FORM

Review of any AAOS confidential draft allows us to improve the overall guideline but does not imply endorsement by any given individual or any specialty society who participates in our review processes. The AAOS review process may result in changes to the documents; therefore, endorsement cannot be solicited until the AAOS Board of Directors officially approves the final guideline.

Reviewer Information:

Name of Reviewer_____

Address_____

City_____ State_____ Zip Code_____

Phone _____Fax _____E-mail_____

Specialty Area/Discipline: _____

Work setting: _____Credentials: _____

May we list you as a Peer Reviewer in the final Guidelines (GL)? ☐ Yes ☐ No
If you do not wish to be listed, your name will be removed for identification purposes. However, your COI will still be available for review with the comments you have made.

Are you reviewing this guideline as a representative of a professional society? ☐ Yes ☐ No

If yes, may we list your society as a reviewer of this guideline? ☐ Yes ☐ No

Society Name: _____
(Listing the specialty society as a reviewing society does not imply or otherwise indicate endorsement of this guideline.)

Conflicts of Interest (COI): All Reviewers must declare their conflicts of interest.

If the boxes below are not checked and/or the reviewer does not attach his/her conflicts of interest, the reviewer's comments will not be addressed by the AAOS nor will the reviewer's name or society be listed as a reviewer of this GL. If a committee reviews the guideline, only the chairperson/or lead of the review must declare their relevant COI.

☐ **I have declared my conflicts of interest on page 2 of this form.**

☐ **I have declared my conflicts of interest in the AAOS database; my customer # is** _____

☐ **I understand that the AAOS will post my declared conflicts of interest with my comments concerning review of this guideline or technology overview on the AAOS website.**

REVIEWER CONFLICT OF INTEREST - The Orthopaedic Disclosure Program

Each item below requires an answer. Please report information for the last 12-months as required by the Accreditation Council for Continuing Medical Education (ACCME) guidelines.

Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device? If YES, please identify product or device:	☐ Yes ☐ No
Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company? If YES, please identify company:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds) If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers? If YES, please identify publisher:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication? If YES, please identify:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the Board of Directors or a committee of any medical and/or orthopaedic professional society? If YES, please identify:	☐ Yes ☐ No

Reviewer Instructions

Please read and review this Draft Clinical Practice Guideline and its associated Technical Report with particular focus on your area of expertise. Your responses are confidential and will be used only to assess the validity, clarity and accuracy of the interpretation of the evidence. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the guideline and Technical Report. If you need more space than is provided, please attach additional pages.

Please complete and return this form electronically to wies@aaos.org or fax the form back to Jan Wies at (847) 823-9769. Thank you in advance for your time in completing this form and giving us your feedback. We value your input and greatly appreciate your efforts. Please send the completed form and comments by end of day **DATE**.

Please indicate your level of agreement with each of the following statements by placing an "X" in the appropriate box.

	Disagree	Somewhat Disagree	Somewhat Agree	Agree
1. The recommendations are clearly stated	☐	☐	☐	☐
2. There is an explicit link between the recommendations and the supporting evidence	☐	☐	☐	☐
3. Given the nature of the topic and the data, all clinically important outcomes are considered	☐	☐	☐	☐
4. The guideline's target audience is clearly described	☐	☐	☐	☐
5. The patients to whom this guideline is meant to apply are specifically described	☐	☐	☐	☐
6. The criteria used to select articles for inclusion are appropriate	☐	☐	☐	☐
7. The reasons why some studies were excluded are clearly described	☐	☐	☐	☐
8. All important studies that met the article inclusion criteria are included	☐	☐	☐	☐
9. The validity of the studies is appropriately appraised	☐	☐	☐	☐
10. The methods are described in such a way as to be reproducible.	☐	☐	☐	☐
11. The statistical methods are appropriate to the material and the objectives of this guideline	☐	☐	☐	☐
12. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed	☐	☐	☐	☐
13. Health benefits, side effects, and risks are adequately addressed	☐	☐	☐	☐
14. The writing style is appropriate for health care professionals.	☐	☐	☐	☐
15. The grades assigned to each recommendation are appropriate	☐	☐	☐	☐

COMMENTS

Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the guideline and Technical Report

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OVERALL ASSESSMENT

Would you recommend these guidelines for use in practice? (check one)

☐ Strongly recommend

☐ Recommend (with provisions or alterations)

☐ Would not recommend

☐ Unsure

APPENDIX X
PARTICIPATING PEER REVIEW ORGANIZATIONS

Participation in the AAOS peer review process does not constitute an endorsement of this guideline by the participating organization.

Peer review of the draft guideline is completed by external organizations with an interest in the guideline. Outside peer reviewers are solicited for each AAOS guideline and consist of experts in the guideline's topic area. These experts represent professional societies other than AAOS and are nominated by the guideline work group prior to beginning work on the guideline. For this guideline, twenty-six outside peer review organizations were invited to review the draft guideline and all supporting documentation. Eleven societies participated in the review of the guideline on Preventing Venous Thromboembolic Disease in patients Undergoing Elecitve Hip or Knee Arthroplasty. Seven organizations explicitly consented to be listed as a peer review organization in this appendix.

The organizations that reviewed the document and consented to be listed as a peer review organization are listed below:

American Academy of Family Physicians (AAFP)

American Association of Hip and Knee Surgeons (AAHKS)

American College of Chest Physicians (ACCP)

American Society of Regional Anesthesia and Pain Medicine (ASRAPM)

American Surgical Association, Society of Surgical Chairs

International Society on Thrombosis and Hemostasis

Joint Commission on Accreditation of Healthcare Organizations

Individuals who participated in the peer review of this document and gave their explicit written consent to be listed as reviewers of this document are:

Ethan Balk, M.D. MPH

Henri Bounameaux, M.D.

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Yngve Falck-Ytter, M.D.

Terese T. Horlocker, M.D.

K. Craig Kent M.D.

Gregory R. Wise, MD, CPE, FACP, FACHE, CPHQ

These reviewers' comments are available with all other guideline documentation on our website.

Participation in the AAOS guideline peer review process does not constitute an endorsement of the guideline by the participating organizations or the individuals listed above nor does it is any way imply the reviewer supports this document.

PUBLIC COMMENTATORS

A period of public commentary follows the peer review of the draft guideline. If significant non-editorial changes are made to the document as a result of public commentary, these changes are also documented and forwarded to the AAOS bodies that approve the final guideline.

Public commentators who gave explicit consent to be listed in this document include the following:

Participation in the AAOS guideline public commentary review process does not constitute an endorsement of the guideline by the participating organizations or the individual listed nor does it in any way imply the reviewer supports this document.

APPENDIX XI

INTERPRETING FOREST PLOTS

We use descriptive diagrams known as forest plots to present data from studies comparing the differences in outcomes between two treatment groups when a meta-analysis has been performed (combining results of multiple studies into a single estimate of overall effect). The estimate of overall effect is presented at the bottom of the graph using a diamond to illustrate the confidence intervals of the estimated overall effect. The odds ratio is the effect measure used to depict differences in outcomes between the two treatment groups of a study. The horizontal line running through each point represents the 95% confidence interval for that point. The solid vertical line represents "no effect" where the odds ratio is equal to one.

ABBREVIATIONS USED IN THIS REPORT

µL	microliter
95% CI	95% Confidence Interval
AAOS	American Academy of Orthopaedic Surgeons
APC	Activated protein C
aPTT	activated partial thromboplastin time
BMI	Body mass index
BOC	AAOS Board of Councilors
BOD	AAOS Board of Directors
BOS	AAOS Board of Specialty Societies
COI	Conflict of interest
CORQ	AAOS Council on Research and Quality
CPG	Clinical practice guidelines
dL	deciliter
DVT	Deep vein thrombosis
EBM	Evidence-based medicine
EBP	Evidence-based practice
EBPC	AAOS Evidence-Based Practice Committee
FDA	United States Food and Drug Administration
g	gram
GCS	Graduated compression stocking
GI	Gastrointestinal
GOC	AAOS Guidelines Oversight Committee
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HD	High dose
HR	Hazard ratio
INR	International normalized ratio
IOM	Institute of Medicine
IPC	Intermittent pneumatic compression
IU	International unit
IVC	Inferior vena cava
LD	Low dose
LMWH	Low molecular weight heparin

µL	microliter
Mg	milligram
mL	milliliter
MR	Magnetic resonance
NR	Not reported
NS	Not significant
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
OREF	Orthopaedic Research and Education Foundation
ORS	Orthopaedic Research Society
PE	Pulmonary embolism
PRECIS	pragmatic-explanatory continuum indicator summary
PT	Prothrombin time
PTT	Partial throboplastin time
QUADAS	Quality Assessment of Diagnostic Accuracy Studies instrument
RR	Relative risk
SCD	Sequential compression device
THA	Total hip arthroplasty
THR	Total hip replacement
TKA	Total knee arthroplasty
TKR	Total knee replacement
USPSTF	United States Preventive Services Task Force
VTE	Venous thromboembolism
VTED	Venous thromboembolic disease

APPENDIX XII
CONFLICT OF INTEREST

All members of the AAOS work group disclosed any conflicts of interest prior to the development of the recommendations for this guideline. Conflicts of interest are disclosed in writing with the American Academy of Orthopaedic Surgeons via a private on-line reporting database and also verbally at the recommendation approval meeting.

Disclosure Items: (n) = Respondent answered 'No' to all items indicating no conflicts. 1=Board member/owner/officer/committee appointments; 2= Medical/Orthopaedic Publications; 3= Royalties; 4= Speakers bureau/paid presentations;5A= Paid consultant; 5B= Unpaid consultant; 6= Research or institutional support from a publisher; 7= Research or institutional support from a company or supplier; 8= Stock or Stock Options; 9= Other financial/material support from a publisher; 10= Other financial/material support from a company or supplier.

APPENDIX XIII
QUALITY AND APPLICABILITY OF INCLUDED STUDIES
ROUTINE SCREENING
Table 47 Quality and Applicability of Treatment Studies for Routine Screening

●: Domain free of flaws

○: Domain flaws present

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Schmidt 2003	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Schmidt 2003	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Schmidt 2003	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Schmidt 2003	Asymptomatic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Robinson 1997	Symptomatic PE	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Robinson 1997	Symptomatic proximal DVT	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Robinson 1997	Fatal PE	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate

Table 47 Quality and Applicability of Treatment Studies for Routine Screening

●: Domain free of flaws

○: Domain flaws present

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Robinson 1997	Major bleeding	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Pellegrini 2005	Readmission for PE	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate
Pellegrini 2005	Fatal PE	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate
Pellegrini 2005	Readmission for DVT	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate
Pellegrini 2006	Readmission for PE	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate
Pellegrini 2006	Fatal PE	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate
Pellegrini 2006	Readmission for DVT	●	●	○	○	○	○	●	●	Low	○	●	●	●	Moderate

Table 48 Quality and Applicability of Diagnostic Studies for Routine Screening

●: Domain free of flaws

○: Domain flaws present

Study	Test	Reporting (Penalty)	Index Test	Reference Test	Participants	Information	Study Design	*Quality*	Participants	Index Test	Directness of Results	Analysis	*Applicability*
Bounameaux 1998	D-dimer	○	●	●	●	●	●	High	●	○	●	○	Moderate
Abraham 1999	D-dimer	○	●	●	●	●	○	Moderate	●	○	○	○	Moderate
Niimi 2010	D-dimer	○	●	●	●	●	○	Moderate	●	○	●	○	Moderate
Larcom 1996	MR Venography	○	●	●	●	●	●	High	●	●	○	○	Moderate

RISK FACTORS FOR VTED

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Fujita 2000	Age	●	●	○	○	●	Low	●	○	○	Moderate
Joseph 2005	Age	●	●	○	○	●	Low	●	○	○	Moderate
Warwick 2007	Age	●	●	○	○	●	Low	○	○	●	Moderate
Leizorovicz 2007	Age	●	●	○	○	●	Low	●	○	○	Moderate
Pedersen 2010	Age	●	●	○	○	●	Low	●	●	●	High
Guijarro 2011	Age	●	●	○	○	●	Low	●	○	●	Moderate
Guijarro 2011	Cancer	●	●	○	○	●	Low	●	○	●	Moderate
Leizorovicz 2007	Cancer	●	●	○	○	●	Low	●	○	○	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Pedersen 2010	Cancer	●	●	○	○	●	Low	●	●	●	High
Guijarro 2011	Cardiovascular Diseases	●	●	○	○	●	Low	●	○	●	Moderate
Pedersen 2010	Cardiovascular Diseases	●	●	○	○	●	Low	●	●	●	High
Leizorovicz 2007	Chronic Heart Failure	●	●	○	○	●	Low	●	○	○	Moderate
Leizorovicz 2007	Chronic Respiratory Failure	●	●	○	○	●	Low	●	○	○	Moderate
Guijarro 2011	Diabetes	●	●	○	○	●	Low	●	○	●	Moderate
Pedersen 2010	Diabetes	●	●	○	○	●	Low	●	●	●	High
Lemos 1992	Estrogen	○	○	○	○	●	Very Low	○	○	●	Moderate
Joseph 2005	History of Blood Clotting Disorders	●	●	○	○	●	Low	●	○	○	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Lowe 1999	History of Blood Clotting Disorders	●	●	○	○	●	Low	○	○	○	Low
Warwick 2007	History of Heart Disease	●	●	○	○	●	Low	○	○	●	Moderate
Joseph 2005	History of Malignancy	●	●	○	○	●	Low	●	○	○	Moderate
Joseph 2005	History of VTE	●	●	○	○	●	Low	●	○	○	Moderate
Warwick 2007	History of VTE	●	●	○	○	●	Low	○	○	●	Moderate
Pedersen 2010	History of VTE	●	●	○	○	●	Low	●	●	●	High
Pearse 2007	Hormone Replacement Therapy	○	○	○	○	●	Very Low	●	○	○	Moderate
Hurbanek 2004	Hormone Replacement Therapy	○	●	○	○	●	Very Low	○	○	○	Low
White 2000	Hormone Replacement Therapy	○	●	○	●	●	Low	○	○	●	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Guijarro 2011	Hypertension	●	●	○	○	●	Low	●	○	●	Moderate
Gandhi 2009	Hypertension	○	●	○	○	●	Very Low	●	○	●	Moderate
Ryu 2010	Hypertension	○	○	○	○	●	Very Low	●	○	●	Moderate
Mraovic 2010	Hypertension	○	○	○	○	●	Very Low	○	○	●	Moderate
Guijarro 2011	Lung Disease	●	●	○	○	●	Low	●	○	●	Moderate
Leizorovicz 2007	Lung Disease	●	●	○	○	●	Low	●	○	○	Moderate
Guijarro 2011	Obesity	●	●	○	○	●	Low	●	○	●	Moderate
Fujita 2000	Obesity	●	●	○	○	●	Low	●	○	○	Moderate
Joseph 2005	Obesity	●	●	○	○	●	Low	●	○	○	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Warwick 2007	Obesity	●	●	○	○	●	Low	○	○	●	Moderate
Leizorovicz 2007	Obesity	●	●	○	○	●	Low	●	○	○	Moderate
Fujita 2000	Operating Time	●	●	○	○	●	Low	●	○	○	Moderate
Joseph 2005	Operating Time	●	●	○	○	●	Low	●	○	○	Moderate
Leizorovicz 2007	Operating Time	●	●	○	○	●	Low	●	○	○	Moderate
Lemos 1992	Peripheral Vascular Disease	○	○	○	○	●	Very Low	○	○	●	Moderate
SooHoo 2010	Peripheral Vascular Disease	○	●	○	○	●	Very Low	●	○	●	Moderate
Mahomed 2003	Race	○	●	○	○	●	Very Low	●	○	●	Moderate
Mahomed 2005	Race	○	●	○	○	●	Very Low	●	○	●	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Memtsoudis 2009	Race	○	●	○	○	●	Very Low	●	○	●	Moderate
SooHoo 2006	Race	○	●	○	○	●	Very Low	●	○	●	Moderate
Keeney 2006	Race	○	○	○	○	●	Very Low	●	○	○	Moderate
White 1998	Race	○	●	○	○	●	Very Low	●	○	●	Moderate
SooHoo 2010	Race	○	●	○	○	●	Very Low	●	○	●	Moderate
Joseph 2005	Recent Surgery	●	●	○	○	●	Low	●	○	○	Moderate
Joseph 2005	Restricted Mobility	●	●	○	○	●	Low	●	○	○	Moderate
Nathan 2003	Restricted Mobility	●	○	○	○	●	Very Low	○	○	○	Low
Beksac 2006	Smoking	●	○	○	○	●	Very Low	●	○	●	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Eriksson 1991	Smoking	●	○	○	○	○	Very Low	●	○	○	Moderate
Lowe 1999	Smoking	●	●	○	○	●	Low	○	○	○	Low
Leizorovicz 2007	Smoking	●	●	○	○	●	Low	●	○	○	Moderate
Won 2011	Smoking	●	○	○	○	○	Very Low	●	○	●	Moderate
Eriksson 1991	Varicose Veins	●	○	○	○	○	Very Low	●	○	○	Moderate
Lowe 1999	Varicose Veins	●	●	○	○	●	Low	○	○	○	Low
Leizorovicz 2007	Varicose Veins	●	●	○	○	●	Low	●	○	○	Moderate
Warwick 2007	History of Venous Stasis	●	●	○	○	●	Low	○	○	●	Moderate
Pearse 2007	Venous Stasis	○	○	○	○	●	Very Low	●	○	○	Moderate

Table 49. Quality and Applicability of Prognostic Studies for Risk Factors for VTED

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Hatef 2008	Screening Instrument	○	●	○	○	●	Very Low	○	○	○	Low
Kosir 1996	Screening Instrument	○	○	○	○	●	Very Low	○	○	○	Low
Bahl 2010	Screening Instrument	○	●	○	○	●	Very Low	○	○	○	Low
Bahl 2010	Inflammatory Bowel Disease	○	○	○	○	●	Very Low	○	○	○	Low
Bahl 2010	Central Venous Access	○	○	○	○	●	Very Low	○	○	○	Low
Frizzelli 2008	Central Venous Catheter	●	○	○	○	●	Very Low	○	○	●	Moderate

RISK FACTORS FOR BLEEDING

Table 50. Quality and Applicability of Prognostic Studies for Risk Factors for Bleeding

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Shih 2004	Cirrhosis	○	●	○	○	●	Very Low	○	○	●	Moderate
Sikkema 2010	Hemophilia	○	●	○	○	●	Very Low	○	○	●	Moderate
Innocenti 2007	Hemophilia	●	○	○	○	●	Very Low	○	○	●	Moderate
Kim 2000	Aplastic Anemia	●	○	○	○	●	Very Low	○	○	●	Moderate
Gravlee 1994	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate
Dorman 1993	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate
Despotis 1982	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate
ElMalik 2000	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate

Table 50. Quality and Applicability of Prognostic Studies for Risk Factors for Bleeding

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bia s	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Gerlach 2002	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate
Karlsson 2008	Platelet Count	●	●	○	○	●	Low	○	○	●	Moderate
Gravlee 1994	PT	●	●	○	○	●	Low	○	○	●	Moderate
Dorman 1993	PT	●	●	○	○	●	Low	○	○	●	Moderate
Despotis 1982	PT	●	●	○	○	●	Low	○	○	●	Moderate
ElMalik 2000	PT	●	●	○	○	●	Low	○	○	●	Moderate
Gerlach 2002	PT	●	●	○	○	●	Low	○	○	●	Moderate
Karlsson 2008	PT	●	●	○	○	●	Low	○	○	●	Moderate
Dorman 1993	Fibrinogen	●	●	○	○	●	Low	○	○	●	Moderate

Table 50. Quality and Applicability of Prognostic Studies for Risk Factors for Bleeding

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bia s	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Gerlach 2002	Fibrinogen	●	●	○	○	●	Low	○	○	●	Moderate
Karlsson 2008	Fibrinogen	●	●	○	○	●	Low	○	○	●	Moderate
Gravlee 1994	aPTT	●	●	○	○	●	Low	○	○	●	Moderate
Dorman 1993	aPTT	●	●	○	○	●	Low	○	○	●	Moderate
Despotis 1982	aPTT	●	●	○	○	●	Low	○	○	●	Moderate
ElMalik 2000	aPTT	●	●	○	○	●	Low	○	○	●	Moderate
Karlsson 2008	aPTT	●	●	○	○	●	Low	○	○	●	Moderate
Dorman 1993	Bleeding Time	●	●	○	○	●	Low	○	○	●	Moderate
Despotis 1982	Bleeding Time	●	●	○	○	●	Low	○	○	●	Moderate

Table 50. Quality and Applicability of Prognostic Studies for Risk Factors for Bleeding

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bia s	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Gerlach 2002	PTT	●	●	○	○	●	Low	○	○	●	Moderate
Gravlee 1994	Earlobe Bleeding Time	●	●	○	○	●	Low	○	○	●	Moderate
Chan 1989	Thrombocytopenia	○	●	○	○	●	Very Low	○	○	●	Moderate
Della Ratta 1993	History of GI bleeding	○	●	○	○	●	Very Low	○	○	●	Moderate
Nuttall 2006	History of Bleeding with prior surgery	○	○	○	○	●	Very Low	○	○	●	Moderate
Woods 2008	Epistaxis	○	●	○	○	●	Very Low	○	○	●	Moderate
Woods 2008	History of bleeding after dental extraction	○	●	○	○	●	Very Low	○	○	●	Moderate

Table 51. Quality and Applicability of Prognostic Studies for Risk Factors for Hemorrhage-Associated Complications

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Borghi 2000	Revision	●	●	○	○	●	Low	●	○	●	Moderate
Rashiq 2004	Revision	○	●	○	○	●	Very Low	●	○	●	Moderate
Saleh 2007	Revision	○	●	○	○	●	Very Low	●	○	●	Moderate
Larocque 1997	Revision	○	●	○	○	●	Very Low	●	○	●	Moderate
Marx 2001	Revision	○	●	○	○	●	Very Low	●	○	●	Moderate
White 1990	Inflammatory Arthritis	○	●	○	○	●	Very Low	●	○	●	Moderate
Bong 2004	Inflammatory Arthritis	○	●	○	○	●	Very Low	●	○	●	Moderate
Walsh 2007	Inflammatory Arthritis	○	●	○	○	●	Very Low	●	○	●	Moderate
Marx 2001	Inflammatory Arthritis	○	●	○	○	●	Very Low	●	○	●	Moderate
SooHoo 2010	Inflammatory Arthritis	○	●	○	○	●	Very Low	●	○	●	Moderate
Moran 2005	Obesity	●	○	○	○	●	Very Low	●	○	●	Moderate
Aderinto 2004	Obesity	●	●	○	○	●	Low	●	○	●	Moderate
Mesa-Ramos 2008	Obesity	●	○	○	○	●	Very Low	○	○	●	Moderate
Amin 2006	Obesity	●	○	○	○	●	Very Low	○	○	●	Moderate

Table 51. Quality and Applicability of Prognostic Studies for Risk Factors for Hemorrhage-Associated Complications

●: Domain free of flaws

○: Domain flaws present

Study	Prognostic	Prospective	Power	Analysis	Model	Investigator Bias	*Quality*	Patients	Analysis	Outcomes	*Applicability*
Chee 2010	Obesity	●	○	○	○	●	Very Low	○	○	●	Moderate
Guerin 2007	Hemoglobin	●	●	○	○	●	Low	●	○	●	Moderate
Aderinto 2004	Hemoglobin	●	●	○	○	●	Low	●	○	●	Moderate
Mesa-Ramos 2008	Hemoglobin	●	○	○	○	●	Very Low	○	○	●	Moderate
Borghi 2000	Hemoglobin	●	●	○	○	●	Low	●	○	●	Moderate
Marchant 2009	Diabetes	○	●	○	○	●	Very Low	●	○	●	Moderate
SooHoo 2010	Diabetes	○	●	○	○	●	Very Low	●	○	●	Moderate
Sikkema 2010	Hemophilia	○	○	○	○	●	Very Low	○	○	●	Moderate

PREOPERATIVE ANTIPLATELET USE

Table 52. Quality and Applicability of Treatment Studies for Preoperative Antiplatelet Use

●: Domain free of flaws

○: Domain flaws present

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Kallis 1994	Reoperation for bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Ghaffarinejad 2007	Reoperation for bleeding	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Firanescu 2009	Reoperation for bleeding	●	○	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Kallis 1994	Blood Loss	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Ghaffarinejad 2007	Blood Loss	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate
Firanescu 2009	Blood Loss	●	●	○	○	●	●	●	●	Moderate	○	○	●	●	Moderate

PROPHYLAXIS

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Agnelli 2007	Bleeding events (major and minor)	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Agnelli 2007	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Avikainen 1995	Postoperative Transfusions	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Avikainen 1995	Revisions due to wound hematomas	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Avikainen 1995	Wound Infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Bailey 1991	Clinically important bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Barber 1977	Deep wound infection	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Barber 1977	Wound Hematoma	●	◐	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate
Barrellier 2010	All Cause Mortality	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate
Barrellier 2010	Fatal Bleeding	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Barrellier 2010	Heparin-associated Thrombocytopenia	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate
Barrellier 2010	Major Bleeding	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate
Barrellier 2010	New Asymptomatic DVT (none at day7)	●	●	●	○	●	●	○	●	Moderate	○	○	○	●	Moderate
Barrellier 2010	Proximal DVT	●	●	●	○	●	●	○	●	Moderate	○	○	○	●	Moderate
Barrellier 2010	Symptomatic DVT	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate
Barrellier 2010	Symptomatic PE	●	●	●	○	●	●	●	●	High	○	○	○	●	Moderate
Bauer 2001	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Any DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Bauer 2001	Bleeding leading to reoperation	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Distal DVT only	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Bauer 2001	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Bauer 2001	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Other Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Postoperative Transfusions	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Bauer 2001	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bauer 2001	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Bergqvist 1996	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Bergqvist 1996	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Bergqvist 1996	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Bergqvist 1996	Hemoglobin decrease of 2g/dL	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Bergqvist 1996	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Bergqvist 1996	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Bergqvist 1996	Rehospitalization due to DVT	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Bergqvist 1996	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Bergqvist 1996	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Bergqvist 1996	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Berkowitz 2003	Major Bleeding	●	◐	○	●	●	●	●	●	High	○	○	○	●	Moderate
Berkowitz 2003	Minor Bleeding	●	◐	○	●	●	●	●	●	High	○	○	○	●	Moderate
Berkowitz 2003	Patients receiving 2+ transfusions	●	◐	○	●	●	●	●	●	High	○	○	○	●	Moderate
Berkowitz 2003	Patients receiving any postop transfusions	●	◐	○	●	●	●	●	●	High	○	○	○	●	Moderate
Bonneux 2006	Postoperative Transfusions	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Bonneux 2006	Wound Problems	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Chin 2009	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Chin 2009	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Chin 2009	DVT (ultrasound)	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Chin 2009	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Chin 2009	Major Bleeding necessitating intervention	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Chin 2009	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Chin 2009	Superficial wound infections	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Chin 2009	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Asymptomatic proximal DVT	●	●	●	●	●	●	○	●	High	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Cohen 2007	Clinically significant minor bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Hemoglobin decreased	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Cohen 2007	Need for transfusion	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Colwell 1994	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate
Colwell 1994	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Heparin-associated Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Colwell 1994	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate
Colwell 1994	Rehospitalization due to VTE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1994	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate
Colwell 1995	Bleeding at nonoperative site	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1995	Bleeding at operative site	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1995	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate
Colwell 1995	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1995	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1995	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Colwell 1995	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 1995	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	●	Moderate
Colwell 1999	All Cause Mortality	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Both Major and Minor Bleeding	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Fatal PE	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Heparin-induced Thrombocytopenia	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Major Bleeding	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Minor Bleeding	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Symptomatic PE	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 1999	Transfusions for replacement of operative blood loss	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Colwell 1999	Transfusions for replacement of postoperative blood loss	●	●	○	●	●	●	●	●	High	●	○	○	●	Moderate
Colwell 2006	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2006	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Colwell 2010	Anemia requiring prolonged hospitalization	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Anemia with hypotension requiring intervention	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Colwell 2010	Distal DVT	●	●	○	●	○	○	○	●	Low	○	○	○	●	Moderate
Colwell 2010	Hematoma requiring prolonged hospitalization	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Hematoma requiring rehospitalization	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Major Bleeding	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Minor Bleeding	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Proximal DVT	●	●	○	●	○	○	○	●	Low	○	○	○	●	Moderate
Colwell 2010	Symptomatic PE	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Ultrasound DVT	●	●	○	●	○	○	○	●	Low	○	○	○	●	Moderate
Colwell 2010	Urinary bleeding requiring rehospitalization	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate
Colwell 2010	Wound drainage requiring rehospitalization	●	●	○	●	○	○	●	●	Moderate	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Comp 2001	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Comp 2001	Ecchymosis	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Injection-site Hemorrhage	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Comp 2001	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Comp 2001	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	○	●	Moderate
Dahl 1997	Adverse Events	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Dahl 1997	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Proximal DVT	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Serious Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dahl 1997	Venographic DVT	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dechavanne 1989	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Dechavanne 1989	Superficial wound infections	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Dechavanne 1989	Thrombocytopenia	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Dechavanne 1989	Wound Hematoma	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Edwards 2008	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Edwards 2008	DVT (ultrasound)	●	●	○	●	●	●	○	●	Moderate	○	○	○	○	Low
Edwards 2008	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Edwards 2008	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Edwards 2008	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Eriksson 1991	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1991	Evacuation of hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1991	Excessive bleeding (>3000 ml)	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1991	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1991	Reoperation due to Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1991	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 1996	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Dehiscence	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 1996	Reoperation due to Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Reoperation due to Infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Surgical bleeding complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1996	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Eriksson 1996	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 1996	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	All Cause Mortality	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Deep Infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Fatal PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Reoperation due to Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Serious Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997	Severe Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 1997	Symptomatic DVT	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 1997	Wound Rupture	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Eriksson 1997b	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Deep wound infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Eriksson 1997b	Injection-site Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 1997b	Serious Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Eriksson 1997b	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Eriksson 1997b	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 1997b	Wound Dehiscence	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 1997b	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Clinically relevant thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Clinically significant bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Composite major or clinically significant bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2005	Fatal PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2005	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2005	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	●	Moderate
Eriksson 2005	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2005	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2006	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006	Clinically relevant nonmajor bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2006	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2006	Reoperation due to Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2006b	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Clinically relevant nonmajor bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2006b	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2006b	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2006b	Reoperation due to Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2006b	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007	Clinically relevant nonmajor bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2007b	Asymptomatic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007b	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007b	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007b	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007b	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2007b	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2007b	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2007c	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Asymptomatic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007c	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007c	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007c	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007c	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2007c	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2007c	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2007d	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007d	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2007d	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Any Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2008	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2008	Nonmajor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2008	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2008	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2008	Wound Infection	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Any Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Any DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2010	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Distal DVT only	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2010	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Major or clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Eriksson 2010	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2010	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2010	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Eriksson 2010	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Eriksson 2011	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Eriksson 2011	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Eriksson 2011	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Eriksson 2011	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Eriksson 2011	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Eriksson 2011	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Eriksson 2011	Total DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Eriksson 2011	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Fauno 1994	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Fauno 1994	Wound Infection	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Feller 1992	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Feller 1992	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Feller 1992	PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Feller 1992	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Feller 1992	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Fitzgerald 2001	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Any Clinically Important Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Any DVT	●	●	●	●	○	●	○	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Distal DVT	●	●	●	●	○	●	○	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Proximal DVT	●	●	●	●	○	●	○	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Fitzgerald 2001	Thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Fordyce 1991	Wound Complications	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Fordyce 1991	Wound Hematoma	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Fordyce 1991	Wound Sepsis	●	●	●	●	●	●	●	●	High	●	○	●	●	Moderate
Fordyce 1992	Bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Fordyce 1992	Serious Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Francis 1992	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1992	Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1992	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1992	Distal DVT only	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1992	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1992	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Francis 1996	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1996	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1996	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1996	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1996	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1996	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Francis 1996	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1997	Bleeding Complications	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Francis 1997	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1997	Major Bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Francis 1997	Operative-site Bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Francis 1997	Other Bleeding complications	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Francis 1997	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Francis 1997	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Francis 1997	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Fuji 2008	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2008	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2008	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Fuji 2008	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Fuji 2008b	Any Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2008b	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2008b	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Fuji 2010	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Any Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Asymptomatic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Fuji 2010	Bleeding leading to reoperation	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Clinically relevant bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Fuji 2010	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Fuji 2010	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Fuji 2010	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Gelfer 2002	Adverse Events	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Ginsberg 2009	All Cause Mortality	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Ginsberg 2009	Any DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Ginsberg 2009	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Ginsberg 2009	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Ginsberg 2009	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Ginsberg 2009	Fatal PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Ginsberg 2009	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Ginsberg 2009	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Ginsberg 2009	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Ginsberg 2009	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Ginsberg 2009	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Ginsberg 2009	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Haas 1990	Adverse Events	●	●	○	●	○	●	●	●	Moderate	●	○	○	○	Moderate
Haas 1990	GI Bleeding	●	●	○	●	○	●	●	●	Moderate	●	○	○	○	Moderate
Haas 1990	Wound Complications	●	●	○	●	○	●	●	●	Moderate	●	○	○	○	Moderate
Hampson 1974	Bleeding	●	◐	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Harris 1974	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Harris 1977	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Harris 1977	Major Bleeding Complication		◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Harris 1977	Wound Hematoma	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Harris 1982	Bleeding Complications	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Harris 1985	Bleeding Complications	●	○	○	●	●	●	●	●	High	○	○	●	○	Moderate
Harris 1985	Major Bleeding Complication	●	○	○	●	●	●	●	●	High	○	○	●	○	Moderate
Hull 1990	All Cause Mortality	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Hull 1990	Fatal PE	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Hull 1990	Proximal DVT	●	●	○	○	●	●	○	●	Moderate	○	○	○	●	Moderate
Hull 1990	Symptomatic DVT	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Hull 1990	Symptomatic PE	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Hull 1990	Venographic DVT	●	●	○	○	●	●	○	●	Moderate	○	○	○	●	Moderate
Hull 1993	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Complicated wound hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Hull 1993	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Hull 1993	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Uncomplicated wound hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 1993	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Hull 1993	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Hull 2000	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Hull 2000	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Trivial Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Hull 2000	Wound Hematoma, complicated	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000	Wound Hematoma, uncomplicated	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Hull 2000b	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Hull 2000b	Symptomatic DVT	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Hull 2000b	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Hull 2000b	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Trivial Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hull 2000b	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Hull 2000b	Wound Hematoma, complicated	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Hull 2000b	Wound Hematoma, uncomplicated	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hume 1973	Wound Hematoma	●	●	○	○	○	●	●	●	Moderate	○	○	●	●	Moderate
Kakkar 2008	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kakkar 2008	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kakkar 2008	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Kakkar 2008	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kakkar 2008	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Kakkar 2008	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kakkar 2008	Nonmajor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kakkar 2008	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Kakkar 2008	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

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●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Kakkar 2008	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	○	Moderate
Kakkar 2008	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Kakkar 2008	Wound Infection	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Kim 1998	Bleeding Complications	●	◐	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
Kim 1998	Major Bleeding Complication	●	◐	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
Kim 1998	Wound Hematoma	●	◐	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
Lachiewicz 2004	All Cause Mortality	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate
Lachiewicz 2004	Complications	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate
Lachiewicz 2004	Fatal Bleeding	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate
Lachiewicz 2004	Symptomatic DVT	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate
Lachiewicz 2004	Symptomatic PE	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate

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●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lachiewicz 2004	Ultrasound DVT	●	●	○	●	●	●	○	●	Moderate	●	○	●	○	Moderate
Lassen 1991	All Cause Mortality	●	●	○	●	●	○	●	●	Moderate	○	○	●	○	Moderate
Lassen 1991	Bleeding Complications	●	●	○	●	●	○	●	●	Moderate	○	○	●	●	Moderate
Lassen 1991	Fatal PE	●	●	○	●	●	○	●	●	Moderate	○	○	●	○	Moderate
Lassen 1991	Injection-site Hematoma	●	●	○	●	●	○	●	●	Moderate	○	○	●	●	Moderate
Lassen 1991	Symptomatic PE	●	●	○	●	●	○	●	●	Moderate	○	○	●	○	Moderate
Lassen 1991	Venographic DVT	●	●	○	●	●	○	○	●	Moderate	○	○	●	○	Moderate
Lassen 1998	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 1998	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 1998	Proximal DVT	●	●	○	●	○	●	●	●	Moderate	○	○	○	○	Low
Lassen 1998	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	○	○	Low

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2000	Heparin-associated Thrombocytopenia	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Lassen 2000	Unusual Wound Evolution	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Lassen 2000	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2002	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Any DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2002	Bleeding leading to reoperation	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Distal DVT only	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2002	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2002	Other Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Postoperative Transfusions	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2002	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2002	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	All Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Asymptomatic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2007	Bleeding with surgical intervention	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Fatal PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2007	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Potentially significant non-overt bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2007	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2007	Symptomatic DVT	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Lassen 2007	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Lassen 2007	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2007	Wound-related Infections	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Any Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2008	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2008	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Nonmajor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2008	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2008	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2008	Wound Infection	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	All Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	All Cause Mortality	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2009	All DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2009	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	Fatal PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Lassen 2009	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2009	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Lassen 2009	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Lassen 2009	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Lassen 2009	Thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Lassen 2010	All Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate

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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2010	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	All DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Lassen 2010	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Lassen 2010	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2010b	All Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Lassen 2010b	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lassen 2010b	Thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Lassen 2010b	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Leclerc 1996	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Leclerc 1996	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Leclerc 1996	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Transfusions after recovery room	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Leclerc 1996	Transfusions during surgery or in recovery room	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Leclerc 1996	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Levine 1991	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Levine 1991	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Leyvraz 1983	Wound Hematoma	●	◐	●	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lieberman 1994	Any DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Lieberman 1994	Complications	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Lieberman 1994	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	GI Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	Major Complications	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Lieberman 1994	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Lieberman 1994	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Lotke 1996	Asymptomatic PE	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Lotke 1996	Bleeding Complications	●	●	○	●	○	●	●	●	Moderate	●	○	●	○	Moderate
Lotke 1996	Distal DVT	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Lotke 1996	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Lotke 1996	Transfusion after 48h	●	●	○	●	○	●	●	●	Moderate	●	○	●	○	Moderate
Lotke 1996	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Manganelli 1998	Bleeding Complications	●	◐	○	○	○	●	●	●	Moderate	○	○	●	○	Moderate
Manganelli 1998	Major Bleeding	●	◐	○	○	○	●	●	●	Moderate	○	○	●	○	Moderate
Mannucci 1976	Bleeding Complications	●	●	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
Mannucci 1976	Excessive operative bleeding	●	●	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
Mannucci 1976	Severe Postoperative Bleeding	●	●	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Mannucci 1976	Wound Hematoma	●	●	○	○	●	●	●	●	Moderate	●	○	●	●	Moderate
McKenna 1980	Active Bleeding	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
McKenna 1980	Bleeding	●	●	○	●	●	●	●	○	Moderate	○	○	●	○	Moderate
Moskovitz 1978	Bleeding Complications	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Moskovitz 1978	Wound Infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Paiement 1987	Bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Paiement 1987	Major bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Paiement 1987	Minor Bleeding	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
PEP 2000	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Bleed requiring transfusion: hematemesis or melena	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Bleed requiring transfusion: other bleed	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
PEP 2000	Bleed requiring transfusion: wound bleed >=4 days	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Evacuation of hematoma	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
PEP 2000	Wound Infection with frank pus	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Planes 1988	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Planes 1988	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Planes 1988	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1988	Venographic DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	○	Moderate
Planes 1991	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Major bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Minor Bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Thrombocytopenia	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Wound Hematoma	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Wound Hematoma requiring reoperation	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Planes 1991	Wound Infection	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Planes 1996	Hematemesis	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Planes 1996	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Planes 1996	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	○	●	Moderate
Planes 1999	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Heparin-induced Thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Proximal DVT	●	●	●	●	●	●	○	●	High	○	○	●	●	Moderate
Planes 1999	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Planes 1999	Venographic DVT	●	●	●	●	●	●	○	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Poller 1995	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Poller 1995	Other Major Bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Poller 1995	Patients requiring at least 3 units of red cells during surgery	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Prandoni 2002	All Cause Mortality	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Prandoni 2002	Fatal Bleeding	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Prandoni 2002	Major Bleeding	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Prandoni 2002	Symptomatic PE	●	●	○	○	●	●	●	●	Moderate	○	○	○	●	Moderate
Prandoni 2002	Ultrasound DVT	●	●	○	○	●	●	○	●	Moderate	○	○	○	●	Moderate
Rader 1998	DVT (ultrasound with venography confirmation)	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Rader 1998	Fatal PE	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Rader 1998	Reoperation for hematoma	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Rader 1998	Surgical intervention due to hematoma or infection	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Rader 1998	Symptomatic PE	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Salzman 1971	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate
Samama 1997	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Samama 1997	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Santori 1994	Bleeding Problems	●	●	●	●	●	●	○	○	Moderate	○	○	○	●	Moderate
Senaran 2006	Heparin-induced Thrombocytopenia	●	●	○	●	●	●	●	●	High	●	○	●	●	Moderate
Senaran 2006	Major Bleeding	●	●	○	●	●	●	●	●	High	●	○	●	●	Moderate
Senaran 2006	Minor Bleeding Complications	●	●	○	●	●	●	●	●	High	●	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Sharrock 1990	Bleeding Complications	●	◐	○	●	●	●	●	●	High	●	○	●	○	Moderate
Sharrock 1990	Deep Hematoma	●	◐	○	●	●	●	●	●	High	●	○	●	○	Moderate
Sharrock 1990	Superficial wound hematoma	●	◐	○	●	●	●	●	●	High	●	○	●	○	Moderate
Sharrock 1990	Thrombocytopenia	●	◐	○	●	●	●	●	●	High	●	○	●	○	Moderate
Spiro 1994	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Spiro 1994	Any DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Spiro 1994	Distal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Spiro 1994	DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Spiro 1994	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Spiro 1994	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Spiro 1994	PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Spiro 1994	Proximal DVT	●	●	○	●	●	●	○	●	Moderate	○	○	●	●	Moderate
Stone 1996	Transfusion of at least 2 units	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Stone 1996	Wound Complications	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Stone 1996	Wound Problems	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Torholm 1991	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Torholm 1991	Injection-site Hematoma	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Torholm 1991	Severe wound hematoma	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Torholm 1991	Wound Infection	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Torholm 1991	Wound Rupture	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Turpie 1986	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 1986	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

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Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Turpie 2001	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2001	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2001	Fatal PE	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2001	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2001	Minor Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2001	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2001	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	●	Moderate
Turpie 2001	Thrombocytopenia	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2001	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2002	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Any DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Turpie 2002	Bleeding leading to reoperation	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Distal DVT only	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2002	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Other Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Postoperative Transfusions	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2002	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2002	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	All Cause Mortality	●	●	●	●	○	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Turpie 2005	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Clinically relevant thrombocytopenia	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2005	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Fatal PE	●	●	●	●	○	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Minor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2005	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	●	Moderate
Turpie 2005	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Turpie 2005	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2009	All Cause Mortality	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Turpie 2009	Any Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Asymptomatic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2009	Clinically relevant nonmajor bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2009	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Fatal PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Turpie 2009	Major Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Nonmajor Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Turpie 2009	Reoperation due to Bleeding	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Turpie 2009	Symptomatic DVT	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Turpie 2009	Symptomatic PE	●	●	●	●	○	●	●	●	High	○	○	●	○	Moderate
Turpie 2009	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Turpie 2009	Wound Infection	●	●	●	●	●	●	●	●	High	○	○	●	●	Moderate
Vives 2001	All Cause Mortality	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Vives 2001	Fatal Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Vives 2001	Hematoma	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Vives 2001	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Vives 2001	Symptomatic DVT	●	●	○	●	●	●	●	●	High	○	○	○	○	Low
Vives 2001	Symptomatic PE	●	●	○	●	●	●	●	●	High	○	○	○	○	Low

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
VTCSG 1975	Wound Hematoma	●	◐	○	○	○	●	●	●	Moderate	●	○	●	○	Moderate
Warwick 1995	Discharge from drain sites which persisted beyond the 6th postop day	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Warwick 1995	Wound Hematoma	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Warwick 1998	All Cause Mortality	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Distal DVT	●	●	●	●	●	●	○	●	High	○	○	○	○	Low
Warwick 1998	Fatal Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Hematoma necessitating treatment	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Proximal DVT	●	●	●	●	●	●	○	●	High	○	○	○	○	Low

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Warwick 1998	Symptomatic DVT	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 1998	Venographic DVT	●	●	●	●	●	●	○	●	High	○	○	○	○	Low
Warwick 2002	Bleeding	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 2002	Bleeding Complications	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 2002	Distal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Warwick 2002	Fatal PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 2002	Proximal DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Warwick 2002	Symptomatic PE	●	●	●	●	●	●	●	●	High	○	○	○	●	Moderate
Warwick 2002	Venographic DVT	●	●	●	●	○	●	○	●	Moderate	○	○	○	○	Low
Westrich 2005	Bleeding Complications	●	●	○	○	●	●	●	●	Moderate	○	○	●	○	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Westrich 2006	Bleeding Complications	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Westrich 2006	Distal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Westrich 2006	Internal Bleeding Complication	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Westrich 2006	Proximal DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Westrich 2006	Symptomatic PE	●	●	○	●	○	●	●	●	Moderate	○	○	●	○	Moderate
Westrich 2006	Ultrasound DVT	●	●	○	●	○	●	○	●	Moderate	○	○	●	○	Moderate
Wilson 1994	Bleeding Complications	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Wilson 1994	Major Bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Wilson 1994	Minor Bleeding	●	◐	○	●	●	●	●	●	High	○	○	●	○	Moderate
Windisch 2010	Reoperation due to Bleeding	●	◐	○	●	○	●	●	●	Moderate	○	○	○	●	Moderate
Woolson 1991	Wound Hematoma	●	●	○	●	○	●	●	○	Moderate	○	○	●	●	Moderate

Table 53. Quality and Applicability of Treatment Studies for Prophylaxis

●: Domain free of flaws
○: Domain flaws present
◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Yokote 2011	Major Bleeding	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

EARLY MOBILIZATION

Table 54. Quality and Applicability of Treatment Studies for Early Mobilization

●: Domain free of flaws

○: Domain flaws present

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Husted 2010	All-Cause Mortality	●	●	○	○	○	●	●	●	Moderate	●	○	●	●	Moderate
Kelsey 1976	DVT	○	●	○	○	○	●	○	●	Low	●	●	●	○	Moderate
Husted 2010	DVT Re-admission	●	●	○	○	○	●	●	●	Moderate	●	○	●	●	Moderate
Johnson 1977	Fatal PE	○	●	○	○	○	○	●	●	Low	●	●	●	○	Moderate
Pearse 2007	Minor wound problems	●	●	○	○	○	●	●	●	Moderate	●	○	●	●	Moderate
Kelsey 1976	PE	○	●	○	○	○	●	○	●	Low	●	●	●	○	Moderate
Johnson 1977	PE	○	●	○	○	○	○	●	●	Low	●	●	●	○	Moderate
Husted 2010	PE Re-admission	●	●	○	○	○	●	●	●	Moderate	●	○	●	●	Moderate

Table 54. Quality and Applicability of Treatment Studies for Early Mobilization

●: Domain free of flaws

○: Domain flaws present

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Samama 2007	Symptomatic VTE	●	●	○	○	○	○	●	●	Low	●	●	●	○	Moderate
Kelsey 1976	VTE	○	●	○	○	○	●	○	●	Low	●	●	●	○	Moderate
Leizorovicz 2007	VTE	●	●	○	○	○	○	○	●	Low	○	●	●	○	Moderate
White 2000	VTE Re-admission	○	●	○	○	○	●	●	●	Low	○	●	●	○	Moderate

ANESTHESIA

Table 55. Quality and Applicability of Treatment Studies for Anesthesia

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Maurer 2007	Symptomatic VTE	●	●	○	●	○	●	●	●	Moderate	●	○	●	●	Moderate
Warwick 2007	Symptomatic VTE	●	●	○	●	○	○	●	●	Moderate	●	●	●	○	Moderate
Williams-Russo 1996	Venographic DVT	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Williams-Russo 1996	Lung Perfusion Defects	●	●	○	●	○	●	○	●	Moderate	●	○	●	○	Moderate
Williams-Russo 1996	All-Cause Mortality	●	●	○	●	●	●	●	●	High	●	○	●	○	Moderate
Eroglu 2005	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Hole 1980	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Modig 1986	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate

Table 55. Quality and Applicability of Treatment Studies for Anesthesia

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Modig 1987	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Modig 1983	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Borghi 2005	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Jorgensen 1991	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Dauphin 1997	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
D'Ambrosio 1999	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Borghi 2002	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate
Stevens 2000	Blood loss	●	●	○	●	●	●	●	●	High	○	○	●	○	Moderate
Chu 2006	Blood loss	●	◐	○	●	●	●	●	●	High	○	○	●	●	Moderate

Table 55. Quality and Applicability of Treatment Studies for Anesthesia

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Niemi 2000	Blood loss	●	●	○	●	●	●	●	●	High	●	○	●	●	Moderate
Twyman 1990	Blood loss	●	●	○	●	●	●	●	●	High	●	○	●	●	Moderate
Juelsgaard 2001	Blood Loss	●	●	○	●	●	●	●	●	High	○	○	●	●	Moderate

IVC FILTERS

Table 56. Quality and Applicability of Treatment Studies for IVC Filters

●: Domain free of flaws

○: Domain flaws present

◐: Moderate power

Study	Outcome	Prospective	Power	Group Assignment	Blinding	Group Comparability	Treatment Integrity	Measurement	Investigator Bias	*Quality*	Participants	Intervention and Expertise	Compliance and Adherence	Analysis	*Applicability*
Khansarinia 1995	PE	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Obeid 2007	PE	○	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Obeid 2007	DVT	○	●	○	○	○	○	○	●	Very Low	○	○	●	●	Moderate
Obeid 2007	Death	○	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Khansarinia 1995	All-cause Mortality	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate
Khansarinia 1995	PE-related Death	●	●	○	○	○	○	●	●	Low	○	○	●	●	Moderate

APPENDIX XIV
EXCLUDED STUDIES
ROUTINE SCREENING

Table 57. Excluded Studies Considered for Routine Screening

Author	Title	Reason for Exclusion
Uehara et al. 2009	Comparison of three techniques for evaluation of de novo asymptomatic pulmonary arterial thrombosis following deep vein thrombosis in total knee arthroplasty	Fewer than 100 patients
Yoo et al. 2009	Deep vein thrombosis after total hip arthroplasty in Korean patients and D-dimer as a screening tool	Not best available evidence
Borris et al. 2007	Prothrombin fragment 1+2 in urine as an indicator of sustained coagulation activation after total hip arthroplasty	Does not examine diagnostic test of interest
Schellong et al. 2007	Ultrasound screening for asymptomatic deep vein thrombosis after major orthopaedic surgery: the VENUS study	Not best available evidence
Dhupar et al. 2006	A comparison of discharge and two-week duplex ultrasound screening protocols for deep venous thrombosis detection following primary total joint arthroplasty	Not best available evidence
Iorio et al. 2006	Routine duplex ultrasound screening after TKA is not necessary	Not best available evidence
Kluge et al. 2006	Experience in 207 combined MRI examinations for acute pulmonary embolism and deep vein thrombosis	Not specific to arthroplasty patients
Schwarcz et al. 2004	Surveillance venous duplex is not clinically useful after total joint arthroplasty when effective deep venous thrombosis prophylaxis is used	Not best available evidence
Arnesen et al. 2003	Sustained prothrombotic profile after hip replacement surgery: the influence of prolonged prophylaxis with dalteparin	Insufficient data for diagnostic accuracy
Abraham et al. 2002	Despite imperfect sensitivity, ultrasound thrombosis detection following arthroplasty is useful	Not best available evidence
Cipolle et al. 2002	The role of surveillance duplex scanning in preventing venous thromboembolism in trauma patients	Not specific to elective arthroplasty
Shiota et al. 2002	Changes in LPIA D-dimer levels after total hip or knee arthroplasty relevant to deep-vein thrombosis diagnosed by bilateral ascending venography	Fewer than 100 patients
Berry 2001	Surveillance for venous thromboembolic disease after total knee arthroplasty	Systematic review, bibliography screened
Verlato et al. 2001	The value of ultrasound screening for proximal vein thrombosis after total hip arthroplasty--a prospective cohort study	Not best available evidence
Eskandari et al. 2000	Is color-flow duplex a good diagnostic test for detection of isolated calf vein thrombosis in high-risk patients?	Fewer than 100 arthroplasty patients

Table 57. Excluded Studies Considered for Routine Screening

Author	Title	Reason for Exclusion
Peetz et al. 2000	Dose-adjusted thrombosis prophylaxis in trauma surgery according to levels of D-Dimer	Not specific to elective arthroplasty
Bara et al. 1999	Occurrence of thrombosis and haemorrhage, relationship with anti-Xa, anti-IIa activities, and D-dimer plasma levels in patients receiving a low molecular weight heparin, enoxaparin or tinzaparin, to prevent deep vein thrombosis after hip surgery	Insufficient data for diagnostic accuracy
Beuhler et al. 1999	Venous thromboembolic disease after hybrid hip arthroplasty with negative duplex screening	Not best available evidence
Corradi et al. 1999	Preoperative plasma levels of prothrombin fragment 1 + 2 correlate with the risk of venous thrombosis after elective hip replacement	Does not investigate post-operative screening
Kalebo et al. 1999	Central assessment of bilateral phlebograms in a major multicentre thromboprophylactic trial. Reasons for inadequate results	Not diagnostic accuracy study
Anderson et al. 1998	Ultrasonographic screening for deep vein thrombosis following arthroplasty fails to reduce posthospital thromboembolic complications: the Postarthroplasty Screening Study (PASS)	Report of previously published study
Ciccone et al. 1998	Ultrasound surveillance for asymptomatic deep venous thrombosis after total joint replacement	Not best available evidence
Cofrancesco et al. 1998	Clinical utility of prothrombin fragment 1+2, thrombin antithrombin III complexes and D-dimer measurements in the diagnosis of deep vein thrombosis following total hip replacement	Not best available evidence
Comp et al. 1998	A comparison of danaparoid and warfarin for prophylaxis against deep vein thrombosis after total hip replacement: The Danaparoid Hip Arthroplasty Investigators Group	Not best available evidence
Hartford et al. 1998	Preoperative duplex ultrasonography evaluation for deep vein thrombosis in hip and knee arthroplasty patients	Not best available evidence
Kalodiki et al. 1998	How 'gold' is the standard? Interobservers' variation on venograms	Fewer than 100 patients
Kearon et al. 1998	Noninvasive diagnosis of deep venous thrombosis. McMaster Diagnostic Imaging Practice Guidelines Initiative	Systematic review, bibliography screened
Robinson et al. 1998	Accuracy of screening compression ultrasonography and clinical examination for the diagnosis of deep vein thrombosis after total hip or knee arthroplasty	Not best available evidence
Westrich et al. 1998	Ultrasound screening for deep venous thrombosis after total knee arthroplasty. 2-year reassessment	Not best available evidence
Brothers et al. 1997	Is duplex venous surveillance worthwhile after arthroplasty?	Not best available evidence
Cofrancesco et al. 1997	Coagulation activation markers in the prediction of venous thrombosis after elective hip surgery	Does not investigate post-operative screening

Table 57. Excluded Studies Considered for Routine Screening

Author	Title	Reason for Exclusion
Crippa et al. 1997	The utility and cost-effectiveness of D-dimer measurements in the diagnosis of deep vein thrombosis	Narrative review, bibliography screened
Kalodiki et al. 1997	Duplex scanning in the postoperative surveillance of patients undergoing total hip arthroplasty	Fewer than 100 patients
Lensing et al. 1997	A comparison of compression ultrasound with color Doppler ultrasound for the diagnosis of symptomless postoperative deep vein thrombosis	Not best available evidence
Westrich et al. 1997	Comparison between color Doppler imaging and ascending venography in the detection of deep venous thrombosis following total joint arthroplasty: a prospective study	Not best available evidence
Ascani et al. 1996	Distribution and occlusiveness of thrombi in patients with surveillance detected deep vein thrombosis after hip surgery	Not specific to elective arthroplasty patients
Garino et al. 1996	Deep venous thrombosis after total joint arthroplasty. The role of compression ultrasonography and the importance of the experience of the technician	Not best available evidence
Kalebo et al. 1996	Percentage of inadequate phlebograms and observer agreement in thromboprophylactic multicenter trials using standardized methodology and central assessment	Not diagnostic accuracy, observer reliability study
Magnusson et al. 1996	Is colour Doppler ultrasound a sensitive screening method in diagnosing deep vein thrombosis after hip surgery?	Not specific to elective arthroplasty
Pellegrini et al. 1996	Natural history of thromboembolic disease after total hip arthroplasty	Patients reported in a more recent publication
Bombardini et al. 1995	Proximal deep vein thrombosis: the use of the echoDoppler for diagnosis and therapeutic indications	Not best available evidence
Dahl et al. 1995	Increased activation of coagulation and formation of late deep venous thrombosis following discontinuation of thromboprophylaxis after hip replacement surgery	Fewer than 100 patients
Wells et al. 1995	Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery. A meta-analysis	Systematic review, bibliography screened
Bongard et al. 1994	D-dimer plasma measurement in patients undergoing major hip surgery: use in the prediction and diagnosis of postoperative proximal vein thrombosis	Not specific to elective arthroplasty patients
Grady-Benson et al. 1994	Postoperative surveillance for deep venous thrombosis with duplex ultrasonography after total knee arthroplasty	Not best available evidence
Grady-Benson et al. 1994	Routine postoperative duplex ultrasonography screening and monitoring for the detection of deep vein thrombosis. A survey of 110 total hip arthroplasties	Not best available evidence

Table 57. Excluded Studies Considered for Routine Screening

Author	Title	Reason for Exclusion
Oishi et al. 1994	The clinical course of distal deep venous thrombosis after total hip and total knee arthroplasty, as determined with duplex ultrasonography	Not diagnostic accuracy study
Walker 1994	Secondary prevention of venous thromboembolism in joint replacement using duplex ultrasonography	Not best available evidence
Wicky et al. 1994	Screening for proximal deep venous thrombosis using B-mode venous ultrasonography following major hip surgery: implications for clinical management	Not specific to elective arthroplasty
Elliott et al. 1993	Duplex ultrasonography for the detection of deep vein thrombi after total hip or knee arthroplasty	Not best available evidence
Kraay et al. 1993	Vascular ultrasonography for deep venous thrombosis after total knee arthroplasty	Not best available evidence
Agnelli et al. 1992	Detection of asymptomatic deep vein thrombosis by real-time B-mode ultrasonography in hip surgery patients	Not specific to elective arthroplasty
Davidson et al. 1992	Low accuracy of color Doppler ultrasound in the detection of proximal leg vein thrombosis in asymptomatic high-risk patients. The RD Heparin Arthroplasty Group	Not best available evidence
Mattos et al. 1992	Color-flow duplex scanning for the surveillance and diagnosis of acute deep venous thrombosis	Fewer than 100 arthroplasty patients
Wille-Jorgensen et al. 1992	Phlebography as the gold standard in thromboprophylactic studies? A multicenter interobserver variation study	Not diagnostic accuracy, observer reliability study
Wille-Jorgensen et al. 1992	Potential influence of observer variation in thromboprophylactic trials	Not diagnostic accuracy, observer reliability study
Barnes et al. 1991	Duplex scanning versus venography as a screening examination in total hip arthroplasty patients	Not best available evidence
Ginsberg et al. 1991	Venous thrombosis in patients who have undergone major hip or knee surgery: detection with compression US and impedance plethysmography	Not specific to elective arthroplasty
Comerota et al. 1990	Venous duplex imaging: should it replace hemodynamic tests for deep venous thrombosis?	Fewer than 100 arthroplasty patients
Lensing et al. 1990	Lower extremity venography with iohexol: results and complications	Not specific to elective arthroplasty
Woolson et al. 1990	B-mode ultrasound scanning in the detection of proximal venous thrombosis after total hip replacement	Not best available evidence

RISK FACTORS FOR VTED

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Chung et al. 2011	Deep vein thrombosis after total knee arthroplasty in asian patients without prophylactic anticoagulation	Not best available evidence
Bedair et al. 2011	Hematologic genetic testing in high-risk patients before knee arthroplasty: a pilot study	Fewer than 100 patients
Caprini 2010	Risk assessment as a guide for the prevention of the many faces of venous thromboembolism	Systematic review, bibliography screened
Caprini 2010	Risk assessment as a guide to thrombosis prophylaxis	Narrative review, bibliography screened
Cha et al. 2010	Venous thromboembolism in Korean patients undergoing major orthopedic surgery: a prospective observational study using computed tomographic (CT) pulmonary angiography and indirect CT venography	Not specific to elective arthroplasty
Chee et al. 2010	Total hip replacement in morbidly obese patients with osteoarthritis: Results of a prospectively matched study	Not best available evidence
Healy et al. 2010	Venous thromboembolism following prolonged cast immobilisation for injury to the tendo Achillis	Not specific to surgical patients
Kapoor et al. 2010	Risk of venous thromboembolism after total hip and knee replacement in older adults with comorbidity and co-occurring comorbidities in the Nationwide Inpatient Sample (2003-2006)	Not best available evidence
Kerr et al. 2010	High incidence of in-hospital pulmonary embolism following joint arthroplasty with dalteparin prophylaxis	Not best available evidence
Mouravas et al. 2010	Homocysteine and its relationship to deep venous thrombosis in patients undergoing total knee or hip arthroplasty	Not best available evidence
Niki et al. 2010	Rheumatoid arthritis: a risk factor for deep venous thrombosis after total knee arthroplasty? Comparative study with osteoarthritis	Does not examine risk factor of interest
Novis et al. 2010	Prevention of thromboembolic events in surgical patients through the creation and implementation of a computerized risk assessment program	Insufficient Data
Paffrath et al. 2010	Venous thromboembolism after severe trauma: incidence, risk factors and outcome	Does not investigate risk factor of interest
Zarowitz et al. 2010	Thrombotic risk and immobility in residents of long-term care facilities	Not specific to surgical patients
Awidi et al. 2009	Risk stratification for venous thromboembolism in hospitalized patients in a developing country: A prospective study	Does not report VTE
Caruana et al. 2009	The pulmonary embolism risk score system reduces the incidence and mortality of pulmonary embolism after gastric bypass	Insufficient Data
Felcher et al. 2009	Incidence and risk factors for venous thromboembolic disease in podiatric surgery	Not specific to elective arthroplasty

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Galanaud et al. 2009	Comparative study on risk factors and early outcome of symptomatic distal versus proximal deep vein thrombosis: results from the OPTIMEV study	Not specific to surgical patients
Khan et al. 2009	The complication rate and medium-term functional outcome after total hip replacement in smokers	Does not report VTE
Lutsey et al. 2009	Correlates and Consequences of Venous Thromboembolism: The Iowa Women's Health Study	Not best available evidence (not specific to elective arthroplasty)
Marchant et al. 2009	The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty	Not best available evidence
Nokes et al. 2009	Thromboprophylaxis in patients with lower limb immobilisation - review of current status	Narrative review, bibliography screened
Obalum et al. 2009	Deep vein thrombosis: risk factors and prevention in surgical patients	Narrative review, bibliography screened
Ringwald et al. 2009	Genetic polymorphisms in venous thrombosis and pulmonary embolism after total hip arthroplasty: a pilot study	Not best available evidence
Severinsen et al. 2009	Anthropometry, body fat, and venous thromboembolism: a Danish follow-up study	Not specific to surgical patients
Szucs et al. 2009	Assessment of thrombotic risk factors predisposing to thromboembolic complications in prosthetic orthopedic surgery	Fewer than 100 patients
Wilasrusmee et al. 2009	Deep venous thrombosis in surgical intensive care unit: prevalence and risk factors	Not specific to elective arthroplasty
Yasunaga et al. 2009	High-volume surgeons in regard to reductions in operating time, blood loss, and postoperative complications for total hip arthroplasty	Not specific to VTE
Yasunaga et al. 2009	Analysis of factors affecting operating time, postoperative complications, and length of stay for total knee arthroplasty: Nationwide web-based survey	Insufficient data
Basilico et al. 2008	Risk factors for cardiovascular complications following total joint replacement surgery	Not specific to VTE
Bolognesi et al. 2008	The impact of diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the United States	Not most recent publication of these data
Buchan et al. 2008	Incidence of venous thromboembolism and thromboprophylaxis after total hip or knee arthroplasty	Not best available evidence
Busato et al. 2008	Influence of high BMI on functional outcome after total hip arthroplasty	Not relevant - no relevant outcome
Gerkens et al. 2008	Assessing the quality of pharmacological treatments from administrative databases: the case of low-molecular-weight heparin after major orthopaedic surgery	Not specific to elective arthroplasty
Kable et al. 2008	Predictors of adverse events in surgical admissions in Australia	Insufficient data

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Kim et al. 2008	The use of spiral computed tomography scans for the detection of pulmonary embolism	Not best available evidence
Monreal et al. 2008	Limited diagnostic workup for deep vein thrombosis after major joint surgery: findings from a prospective, multicentre, cohort study	Not best available evidence (not specific to elective arthroplasty)
Otero-Fernandez et al. 2008	Evaluation of the effectiveness and safety of bemiparin in a large population of orthopedic patients in a normal clinical practice	Not best available evidence (not specific to elective arthroplasty)
Patel et al. 2008	Relationship of body mass index to early complications in knee replacement surgery	Insufficient data
Seruya et al. 2008	Efficacy and safety of venous thromboembolism prophylaxis in highest risk plastic surgery patients	Does not address question of interest
Vu et al. 2008	Determination of risk factors for deep venous thrombosis in hospitalized children	Not specific to surgical patients
Ansari et al. 2007	Risk stratification and utilisation of thrombo-embolism prophylaxis in a medical-surgical ICU: a hospital-based study	Does not address question of interest
Bowler et al. 2007	Factor V Leiden: prevalence and thromboembolic complications after total hip replacement in Ireland	Not best available evidence
Burnett et al. 2007	Failure of the American College of Chest Physicians-1A protocol for lovenox in clinical outcomes for thromboembolic prophylaxis	Not best available evidence
Chotanaphuti et al. 2007	The prevalence of thrombophilia and venous thromboembolism in total knee arthroplasty	Not best available evidence
Chotanaphuti et al. 2007	Risk factors of deep vein thrombosis (DVT) after total knee arthroplasty (TKA) at Phramongkutklao Hospital	Not best available evidence
Dorr et al. 2007	Multimodal thromboprophylaxis for total hip and knee arthroplasty based on risk assessment	Not best available evidence
Gangireddy et al. 2007	Risk factors and clinical impact of postoperative symptomatic venous thromboembolism	Not best available evidence (not specific to elective arthroplasty)
Kahan et al. 2007	High incidence of venous thromboembolic events in lung transplant recipients	Not specific to elective arthroplasty
Kim et al. 2007	Factors leading to decreased rates of deep vein thrombosis and pulmonary embolism after total knee arthroplasty	Not best available evidence
Kim et al. 2007	The 2007 John Charnley Award. Factors leading to low prevalence of DVT and pulmonary embolism after THA: analysis of genetic and prothrombotic factors	Not best available evidence
Kiyoshige et al. 2007	Inherited risk factors for deep venous thrombosis following total hip arthroplasty in Japanese patients: matched control study	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Parvizi et al. 2007	The rise in the incidence of pulmonary embolus after joint arthroplasty: is modern imaging to blame?	Not best available evidence
Samama et al. 2007	Epidemiology of venous thromboembolism after lower limb arthroplasty: the FOTO study	Not best available evidence
Seddighzadeh et al. 2007	Venous thromboembolism in patients undergoing surgery: low rates of prophylaxis and high rates of filter insertion	Does not investigate relevant comparison
Yegen et al. 2007	Risk factors for venous thromboembolism after lung transplantation	Fewer than 100 patients
Zhan et al. 2007	Incidence and short-term outcomes of primary and revision hip replacement in the United States	Not best available evidence
Agnelli et al. 2006	A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS project	Not best available evidence (not specific to elective arthroplasty)
Amin et al. 2006	Does obesity influence the clinical outcome at five years following total knee replacement for osteoarthritis?	Not best available evidence
Bagaria et al. 2006	Incidence and risk factors for development of venous thromboembolism in Indian patients undergoing major orthopaedic surgery: results of a prospective study	Not best available evidence (not specific to elective arthroplasty)
Biau et al. 2006	Is anyone too old for a total knee replacement?	Not best available evidence
Gonzalez et al. 2006	Venous thromboembolism is rare with a multimodal prophylaxis protocol after total hip arthroplasty	Not best available evidence
Hernandez-Vaquero et al. 2006	Total Knee Arthroplasty in the Elderly. Is There an Age Limit?	Does not report VTE
Lachiewicz et al. 2006	Multimodal prophylaxis for THA with mechanical compression	Not best available evidence
Lyman et al. 2006	Prevalence and risk factors for symptomatic thromboembolic events after shoulder arthroplasty	Not best available evidence
McLaughlin et al. 2006	The outcome of total hip replacement in obese and non-obese patients at 10- to 18-years	Not best available evidence
Sadr et al. 2006	The impact of tobacco use and body mass index on the length of stay in hospital and the risk of post-operative complications among patients undergoing total hip replacement	Does not examine VTE
Sakon et al. 2006	Incidence of venous thromboembolism following major abdominal surgery: a multi-center, prospective epidemiological study in Japan	Not specific to elective arthroplasty
Solomon et al. 2006	Development of a preliminary index that predicts adverse events after total knee replacement	Not specific to VTE

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Soohoo et al. 2006	Primary total knee arthroplasty in California 1991 to 2001: does hospital volume affect outcomes?	Insufficient data
Soohoo et al. 2006	Factors predicting complication rates following total knee replacement	Patients reported in a more recent publication
Crowther et al. 2005	Deep venous thrombosis: clinically silent in the intensive care unit	Not specific to surgical patients
Dahl et al. 2005	Postoperative Melagatran/Ximelagatran for the Prevention of Venous Thromboembolism following Major Elective Orthopaedic Surgery : Effects of Timing of First Dose and Risk Factors for Thromboembolism and Bleeding Complications on Efficacy and Safety	Not best available evidence
Gray et al. 2005	Outcome of hip arthroplasty in octogenarians compared with younger patients	Not best available evidence
Gregory et al. 2005	Prevalence of venous thromboembolism in hip and knee arthroplasty patients admitted for comprehensive inpatient rehabilitation	Not best available evidence
Jaffer et al. 2005	Duration of anesthesia and venous thromboembolism after hip and knee arthroplasty	Not best available evidence
Kreder et al. 2005	Arthroplasty in the octogenarian: Quantifying the risks	Does not report VTE
Leizorovicz et al. 2005	Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study	Not best available evidence (not specific to elective arthroplasty)
Piovella et al. 2005	Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography	Not best available evidence (not specific to elective arthroplasty)
Salvati et al. 2005	The John Charnley Award: heritable thrombophilia and development of thromboembolic disease after total hip arthroplasty	Not best available evidence
Schiff et al. 2005	Identifying orthopedic patients at high risk for venous thromboembolism despite thromboprophylaxis	Not best available evidence (not specific to elective arthroplasty)
Syed et al. 2005	Lower-limb deep-vein thrombosis in a general hospital: risk factors, outcomes and the contribution of intravenous drug use	Not specific to surgical patients
Edmonds et al. 2004	Evidence-based risk factors for postoperative deep vein thrombosis	Systematic review, bibliography screened
Hilton et al. 2004	The octogenarian total knee arthroplasty	Not best available evidence
Mont et al. 2004	Risk factors for pulmonary emboli after total hip or knee arthroplasty	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Pookarnjanamorakot et al. 2004	The incidence of deep vein thrombosis and pulmonary embolism after total knee arthroplasty: the screening study by radionuclide venography	Not best available evidence
Weill-Engerer et al. 2004	Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case-control multicenter study	Not specific to surgical patients
White et al. 2004	Effect of age on the incidence of venous thromboembolism after major surgery	Not best available evidence (not specific to elective arthroplasty)
Clarke-Pearson et al. 2003	Venous thromboembolism prophylaxis: patients at high risk to fail intermittent pneumatic compression	Not specific to elective arthroplasty
Czerwinski et al. 2003	Thromboembolic complications after total hip arthroplasty and prevention of thrombosis: own experience	Cannot locate publication
Dowling et al. 2003	The epidemiology of venous thromboembolism in Caucasians and African-Americans: the GATE Study	Not specific to surgical patients
Kim et al. 2003	Incidence and natural history of deep-vein thrombosis after total hip arthroplasty. A prospective and randomised clinical study	Not best available evidence
Kinkel et al. 2003	Revision total hip arthroplasty: the influence of gender and age on the perioperative complication rate	Not best available evidence
Lawton et al. 2003	Validity of index of suspicion for pulmonary embolism after hip arthroplasty	Not best available evidence
Mantilla et al. 2003	Risk factors for clinically relevant pulmonary embolism and deep venous thrombosis in patients undergoing primary hip or knee arthroplasty	Not best available evidence
Moller et al. 2003	Effect of smoking on early complications after elective orthopaedic surgery	Does not report VTE
Samama et al. 2003	Quantification of risk factors for venous thromboembolism: a preliminary study for the development of a risk assessment tool	Systematic review, bibliography screened
White et al. 2003	Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures	Not best available evidence (not specific to elective arthroplasty)
Wurtz et al. 2003	Elective primary total hip arthroplasty in octogenarians	Fewer than 100 patients
Bergqvist et al. 2002	Venous thromboembolism in patients undergoing laparoscopic and arthroscopic surgery and in leg casts	Narrative review, bibliography screened
Kim et al. 2002	Incidence and natural history of deep-vein thrombosis after total knee arthroplasty. A prospective, randomised study	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Mantilla et al. 2002	Frequency of myocardial infarction, pulmonary embolism, deep venous thrombosis, and death following primary hip or knee arthroplasty	Not best available evidence
Solis et al. 2002	Incidence of DVT following surgery of the foot and ankle	Not specific to elective arthroplasty
Ting et al. 2002	Perioperative deep vein thrombosis in Chinese patients undergoing craniotomy	Not best available evidence (not specific to elective arthroplasty)
Wahlander et al. 2002	Factor V Leiden (G1691A) and prothrombin gene G20210A mutations as potential risk factors for venous thromboembolism after total hip or total knee replacement surgery	Not best available evidence
Westrich et al. 2002	Correlation of thrombophilia and hypofibrinolysis with pulmonary embolism following total hip arthroplasty: an analysis of genetic factors	Not best available evidence
Caprini et al. 2001	Effective risk stratification of surgical and nonsurgical patients for venous thromboembolic disease	Narrative review, bibliography screened
Della et al. 2001	The relationship of the factor V Leiden mutation or the deletion-deletion polymorphism of the angiotensin converting enzyme to postoperative thromboembolic events following total joint arthroplasty	Not best available evidence
Larson et al. 2001	Thromboembolism after total knee arthroplasty: intermittent pneumatic compression and aspirin prophylaxis	Not best available evidence
Nguyen et al. 2001	Systemic coagulation and fibrinolysis after laparoscopic and open gastric bypass	Fewer than 100 patients
Tveit et al. 2001	Risk factors for hospitalizations resulting from pulmonary embolism after renal transplantation in the United States	Not best available evidence
Della et al. 2000	Anticoagulant treatment of thromboembolism with intravenous heparin therapy in the early postoperative period following total joint arthroplasty	Not best available evidence
Hansson et al. 2000	Recurrent venous thromboembolism after deep vein thrombosis: incidence and risk factors	Not specific to surgical patients
Joynt et al. 2000	Deep venous thrombosis caused by femoral venous catheters in critically ill adult patients	Not specific to surgical patients
Perka et al. 2000	Influencing factors on perioperative morbidity in knee arthroplasty	Data not specific to VTE
Perka et al. 2000	The influence of obesity on perioperative morbidity and mortality in revision total hip arthroplasty	Not best available evidence
Ruban et al. 2000	Deep vein thrombosis after total knee replacement	Not best available evidence
Wang et al. 2000	Deep vein thrombosis after total knee arthroplasty	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
de Thomasson et al. 1999	Detection of asymptomatic venous thrombosis following hip replacement surgery: Retrospective evaluation of routine screening by duplex ultrasonography based on 286 cases	Not best available evidence
Hooker et al. 1999	Efficacy of prophylaxis against thromboembolism with intermittent pneumatic compression after primary and revision total hip arthroplasty	Not best available evidence
Lindahl et al. 1999	APC-resistance is a risk factor for postoperative thromboembolism in elective replacement of the hip or knee--a prospective study	Not best available evidence
Messieh 1999	Preoperative risk factors associated with symptomatic pulmonary embolism after total knee arthroplasty	Not best available evidence
Warbel et al. 1999	Venous thromboembolism: risk factors in the craniotomy patient population	Not best available evidence (not specific to elective arthroplasty)
Mizel et al. 1998	Thromboembolism after foot and ankle surgery: A multicenter study	Not specific to elective arthroplasty
Ryan et al. 1998	Relation of factor V Leiden genotype to risk for acute deep venous thrombosis after joint replacement surgery	Not best available evidence
White et al. 1998	Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty	Not best available evidence
Woolson et al. 1998	Deep venous thrombosis prophylaxis for knee replacement: warfarin and pneumatic compression	Not best available evidence
Woolson et al. 1998	Factor V Leiden and the risk of proximal venous thrombosis after total hip arthroplasty	Not best available evidence
Andersen et al. 1997	Location of postoperative deep vein thrombosis in relation to age and survival	Not best available evidence
Lieberman et al. 1997	The efficacy of prophylaxis with low-dose warfarin for prevention of pulmonary embolism following total hip arthroplasty	Not best available evidence
Svensson et al. 1997	Female gender and resistance to activated protein C (FV:Q506) as potential risk factors for thrombosis after elective hip arthroplasty	Not best available evidence
Warwick et al. 1997	Symptomatic venous thromboembolism after total knee replacement	Not best available evidence
Woolson 1996	Intermittent pneumatic compression prophylaxis for proximal deep venous thrombosis after total hip replacement	Not best available evidence
Babcock et al. 1994	Venous duplex imaging for surveillance of patients undergoing total joint arthroplasty: A three-year study	Not best available evidence
Lehman et al. 1994	Total hip arthroplasty without cement in obese patients. A minimum two-year clinical and radiographic follow-up study	Not best available evidence
Jiganti et al. 1993	A comparison of the perioperative morbidity in total joint arthroplasty in the obese and nonobese patient	Not best available evidence
Sharrock et al. 1993	Factors affecting deep vein thrombosis rate following total knee arthroplasty under epidural anesthesia	Not best available evidence
Sharrock et al. 1993	Factors influencing deep vein thrombosis following total hip arthroplasty under epidural anesthesia	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Vresilovic et al. 1993	Incidence of pulmonary embolism after total knee arthroplasty with low-dose coumadin prophylaxis	Not best available evidence
Clagett et al. 1992	Prevention of venous thromboembolism	Narrative review, bibliography screened
Gillinov et al. 1992	Pulmonary embolism in the cardiac surgical patient	Fewer than 100 patients
Caprini et al. 1991	Clinical assessment of venous thromboembolic risk in surgical patients	Does not address question of interest
Kim et al. 1991	Factors leading to low incidence of deep vein thrombosis after cementless and cemented total knee arthroplasty	Not best available evidence
Kim 1990	The incidence of deep vein thrombosis after cementless and cemented knee replacement	Not best available evidence
Stern et al. 1990	Total knee arthroplasty in obese patients	Not best available evidence
Balderston et al. 1989	The prevention of pulmonary embolism in total hip arthroplasty. Evaluation of low-dose warfarin therapy	Not best available evidence
Hu 1989	Prophylaxis of deep-vein thrombosis in total hip surgery	Not best available evidence
Stringer et al. 1989	Deep vein thrombosis after elective knee surgery. An incidence study in 312 patients	Not best available evidence (not specific to elective arthroplasty)
Kim et al. 1988	Low incidence of deep-vein thrombosis after cementless total hip replacement	Insufficient data
Lynch et al. 1988	Deep-vein thrombosis and continuous passive motion after total knee arthroplasty	Not best available evidence
Rocha et al. 1988	Preoperative identification of patients at high risk of deep venous thrombosis despite prophylaxis in total hip replacement	Not best available evidence
Stulberg et al. 1984	Deep-vein thrombosis following total knee replacement. An analysis of six hundred and thirty-eight arthroplasties	Not best available evidence
Suomalainen et al. 1983	Postoperative thromboembolism and risk factors in elective hip surgery	Not best available evidence
Stulberg et al. 1982	Aspirin prophylaxis for pulmonary embolism following total hip arthroplasty. An incidence study	Not best available evidence
Sikorski et al. 1981	The natural history and aetiology of deep vein thrombosis after total hip replacement	Not best available evidence
Sorensen et al. 1981	Mechanical prophylaxis against deep vein thrombosis in Charnley hip arthroplasty	Not best available evidence
Buchanan et al. 1980	Is there a lower incidence of deep venous thrombosis after joint replacement in rheumatoid arthritis?	Does not report risk factor of interest
Anderson et al. 1979	Risk factor assessment in 101 total hip arthroplasties: a medical perspective	Not best available evidence

Table 58. Excluded Studies Considered for Risk Factors for VTED

Author	Title	Reason for Exclusion
Nillius et al. 1979	Deep vein thrombosis after total hip replacement: a clinical and phlebographic study	Not best available evidence
van et al. 1977	Comparison of postoperative coumarin, dextran 40 and subcutaneous heparin in the prevention of postoperative deep vein thrombosis	Not best available evidence
Kelsey et al. 1976	Prediction of thromboembolism following total hip replacement	Not best available evidence
Smith et al. 1975	Complications of Austin Moore arthroplasty. Their incidence and relationship to potential predisposing factors	Not specific to elective arthroplasty
Ilstrup et al. 1973	Factors influencing the results in 2,012 total hip arthroplasties	Insufficient data

RISK FACTORS FOR BLEEDING

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Goddard et al. 2010	Total knee replacement in patients with end-stage haemophilic arthropathy: 25-year results	Not best available evidence
Karkouti et al. 2010	The influence of perioperative coagulation status on postoperative blood loss in complex cardiac surgery: a prospective observational study	Excludes patients with pre-existing coagulopathy
Thompson et al. 2010	Systemic AL amyloidosis with acquired factor X deficiency: A study of perioperative bleeding risk and treatment outcomes in 60 patients	Not best available evidence (case series)
Tsuji et al. 2010	Risk factors for bleeding after endoscopic submucosal dissection for gastric lesions	Does not investigate risk factor of interest
Cosmi et al. 2009	Assessment of the risk of bleeding in patients undergoing surgery or invasive procedures: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISET)	Clinical guideline
Fuchs et al. 2009	Major bleeding complicating contemporary primary percutaneous coronary interventions-incidence, predictors, and prognostic implications	Does not address question of interest
Kinnaird et al. 2009	Bleeding during percutaneous intervention: Tailoring the approach to minimise risk	Systematic review, bibliography screened
Manoukian 2009	Predictors and impact of bleeding complications in percutaneous coronary intervention, acute coronary syndromes, and ST-segment elevation myocardial infarction	Narrative review, bibliography screened
Nardell et al. 2009	Risk factors for bleeding in pediatric post-cardiotomy patients requiring ECLS	Does not investigate risk factor of interest
Ng et al. 2009	Value of a single preoperative PFA-100 measurement in assessing the risk of bleeding in patients taking cyclooxygenase inhibitors and undergoing total knee replacement	Does not address question of interest
Solimeno et al. 2009	Factors influencing the long-term outcome of primary total knee replacement in haemophiliacs: a review of 116 procedures at a single institution	Not best available evidence (retrospective case series)
Vieira et al. 2009	A prospective study of conventional and expanded coagulation indices in predicting ulcer bleeding after variceal band ligation	Not best available evidence (coagulation screening)
Witmer et al. 2009	Incidence of bleeding complications in pediatric patients with type 1 von Willebrand disease undergoing adenotonsillar procedures	Not best available evidence
Yasunaga et al. 2009	High-volume surgeons in regard to reductions in operating time, blood loss, and postoperative complications for total hip arthroplasty	Does not examine risk factor of interest
Yoo et al. 2009	The outcome of cementless total hip arthroplasty in haemophilic hip arthropathy	Not best available evidence (retrospective case series)
Blasdale et al. 2008	Perioperative international normalized ratio level is a poor predictor of postoperative bleeding complications in dermatological surgery patients taking warfarin	Not best available evidence (coagulation screening)

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Chee et al. 2008	Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Haematology	Systematic review, bibliography screened
Chiang et al. 2008	Total knee arthroplasty for severe haemophilic arthropathy: long-term experience in Taiwan	Insufficient data
Gerber et al. 2008	The incidence of and risk factors for venous thromboembolism (VTE) and bleeding among 1514 patients undergoing hematopoietic stem cell transplantation: implications for VTE prevention	Does not investigate risk factor of interest
Licameli et al. 2008	Use of a preoperative bleeding questionnaire in pediatric patients who undergo adenotonsillectomy	Not best available evidence (coagulation screening)
Miles et al. 2008	The impact of haemophilia on the success of total hip arthroplasty	Not best available evidence (retrospective case series)
Modig et al. 2008	Template bleeding time for preoperative screening in patients having orthognathic surgery	Not best available evidence (coagulation screening)
Beiderlinden et al. 2007	Risk factors associated with bleeding during and after percutaneous dilational tracheostomy	Not best available evidence (coagulation screening)
Feit et al. 2007	Predictors and Impact of Major Hemorrhage on Mortality Following Percutaneous Coronary Intervention from the REPLACE-2 Trial	Does not address question of interest
Habermann et al. 2007	Total hip replacement in patients with severe bleeding disorders. A 30 years single center experience	Not best available evidence (retrospective case series)
Iwata et al. 2007	Factors predicting early postoperative liver cirrhosis-related complications after lung cancer surgery in patients with liver cirrhosis	Not best available evidence (coagulation screening)
Lethagen et al. 2007	von Willebrand factor/factor VIII concentrate (Haemate(registered trademark) P) dosing based on pharmacokinetics: A prospective multicenter trial in elective surgery	Not best available evidence (bleeding disorder)
Rodriguez-Merchan et al. 2007	Total knee replacement in haemophilic arthropathy	Not best available evidence (retrospective case series)
Valerin et al. 2007	Modified Child-Pugh score as a marker for postoperative bleeding from invasive dental procedures	Not best available evidence (coagulation screening)
Welsby et al. 2007	ABO blood group and bleeding after coronary artery bypass graft surgery	Excludes patients with pre-existing coagulopathy
Carroll et al. 2006	Correlation of perioperative platelet function and coagulation tests with bleeding after cardiopulmonary bypass surgery	Not best available evidence (coagulation screening)

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Gerrah et al. 2006	Using cone and plate(let) analyzer to predict bleeding in cardiac surgery	Not best available evidence (coagulation screening)
Giles et al. 2006	Routine coagulation screening in children undergoing gastrointestinal endoscopy does not predict those at risk of bleeding	Not best available evidence (coagulation screening)
Kirtane et al. 2006	Correlates of bleeding events among moderate- to high-risk patients undergoing percutaneous coronary intervention and treated with eptifibatide: observations from the PROTECT-TIMI-30 trial	Not best available evidence (coagulation screening)
Ward et al. 2006	Long-term postoperative bleeding after dentoalveolar surgery in the pretransplant liver failure patient	Not best available evidence (coagulation screening)
Welsby et al. 2006	The kaolin-activated Thrombelastograph predicts bleeding after cardiac surgery	Not best available evidence (coagulation screening)
Bae et al. 2005	Total knee arthroplasty in hemophilic arthropathy of the knee	Not best available evidence (retrospective case series)
Blome et al. 2005	Relationship between factor XIII activity, fibrinogen, haemostasis screening tests and postoperative bleeding in cardiopulmonary bypass surgery	Excludes patients with pre-existing coagulopathy
Farouque et al. 2005	Risk factors for the development of retroperitoneal hematoma after percutaneous coronary intervention in the era of glycoprotein IIb/IIIa inhibitors and vascular closure devices	Not best available evidence (coagulation screening)
Magann et al. 2005	Postpartum hemorrhage after cesarean delivery: an analysis of risk factors	Not best available evidence
Ohta et al. 2005	Analysis of risk factors for massive intraoperative bleeding during laparoscopic splenectomy	Not best available evidence
Segal et al. 2005	Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: An evidence-based review	Systematic review, bibliography screened
Sirichindakul et al. 2005	Risk factors associated with major intraoperative blood loss in hepatic resection for hepatobiliary tumor	Not best available evidence
Villiger et al. 2005	Prevention of bleeding after islet transplantation: lessons learned from a multivariate analysis of 132 cases at a single institution	Not best available evidence (coagulation screening)
Chang et al. 2004	Predicting blood loss and transfusion requirements during radical prostatectomy: the significant negative impact of increasing body mass index	Not best available evidence (not elective arthroplasty)
Ho et al. 2004	Blood loss and transfusion in elective abdominal aortic aneurysm surgery	Not best available evidence (coagulation screening)
Karthik et al. 2004	Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay	Does not investigate risk factor of interest
Kukreja et al. 2004	Factors affecting blood loss during percutaneous nephrolithotomy: prospective study	Does not investigate risk factor of interest

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Castellano et al. 2003	American Society of Anesthesiology classification may predict severe post-tonsillectomy haemorrhage in children	Not best available evidence (coagulation screening)
Fattorutto et al. 2003	Does the platelet function analyser (PFA-100) predict blood loss after cardiopulmonary bypass?	Not best available evidence (coagulation screening)
Herwaldt et al. 2003	Hemorrhage after coronary artery bypass graft procedures	Not best available evidence
Hsieh et al. 2003	Hip arthroplasty in patients with cirrhosis of the liver	Not best available evidence (retrospective case series)
Legroux-Gerot et al. 2003	Total knee arthroplasty in hemophilic arthropathy	Not best available evidence (retrospective case series)
Terjung et al. 2003	Bleeding complications after percutaneous liver biopsy. An analysis of risk factors	Not best available evidence
Winkelmayer et al. 2003	Chronic kidney disease as a risk factor for bleeding complications after coronary artery bypass surgery	Not best available evidence (coagulation screening)
Hall et al. 2002	Hemorrhage related reexploration following open heart surgery: the impact of pre-operative and post-operative coagulation testing	Not best available evidence (coagulation screening)
Isgro et al. 2002	Platelet function test HemoSTATUS 2: tool or toy for an optimized management of hemostasis?	Not best available evidence (coagulation screening)
Ti et al. 2002	Prediction of excessive bleeding after coronary artery bypass graft surgery: the influence of timing and heparinase on thromboelastography	Not best available evidence (coagulation screening)
Asaf et al. 2001	The need for routine pre-operative coagulation screening tests (prothrombin time PT/partial thromboplastin time PTT) for healthy children undergoing elective tonsillectomy and/or adenoidectomy	Not best available evidence (coagulation screening)
Blinder et al. 2001	Dental extractions in patients maintained on oral anticoagulant therapy: comparison of INR value with occurrence of postoperative bleeding	Not best available evidence (coagulation screening)
Ereth et al. 2001	Platelet glass bead retention predicts bleeding after cardiac surgery	Insufficient data
Friedman et al. 2001	Remote cerebellar hemorrhage after supratentorial surgery	Not best available evidence (coagulation screening)
Krishna et al. 2001	Post-tonsillectomy bleeding: a meta-analysis	Systematic review, bibliography screened
Lehman et al. 2001	Discontinuation of the bleeding time test without detectable adverse clinical impact	Not best available evidence
Nevo et al. 2001	Acute bleeding and thrombocytopenia after bone marrow transplantation	Does not address question of interest

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Steib et al. 2001	Intraoperative blood losses and transfusion requirements during adult liver transplantation remain difficult to predict	Not best available evidence (coagulation screening)
Stiles et al. 2001	The impact of bleeding times on major complication rates after percutaneous real-time ultrasound-guided renal biopsies	Not best available evidence (coagulation screening)
Christiansen et al. 2000	Are patients with Werlhof's disease at increased risk for bleeding complications when undergoing cardiac surgery?	Not best available evidence (coagulation screening)
Cohen et al. 2000	Orthopaedic outcome of total knee replacement in haemophilia A	Not best available evidence (retrospective case series)
Gabriel et al. 2000	Relationship between clinical history, coagulation tests, and perioperative bleeding during tonsillectomies in pediatrics	Not best available evidence (coagulation screening)
Gerlach et al. 2000	Factor XIII deficiency and postoperative hemorrhage after neurosurgical procedures	Not best available evidence (bleeding disorder)
Boberg et al. 1999	Is a prolonged bleeding time associated with an increased risk of hemorrhage after liver biopsy?	Not best available evidence
Oren et al. 1999	Abnormal clotting parameters before therapeutic ERCP: do they predict major bleeding?	Not best available evidence (coagulation screening)
Schick et al. 1999	Haemophilic; arthropathy: Assessment of quality of life after total knee arthroplasty	Not best available evidence (retrospective case series)
Bjortuft et al. 1998	Bronchoscopy with transbronchial biopsies: measurement of bleeding volume and evaluation of the predictive value of coagulation tests	Not best available evidence
Dacey et al. 1998	Reexploration for hemorrhage following coronary artery bypass grafting: incidence and risk factors. Northern New England Cardiovascular Disease Study Group	Not best available evidence
Ereth et al. 1998	The relation between the platelet-activated clotting test (HemoSTATUS) and blood loss after cardiopulmonary bypass	Not best available evidence (coagulation screening)
Kabakibi et al. 1998	Collagen-induced whole blood platelet aggregation in patients undergoing surgical procedures associated with minimal to moderate blood loss	Not best available evidence (coagulation screening)
Korte et al. 1998	Preoperative values of molecular coagulation markers identify patients at low risk for intraoperative haemostatic disorders and excessive blood loss	Not best available evidence (coagulation screening)
Mandak et al. 1998	Modifiable risk factors for vascular access site complications in the	Does not address question of interest
Wahba et al. 1998	Are in-vitro platelet function tests useful in predicting blood loss following open heart surgery?	Not best available evidence (coagulation screening)

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Ereth et al. 1997	Does the platelet-activated clotting test (HemoSTATUS) predict blood loss and platelet dysfunction associated with cardiopulmonary bypass?	Not best available evidence (coagulation screening)
Howells et al. 1997	Value of preoperative prothrombin time/partial thromboplastin time as a predictor of postoperative hemorrhage in pediatric patients undergoing tonsillectomy	Not best available evidence (coagulation screening)
Nuttall et al. 1997	Coagulation tests predict bleeding after cardiopulmonary bypass	Not best available evidence (coagulation screening)
Despotis et al. 1996	Evaluation of a new point-of-care test that measures PAF-mediated acceleration of coagulation in cardiac surgical patients	Insufficient data
Gelb et al. 1996	Changes in blood coagulation during and following cardiopulmonary bypass: lack of correlation with clinical bleeding	Not best available evidence (coagulation screening)
Gewirtz et al. 1996	The clinical usefulness of the preoperative bleeding time	Not best available evidence (coagulation screening)
Lofqvist et al. 1996	Total hip replacement in patients with hemophilia. 13 hips in 11 patients followed for 1-16 years	Not best available evidence (retrospective case series)
Monreal et al. 1996	Preoperative platelet count and postoperative blood loss in patients undergoing hip surgery: an inverse correlation	Not best available evidence
Moulton et al. 1996	Reexploration for bleeding is a risk factor for adverse outcomes after cardiac operations	Not best available evidence
Winter et al. 1996	Perioperative blood loss: the effect of valproate	Not best available evidence (coagulation screening)
Aleskog et al. 1995	Preoperative evaluation of primary hemostasis in patients with thrombocytopenia using the Thrombostat 4000	Does not report patient oriented outcomes
Davis et al. 1995	Thromboelastography for the prediction of bleeding after transplant renal biopsy	Not best available evidence (coagulation screening)
Grosflam et al. 1995	Predictors of blood loss during total hip replacement surgery	Does not investigate risk factor of interest
Irani et al. 1995	Platelet function, coagulation tests, and cardiopulmonary bypass: lack of correlation between pre-operative and intra-operative whole blood lumiaggregometry and peri-operative blood loss in patients receiving autologous platelet-rich plasma	Not best available evidence (coagulation screening)
Kelley et al. 1995	Hip arthroplasty in hemophilic arthropathy	Insufficient data
Ozier et al. 1995	Intraoperative blood loss in pediatric liver transplantation: analysis of preoperative risk factors	Not best available evidence (coagulation screening)
De Caterina et al. 1994	Bleeding time and bleeding: an analysis of the relationship of the bleeding time test with parameters of surgical bleeding	Excludes patients with pre-existing coagulopathy

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Kozak et al. 1994	Do 'screening' coagulation tests predict bleeding in patients undergoing fiberoptic bronchoscopy with biopsy?	Not best available evidence (coagulation screening)
Naef et al. 1994	Prediction of hemorrhage at cesarean delivery	Does not address question of interest
Nelson et al. 1994	Major hemorrhage from endoscopic sphincterotomy: risk factor analysis	Not best available evidence (coagulation screening)
Ray et al. 1994	Relationship of platelet aggregation to bleeding after cardiopulmonary bypass	Not best available evidence (coagulation screening)
Macpherson et al. 1993	Abnormal peri-operative haemorrhage in asymptomatic patients is not predicted by laboratory testing	Not best available evidence (coagulation screening)
Mor et al. 1993	The impact of operative bleeding on outcome in transplantation of the liver	Not best available evidence (coagulation screening)
Teigland et al. 1993	Knee arthroplasty in hemophilia. 5-12 year follow-up of 15 patients	Not best available evidence (retrospective case series)
Davenport 1992	Predicting postprocedure bleeding in liver disease	Commentary
Nelson et al. 1992	Total hip arthroplasty for hemophilic arthropathy	Insufficient data
Wang et al. 1992	Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients	Not best available evidence (coagulation screening)
Lebovics et al. 1991	Upper gastrointestinal bleeding following open heart surgery. Predominant finding of aggressive duodenal ulcer disease	Does not address question of interest
Lind 1991	The bleeding time does not predict surgical bleeding	Systematic review, bibliography screened
Martin et al. 1991	Monitoring of coagulation status using thrombelastography during paediatric open heart surgery	Not best available evidence (coagulation screening)
Hay et al. 1990	Bleeding complications in thrombocytopenic patients undergoing ophthalmic surgery	Letter
Smith et al. 1990	Predicting bleeding in common ear, nose, and throat procedures: a prospective study	Insufficient data
Figgie et al. 1989	Total knee arthroplasty for the treatment of chronic hemophilic arthropathy	Not best available evidence (retrospective case series)
Berman et al. 1988	Blood loss with total knee arthroplasty	Does not investigate risk factor of interest
Halonen et al. 1987	Evaluation of risk factors in intraoperative bleeding tendency	Not best available evidence (coagulation screening)

Table 59. Excluded Studies Considered for Risk Factors for Bleeding

Author	Title	Reason for Exclusion
Tami et al. 1987	Post-tonsillectomy bleeding: an evaluation of risk factors	Not best available evidence (coagulation screening)
Burns et al. 1986	The preoperative bleeding time as a predictor of postoperative hemorrhage after cardiopulmonary bypass	Not best available evidence (coagulation screening)
Suchman et al. 1986	How well does the activated partial thromboplastin time predict postoperative hemorrhage?	Not best available evidence
Barber et al. 1985	The bleeding time as a preoperative screening test	Insufficient data
Lachiewicz et al. 1985	Total knee arthroplasty in hemophilia	Insufficient data
Sharma et al. 1982	The risk of bleeding after percutaneous liver biopsy: relation to platelet count	Not best available evidence (coagulation screening)
Goldberg et al. 1981	Total knee arthroplasty in classic hemophilia	Not best available evidence (retrospective case series)
McCollough et al. 1979	Synovectomy or total replacement of the knee in hemophilia	Less than 10 arthroplasty patients
D'Ambrosia et al. 1974	Total hip replacement for patients with hemophilia and hemorrhagic diathesis	Case report

Table 60. Excluded Studies Considered for Risk Factors for Hemorrhage-Associated Complications

Author	Title	Reason for Exclusion
Baker et al. 2011	The effect of surgeon volume on the need for transfusion following primary unilateral hip and knee arthroplasty	Not best available evidence
Goddard et al. 2010	Does the preoperative iron status predict transfusion requirement of orthopedic patients?	Not best available evidence
Mahadevan et al. 2010	Revision total hip replacement: predictors of blood loss, transfusion requirements, and length of hospitalisation	Not best available evidence
Fotland et al. 2009	Does the preoperative iron status predict transfusion requirement of orthopedic patients?	Not best available evidence
Mourao et al. 2009	An analysis of joint replacement in patients with systemic lupus erythematosus	Not best available evidence
Andrew et al. 2008	Obesity in total hip replacement	Not best available evidence
Bolognesi et al. 2008	The impact of diabetes on perioperative patient outcomes after total hip and total knee arthroplasty in the United States	Not most recent publication of these data
Chelly et al. 2008	Throbmoprophylaxis and peripheral nerve blocks in patients undergoing joint arthroplasty	Retrospective case series
Chelly et al. 2008b	International normalized ratio and prothrombin time values before the removal of a lumbar plexus catheter in patients receiving warfarin after total hip replacement	Retrospective case series
Gunningberg et al. 2008	Pre- and postoperative nutritional status and predictors for surgical-wound infections in elective orthopaedic and thoracic patients	Not best available evidence
Habermann et al. 2008	Total joint replacement in HIV positive patients	Not best available evidence
Hamilton et al. 2008	Deep infection in total hip arthroplasty	Not best available evidence
Moon et al. 2008	Factors affecting outcome after total knee arthroplasty in patients with diabetes mellitus	Not best available evidence
Pulido et al. 2008	In hospital complications after total joint arthroplasty	Not best available evidence
Rogers et al. 2008	Identification and treatment of anaemia in patients awaiting hip replacement	Not best available evidence
Burnett et al. 2007	Failure of the American College of Chest Physicians-1A protocol for lovenox in clinical outcomes for thromboembolic prophylaxis	Not best available evidence
Moon et al. 2007	Perioperative risk of hip arthroplasty in patients with cirrhotic liver disease	Not best available evidence
Patel et al. 2007	Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty	Not best available evidence
Prasad et al. 2007	Blood loss in total knee arthroplasty: an analysis of risk factors	Not best available evidence
Wood et al. 2007	Wound oozing after total hip arthroplasty	Not best available evidence

Table 60. Excluded Studies Considered for Risk Factors for Hemorrhage-Associated Complications

Author	Title	Reason for Exclusion
Amin et al. 2006	Does obesity influence the clinical outcome at five years following total knee replacement for osteoarthritis?	Not best available evidence
McLaughlin et al. 2006	The outcome of total hip replacement in obese and non-obese patients at 10- to 18-years	Not best available evidence
Parvizi et al. 2006	Can epidural anesthesia and warfarin be coadministered	Retrospective case series
Rashiq et al. 2006	The effect of spinal anesthesia on blood transfusion rate in total joint arthroplasty	Data from previously published study
Sadr et al. 2006	The impact of tobacco use and body mass index on the length of stay in hospital and the risk of post-operative complications among patients undergoing total hip replacement	Does not examine hemorrhage-associated complications
Yercan et al. 2006	Stiffness after total knee arthroplasty: Prevalence, management and outcomes	Insufficien data
Powell et al. 2005	Knee and hip arthroplasty infection rates in persons with haemophilia: a 27 year single center experience during the HIV epidemic	Not best available evidence
Al-Mousawi 2004	Complications and failures of hip replacement in sickle cell disease	Not best available evidence
Pola et al. 2004	Clinical factors associated with an increased risk of perioperative blood transfusion in nonanemic patients undergoing total hip arthroplasty	Not best available evidence
Rose et al. 2004	Total knee arthroplasty in Ehlers-Danlos Syndrome	Retrospective case series
Yau et al. 2004	Factors leading to blood transfusion among Chinese patients undergoing total knee replacements: a retrospective study	Not best available evidence
Parvizi et al. 2003	Total joint arthroplasty in human immunodeficiency virus-positive patients: An alarming rate of early failure	Not best available evidence
Shrader et al. 2003	Insall Award paper. Primary TKA in patients with lymphedema	Not best available evidence
Al-Mousawi et al. 2002	Total hip replacement in sickle cell disease	Not best available evidence
Ilyas et al. 2002	Simultaneous bilateral total hip arthroplasty in sickle cell disease	Not best available evidence
Saleh et al. 2002	Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program	Not best available evidence
Salido et al. 2002	Preoperative hemoglobin levels and the need for transfusion after prosthetic hip and knee surgery: analysis of predictive factors	Not best available evidence
Hatzidakis et al. 2000	Preoperative autologous donation for total joint arthroplasty. An analysis of risk factors for allogenic transfusion	Not best available evidence
Perka et al. 2000	The influence of obesity on perioperative morbidity and mortality in revision total hip arthroplasty	Not best available evidence
Bowditch et al. 1999	Do obese patients bleed more? A prospective study of blood loss at total hip replacement	Does not report outcome of interest

Table 60. Excluded Studies Considered for Risk Factors for Hemorrhage-Associated Complications

Author	Title	Reason for Exclusion
Faris et al. 1999	The predictive power of baseline hemoglobin for transfusion risk in surgery patients	Narrative review, bibliography screened
Nelson et al. 1999	Primary and revision total hip replacement in patients who are Jehovah's Witnesses	Narrative review, bibliography screened
Vichinsky et al. 1999	The perioperative complication rate of orthopedic surgery in sickle cell disease: report of the National Sickle Cell Surgery Study Group	Not best available evidence
Kageyama et al. 1998	Outcomes for patients undergoing one or more total hip and knee arthroplasties	Does not report outcome of interest
Keating et al. 1998	Predictors of transfusion risk in elective knee surgery	Not best available evidence
Larocque et al. 1998	Prospective validation of a point score system for predicting blood transfusion following hip or knee replacement	Insufficient data
Nuttall et al. 1996	The predictors of red cell transfusions in total hip arthroplasties	Not best available evidence
Wu et al. 1996	Oral anticoagulant prophylaxis and epidural catheter removal	Retrospective case series
Deo et al. 1995	Total hip replacement in renal transplant patients	Not best available evidence
Escalante et al. 1995	Risk factors for early wound complications after orthopedic surgery for rheumatoid arthritis	Not specific to hip and knee arthroplasty
Hasley et al. 1995	Variation in the use of red blood cell transfusions. A study of four common medical and surgical conditions	Does not investigate risk factor of interest
McGrory et al. 1995	Total hip arthroplasty in patients who have chronic lymphocytic leukemia	Not best available evidence
Horlocker et al. 1994	Postoperative epidural anesthesia and oral anticoagulant therapy	Retrospective case series
Lehman et al. 1994	Total hip arthroplasty without cement in obese patients. A minimum two-year clinical and radiographic follow-up study	Not best available evidence
Jiganti et al. 1993	A comparison of the perioperative morbidity in total joint arthroplasty in the obese and nonobese patient	Not best available evidence
Moran et al. 1993	Total hip arthroplasty in sickle cell hemoglobinopathy	Not best available evidence
Wittmann et al. 1992	Total hip replacement surgery without blood transfusion in Jehovah’s Witnesses	Retrospective case series
Flordal et al. 1991	Blood loss in total hip replacement. A retrospective study	Not best available evidence
England et al. 1990	Total knee arthroplasty in diabetes mellitus	Not best available evidence
Bonnett et al. 1987	Total hip replacement in Jehovah’s Witnesses under spinal anesthesia without transfusion	Retrospective case series
Isono et al. 1987	Total joint arthroplasty for steroid-induced osteonecrosis in cardiac transplant patients	Not best available evidence

Table 60. Excluded Studies Considered for Risk Factors for Hemorrhage-Associated Complications

Author	Title	Reason for Exclusion
Soballe et al. 1987	Hip replacement in obese patients	Not best available evidence
Nelson et al. 1986	Total hip arthroplasty in Jehovah's Witnesses without blood transfusion	Retrospective case series
Chmell et al. 1983	Total hip replacement in patients with renal transplants	Not best available evidence
Colville et al. 1978	Charnley low-friction arthroplasties of the hip in rheumatoid arthritis. A study of the complications and results of 378 arthroplasties	Not best available evidence
Riley et al. 1978	Geometric total knee replacement for treatment of the rheumatoid knee	Not best available evidence
Salvati et al. 1972	Total hip replacement in rheumatoid arthritis	Not best available evidence

PREOPERATIVE ANTIPLATELET USE

Table 61. Excluded Studies Considered for Preoperative Antiplatelet Use

Author	Title	Reason for Exclusion
Badreldin et al. 2010	Effect of clopidogrel on perioperative blood loss and transfusion in coronary artery bypass graft surgery	Not best available evidence (non-randomized study)
Herman et al. 2010	Clopidogrel increases blood transfusion and hemorrhagic complications in patients undergoing cardiac surgery	Not best available evidence (non-randomized study)
Tompkins et al. 2010	Dual antiplatelet therapy and heparin 'bridging' significantly increase the risk of bleeding complications after pacemaker or implantable cardioverter-defibrillator device implantation	Not best available evidence (non-randomized study)
Grujic et al. 2009	Perioperative clopidogrel is seven days enough?	Not best available evidence (non-randomized study)
Gulbins et al. 2009	Preoperative platelet inhibition with ASA does not influence postoperative blood loss following coronary artery bypass grafting	Not best available evidence (non-randomized study)
Jeon et al. 2009	Predictors of immediate bleeding during endoscopic submucosal dissection in gastric lesions	Not best available evidence (non-randomized study)
Napenas et al. 2009	The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual antiplatelet therapy	Not best available evidence (non-randomized study)
Nardell et al. 2009	Risk factors for bleeding in pediatric post-cardiotomy patients requiring ECLS	Does not investigate risk factor of interest
O'Riordan et al. 2009	Antiplatelet agents in the perioperative period	Systematic review, bibliography screened
Vaccarino et al. 2009	Impact of preoperative clopidogrel in off pump coronary artery bypass surgery: a propensity score analysis	Not best available evidence (non-randomized study)
Berger et al. 2008	Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: a multicenter analysis	Not best available evidence (non-randomized study)
Filsoufi et al. 2008	Clopidogrel treatment before coronary artery bypass graft surgery increases postoperative morbidity and blood product requirements	Not best available evidence (non-randomized study)
Halliwell et al. 2008	Transrectal ultrasound-guided biopsy of the prostate: aspirin increases the incidence of minor bleeding complications	Not best available evidence (non-randomized study)
Kamran et al. 2008	Effect of aspirin on postoperative bleeding in coronary artery bypass grafting	Not best available evidence (non-randomized study)
Krishnan et al. 2008	Exodontia and antiplatelet therapy	Not best available evidence (non-randomized study)
Law et al. 2008	Hemorrhagic complications from glaucoma surgery in patients on anticoagulation therapy or antiplatelet therapy	Not best available evidence (non-randomized study)

Table 61. Excluded Studies Considered for Preoperative Antiplatelet Use

Author	Title	Reason for Exclusion
Maltais et al. 2008	Effect of clopidogrel on bleeding and transfusions after off-pump coronary artery bypass graft surgery: impact of discontinuation prior to surgery	Not best available evidence (non-randomized study)
Morimoto et al. 2008	Hemostatic management of tooth extractions in patients on oral antithrombotic therapy	Not best available evidence (non-randomized study)
Ozao-Choy et al. 2008	Clopidogrel and bleeding after general surgery procedures	Not best available evidence (non-randomized study)
Partridge et al. 2008	The effect of platelet-altering medications on bleeding from minor oral surgery procedures	Not best available evidence (non-randomized study)
Pinkau et al. 2008	Glycoprotein IIb/IIIa receptor inhibition with abciximab during percutaneous coronary interventions increases the risk of bleeding in patients with impaired renal function	Does not address question of interest
Ruiz-Nodar et al. 2008	Anticoagulant and antiplatelet therapy use in 426 patients with atrial fibrillation undergoing percutaneous coronary intervention and stent implantation implications for bleeding risk and prognosis	Does not investigate risk factor of interest
Shalom et al. 2008	Lack of complications in minor skin lesion excisions in patients taking aspirin or warfarin products	Not best available evidence (non-randomized study)
Shimizu et al. 2008	Multiple antithrombotic agents increase the risk of postoperative hemorrhage in dermatologic surgery	Not best available evidence (non-randomized study)
Sun et al. 2008	The effect of pre-operative aspirin on bleeding, transfusion, myocardial infarction, and mortality in coronary artery bypass surgery: A systematic review of randomized and observational studies	Systematic review, bibliography screened
Widimsky et al. 2008	Clopidogrel pre-treatment in stable angina: For all patients >6 h before elective coronary angiography or only for angiographically selected patients a few minutes before PCI? A randomized multicentre trial PRAGUE-8	Does not address question of interest
Alghamdi et al. 2007	Does the use of preoperative aspirin increase the risk of bleeding in patients undergoing coronary artery bypass grafting surgery? Systematic review and meta-analysis	Systematic review, bibliography screened
Dixon et al. 2007	Bleeding complications in skin cancer surgery are associated with warfarin but not aspirin therapy	Not best available evidence (non-randomized study)
Mehilli et al. 2007	Sex and effect of abciximab in patients with acute coronary syndromes treated with percutaneous coronary interventions: results from Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment 2 trial	Does not address question of interest
Ouattara et al. 2007	Impact of aspirin with or without clopidogrel on postoperative bleeding and blood transfusion in coronary surgical patients treated prophylactically with a low-dose of aprotinin	Not best available evidence (non-randomized study)

Table 61. Excluded Studies Considered for Preoperative Antiplatelet Use

Author	Title	Reason for Exclusion
Picker et al. 2007	Antiplatelet therapy preceding coronary artery surgery: implications for bleeding, transfusion requirements and outcome	Not best available evidence (non-randomized study)
Pristipino et al. 2007	Comparison of access-related bleeding complications in women versus men undergoing percutaneous coronary catheterization using the radial versus femoral artery	Not best available evidence (non-randomized study)
Robinson et al. 2007	Factors associated with deep sternal wound infection and haemorrhage following cardiac surgery in Victoria	Not best available evidence (non-randomized study)
Dhiwakar et al. 2006	Surgical resection of cutaneous head and neck lesions: does aspirin use increase hemorrhagic risk?	Not best available evidence
Ellis et al. 2006	Correlates and outcomes of retroperitoneal hemorrhage complicating percutaneous coronary intervention	Not best available evidence (non-randomized study)
Foss et al. 2006	Hidden blood loss after surgery for hip fracture	Not best available evidence (non-randomized study)
Haydar et al. 2006	Bleeding post coronary artery bypass surgery. Clopidogrel--cure or culprit?	Not best available evidence (non-randomized study)
Kennedy et al. 2006	The association between aspirin and blood loss in hip fracture patients	Not best available evidence (non-randomized study)
McCaslin et al. 2006	Oral antiplatelet agents and bleeding risk in relation to major cardiovascular surgery	Narrative review, bibliography screened
Zhang et al. 2006	Administrative claims analysis of the relationship between warfarin use and risk of hemorrhage including drug-drug and drug-disease interactions	Not specific to surgical patients
Akowuah et al. 2005	Comparison of two strategies for the management of antiplatelet therapy during urgent surgery	Does not address question of interest
Exaire et al. 2005	Closure devices and vascular complications among percutaneous coronary intervention patients receiving enoxaparin, glycoprotein IIb/IIIa inhibitors, and clopidogrel	Not best available evidence (non-randomized study)
Giger et al. 2005	Hemorrhage risk after quinsy tonsillectomy	Not best available evidence (non-randomized study)
Leong et al. 2005	Clopidogrel and bleeding after coronary artery bypass graft surgery	Not best available evidence (non-randomized study)
McDonald et al. 2005	Preoperative use of enoxaparin increases the risk of postoperative bleeding and re-exploration in cardiac surgery patients	Not best available evidence (non-randomized study)
Morawski et al. 2005	Prediction of the excessive perioperative bleeding in patients undergoing coronary artery bypass grafting: Role of aspirin and platelet glycoprotein IIIa polymorphism	Does not address question of interest
Chen et al. 2004	Clopidogrel and bleeding in patients undergoing elective coronary artery bypass grafting	Not best available evidence (non-randomized study)

Table 61. Excluded Studies Considered for Preoperative Antiplatelet Use

Author	Title	Reason for Exclusion
Chu et al. 2004	Does clopidogrel increase blood loss following coronary artery bypass surgery?	Not best available evidence (non-randomized study)
Karabulut et al. 2004	Clopidogrel does not increase bleeding and allogenic blood transfusion in coronary artery surgery	Not best available evidence (non-randomized study)
Pothula et al. 2004	The effect of preoperative antiplatelet/anticoagulant prophylaxis on postoperative blood loss in cardiac surgery	Not best available evidence (non-randomized study)
Cammerer et al. 2003	The predictive value of modified computerized thromboelastography and platelet function analysis for postoperative blood loss in routine cardiac surgery	Not best available evidence (non-randomized study)
Srinivasan et al. 2003	Effect of preoperative aspirin use in off-pump coronary artery bypass operations	Not best available evidence (non-randomized study)
Blankenship et al. 2002	Reduction in vascular access site bleeding in sequential abciximab coronary intervention trials	Does not address question of interest
Ferraris et al. 2002	Aspirin and postoperative bleeding after coronary artery bypass grafting	Not best available evidence (non-randomized study)
Hongo et al. 2002	The effect of clopidogrel in combination with aspirin when given before coronary artery bypass grafting	Not best available evidence (non-randomized study)
Hui et al. 2002	Does withholding aspirin for one week reduce the risk of post-sphincterotomy bleeding?	Not best available evidence (non-randomized study)
Bizzarri et al. 2001	Perioperative use of tirofiban hydrochloride (Aggrastat) does not increase surgical bleeding after emergency or urgent coronary artery bypass grafting	Not best available evidence (non-randomized study)
Grubitzsch et al. 2001	Emergency coronary artery bypass grafting: does excessive preoperative anticoagulation increase bleeding complications and transfusion requirements?	Not best available evidence (non-randomized study)
Mehta et al. 2001	Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: The PCI-CURE study	Does not address question of interest
Yende et al. 2001	Effect of clopidogrel on bleeding after coronary artery bypass surgery	Not best available evidence (non-randomized study)
Lincoff et al. 2000	Abciximab and bleeding during coronary surgery: results from the EPILOG and EPISTENT trials. Improve Long-term Outcome with abciximab GP IIb/IIIa blockade.	Does not address question of interest
Van et al. 2000	Evaluation of Platelet IIb/IIIa Inhibition in STENTing Abciximab and bleeding during coronary surgery: Results from the EPILOG and	Does not address question of interest
Herget et al. 1999	Transrectal ultrasound-guided biopsy of the prostate: relation between ASA use and bleeding complications	Not best available evidence (non-randomized study)

Table 61. Excluded Studies Considered for Preoperative Antiplatelet Use

Author	Title	Reason for Exclusion
Assia et al. 1998	Effect of aspirin intake on bleeding during cataract surgery	Does not report patient oriented outcomes
Gammie et al. 1998	Abciximab and excessive bleeding in patients undergoing emergency cardiac operations	Not best available evidence (non-randomized study)
Wierod et al. 1998	Risk of haemorrhage from transurethral prostatectomy in acetylsalicylic acid and NSAID-treated patients	Does not address question of interest
Billingsley et al. 1997	Intraoperative and postoperative bleeding problems in patients taking warfarin, aspirin, and nonsteroidal antiinflammatory agents. A prospective study	Not best available evidence (non-randomized study)
Cohen et al. 1997	Risk factors for bleeding in major abdominal surgery using heparin thromboprophylaxis	Not best available evidence (non-randomized study)
Aguirre et al. 1995	Bleeding complications with the chimeric antibody to platelet glycoprotein IIb/IIIa integrin in patients undergoing percutaneous coronary intervention. EPIC Investigators	Does not address question of interest
Lawrence et al. 1994	Effect of aspirin and nonsteroidal antiinflammatory drug therapy on bleeding complications in dermatologic surgical patients	Not best available evidence (non-randomized study)
Shiffman et al. 1994	Risk of bleeding after endoscopic biopsy or polypectomy in patients taking aspirin or other NSAIDS	Not best available evidence (non-randomized study)
Landefeld et al. 1993	Anticoagulant-related bleeding: clinical epidemiology, prediction, and prevention	Systematic review, bibliography screened
Thurston et al. 1993	Aspirin and post-prostatectomy haemorrhage	Not best available evidence (non-randomized study)
Ferraris et al. 1988	Preoperative aspirin ingestion increases operative blood loss after coronary artery bypass grafting	Does not address question of interest

PROPHYLAXIS

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Dranitsaris et al. 2011	Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement	Systematic review, bibliography screened
Kalyani et al. 2011	Low molecular weight heparin: Current evidence for its application in orthopaedic surgery	Systematic review, bibliography screened
Ma et al. 2011	Dabigatran etexilate versus warfarin as the oral anticoagulant of choice? A review of clinical data	Narrative review, bibliography screened
Papakostidis et al. 2011	The timing of drug administration for thromboprophylaxis following orthopaedic surgery: Evidence and controversies related to treatment initiation and duration	Narrative review, bibliography screened
Borgen et al. 2010	Preoperative versus postoperative initiation of dalteparin thromboprophylaxis in THA	Not best available evidence (retrospective comparative)
Bozic et al. 2010	Does aspirin have a role in venous thromboembolism prophylaxis in total knee arthroplasty patients?	Not best available evidence
Cao et al. 2010	Rivaroxaban versus enoxaparin for thromboprophylaxis after total hip or knee arthroplasty: a meta-analysis of randomized controlled trials	Systematic review, bibliography screened
Diamantopoulos et al. 2010	Cost-effectiveness of rivaroxaban versus enoxaparin for the prevention of postsurgical venous thromboembolism in Canada	Cost-Effectiveness Study
Friedman et al. 2010	Dabigatran versus enoxaparin for prevention of venous thromboembolism after hip or knee arthroplasty: a pooled analysis of three trials	Systematic review, bibliography screened
Haas et al. 2010	Rivaroxaban, a new oral anticoagulant for the prevention of venous thromboembolism after elective hip or knee replacement surgery	Narrative review, bibliography screened
Huisman et al. 2010	Enoxaparin versus dabigatran or rivaroxaban for thromboprophylaxis after hip or knee arthroplasty: Results of separate pooled analyses of phase III multicenter randomized trials	Systematic review, bibliography screened
Jameson et al. 2010	The impact of national guidelines for the prophylaxis of venous thromboembolism on the complications of arthroplasty of the lower limb	Ecological study
Kapoor et al. 2010	Cost effectiveness of venous thromboembolism pharmacological prophylaxis in total hip and knee replacement: a systematic review	Systematic review, bibliography screened
Melillo et al. 2010	Rivaroxaban for thromboprophylaxis in patients undergoing major orthopedic surgery	Systematic review, bibliography screened
Pendleton et al. 2010	A safe, effective, and easy to use warfarin initiation dosing nomogram for post-joint arthroplasty patients	Not best available evidence (case series)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Salazar et al. 2010	Direct thrombin inhibitors versus vitamin K antagonists or low molecular weight heparins for prevention of venous thromboembolism following total hip or knee replacement	Systematic review, bibliography screened
Tasker et al. 2010	Meta-analysis of low molecular weight heparin versus placebo in patients undergoing total hip replacement and post-operative morbidity and mortality since their introduction	Systematic review, bibliography screened
Trkulja et al. 2010	Rivaroxaban vs dabigatran for thromboprophylaxis after joint-replacement surgery: exploratory indirect comparison based on meta-analysis of pivotal clinical trials	Review, bibliography screened
Turpie et al. 2010	Rivaroxaban for the prevention of venous thromboembolism after hip or knee arthroplasty. Pooled analysis of four studies	Systematic review, bibliography screened
Wilke et al. 2010	Nonadherence in outpatient thromboprophylaxis after major orthopedic surgery: a systematic review	Systematic review, bibliography screened
Agnelli et al. 2009	Safety assessment of new antithrombotic agents: lessons from the EXTEND study on ximelagatran	Does not investigate comparison of interest
Bell et al. 2009	Factors affecting perioperative blood loss and transfusion rates in primary total joint arthroplasty: a prospective analysis of 1642 patients	Not best available evidence (non-randomized)
Bozic et al. 2009	Does Aspirin Have a Role in Venous Thromboembolism Prophylaxis in Total Knee Arthroplasty Patients?	Not best available evidence (retrospective comparative)
Brown 2009	Venous Thromboembolism Prophylaxis After Major Orthopaedic Surgery: A Pooled Analysis of Randomized Controlled Trials	Systematic review, bibliography screened
Cusick et al. 2009	The incidence of fatal pulmonary embolism after primary hip and knee replacement in a consecutive series of 4253 patients	Not best available evidence (retrospective comparative)
Darwish et al. 2009	Total knee replacement in King Abdullah University Hospital, early results	Not best available evidence (case series)
Eriksson et al. 2009	Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement	Systematic review, bibliography screened
Froimson et al. 2009	Venous thromboembolic disease reduction with a portable pneumatic compression device	Not best available evidence (retrospective comparative)
Hitos et al. 2009	Venous thromboembolism following primari total hip arthroplastydrome	Not best available evidence (retrospective comparative)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Holmes et al. 2009	Dabigatran etexilate for the prevention of venous thromboembolism in patients undergoing elective hip and knee surgery: a single technology appraisal	Systematic review, bibliography screened
Hull et al. 2009	State-of-the-art review: Assessing the safety profiles of new anticoagulants for major orthopedic surgery thromboprophylaxis	Systematic review, bibliography screened
Kimura et al. 2009	Anticoagulation therapy with heparin and warfarin in total knee arthroplasty for osteoarthritis knee	Not best available evidence (non-randomized)
Lassen et al. 2009	AVE5026, a new hemisynthetic ultra-low-molecular-weight heparin for the prevention of venous thromboembolism in patients after total knee replacement surgery--TREK: a dose-ranging study	Does not investigate comparison of interest
Lassen 2009	Is the preoperative administration of enoxaparin 40 mg necessary to optimally prevent the occurrence of venous thromboembolism after hip surgery? A subanalysis of two pooled randomized trials	Narrative review, bibliography screened
Lazo-Langner et al. 2009	Lessons from ximelagatran: issues for future studies evaluating new oral direct thrombin inhibitors for venous thromboembolism prophylaxis in orthopedic surgery	Systematic review, bibliography screened
Sugano et al. 2009	Clinical efficacy of mechanical thromboprophylaxis without anticoagulant drugs for elective hip surgery in an Asian population	Not best available evidence (case series)
Turpie et al. 2009	Pharmacokinetic and clinical data supporting the use of fondaparinux 1.5 mg once daily in the prevention of venous thromboembolism in renally impaired patients	Systematic review, bibliography screened
Turpie et al. 2009	A randomized evaluation of betrixaban, an oral factor Xa inhibitor, for prevention of thromboembolic events after total knee replacement (EXPERT)	Does not investigate comparison of interest
Van Thiel et al. 2009	Interpretation of benefit-risk of enoxaparin as comparator in the RECORD program: rivaroxaban oral tablets (10 milligrams) for use in prophylaxis in deep vein thrombosis and pulmonary embolism in patients undergoing hip or knee replacement surgery	Commentary
Vavken et al. 2009	A prospective cohort study on the effectiveness of 3500 IU versus 5000 IU bemiparin in the prophylaxis of postoperative thrombotic events in obese patients undergoing orthopedic surgery	Not specific to elective arthroplasty
Wolowacz et al. 2009	Efficacy and safety of dabigatran etexilate for the prevention of venous thromboembolism following total hip or knee arthroplasty. A meta-analysis	Systematic review, bibliography screened
Ares-Rodriguez et al. 2008	Survival curve and factors related to drainage during the first 24 h after total knee arthroplasty	Not best available evidence (retrospective comparative)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Callaghan et al. 2008	Evaluation of deep venous thrombosis prophylaxis in low-risk patients undergoing total knee arthroplasty	Not best available evidence (retrospective comparative)
Camporese et al. 2008	Low-molecular-weight heparin versus compression stockings for thromboprophylaxis after knee arthroscopy: a randomized trial	Incorrect patient population (arthroscopy patients)
Daniel et al. 2008	Multimodal thromboprophylaxis following primary hip arthroplasty: the role of adjuvant intermittent pneumatic calf compression	Not best available evidence (retrospective comparative)
Happe et al. 2008	Cost and occurrence of thrombocytopenia in patients receiving venous thromboembolism prophylaxis following major orthopaedic surgeries	Less than 80% elective arthroplasty patients
Kakkos et al. 2008	Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients	Systematic review, bibliography screened
Lassen et al. 2008	SR123781A: a new once-daily synthetic oligosaccharide anticoagulant for thromboprophylaxis after total hip replacement surgery: the DRIVE (Dose Ranging Study in Elective Total Hip Replacement Surgery) study	Does not investigate comparison of interest
Madhusudhan et al. 2008	Gastric protection and gastrointestinal bleeding with aspirin thromboprophylaxis in hip and knee joint replacements	Does not investigate comparison of interest
Maezawa et al. 2008	Changes of D-dimer after total hip arthroplasty in patients with and without intraoperative heparin	Not best available evidence (non-randomized)
Novicoff et al. 2008	Mandated venous thromboembolism prophylaxis: possible adverse outcomes	Not best available evidence (retrospective comparative)
Parry et al. 2008	Ninety-day mortality after elective total hip replacement: 1549 patients using aspirin as a thromboprophylactic agent	Not best available evidence (case series)
Pitto et al. 2008	Foot pumps without graduated compression stockings for prevention of deep-vein thrombosis in total joint replacement: efficacy, safety and patient compliance. A comparative, prospective clinical trial	Not best available evidence (non-randomized)
Rahme et al. 2008	Postdischarge thromboprophylaxis and mortality risk after hip-or knee-replacement surgery	Not best available evidence (retrospective comparative)
Sharrock et al. 2008	Potent anticoagulants are associated with a higher all-cause mortality rate after hip and knee arthroplasty	Systematic review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Wolowacz et al. 2008	Cost-effectiveness of venous thromboembolism prophylaxis in total hip and knee replacement surgery: the evolving application of health economic modelling over 20 years	Cost-effectiveness study
Xing et al. 2008	Has the incidence of deep vein thrombosis in patients undergoing total hip/knee arthroplasty changed over time? A systematic review of randomized controlled trials	Systematic review, bibliography screened
Xu et al. 2008	A review of clinical pathway data of 1,663 total knee arthroplasties in a tertiary institution in Singapore	Not best available evidence (case series)
Abad et al. 2007	A prospective observational study on the effectiveness and safety of bemiparin, first dose administered 6 h after knee or hip replacement surgery	Not best available evidence (case series)
Anand et al. 2007	Patient acceptance of a foot pump device used for thromboprophylaxis	Not best available evidence (case series)
Beksac et al. 2007	Symptomatic thromboembolism after one-stage bilateral THA with a multimodal prophylaxis protocol	Not best available evidence (retrospective comparative)
Bern et al. 2007	Low-dose warfarin coupled with lower leg compression is effective prophylaxis against thromboembolic disease after hip arthroplasty	Not best available evidence (case series)
Chan et al. 2007	Compliance and satisfaction with foot compression devices: an orthopaedic perspective	Does not address question of interest
Eisele et al. 2007	Rapid-inflation intermittent pneumatic compression for prevention of deep venous thrombosis	Does not address comparison of interest
Fisher et al. 2007	Rivaroxaban for thromboprophylaxis after orthopaedic surgery: pooled analysis of two studies	Systematic review, bibliography screened
Ivanovic et al. 2007	Thromboprophylaxis in total hip-replacement surgery in Europe: Acenocoumarol, fondaparinux, dabigatran and rivaroxban	Systematic review, bibliography screened
Khan et al. 2007	Fatal pulmonary embolism, death rates and standardised mortality ratios after primary total hip replacement in a joint replacement centre	Not best available evidence (case series)
Lachiewicz et al. 2007	Mechanical calf compression and aspirin prophylaxis for total knee arthroplasty	Not best available evidence (case series)
Lombardi et al. 2007	The incidence and prevention of symptomatic thromboembolic disease following unicompartmental knee arthroplasty	Not best available evidence (retrospective comparative)
Muntz et al. 2007	Factors associated with thromboprophylaxis for orthopedic patients and their impact on outcome	Not best available evidence (retrospective comparative)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Parvizi et al. 2007	Total joint arthroplasty: When do fatal or near-fatal complications occur?	Not best available evidence (case series)
Prejbeanu et al. 2007	Thromboembolic risk after knee endoprosthesis	Not best available evidence (case series)
Salvati et al. 2007	The 2007 ABJS Nicolas Andry Award: three decades of clinical, basic, and applied research on thromboembolic disease after THA: rationale and clinical results of a multimodal prophylaxis protocol	Narrative review, bibliography screened
Seah et al. 2007	Thirty-day mortality and morbidity after total knee arthroplasty	Not best available evidence (case series)
Shorr et al. 2007	Venous thromboembolism after orthopedic surgery: implications of the choice for prophylaxis	Less than 80% elective arthroplasty patients
Skedgel et al. 2007	The cost-effectiveness of extended-duration antithrombotic prophylaxis after total hip arthroplasty	Systematic review, bibliography screened
Tudor et al. 2007	Overview of current trends and the future of thromboprophylaxis in orthopaedic surgery	Narrative review, bibliography screened
Wang et al. 2007	Clinical significance of muscular deep-vein thrombosis after total knee arthroplasty	Insufficient data
Yen et al. 2007	Results of adjusted-dose heparin for thromboembolism prophylaxis in knee replacement compared to those found for its use in hip fracture surgery and elective hip replacement	Not best available evidence (case series)
Bischof et al. 2006	Cost-effectiveness of extended venous thromboembolism prophylaxis with fondaparinux in hip surgery patients	Cost-effectiveness study
Bjornara et al. 2006	Frequency and timing of clinical venous thromboembolism after major joint surgery	Not best available evidence (case series)
Blom et al. 2006	Early death following primary total hip arthroplasty: 1,727 procedures with mechanical thrombo-prophylaxis	Not best available evidence (case series)
Chan 2006	Role for aspirin after total hip replacement?	Systematic review, bibliography screened
Dahl et al. 2006	Assessment of bleeding after concomitant administration of antiplatelet and anticoagulant agents in lower limb arthroplasty	Not best available evidence (retrospective comparative)
Gomez-Outes et al. 2006	Cost-effecttiveness of bemiparin in the prevention and treatment of venous thromboembolism	Narrative review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Haas et al. 2006	Prevention of major venous thromboembolism following total hip or knee replacement: a randomized comparison of low-molecular-weight heparin with unfractionated heparin (ECHOS Trial)	Does not address comparison of interest
Hitos et al. 2006	Venous thromboembolism following primary total knee arthroplasty	Not best available evidence (retrospective comparative)
Lotke et al. 2006	The benefit of aspirin chemoprophylaxis for thromboembolism after total knee arthroplasty	Not best available evidence (case series)
Ottinger 2006	Retrospective evaluation of delayed administration of fondaparinux in providing comparable safety and efficacy outcomes in patients undergoing elective-arthroplasty procedures	Not best available evidence (retrospective comparative)
Shepherd et al. 2006	Fatal pulmonary embolism following hip and knee replacement. A study of 2153 cases using routine mechanical prophylaxis and selective chemoprophylaxis	Not best available evidence (retrospective comparative)
Williams et al. 2006	Above-knee versus below-knee stockings in total knee arthroplasty	Not best available evidence (non-randomized)
Bauersachs et al. 2005	Prophylaxis, diagnosis and therapy of surgery-related complications in orthopedic and trauma surgery: An observational survey (CHANGE)	Not best available evidence (case series)
Colwell et al. 2005	Oral direct thrombin inhibitor ximelagatran compared with warfarin for the prevention of venous thromboembolism after total knee arthroplasty	Does not investigate comparison of interest
Dahl et al. 2005	Postoperative Melagatran/Ximelagatran for the Prevention of Venous Thromboembolism following Major Elective Orthopaedic Surgery : Effects of Timing of First Dose and Risk Factors for Thromboembolism and Bleeding Complications on Efficacy and Safety	Does not investigate comparison of interest
Enyart et al. 2005	Low-dose warfarin for prevention of symptomatic thromboembolism after orthopedic surgery	Not best available evidence (retrospective comparative)
Larson et al. 2005	A feasibility study of continuing dose-reduced warfarin for invasive procedures in patients with high thromboembolic risk	Not best available evidence (case series)
O'Reilly et al. 2005	The prevalence of venous thromboembolism after hip and knee replacement surgery	Not best available evidence (retrospective comparative)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Walton et al. 2005	Arthrofibrosis following total knee replacement; does therapeutic warfarin make a difference?	Not best available evidence (retrospective comparative)
Ben-Galim et al. 2004	A miniature and mobile intermittent pneumatic compression device for the prevention of deep-vein thrombosis after joint replacement	Fewer than 100 patients and no non-VTE outcomes
Brotman et al. 2004	Warfarin prophylaxis and venous thromboembolism in the first 5 days following hip and knee arthroplasty	Not best available evidence (retrospective comparative)
Dranitsaris et al. 2004	Pharmacoeconomic analysis of fondaparinux versus enoxaparin for the prevention of thromboembolic events in orthopedic surgery patients	Cost-effectiveness study
Eikelboom et al. 2004	Thromboprophylaxis practice patterns in two Western Australian teaching hospitals	Not best available evidence (non-randomized)
Eriksson et al. 2004	Dose escalating safety study of a new oral direct thrombin inhibitor, dabigatran etexilate, in patients undergoing total hip replacement: BISTRO I	Not best available evidence (non-randomized)
Eriksson et al. 2004	Significantly lower need for blood transfusions associated with post-operatively initiated subcutaneous melagatran/oral ximelagatran compared with enoxaparin	Letter
Frosch et al. 2004	Complications after total knee arthroplasty: A comprehensive report	Not best available evidence (case series)
Haentjens et al. 2004	Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. A cost-utility analysis	Cost-effectiveness study
Jain et al. 2004	Deep vein thrombosis after total hip arthroplasty in Indian patients with and without enoxaparin	Not best available evidence (non-randomized)
Lobo 2004	Emerging options for thromboprophylaxis after orthopedic surgery: a review of clinical data	Narrative review, bibliography screened
Mismetti et al. 2004	Prevention of venous thromboembolism in orthopedic surgery with vitamin K antagonists: A meta-analysis	Systematic review, bibliography screened
Pitto et al. 2004	Mechanical prophylaxis of deep-vein thrombosis after total hip replacement a randomised clinical trial	Does not address comparison of interest
Silbersack et al. 2004	Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression	Fewer than 100 patients per group and no non-VTE outcomes

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Turpie 2004	Venous thromboembolism prophylaxis: role of factor xa inhibition by fondaparinux	Narrative review, bibliography screened
Wang et al. 2004	Prevention of deep-vein thrombosis after total knee arthroplasty in Asian patients. Comparison of low-molecular-weight heparin and indomethacin	Does not address comparison of interest
Wenzl et al. 2004	Prevention of thromboembolism with low-molecular-weight heparin in orthopedic surgery: a 5-year experience	Not best available evidence (case series)
Charalambous et al. 2003	Foot pump prophylaxis for deep venous thrombosis-rate of effective usage following knee and hip arthroplasty	Does not examine outcome of interest
Colwell et al. 2003	Comparison of ximelagatran, an oral direct thrombin inhibitor, with enoxaparin for the prevention of venous thromboembolism following total hip replacement. A randomized, double-blind study	Does not investigate comparison of interest
Dahl et al. 2003	Risk of clinical pulmonary embolism after joint surgery in patients receiving low-molecular-weight heparin prophylaxis in hospital: a 10-year prospective register of 3,954 patients	Not best available evidence (case series)
Dahl et al. 2003	Investment in prolonged thromboprophylaxis with dalteparin improves clinical outcomes after hip replacement	Cost-effectiveness study
Deitelzweig et al. 2003	Venous thromboembolism prevention with LMWHs in medical and orthopedic surgery patients	
Eriksson et al. 2003	The direct thrombin inhibitor melagatran followed by oral ximelagatran compared with enoxaparin for the prevention of venous thromboembolism after total hip or knee replacement: the EXPRESS study	Does not investigate comparison of interest
Eriksson et al. 2003	Direct thrombin inhibitor melagatran followed by oral ximelagatran in comparison with enoxaparin for prevention of venous thromboembolism after total hip or knee replacement	Does not investigate comparison of interest
Francis et al. 2003	Comparison of ximelagatran with warfarin for the prevention of venous thromboembolism after total knee replacement	Does not investigate comparison of interest
Fujisawa et al. 2003	Effect of calf-thigh intermittent pneumatic compression device after total hip arthroplasty: comparative analysis with plantar compression on the effectiveness of reducing thrombogenesis and leg swelling	Fewer than 100 patients per group and no non-VTE outcomes
Keays et al. 2003	The effect of anticoagulation on the restoration of range of motion after total knee arthroplasty: enoxaparin versus aspirin	Not best available evidence (retrospective comparative)
Kolb et al. 2003	Reduction of venous thromboembolism following prolonged prophylaxis with the low molecular weight heparin Certoparin after endoprothetic joint replacement or osteosynthesis of the lower limb in elderly patients	Fewer than 80% arthroplasty patients

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Navarro-Quilis et al. 2003	Efficacy and safety of bemiparin compared with enoxaparin in the prevention of venous thromboembolism after total knee arthroplasty: a randomized, double-blind clinical trial	Does not address comparison of interest
Nunley et al. 2003	Mortality after total hip and knee arthroplasty in a medium-volume university practice	Not best available evidence (case series)
O'Donnell et al. 2003	Reduction of out-of-hospital symptomatic venous thromboembolism by extended thromboprophylaxis with low-molecular-weight heparin following elective hip arthroplasty: a systematic review	Systematic review, bibliography screened
Ragucci et al. 2003	Comprehensive deep venous thrombosis prevention strategy after total-knee arthroplasty	Not best available evidence (case series)
Reitman et al. 2003	A multimodality regimen for deep venous thrombosis prophylaxis in total knee arthroplasty	Not best available evidence (case series)
Sachs et al. 2003	Does anticoagulation do more harm than good?: A comparison of patients treated without prophylaxis and patients treated with low-dose warfarin after total knee arthroplasty	Not best available evidence (retrospective comparative)
Tran et al. 2003	Fondaparinux for prevention of venous thromboembolism in major orthopedic surgery	Systematic review, bibliography screened
Westrich et al. 2003	Compliance in using a pneumatic compression device after total knee arthroplasty	Does not report patient oriented outcomes
Zufferey et al. 2003	Optimal low-molecular-weight heparin regimen in major orthopaedic surgery: A meta-analysis of randomised trials	Systematic review, bibliography screened
Anderson et al. 2002	Comparison of a nomogram and physician-adjusted dosage of warfarin for prophylaxis against deep-vein thrombosis after arthroplasty	Not best available evidence (retrospective comparative)
Bern et al. 2002	Very low dose warfarin as prophylaxis against ultrasound detected deep vein thrombosis following primary hip replacement	Fewer than 100 patients and no non-VTE outcomes
Borghi et al. 2002	Thromboembolic complications after total hip replacement	Not best available evidence (retrospective comparative)
Cheng 2002	Fondaparinux: a new antithrombotic agent	Systematic review, bibliography screened
Douketis et al. 2002	Short-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of prospective studies investigating symptomatic outcomes	Systematic review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Douketis et al. 2002	Anticoagulant effect at the time of epidural catheter removal in patients receiving twice-daily or once-daily low-molecular-weight heparin and continuous epidural analgesia after orthopedic surgery	Does not report patient oriented outcomes
Eriksson et al. 2002	Ximelagatran and melagatran compared with dalteparin for prevention of venous thromboembolism after total hip or knee replacement: the METHRO II randomised trial	Does not investigate comparison of interest
Eriksson et al. 2002	A dose-ranging study of the oral direct thrombin inhibitor, ximelagatran, and its subcutaneous form, melagatran, compared with dalteparin in the prophylaxis of thromboembolism after hip or knee replacement: METHRO I. MElagatran for THRombin inhibition in	Does not investigate comparison of interest
Francis et al. 2002	Ximelagatran versus warfarin for the prevention of venous thromboembolism after total knee arthroplasty. A randomized, double-blind trial	Does not investigate comparison of interest
Khan et al. 2002	Standardized mortality ratios and fatal pulmonary embolism rates following total knee replacement: a cohort of 936 consecutive cases	Not best available evidence (case series)
Kwong et al. 2002	Thromboprophylaxis dosing: the relationship between timing of first administration, efficacy, and safety	Narrative review, bibliography screened
Leali et al. 2002	Prevention of thromboembolic disease after non-cemented hip arthroplasty. A multimodal approach	Not best available evidence (case series)
Macdonald et al. 2002	Computerized management of oral anticoagulant therapy: experience in major joint arthroplasty	Not best available evidence (case series)
Moretti et al. 2002	Combined pharmacological and mechanical prophylaxis for DVT following hip and knee arthroplasty	Does not address comparison of interest
Nerurkar et al. 2002	Cost/death averted with venous thromboembolism prophylaxis in patients undergoing total knee replacement or knee arthroplasty	Systematic review, bibliography screened
Ryan et al. 2002	Effect of mechanical compression on the prevalence of proximal deep venous thrombosis as assessed by magnetic resonance venography	Fewer than 100 patients per group and no non-VTE outcomes
Samama et al. 2002	Extended venous thromboembolism prophylaxis after total hip replacement: a comparison of low-molecular-weight heparin with oral anticoagulant	Does not investigate comparison of interest
Sculco et al. 2002	Prophylaxis against venous thromboembolic disease in patients having a total hip or knee arthroplasty	Narrative review, bibliography screened
Strebel et al. 2002	Preoperative or postoperative start of prophylaxis for venous thromboembolism with low-molecular-weight heparin in elective hip surgery?	Systematic review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Turpie et al. 2002	A meta-analysis of fondaparinux versus enoxaparin in the prevention of venous thromboembolism after major orthopaedic surgery	Systematic review, bibliography screened
Turpie et al. 2002	Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery: a meta-analysis of 4 randomized double-blind studies	Systematic review, bibliography screened
Asano et al. 2001	Prevention of pulmonary embolism by a foot sole pump	Not specific to elective arthroplasty
Benko et al. 2001	Graduated compression stockings: Knee length or thigh length	Does not report outcome of interest
Brookenthal et al. 2001	A meta-analysis of thromboembolic prophylaxis in total knee arthroplasty	Systematic review, bibliography screened
Cohen et al. 2001	Extended thromboprophylaxis with low molecular weight heparin reduces symptomatic venous thromboembolism following lower limb arthroplasty--a meta-analysis	Letter
Eikelboom et al. 2001	Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials	Systematic review, bibliography screened
Finsen 2001	Duration of thrombosis prophylaxis in orthopaedic surgery	Not best available evidence (case series)
Goldstein et al. 2001	Safety of a clinical surveillance protocol with 3- and 6-week warfarin prophylaxis after total joint arthroplasty	Not best available evidence (retrospective comparative)
Haddad et al. 2001	Unanticipated variations between expected and delivered pneumatic compression therapy after elective hip surgery: a possible source of variation in reported patient outcomes	Does not address question of interest
Heit et al. 2001	Comparison of the oral direct thrombin inhibitor ximelagatran with enoxaparin as prophylaxis against venous thromboembolism after total knee replacement: a phase 2 dose-finding study	Does not investigate comparison of interest
Heit 2001	Low-molecular-weight heparin: the optimal duration of prophylaxis against postoperative venous thromboembolism after total hip or knee replacement	Narrative review, bibliography screened
Hull et al. 2001	Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review	Systematic review, bibliography screened
Hull et al. 2001	Timing of initial administration of low-molecular-weight heparin prophylaxis against deep vein thrombosis in patients following elective hip arthroplasty: a systematic review	Systematic review, bibliography screened
Hull et al. 2001	Low-molecular-weight heparin prophylaxis: preoperative versus postoperative initiation in patients undergoing elective hip surgery	Systematic review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Krotenberg et al. 2001	Dalteparin vs. enoxaparin as prophylaxis for deep-vein thrombosis after total hip or knee arthroplasty: a retrospective analysis	Not best available evidence (retrospective comparative)
van Heereveld et al. 2001	Prevention of symptomatic thrombosis with short term (low molecular weight) heparin in patients with rheumatoid arthritis after hip or knee replacement	Not best available evidence (case series)
Amaragiri et al. 2000	Elastic compression stockings for prevention of deep vein thrombosis (Cochrane Review) [with con sumer summary]	Systematic review, bibliography screened
Best et al. 2000	Graded compression stockings in elective orthopaedic surgery. An assessment of the in vivo performance of commercially available stockings in patients having hip and knee arthroplasty	Not best available evidence (non-randomized)
DiGiovanni et al. 2000	The safety and efficacy of intraoperative heparin in total hip arthroplasty	Not best available evidence (case series)
Fong et al. 2000	Use of low molecular weight heparin for prevention of deep vein thrombosis in total knee arthroplasty--a study of its efficacy in an Asian population	Not best available evidence (non-randomized)
Freedman et al. 2000	A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty	Systematic review, bibliography screened
Heit et al. 2000	Ardeparin sodium for extended out-of-hospital prophylaxis against venous thromboembolism after total hip or knee replacement. A randomized, double-blind, placebo-controlled trial	Does not address comparison of interest
Kakkar et al. 2000	A comparative double-blind, randomised trial of a new second generation LMWH (bemiparin) and UFH in the prevention of post-operative venous thromboembolism. The Bemiparin Assessment group	Does not address comparison of interest
Mant et al. 2000	Intraoperative heparin in addition to postoperative low-molecular-weight heparin for thromboprophylaxis in total knee replacement	Not best available evidence (case series)
McEvoy et al. 2000	Noncompliance in the inpatient administration of enoxaparin in conjunction with epidural or spinal anesthesia	Does not report patient oriented outcomes
Nassif et al. 2000	The effect of intraoperative intravenous fixed-dose heparin during total joint arthroplasty on the incidence of fatal pulmonary emboli	Not best available evidence (case series)
Planes 2000	An equivalence study of two low-molecular-weight heparins in the prevention and treatment of deep-vein thrombosis after total hip replacement	Report of previously published study
Robertson et al. 2000	Patient compliance and satisfaction with mechanical devices for preventing deep venous thrombosis after joint replacement	Does not report VTE outcomes

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Stern et al. 2000	Evaluation of the safety and efficacy of enoxaparin and warfarin for prevention of deep vein thrombosis after total knee arthroplasty	Not best available evidence (retrospective comparative)
Westrich et al. 2000	Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty	Systematic review, bibliography screened
Adolf et al. 1999	Comparison of 3,000 IU aXa of the low molecular weight heparin certoparin with 5,000 IU aXa in prevention of deep vein thrombosis after total hip replacement. German Thrombosis Study Group	Does not address comparison of interest
Agu et al. 1999	Graduated compression stockings in the prevention of venous thromboembolism	Systematic review, bibliography screened
Blanchard et al. 1999	Prevention of deep-vein thrombosis after total knee replacement. Randomised comparison between a low-molecular-weight heparin (nadroparin) and mechanical prophylaxis with a foot-pump system	Does not address comparison of interest
Bounameaux 1999	Integrating pharmacologic and mechanical prophylaxis of venous thromboembolism	Narrative review, bibliography screened
Dahl et al. 1999	Combined administration of dextran 70 and dalteparin does not increase perioperative blood loss compared to dextran 70 alone in major orthopedic surgery	Not best available evidence (non-randomized)
Hull et al. 1999	Preoperative vs postoperative initiation of low-molecular-weight heparin prophylaxis against venous thromboembolism in patients undergoing elective hip replacement	Systematic review, bibliography screened
Lawton et al. 1999	The use of heparin in patients in whom a pulmonary embolism is suspected after total hip arthroplasty	Not best available evidence (retrospective comparative)
Marchetti et al. 1999	Long-term cost-effectiveness of low molecular weight heparin versus unfractionated heparin for the prophylaxis of venous thromboembolism in elective hip replacement	Cost-effectiveness study
Messieh et al. 1999	Warfarin responses in total joint and hip fracture patients	Not best available evidence (case series)
Pineo et al. 1999	Prophylaxis of venous thromboembolism following orthopedic surgery: Mechanical and pharmacological approaches and the need for extended prophylaxis	Narrative review, bibliography screened
Shaieb et al. 1999	Bleeding complications with enoxaparin for deep venous thrombosis prophylaxis	Not best available evidence (retrospective comparative)
Sharrock et al. 1999	Dose response of intravenous heparin on markers of thrombosis during primary total hip replacement	Not best available evidence (quality)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Tamir et al. 1999	Sequential foot compression reduces lower limb swelling and pain after total knee arthroplasty	Does not report critical outcome of interest
Wade 1999	Cost effectiveness of danaparoid compared with enoxaparin as deep vein thrombosis prophylaxis after hip replacement surgery	Systematic review, bibliography screened
Ward et al. 1999	Simple, hybrid deep venous thrombosis/pulmonary embolus prophylaxis after total hip arthroplasty	Not best available evidence (case series)
Westrich et al. 1999	Thromboembolic disease prophylaxis in total knee arthroplasty using intraoperative heparin and postoperative pneumatic foot compression	Not best available evidence (non-randomized)
Westrich et al. 1999	The incidence of venous thromboembolism after total hip arthroplasty: a specific hypotensive epidural anesthesia protocol	Not best available evidence (case series)
Comp et al. 1998	A comparison of danaparoid and warfarin for prophylaxis against deep vein thrombosis after total hip replacement: The Danaparoid Hip Arthroplasty Investigators Group	Does not investigate comparison of interest
Davidson 1998	Out-of-hospital prophylaxis with low-molecular-weight heparin in hip surgery: the Swedish study	Commentary
Dearborn et al. 1998	Postoperative mortality after total hip arthroplasty. An analysis of deaths after two thousand seven hundred and thirty-six procedures	Not best available evidence (case series)
Howard et al. 1998	Low molecular weight heparin decreases proximal and distal deep venous thrombosis following total knee arthroplasty. A meta-analysis of randomized trials	Systematic review, bibliography screened
Kalodiki et al. 1998	How 'gold' is the standard? Interobservers' variation on venograms	Fewer than 100 patients
LaRusso et al. 1998	Sonographic incidence of deep venous thrombosis contralateral to hip or knee replacement surgery	Not best available evidence (case series)
Leclerc et al. 1998	The incidence of symptomatic venous thromboembolism after enoxaparin prophylaxis in lower extremity arthroplasty: a cohort study of 1,984 patients. Canadian Collaborative Group	Report of previously published study
Leclerc et al. 1998	The incidence of symptomatic venous thromboembolism during and after prophylaxis with enoxaparin: a multi-institutional cohort study of patients who underwent hip or knee arthroplasty. Canadian Collaborative Group	Not best available evidence (case series)
Montebugnoli et al. 1998	Thromboembolic complications and pharmacological prophylaxis in orthopaedic surgery	Not best available evidence (retrospective comparative)
Norgren et al. 1998	Prevention of deep vein thrombosis in knee arthroplasty. Preliminary results from a randomized controlled study of low molecular weight heparin vs foot pump compression	Not best available evidence

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Planes et al. 1998	Comparison of two low-molecular-weight heparins for the prevention of postoperative venous thromboembolism after elective hip surgery. Reviparin Study Group	Does not address comparison of interest
Planes et al. 1998	Out-of-hospital prophylaxis with low-molecular-weight heparin in hip surgery: the French study--venographic outcome at 35 days	Report of previously published study
Vanek 1998	Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves	Systematic review, bibliography screened
Anderson et al. 1997	Cost effectiveness of the prevention and treatment of deep vein thrombosis and pulmonary embolism	Cost-effectiveness study
Ansari et al. 1997	Incidence of fatal pulmonary embolism after 1,390 knee arthroplasties without routine prophylactic anticoagulation, except in high-risk cases	Not best available evidence (retrospective comparative)
Clarke et al. 1997	Screening for deep-venous thrombosis after hip and knee replacement without prophylaxis	Not best available evidence (case series)
Fender et al. 1997	Mortality and fatal pulmonary embolism after primary total hip replacement. Results from a regional hip register	Not best available evidence (retrospective comparative)
Gallay et al. 1997	A short course of low-molecular-weight heparin to prevent deep venous thrombosis after elective total hip replacement	Not best available evidence (retrospective comparative)
Heit et al. 1997	Efficacy and safety of low molecular weight heparin (ardeparin sodium) compared to warfarin for the prevention of venous thromboembolism after total knee replacement surgery: a double-blind, dose-ranging study. Ardeparin Arthroplasty Study Group	Does not address comparison of interest
Howard 1997	Dalteparin: a low-molecular-weight heparin	Systematic review, bibliography screened
Kim et al. 1997	Deep vein thrombosis after uncemented total hip replacement	Does not investigate comparison of interest
Knelles et al. 1997	Prevention of heterotopic ossification after total hip replacement. A prospective, randomised study using acetylsalicylic acid, indomethacin and fractional or single-dose irradiation	Not relevant - does not investigate VTE
Lieberman et al. 1997	Low-dose warfarin prophylaxis to prevent symptomatic pulmonary embolism after total knee arthroplasty	Not best available evidence (case series)
Nilsson et al. 1997	The post-discharge prophylactic management of the orthopedic patient with low-molecular-weight heparin: enoxaparin	Summary of previously published study

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Author	Title	Reason for Exclusion
Planes et al. 1997	The post-hospital discharge venous thrombosis risk of the orthopedic patient	Report of previously published study
Skoutakis 1997	Danaparoid in the prevention of thromboembolic complications	Systematic review, bibliography screened
Yoo et al. 1997	A prospective randomized study on the use of nadroparin calcium in the prophylaxis of thromboembolism in Korean patients undergoing elective total hip replacement	Does not address comparison of interest
Andersen et al. 1996	Survival in patients undergoing total hip arthroplasty in relation to thromboprophylaxis with low molecular weight heparin: A long-term follow-up study	Systematic review, bibliography screened
Horbach et al. 1996	A fixed-dose combination of low molecular weight heparin with dihydroergotamine versus adjusted-dose unfractionated heparin in the prevention of deep-vein thrombosis after total hip replacement	Does not investigate comparison of interest
Hui et al. 1996	Graded compression stockings for prevention of deep-vein thrombosis after hip and knee replacement	Fewer than 100 patients per group and no non-VTE outcomes
Kalodiki et al. 1996	Deep venous thrombosis prophylaxis with low molecular weight heparin and elastic compression in patients having total hip replacement. A randomised controlled trial	Fewer than 100 patients and insufficient data
Lachiewicz et al. 1996	Pneumatic compression or aspirin prophylaxis against thromboembolism in total hip arthroplasty	Not best available evidence (non-randomized)
Levine et al. 1996	Ardeparin (low-molecular-weight heparin) vs graduated compression stockings for the prevention of venous thromboembolism. A randomized trial in patients undergoing knee surgery	Does not address comparison of interest
Mcgrath et al. 1996	Death rate from pulmonary embolism following joint replacement surgery	Not best available evidence (case series)
Murray et al. 1996	Thromboprophylaxis and death after total hip replacement	Systematic review, bibliography screened
Norgren et al. 1996	Low incidence of deep vein thrombosis after total hip replacement: An interim analysis of patients on low molecular weight heparin vs sequential gradient compression prophylaxis	Fewer than 100 patients per group and no non-VTE outcomes
Perhoniemi et al. 1996	The effect of enoxaparin in prevention of deep venous thrombosis in hip and knee surgery--a comparison with the dihydroergotamine-heparin combination	Does not investigate comparison of interest
Planes et al. 1996	Efficacy and safety of postdischarge administration of enoxaparin in the prevention of deep venous thrombosis after total hip replacement. A prospective randomised double-blind placebo-controlled trial	Report of previously published study

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Sarasin et al. 1996	Antithrombotic strategy after total hip replacement. A cost-effectiveness analysis comparing prolonged oral anticoagulants with screening for deep vein thrombosis	Systematic review, bibliography screened
Stannard et al. 1996	Prophylaxis of deep venous thrombosis after total hip arthroplasty by using intermittent compression of the plantar venous plexus	Fewer than 100 patients and no non-VTE outcomes
Suomalainen et al. 1996	Prevention of fatal pulmonary embolism with warfarin after total hip replacement	Not best available evidence (case series)
Vresilovic et al. 1996	Comparative risk of early postoperative pulmonary embolism after cemented total knee versus total hip arthroplasty with low-dose warfarin prophylaxis	Not best available evidence (case series)
Westrich et al. 1996	Prophylaxis against deep venous thrombosis after total knee arthroplasty. Pneumatic plantar compression and aspirin compared with aspirin alone	Fewer than 100 patients and no non-VTE outcomes
Agnelli et al. 1995	Clinical outcome of orthopaedic patients with negative lower limb venography at discharge	Not best available evidence (case series)
Colwell et al. 1995	Efficacy and safety of enoxaparin to prevent deep vein thrombosis after hip arthroplasty	Report of previously published studies
Hamulyak et al. 1995	Subcutaneous low-molecular weight heparin or oral anticoagulants for the prevention of deep-vein thrombosis in elective hip and knee replacement? Fraxiparine Oral Anticoagulant Study Group	Does not investigate comparison of interest
Kalodiki et al. 1995	V/Q defects and deep venous thrombosis following total hip replacement	Fewer than 100 patients and no non-VTE outcomes
Menzin et al. 1995	Cost-effectiveness of enoxaparin vs low-dose warfarin in the prevention of deep-vein thrombosis after total hip replacement surgery	Cost-effectiveness study
Monreal et al. 1995	Platelet count, antiplatelet therapy and pulmonary embolism--a prospective study in patients with hip surgery	Not specific to elective arthroplasty
Tremaine et al. 1995	Duplex ultrasound evaluation for acute deep venous thrombosis in 962 total joint arthroplasty patients	Not best available evidence (case series)
Warwick et al. 1995	Death and thromboembolic disease after total hip replacement. A series of 1162 cases with no routine chemical prophylaxis	Not best available evidence (case series)
Antiplatelet Trialists' Collaboration 1994	Collaborative overview of randomised trials of antiplatelet therapy--III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients.	Systematic review, bibliography screened
Borris et al. 1994	Perioperative thrombosis prophylaxis with low molecular weight heparins in elective hip surgery. Clinical and economic considerations	Systematic review, bibliography screened

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Eriksson et al. 1994	Direct thrombin inhibition with Rec-hirudin CGP 39393 as prophylaxis of thromboembolic complications after total hip replacement	Not best available evidence (case series)
Friedman et al. 1994	RD heparin compared with warfarin for prevention of venous thromboembolic disease following total hip or knee arthroplasty. RD Heparin Arthroplasty Group	Does not address comparison of interest
Ginsberg et al. 1994	Use of Hirulog in the prevention of venous thrombosis after major hip or knee surgery	Fewer than 80% elective arthroplasty patients
Imperiale et al. 1994	A meta-analysis of methods to prevent venous thromboembolism following total hip replacement	Systematic review, bibliography screened
Lieberman et al. 1994	Prevention of venous thromboembolism after total hip and knee arthroplasty	Narrative review, bibliography screened
Menzin et al. 1994	Prevention of deep-vein thrombosis following total hip replacement surgery with enoxaparin versus unfractionated heparin: a pharmacoeconomic evaluation	Economic evaluation
O'Brien et al. 1994	Cost-effectiveness of enoxaparin versus warfarin prophylaxis against deep-vein thrombosis after total hip replacement	Systematic review, bibliography screened
Anderson et al. 1993	Efficacy and cost of low-molecular-weight heparin compared with standard heparin for the prevention of deep vein thrombosis after total hip arthroplasty	Systematic review, bibliography screened
Bradley et al. 1993	The effectiveness of intermittent plantar venous compression in prevention of deep venous thrombosis after total hip arthroplasty	Fewer than 100 patients and no non-VTE outcomes
Carter et al. 1993	Enoxaparin: The low-molecular-weight heparin for prevention of postoperative thromboembolic complications	Systematic review, bibliography screened
Khaw et al. 1993	The incidence of fatal pulmonary embolism after knee replacement with no prophylactic anticoagulation	Not best available evidence (case series)
Mohr et al. 1993	Prophylactic agents for venous thrombosis in elective hip surgery. Meta-analysis of studies using venographic assessment	Systematic review, bibliography screened
Paiement et al. 1993	Routine use of adjusted low-dose warfarin to prevent venous thromboembolism after total hip replacement	Not best available evidence (case series)
Planes 1993	Comparison of antithrombotic efficacy and haemorrhagic side-effects of Clivarin versus enoxaparin in patients undergoing total hip replacement surgery	Abstract
Breyer et al. 1992	Prevention of deep vein thrombosis with low molecular-weight heparin in patients undergoing total hip replacement. A randomized trial. The German Hip Arthroplasty Trial (GHAT) Group	Does not address comparison of interest

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Clagett et al. 1992	Prevention of venous thromboembolism	Narrative review, bibliography screened
Gallus et al. 1992	Apparent lack of synergism between heparin and dihydroergotamine in prevention of deep vein thrombosis after elective hip replacement: a randomised double-blind trial reported in conjunction with an overview of previous results	Does not investigate comparison of interest
Hoek et al. 1992	Prevention of deep vein thrombosis following total hip replacement by low molecular weight heparinoid	Does not investigate comparison of interest
Huo et al. 1992	Intraoperative heparin thromboembolic prophylaxis in primary total hip arthroplasty. A prospective, randomized, controlled, clinical trial	Report of previously published data
Laguardia et al. 1992	Prevention of deep vein thrombosis in orthopaedic surgery. Comparison of two different treatment protocols with low molecular weight heparin ('Fluxum')	Does not address comparison of interest
Leclerc et al. 1992	Prevention of deep vein thrombosis after major knee surgery--a randomized, double-blind trial comparing a low molecular weight heparin fragment (enoxaparin) to placebo	Not specific to elective arthroplasty
Leizorovicz et al. 1992	Low molecular weight heparin in prevention of perioperative thrombosis	Systematic review, bibliography screened
Leyvraz et al. 1992	Thromboembolic prophylaxis in total hip replacement: a comparison between the low molecular weight heparinoid Lomoparan and heparin-dihydroergotamine	Does not investigate comparison of interest
Mohr et al. 1992	Venous thromboembolism associated with hip and knee arthroplasty: current prophylactic practices and outcomes	Not best available evidence (retrospective comparative)
Nurmohamed et al. 1992	Low-molecular-weight heparin versus standard heparin in general and orthopaedic surgery: a meta-analysis	Systematic review, bibliography screened
Ofosu et al. 1992	The low molecular weight heparin Enoxaparin inhibits the consumption of factor VII and prothrombin activation in vivo associated with elective knee replacement surgery	Does not report patient oriented outcomes
Paiement et al. 1992	Influence of prophylaxis on proximal venous thrombus formation after total hip arthroplasty	Narrative review, bibliography screened
Pidala et al. 1992	A prospective study on intermittent pneumatic compression in the prevention of deep vein thrombosis in patients undergoing total hip or total knee replacement	Not best available evidence (case series)
Solis et al. 1992	Is anticoagulation indicated for asymptomatic postoperative calf vein thrombosis?	Not best available evidence (case series)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Wilson et al. 1992	Thrombo-embolic prophylaxis in total knee replacement. Evaluation of the A-V Impulse System	Fewer than 100 patients and no-non VTE outcomes
Wolf et al. 1992	Pulmonary embolism. Incidence in primary cemented and uncemented total hip arthroplasty using low-dose sodium warfarin prophylaxis	Not best available evidence (case series)
Borris et al. 1991	Low-molecular-weight heparin (enoxaparin) vs dextran 70. The prevention of postoperative deep vein thrombosis after total hip replacement. The Danish Enoxaparin Study Group	Does not investigate comparison of interest
Borris et al. 1991	Components of coagulation and fibrinolysis during thrombosis prophylaxis with a low molecular weight heparin (Enoxaparin) versus Dextran 70 in hip arthroplasty	Does not investigate comparison of interest
Dale et al. 1991	Prevention of venous thrombosis with minidose warfarin after joint replacement	Not best available evidence (retrospective)
Eriksson et al. 1991	Impaired fibrinolysis and postoperative thromboembolism in orthopedic patients	Fewer than 100 patients per group and no non-VTE outcomes
Freick et al. 1991	Prevention of deep vein thrombosis by low-molecular-weight heparin and dihydroergotamine in patients undergoing total hip replacement	Does not investigate comparison of interest
Hodge 1991	Prevention of deep vein thrombosis after total knee arthroplasty. Coumadin versus pneumatic calf compression	Not best available evidence (non-randomized)
Kaempffe et al. 1991	Intermittent pneumatic compression versus coumadin. Prevention of deep vein thrombosis in lower-extremity total joint arthroplasty	Fewer than 100 patients per group and no non-VTE outcomes
Leyvraz et al. 1991	Prevention of deep vein thrombosis after hip replacement: randomised comparison between unfractionated heparin and low molecular weight heparin	Does not address comparison of interest
Matzsch et al. 1991	Comparison of the thromboprophylactic effect of a low molecular weight heparin versus dextran in total hip replacement	Does not investigate comparison of interest
Planes et al. 1991	Efficacy and safety of a perioperative enoxaparin regimen in total hip replacement under various anesthesias	Narrative review, bibliography screened
Putz et al. 1991	Triflusal versus acetylsalicylic acid: a double-blind study for the prophylaxis of deep vein thrombosis after hip surgery	Does not investigate comparison of interest
Turpie 1991	Efficacy of a postoperative regimen of enoxaparin in deep vein thrombosis prophylaxis	Report of previously published RCT
Francis et al. 1990	Prevention of venous thrombosis after total knee arthroplasty. Comparison of antithrombin III and low-dose heparin with dextran	Does not investigate comparison of interest

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Kristensen et al. 1990	Combined treatment with indomethacin and low-dose heparin after total hip replacement. A double-blind placebo-controlled clinical trial	Not relevant treatment comparison
Lynch et al. 1990	Mechanical measures in the prophylaxis of postoperative thromboembolism in total knee arthroplasty	Not best available evidence (retrospective comparative)
Matzsch et al. 1990	Low molecular weight heparin compared with dextran as prophylaxis against thrombosis after total hip replacement	Does not investigate comparison of interest
Planes et al. 1990	Total hip replacement and deep vein thrombosis. A venographic and necropsy study	Not best available evidence (case series)
Planes et al. 1990	Once-daily dosing of enoxaparin (a low molecular weight heparin) in prevention of deep vein thrombosis after total hip replacement	Commentary
Sorensen et al. 1990	Levels of thrombin--antithrombin-III complex and factor VIII activity in relation to post-operative deep vein thrombosis and influence of prophylaxis with a low-molecular-weight heparin	Fewer than 100 patients per group and no non-VTE outcomes
Sorensen et al. 1990	Association between plasma levels of tissue plasminogen activator and postoperative deep vein thrombosis--influence of prophylaxis with a low molecular weight heparin. The Venous Thrombosis Group	Fewer than 100 patients per group and no non-VTE outcomes
Turpie 1990	Enoxaparin prophylaxis in elective hip surgery	Report of previously published RCT
Amstutz et al. 1989	Warfarin prophylaxis to prevent mortality from pulmonary embolism after total hip replacement	Not best available evidence (case series)
Christensen et al. 1989	Prevention of deep venous thrombosis following total hip replacement, using epidural analgesia	Does not investigate comparison of interest
Francis et al. 1989	Antithrombin III prophylaxis of venous thromboembolic disease after total hip or total knee replacement	Insufficient data
Francis et al. 1989	Prevention of venous thrombosis after total hip arthroplasty. Antithrombin III and low-dose heparin compared with dextran 40	Does not investigate comparison of interest
Fredin et al. 1989	Thromboprophylaxis in hip arthroplasty. Dextran with graded compression or preoperative dextran compared in 150 patients	Does not investigate comparison of interest
Levine et al. 1989	The relationship between anti-factor Xa level and clinical outcome in patients receiving enoxaparine low molecular weight heparin to prevent deep vein thrombosis after hip replacement	Not best available evidence (case series)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Patterson et al. 1989	Complications of heparin therapy after total joint arthroplasty	Not relevant - treatment, not prevention of VTE
Stulberg et al. 1989	Antithrombin III/low-dose heparin in the prevention of deep-vein thrombosis after total knee arthroplasty. A preliminary report	Does not investigate comparison of interest
Taberner et al. 1989	Randomized study of adjusted versus fixed low dose heparin prophylaxis of deep vein thrombosis in hip surgery	Fewer than 100 patients per group and insufficient data on bleeding outcomes
Beisaw et al. 1988	Dihydroergotamine/heparin in the prevention of deep-vein thrombosis after total hip replacement. A controlled, prospective, randomized multicenter trial	Does not investigate comparison of interest
Chiapuzzo et al. 1988	The use of low molecular weight heparins for postsurgical deep vein thrombosis prevention in orthopaedic patients	Not specific to elective arthroplasty
Eriksson et al. 1988	Thrombosis prophylaxis with low molecular weight heparin in total hip replacement	Does not investigate comparison of interest
Lassen et al. 1988	Heparin/dihydroergotamine for venous thrombosis prophylaxis: comparison of low-dose heparin and low molecular weight heparin in hip surgery	Does not investigate comparison of interest
Leyvraz et al. 1988	Adjusted subcutaneous heparin versus heparin plus dihydroergotamine in prevention of deep vein thrombosis after total hip arthroplasty	Does not investigate comparison of interest
Matzsch et al. 1988	Safety and efficacy of a low molecular weight heparin (Logiparin) versus dextran as prophylaxis against thrombosis after total hip replacement	Does not investigate comparison of interest
Swierstra et al. 1988	Prevention of thrombosis after hip arthroplasty. A prospective study of preoperative oral anticoagulants	Does not investigate comparison of interest
Christensen et al. 1987	Bleeding after hip arthroplasty not increased by heparin plus dihydroergotamine	Does not investigate comparison of interest
Clayton et al. 1987	Activity, air boots, and aspirin as thromboembolism prophylaxis in knee arthroplasty. A multiple regimen approach	Not best available evidence (case series)
Haas et al. 1987	Prophylaxis of deep vein thrombosis in high risk patients undergoing total hip replacement with low molecular weight heparin plus dihydroergotamine	Does not investigate comparison of interest
Josefsson et al. 1987	Prevention of thromboembolism in total hip replacement. Aspirin versus dihydroergotamine-heparin	Does not investigate comparison of interest
Alfaro et al. 1986	Prophylaxis of thromboembolic disease and platelet-related changes following total hip replacement: a comparative study of aspirin and heparin-dihydroergotamine	Fewer than 100 patients per group and no non-VTE outcomes

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Bergqvist et al. 1986	Low molecular weight heparin once daily compared with conventional low-dose heparin twice daily. A prospective double-blind multicentre trial on prevention of postoperative thrombosis	Not specific to elective arthroplasty
Planes et al. 1986	Enoxaparine low molecular weight heparin: its use in the prevention of deep venous thrombosis following total hip replacement	Not best available evidence (non-randomized)
Bergqvist et al. 1985	Does thromboprophylaxis increase the risk for infectious complications after total hip replacement?	Subgroup of study previously published
Kakkar et al. 1985	Heparin and dihydroergotamine prophylaxis against thrombo-embolism after hip arthroplasty	Not best available evidence (case series)
Fredin et al. 1984	Hypotensive anesthesia, thromboprophylaxis and postoperative thromboembolism in total hip arthroplasty	Does not investigate comparison of interest
Fredin et al. 1984	On thrombo-embolism after total hip replacement in epidural analgesia: a controlled study of dextran 70 and low-dose heparin combined with dihydroergotamine	Does not investigate comparison of interest
Eyb et al. 1983	The effect of prophylaxis for thrombosis on heterotopic ossification following total hip joint replacement	Does not report outcome of interest
Figus et al. 1983	Thromboembolism in total hip replacement	Not best available evidence (retrospective comparative)
Francis et al. 1983	Two-step warfarin therapy. Prevention of postoperative venous thrombosis without excessive bleeding	Does not investigate comparison of interest
Fredin et al. 1983	Pre- and postoperative levels of antithrombin III with special reference to thromboembolism after total hip replacement	Does not investigate comparison of interest
Gallus et al. 1983	Venous thrombosis after elective hip replacement--the influence of preventive intermittent calf compression and of surgical technique	Fewer than 100 patients per group and no non-VTE outcomes
Ohlund et al. 1983	Calf compression for prevention of thromboembolism following hip surgery	Fewer than 100 patients and no non-VTE outcomes
Sautter et al. 1983	Aspirin-sulfinpyrazone in prophylaxis of deep venous thrombosis in total hip replacement	Does not investigate comparison of interest
Fredin et al. 1982	Fatal pulmonary embolism after total hip replacement	Not best available evidence (case series)
Guyer et al. 1982	The detection and prevention of pulmonary embolism in total hip replacement. A study comparing aspirin and low-dose warfarin	Not best available evidence (non-randomized)

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Hartman et al. 1982	Cyclic sequential compression of the lower limb in prevention of deep venous thrombosis	Fewer than 100 patients and no non-VTE outcomes
Welin-Berger et al. 1982	Deep vein thrombosis following hip surgery. Relation to activated factor X inhibitor activity: effect of heparin and dextran	Fewer than 100 patients and no non-VTE outcomes
Amrein et al. 1981	Aspirin-induced prolongation of bleeding time and perioperative blood loss	Not best available evidence (retrospective comparative)
Ishak et al. 1981	Deep venous thrombosis after total hip arthroplasty: a prospective controlled study to determine the prophylactic effect of graded pressure stockings	Does not address comparison of interest
Morris et al. 1981	The effect of dihydroergotamine and heparin on the incidence of thromboembolic complications following total hip replacement: a randomized controlled clinical trial	Does not investigate comparison of interest
Sheppeard et al. 1981	A clinico-pathological study of fatal pulmonary embolism in a specialist orthopaedic hospital	Not best available evidence (case series)
Westermann et al. 1981	Thromboembolism after hip surgery	Not best available evidence (non-randomized)
Gnudi et al. 1980	Thrombo-embolism as a complication of prosthetic replacement operations of the hip: prophylaxis with heparin at low doses	Not best available evidence (retrospective comparative)
Schondorf et al. 1980	Prevention of deep vein thrombosis in orthopedic surgery with the combination of low dose heparin plus either dihydroergotamine or dextran	Does not investigate comparison of interest
Bergzvist et al. 1979	Thromboembolism after elective and post-traumatic hip surgery--a controlled prophylactic trial with dextran 70 and low-dose heparin	Not best available evidence
Goss et al. 1979	The efficacy of low-dose heparin--warfarin anticoagulation prophylaxis after total hip replacement arthroplasty	Not best available evidence (case series)
Hull et al. 1979	Effectiveness of intermittent pulsatile elastic stockings for the prevention of calf and thigh vein thrombosis in patients undergoing elective knee surgery	Fewer than 100 patients per group and no non-VTE outcomes
Kakkar et al. 1979	Prophylaxis for postoperative deep-vein thrombosis. Synergistic effect of heparin and dihydroergotamine	Does not investigate comparison of interest
Barnes et al. 1978	Efficacy of graded-compression antiembolism stockings in patients undergoing total hip arthroplasty	Less than 10 patients per group
Rogers et al. 1978	Controlled trial of low-dose heparin and sulfinpyrazone to prevent venous thromboembolism after operation on the hip	Does not investigate comparison of interest

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Silvergleid et al. 1978	ASA-dipyridamole prophylaxis in elective total hip replacement	Does not investigate comparison of interest
Stamatakis et al. 1978	Failure of aspirin to prevent postoperative deep vein thrombosis in patients undergoing total hip replacement	Not best available evidence (case series)
Williams et al. 1978	Failure of low dose heparin to prevent pulmonary embolism after hip surgery or above the knee amputation	Not specific to elective arthroplasty
Flicoteaux et al. 1977	Comparision of low dose heparin and low dose heparin combined with aspirin in prevention of deep vein thrombosis after total hip replacement	Not best available evidence (low power)
Hume et al. 1977	Prevention of postoperative thrombosis by aspirin	Fewer than 100 patients and no non-VTE outcomes
Johnson et al. 1977	Pulmonary embolism and its prophylaxis following the Charnley total hip replacement	Not best available evidence (retrospective comparative)
Pedegana et al. 1977	Prevention of thromboembolic disease by external pneumatic compression in patients undergoing total hip arthroplasty	Fewer than 100 patients per group and no non-VTE outcomes
van Geloven et al. 1977	Comparison of postoperative coumarin, dextran 40 and subcutaneous heparin in the prevention of postoperative deep vein thrombosis	Not specific to arthoplasty
Jennings et al. 1976	A clinical evaluation of aspirin prophylaxis of thromboembolic disease after total hip arthroplasty	Not best available evidence (case series)
Sagar et al. 1976	Efficacy of low-dose heparin in prevention of extensive deep-vein thrombosis in patients undergoing total-hip replacement	Does not investigate comparison of interest
Sakai et al. 1976	Prevention of thromboembolic phenomena	Not best available evidence (case series)
Salvati et al. 1976	Thromboembolism following total hip-replacement arthroplasty. The efficicy of dextran-aspirin and dextran-warfarin in prophylaxis	Not best available evidence (retrospective comparative)
Gruber 1975	Dextran and the prevention of postoperative thromboembolic complications	Narrative review, bibliography screened
Ritter et al. 1975	A comparative analysis of warfarin and low-dose heparin as thromboembolism prophylaxis in total hip replacement patinets	Not best available evidence (non-randomized)
Soreff et al. 1975	Acetylsalicylic acid in a trial to diminish thromboembolic complications after elective hip surgery	Not specific to elective arthroplasty

Table 62. Excluded Studies Considered for Prophylaxis

Author	Title	Reason for Exclusion
Morris et al. 1974	Prevention of deep-vein thrombosis by low-dose heparin in patients undergoing total hip replacement	Does not investigate comparison of interest
Coventry et al. 1973	'Delayed' prophylactic anticoagulation: a study of results and complications in 2,012 total hip arthroplasties	Not best available evidence (retrospective comparative)
Evarts et al. 1973	Thromboembolism after total hip reconstruction. Failure of low doses of heparin in prevention	Not best available evidence (case series)
Gallus et al. 1973	Small subcutaneous doses of heparin in prevention of venous thrombosis	Not specific to elective arthroplasty
Daniel et al. 1972	Pulmonary complications after total hip arthroplasty with Charnley prosthesis as revealed by chest roentgenograms	Not best available evidence (case series)
Harris et al. 1972	Prevention of venous thromboembolism following total hip replacement. Warfarin vs dextran 40	Does not investigate comparison of interest
	Effect of aspirin on postoperative venous thrombosis. Report of the Steering Committee of a trial sponsored by the Medical Research Council	Does not report critical outcome (DVT diagnosed by 125I-fibrinogen)
Evarts et al. 1971	Prevention of thromboembolic disease after elective surgery of the hip	Not best available evidence (non-randomized)
Pinto 1970	Controlled trial of an anticoagulant (warfarin sodium) in the prevention of venous thrombosis following hip surgery	Not specific to elective arthroplasty
Harris et al. 1967	The prevention of thromboembolic disease by prophylactic anticoagulation. A controlled study in elective hip surgery	Not best available evidence (non-randomized)

EARLY MOBILIZATION

Table 63. Excluded Studies Considered for Early Mobilization

Author	Title	Reason for Exclusion
Chandrasek-aran et al. 2009	Early mobilization after total knee replacement reduces the incidence of deep venous thrombosis	Fewer than 100 patients and no non-VTE outcomes
Thien et al. 2007	Immediate weight bearing after uncemented total hip arthroplasty with an anteverted stem: A prospective randomized comparison using radiostereometry	No relevant outcomes
Buehler et al. 1999	Late deep venous thrombosis and delayed weightbearing after total hip arthroplasty	Fewer than 100 patients per group
Wasilewski et al. 1990	Value of continuous passive motion in total knee arthroplasty	Does not address question of interest
Vince et al. 1987	Continuous passive motion after total knee arthroplasty	Does not address question of interest
Stulberg et al. 1982	Aspirin prophylaxis for pulmonary embolism following total hip arthroplasty. An incidence study	Not best available evidence
Nillius et al. 1979	Deep vein thrombosis after total hip replacement: a clinical and phlebographic study	Not best available evidence

ANESTHESIA

Table 64. Excluded Studies Considered for Anesthesia

Author	Title	Reason for Exclusion
Kerr et al. 2010	High incidence of in-hospital pulmonary embolism following joint arthroplasty with dalteparin prophylaxis	Not best available evidence
Duarte et al. 2009	Posterior lumbar plexus block in postoperative analgesia for total hip arthroplasty: a comparative study between 0.5% Bupivacaine with Epinephrine and 0.5% Ropivacaine	Does not address question of interest
Duarte et al. 2009	Epidural lumbar block or lumbar plexus block combined with general anesthesia: efficacy and hemodynamic effects on total hip arthroplasty	Not best available evidence
Frassanito et al. 2009	Anaesthesia for total knee arthroplasty: Efficacy of single-injection or continuous lumbar plexus associated with sciatic nerve blocks - A randomized controlled study	Does not report critical outcome of interest
Hu et al. 2009	A comparison of regional and general anaesthesia for total replacement of the hip or knee: a meta-analysis	Systematic review, bibliography screened
Ilfeld et al. 2009	Health-related quality of life after hip arthroplasty with and without an extended-duration continuous posterior lumbar plexus nerve block: A prospective, 1-year follow-up of a randomized, triple-masked, placebo-controlled study	Does not address question of interest
Krenzel et al. 2009	Posterior Capsular Injections of Ropivacaine During Total Knee Arthroplasty: A Randomized, Double-Blind, Placebo-Controlled Study	Does not address question of interest
Macfarlane et al. 2009	Does regional anaesthesia improve outcome after total hip arthroplasty? A systematic review	Systematic review, bibliography screened
Macfarlane et al. 2009	Does regional anesthesia improve outcome after total knee arthroplasty?	Systematic review, bibliography screened
Ilfeld et al. 2008	Ambulatory continuous posterior lumbar plexus nerve blocks after hip arthroplasty: A dual-center, randomized, triple-masked, placebo-controlled trial	Does not address question of interest
Bowler et al. 2007	Factor V Leiden: prevalence and thromboembolic complications after total hip replacement in Ireland	Not best available evidence
Brooks et al. 2007	Thromboembolism in patients undergoing total knee arthroplasty with epidural analgesia	Not best available evidence
Donatelli et al. 2007	Epidural anesthesia and analgesia decrease the postoperative incidence of insulin resistance in preoperative insulin-resistant subjects only	Not best available evidence
Kardash et al. 2007	Obturator versus femoral nerve block for analgesia after total knee arthroplasty	Does not address question of interest
Kita et al. 2007	Caudal epidural anesthesia administered intraoperatively provides for effective postoperative analgesia after total hip arthroplasty	Does not address question of interest

Table 64. Excluded Studies Considered for Anesthesia

Author	Title	Reason for Exclusion
Rosencher et al. 2007	Selected new antithrombotic agents and neuraxial anaesthesia for major orthopaedic surgery: management strategies	Systematic review, bibliography screened
Samama et al. 2007	Epidemiology of venous thromboembolism after lower limb arthroplasty: the FOTO study	Not best available evidence
Siddiqui et al. 2007	Continuous lumbar plexus block provides improved analgesia with fewer side effects compared with systemic opioids after hip arthroplasty: a randomized controlled trial	Does not address question of interest
Stevens et al. 2007	A modified fascia iliaca compartment block has significant morphine-sparing effect	Does not address question of interest
Guay 2006	The effect of neuraxial blocks on surgical blood loss and blood transfusion requirements: a meta-analysis	Systematic review, bibliography screened
Mauermann et al. 2006	A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis	Systematic review, bibliography screened
Peters et al. 2006	The Effect of a New Multimodal Perioperative Anesthetic Regimen on Postoperative Pain, Side Effects, Rehabilitation, and Length of Hospital Stay After Total Joint Arthroplasty	Not best available evidence
Axelsson et al. 2005	Postoperative extradural analgesia with morphine and ropivacaine. A double-blind comparison between placebo and ropivacaine 10 mg/h or 16 mg/h	Does not address question of interest
Dahl et al. 2005	Postoperative Melagatran/Ximelagatran for the Prevention of Venous Thromboembolism following Major Elective Orthopaedic Surgery : Effects of Timing of First Dose and Risk Factors for Thromboembolism and Bleeding Complications on Efficacy and Safety	Not best available evidence
Farag et al. 2005	Epidural analgesia improves early rehabilitation after total knee replacement	Does not address question of interest
Hebl et al. 2005	A comprehensive anesthesia protocol that emphasizes peripheral nerve blockade for total knee and total hip arthroplasty	Not best available evidence
Jaffer et al. 2005	Duration of anesthesia and venous thromboembolism after hip and knee arthroplasty	Not best available evidence
Sarmiento et al. 2005	Thromboembolic disease prophylaxis in total hip arthroplasty	Not best available evidence
Singelyn et al. 2005	Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous femoral nerve sheath block on rehabilitation after unilateral total-hip arthroplasty	Does not address question of interest
Kudoh et al. 2004	A comparison of anesthetic quality in propofol-spinal anesthesia and propofol-fentanyl anesthesia for total knee arthroplasty in elderly patients	Does not address question of interest

Table 64. Excluded Studies Considered for Anesthesia

Author	Title	Reason for Exclusion
Macalou et al. 2004	Postoperative analgesia after total knee replacement: the effect of an obturator nerve block added to the femoral 3-in-1 nerve block	Does not address question of interest
Brueckner et al. 2004	Comparison of general and spinal anesthesia and their influence on hemostatic markers in patients undergoing total hip arthroplasty	Does not report critical outcome of interest
Horlocker et al. 2003	Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation)	Narrative review, bibliography screened
Mantilla et al. 2003	Risk factors for clinically relevant pulmonary embolism and deep venous thrombosis in patients undergoing primary hip or knee arthroplasty	Not best available evidence
Buckenmaier et al. 2002	Lumbar plexus block with perineural catheter and sciatic nerve block for total hip arthroplasty	Not best available evidence
Westrich et al. 2002	Correlation of thrombophilia and hypofibrinolysis with pulmonary embolism following total hip arthroplasty: an analysis of genetic factors	Not best available evidence
Chelly et al. 2001	Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty	Not best available evidence
Della Valle et al. 2001	The relationship of the factor V Leiden mutation or the deletion-deletion polymorphism of the angiotensin converting enzyme to postoperative thromboembolic events following total joint arthroplasty	Not best available evidence
DeWeese et al. 2001	Pain control after knee arthroplasty: Intraarticular versus epidural anesthesia	Not best available evidence
Della Valle et al. 2000	Anticoagulant treatment of thromboembolism with intravenous heparin therapy in the early postoperative period following total joint arthroplasty	Not best available evidence
Wang et al. 2000	Deep vein thrombosis after total knee arthroplasty	Not best available evidence
Capdevila et al. 1999	Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery	Does not address question of interest
Caprini et al. 1999	The influence of oral anticoagulation therapy on deep vein thrombosis rates four weeks after total hip replacement	Not best available evidence
Ganapathy et al. 1999	Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty	Does not address question of interest
Hooker et al. 1999	Efficacy of prophylaxis against thromboembolism with intermittent pneumatic compression after primary and revision total hip arthroplasty	Not best available evidence
Sarmiento et al. 1999	Thromboembolic prophylaxis with use of aspirin, exercise, and graded elastic stockings or intermittent compression devices in patients managed with total hip arthroplasty	Not best available evidence

Table 64. Excluded Studies Considered for Anesthesia

Author	Title	Reason for Exclusion
Wulf et al. 1999	Ropivacaine epidural anesthesia and analgesia versus general anesthesia and intravenous patient-controlled analgesia with morphine in the perioperative management of hip replacement. Ropivacaine Hip Replacement Multicenter Study Group	Does not report critical outcome of interest
Allen et al. 1998	Peripheral nerve blocks improve analgesia after total knee replacement surgery	Does not address question of interest
Lau et al. 1998	Regional nerve block for total knee arthroplasty	Not best available evidence
Singelyn et al 1998	Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty	Does not address question of interest
Woolson et al. 1998	Deep venous thrombosis prophylaxis for knee replacement: warfarin and pneumatic compression	Not best available evidence
Woolson et al. 1998	Factor V Leiden and the risk of proximal venous thrombosis after total hip arthroplasty	Not best available evidence
Brinker et al. 1997	Comparison of general and epidural anesthesia in patients undergoing primary unilateral THR	Not best available evidence
Babcock et al. 1994	Venous duplex imaging for surveillance of patients undergoing total joint arthroplasty: A three-year study	Not best available evidence
Dalldorf et al. 1994	Deep venous thrombosis following total hip arthroplasty. Effects of prolonged postoperative epidural anesthesia	Not best available evidence
Haas 1994	Effects of epidural anesthesia on incidence of venous thromboembolism following joint replacement	Fewer than 100 patients per group and no non-VTE outcome
M°iniche et al. 1994	The effect of balanced analgesia on early convalescence after major orthopaedic surgery	Does not report critical outcomes of interest
Vresilovic et al. 1993	Incidence of pulmonary embolism after total knee arthroplasty with low-dose coumadin prophylaxis	Not best available evidence
Lemos et al. 1992	Pulmonary embolism in total hip and knee arthroplasty. Risk factors in patients on warfarin prophylaxis and analysis of the prothrombin time as an indicator of warfarin's prophylactic effect	Not best available evidence
McQueen et al. 1992	A comparison of epidural and non-epidural anesthesia and analgesia in total hip or knee arthroplasty patients	Not best available evidence
Uhrbrand et al. 1992	Perioperative analgesia by 3-in-one block in total hip arthroplasty. Prospective randomized blind study	Does not address question of interest
Hoek et al. 1991	The effect of different anaesthetic techniques on the incidence of thrombosis following total hip replacement	Not best available evidence
Mitchell et al. 1991	Prevention of thromboembolic disease following total knee arthroplasty. Epidural versus general anesthesia	Insufficient data
Sharrock et al. 1991	Effects of epidural anesthesia on the incidence of deep-vein thrombosis after total knee arthroplasty	Not best available evidence

Table 64. Excluded Studies Considered for Anesthesia

Author	Title	Reason for Exclusion
McCardel et al. 1990	Aspirin prophylaxis and surveillance of pulmonary embolism and deep vein thrombosis in total hip arthroplasty	Not best available evidence
Jones et al. 1990	Cognitive and functional competence after anaesthesia in patients aged over 60: Controlled trial of general and regional anaesthesia for elective hip or knee replacement	Does not report critical outcome
Nielsen et al. 1990	Long-term cognitive and social sequelae of general versus regional anesthesia during arthroplasty in the elderly	Does not address critical outcome of interest
Nielsen et al. 1990	Lower thrombosis risk with epidural blockade in knee arthroplasty	Not best available evidence
Prins et al. 1990	A comparison of general anesthesia and regional anesthesia as a risk factor for deep vein thrombosis following hip surgery: a critical review	Systematic review, bibliography screened
Balderston et al. 1989	The prevention of pulmonary embolism in total hip arthroplasty. Evaluation of low-dose warfarin therapy	Not best available evidence
Davis et al. 1989	Deep vein thrombosis after total hip replacement. A comparison between spinal and general anaesthesia	Fewer than 100 patients per group and no non-VTE outcomes
Modig 1989	Beneficial effects on intraoperative and postoperative blood loss in total hip replacement when performed under lumbar epidural anesthesia. An explanatory study	Report of previously published study
Wille-Jorgensen et al. 1989	Prevention of thromboembolism following elective hip surgery. The value of regional anesthesia and graded compression stockings	Not best available evidence
Fredin et al. 1986	Anaesthetic techniques and thromboembolism in total hip arthroplasty	Not best available evidence
Modig et al. 1983	Role of extradural and of general anaesthesia in fibrinolysis and coagulation after total hip replacement	Not best available evidence
Chin et al. 1982	Blood loss in total hip replacement: extradural v. phenoperidine analgesia	Does not address question of interest
Rosberg et al. 1982	Anesthetic techniques and surgical blood loss in total hip arthroplasty	Not best available evidence
Modig et al. 1981	Comparative influences of epidural and general anaesthesia on deep venous thrombosis and pulmonary embolism after total hip replacement	Not best available evidence
Thorburn et al. 1980	Spinal and general anaesthesia in total hip replacement: frequency of deep vein thrombosis	Not best available evidence
Keith 1977	Anaesthesia and blood loss in total hip replacement	Less than 10 patients per group
Amaranath et al. 1975	Relation of anesthesia to total hip replacement and control of operative blood loss	Not best available evidence
Sculco et al. 1975	The use of spinal anesthesia for total hip-replacement arthroplasty	Not best available evidence

IVC FILTERS

Table 65. Excluded Studies Considered for IVC Filters

Author	Title	Reason for Exclusion
Smoot et al. 2010	Inferior vena cava filters in trauma patients: Efficacy, morbidity, and retrievability	Not best available evidence
Binkert et al. 2009	Technical success and safety of retrieval of the G2 filter in a prospective, multicenter study	Not best available evidence
Charles et al. 2009	G2 inferior vena cava filter: retrievability and safety	Not specific to surgical patients
Helling et al. 2009	Practice patterns in the use of retrievable inferior vena cava filters in a trauma population: A single-center experience	Not best available evidence
Ishihara et al. 2009	Clinical outcome of perioperative nonpermanent vena cava filter placement in patients with deep venous thrombosis or blood stasis of the vein	Not best available evidence
Ko et al. 2009	Institutional protocol improves retrievable inferior vena cava filter recovery rate	Not best available evidence
Kuo et al. 2009	High-risk retrieval of adherent and chronically implanted IVC filters: techniques for removal and management of thrombotic complications	Not best available evidence
Lyon et al. 2009	Short- and long-term retrievability of the Celect vena cava filter: results from a multi-institutional registry	Not best available evidence
Onat et al. 2009	OptEase and TrapEase vena cava filters: a single-center experience in 258 patients	Narrative review, bibliography screened
Overby et al. 2009	Risk-group targeted inferior vena cava filter placement in gastric bypass patients	Not best available evidence
Rosenthal et al. 2009	Gunther Tulip and Celect IVC filters in multiple-trauma patients	Not best available evidence
Saour et al. 2009	Inferior vena caval filters: 5 years of experience in a tertiary care center	Not best available evidence
Vaziri et al. 2009	Retrievable inferior vena cava filters in high-risk patients undergoing bariatric surgery	Not best available evidence
Adib et al. 2008	The use of inferior vena caval filters prior to major surgery in women with gynaecological cancer	Does not investigate prophylaxis
Chung et al. 2008	Using inferior vena cava filters to prevent pulmonary embolism	Systematic review, bibliography screened
de Villiers et al. 2008	Initial Australian experience with the recovery inferior vena cava filter in patients with increased risk of thromboembolic disease	Not best available evidence
Given et al. 2008	Retrievable Gunther Tulip inferior vena cava filter: experience in 317 patients	Not best available evidence
Hermsen et al. 2008	Retrievable inferior vena cava filters in high-risk trauma and surgical patients: factors influencing successful removal	Not best available evidence
Kardys et al. 2008	Safety and efficacy of intravascular ultrasound-guided inferior vena cava filter in super obese bariatric patients	Not best available evidence
Lo et al. 2008	Inferior vena cava filters and lower limb flap reconstructions	Not best available evidence

Table 65. Excluded Studies Considered for IVC Filters

Author	Title	Reason for Exclusion
Oliva et al. 2008	Recovery G2 inferior vena cava filter: technical success and safety of retrieval	Not specific to surgical patients
Seshadri et al. 2008	Ins and outs of inferior vena cava filters in patients with venous thromboembolism: the experience at Monash Medical Centre and review of the published reports	Not specific to surgical patients
Spaniolas et al. 2008	Bedside placement of removable vena cava filters guided by intravascular ultrasound in the critically injured	Not best available evidence
Strauss et al. 2008	The use of retrievable inferior vena cava filters in orthopaedic patients	Not best available evidence
Zakhary et al. 2008	Optional filters in trauma patients: can retrieval rates be improved?	Not best available evidence
Ahmed et al. 2007	Role of inferior vena cava filter implantation in preventing pulmonary embolism	Not specific to surgical patients
Austin et al. 2007	The inferior vena cava filter is effective in preventing fatal pulmonary embolus after hip and knee arthroplasties	Not specific to prophylaxis
Aziz et al. 2007	Changing Patterns in the Use of Inferior Vena Cava Filters: Review of a Single Center Experience	Not best available evidence
Berczi et al. 2007	Long-term retrievability of IVC filters: should we abandon permanent devices?	Narrative review, bibliography screened
Corriere et al. 2007	Vena cava filters and inferior vena cava thrombosis	Not specific to surgical patients
Halmi et al. 2007	Preoperative placement of retreivable inferior vena cava filters in bariatric surgery	Not best available evidence
Hulse et al. 2007	Role of vena cava filters in high-risk trauma and elective orthopaedic procedures	Narrative review, bibliography screened
Kardys et al. 2007	The use of intravascular ultrasound imaging to improve use of inferior vena cava filters in a high-risk bariatric population	Not best available evidence
Karmy-Jones et al. 2007	Practice patterns and outcomes of retrievable vena cava filters in trauma patients: an AAST multicenter study	Not best available evidence
Keller et al. 2007	Clinical comparison of two optional vena cava filters	Not best available evidence
Martin et al. 2007	Vena cava filters in surgery and trauma	Narrative review, bibliography screened
Mismetti et al. 2007	A prospective long-term study of 220 patients with a retrievable vena cava filter for secondary prevention of venous thromboembolism	Not best available evidence
Piano et al. 2007	Safety, feasibility, and outcome of retrievable vena cava filters in high-risk surgical patients	Not best available evidence
Schuster et al. 2007	Retrievable inferior vena cava filters may be safely applied in gastric bypass surgery	Not best available evidence
Trigilio-Black et al. 2007	Inferior vena cava filter placement for pulmonary embolism risk reduction in super morbidly obese undergoing bariatric surgery	Not best available evidence

Table 65. Excluded Studies Considered for IVC Filters

Author	Title	Reason for Exclusion
Young et al. 2007	Vena caval filters for the prevention of pulmonary embolism	Systematic review, bibliography screened
Antevil et al. 2006	Retrievable vena cava filters for preventing pulmonary embolism in trauma patients: a cautionary tale	Not best available evidence
Dovrish et al. 2006	Retrospective analysis of the use of inferior vena cava filters in routine hospital practice	Not specific to surgical patients
Hoppe et al. 2006	Gunther Tulip filter retrievability multicenter study including CT follow-up: final report	Not specific to surgical patients
Meier et al. 2006	Early experience with the retrievable OptEase vena cava filter in high-risk trauma patients	Not best available evidence
Pancione et al. 2006	Use of the ALN permanent/removable vena cava filter. A multi-centre experience	Not specific to surgical patients
Rosenthal et al. 2006	Retrievable inferior vena cava filters: Initial clinical results	Not best available evidence
Stefanidis et al. 2006	Extended interval for retrieval of vena cava filters is safe and may maximize protection against pulmonary embolism	Not best available evidence
Grande et al. 2005	Experience with the recovery filter as a retrievable inferior vena cava filter	Not best available evidence
Imberti et al. 2005	Clinical experience with retrievable vena cava filters: results of a prospective observational multicenter study	Not specific to surgical patients
Keeling et al. 2005	Current indications for preoperative inferior vena cava filter insertion in patients undergoing surgery for morbid obesity	Not best available evidence
Kurtoglu et al. 2005	Intermittent pneumatic compression in the prevention of venous thromboembolism in high-risk trauma and surgical ICU patients	Fewer than 100 patients and no non-VTE outcomes
Leon et al. 2005	The prophylactic use of inferior vena cava filters in patients undergoing high-risk spinal surgery	Fewer than 100 patients and no non-VTE outcomes
Oliva et al. 2005	The Jonas study: evaluation of the retrievability of the Cordis OptEase inferior vena cava filter	Not specific to surgical patients
Prokubovsky et al. 2005	The use of the Zontik cava filter for temporary implantation to the inferior vena cava	Not best available evidence
Rosenthal et al. 2005	OptEase retrievable inferior vena cava filter: initial multicenter experience	Not specific to surgical patients
Sarani et al. 2005	Role of optional (retrievable) IVC filters in surgical patients at risk for venous thromboembolic disease	Narrative review, bibliography screened
Benevenia et al. 2004	Inferior vena cava filters prevent pulmonary emboli in patients with metastatic pathologic fractures of the lower extremity	Not best available evidence
Dawson et al. 2004	Best evidence topic reports. Safety of inferior vena cava filters as primary treatment for proximal deep vein thrombosis	Systematic review, bibliography screened

Table 65. Excluded Studies Considered for IVC Filters

Author	Title	Reason for Exclusion
Rosner et al. 2004	Prophylactic placement of an inferior vena cava filter in high-risk patients undergoing spinal reconstruction	Not best available evidence
Terhaar et al. 2004	Extended interval for retrieval of Gunther Tulip filters	Not best available evidence
De Gregorio et al. 2003	The Gunther Tulip retrievable filter: prolonged temporary filtration by repositioning within the inferior vena cava	Not specific to surgical patients
Lin et al. 2003	Factors associated with recurrent venous thromboembolism in patients with malignant disease	Not specific to surgical patients
Offner et al. 2003	The role of temporary inferior vena cava filters in critically ill surgical patients	Not best available evidence
Pieri et al. 2003	Optional vena cava filters: preliminary experience with a new vena cava filter	Not best available evidence
Donat et al. 2002	Incidence of thromboembolism after transurethral resection of the prostate (TURP)--a study on TED stocking prophylaxis and literature review	Does not address question of interest
Jarrett et al. 2002	Inferior vena cava filters in malignant disease	Does not investigate prophylaxis
Millward et al. 2001	Gunther Tulip Retrievable Vena Cava Filter: results from the Registry of the Canadian Interventional Radiology Association	Fewer than 100 patients; not specific to elective arthroplasty
Schleich et al. 2001	Long-term follow-up of percutaneous vena cava filters: a prospective study in 100 consecutive patients	Not best available evidence
McMurtry et al. 1999	Increased use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism	Not best available evidence
Rogers et al. 1998	Five-year follow-up of prophylactic vena cava filters in high-risk trauma patients	Not best available evidence
Gosin et al. 1997	Efficacy of prophylactic vena cava filters in high-risk trauma patients	Not best available evidence
Rogers et al. 1997	Prophylactic vena cava filter insertion in selected high-risk orthopaedic trauma patients	Not best available evidence
Rodriguez et al. 1996	Early placement of prophylactic vena caval filters in injured patients at high risk for pulmonary embolism	Not best available evidence
Crystal et al. 1995	Utilization patterns with inferior vena cava filters: surgical versus percutaneous placement	Not relevant - examines VTE treatment, not prevention
Ricco et al. 1995	The LGM Vena-Tech caval filter: Results of a multicenter study	Not specific to surgical patients
Rogers et al. 1995	Routine prophylactic vena cava filter insertion in severely injured trauma patients decreases the incidence of pulmonary embolism	Not best available evidence
Greenfield et al. 1994	Extended evaluation of the titanium Greenfield vena caval filter	Not specific to surgical patients

Table 65. Excluded Studies Considered for IVC Filters

Author	Title	Reason for Exclusion
Kniemeyer et al. 1994	Complications following caval interruption	Does not address question of interest
Leach et al. 1994	Surgical prophylaxis for pulmonary embolism	Not best available evidence
Lord et al. 1994	Early and late results after Bird's Nest filter placement in the inferior vena cava: clinical and duplex ultrasound follow up	Not best available evidence
Rosenthal et al. 1994	Use of the Greenfield filter in patients with major trauma	Not best available evidence
Collins et al. 1992	Vena caval filter use in orthopaedic trauma patients with recognized preoperative venous thromboembolic disease	Not best available evidence
Magnant et al. 1992	Current use of inferior vena cava filters	Less than 10 surgical prophylaxis patients
Webb et al. 1992	Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture	Not best available evidence
Emerson et al. 1991	Prophylactic and early therapeutic use of the Greenfield filter in hip and knee joint arthroplasty	Not specific to prophylaxis
Bucci et al. 1989	Mechanical prophylaxis of venous thrombosis in patients undergoing craniotomy: a randomized trial	Patient population not relevant
Vaughn et al. 1989	Use of the Greenfield filter to prevent fatal pulmonary embolism associated with total hip and knee arthroplasty	Retrospective case series
Clagett et al. 1988	Prevention of venous thromboembolism in general surgical patients. Results of meta-analysis	Systematic review, bibliography screened
Golueke et al. 1988	Interruption of the vena cava by means of the Greenfield filter: Expanding the indications	Retrospective case series
Thomas et al. 1988	A retrospective analysis of inferior vena caval filtration for prevention of pulmonary embolization	Not specific to surgical patients
Colditz et al. 1986	Rates of venous thrombosis after general surgery: combined results of randomised clinical trials	Systematic review, bibliography screened
Fullen et al. 1973	Prophylactic vena caval interruption in hip fractures	Not best available evidence

OTHER EXCLUDED STUDIES

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Babis et al. 2011	Incidence and prevention of thromboembolic events in one stage bilateral total hip arthroplasty: a systematic review	Systematic review, bibliography screened
Dushey et al. 2011	Short-Term Coagulation Complications Following Total Knee Arthroplasty A Comparison of Patient-Reported and Surgeon-Verified Complication Rates	Incidence study
Fitzgerald et al. 2011	Incidence of postthrombotic syndrome in patients undergoing primary total hip arthroplasty for osteoarthritis	Background article
Asensio et al. 2010	Timing of DVT prophylaxis and risk of postoperative knee prosthesis infection	Does not address question of interest
Baser et al. 2010	Impact of postoperative venous thromboembolism on Medicare recipients undergoing total hip replacement or total knee replacement surgery	Background article
Baser et al. 2010	Clinical and cost outcomes of venous thromboembolism in Medicare patients undergoing total hip replacement or total knee replacement surgery	Incidence study
Berend et al. 2010	Unicompartmental knee arthroplasty: incidence of transfusion and symptomatic thromboembolic disease	Incidence study
Bottaro et al. 2010	How should we define major bleeding events in thromboprophylaxis?	Letter
Bozic et al. 2010	The influence of procedure volumes and standardization of care on quality and efficiency in total joint replacement surgery	Does not address question of interest
Clifford et al. 2010	How should we define major bleeding events in thromboprophylaxis?: Reply	Letter
Cushner et al. 2010	Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY)	Incidence study
Dahl et al. 2010	A critical appraisal of bleeding events reported in venous thromboembolism prevention trials of patients undergoing hip and knee arthroplasty	Background article
Kurmis et al. 2010	Review article: thromboprophylaxis after total hip replacement	Systematic review, bibliography screened
Lanes et al. 2010	Incidence rates of thromboembolic, bleeding, and hepatic outcomes in patients undergoing hip or knee replacement surgery	Incidence study
Maynard et al. 2010	Optimizing prevention of hospital-acquired venous thromboembolism (VTE): prospective validation of a VTE risk assessment model	Not specific to elective arthroplasty
McAndrew et al. 2010	Incidence of postthrombotic syndrome in patients undergoing primary total knee arthroplasty for osteoarthritis	Does not address question of interest
McNally 2010	The impact of national guidelines for the prophylaxis of venous thromboembolism on the complications of arthroplasty of the lower limb	Letter

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Memtsoudis et al. 2010	Risk factors for perioperative mortality after lower extremity arthroplasty: a population-based study of 6,901,324 patient discharges	Does not address question of interest
Moganasundram et al. 2010	The relationship among thromboelastography, hemostatic variables, and bleeding after cardiopulmonary bypass surgery in children	Incorrect patient population
Muntz et al. 2010	Prevention and management of venous thromboembolism in the surgical patient: options by surgery type and individual patient risk factors	Systematic review, bibliography screened
Parvizi et al. 2010	Is deep vein thrombosis a good proxy for pulmonary embolus?	Background article
Plumb et al. 2010	Cost effectiveness of venous thromboembolism pharmacological prophylaxis in total hip and knee replacement: A systematic review	Letter
Raslan et al. 2010	Prophylaxis for venous thrombo-embolism in neurocritical care: a critical appraisal	Does not address question of interest
Rhodes et al. 2010	Discontinuation of warfarin is unnecessary in total knee arthroplasty	Does not address question of interest
Rosencher et al. 2010	Definition of major bleeding in surgery: An anesthesiologist's point of view: A rebuttal	Background article
Sheth et al. 2010	DVT Prophylaxis in Total Joint Reconstruction	Narrative review, bibliography screened
Struijk-Mulder et al. 2010	Comparing consensus guidelines on thromboprophylaxis in orthopedic surgery	Systematic review, bibliography screened
Van Herck et al. 2010	Key interventions and outcomes in joint arthroplasty clinical pathways: a systematic review	Does not address question of interest
Wuerz et al. 2010	The Surgical Apgar Score in Hip and Knee Arthroplasty	Does not address question of interest
Al Sayegh et al. 2009	Global Risk Profile Verification in Patients with Venous Thromboembolism (GRIP VTE) in 5 Gulf countries	Does not address question of interest
Andrade et al. 2009	Risk factors and prophylaxis for venous thromboembolism in hospitals in the city of Manaus, Brazil	Does not address question of interest
Arnold et al. 2009	Rational testing: Preoperative risk assessment for bleeding and thromboembolism	Commentary
Bono et al. 2009	An evidence-based clinical guideline for the use of antithrombotic therapies in spine surgery	Does not address question of interest
Clayton et al. 2009	Thromboembolic disease after total knee replacement: experience of 5100 cases	Incidence study
Dall et al. 2009	The influence of pre-operative factors on the length of in-patient stay following primary total hip replacement for osteoarthritis: A multivariate analysis of 2302 patients	No relevant outcomes
De Luca et al. 2009	Risk profile and benefits from Gp IIb-IIIa inhibitors among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: A meta-regression analysis of randomized trials	Does not address question of interest

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Dowsey et al. 2009	Obese diabetic patients are at substantial risk for deep infection after primary TKA	Does not address question of interest
Hooper et al. 2009	Bilateral Total Joint Arthroplasty. The Early Results from the New Zealand National Joint Registry	Does not address question of interest
Huddleston et al. 2009	Adverse events after total knee arthroplasty: a national Medicare study	Incidence study
Khuangsirikul et al. 2009	Lower extremities' postthrombotic syndrome after total knee arthroplasty	Does not address question of interest
Li et al. 2009	Experimental study of COX-2 selective and traditional non-steroidal anti-inflammatory drugs in total hip replacement	Does not address question of interest
Memtsoudis et al. 2009	Perioperative outcomes after unilateral and bilateral total knee arthroplasty	Does not address question of interest
Sharma et al. 2009	Factors influencing early rehabilitation after tha: A systematic review	Does not address question of interest
Sweetland et al. 2009	Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: prospective cohort study	Incidence study
Teasell et al. 2009	Venous thromboembolism after spinal cord injury	Does not address question of interest
Urwyler et al. 2009	Is perioperative point-of-care prothrombin time testing accurate compared to the standard laboratory test?	Does not address question of interest
Arcelus et al. 2008	Clinical presentation and time-course of postoperative venous thromboembolism: Results from the RIETE Registry	Does not address question of interest
Borris et al. 2008	Differences in urinary prothrombin fragment 1 + 2 levels after total hip replacement in relation to venous thromboembolism and bleeding events	Does not address question of interest
Collen et al. 2008	Prevention of venous thromboembolism in neurosurgery: a metaanalysis	Does not address question of interest
Dowsey et al. 2008	Obesity is a major risk factor for prosthetic infection after primary hip arthroplasty	Does not address question of interest
Grella 2008	Continuous passive motion following total knee arthroplasty: a useful adjunct to early mobilisation? (Provisional abstract)	Does not address question of interest
Khan et al. 2008	Multidisciplinary rehabilitation programmes following joint replacement at the hip and knee in chronic arthropathy	Does not address question of interest
Khatod et al. 2008	Knee replacement: epidemiology, outcomes, and trends in Southern California: 17,080 replacements from 1995 through 2004	Incidence study
Mant et al. 2008	Post-thrombotic syndrome after total hip arthroplasty is uncommon	Does not address question of interest
Osborne et al. 2008	Venous thromboembolism in cancer patients undergoing major surgery	Systematic review, bibliography screened
Pulido et al. 2008	Periprosthetic joint infection: the incidence, timing, and predisposing factors	Does not address question of interest

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Ramos et al. 2008	Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy	Not specific to elective arthroplasty
Tsiridis et al. 2008	The safety and efficacy of bilateral simultaneous total hip replacement: an analysis of 2063 cases	Does not address question of interest
Wu et al. 2008	Does different time interval between staggered bilateral total knee arthroplasty affect perioperative outcome? A retrospective study	Does not address question of interest
Agren et al. 2007	Low PAI-1 activity in relation to the risk for perioperative bleeding complications in transurethral resection of the prostate	Does not address question of interest
Becattini et al. 2007	Acute pulmonary embolism: risk stratification in the emergency department	Not specific to elective arthroplasty
Chan et al. 2007	Systemic anticoagulant prophylaxis for central catheter-associated venous thrombosis in cancer patients	Not specific to surgical patients
Einstein et al. 2007	Venous thromboembolism prevention in gynecologic cancer surgery: a systematic review	Not specific to elective arthroplasty
Ferreira et al. 2007	Clinically significant delayed postsphincterotomy bleeding: a twelve year single center experience	Does not address question of interest
Hashmi et al. 2007	Staged bilateral hip or knee arthroplasties	Does not address question of interest
Parvizi et al. 2007	Does 'excessive' anticoagulation predispose to periprosthetic infection?	Does not address question of interest
Patiar et al. 2007	Prevention of venous thromboembolism in surgical patients with breast cancer	Systematic review, bibliography screened
Quinlan et al. 2007	Association between asymptomatic deep vein thrombosis detected by venography and symptomatic venous thromboembolism in patients undergoing elective hip or knee surgery	Systematic review, bibliography screened
Restrepo et al. 2007	Safety of simultaneous bilateral total knee arthroplasty. A meta-analysis	Does not address question of interest
Salam et al. 2007	Bleeding after dental extractions in patients taking warfarin	Does not address question of interest
Barrett et al. 2006	Bilateral total knee replacement: staging and pulmonary embolism	Does not address question of interest
Hutchinson et al. 2006	A comparison of bilateral uncemented total knee arthroplasty: simultaneous or staged?	Does not address question of interest
Lonner et al. 2006	Postthrombotic syndrome after asymptomatic deep vein thrombosis following total knee and hip arthroplasty	Does not address question of interest
Martino et al. 2006	Pulmonary embolism after major abdominal surgery in gynecologic oncology	Not specific to elective arthroplasty
Negus et al. 2006	Thromboprophylaxis in major abdominal surgery for cancer	Systematic review, bibliography screened
Powell et al. 2006	Bilateral vs Unilateral Total Knee Arthroplasty: A Patient-Based Comparison of Pain Levels and Recovery of Ambulatory Skills	Does not address question of interest

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Rocha et al. 2006	Risk of venous thromboembolism and efficacy of thromboprophylaxis in hospitalized obese medical patients and in obese patients undergoing bariatric surgery	Systematic review, bibliography screened
Samama et al. 2006	An electronic tool for venous thromboembolism prevention in medical and surgical patients	Does not address question of interest
Samama et al. 2006	Venous thromboembolism prevention in surgery and obstetrics: clinical practice guidelines	Clinical guideline
Wu et al. 2006	Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study	Systematic review, bibliography screened
Asensio et al. 2005	Preoperative low molecular weight heparin as venous thromboembolism prophylaxis in patients at risk for prosthetic infection after knee arthroplasty	Does not address question of interest
Borly et al. 2005	Systematic review of thromboprophylaxis in colorectal surgery -- an update	Does not address question of interest
Cotter et al. 2005	Efficacy of venous thromboembolism prophylaxis in morbidly obese patients undergoing gastric bypass surgery	Does not address question of interest
Goodacre et al. 2005	Meta-analysis: The value of clinical assessment in the diagnosis of deep venous thrombosis	Systematic review, bibliography screened
Howie et al. 2005	Venous thromboembolism associated with hip and knee replacement over a ten-year period: a population-based study	Incidence study
Schindler et al. 2005	Post-thrombotic syndrome after total hip or knee arthroplasty: incidence in patients with asymptomatic deep venous thrombosis	Does not address question of interest
Sliva et al. 2005	Staggered bilateral total knee arthroplasty performed four to seven days apart during a single hospitalization	Does not address question of interest
Cordell-Smith et al. 2004	Lower limb arthroplasty complicated by deep venous thrombosis. Prevalence and subjective outcome	Incidence study
Friis et al. 2004	Thromboembolic prophylaxis as a risk factor for postoperative complications after breast cancer surgery	Does not address question of interest
Gonzalez et al. 2004	Incidence of clinically evident deep venous thrombosis after laparoscopic Roux-en-Y gastric bypass	Not specific to elective arthroplasty
Howard et al. 2004	Randomized clinical trial of low molecular weight heparin with thigh-length or knee-length antiembolism stockings for patients undergoing surgery	Not specific to elective arthroplasty
Lee et al. 2004	Bilateral vs. ipsilateral venography as the primary efficacy outcome measure in thromboprophylaxis clinical trials: a systematic review	Systematic review, bibliography screened
Miller et al. 2004	An approach to venous thromboembolism prophylaxis in laparoscopic Roux-en-Y gastric bypass surgery	Does not address question of interest
Minnema et al. 2004	Risk factors for surgical-site infection following primary total knee arthroplasty	Does not address question of interest
Smith et al. 2004	Prophylaxis for deep venous thrombosis in neurosurgical oncology: review of 2779 admissions over a 9-year period	Not specific to elective arthroplasty

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Windfuhr et al. 2004	Unidentified coagulation disorders in post-tonsillectomy hemorrhage	Insufficient data
Grabowska-Gawel et al. 2003	Combined subarachnoid and epidural anaesthesia for endoprosthetoplasty of the knee joint	Cannot locate publication
Major et al. 2003	The incidence of thromboembolism in the surgical intensive care unit	Does not address question of interest
Mehta et al. 2003	Venous leg ulcers after hip replacement	Does not address question of interest
Nutescu et al. 2003	Tinzaparin: Considerations for Use in Clinical Practice	Systematic review, bibliography screened
Phillips et al. 2003	Incidence rates of dislocation, pulmonary embolism, and deep infection during the first six months after elective total hip replacement	Incidence study
Ramirez et al. 2003	Sequential compression devices as prophylaxis for venous thromboembolism in high-risk colorectal surgery patients: reconsidering American Society of Colorectal Surgeons parameters	Not specific to elective arthroplasty
Ritter et al. 2003	Simultaneous bilateral, staged bilateral, and unilateral total knee arthroplasty. A survival analysis	Does not address question of interest
Rodriguez-Merchan et al. 2003	Elective orthopaedic surgery for inhibitor patients	Less than 10 arthroplasty patients
Sapala et al. 2003	Fatal pulmonary embolism after bariatric operations for morbid obesity: a 24-year retrospective analysis	Insufficient data
Wang et al. 2003	Outcome of calf deep-vein thrombosis after total knee arthroplasty	DVT-PE Correlation
Zenios et al. 2003	Post-thrombotic syndrome after total hip arthroplasty	Does not address question of interest
Handoll et al. 2002	Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures	Systematic review, bibliography screened
Piovella et al. 2002	Normalization rates of compression ultrasonography in patients with a first episode of deep vein thrombosis of the lower limbs: association with recurrence and new thrombosis	Not relevant - examines VTE treatment, not prevention
Williams et al. 2002	Mortality, morbidity, and 1-year outcomes of primary elective total hip arthroplasty	Incidence study
Deehan et al. 2001	Postphlebitic syndrome after total knee arthroplasty: 405 patients examined 2-10 years after surgery	Does not address question of interest
Maxwell et al. 2001	Pneumatic compression versus low molecular weight heparin in gynecologic oncology surgery: a randomized trial	Not specific to elective arthroplasty
Ziegler et al. 2001	Post-thrombotic syndrome after primary event of deep venous thrombosis 10 to 20 years ago	Not specific to elective arthroplasty

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Dahl et al. 2000	Late occurring clinical deep vein thrombosis in joint-operated patients	Not specific to elective arthroplasty
Ginsberg et al. 2000	Postthrombotic syndrome after hip or knee arthroplasty: a cross-sectional study	Does not address question of interest
Neal et al. 2000	No effect of low-dose aspirin for the prevention of heterotopic bone formation after total hip replacement: a randomized trial of 2,649 patients	Does not address question of interest
Wroblewski et al. 2000	Fatal pulmonary embolism and mortality after revision of failed total hip arthroplasties	Incidence study
Alfaro-Adrian et al. 1999	One- or two-stage bilateral total hip replacement	Does not address question of interest
Perkins et al. 1999	Vascular surgical society of great britain and ireland: randomized controlled trial of heparin plus graduated compression stocking for the prophylaxis of deep venous thrombosis in general surgical patients	Abstract
Williams et al. 1999	Coagulation tests during cardiopulmonary bypass correlate with blood loss in children undergoing cardiac surgery	Incorrect patient population
Bould et al. 1998	Blood loss in sequential bilateral total knee arthroplasty	Does not address question of interest
Cafferata et al. 1998	Venous thromboembolism in trauma patients: standardized risk factors	Does not address question of interest
Heck et al. 1998	Patient outcomes after knee replacement	Incidence study
Wroblewski et al. 1998	Fatal pulmonary embolism after total hip arthroplasty: diurnal variations	Does not address question of interest
Koch et al. 1997	Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses	Systematic review, bibliography screened
Palmer et al. 1997	Efficacy and safety of low molecular weight heparin, unfractionated heparin and warfarin for thrombo-embolism prophylaxis in orthopaedic surgery: a meta-analysis of randomised clinical trials	Systematic review, bibliography screened
Rader et al. 1997	Comparison of low molecular weight and PTT adjusted heparin for thromboprophylaxis in patients with total hip and total knee arthroplasty	Foreign language
Baron et al. 1996	Total hip arthroplasty: use and select complications in the US Medicare population	Incidence study
Eggli et al. 1996	Bilateral total hip arthroplasty: one stage versus two stage procedure	Does not address question of interest
Flinn et al. 1996	Prospective surveillance for perioperative venous thrombosis. Experience in 2643 patients	Does not address question of interest
Hynson et al. 1996	Epidural hematoma associated with enoxaparin	Case report
Lisander et al. 1996	Giving both enoxaparin and dextran increases the need for transfusion in revision hip arthroplasty	Does not address question of interest
Ramos et al. 1996	The efficacy of pneumatic compression stockings in the prevention of pulmonary embolism after cardiac surgery	Not specific to elective arthroplasty

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
Ricotta et al. 1996	Post discharge clinically overt venous thromboembolism in orthopaedic surgery patients with negative venography--an overview analysis	Systematic review, bibliography screened
Schwartsmann et al. 1996	Randomized controlled trial, comparative to evaluate the efficacy and security of enoxaparin comparated by heparin in prophylaxis of thromboembolism in patients with arthroplasty replacement hip	Foreign language
Siddique et al. 1996	Thirty-day case-fatality rates for pulmonary embolism in the elderly	Does not address question of interest
Warwick et al. 1996	Does total hip arthroplasty predispose to chronic venous insufficiency?	Does not address question of interest
Despotis et al. 1995	The impact of heparin concentration and activated clotting time monitoring on blood conservation. A prospective, randomized evaluation in patients undergoing cardiac operation	Does not address question of interest
Goldhaber et al. 1995	Prevention of venous thrombosis after coronary artery bypass surgery (a randomized trial comparing two mechanical prophylaxis strategies)	Not specific to elective arthroplasty
Rosenow 1995	Venous and pulmonary thromboembolism: an algorithmic approach to diagnosis and management	Narrative review, bibliography screened
Sharrock et al. 1995	Changes in mortality after total hip and knee arthroplasty over a ten- year period	Incidence study
Unsworth-White et al. 1995	Resternotomy for bleeding after cardiac operation: a marker for increased morbidity and mortality	Does not address question of interest
Jankiewicz et al. 1994	One-stage versus 2-stage bilateral total knee arthroplasty	Does not address question of interest
Lotke et al. 1994	Significance of deep venous thrombosis in the lower extremity after total joint arthroplasty	DVT-PE Correlation
McNally et al. 1994	Postphlebitic syndrome after hip arthroplasty. 43 patients followed at least 5 years	Does not address question of interest
Ferree et al. 1993	Deep venous thrombosis following posterior lumbar spinal surgery	Does not address question of interest
Ivory et al. 1993	Bilateral knee replacements: simultaneous or staged?	Does not address question of interest
Monreal et al. 1993	Venographic assessment of deep vein thrombosis and risk of developing post-thrombotic syndrome: a prospective study	Not specific to elective arthroplasty
Pellegrini et al. 1993	Embolic complications of calf thrombosis following total hip arthroplasty	DVT-PE Correlation
Robinson et al. 1993	Nonsteroidal antiinflammatory drugs, perioperative blood loss, and transfusion requirements in elective hip arthroplasty	Does not address question of interest
Haas et al. 1992	The significance of calf thrombi after total knee arthroplasty	DVT-PE Correlation
Wroblewski et al. 1992	Fatal pulmonary embolism after total hip arthroplasty. Seasonal variation	Does not address question of interest

Table 66. Other Studies Excluded at Full-Text Review (not reported elsewhere)

Author	Title	Reason for Exclusion
An et al. 1991	Effects of hypotensive anesthesia, nonsteroidal antiinflammatory drugs, and polymethylmethacrylate on bleeding in total hip arthroplasty patients	Does not address question of interest
Connelly et al. 1991	Should nonsteroidal anti-inflammatory drugs be stopped before elective surgery?	Does not address question of interest
Paavolainen et al. 1991	Registration of arthroplasties in Finland. A nationwide prospective project	Incidence study
Seagroatt et al. 1991	Elective total hip replacement: incidence, emergency readmission rate, and postoperative mortality	Incidence study
Traverso et al. 1991	The effect of intravenous fixed-dose heparin during total hip arthroplasty on the incidence of deep-vein thrombosis. A randomized, double-blind trial in patients operated on with epidural anesthesia and controlled hypotension	Letter
Kalebo et al. 1990	Phlebographic findings in venous thrombosis following total hip replacement	DVT-PE Correlation
Francis et al. 1988	Long-term clinical observations and venous functional abnormalities after asymptomatic venous thrombosis following total hip or knee arthroplasty	Does not address question of interest
Morrey et al. 1987	Complications and mortality associated with bilateral or unilateral total knee arthroplasty	Does not address question of interest
Brotherton et al. 1986	Staged versus simultaneous bilateral total knee replacement	Does not address question of interest
Shih et al. 1985	One-stage versus two-stage bilateral autophor ceramic total hip arthroplasty	Does not address question of interest
Soudry et al. 1985	Successive bilateral total knee replacement	Does not address question of interest
Clarke-Pearson et al. 1984	Perioperative external pneumatic calf compression as thromboembolism prophylaxis in gynecologic oncology: report of a randomized controlled trial	Not specific to elective arthroplasty
Lotke et al. 1984	Indications for the treatment of deep venous thrombosis following total knee replacement	Incidence study
de Mourgues et al. 1979	Study of efficacy of subcutaneous heparin used by two different methods for prevention of postoperative venous thrombosis after hip prosthesis	Foreign language
Salvati et al. 1978	Bilateral total hip-replacement arthroplasty in one stage	Does not address question of interest
Bachmann et al. 1976	Low pressure intermittent compression to calves and thighs: a successful new method for prevention of postoperative thrombosis. <ORIGINAL> INTERMITTIERENDE PNEUMATISCHE KOMPRESSION VON UNTER- UND OBERSCHENKEL; EINE NEUE ERFOLGREICHE METHODE ZUR POSTOPERAT	Foreign language

SYSTEMATIC REVIEWS SCREENED FOR ADDITIONAL ARTICLES

Author	Title
Babis et al. 2011	Incidence and prevention of thromboembolic events in one stage bilateral total hip arthroplasty: a systematic review
Kalyani et al. 2011	Low molecular weight heparin: Current evidence for its application in orthopaedic surgery
Dranitsaris et al. 2011	Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement
Friedman et al. 2010	Dabigatran versus enoxaparin for prevention of venous thromboembolism after hip or knee arthroplasty: a pooled analysis of three trials
Huang et al. 2010	Apixaban versus enoxaparin in patients with total knee arthroplasty. A meta-analysis of randomised trials
Huisman et al. 2010	Enoxaparin versus dabigatran or rivaroxaban for thromboprophylaxis after hip or knee arthroplasty: Results of separate pooled analyses of phase III multicenter randomized trials
Cao et al. 2010	Rivaroxaban versus enoxaparin for thromboprophylaxis after total hip or knee arthroplasty: a meta-analysis of randomized controlled trials
Melillo et al. 2010	Rivaroxaban for thromboprophylaxis in patients undergoing major orthopedic surgery
Kapoor et al. 2010	Cost effectiveness of venous thromboembolism pharmacological prophylaxis in total hip and knee replacement: a systematic review
Muntz et al. 2010	Prevention and management of venous thromboembolism in the surgical patient: options by surgery type and individual patient risk factors
Caprini 2010	Risk assessment as a guide for the prevention of the many faces of venous thromboembolism
Tasker et al. 2010	Meta-analysis of low molecular weight heparin versus placebo in patients undergoing total hip replacement and post-operative morbidity and mortality since their introduction
Turpie et al. 2010	Rivaroxaban for the prevention of venous thromboembolism after hip or knee arthroplasty. Pooled analysis of four studies
Donohoe et al. 2010	Aspirin for lower limb arthroplasty thromboprophylaxis: review of international guidelines
Wilke et al. 2010	Nonadherence in outpatient thromboprophylaxis after major orthopedic surgery: a systematic review
Struijk-Mulder et al. 2010	Comparing consensus guidelines on thromboprophylaxis in orthopedic surgery
Kurmis 2010	Review article: thromboprophylaxis after total hip replacement
Salazar et al. 2010	Direct thrombin inhibitors versus vitamin K antagonists or low molecular weight heparins for prevention of venous thromboembolism following total hip or knee replacement
Sachdeva et al. 2010	Elastic compression stockings for prevention of deep vein thrombosis (Cochrane review) [with consumer summary]
Holmes et al. 2009	Dabigatran etexilate for the prevention of venous thromboembolism in patients undergoing elective hip and knee surgery: a single technology appraisal
Macfarlane et al. 2009	Does regional anesthesia improve outcome after total knee arthroplasty?
Macfarlane et al. 2009	Does regional anaesthesia improve outcome after total hip arthroplasty? A systematic review
Eriksson et al. 2009	Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement

Author	Title
Lazo-Langner et al. 2009	Lessons from ximelagatran: issues for future studies evaluating new oral direct thrombin inhibitors for venous thromboembolism prophylaxis in orthopedic surgery
Turpie et al. 2009	Pharmacokinetic and clinical data supporting the use of fondaparinux 1.5 mg once daily in the prevention of venous thromboembolism in renally impaired patients
Hu et al. 2009	A comparison of regional and general anaesthesia for total replacement of the hip or knee: a meta-analysis
Wolowacz et al. 2009	Efficacy and safety of dabigatran etexilate for the prevention of venous thromboembolism following total hip or knee arthroplasty. A meta-analysis
Kinnaird et al. 2009	Bleeding during percutaneous intervention: Tailoring the approach to minimise risk
O'Riordan et al. 2009	Antiplatelet agents in the perioperative period
Hull et al. 2009	State-of-the-art review: Assessing the safety profiles of new anticoagulants for major orthopedic surgery thromboprophylaxis
Brown 2009	Venous Thromboembolism Prophylaxis After Major Orthopaedic Surgery: A Pooled Analysis of Randomized Controlled Trials
Chee et al. 2008	Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Haematology
Sharrock et al. 2008	Potent anticoagulants are associated with a higher all-cause mortality rate after hip and knee arthroplasty
Chung et al. 2008	Using inferior vena cava filters to prevent pulmonary embolism
Osborne et al. 2008	Venous thromboembolism in cancer patients undergoing major surgery
Sun et al. 2008	The effect of pre-operative aspirin on bleeding, transfusion, myocardial infarction, and mortality in coronary artery bypass surgery: A systematic review of randomized and observational studies
Kakkos et al. 2008	Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients
Xing et al. 2008	Has the incidence of deep vein thrombosis in patients undergoing total hip/knee arthroplasty changed over time? A systematic review of randomized controlled trials
Rosencher et al. 2007	Selected new antithrombotic agents and neuraxial anaesthesia for major orthopaedic surgery: management strategies
Alghamdi et al. 2007	Does the use of preoperative aspirin increase the risk of bleeding in patients undergoing coronary artery bypass grafting surgery? Systematic review and meta-analysis
Fisher et al. 2007	Rivaroxaban for thromboprophylaxis after orthopaedic surgery: pooled analysis of two studies
Quinlan et al. 2007	Association between asymptomatic deep vein thrombosis detected by venography and symptomatic venous thromboembolism in patients undergoing elective hip or knee surgery
Patiar et al. 2007	Prevention of venous thromboembolism in surgical patients with breast cancer
Skedgel et al. 2007	The cost-effectiveness of extended-duration antithrombotic prophylaxis after total hip arthroplasty
Ivanovic et al. 2007	Thromboprophylaxis in total hip-replacement surgery in Europe: Acenocoumarol, fondaparinux, dabigatran and rivaroxban
Young et al. 2007	Vena caval filters for the prevention of pulmonary embolism

Author	Title
Mauermann et al. 2006	A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis
Negus et al. 2006	Thromboprophylaxis in major abdominal surgery for cancer
Guay 2006	The effect of neuraxial blocks on surgical blood loss and blood transfusion requirements: a meta-analysis
Rocha et al. 2006	Risk of venous thromboembolism and efficacy of thromboprophylaxis in hospitalized obese medical patients and in obese patients undergoing bariatric surgery
Wu et al. 2006	Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study
Chan et al. 2006	Role for aspirin after total hip replacement?
Goodacre et al. 2005	Meta-analysis: The value of clinical assessment in the diagnosis of deep venous thrombosis
Segal et al. 2005	Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: An evidence-based review
Lee et al. 2004	Bilateral vs. ipsilateral venography as the primary efficacy outcome measure in thromboprophylaxis clinical trials: a systematic review
Dawson et al. 2004	Best evidence topic reports. Safety of inferior vena cava filters as primary treatment for proximal deep vein thrombosis
Edmonds et al. 2004	Evidence-based risk factors for postoperative deep vein thrombosis
Mismetti et al. 2004	Prevention of venous thromboembolism in orthopedic surgery with vitamin K antagonists: A meta-analysis
Tran et al. 2003	Fondaparinux for prevention of venous thromboembolism in major orthopedic surgery
O'Donnell et al. 2003	Reduction of out-of-hospital symptomatic venous thromboembolism by extended thromboprophylaxis with low-molecular-weight heparin following elective hip arthroplasty: a systematic review
Samama et al. 2003	Quantification of risk factors for venous thromboembolism: a preliminary study for the development of a risk assessment tool
Nutescu et al. 2003	Tinzaparin: Considerations for Use in Clinical Practice
Zufferey et al. 2003	Optimal low-molecular-weight heparin regimen in major orthopaedic surgery: A meta-analysis of randomised trials
Turpie et al. 2002	Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery: a meta-analysis of 4 randomized double-blind studies
Cehng 2002	Fondaparinux: a new antithrombotic agent
Strebel et al. 2002	Preoperative or postoperative start of prophylaxis for venous thromboembolism with low-molecular-weight heparin in elective hip surgery?
Douketis et al. 2002	Short-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of prospective studies investigating symptomatic outcomes
Nerurkar et al. 2002	Cost/death averted with venous thromboembolism prophylaxis in patients undergoing total knee replacement or knee arthroplasty
Handoll et al. 2002	Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures

Author	Title
Turpie et al. 2002	A meta-analysis of fondaparinux versus enoxaparin in the prevention of venous thromboembolism after major orthopaedic surgery
Hull et al. 2001	Timing of initial administration of low-molecular-weight heparin prophylaxis against deep vein thrombosis in patients following elective hip arthroplasty: a systematic review
Hull et al. 2001	Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review
Berry 2001	Surveillance for venous thromboembolic disease after total knee arthroplasty
Eikelboom et al. 2001	Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials
Hull et al. 2001	Low-molecular-weight heparin prophylaxis: preoperative versus postoperative initiation in patients undergoing elective hip surgery
Krishna et al. 2001	Post-tonsillectomy bleeding: a meta-analysis
Brookenthal et al. 2001	A meta-analysis of thromboembolic prophylaxis in total knee arthroplasty
Freedman et al. 2000	A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty
Westrich et al. 2000	Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty
Amaragiri et al. 2000	Elastic compression stockings for prevention of deep vein thrombosis (Cochrane Review) [with con sumer summary]
Hull et al. 1999	Preoperative vs postoperative initiation of low-molecular-weight heparin prophylaxis against venous thromboembolism in patients undergoing elective hip replacement
Agu et al. 1999	Graduated compression stockings in the prevention of venous thromboembolism
Wade 1999	Cost effectiveness of danaparoid compared with enoxaparin as deep vein thrombosis prophylaxis after hip replacement surgery
Vanek 1998	Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves
Howard et al. 1998	Low molecular weight heparin decreases proximal and distal deep venous thrombosis following total knee arthroplasty. A meta-analysis of randomized trials
Kearon et al. 1998	Noninvasive diagnosis of deep venous thrombosis. McMaster Diagnostic Imaging Practice Guidelines Initiative
Palmer et al. 1997	Efficacy and safety of low molecular weight heparin, unfractionated heparin and warfarin for thrombo-embolism prophylaxis in orthopaedic surgery: a meta-analysis of randomised clinical trials
Koch et al. 1997	Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses
Skoutakis 1997	Danaparoid in the prevention of thromboembolic complications
Howard et al. 1997	Dalteparin: a low-molecular-weight heparin
Murray et al. 1996	Thromboprophylaxis and death after total hip replacement
Ricotta et al. 1996	Post discharge clinically overt venous thromboembolism in orthopaedic surgery patients with negative venography--an overview analysis
Sarasin et al. 1996	Antithrombotic strategy after total hip replacement. A cost-effectiveness analysis comparing prolonged oral anticoagulants with screening for deep vein thrombosis

Author	Title
Andersen et al. 1996	Survival in patients undergoing total hip arthroplasty in relation to thromboprophylaxis with low molecular weight heparin: A long-term follow-up study
Wells et al. 1995	Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery. A meta-analysis
Borris et al. 1994	Perioperative thrombosis prophylaxis with low molecular weight heparins in elective hip surgery. Clinical and economic considerations
Imperiale et al. 1994	A meta-analysis of methods to prevent venous thromboembolism following total hip replacement
Antiplatelet Trialists Collaboration 1994	Collaborative overview of randomised trials of antiplatelet therapy--III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. Antiplatelet Trialists' Collaboration
O'Brien et al. 1994	Cost-effectiveness of enoxaparin versus warfarin prophylaxis against deep-vein thrombosis after total hip replacement
Landefeld et al. 1993	Anticoagulant-related bleeding: clinical epidemiology, prediction, and prevention
Mohr et al. 1993	Prophylactic agents for venous thrombosis in elective hip surgery. Meta-analysis of studies using venographic assessment
Anderson et al. 1993	Efficacy and cost of low-molecular-weight heparin compared with standard heparin for the prevention of deep vein thrombosis after total hip arthroplasty
Carter et al. 1993	Enoxaparin: The low-molecular-weight heparin for prevention of postoperative thromboembolic complications
Leizorovicz et al. 1992	Low molecular weight heparin in prevention of perioperative thrombosis
Nurmohamed et al. 1992	Low-molecular-weight heparin versus standard heparin in general and orthopaedic surgery: a meta-analysis
Lind 1991	The bleeding time does not predict surgical bleeding
Prins et al. 1990	A comparison of general anesthesia and regional anesthesia as a risk factor for deep vein thrombosis following hip surgery: a critical review
Clagett et al. 1988	Prevention of venous thromboembolism in general surgical patients. Results of meta-analysis
Colditz et al. 1986	Rates of venous thrombosis after general surgery: combined results of randomised clinical trials

APPENDIX XV
PROPHYLAXIS RECOMMENDATION ANALYSIS
SUMMARY OF DIRECT COMPARISONS
Table 67. Pulmonary Embolism Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	1 (0.062, 16.089)	No Difference
IPC v None	2	0.138 (0.009, 2.206)	No Difference
Aspirin (<300mg/day) v Placebo	1	0.997 (0.374, 2.661)	No Difference
Enoxaparin v Placebo/None	2	1.037† (0.065, 16.591)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	1.044 (0.065, 16.81)	No Difference
Enoxaparin v GCS	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.133 (0.003, 6.722)	No Difference
Tinzaparin + GCS v GCS	1	1 (0.062, 16.094)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	0.969 (0.135, 6.935)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	7.741 (0.153, 390.51)	No Difference
IPC v GCS	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.964 (0.06, 15.503)	No Difference
Apixaban v Enoxaparin	4	1.125 (0.649, 1.952)	No Difference
Dabigatran v Enoxaparin	4	1.032 (0.503, 2.116)	No Difference
Desirudin v Enoxaparin	1	0.501 (0.135, 1.856)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	1.575 (0.777, 3.19)	No Difference
Heparin v Enoxaparin	4	7.345 (1.982, 27.219)	Enoxaparin
Rivaroxaban v Enoxaparin	5	0.584 (0.285, 1.195)	No Difference
Tinzaparin v Enoxaparin	1	0.991 (0.062, 15.893)	No Difference
Tinzaparin v Warfarin	1	1.008 (0.063, 16.138)	No Difference
Warfarin v Enoxaparin	4	0.898 (0.457, 1.764)	No Difference
Desirudin v Heparin	2	0.306† (0.053, 1.779)	No Difference

† = heterogeneity

Table 68. Pulmonary Embolism Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
IPC v None	1	0.141 (0.003, 7.09)	No Difference
Aspirin (<300mg/day) v Placebo	1	0.997 (0.374, 2.661)	No Difference
Enoxaparin v Placebo/None	1	7.965 (0.158, 402.4)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	1.044 (0.065, 16.81)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.133 (0.003, 6.722)	No Difference
Tinzaparin + GCS v GCS	1	1 (0.062, 16.094)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	0.969 (0.135, 6.935)	No Difference
Apixaban v Enoxaparin	1	0.366 (0.118, 1.136)	No Difference
Dabigatran v Enoxaparin	2	0.999 (0.351, 2.84)	No Difference
Desirudin v Enoxaparin	1	0.501 (0.135, 1.856)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	2.196 (0.967, 4.983)	No Difference
Heparin v Enoxaparin	3	7.295 (1.651, 32.235)	Enoxaparin
Rivaroxaban v Enoxaparin	3	0.857† (0.288, 2.544)	No Difference
Tinzaparin v Enoxaparin	1	0.991 (0.062, 15.893)	No Difference
Tinzaparin v Warfarin	1	1.008 (0.063, 16.138)	No Difference
Warfarin v Enoxaparin	1	0.811 (0.38, 1.729)	No Difference
Desirudin v Heparin	2	0.306† (0.053, 1.779)	No Difference

† = heterogeneity

Table 69. Pulmonary Embolism Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	1 (0.062, 16.089)	No Difference
IPC v None	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin v Placebo/None	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin v GCS	1	0.135 (0.003, 6.82)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	7.741 (0.153, 390.51)	No Difference
IPC v GCS	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.964 (0.06, 15.503)	No Difference
Apixaban v Enoxaparin	3	1.593† (0.848, 2.991)	No Difference
Dabigatran v Enoxaparin	2	1.062 (0.396, 2.846)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	0.604 (0.15, 2.428)	No Difference
Heparin v Enoxaparin	1	7.522 (0.469, 120.6)	No Difference
Rivaroxaban v Enoxaparin	3	0.435 (0.168, 1.128)	No Difference
Warfarin v Enoxaparin	3	1.333 (0.302, 5.884)	No Difference

† = heterogeneity

Table 70. Major Bleeding Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
Dabigatran v Placebo	1	2.644 (0.368, 19.002)	No Difference
Enoxaparin v Placebo/None	4	0.989† (0.316, 3.095)	No Difference
Fondaparinux v Placebo	1	2.811 (0.392, 20.134)	No Difference
Heparin v Placebo/None	1	9.273 (1.54, 55.8)	None
Enoxaparin v GCS	1	7.457 (0.463, 119.98)	No Difference
Enoxaparin + GCS v GCS	1	1 (0.062, 16.12)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	0.126 (0.036, 0.416)	IPC + Low-dose Aspirin
Fondaparinux + GCS v Fondaparinux	1	0.14 (0.003, 7.047)	No Difference
Enoxaparin v IPC	1	7.457 (0.463, 119.98)	No Difference
Apixaban v Enoxaparin	4	0.793 (0.532, 1.183)	No Difference
Dabigatran v Enoxaparin	5	1.285 (0.904, 1.825)	No Difference
Desirudin v Enoxaparin	1	0.995 (0.532, 1.86)	No Difference
Fondaparinux v Enoxaparin	1	1.326 (0.494, 3.557)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	1.766 (1.233, 2.531)	Enoxaparin + GCS
Heparin v Enoxaparin	5	1.335 (0.8, 2.229)	No Difference
Rivaroxaban v Enoxaparin	8	1.552 (0.889, 2.709)	No Difference
Tinzaparin v Enoxaparin	1	0.505 (0.101, 2.524)	No Difference
Tinzaparin v Warfarin	1	2.186 (1.048, 4.56)	Warfarin
Warfarin v Enoxaparin	3	0.563 (0.299, 1.061)	No Difference
LY517717 v Enoxaparin	1	0.848 (0.052, 13.778)	No Difference
YM150 v Enoxaparin	1	0.144 (0.003, 7.258)	No Difference
Apixaban v Warfarin	1	7.201 (0.143, 363.02)	No Difference
Aspirin (≥300mg/day) v Warfarin	1	0.735 (0.158, 3.419)	No Difference
Dalteparin v Warfarin	2	1.94 (1.22, 3.084)	Warfarin
Desirudin v Heparin	1	1.96 (0.393, 9.78)	No Difference

† = heterogeneity

Table 71. Major Bleeding Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
Enoxaparin v Placebo/None	2	1.494† (0.256, 8.734)	No Difference
Fondaparinux v Placebo	1	2.811 (0.392, 20.134)	No Difference
Heparin v Placebo/None	1	9.273 (1.54, 55.8)	Placebo/None
Enoxaparin + GCS v GCS	1	1 (0.062, 16.12)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	0.126 (0.036, 0.416)	IPC + Low-Dose Aspirin
Fondaparinux + GCS v Fondaparinux	1	0.14 (0.003, 7.047)	No Difference
Apixaban v Enoxaparin	1	1.217 (0.653, 2.267)	No Difference
Dabigatran v Enoxaparin	3	1.585 (1.044, 2.405)	Enoxaparin
Desirudin v Enoxaparin	1	0.995 (0.532, 1.86)	No Difference
Fondaparinux v Enoxaparin	1	1.326 (0.494, 3.557)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	1.56 (1.068, 2.28)	Enoxaparin + GCS
Heparin v Enoxaparin	4	1.377 (0.802, 2.365)	No Difference
Rivaroxaban v Enoxaparin	5	1.76 (0.743, 4.173)	No Difference
Tinzaparin v Enoxaparin	1	0.505 (0.101, 2.524)	No Difference
Tinzaparin v Warfarin	1	2.186 (1.048, 4.56)	Warfarin
LY517717 v Enoxaparin	1	0.848 (0.052, 13.778)	No Difference
YM150 v Enoxaparin	1	0.144 (0.003, 7.258)	No Difference
Aspirin (≥300mg/day) v Warfarin	1	0.735 (0.158, 3.419)	No Difference
Dalteparin v Warfarin	2	1.94 (1.22, 3.084)	Warfarin
Desirudin v Heparin	1	1.96 (0.393, 9.78)	No Difference

† = heterogeneity

Table 72. Major Bleeding Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
Dabigatran v Placebo	1	2.644 (0.368, 19.002)	No Difference
Enoxaparin v Placebo/None	2	0.736† (0.165, 3.28)	No Difference
Fondaparinux v Placebo	1	2.811 (0.392, 20.134)	No Difference
Enoxaparin v GCS	1	7.457 (0.463, 119.981)	No Difference
Enoxaparin v IPC	1	7.457 (0.463, 119.981)	No Difference
Apixaban v Enoxaparin	3	0.587 (0.348, 0.989)	Apixaban
Dabigatran v Enoxaparin	2	0.774 (0.405, 1.481)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	5.39 (1.728, 16.815)	Enoxaparin + GCS
Heparin v Enoxaparin	1	1.013 (0.203, 5.067)	No Difference
Rivaroxaban v Enoxaparin	3	1.418 (0.683, 2.941)	No Difference
Apixaban v Warfarin	1	7.201 (0.143, 363.019)	No Difference

† = heterogeneity

Table 73. All Cause Mortality Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
IPC v None	1	7.738 (0.482, 124.327)	No Difference
Aspirin (<300mg/day) v Placebo	1	0.816 (0.339, 1.963)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.379 (0.053, 2.729)	No Difference
Warfarin + GCS v IPC + GCS	1	1 (0.062, 16.089)	No Difference
Tinzaparin + GCS v GCS	1	1 (0.062, 16.094)	No Difference
Aspirin (≥300mg/day) + IPC v Aspirin (≥300mg/day)	1	7.723 (0.153, 390)	No Difference
Fondaparinux + GCS v Fondaparinux	1	0.379 (0.053, 2.699)	No Difference
Apixaban v Enoxaparin	3	1.22 (0.507, 2.932)	No Difference
Warfarin v Enoxaparin	3	1.284 (0.585, 2.819)	No Difference
Dabigatran v Enoxaparin	4	1.231 (0.377, 4.017)	No Difference
Desirudin v Enoxaparin	1	1.91 (0.385, 9.49)	No Difference
Heparin v Enoxaparin	1	1.824 (0.188, 17.659)	No Difference
Fondaparinux v Enoxaparin	1	0.186 (0.003, 10.093)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	0.999 (0.415, 2.402)	No Difference
Rivaroxaban v Enoxaparin	5	0.625 (0.333, 1.171)	No Difference
Desirudin v Heparin	2	0.135 (0.014, 1.299)	No Difference
Dalteparin v Warfarin	1	0.986 (0.138, 7.02)	No Difference
Tinzaparin v Warfarin	1	1.008 (0.291, 3.497)	No Difference

Table 74. All Cause Mortality Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
IPC v None	1	7.738 (0.482, 124.327)	No Difference
Aspirin (<300mg/day) v Placebo	1	0.816 (0.339, 1.963)	No Difference
Warfarin + GCS v IPC + GCS	1	1 (0.062, 16.089)	No Difference
Tinzaparin + GCS v GCS	1	1 (0.062, 16.094)	No Difference
Aspirin (≥300mg/day) + IPC v Aspirin (≥300mg/day)	1	7.723 (0.153, 390)	No Difference
Fondaparinux + GCS v Fondaparinux	1	0.379 (0.053, 2.699)	No Difference
Apixaban v Enoxaparin	1	2.351 (0.534, 10.352)	No Difference
Warfarin v Enoxaparin	1	1.127 (0.457, 2.779)	No Difference
Dabigatran v Enoxaparin	2	1.491† (0.258, 8.611)	No Difference
Desirudin v Enoxaparin	1	1.91 (0.385, 9.49)	No Difference
Heparin v Enoxaparin	1	1.824 (0.188, 17.659)	No Difference
Fondaparinux v Enoxaparin	1	0.186 (0.003, 10.093)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	1.141 (0.414, 3.144)	No Difference
Rivaroxaban v Enoxaparin	3	0.743 (0.315, 1.749)	No Difference
Desirudin v Heparin	2	0.135 (0.014, 1.299)	No Difference
Dalteparin v Warfarin	1	0.986 (0.138, 7.02)	No Difference
Tinzaparin v Warfarin	1	1.008 (0.291, 3.497)	No Difference

† = heterogeneity

Table 75. All Cause Mortality Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
Enoxaparin + GCS v Foot Pump + GCS	1	0.379 (0.053, 2.729)	No Difference
Apixaban v Enoxaparin	2	0.856 (0.288, 2.542)	No Difference
Warfarin v Enoxaparin	2	1.937 (0.389, 9.648)	No Difference
Dabigatran v Enoxaparin	2	1.048 (0.211, 5.202)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	0.669 (0.116, 3.876)	No Difference
Rivaroxaban v Enoxaparin	2	0.511† (0.202, 1.288)	No Difference

† = heterogeneity

Table 76. Symptomatic Deep Vein Thrombosis Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
Apixaban v Enoxaparin	4	0.548 (0.295, 1.02)	No Difference
Apixaban v Warfarin	1	2.036 (0.209, 19.791)	No Difference
Warfarin v Enoxaparin	1	1 (0.062, 16.09)	No Difference
Aspirin (<300mg/day) v Placebo	1	0.786 (0.4, 1.545)	No Difference
Dabigatran v Enoxaparin	5	0.765† (0.364, 1.608)	No Difference
Dabigatran v Placebo	1	0.491 (0.051, 4.761)	No Difference
Dalteparin v Warfarin	1	0.358 (0.147, 0.872)	Dalteparin
Desirudin v Enoxaparin	1	1.12 (0.405, 3.094)	No Difference
Desirudin v Heparin	1	0.797 (0.213, 2.987)	No Difference
Tinzaparin v Enoxaparin	1	0.662 (0.114, 3.851)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	1.929 (0.199, 18.699)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.964 (0.06, 15.503)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	2.121 (0.795, 5.66)	No Difference
IPC v None	1	2.034 (0.21, 19.711)	No Difference
Rivaroxaban v Enoxaparin	3	0.478 (0.194, 1.178)	No Difference

† = heterogeneity

Table 77. Symptomatic DVT Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
Apixaban v Enoxaparin	1	0.21 (0.057, 0.776)	Apixaban
Aspirin (<300mg/day) v Placebo	1	0.786 (0.4, 1.545)	No Difference
Dabigatran v Enoxaparin	3	1.51† (0.548, 4.159)	No Difference
Dalteparin v Warfarin	1	0.358 (0.147, 0.872)	Dalteparin
Desirudin v Enoxaparin	1	1.12 (0.405, 3.094)	No Difference
Desirudin v Heparin	1	0.797 (0.213, 2.987)	No Difference
Tinzaparin v Enoxaparin	1	0.662 (0.114, 3.851)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	1.929 (0.199, 18.699)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	4.743 (1.283, 17.5)	Enoxaparin + GCS
IPC v None	1	2.034 (0.21, 19.711)	No Difference
Rivaroxaban v Enoxaparin	1	0.128 (0.003, 6.458)	No Difference

† = heterogeneity

Table 78. Symptomatic DVT Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
Apixaban v Enoxaparin	3	0.725 (0.358, 1.469)	No Difference
Apixaban v Warfarin	1	2.036 (0.209, 19.791)	No Difference
Warfarin v Enoxaparin	1	1 (0.062, 16.09)	No Difference
Dabigatran v Enoxaparin	2	0.349 (0.117, 1.038)	No Difference
Dabigatran v Placebo	1	0.491 (0.051, 4.761)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.964 (0.06, 15.503)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	0.75 (0.17, 3.315)	No Difference
Rivaroxaban v Enoxaparin	2	0.509 (0.201, 1.287)	No Difference

Table 79. Deep Vein Thrombosis Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	0.531 (0.264, 1.066)	No Difference
IPC v None	2	0.342 (0.231, 0.505)	IPC
Enoxaparin v Placebo/None	2	0.469† (0.289, 0.762)	Enoxaparin
Enoxaparin v GCS	1	0.416 (0.166, 1.042)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	2	0.789 (0.512, 1.216)	No Difference
Tinzaparin + GCS v GCS	1	0.551 (0.307, 0.987)	Tinzaparin + GCS
IPC + Low-dose Aspirin v Enoxaparin	1	0.968 (0.356, 2.631)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	1.323 (0.685, 2.555)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	0.802 (0.291, 2.209)	No Difference
Warfarin + GCS v IPC + GCS	1	1.246 (0.678, 2.291)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	0.482† (0.388, 0.599)	Fondaparinux + GCS
IPC v GCS	1	0.617 (0.261, 1.46)	No Difference
Enoxaparin v IPC	1	0.652 (0.229, 1.857)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.329 (0.132, 0.815)	Enoxaparin + IPC
Apixaban v Enoxaparin	4	0.6† (0.51, 0.705)	Apixaban
Dabigatran v Enoxaparin	5	0.973† (0.846, 1.12)	No Difference
Desirudin v Enoxaparin	1	0.659 (0.518, 0.839)	Desirudin
Fondaparinux v Enoxaparin	1	0.276 (0.104, 0.729)	Fondaparinux
Heparin v Enoxaparin	3	1.857 (1.36, 2.536)	Enoxaparin
Rivaroxaban v Enoxaparin	7	0.462† (0.391, 0.545)	Rivaroxaban
Tinzaparin v Enoxaparin	1	1.103 (0.697, 1.746)	No Difference
Tinzaparin v Warfarin	1	0.764 (0.603, 0.969)	Tinzaparin
Warfarin v Enoxaparin	3	2.065 (1.583, 2.695)	Enoxaparin
YM150 v Enoxaparin	1	1.026 (0.54, 1.95)	No Difference
Apixaban v Warfarin	1	0.362 (0.181, 0.724)	Apixaban
Aspirin (>300mg/day) v Warfarin/Aspirin	1	1.138 (0.728, 1.778)	No Difference
Dalteparin v Warfarin	2	0.434 (0.318, 0.592)	Dalteparin
Desirudin v Heparin	2	0.387 (0.275, 0.546)	Desirudin
Heparin + GCS v Heparin/Enoxaparin + GCS	1	0.323 (0.091, 1.143)	No Difference

† = heterogeneity

Table 80. Deep Vein Thrombosis Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
IPC v None	1	0.34 (0.214, 0.54)	IPC
Enoxaparin v Placebo/None	1	0.71 (0.38, 1.327)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.702 (0.364, 1.354)	No Difference
Tinzaparin + GCS v GCS	1	0.551 (0.307, 0.987)	Tinzaparin + GCS
IPC + Low-dose Aspirin v Enoxaparin	1	0.968 (0.356, 2.631)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	0.802 (0.291, 2.209)	No Difference
Warfarin + GCS v IPC + GCS	1	1.246 (0.678, 2.291)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	0.535† (0.409, 0.7)	Fondaparinux + GCS
Apixaban v Enoxaparin	1	0.345 (0.227, 0.524)	Apixaban
Dabigatran v Enoxaparin	3	0.747 (0.596, 0.936)	Dabigatran
Desirudin v Enoxaparin	1	0.659 (0.518, 0.839)	Desirudin
Fondaparinux v Enoxaparin	1	0.276 (0.104, 0.729)	Fondaparinux
Heparin v Enoxaparin	2	2.388 (1.467, 3.889)	Enoxaparin
Rivaroxaban v Enoxaparin	4	0.316† (0.24, 0.415)	Rivaroxaban
Tinzaparin v Enoxaparin	1	1.103 (0.697, 1.746)	No Difference
Tinzaparin v Warfarin	1	0.764 (0.603, 0.969)	Tinzaparin
YM150 v Enoxaparin	1	1.026 (0.54, 1.95)	No Difference
Dalteparin v Warfarin	2	0.434 (0.318, 0.592)	Dalteparin
Desirudin v Heparin	2	0.387 (0.275, 0.546)	Desirudin
Heparin + GCS v Heparin/Enoxaparin + GCS	1	0.323 (0.091, 1.143)	No Difference

† = heterogeneity

Table 81. Deep Vein Thrombosis Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	0.531 (0.264, 1.066)	No Difference
IPC v None	1	0.345 (0.165, 0.722)	IPC
Enoxaparin v Placebo/None	1	0.251 (0.116, 0.541)	Enoxaparin
Enoxaparin v GCS	1	0.416 (0.166, 1.042)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.863 (0.486, 1.534)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	1.323 (0.685, 2.555)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	0.397 (0.276, 0.573)	Fondaparinux + GCS
IPC v GCS	1	0.617 (0.261, 1.46)	No Difference
Enoxaparin v IPC	1	0.652 (0.229, 1.857)	No Difference
Enoxaparin + IPC v Enoxaparin	1	0.329 (0.132, 0.815)	Enoxaparin + IPC
Apixaban v Enoxaparin	3	0.661† (0.555, 0.788)	Apixaban
Dabigatran v Enoxaparin	2	1.149† (0.961, 1.375)	No Difference
Heparin v Enoxaparin	1	1.561 (1.041, 2.34)	Enoxaparin
Rivaroxaban v Enoxaparin	3	0.574 (0.466, 0.706)	Rivaroxaban
Warfarin v Enoxaparin	3	2.065 (1.583, 2.695)	Enoxaparin
Apixaban v Warfarin	1	0.362 (0.181, 0.724)	Apixaban
Aspirin (>300mg/day) v Warfarin/Aspirin	1	1.138 (0.728, 1.778)	No Difference

† = heterogeneity

Table 82. Proximal DVT Direct Comparisons among Hip and Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	0.363 (0.05, 2.611)	No Difference
IPC v None	2	0.446 (0.262, 0.761)	IPC
Dabigatran v Placebo	1	0.131 (0.026, 0.664)	Dabigatran
Enoxaparin v Placebo/None	2	0.604 (0.237, 1.534)	No Difference
Enoxaparin v GCS	1	1 (0.062, 16.089)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	2	0.548 (0.268, 1.122)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	1.452 (0.249, 8.46)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	0.627 (0.154, 2.555)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	0.141 (0.003, 7.122)	No Difference
Warfarin + GCS v IPC + GCS	1	0.261 (0.091, 0.745)	Warfarin + GCS
IPC v GCS	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin v IPC	1	7.389 (0.147, 372.4)	No Difference
Apixaban v Enoxaparin	4	0.477 (0.313, 0.726)	Apixaban
Dabigatran v Enoxaparin	5	0.649 (0.48, 0.877)	Dabigatran
Desirudin v Enoxaparin	1	0.584 (0.386, 0.884)	Desirudin
Fondaparinux v Enoxaparin	1	0.369 (0.071, 1.915)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	3	0.555† (0.358, 0.861)	Fondaparinux + GCS
Heparin v Enoxaparin	3	2.99 (1.835, 4.878)	Enoxaparin
Rivaroxaban v Enoxaparin	7	0.26 (0.187, 0.362)	Rivaroxaban
Tinzaparin v Enoxaparin	1	0.895 (0.480, 1.67)	No Difference
Tinzaparin v Warfarin	1	0.789 (0.505, 1.233)	No Difference
Warfarin v Enoxaparin	3	1.481† (0.919, 2.387)	No Difference
YM150 v Enoxaparin	1	1.119 (0.316, 3.966)	No Difference
Apixaban v Warfarin	1	1.039 (0.144, 7.48)	No Difference
Aspirin (>300mg/day) v Warfarin/Aspirin	1	0.759 (0.372, 1.547)	No Difference
Dalteparin v Warfarin	2	0.48 (0.254, 0.906)	Dalteparin
Desirudin v Heparin	2	0.212 (0.129, 0.348)	Desirudin
Fondaparinux + GCS v Fondaparinux	1	0.847 (0.43, 1.67)	No Difference

† = heterogeneity

Table 83. Proximal DVT Direct Comparisons among Hip Patients

Comparison	Studies	OR (95% CI)	Favors
IPC v None	1	0.479 (0.276, 0.829)	IPC
Enoxaparin v Placebo/None	1	0.699 (0.242, 2.014)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.67 (0.311, 1.445)	No Difference
IPC + Low-dose Aspirin v Enoxaparin	1	1.452 (0.249, 8.46)	No Difference
IPC + Aspirin (>300mg/day) v Aspirin (>300mg/day)	1	0.141 (0.003, 7.122)	No Difference
Warfarin + GCS v IPC + GCS	1	0.261 (0.091, 0.745)	Warfarin + GCS
Apixaban v Enoxaparin	1	0.379 (0.178, 0.807)	Apixaban
Dabigatran v Enoxaparin	3	0.519 (0.362, 0.746)	Dabigatran
Desirudin v Enoxaparin	1	0.584 (0.386, 0.884)	Desirudin
Fondaparinux v Enoxaparin	1	0.369 (0.071, 1.915)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	2	0.614† (0.357, 1.057)	No Difference
Heparin v Enoxaparin	2	2.533 (1.351, 4.75)	Enoxaparin
Rivaroxaban v Enoxaparin	4	0.199 (0.132, 0.3)	Rivaroxaban
Tinzaparin v Enoxaparin	1	0.895 (0.480, 1.67)	No Difference
Tinzaparin v Warfarin	1	0.789 (0.505, 1.233)	No Difference
YM150 v Enoxaparin	1	1.119 (0.316, 3.966)	No Difference
Dalteparin v Warfarin	2	0.48 (0.254, 0.906)	Dalteparin
Desirudin v Heparin	2	0.212 (0.129, 0.348)	Desirudin
Fondaparinux + GCS v Fondaparinux	1	0.847 (0.430, 1.67)	No Difference

† = heterogeneity

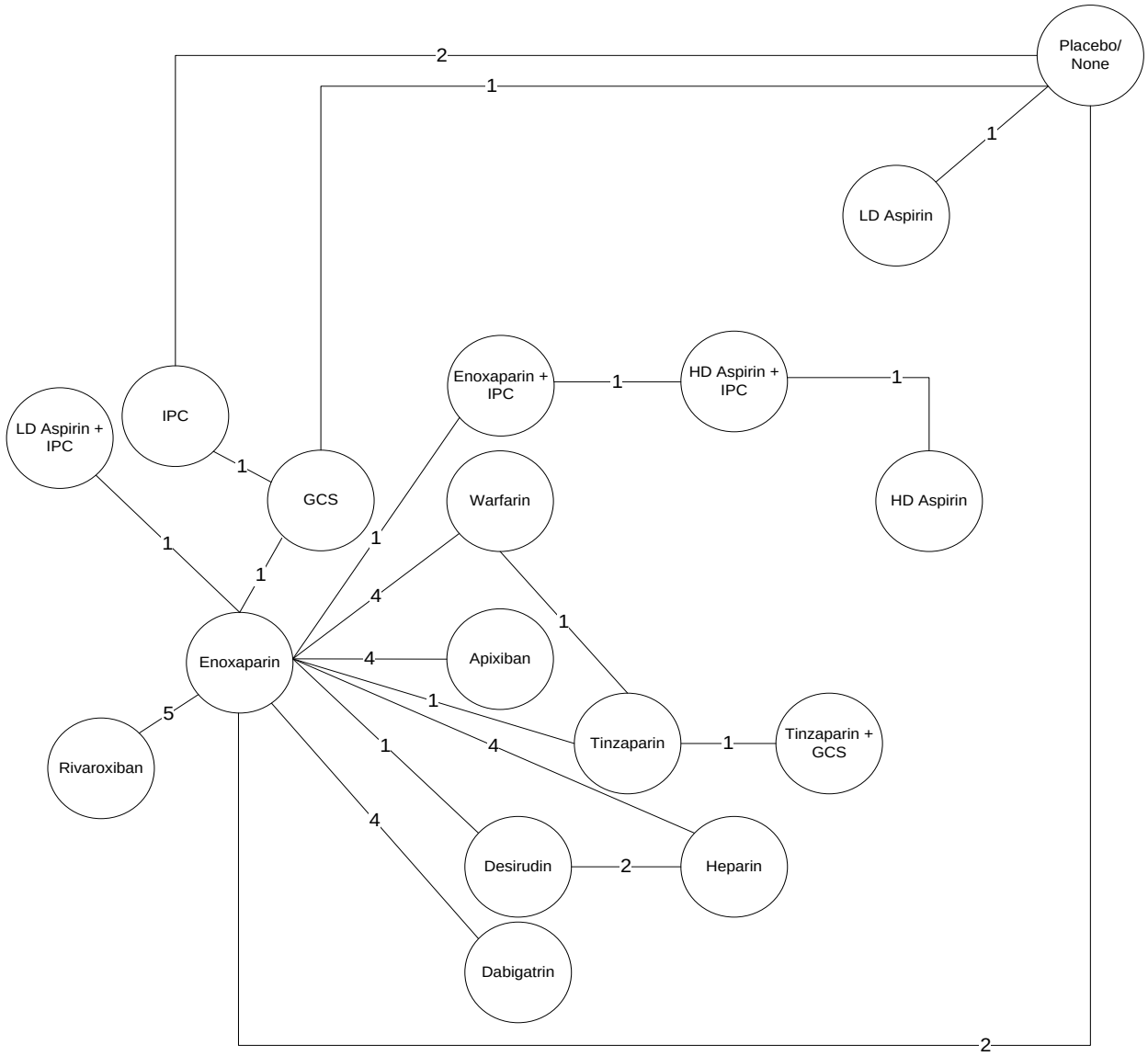
Table 84. Proximal DVT Direct Comparisons among Knee Patients

Comparison	Studies	OR (95% CI)	Favors
GCS v None	1	0.363 (0.05, 2.611)	No Difference
IPC v None	1	0.133 (0.014, 1.291)	No Difference
Dabigatran v Placebo	1	0.131 (0.026, 0.664)	Dabigatran
Enoxaparin v Placebo/None	1	0.363 (0.05, 2.611)	No Difference
Enoxaparin v GCS	1	1 (0.062, 16.089)	No Difference
Enoxaparin + GCS v Foot Pump + GCS	1	0.145 (0.02, 1.05)	No Difference
IPC + Aspirin (>300mg/day) v IPC + Enoxaparin	1	0.627 (0.154, 2.555)	No Difference
IPC v GCS	1	0.135 (0.003, 6.82)	No Difference
Enoxaparin v IPC	1	7.389 (0.147, 372.4)	No Difference
Apixaban v Enoxaparin	3	0.506 (0.304, 0.842)	Apixaban
Dabigatran v Enoxaparin	2	1.075 (0.623, 1.854)	No Difference
Fondaparinux + GCS v Enoxaparin + GCS	1	0.46 (0.219, 0.965)	Fondaparinux + GCS
Heparin v Enoxaparin	1	3.86 (1.77, 8.40)	Enoxaparin
Rivaroxaban v Enoxaparin	3	0.401 (0.228, 0.704)	Rivaroxaban
Warfarin v Enoxaparin	3	1.481† (0.919, 2.387)	No Difference
Apixaban v Warfarin	1	1.039 (0.144, 7.48)	No Difference
Aspirin (>300mg/day) v Warfarin/Aspirin	1	0.759 (0.372, 1.547)	No Difference

† = heterogeneity

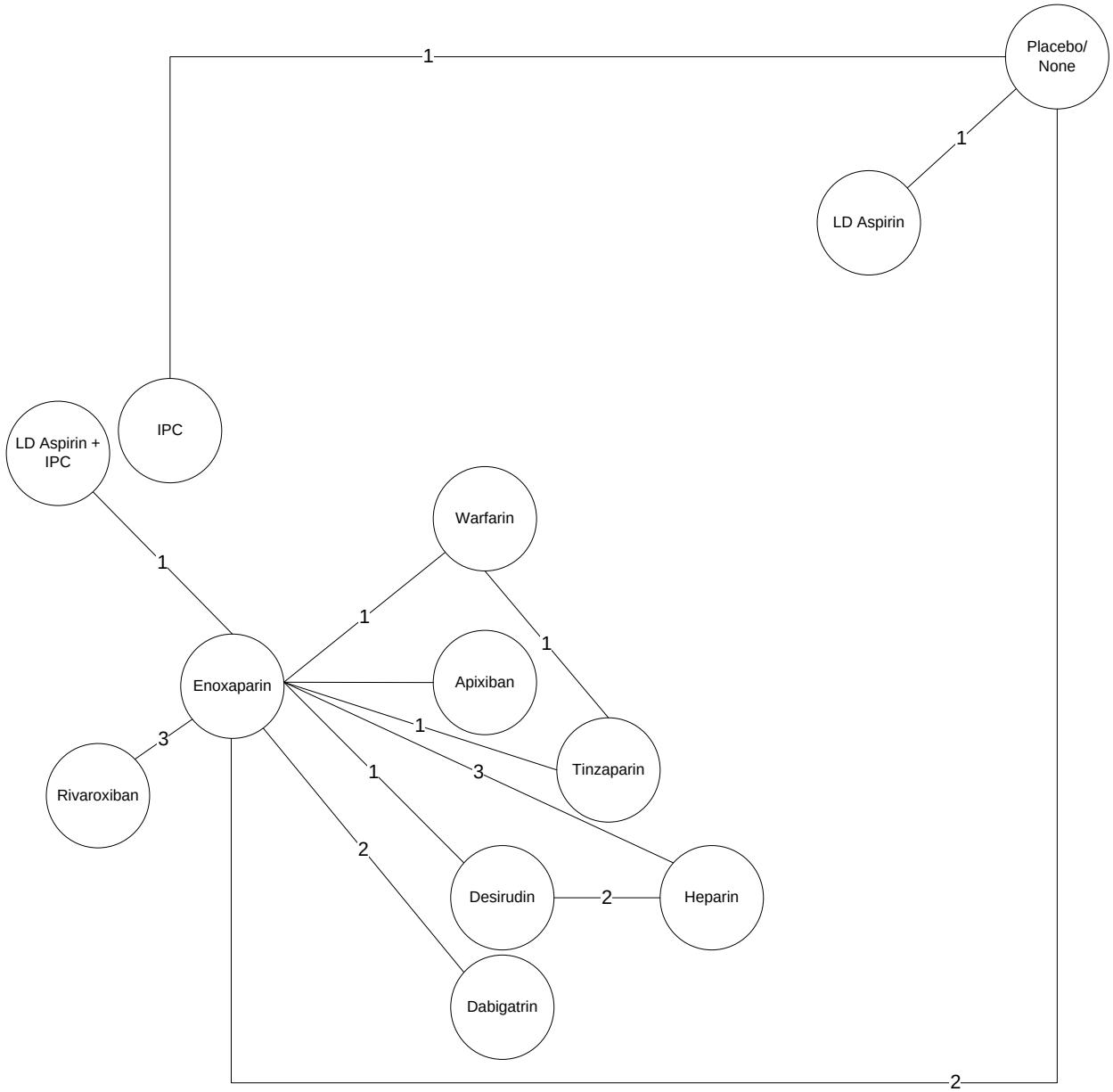
NETWORK META-ANALYSIS SENSITIVITY ANALYSIS MODELS

Figure 60. Pulmonary Embolism Model (All Trials, with Continuity Correction)



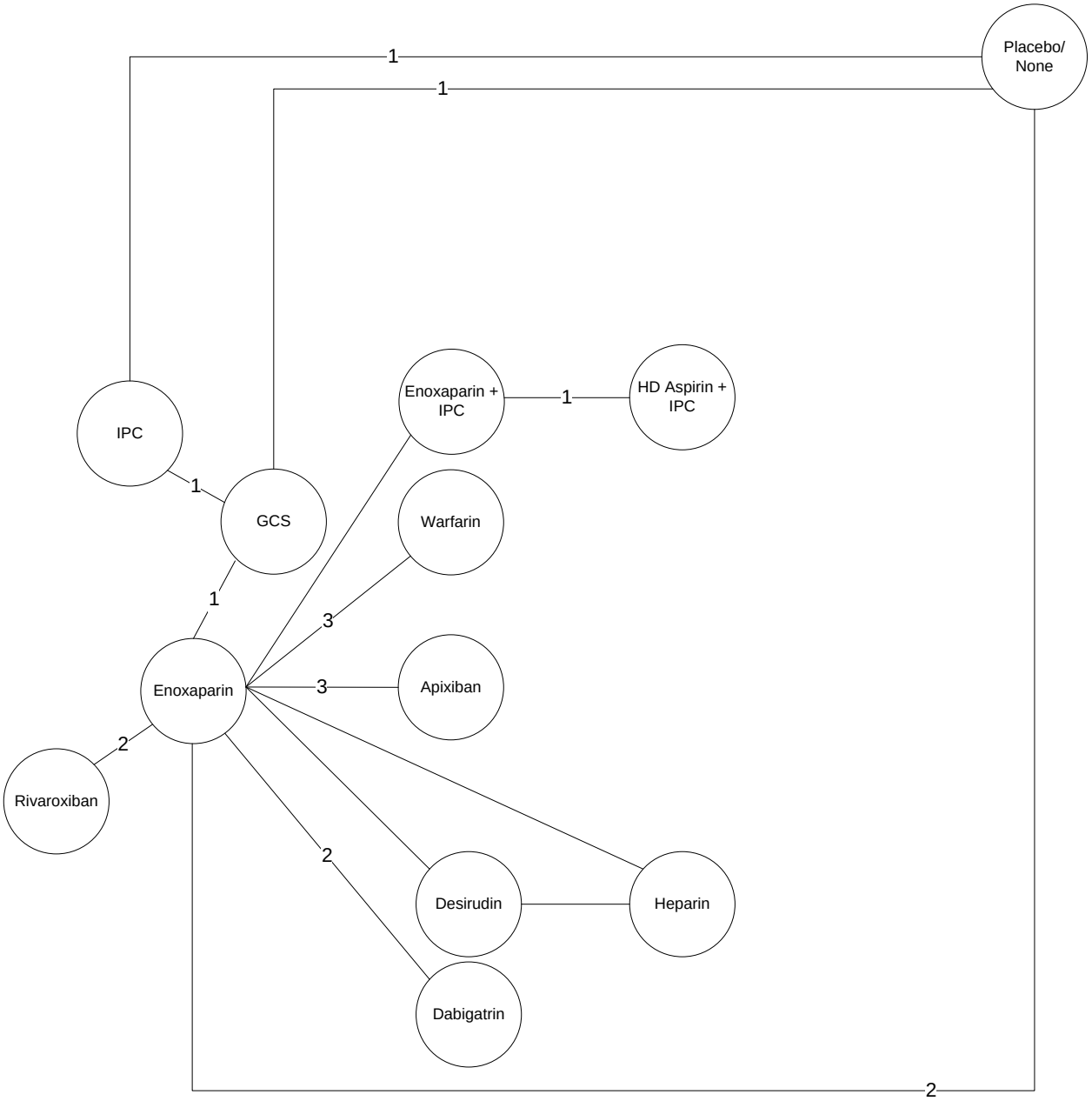
The model depicted in the figure is the base case model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 61. Pulmonary Embolism Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



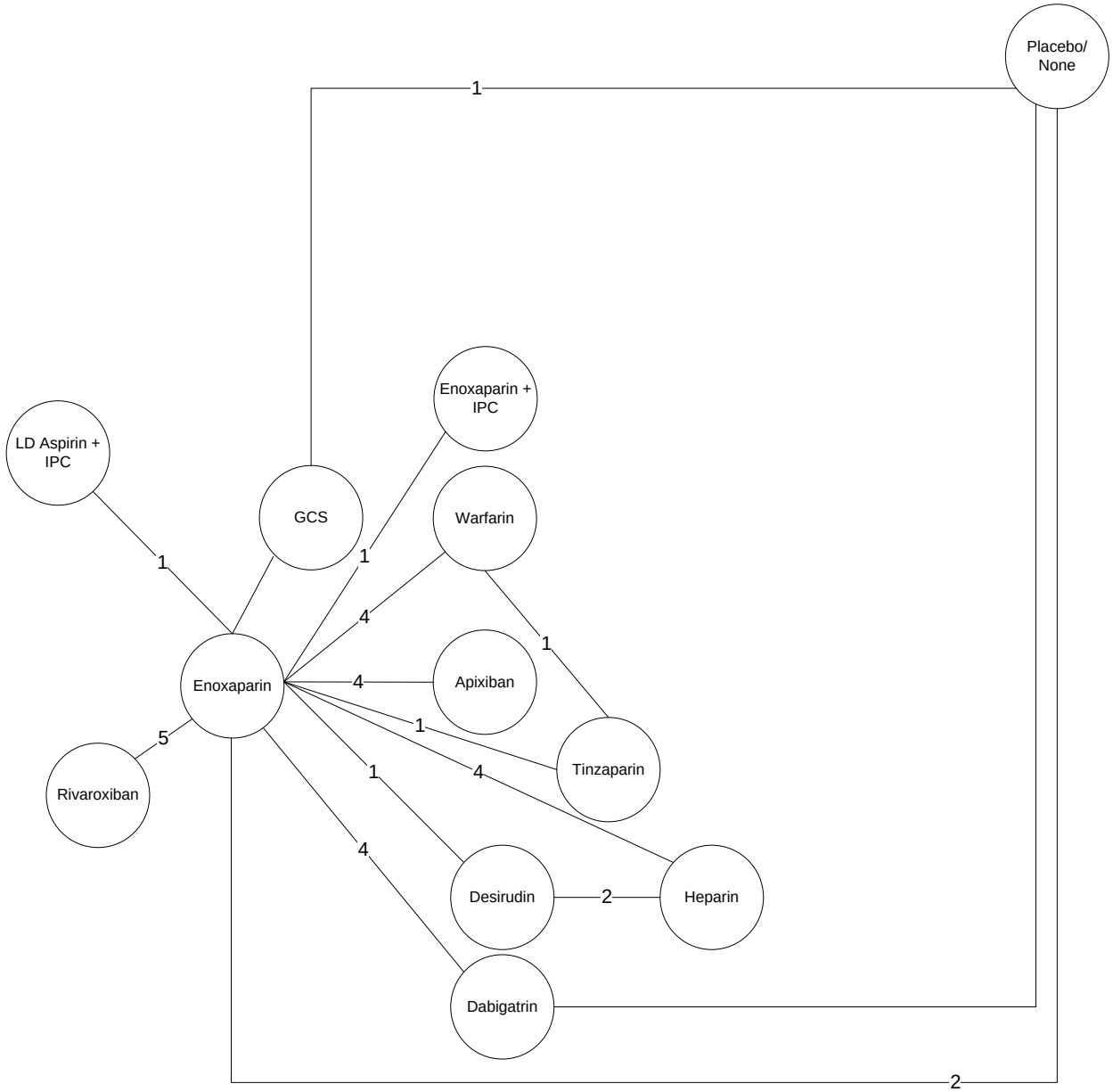
The model depicted in the figure is a model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 62. Pulmonary Embolism Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



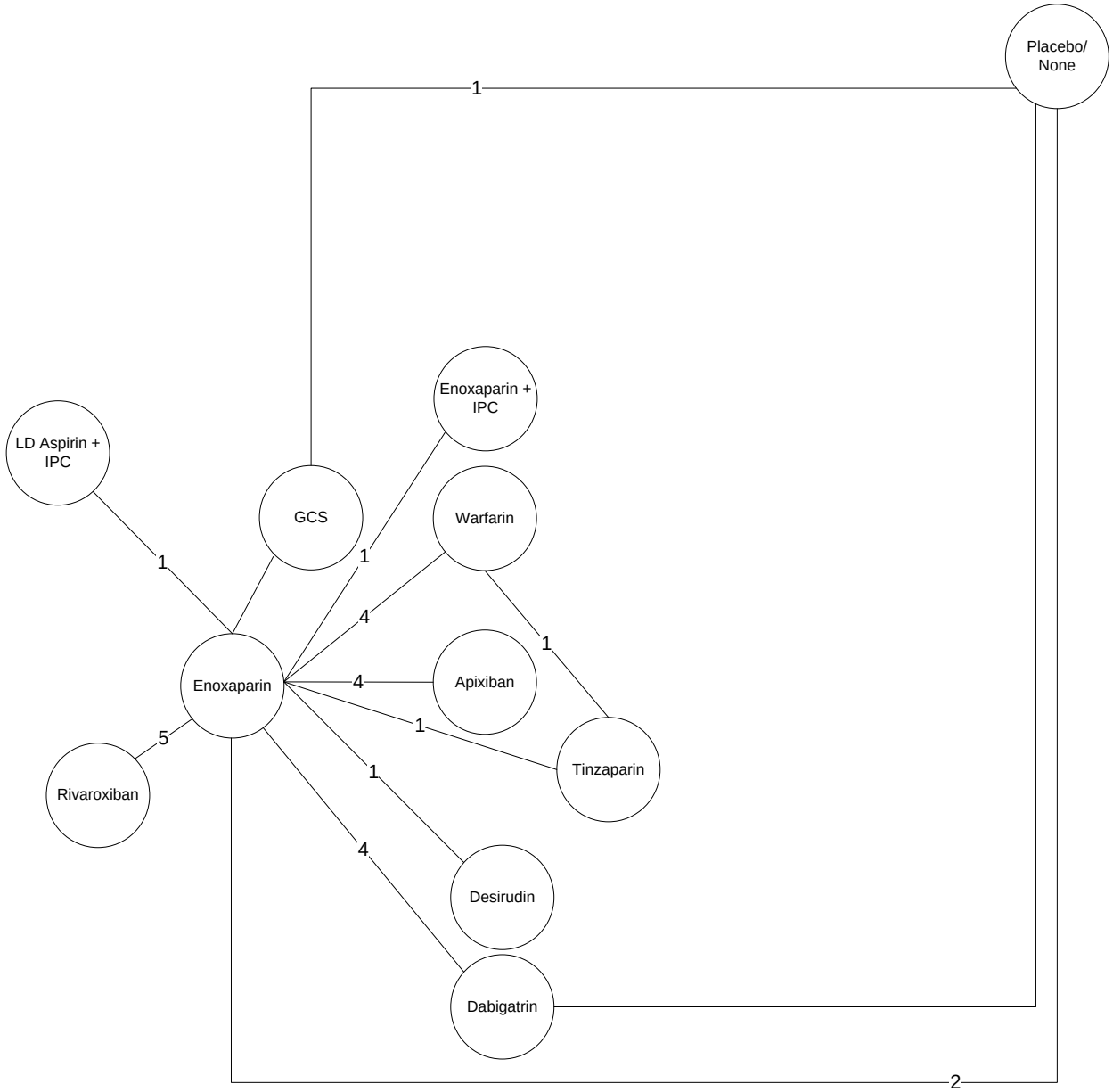
The model depicted in the figure a model for pulmonary embolism. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 63. Pulmonary Embolism Model Omitting Studies that Required a Continuity Correction



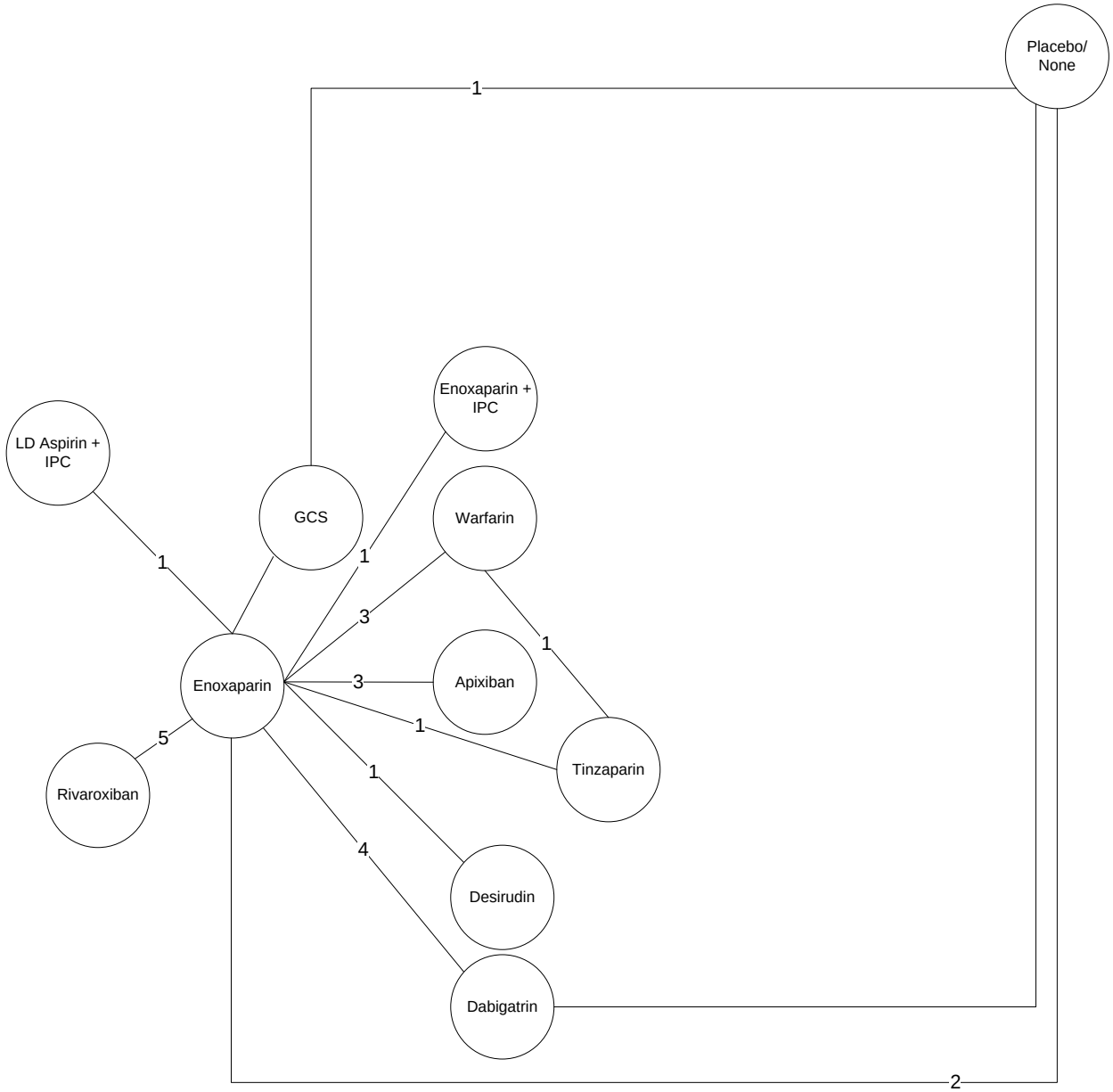
The model depicted in the figure is a model for pulmonary embolism that omits studies for which a continuity correction was required. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 64. Pulmonary Embolism Model Omitting Trials that Required a Continuity Correction and Omitting Trials of Heparin



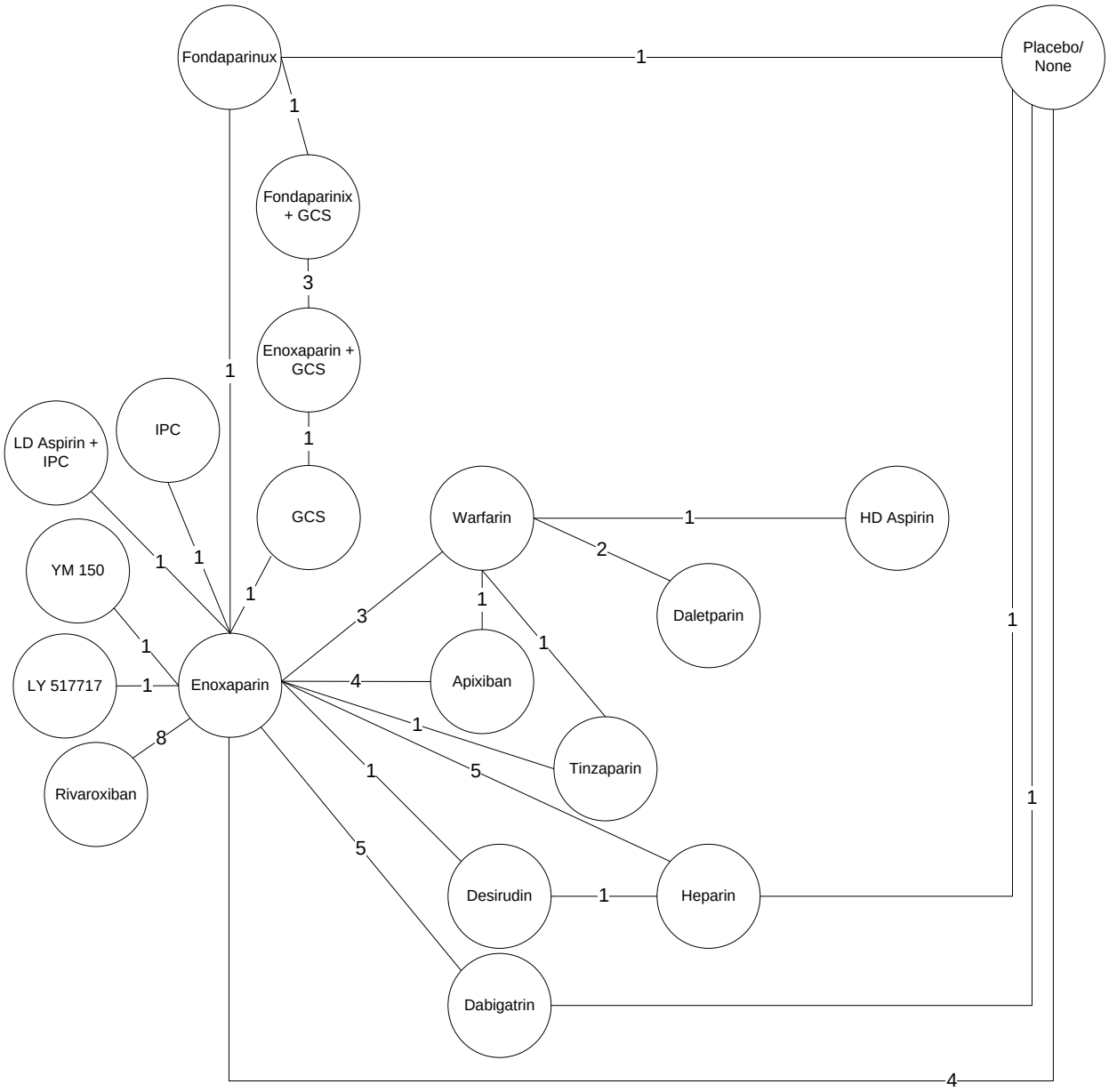
The model depicted in the figure is a model for pulmonary embolism that omits studies for which a continuity correction was required, and that also omits studies of heparin. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 65. Pulmonary Embolism Model Omitting Trials that Required a Continuity Correction, Trials of Heparin, and Trials with > 2 Arms.



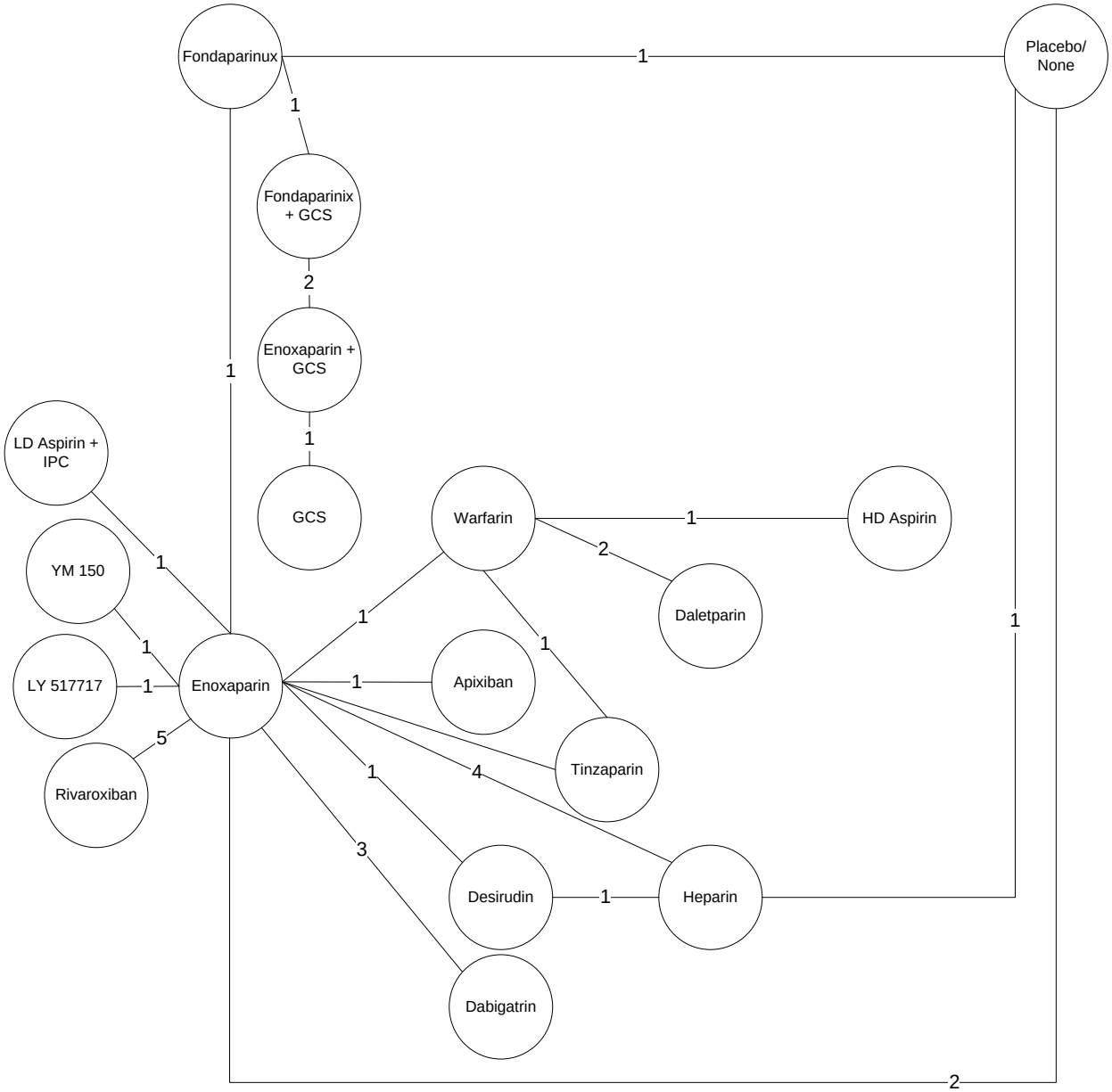
The model depicted in the figure is a model for pulmonary embolism that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 66. Major Bleeding Model (All Trials, with Continuity Correction)



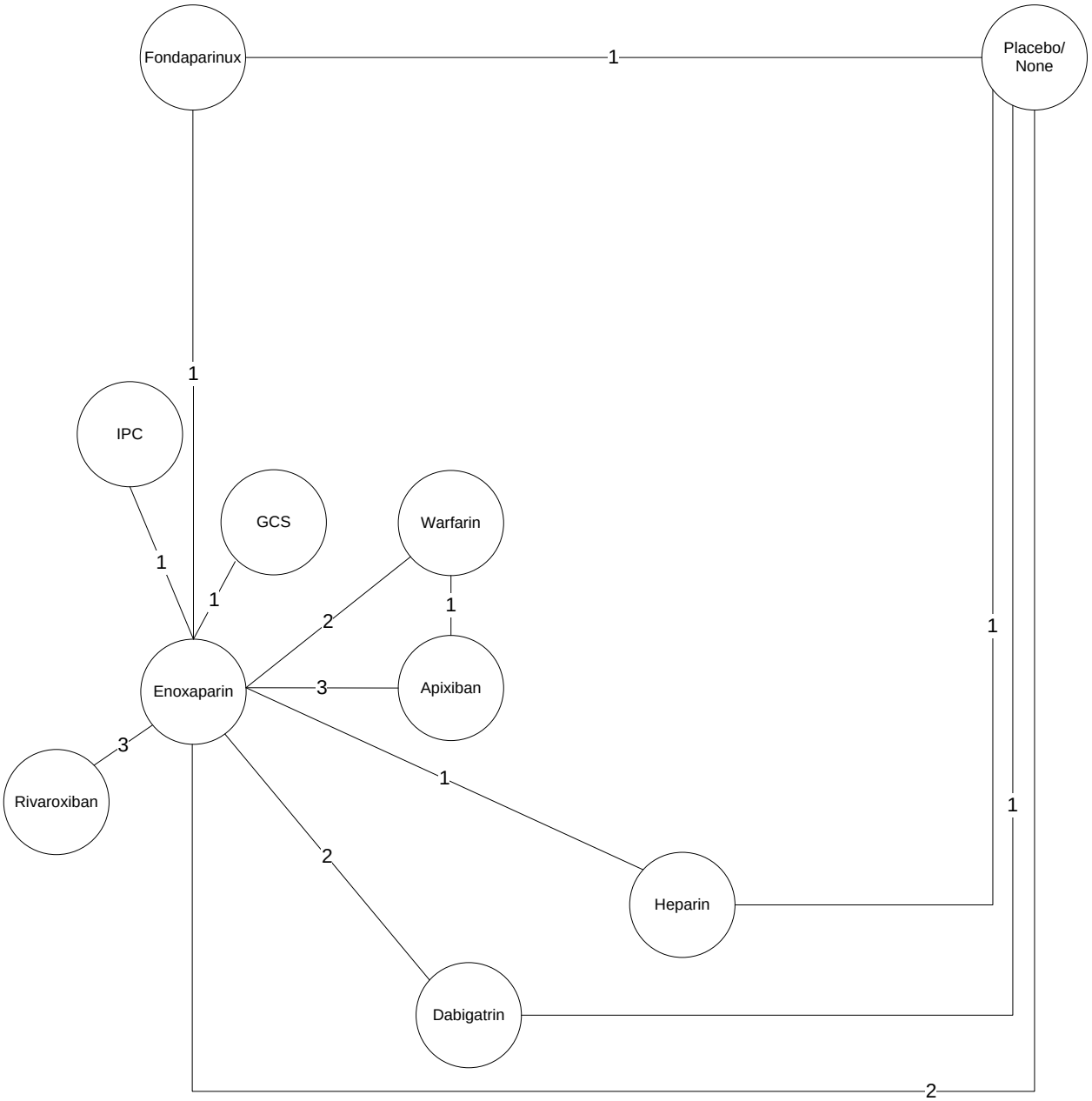
The model depicted in the figure is the base case model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 67. Major Bleeding Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



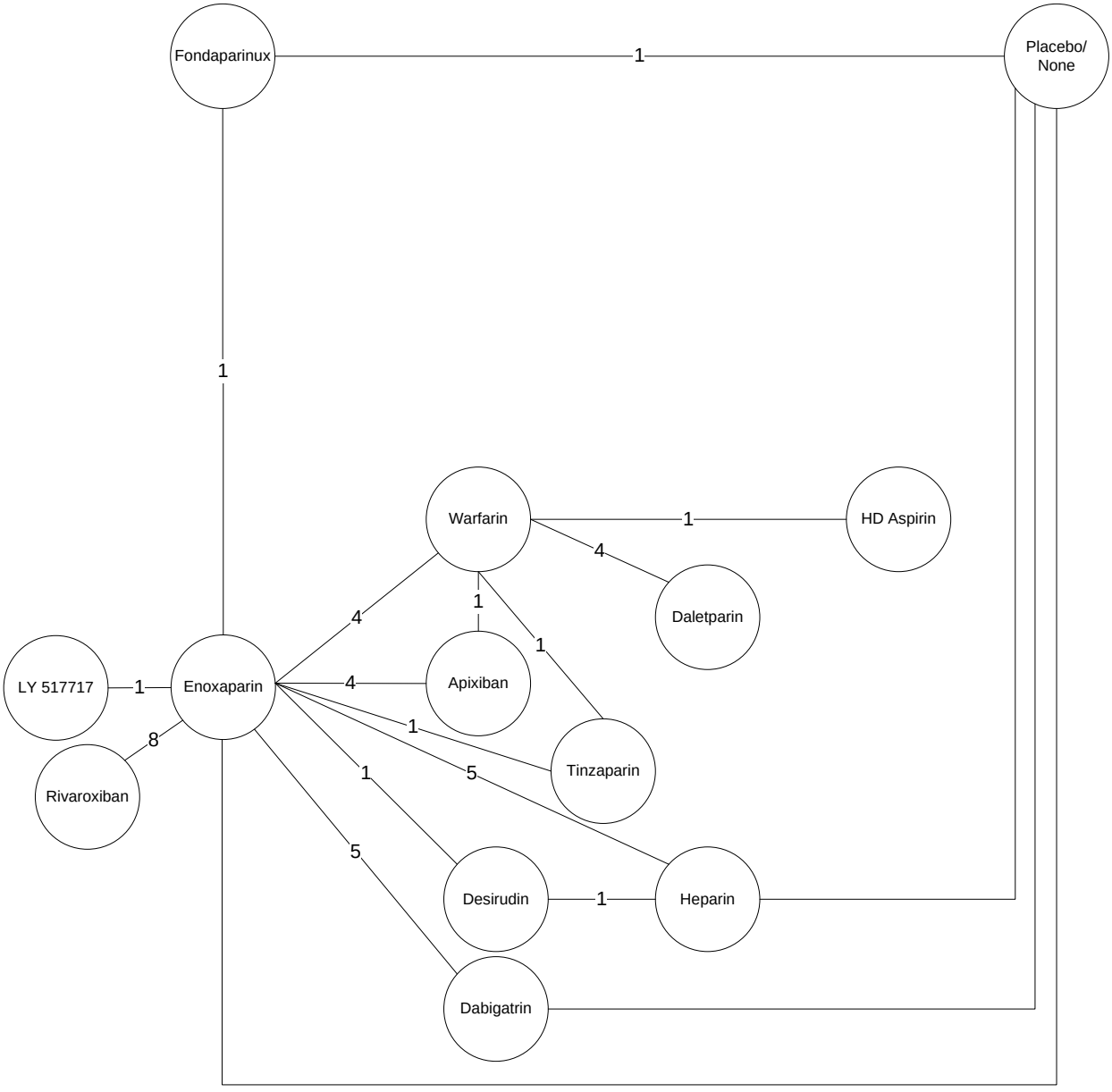
The model depicted in the figure is a model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 68. Major Bleeding Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



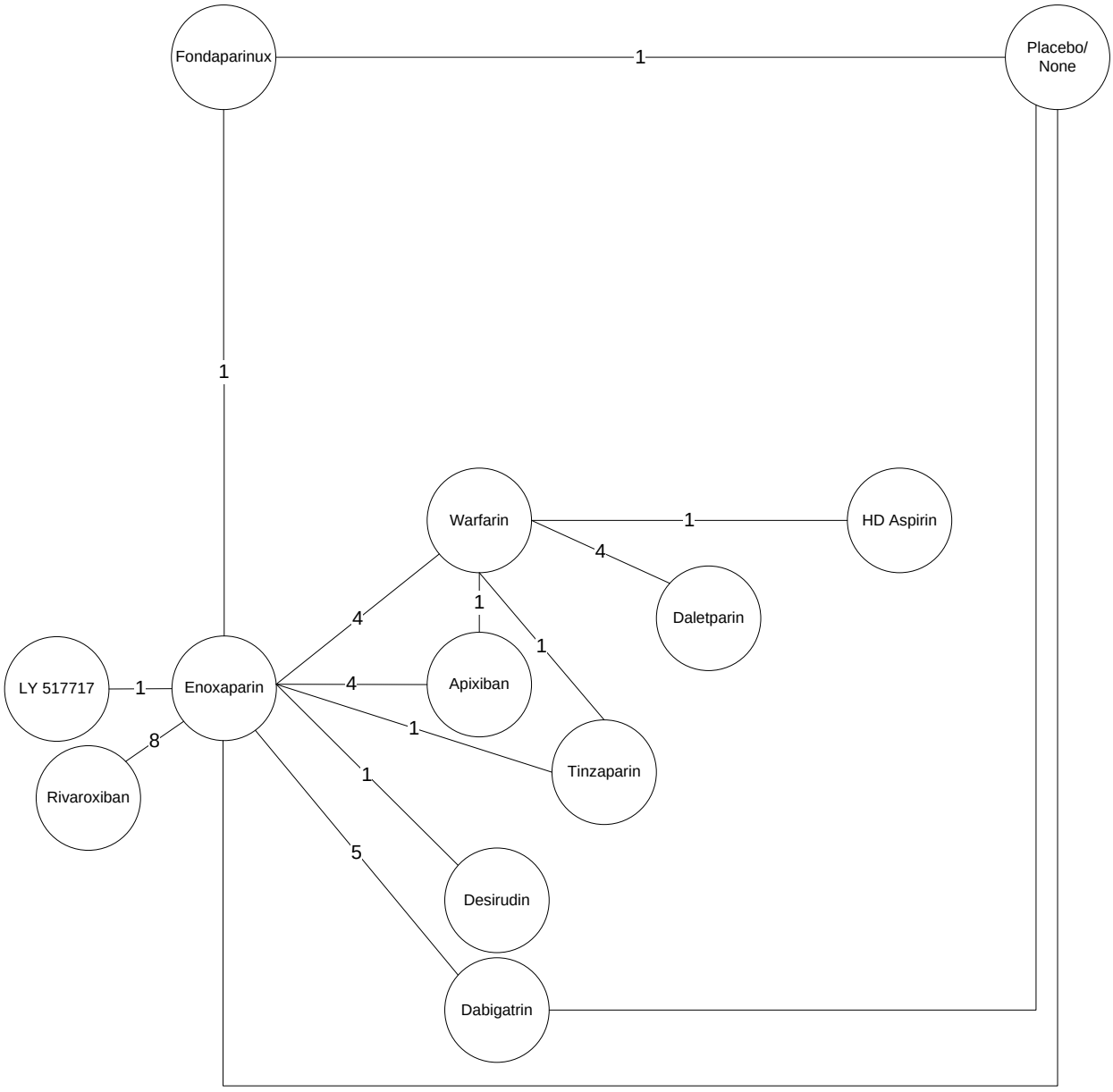
The model depicted in the figure a model for major bleeding. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 69. Major Bleeding Model Omitting Studies that Required a Continuity Correction



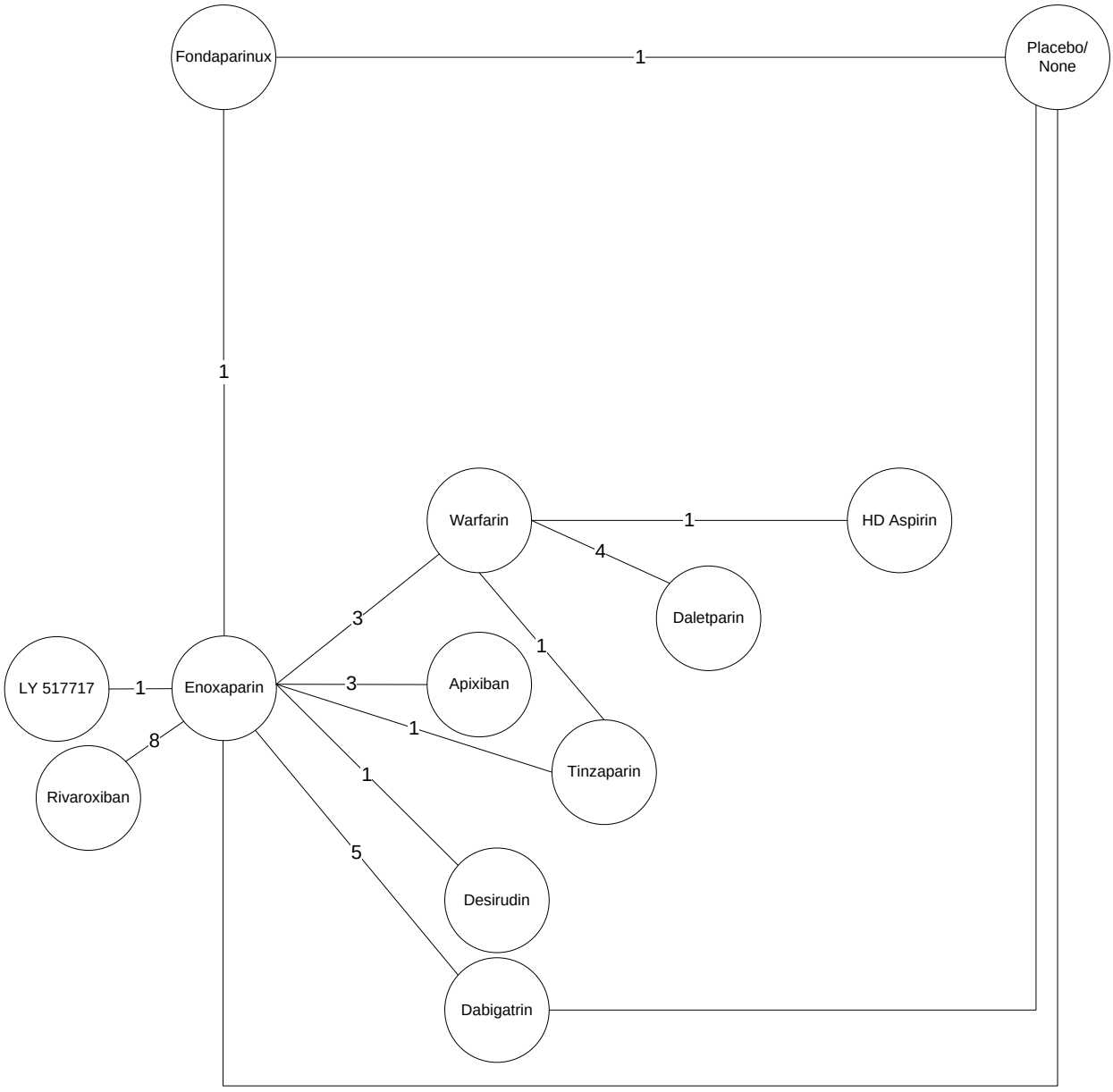
The model depicted in the figure is a model for major bleeding that omits studies for which a continuity correction was required. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 70. Major Bleeding Model Omitting Trials that Required a Continuity Correction and Omitting Trials of Heparin



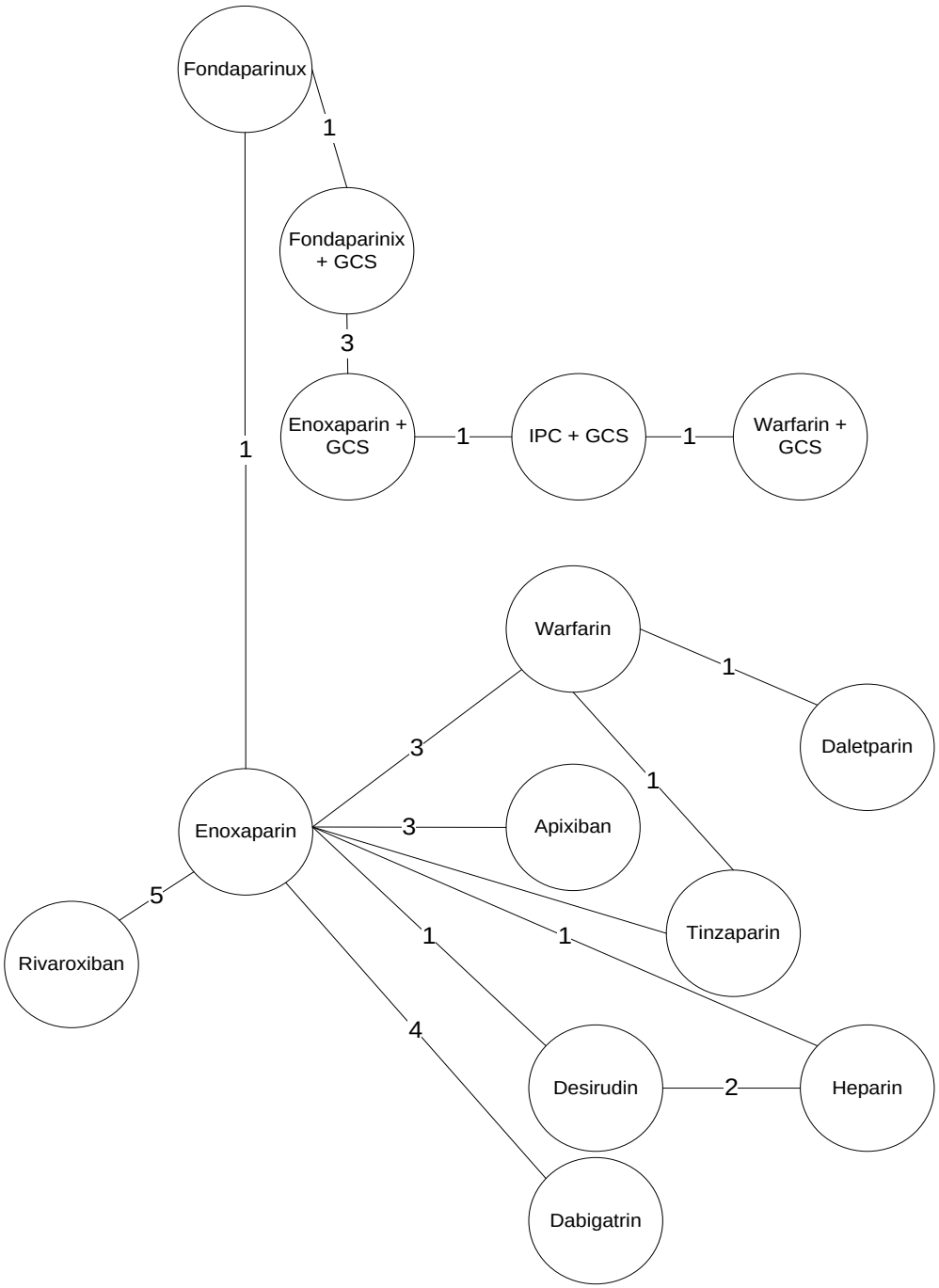
The model depicted in the figure is a model for major bleeding that omits studies for which a continuity correction was required, and that also omits studies of heparin. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 71. Major Bleeding Model Omitting Trials that Required a Continuity Correction, Trials of Heparin, and Trials with > 2 Arms.



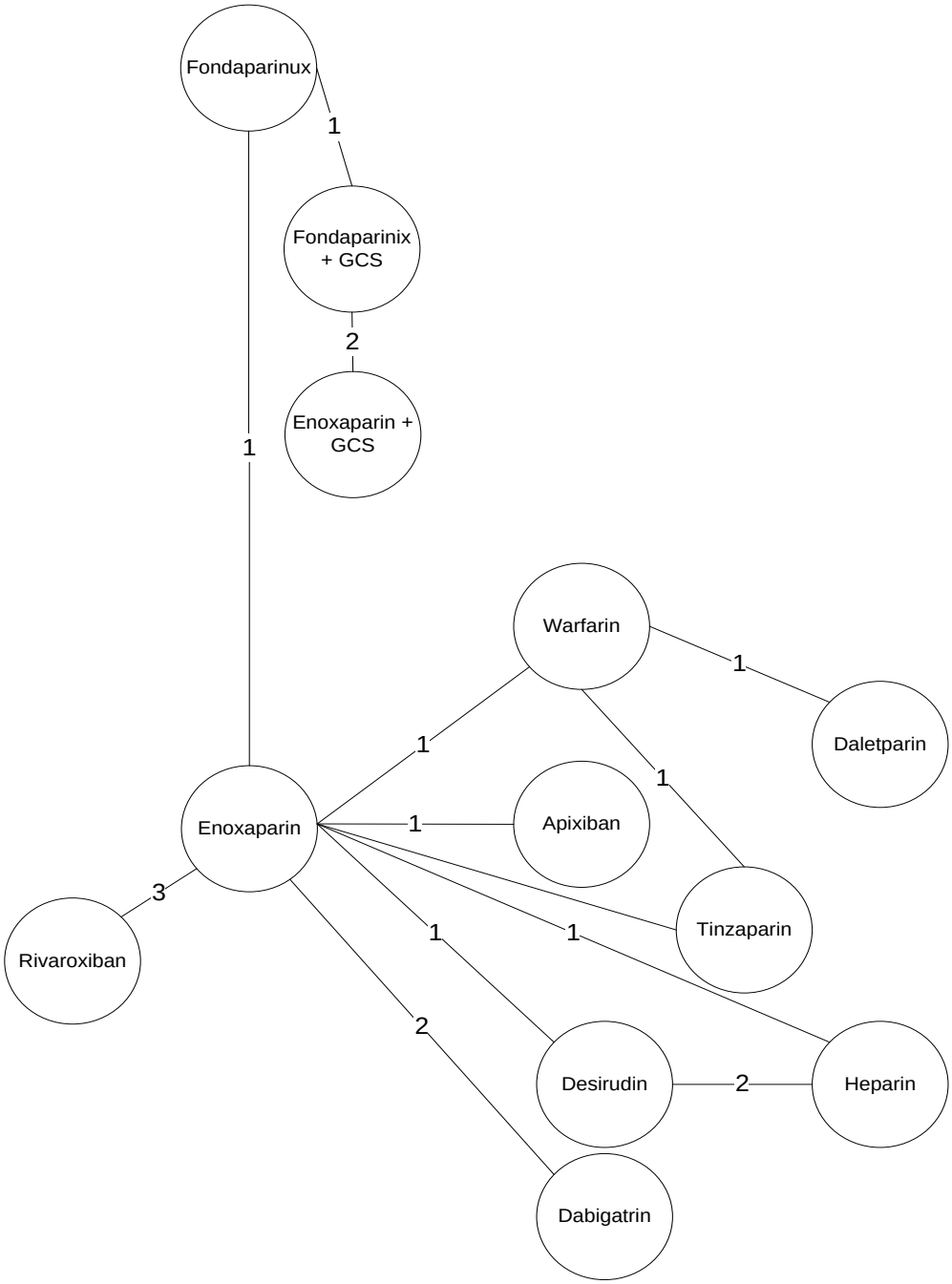
The model depicted in the figure is a model for major bleeding that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 72. All Cause Mortality Model (All Trials, with Continuity Correction)



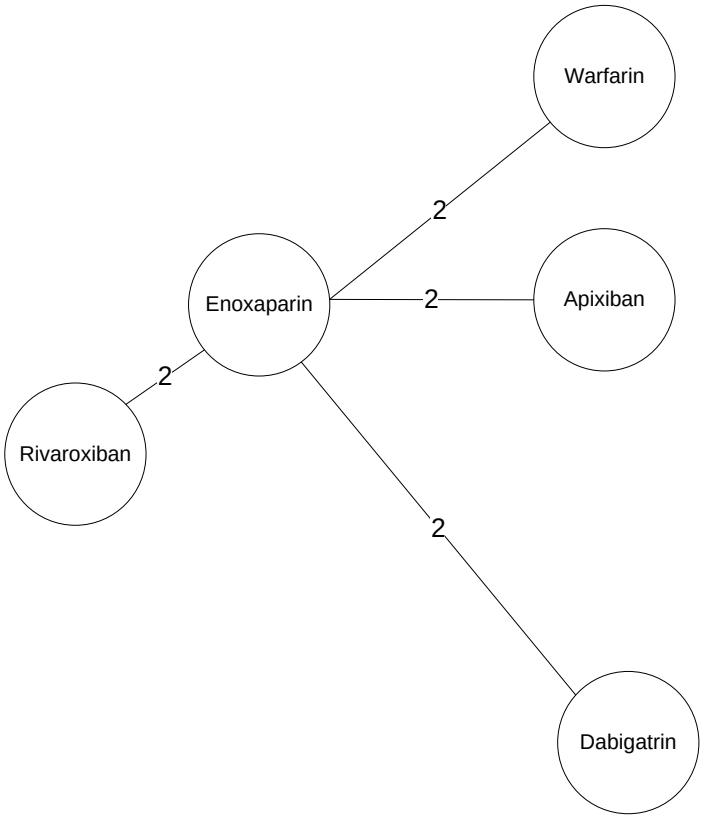
The model depicted in the figure is the base case model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 73. All Cause Mortality Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



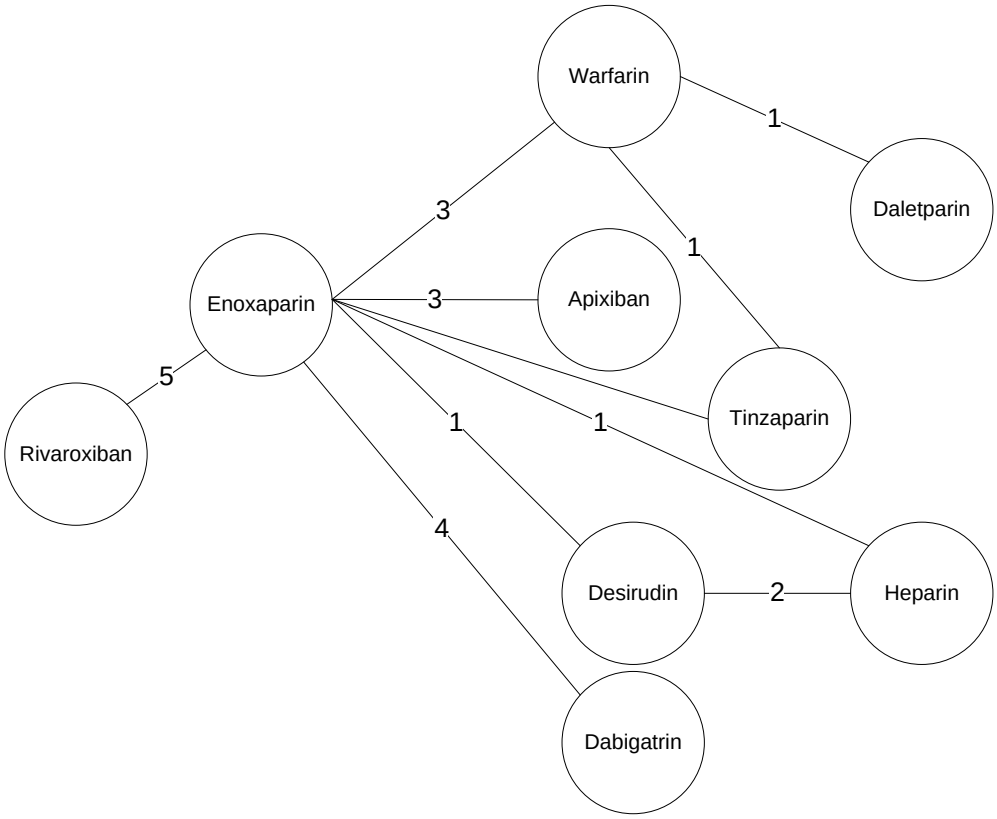
The model depicted in the figure is a model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 74. All Cause Mortality Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



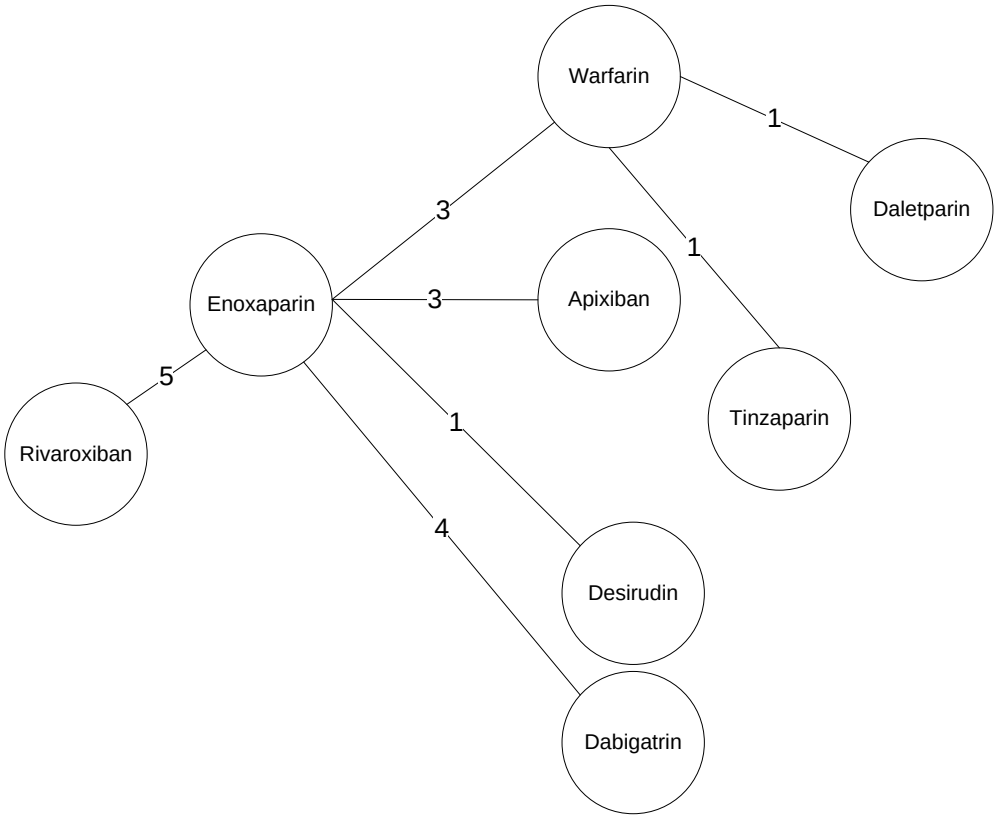
The model depicted in the figure a model for all cause mortality. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 75. All Cause Mortality Model Omitting Studies that Required a Continuity Correction



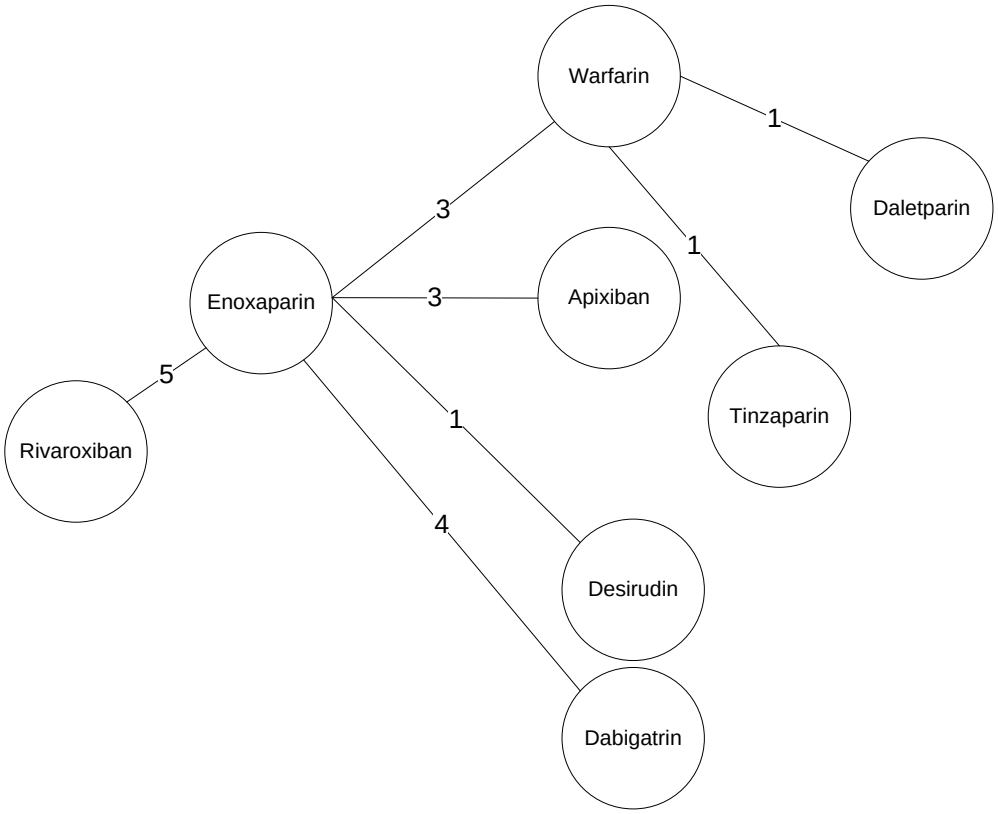
The model depicted in the figure is a model for all cause mortality that omits studies for which a continuity correction was required. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 76. All Cause Mortality Model Omitting Trials that Required a Continuity Correction and Omitting Trials of Heparin



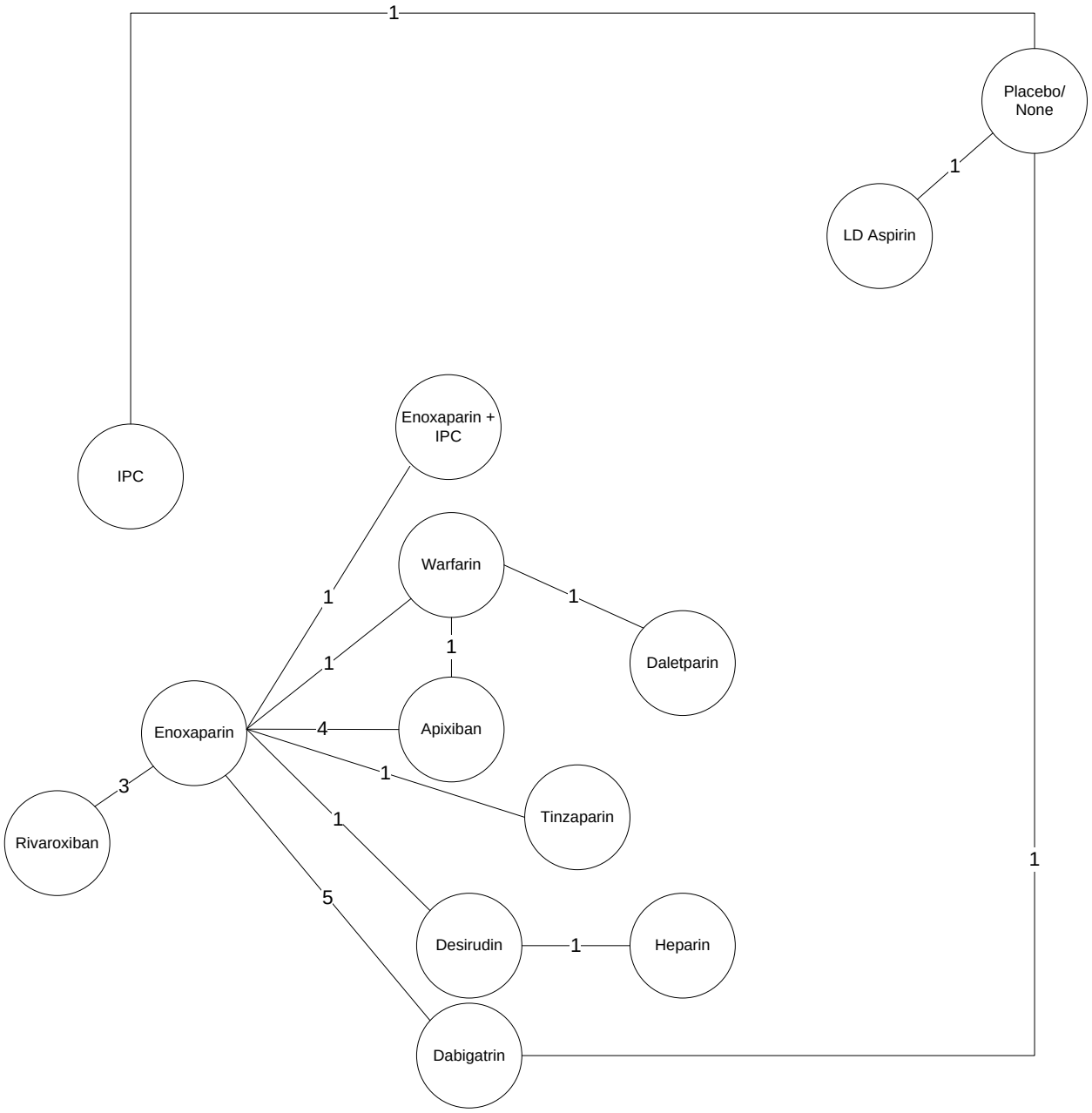
The model depicted in the figure is a model for all cause mortality that omits studies for which a continuity correction was required, and that also omits studies of heparin. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 77. All Cause Mortality Model Omitting Trials that Required a Continuity Correction, Trials of Heparin, and Trials with > 2 Arms.



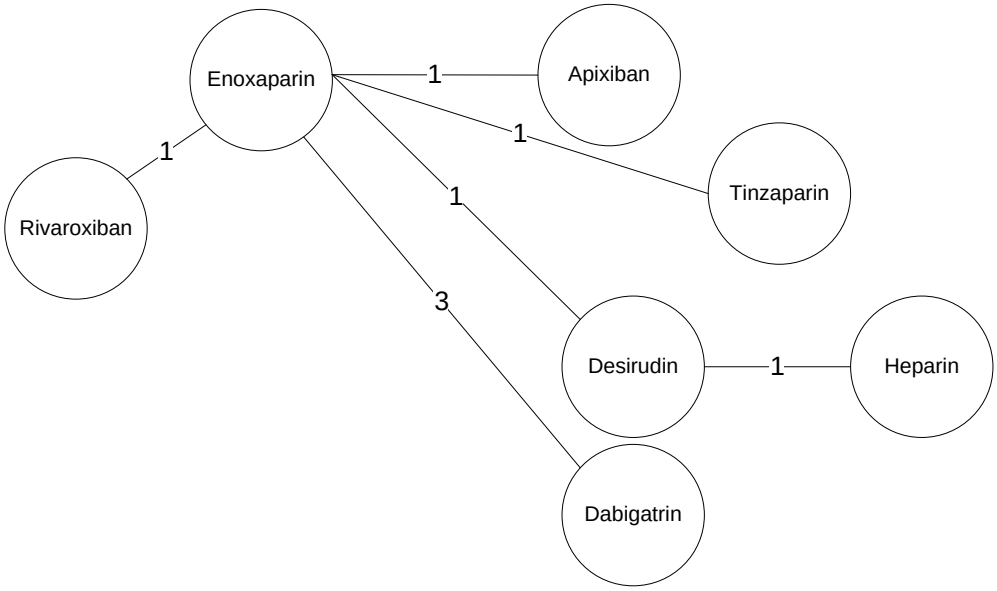
The model depicted in the figure is a model for all cause mortality that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles. Note that there were no studies with > 3 arms, so this model is identical to the model in which studies of heparin were omitted.

Figure 78. Symptomatic DVT Model (All Trials, with Continuity Correction)



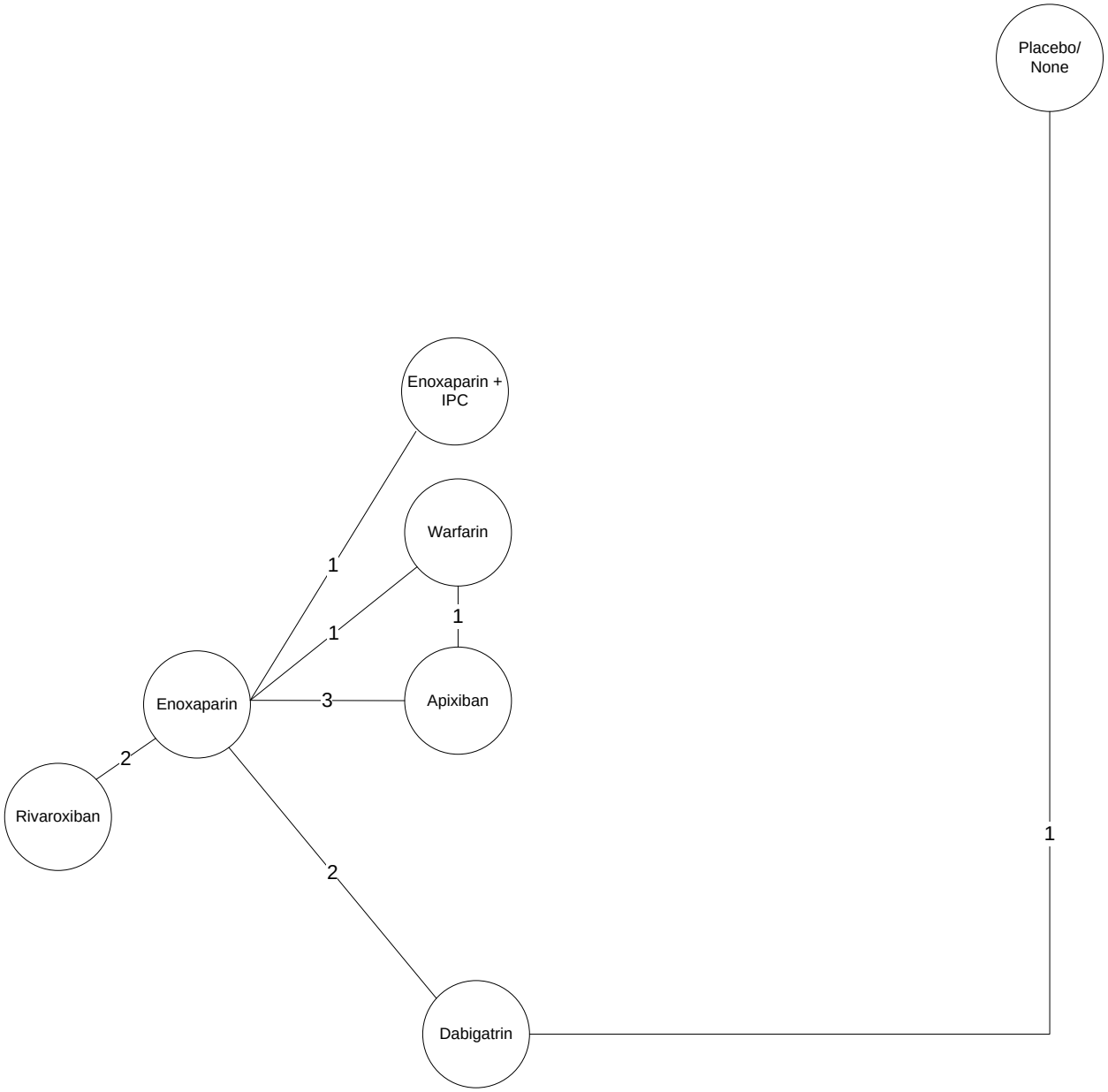
The model depicted in the figure is the base case model for symptomatic DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 79. Symptomatic DVT Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



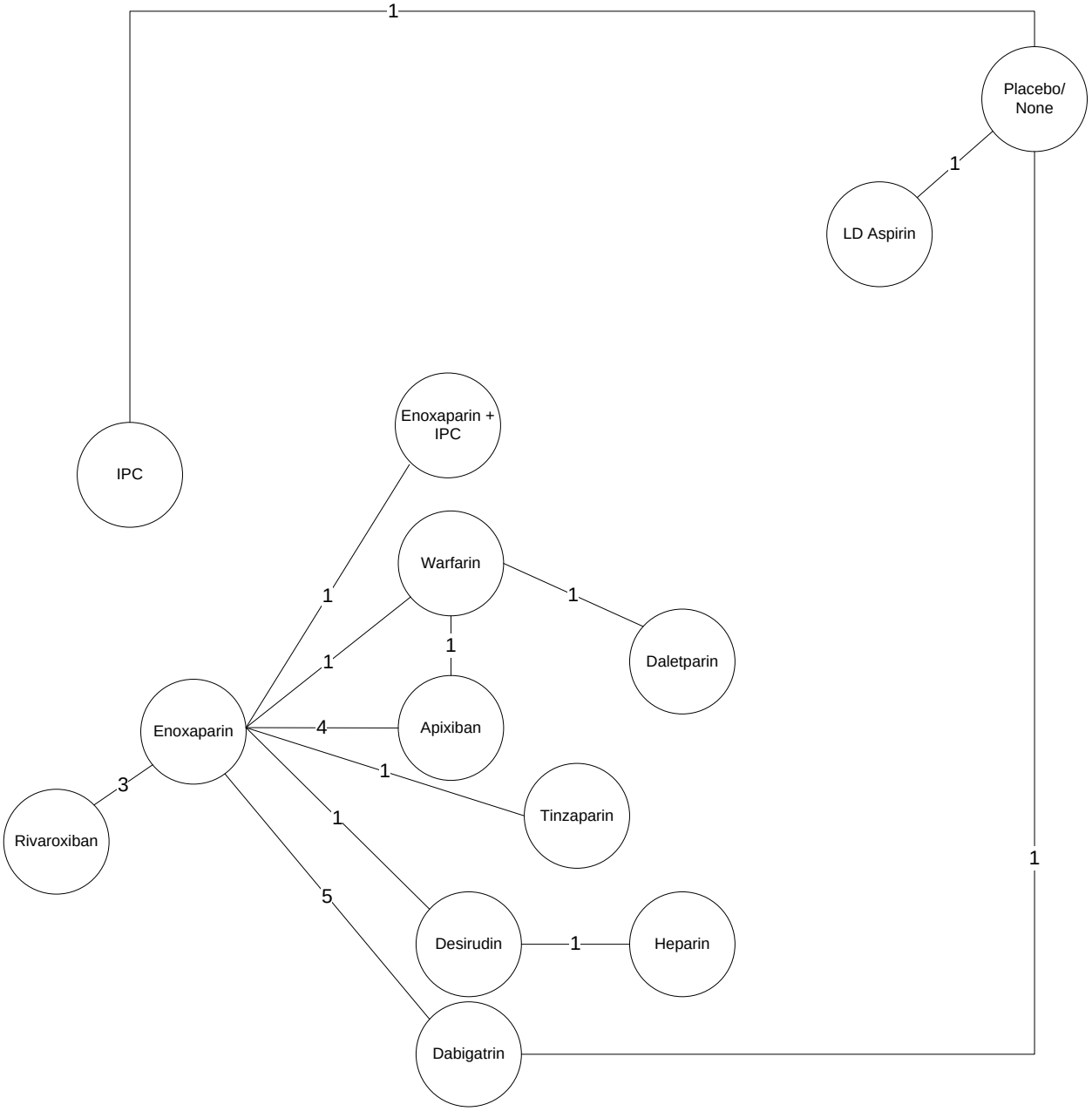
The model depicted in the figure is a model for symptomatic DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 80. Symptomatic DVT Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



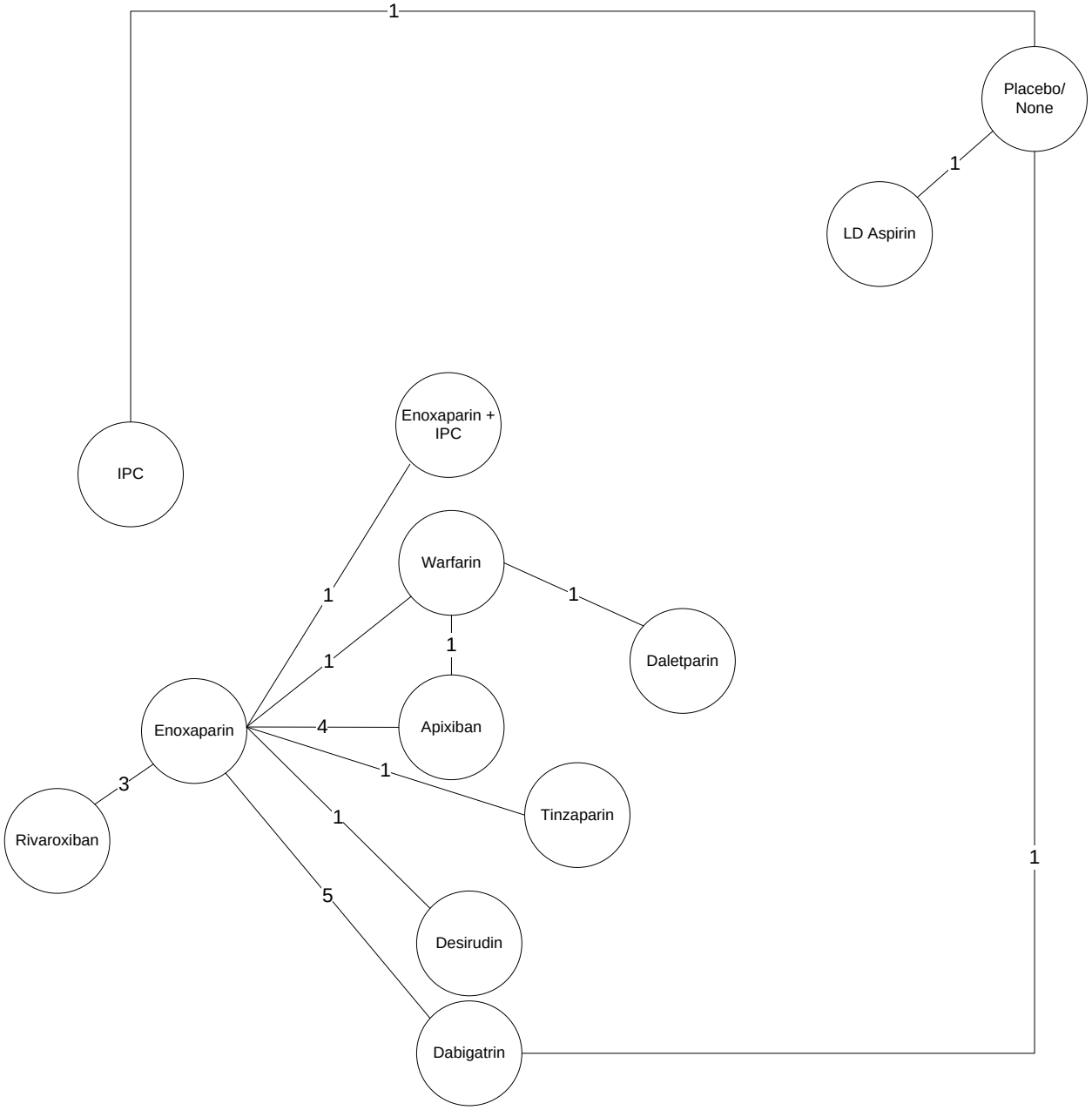
The model depicted in the figure a model for symptomatic DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 81. Symptomatic DVT Model Omitting Studies that Required a Continuity Correction



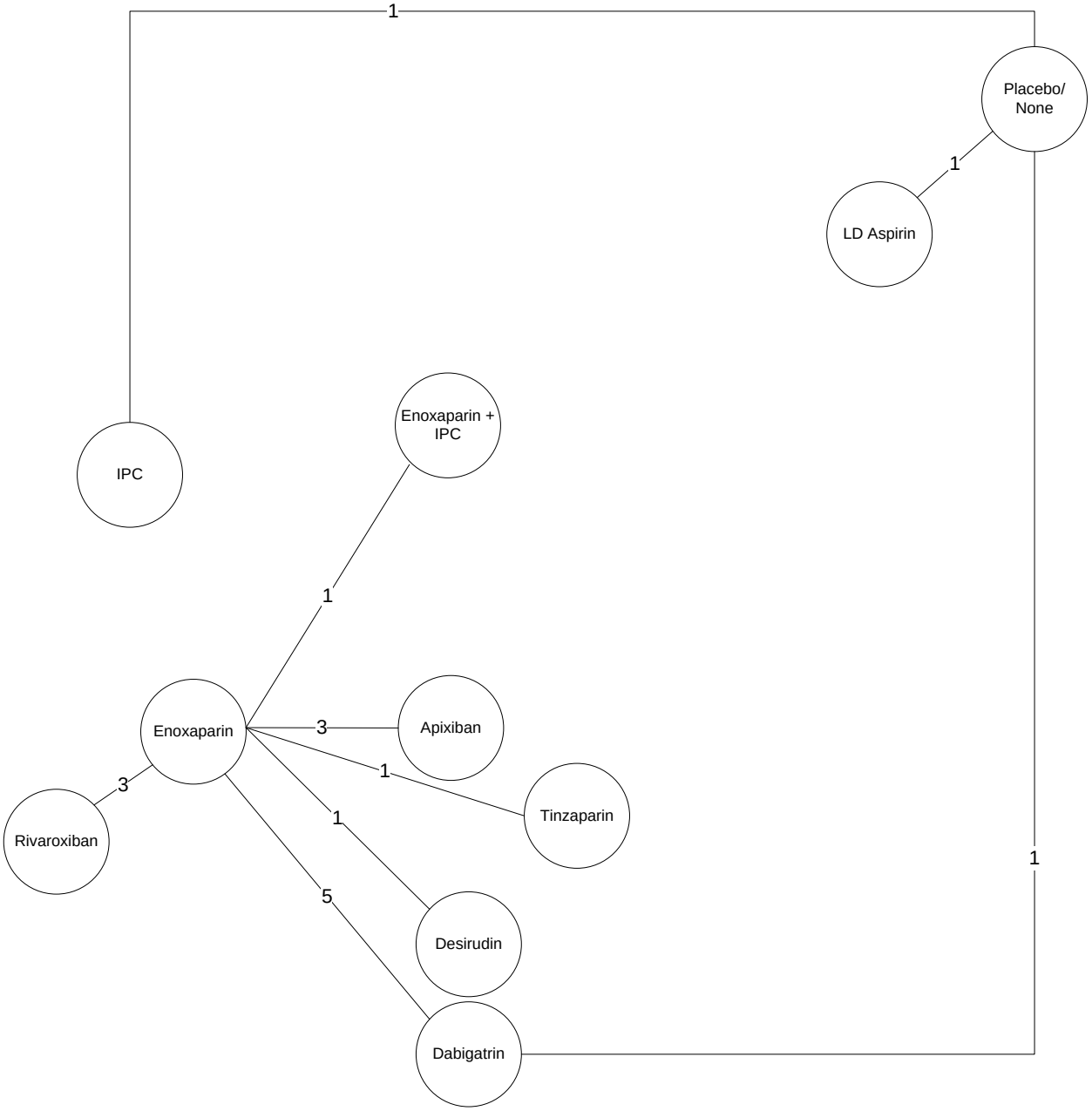
The model depicted in the figure is a model for symptomatic DVT that omits studies for which a continuity correction was required. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles. Note that this is the same as the model with all trials.

Figure 82. Symptomatic DVT Model Omitting Trials that Required a Continuity Correction and Omitting Trials of Heparin



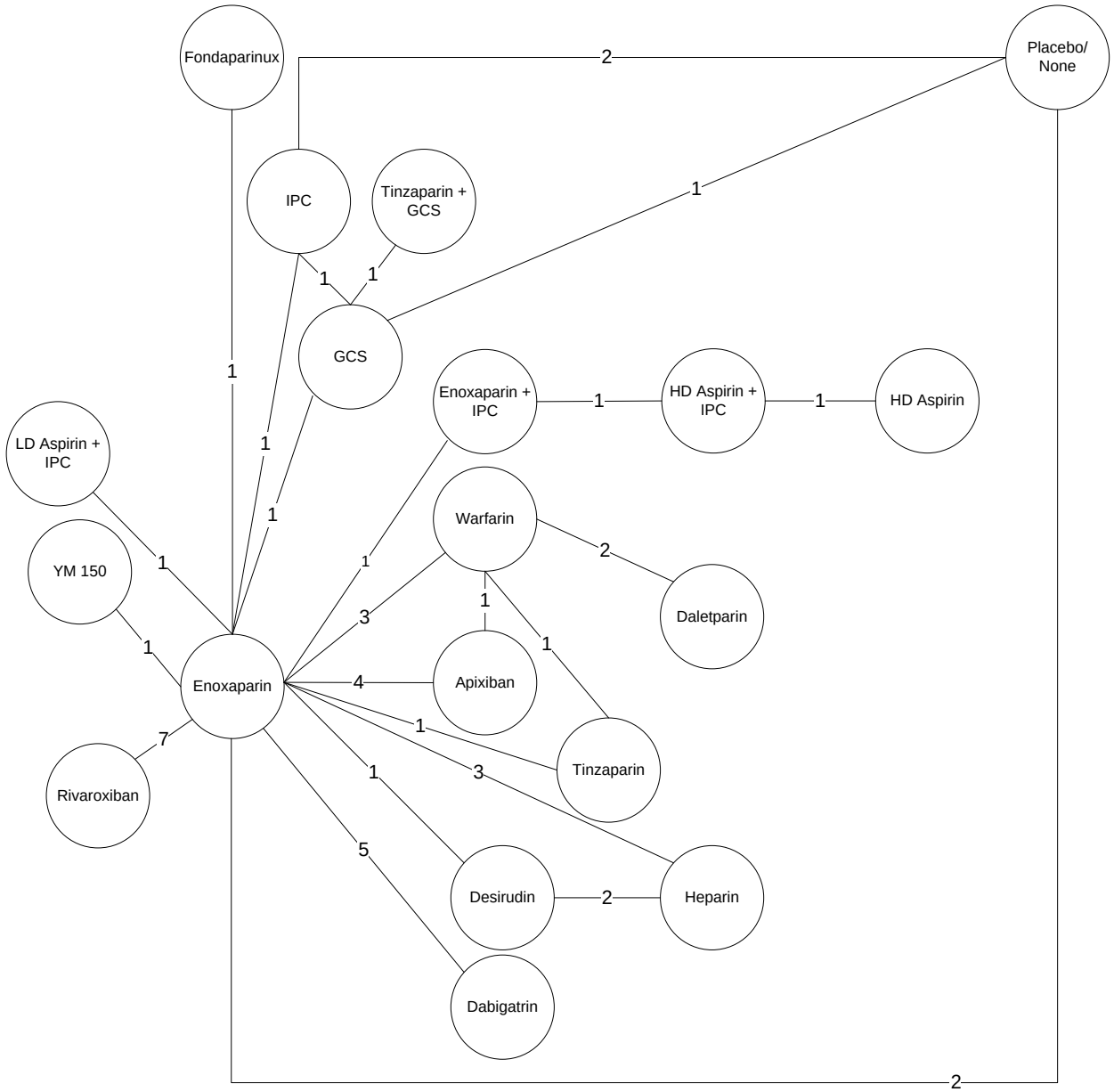
The model depicted in the figure is a model for all symptomatic DVT that omits studies for which a continuity correction was required, and that also omits studies of heparin. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 83. Symptomatic DVT Model Omitting Trials that Required a Continuity Correction, Trials of Heparin, and Trials with > 2 Arms.



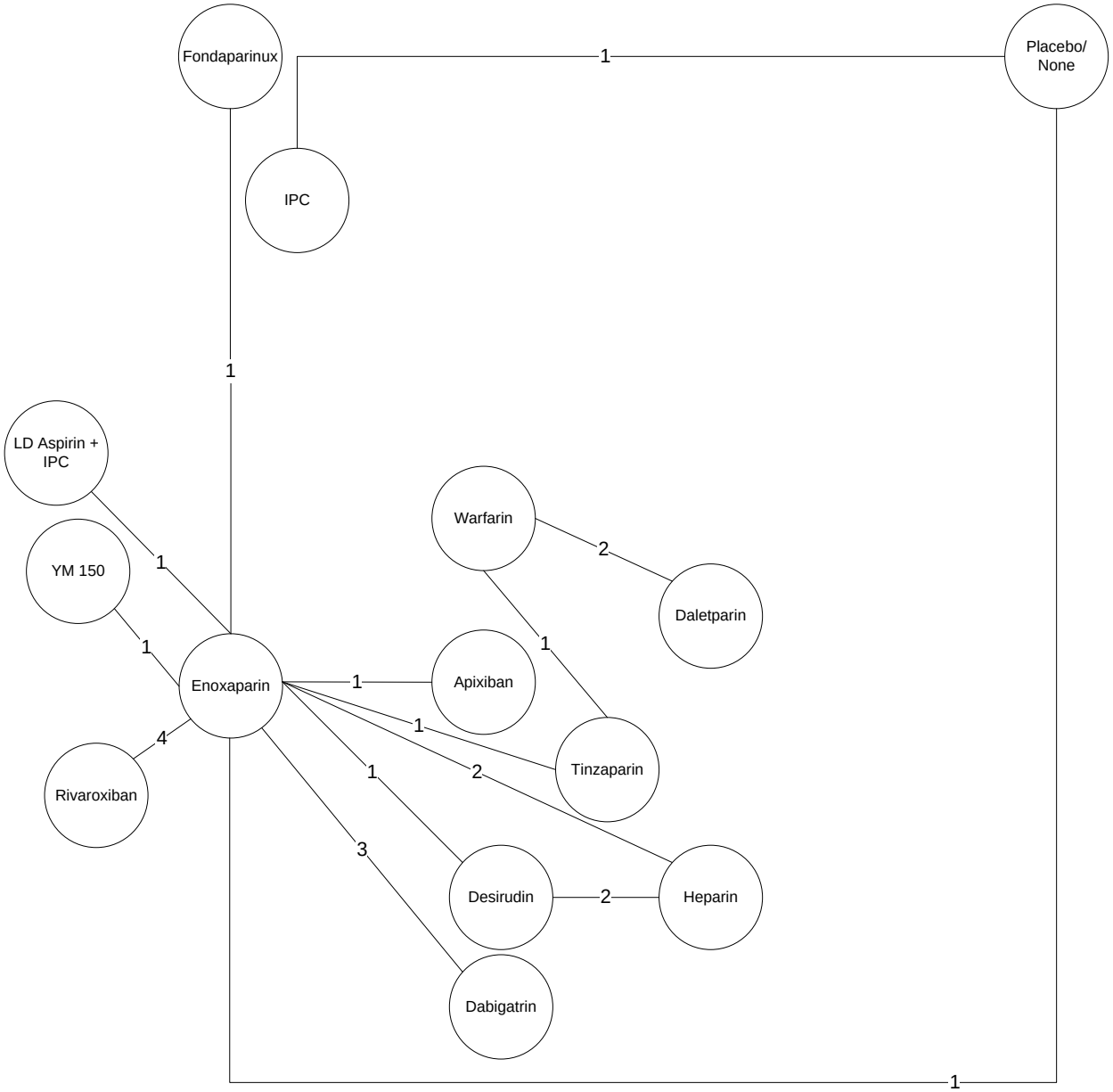
The model depicted in the figure is a model for symptomatic DVT that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 84. Deep Vein Thrombosis Model (All Trials, with Continuity Correction)



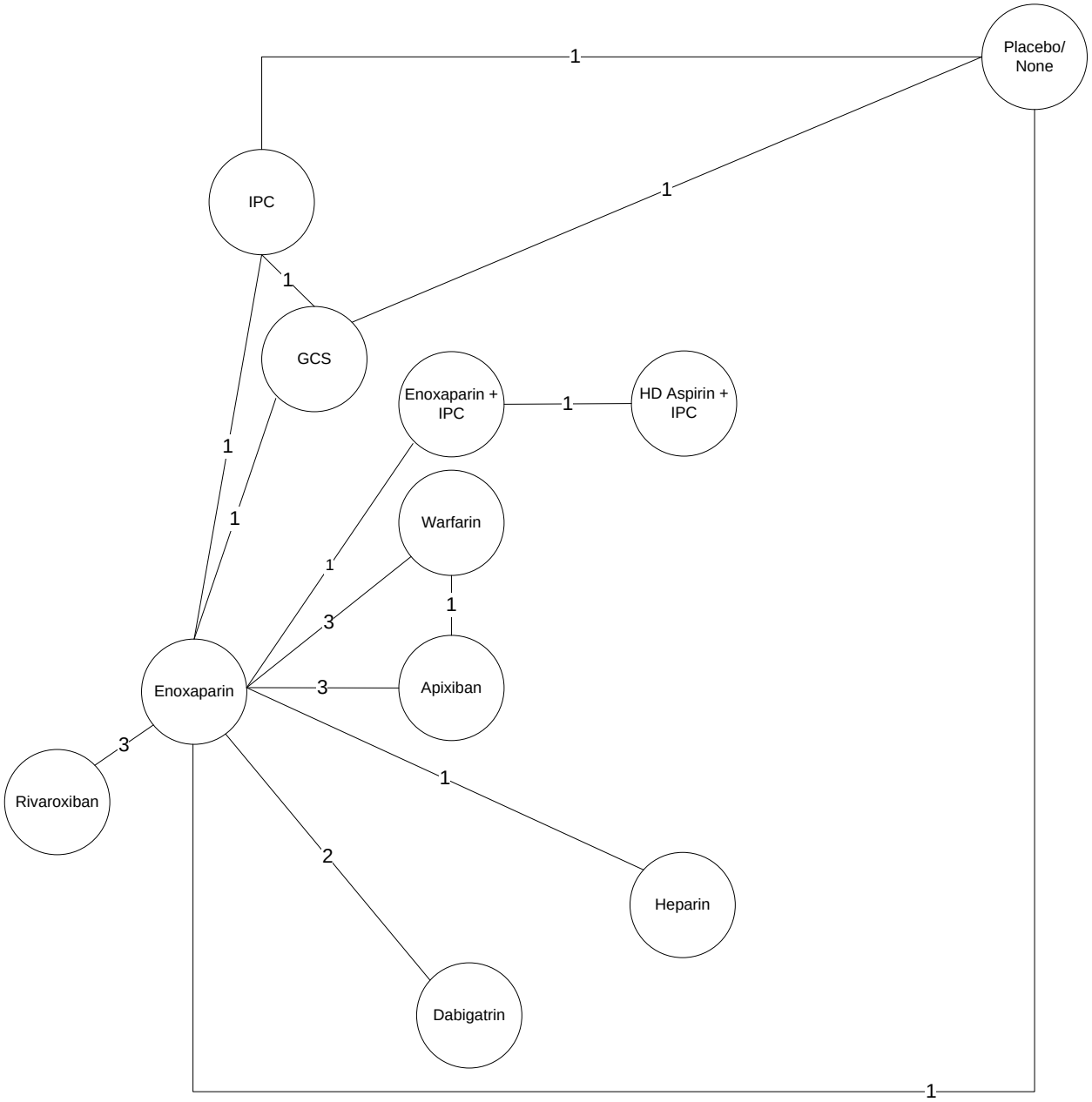
The model depicted in the figure is the base case model for DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 85. Deep Vein Thrombosis Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



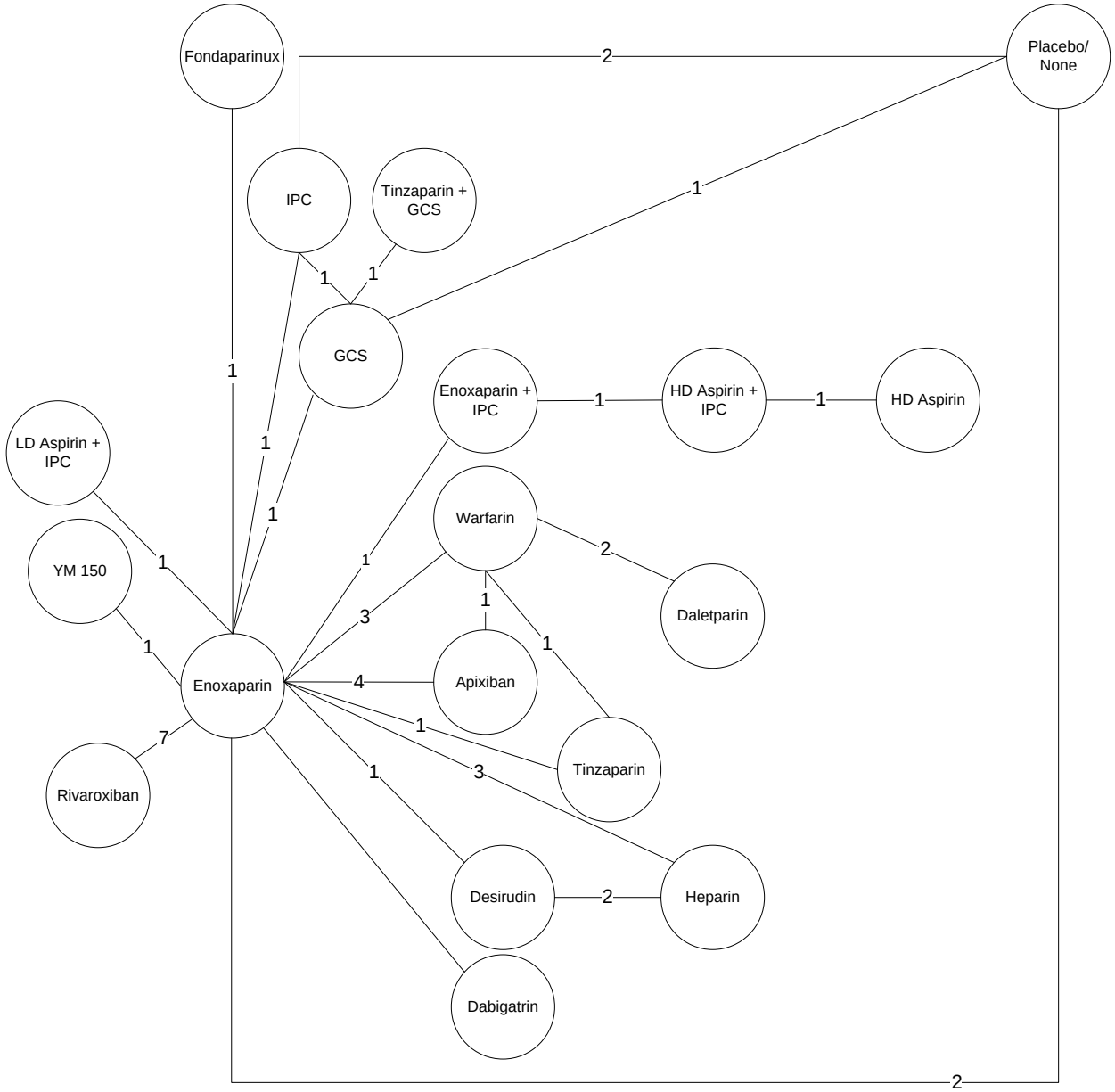
The model depicted in the figure is a model for DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 86. Deep Vein Thrombosis Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



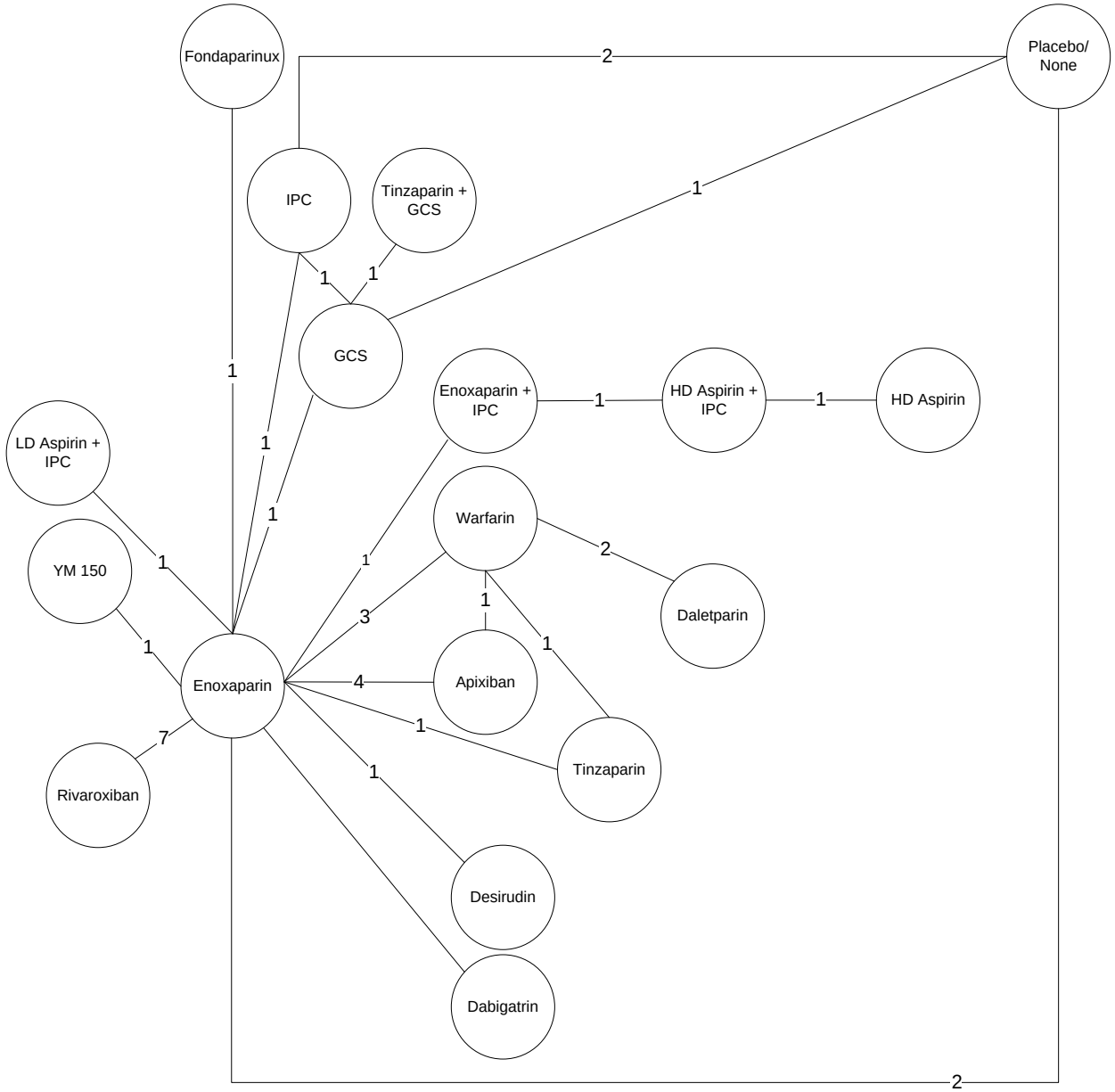
The model depicted in the figure a model for DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 87. Deep Vein Thrombosis Model Omitting Studies that Required a Continuity Correction



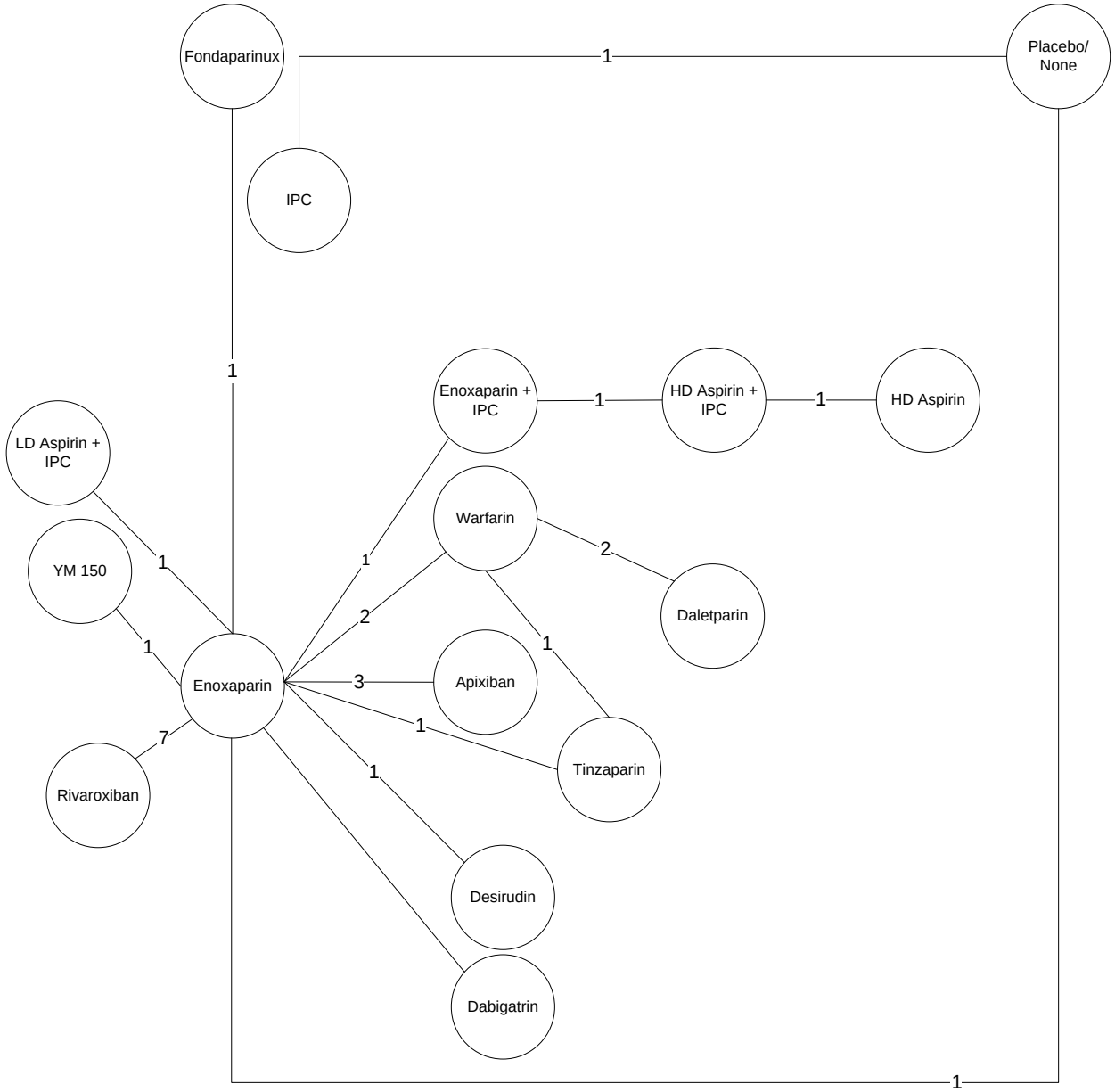
The model depicted in the figure is a model for DVT that omits studies for which a continuity correction was required. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 88. Deep Vein Thrombosis Model Omitting Trials that Required a Continuity Correction and Omitting Trials of Heparin



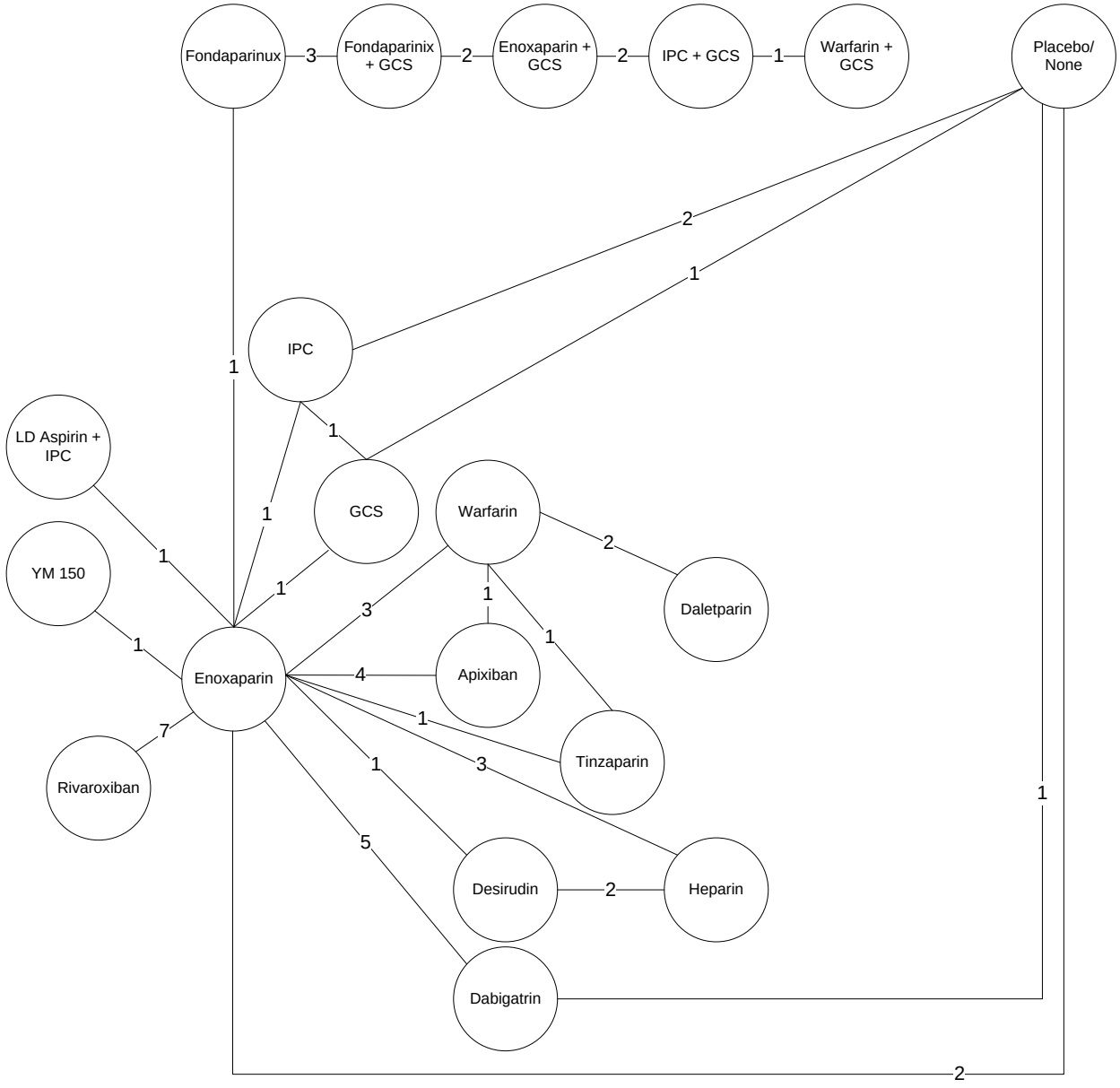
The model depicted in the figure is a model for DVT that omits studies for which a continuity correction was required, and that also omits studies of heparin. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 89. Deep Vein Thrombosis Model Omitting Trials that Required a Continuity Correction, Trials of Heparin, and Trials with > 2 Arms.



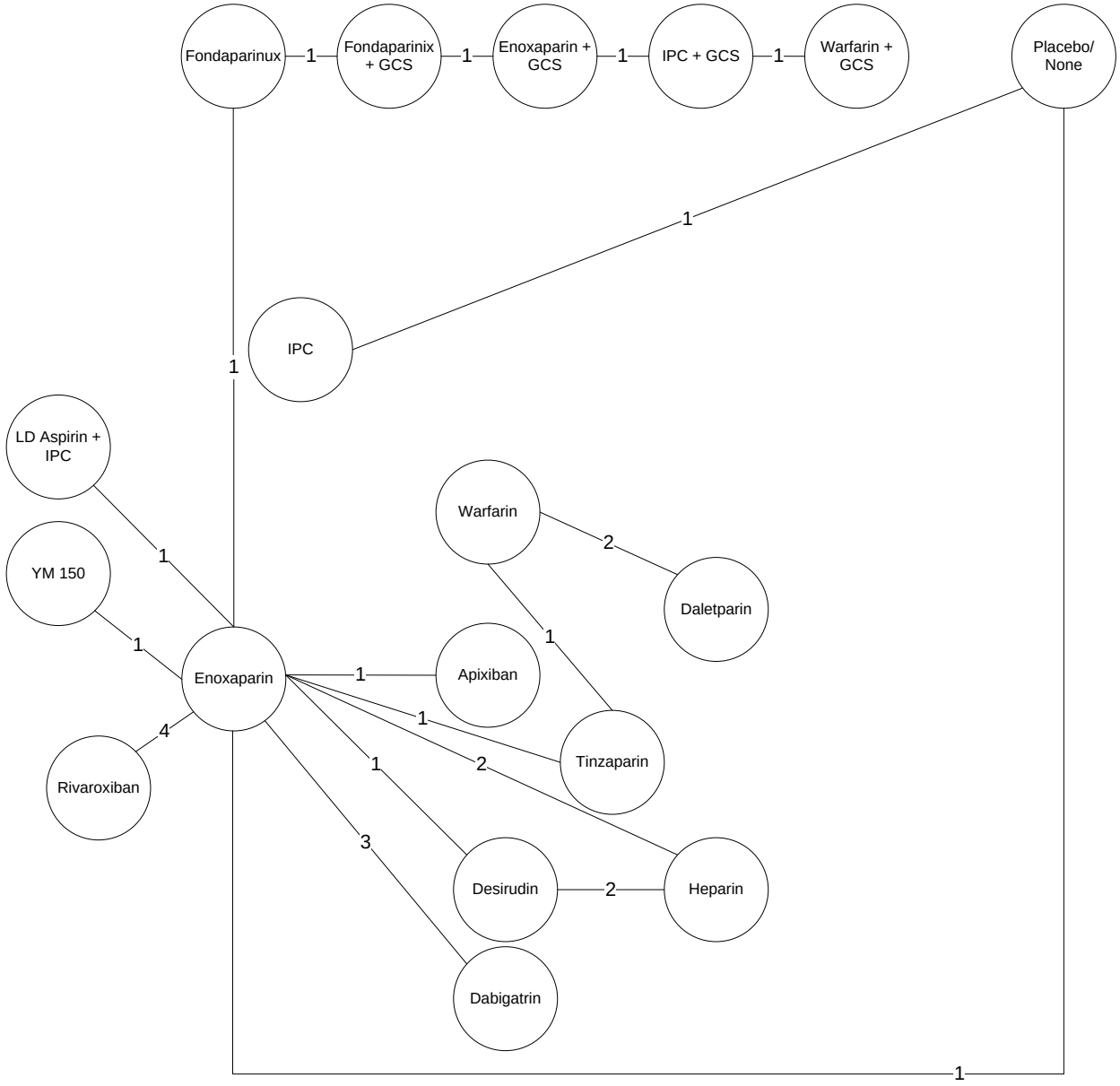
The model depicted in the figure is a model for DVT that omits studies for which a continuity correction was required, studies of heparin, and studies with > 2 arms. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 90. Proximal Deep Vein Thrombosis Model (All Trials, with Continuity Correction)



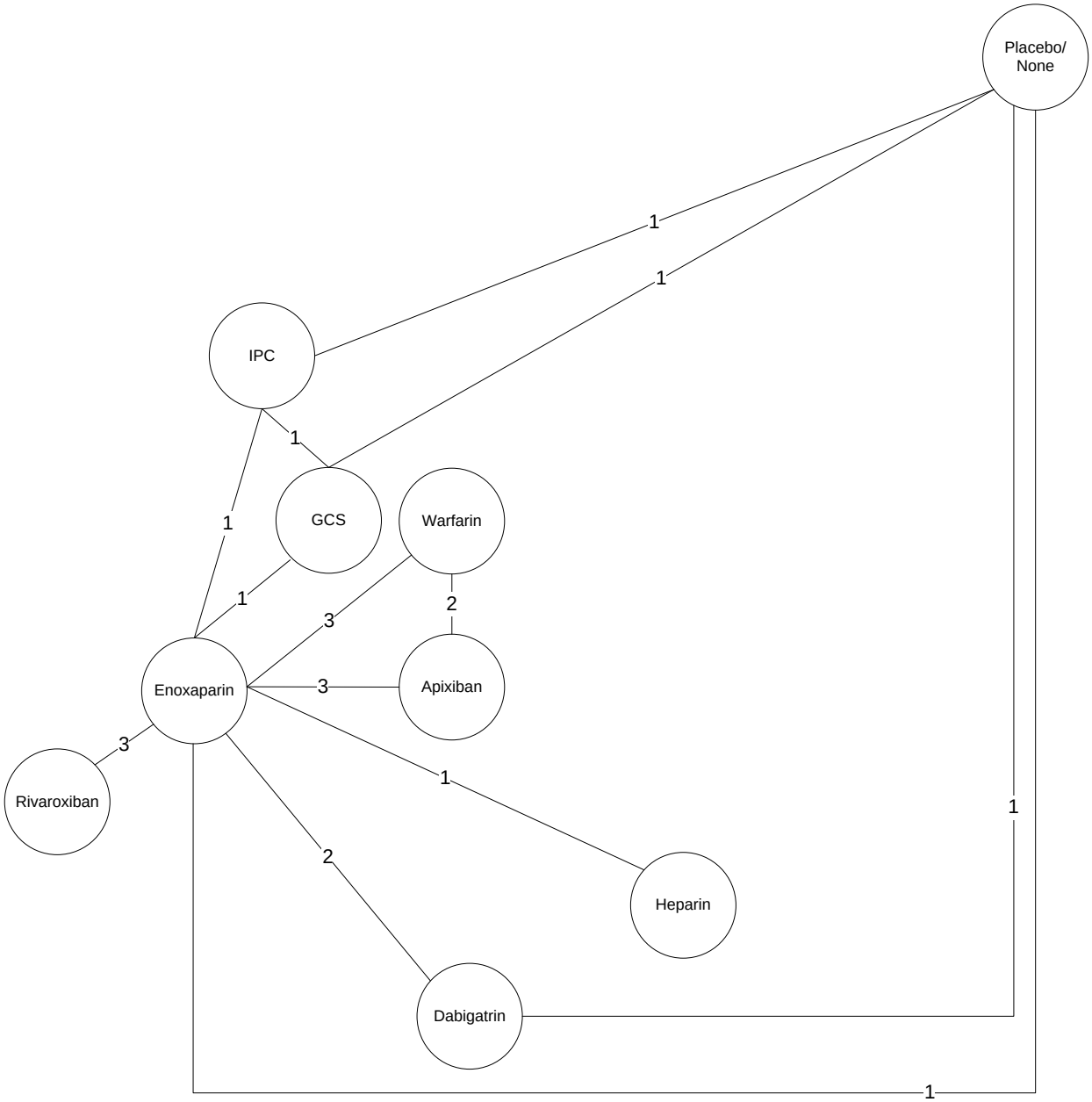
The model depicted in the figure is the initial model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes data from patients who received a hip replacement and those who received a total knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

Figure 91. Proximal Deep Vein Thrombosis Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Hip Replacement



The model depicted in the figure is a model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a hip replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

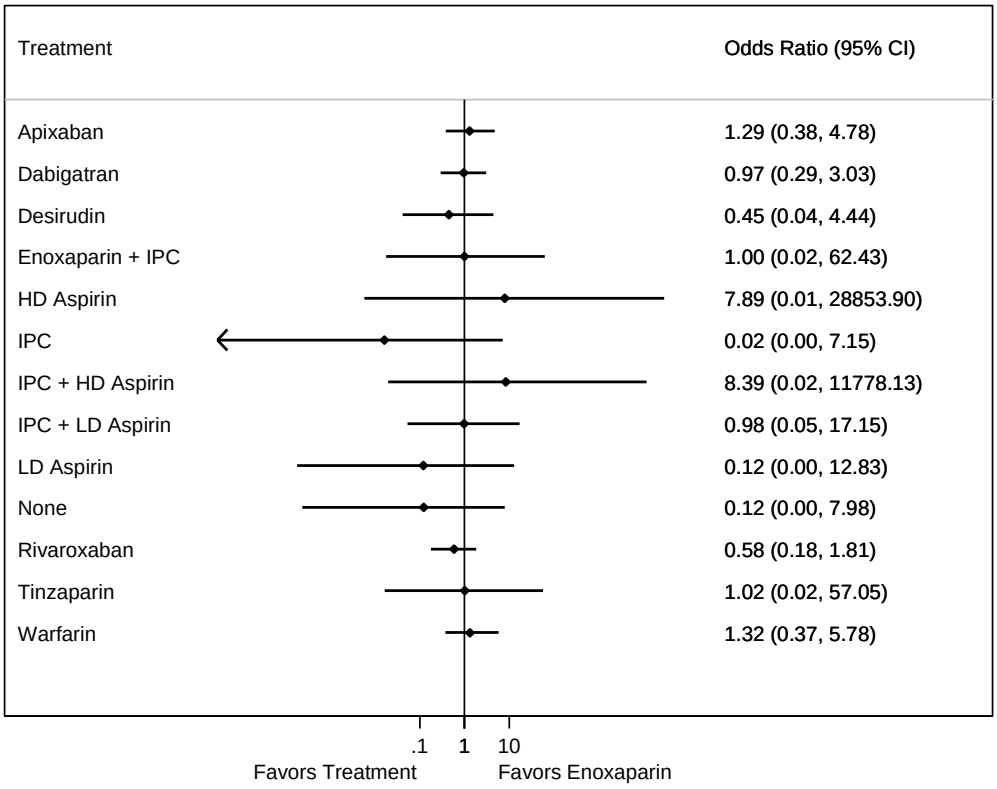
Figure 92. Proximal Deep Vein Thrombosis Model (All Trials, with Continuity Correction) with Only Data from Patients who Received a Knee Replacement



The model depicted in the figure a model for proximal DVT. All trials that observed at least one event in one of its groups are included. A continuity correction was employed for trials that observed no events at least one of its groups. The model includes only data from patients who received a knee replacement. Circles denote the treatments studied. Lines between circles denote treatment comparisons that are addressed by direct evidence. The numbers on these lines show the number of trials that compared the two treatments denoted in the circles.

FINAL MODEL RESULTS AS COMPARED TO ENOXAPARIN

Figure 93. Pumonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



Note: The comparator in this graph is enoxaparin rather than no treatment.

Figure 94. Pumonary Embolism among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

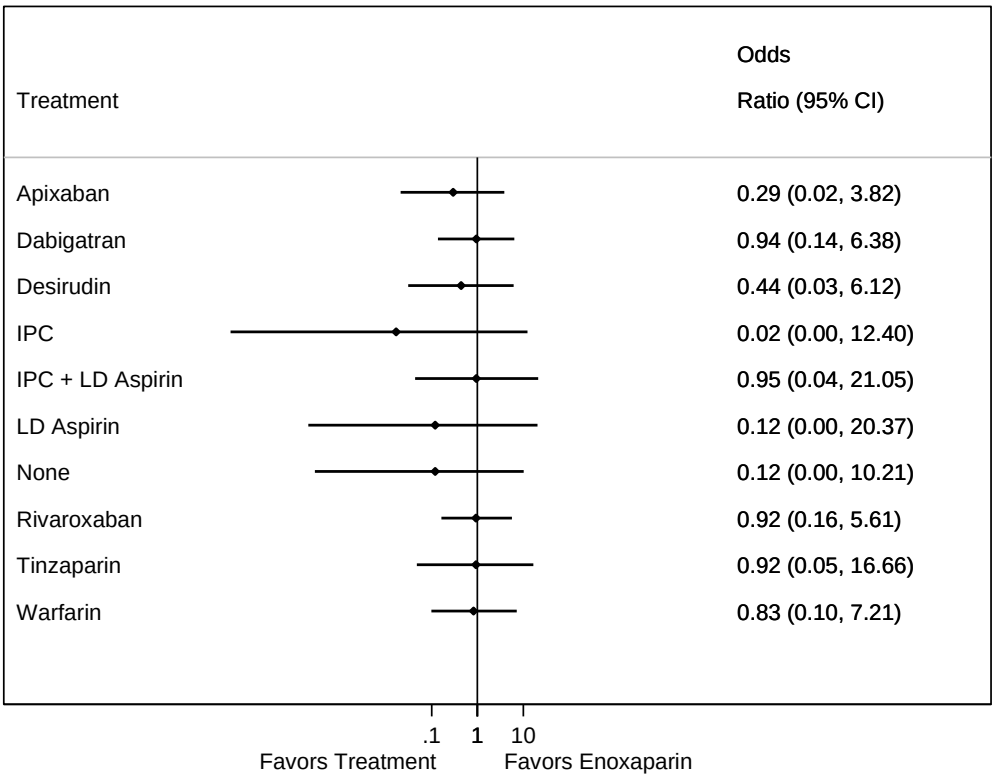


Figure 95. Pumonary Embolism among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

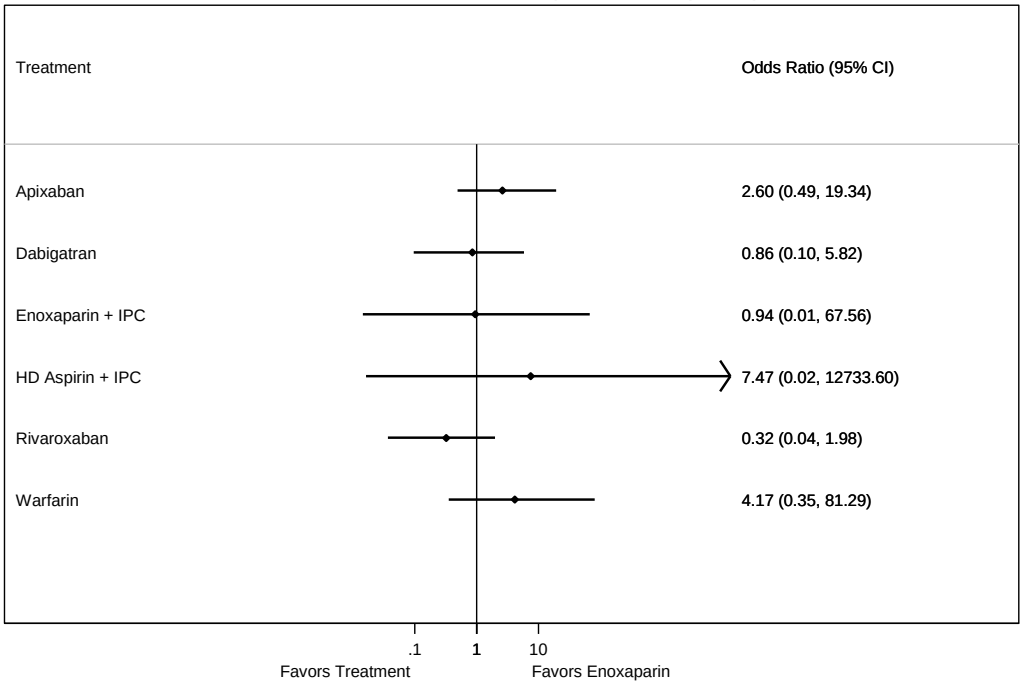


Figure 96. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

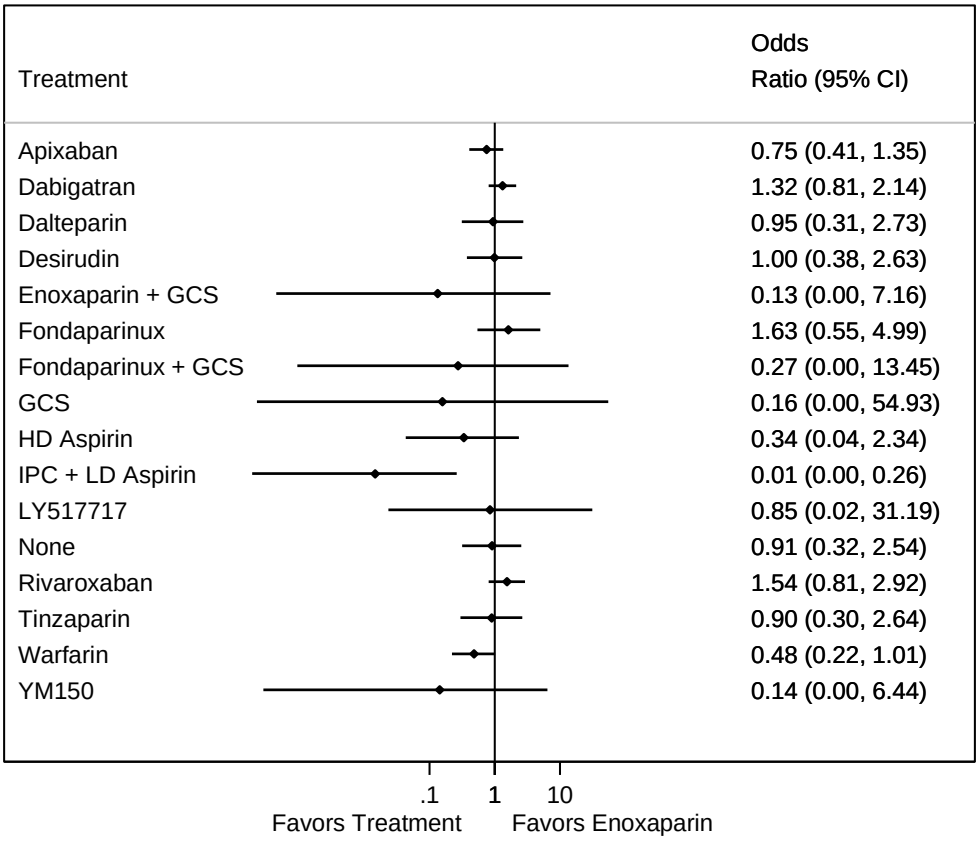


Figure 97. Major Bleeding among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

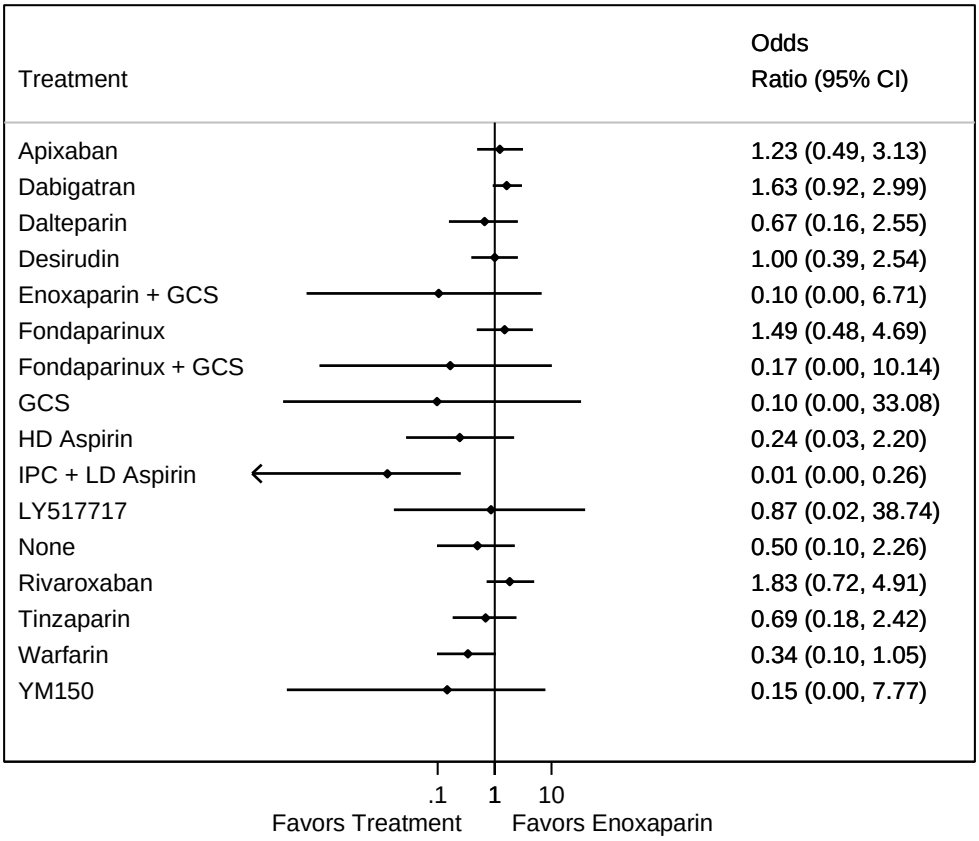


Figure 98. Major Bleeding among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

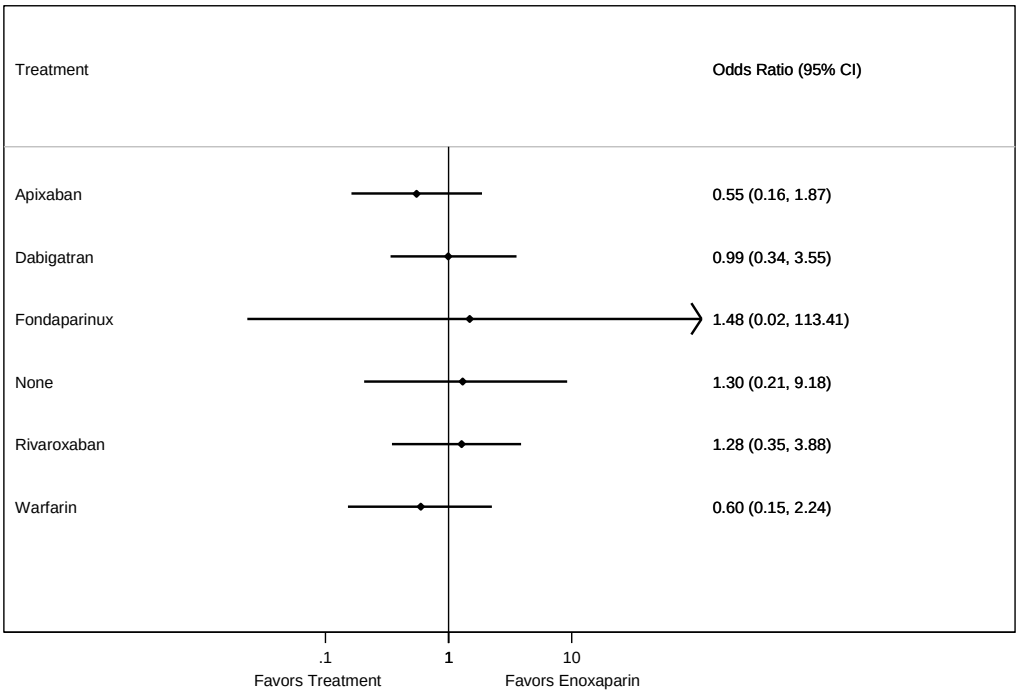


Figure 99. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

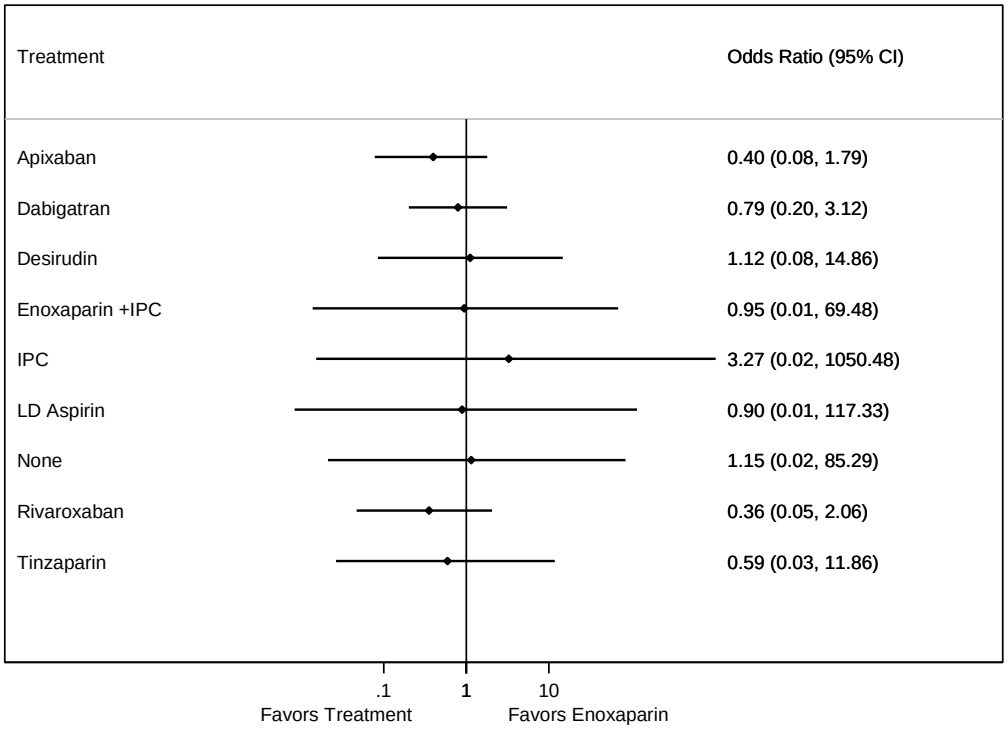


Figure 100. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

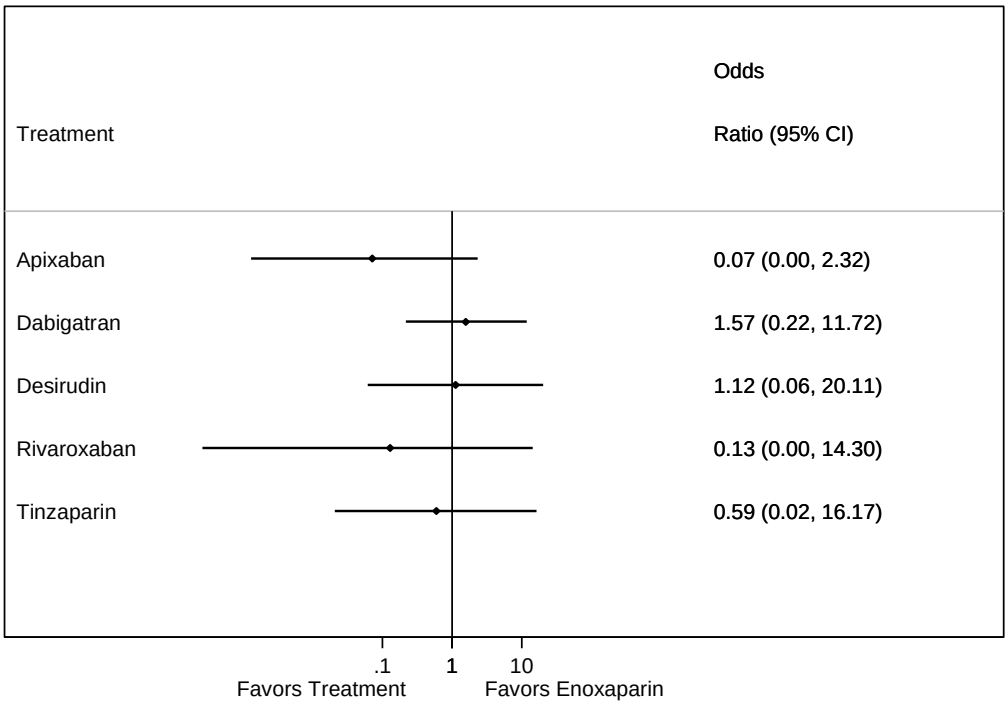


Figure 101. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results with Continuity Correction Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

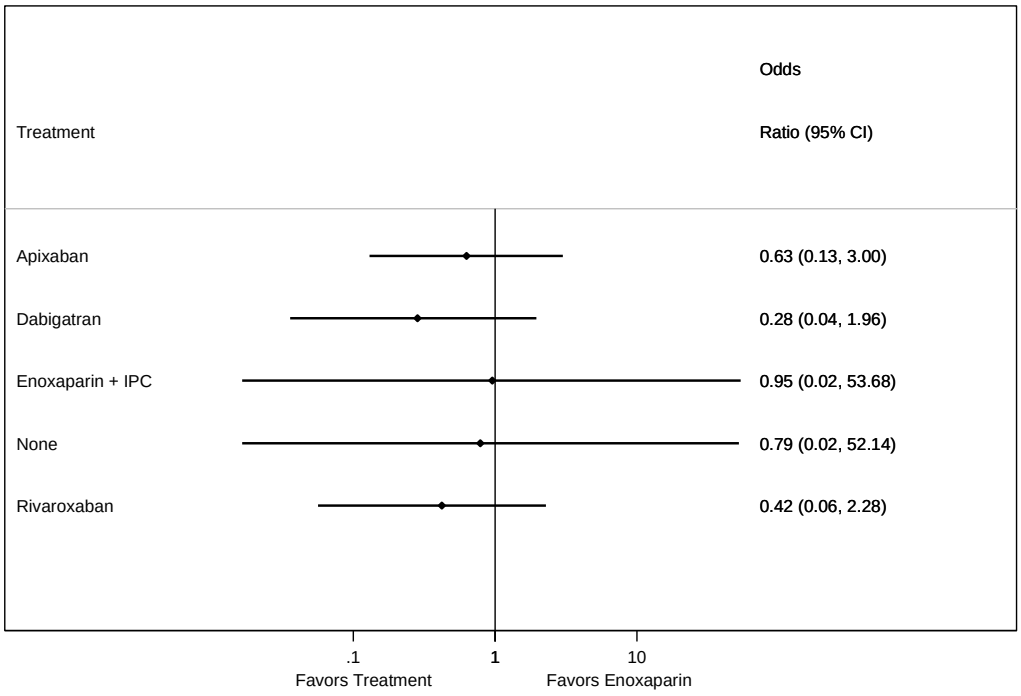


Figure 102. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

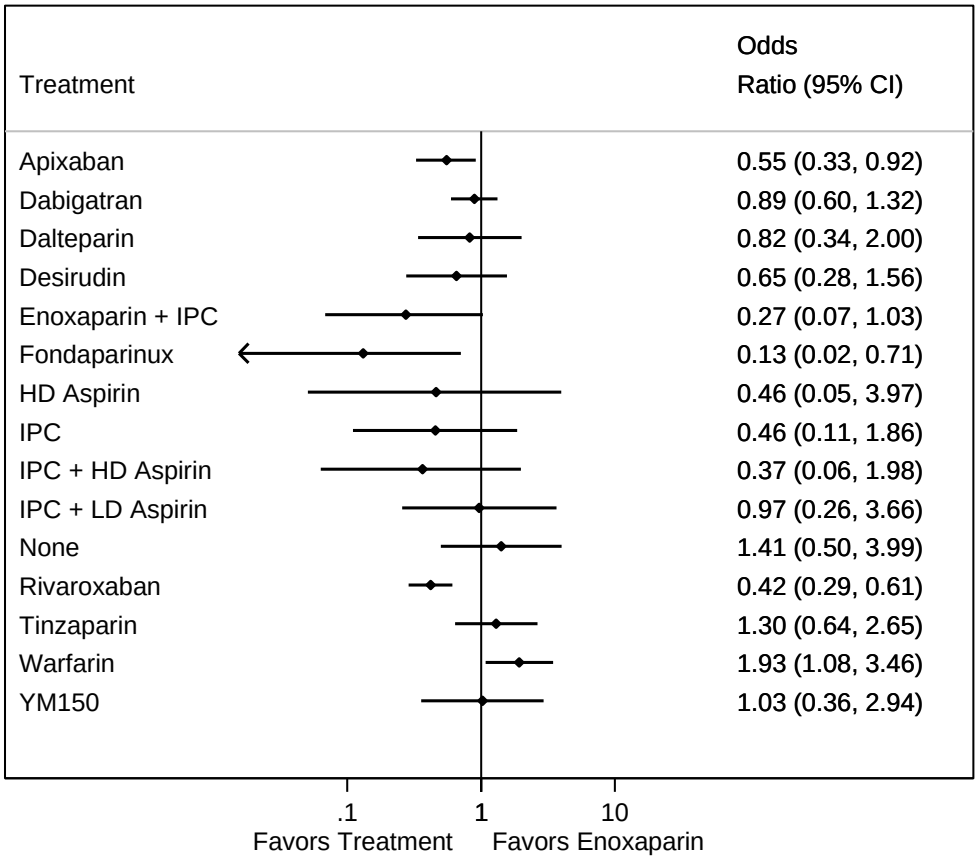


Figure 103. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

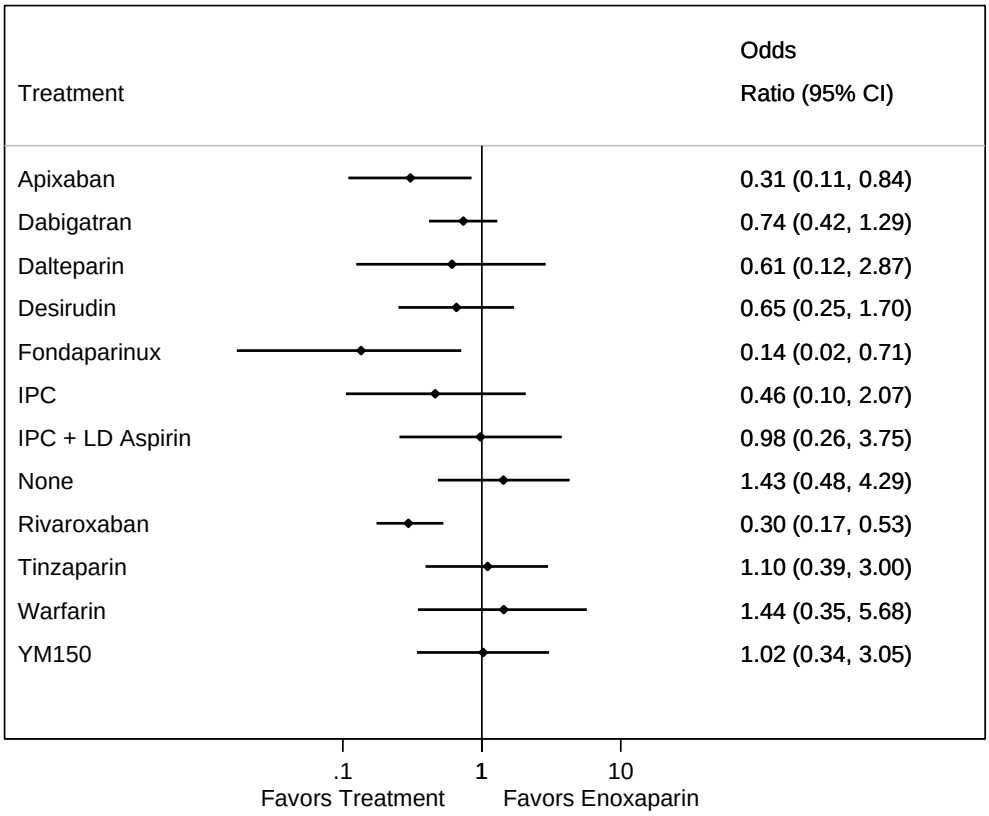


Figure 104. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

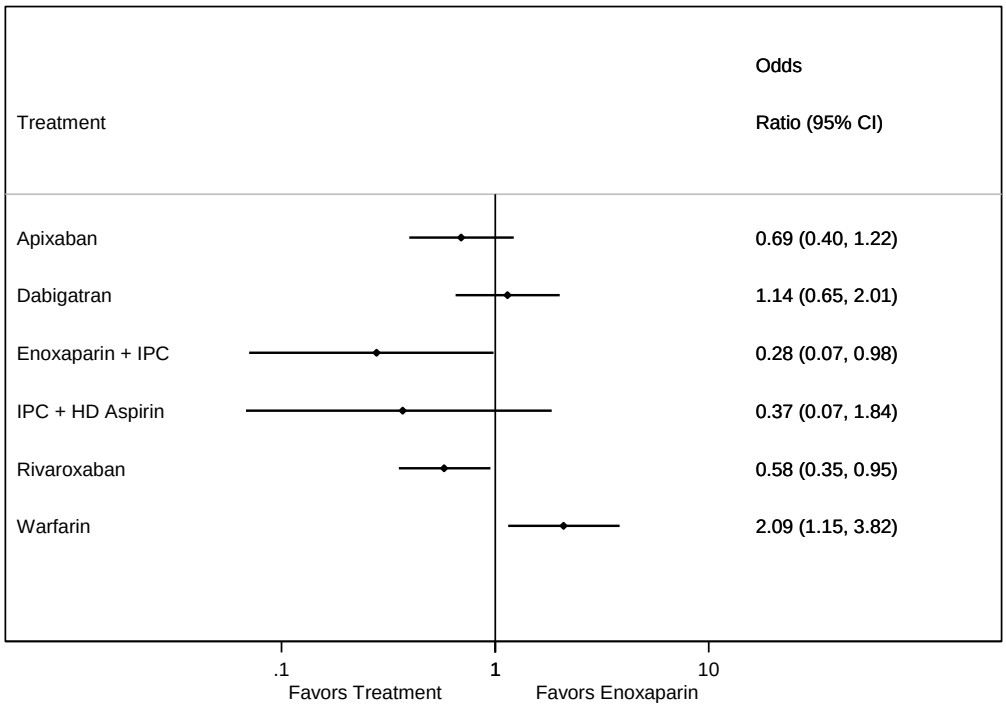


Figure 105. Proximal Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

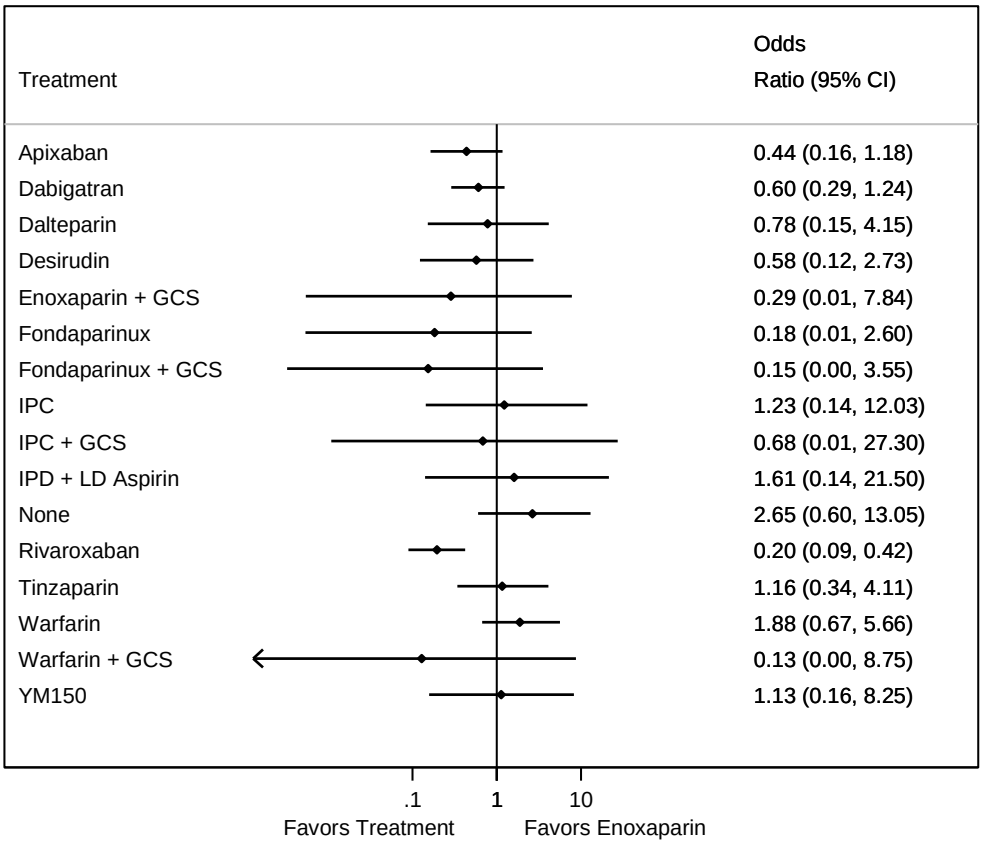


Figure 106. Proximal Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

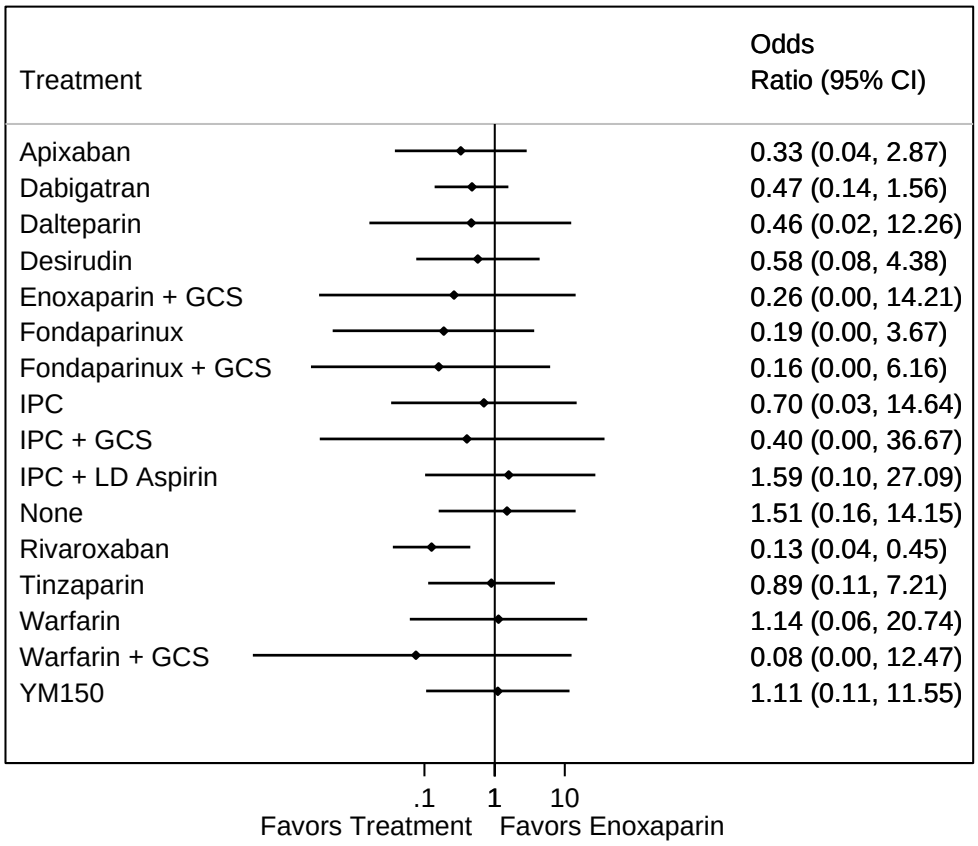
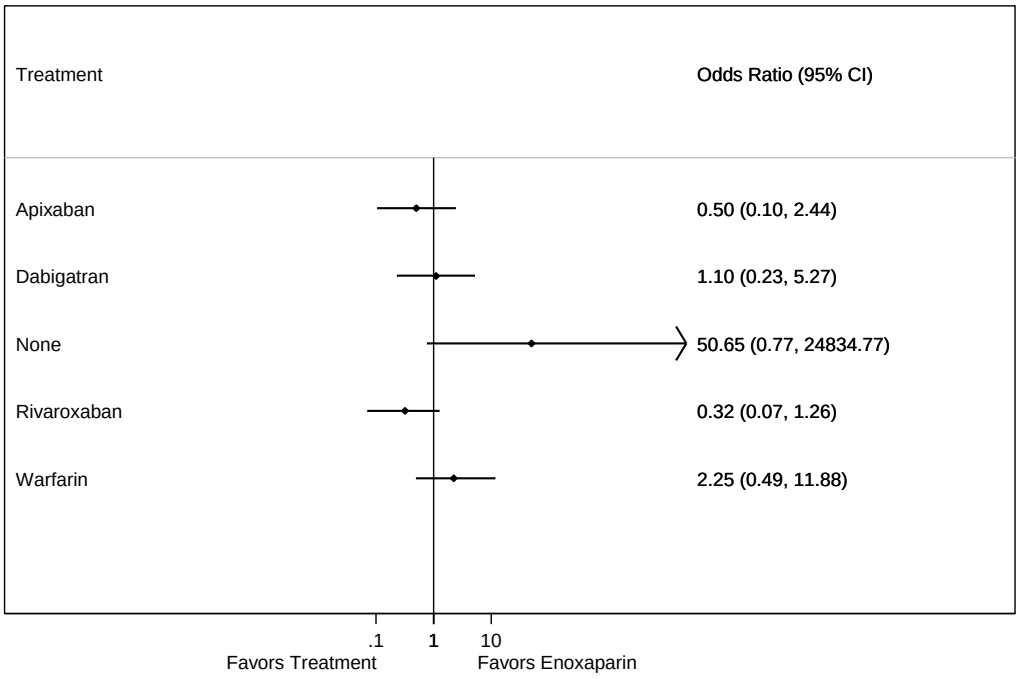


Figure 107. Proximal Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



FINAL MODEL RESULTS – RANKING OF TREATMENTS

The first set of tables below (Table 85 - Table 90) ranks treatments according to the probability that the listed treatment is the best for that particular outcome. These rankings are based on the network meta-analysis of the final model and only includes the treatments included in the final model.

The second set of tables (Table 91- Table 96) presents the same results from the same models but also includes the complete set of probabilities (i.e., probability that a treatment is best, probability that a treatment is second best,… probability that a treatment is the worst) for each outcome.

Table 85. Final Network Meta-Analysis Ranking of Agents - Pulmonary Embolism

Treatment	Probability that Treatment is Best
IPC	56%
LD Aspirin	10%
Tinzaparin	6%
HD Aspirin	6%
Desirudin	6%
None	5%
Enoxaparin + IPC	5%
IPC + LD Aspirin	3%
IPC + HD Aspirin	2%
Rivaroxaban	1%
Dabigatran	0%
Warfarin	0%
Apixaban	0%
Enoxaparin	0%

Table 86. Final Network Meta-Analysis Ranking of Agents - Major Bleeding

Treatment	Probability that Treatment is Best
IPC + LD Aspirin	56%
GCS	16%
YM150	13%
Enoxaparin + GCS	11%
LY517717	2%
HD Aspirin	2%
Fondaparinux + GCS	0%
Warfarin	0%
None	0%
Dalteparin	0%
Tinzaparin	0%
Desirudin	0%
Apixaban	0%

Treatment	Probability that Treatment is Best
Enoxaparin	0%
Dabigatran	0%
Fondaparinux	0%
Rivaroxaban	0%

Table 87. Final Network Meta-Analysis Ranking of Agents – All Cause Mortality

Treatment	Probability that Treatment is Best
Fondaparinux + GCS	27%
Enoxaparin + GCS	23%
Warfarin + GCS	20%
Rivaroxiban	6%
Fondaparinux	6%
IPC + GCS	6%
Dalteparin	6%
Tinzaparin	3%
Dabigatran	2%
Desirudin	2%
Apixaban	1%
Warfarin	0%
Enoxaparin	0%

Table 88. Final Network Meta-Analysis Ranking of Agents – Symptomatic DVT

Treatment	Probability that Treatment is Best
Rivaroxaban	20%
Tinzaparin	17%
Enoxaparin + IPC	17%
LD Aspirin	15%
Apixaban	11%
IPC	7%
Desirudin	5%
None	4%
Dabigatran	3%
Enoxaparin	0%

Table 89. Final Network Meta-Analysis Ranking of Agents - DVT

Treatment	Probability that Treatment is Best
Fondaparinux	62%
Enoxaparin + IPC	13%
HD Aspirin	9%

Treatment	Probability that Treatment is Best
IPC	7%
IPC + HD Aspirin	6%
Rivaroxaban	1%
IPC + LD Aspirin	1%
Desirudin	1%
Apixaban	0%
Dalteparin	0%
YM150	0%
Tinzaparin	0%
None	0%
Dabigatran	0%
Enoxaparin	0%
Warfarin	0%

Table 90. Final Network Meta-Analysis Ranking of Agents – Proximal DVT

Treatment	Probability that Treatment is Best
Warfarin + GCS	38%
Rivaroxaban	23%
Fondaparinux + GCS	16%
Fondaparinux	11%
Desirudin	3%
Apixaban	2%
IPC	2%
IPD + LD Aspirin	2%
Dalteparin	2%
YM150	1%
Enoxaparin + GCS	1%
Dabigatran	0%
Tinzaparin	0%
IPC + GCS	0%
None	0%
Enoxaparin	0%
Warfarin	0%

Table 91. Final Network Meta-Analysis Complete Ranking of Agents - Pulmonary Embolism

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	10	11	12	13	Rank 14 (Worst)
Apixaban	0%	1%	1%	2%	4%	7%	9%	11%	13%	16%	15%	11%	6%	3%
Dabigatran	0%	1%	2%	5%	8%	11%	13%	13%	13%	13%	10%	6%	3%	1%
Desirudin	6%	9%	9%	16%	14%	10%	8%	6%	5%	5%	5%	4%	2%	1%
Enoxaparin	0%	0%	0%	2%	4%	9%	16%	21%	20%	14%	8%	3%	1%	0%
Enoxaparin + IPC	5%	6%	6%	9%	8%	7%	5%	5%	5%	6%	10%	19%	6%	3%
HD Aspirin	6%	5%	3%	5%	4%	3%	2%	2%	2%	2%	4%	7%	21%	35%
IPC	56%	12%	9%	5%	3%	2%	2%	1%	1%	2%	2%	2%	1%	2%
IPC + HD Aspirin	2%	3%	4%	3%	4%	3%	3%	2%	2%	3%	4%	8%	32%	27%
IPC + LD Aspirin	3%	5%	5%	9%	8%	8%	7%	6%	6%	8%	10%	11%	7%	7%
LD Aspirin	10%	23%	21%	9%	6%	4%	3%	3%	3%	3%	4%	4%	3%	3%
None	5%	23%	25%	11%	7%	5%	4%	3%	3%	4%	4%	3%	2%	1%
Rivaroxaban	1%	4%	7%	13%	17%	17%	13%	10%	7%	5%	3%	1%	1%	0%
Tinzaparin	6%	6%	5%	9%	7%	6%	5%	5%	5%	6%	9%	10%	8%	13%
Warfarin	0%	1%	2%	3%	5%	7%	9%	11%	13%	14%	15%	11%	7%	4%

Table 92. Final Network Meta-Analysis Complete Ranking of Agents – Major Bleeding

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Rank 17 (Worst)
Apixaban	0%	0%	1%	3%	6%	10%	13%	15%	16%	13%	9%	6%	4%	2%	1%	1%	0%
Dabigatran	0%	0%	0%	0%	0%	0%	1%	2%	4%	6%	9%	13%	16%	18%	16%	10%	4%
Dalteparin	0%	0%	1%	2%	3%	6%	8%	10%	11%	10%	9%	8%	8%	8%	7%	6%	4%
Desirudin	0%	0%	1%	2%	3%	5%	7%	9%	9%	10%	10%	10%	9%	9%	7%	6%	4%
Enoxaparin	0%	0%	0%	0%	0%	1%	4%	7%	12%	17%	21%	19%	12%	6%	1%	0%	0%
Enoxaparin + GCS	11%	21%	20%	12%	6%	4%	3%	2%	2%	2%	2%	2%	2%	3%	6%	3%	0%
Fondaparinux	0%	0%	0%	0%	0%	1%	2%	3%	4%	5%	5%	7%	9%	13%	14%	19%	17%
Fondaparinux + GCS	0%	5%	14%	18%	12%	7%	4%	3%	2%	2%	2%	2%	2%	3%	4%	9%	9%
GCS	16%	17%	14%	9%	6%	3%	2%	2%	2%	1%	1%	1%	2%	2%	3%	5%	14%
HD Aspirin	2%	11%	14%	12%	14%	14%	8%	5%	4%	3%	2%	2%	2%	2%	2%	2%	2%
IPC + LD Aspirin	56%	18%	9%	10%	5%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
LY517717	2%	7%	8%	6%	7%	7%	5%	4%	3%	3%	3%	3%	3%	4%	4%	7%	23%
None	0%	1%	1%	3%	5%	7%	9%	10%	9%	9%	9%	9%	8%	7%	6%	5%	3%
Rivaroxaban	0%	0%	0%	0%	0%	0%	1%	1%	2%	4%	6%	9%	12%	15%	18%	18%	12%
Tinzaparin	0%	0%	1%	2%	4%	6%	9%	10%	11%	10%	9%	8%	8%	7%	6%	5%	3%
Warfarin	0%	1%	7%	13%	15%	20%	20%	13%	6%	3%	1%	1%	0%	0%	0%	0%	0%
YM150	13%	19%	10%	8%	12%	7%	4%	3%	2%	2%	2%	2%	2%	2%	2%	4%	6%

Table 93. Final Network Meta-Analysis Complete Ranking of Agents – All Cause Mortality

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	10	11	12	Rank 13 (Worst)
Apixaban	1%	2%	2%	3%	5%	8%	11%	12%	14%	13%	13%	11%	6%
Dabigatran	2%	2%	3%	4%	6%	10%	11%	12%	12%	11%	11%	10%	5%
Dalteparin	6%	3%	3%	4%	5%	10%	7%	6%	7%	7%	10%	12%	19%
Desirudin	2%	2%	2%	3%	4%	6%	6%	7%	7%	9%	12%	15%	26%
Enoxaparin	0%	1%	3%	5%	7%	10%	18%	21%	17%	11%	5%	1%	0%
Enoxaparin + GCS	23%	31%	18%	8%	4%	2%	2%	2%	3%	3%	3%	1%	1%
Fondaparinux	6%	5%	15%	13%	24%	7%	5%	4%	5%	4%	5%	4%	3%
Fondaparinux + GCS	27%	29%	16%	10%	3%	2%	2%	2%	3%	2%	2%	1%	0%
IPC + GCS	6%	9%	16%	20%	10%	4%	3%	3%	3%	4%	5%	11%	8%
Rivaroxiban	6%	6%	7%	10%	12%	23%	15%	9%	5%	3%	2%	1%	0%
Tinzaparin	3%	3%	3%	4%	6%	9%	9%	8%	8%	10%	12%	14%	13%
Warfarin	0%	1%	2%	3%	4%	6%	9%	12%	14%	18%	17%	11%	3%
Warfarin + GCS	20%	6%	10%	13%	10%	3%	2%	2%	3%	3%	4%	8%	15%

Table 94. Final Network Meta-Analysis Complete Ranking of Agents – Symptomatic DVT

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	Rank 10 (Worst)
Apixaban	11%	19%	21%	18%	14%	9%	5%	2%	1%	0%
Dabigatran	3%	7%	11%	14%	15%	16%	14%	10%	8%	3%
Desirudin	5%	7%	8%	8%	9%	12%	14%	11%	14%	13%
Enoxaparin	0%	0%	3%	10%	18%	21%	20%	16%	9%	2%
Enoxaparin + IPC	17%	8%	7%	7%	6%	7%	10%	7%	11%	19%
IPC	7%	5%	6%	5%	5%	5%	6%	9%	14%	40%
LD Aspirin	15%	11%	9%	7%	6%	6%	8%	15%	14%	8%
None	4%	11%	11%	9%	8%	8%	10%	17%	19%	5%
Rivaroxaban	20%	20%	16%	13%	11%	8%	6%	4%	2%	1%
Tinzaparin	17%	12%	10%	9%	8%	9%	9%	8%	9%	8%

Table 95. Final Network Meta-Analysis Complete Ranking of Agents – DVT

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Rank 16 (Worst)
Apixaban	0%	2%	5%	9%	14%	19%	21%	15%	9%	4%	2%	1%	0%	0%	0%	0%
Dabigatran	0%	0%	0%	0%	1%	3%	6%	11%	17%	20%	17%	12%	8%	4%	1%	0%
Dalteparin	0%	1%	2%	3%	5%	7%	9%	12%	13%	11%	9%	9%	9%	6%	3%	0%
Desirudin	1%	2%	4%	6%	9%	11%	14%	14%	12%	8%	6%	5%	4%	2%	1%	1%
Enoxaparin	0%	0%	0%	0%	0%	0%	1%	3%	8%	18%	26%	25%	14%	4%	1%	0%
Enoxaparin + IPC	13%	28%	21%	14%	8%	5%	3%	2%	2%	1%	1%	1%	0%	0%	0%	0%
Fondaparinux	62%	12%	8%	8%	4%	2%	2%	1%	1%	1%	0%	0%	0%	0%	0%	0%
HD Aspirin	9%	12%	11%	11%	7%	6%	6%	5%	4%	3%	3%	3%	4%	4%	4%	7%
IPC	7%	14%	10%	10%	12%	9%	8%	7%	5%	4%	3%	3%	3%	2%	2%	0%
IPC + HD Aspirin	6%	16%	20%	14%	9%	7%	6%	5%	3%	3%	2%	2%	2%	2%	2%	1%
IPC + LD Aspirin	1%	2%	3%	3%	5%	5%	6%	7%	8%	7%	6%	7%	9%	10%	9%	11%
None	0%	0%	0%	0%	1%	1%	2%	4%	5%	5%	6%	8%	12%	16%	18%	21%
Rivaroxaban	1%	9%	15%	18%	23%	19%	9%	3%	1%	0%	0%	0%	0%	0%	0%	0%
Tinzaparin	0%	0%	0%	0%	0%	1%	1%	2%	4%	6%	8%	12%	18%	23%	18%	5%
Warfarin	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	1%	2%	6%	14%	31%	45%
YM150	0%	1%	1%	2%	3%	4%	6%	8%	9%	9%	8%	9%	11%	11%	10%	8%

Table 96. Final Network Meta-Analysis Complete Ranking of Agents – Proximal DVT

Treatment	Rank 1 (Best)	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Rank 17 (Worst)
Apixaban	2%	6%	8%	9%	9%	11%	16%	14%	10%	7%	4%	2%	1%	1%	0%	0%	0%
Dabigatran	0%	1%	3%	6%	7%	9%	12%	15%	17%	13%	8%	5%	2%	1%	0%	0%	0%
Dalteparin	2%	3%	4%	4%	5%	6%	8%	9%	9%	9%	9%	8%	8%	7%	5%	3%	2%
Desirudin	3%	5%	5%	6%	7%	8%	11%	11%	10%	8%	7%	6%	5%	4%	3%	2%	1%
Enoxaparin	0%	0%	0%	0%	1%	2%	4%	6%	9%	14%	20%	20%	15%	7%	2%	0%	0%
Enoxaparin + GCS	1%	7%	16%	18%	10%	7%	5%	5%	4%	4%	4%	4%	4%	4%	4%	4%	1%
Fondaparinux	11%	15%	16%	15%	12%	7%	5%	4%	3%	3%	2%	2%	2%	1%	1%	0%	0%
Fondaparinux + GCS	16%	26%	17%	9%	6%	5%	4%	3%	3%	2%	2%	2%	2%	2%	1%	0%	0%
IPC	2%	2%	2%	3%	3%	4%	5%	6%	6%	6%	6%	7%	8%	9%	11%	12%	7%
IPC + GCS	0%	2%	2%	6%	15%	8%	6%	5%	5%	4%	4%	4%	4%	5%	6%	8%	15%
IPD + LD Aspirin	2%	2%	2%	2%	3%	3%	4%	4%	5%	5%	5%	6%	6%	8%	9%	10%	22%
None	0%	0%	0%	0%	0%	0%	1%	1%	2%	3%	4%	5%	7%	10%	15%	24%	28%
Rivaroxaban	23%	17%	11%	10%	11%	18%	6%	2%	1%	0%	0%	0%	0%	0%	0%	0%	0%
Tinzaparin	0%	0%	1%	1%	2%	3%	4%	6%	7%	9%	11%	12%	13%	12%	9%	6%	3%
Warfarin	0%	0%	0%	0%	0%	0%	1%	1%	2%	3%	5%	8%	12%	18%	20%	18%	11%
Warfarin + GCS	38%	11%	9%	8%	5%	4%	3%	3%	2%	2%	2%	2%	2%	2%	2%	3%	1%
YM150	1%	2%	3%	3%	3%	4%	5%	6%	6%	7%	7%	7%	8%	9%	9%	9%	10%

SENSITIVITY ANALYSIS RESULTS

PULMONARY EMBOLISM

Figure 108. Pulmonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

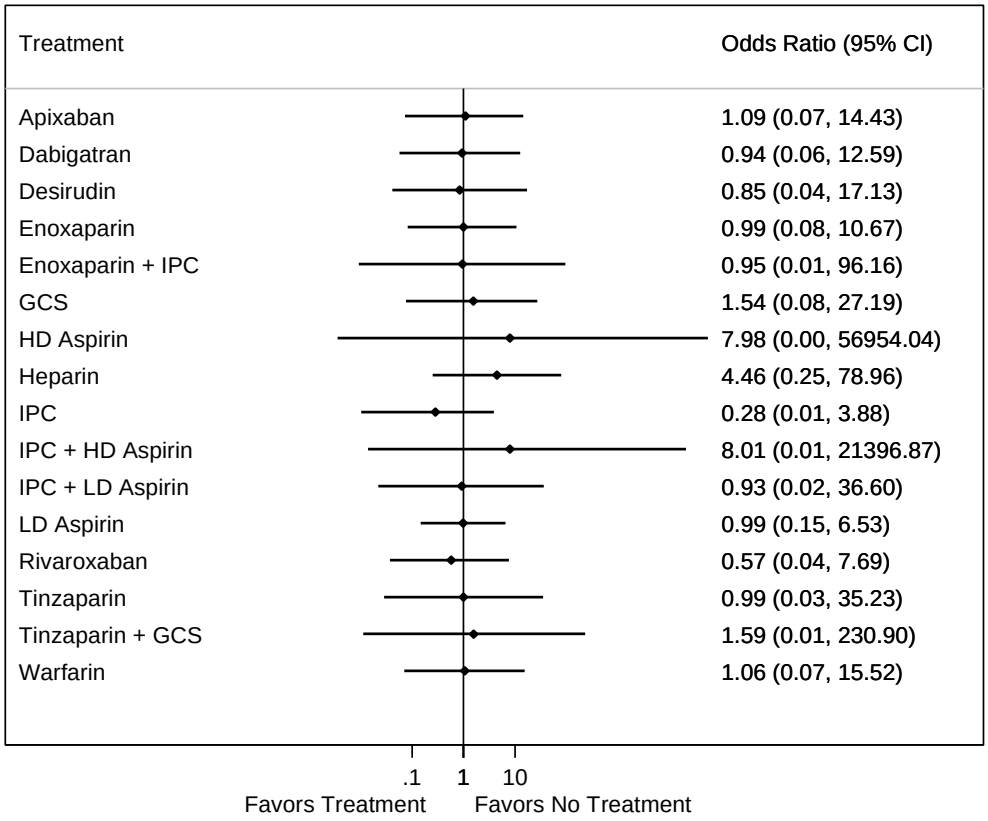


Figure 109. Pulmonary Embolism among Hip Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

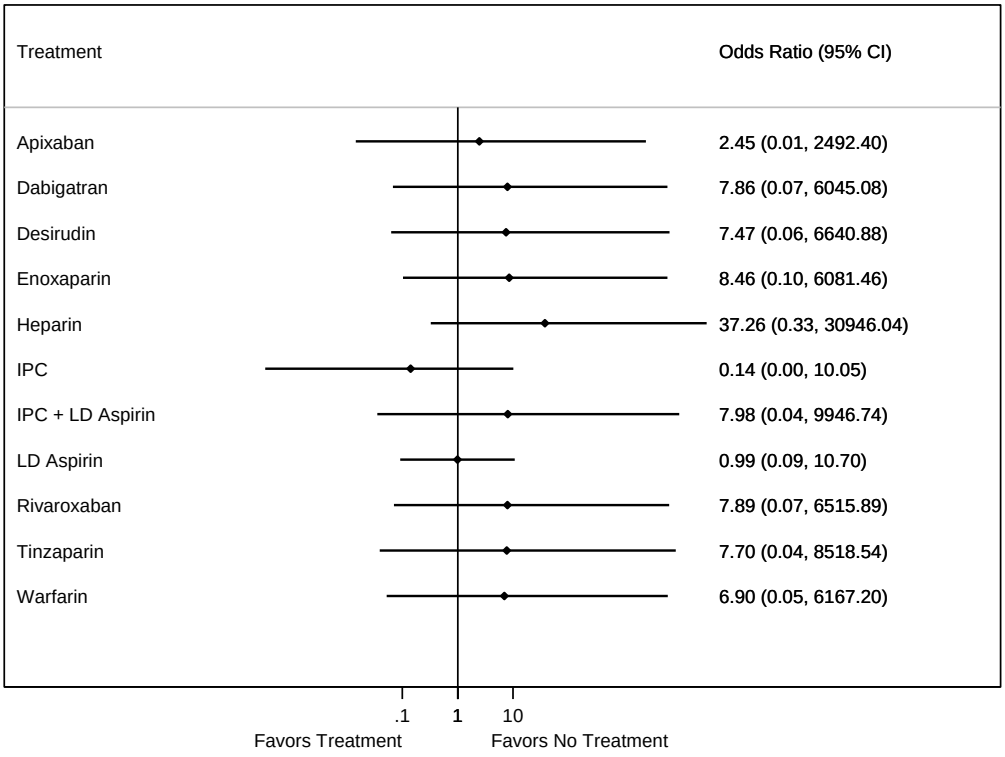


Figure 110. Pulmonary Embolism among Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

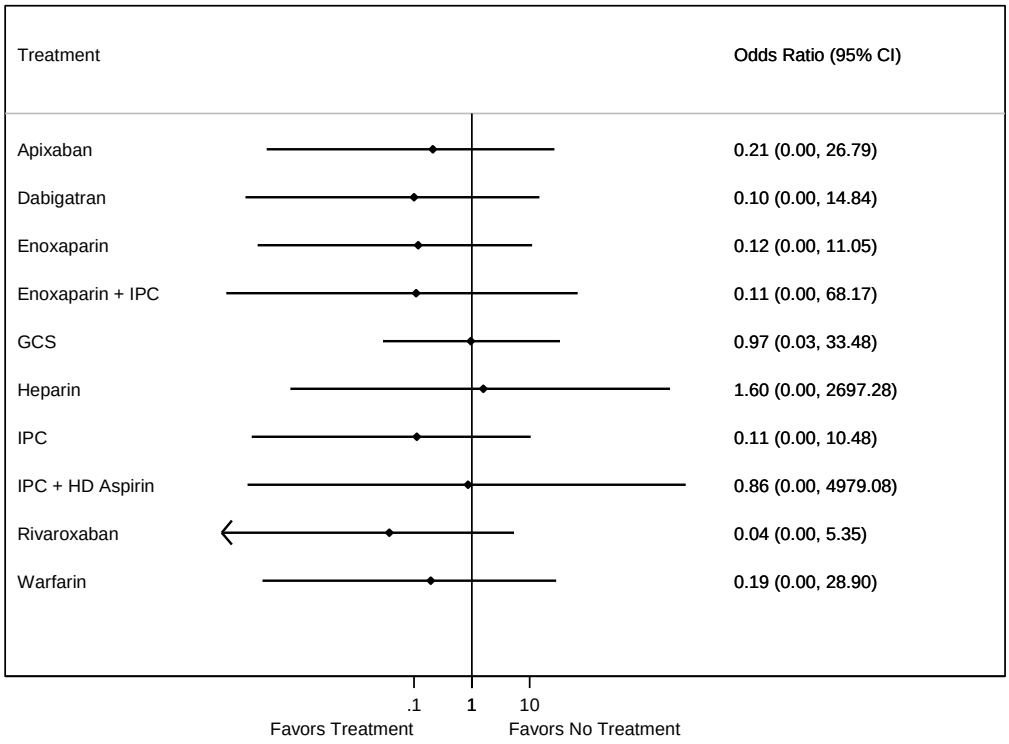


Figure 111. Pulmonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

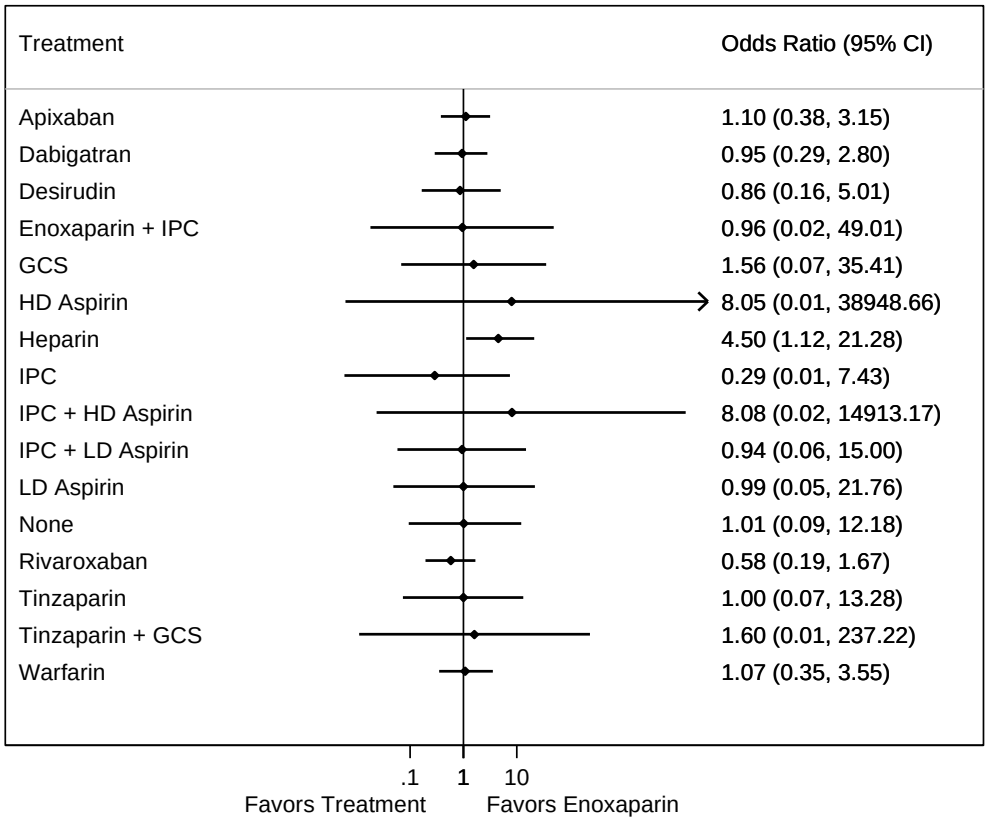


Figure 112. Pulmonary Embolism among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

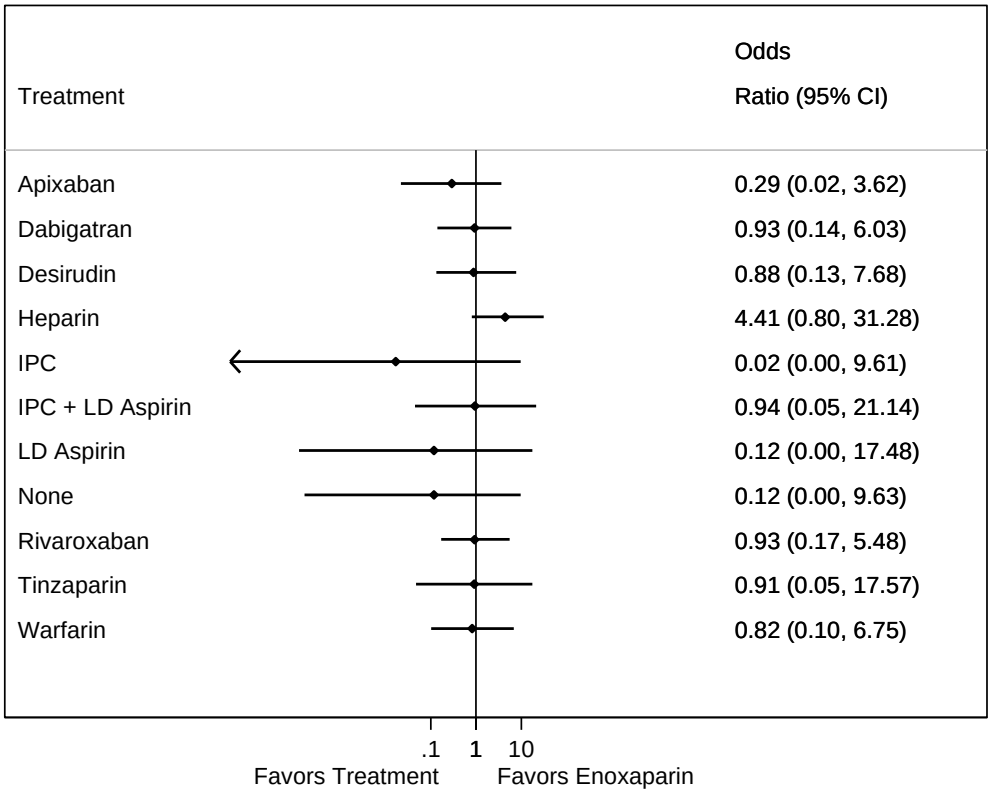


Figure 113. Pulmonary Embolism among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

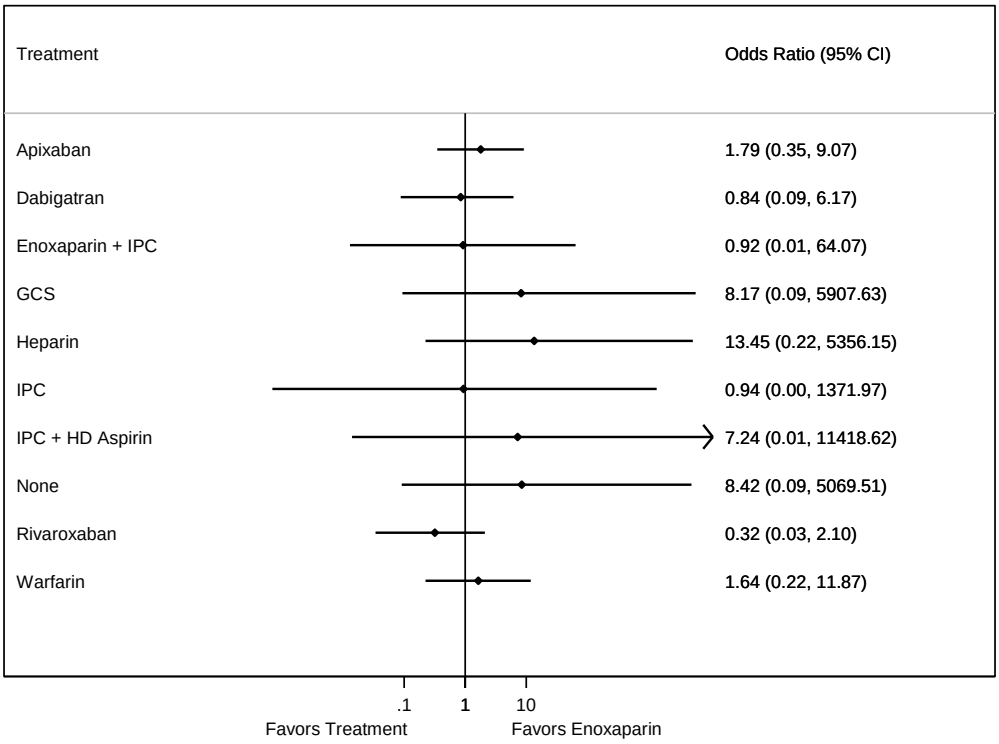


Figure 114. Pulmonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

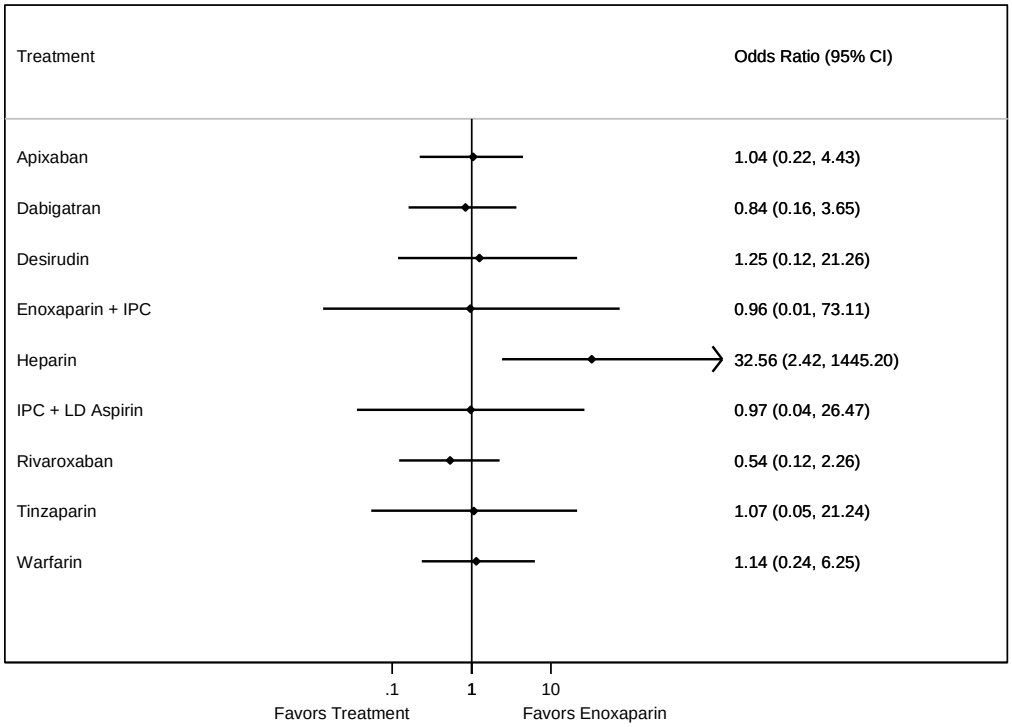


Figure 115. Pulmonary Embolism among Hip Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

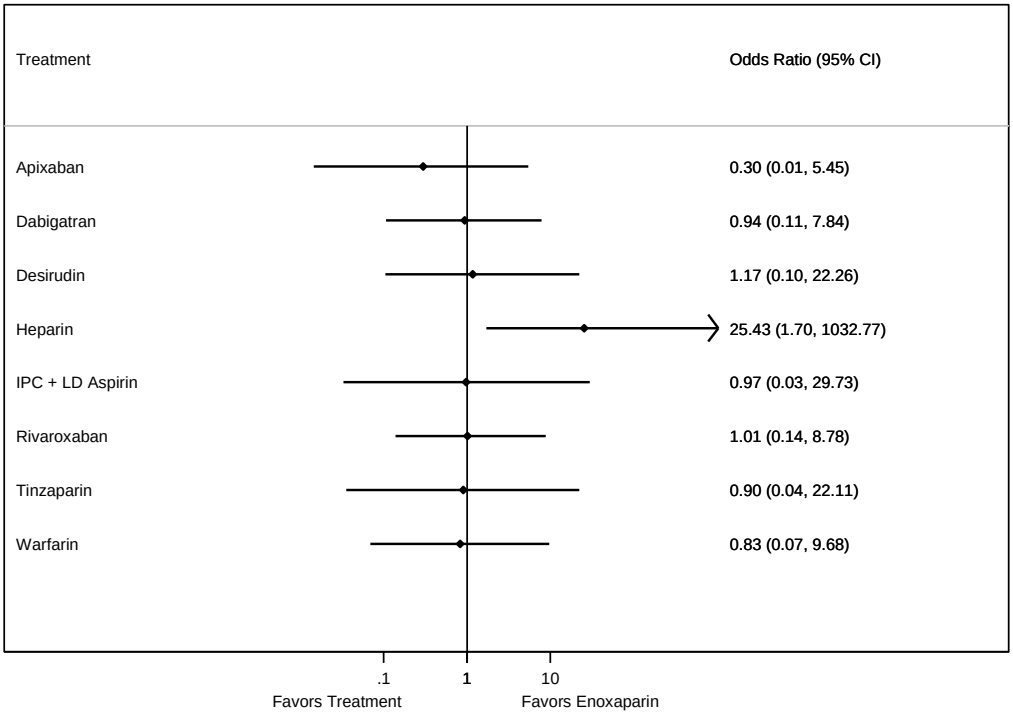


Figure 116. Pulmonary Embolism among Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

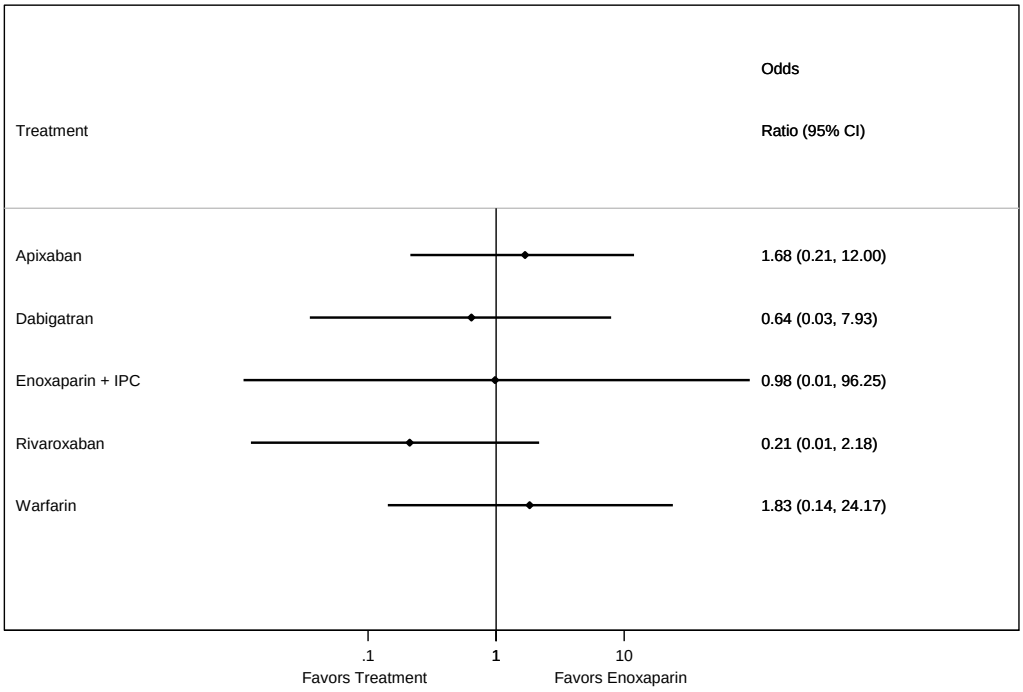


Figure 117. Pulmonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

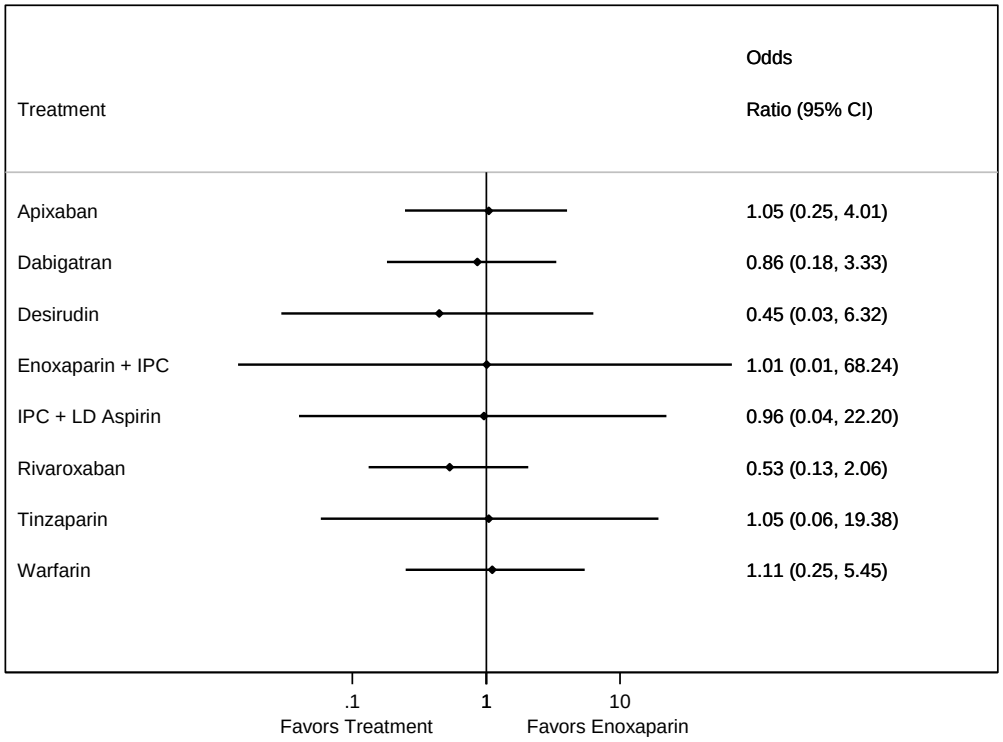


Figure 118. Pulmonary Embolism among Hip Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

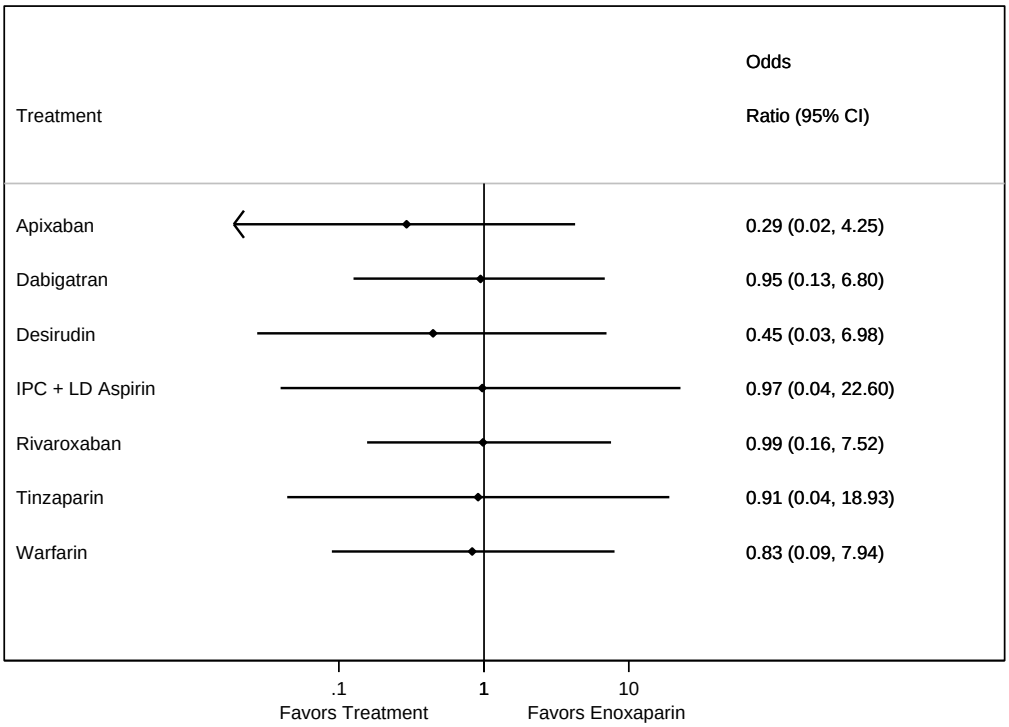


Figure 119. Pulmonary Embolism among Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

Same as prior model

Figure 120. Pulmonary Embolism among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

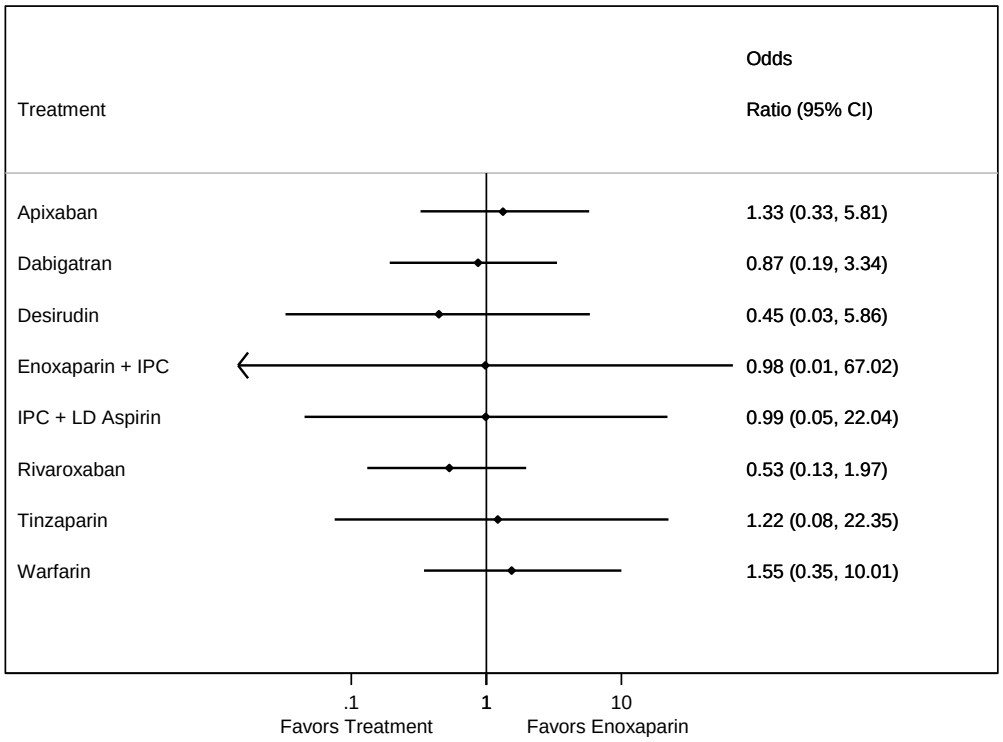
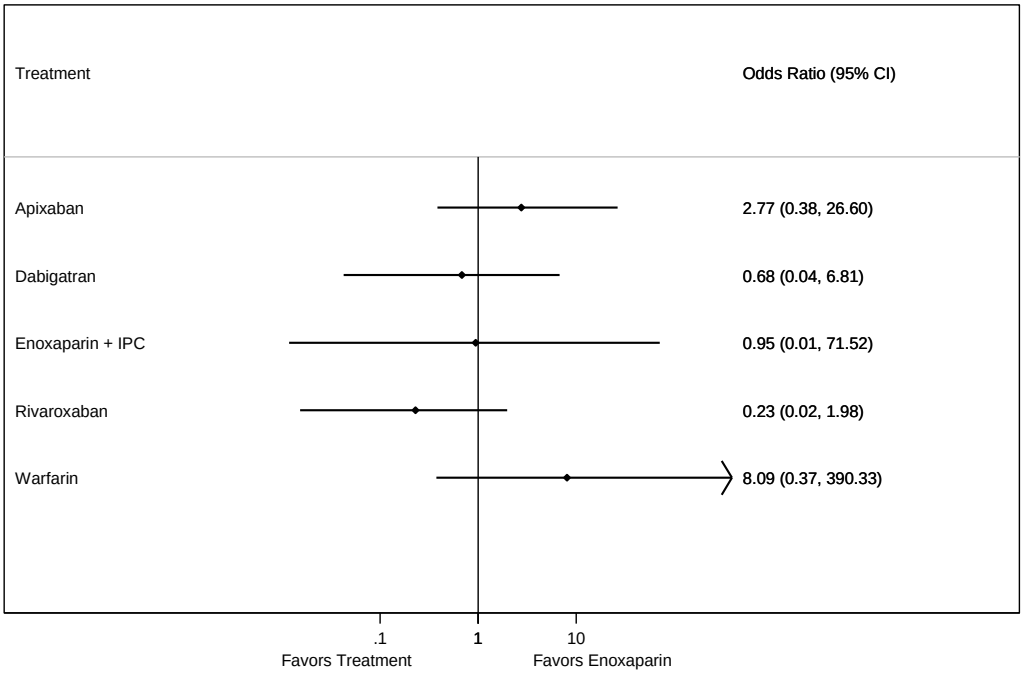


Figure 121. Pulmonary Embolism among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 122. Pulmonary Embolism among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



MAJOR BLEEDING

Figure 123. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

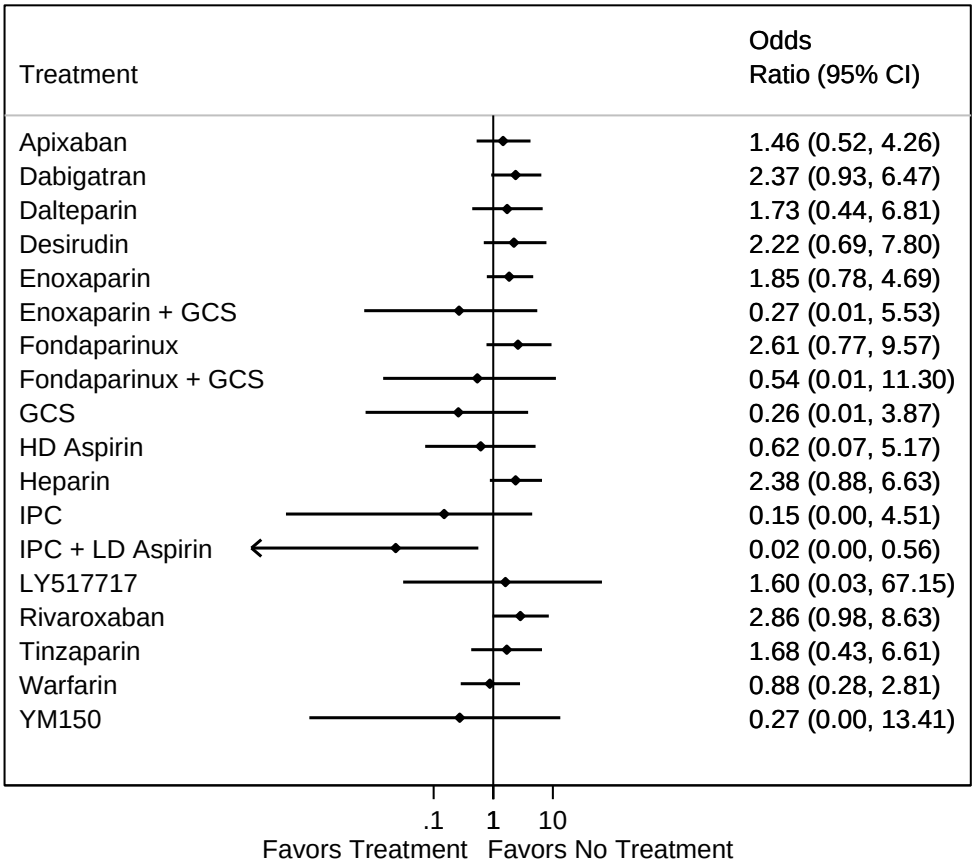


Figure 124. Major Bleeding among Hip Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

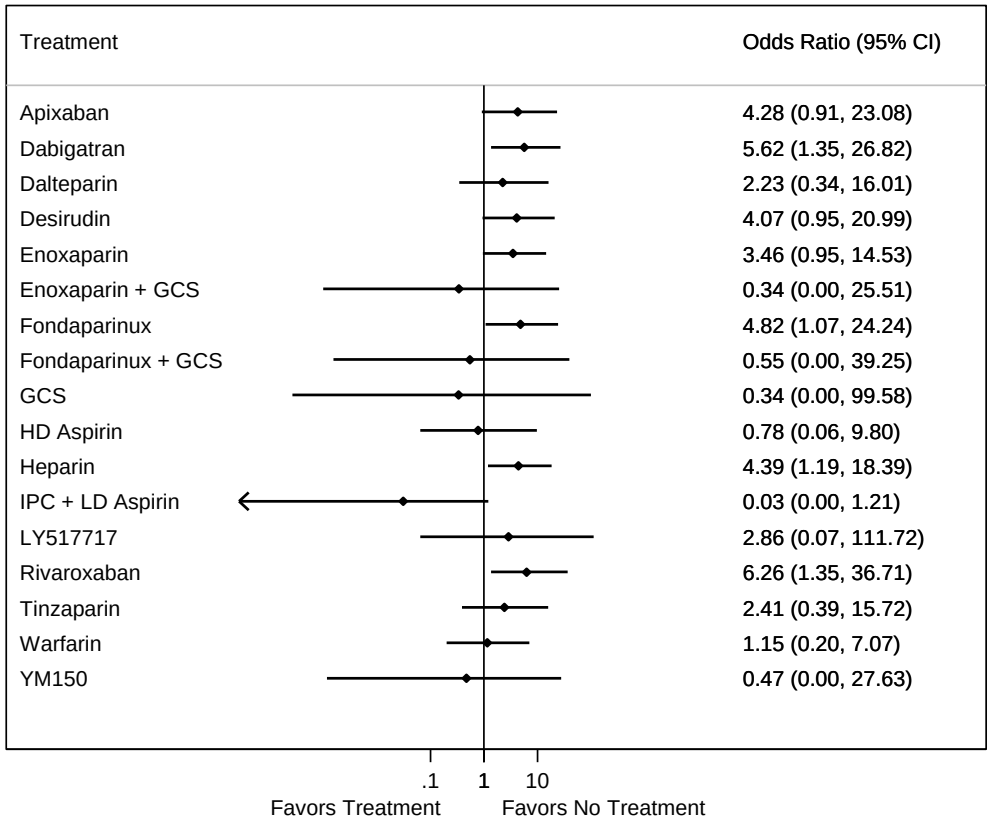


Figure 125. Major Bleeding among Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

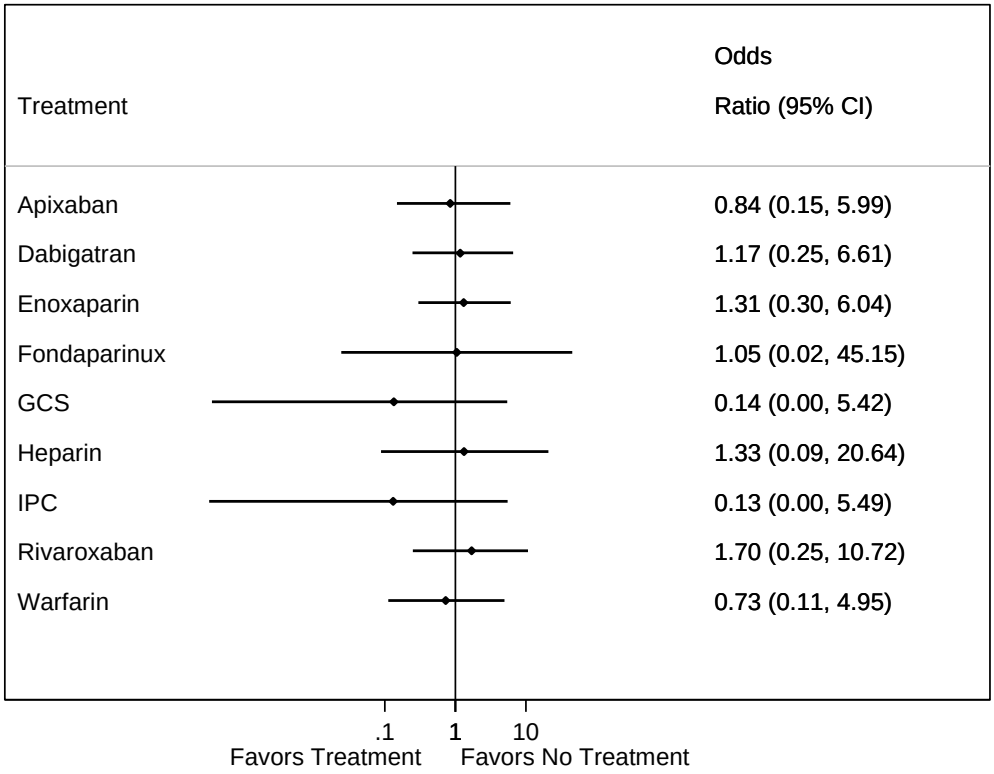


Figure 126. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

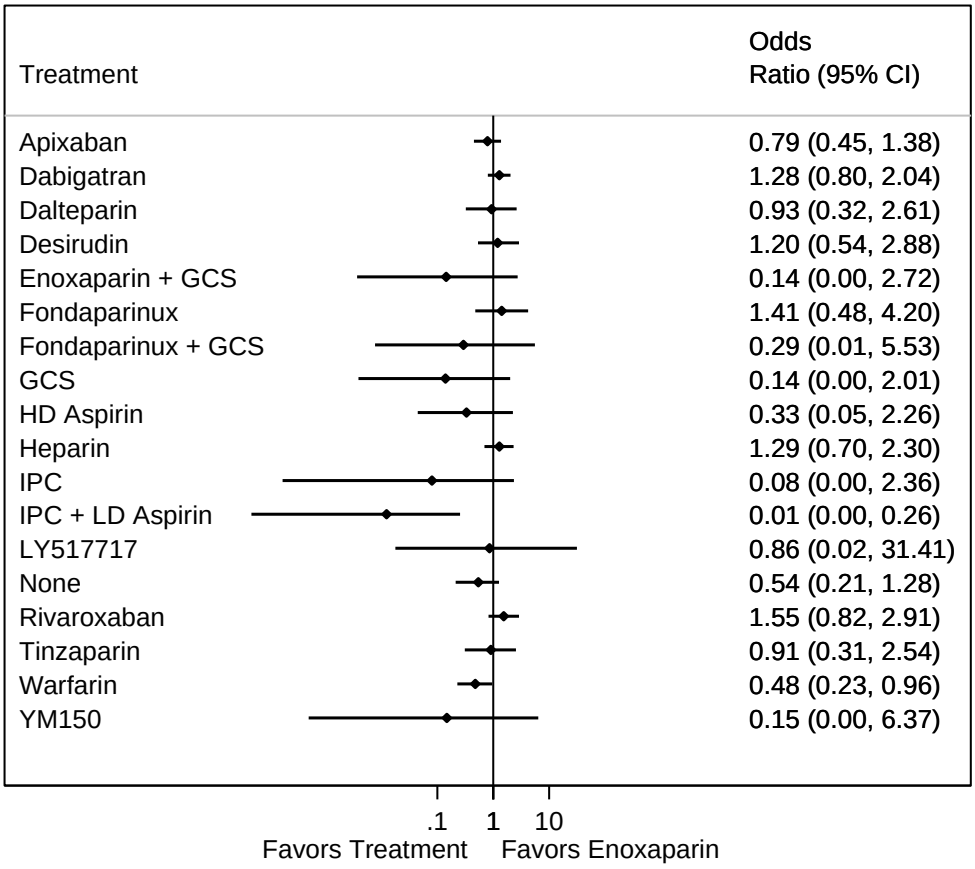


Figure 127. Major Bleeding among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

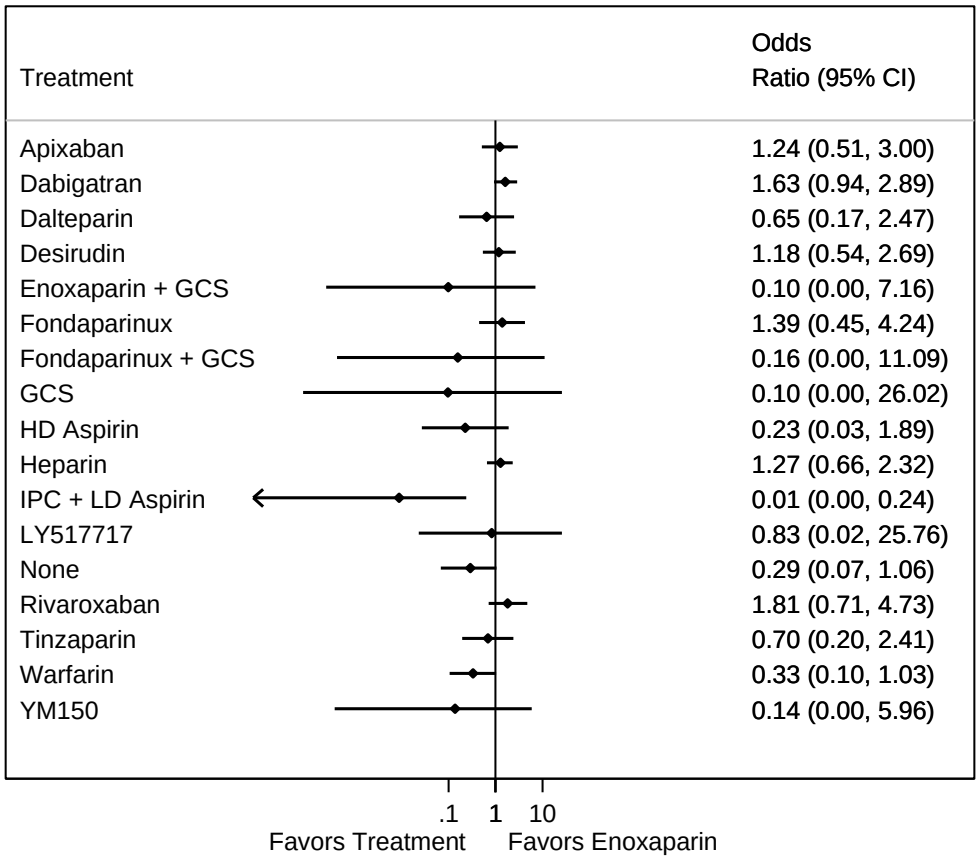


Figure 128. Major Bleeding among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

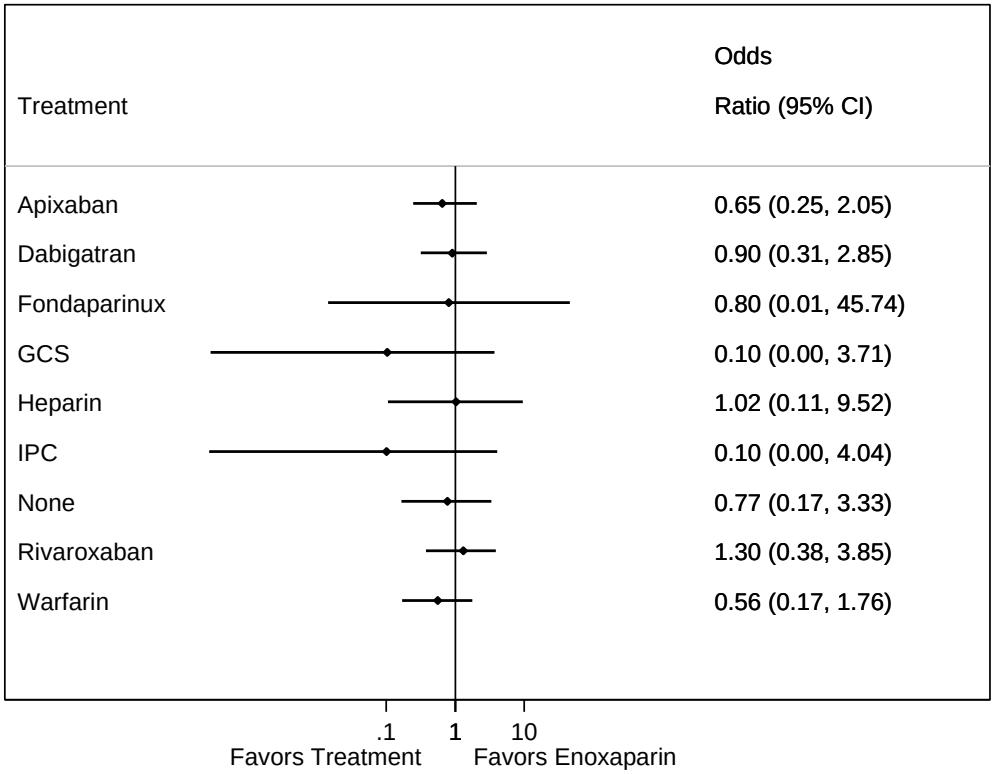


Figure 129. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

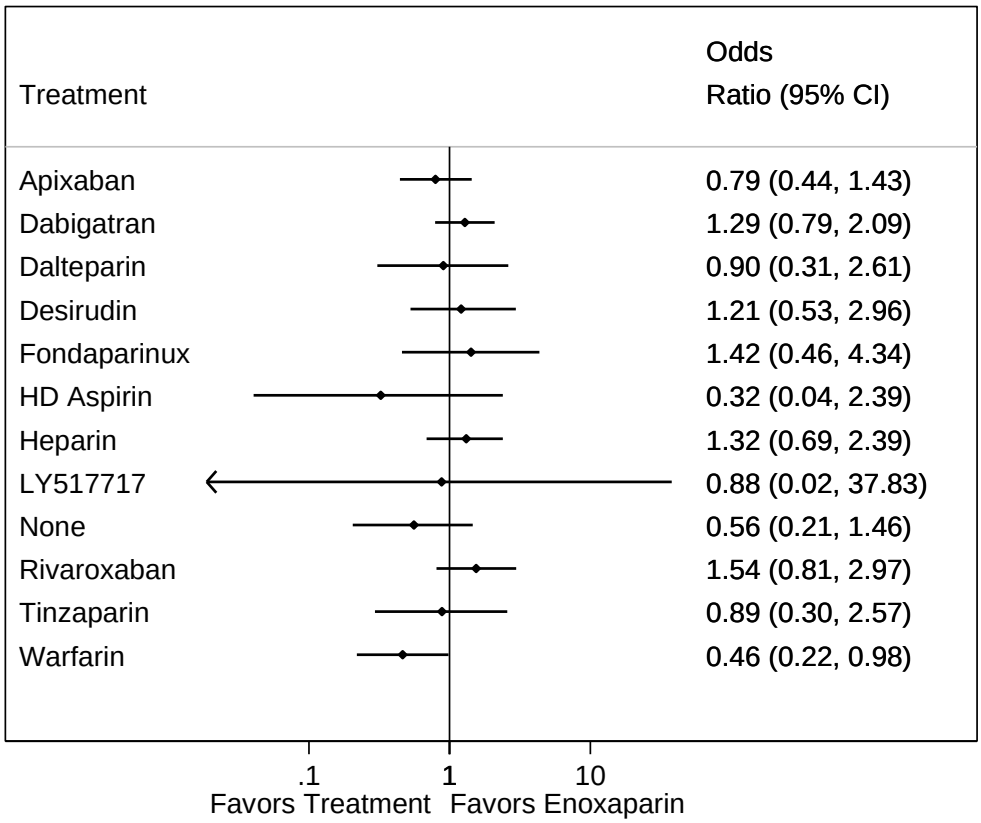


Figure 130. Major Bleeding among Hip Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

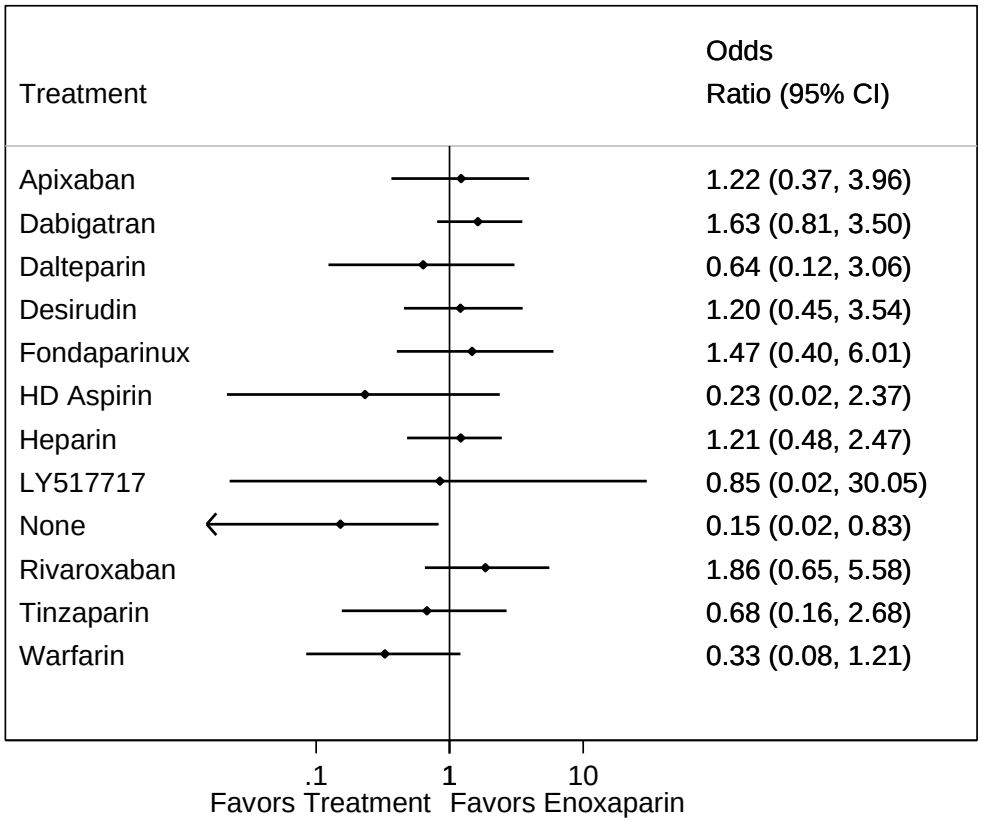


Figure 131. Major Bleeding among Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

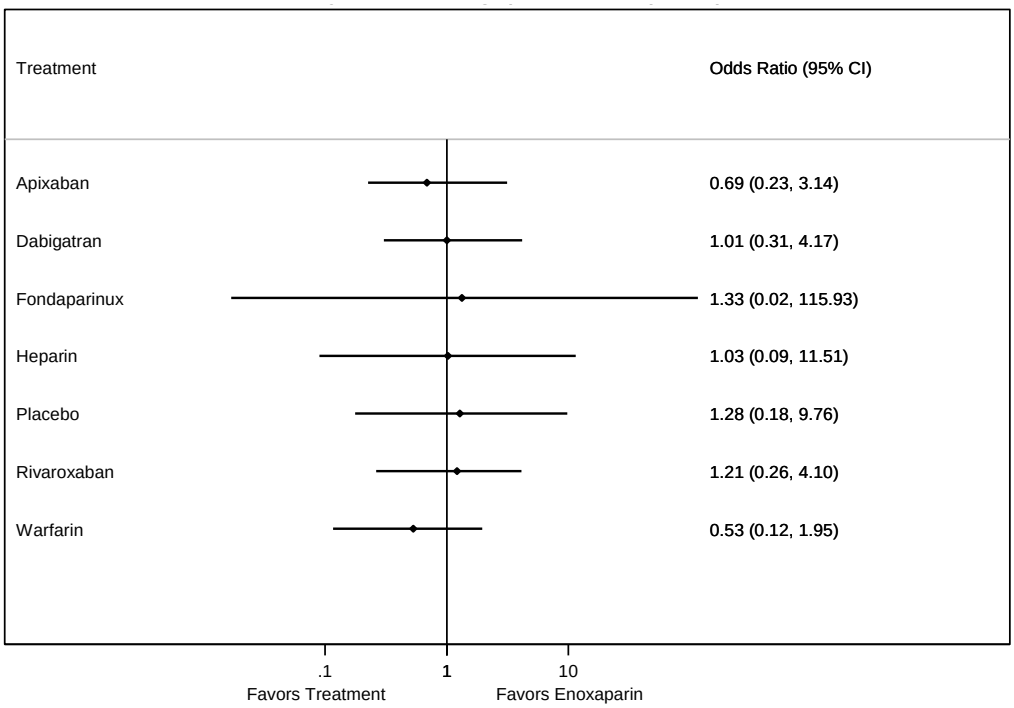


Figure 132. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

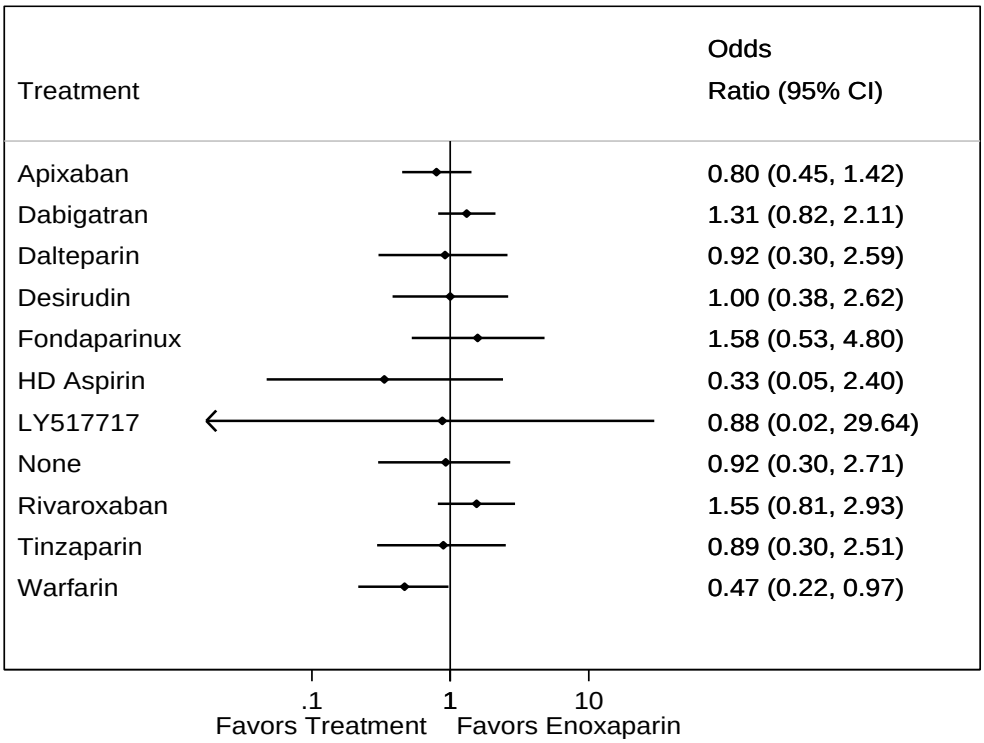


Figure 133. Major Bleeding among Hip Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

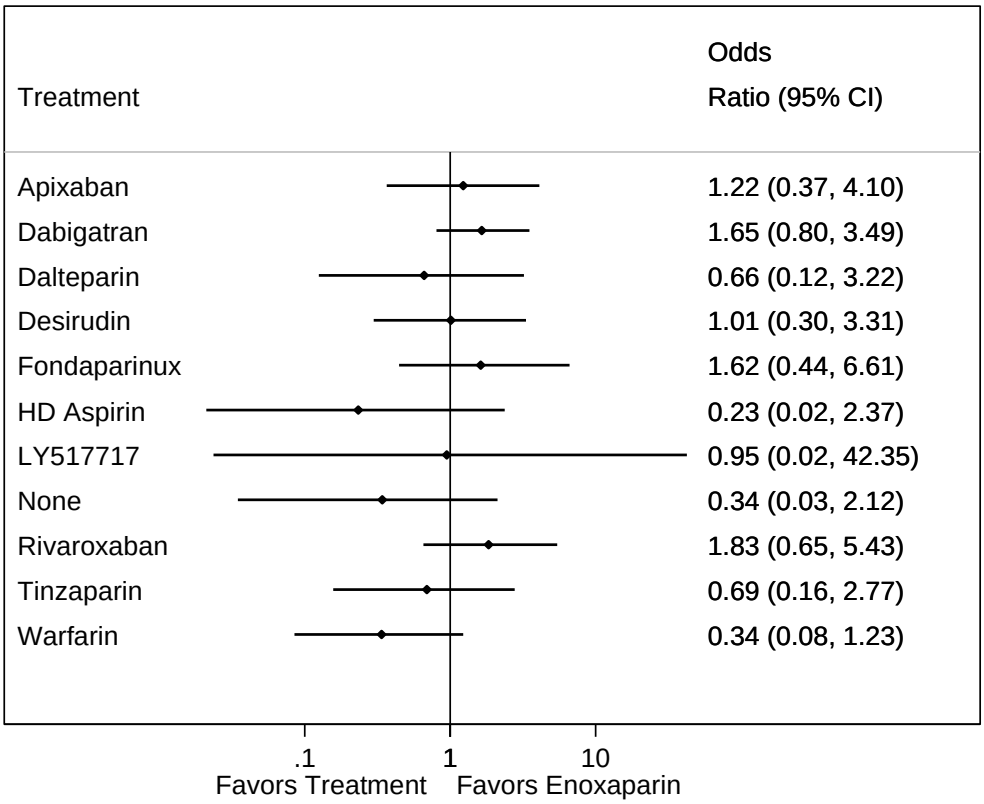


Figure 134. Major Bleeding among Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

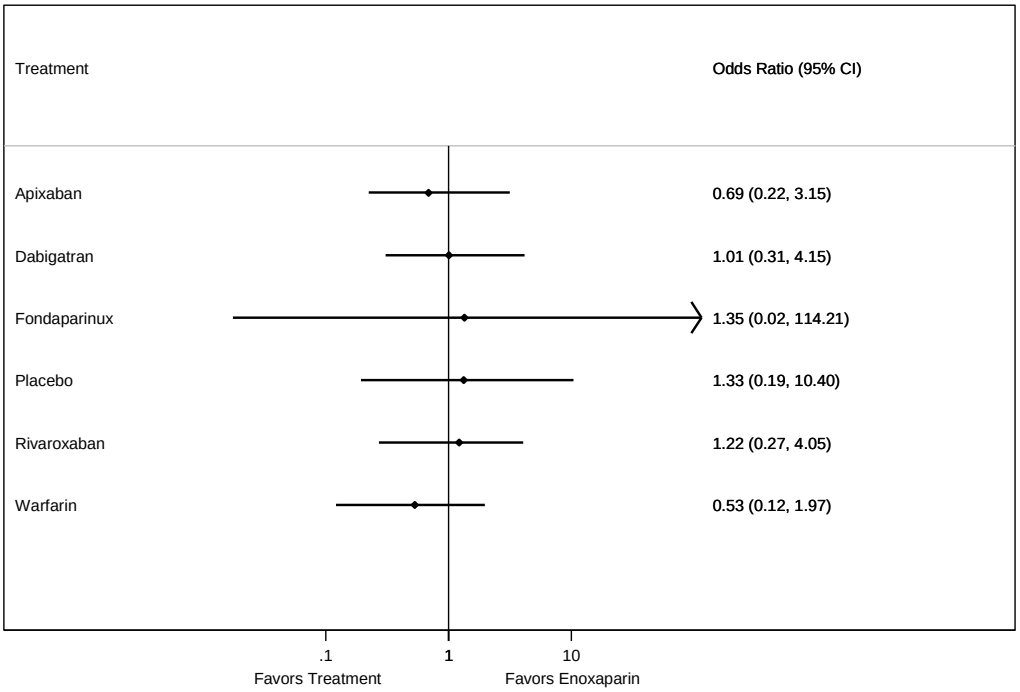


Figure 135. Major Bleeding among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

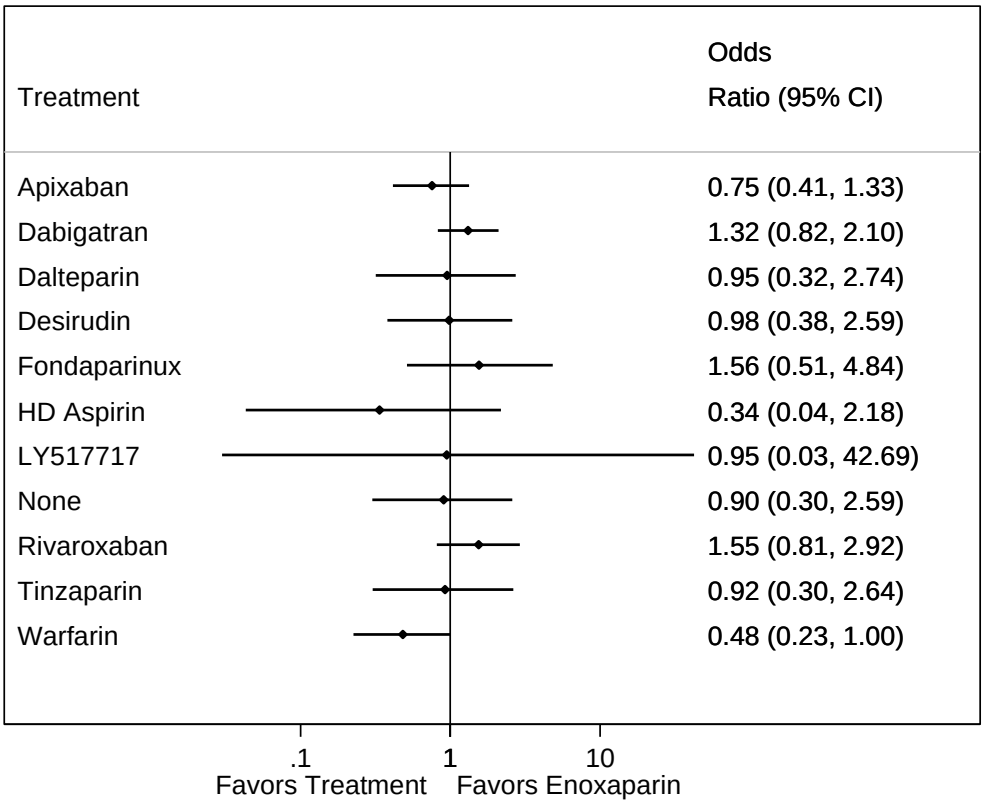
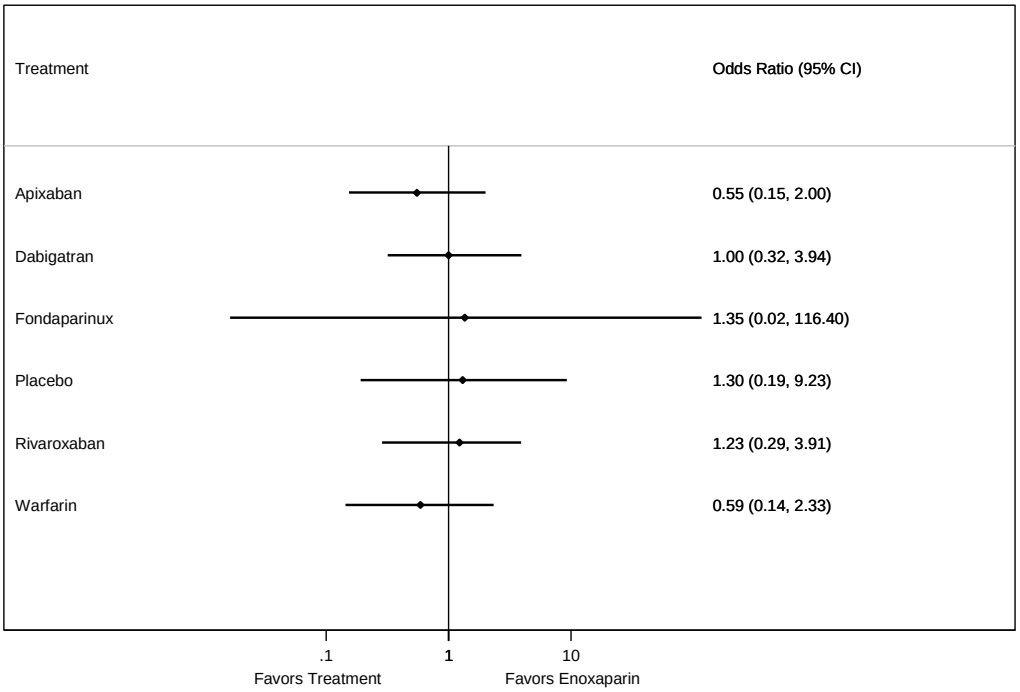


Figure 136. Major Bleeding among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 137. Major Bleeding among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



ALL CAUSE MORTALITY

Figure 138. All Cause Mortality among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

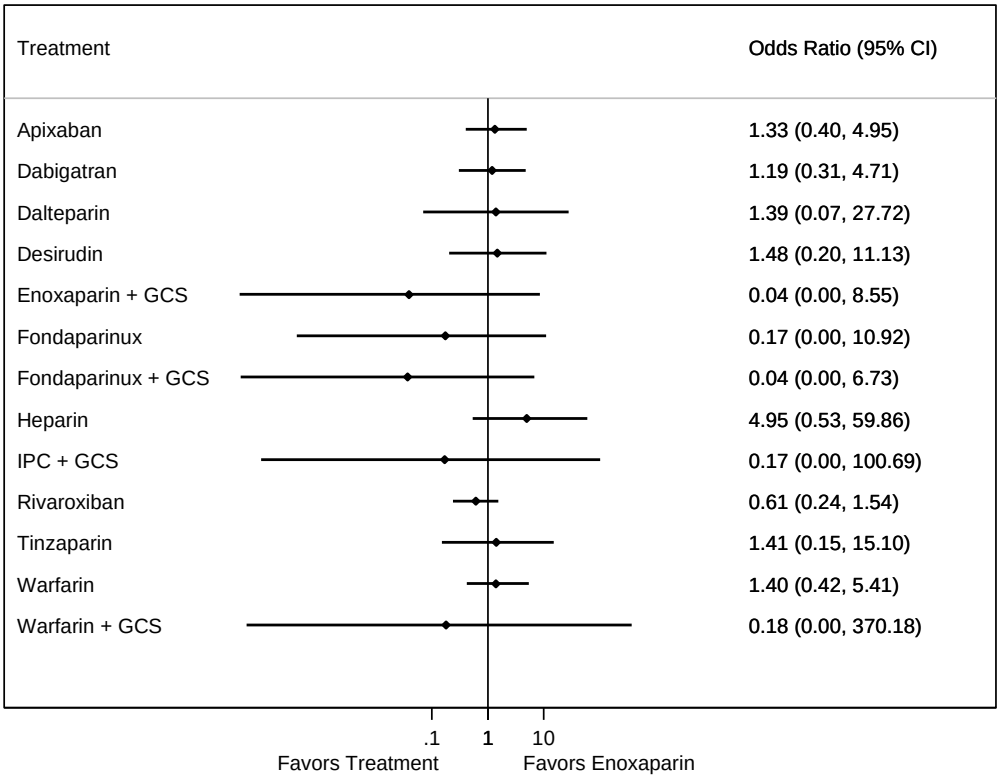


Figure 139. All Cause Mortality among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

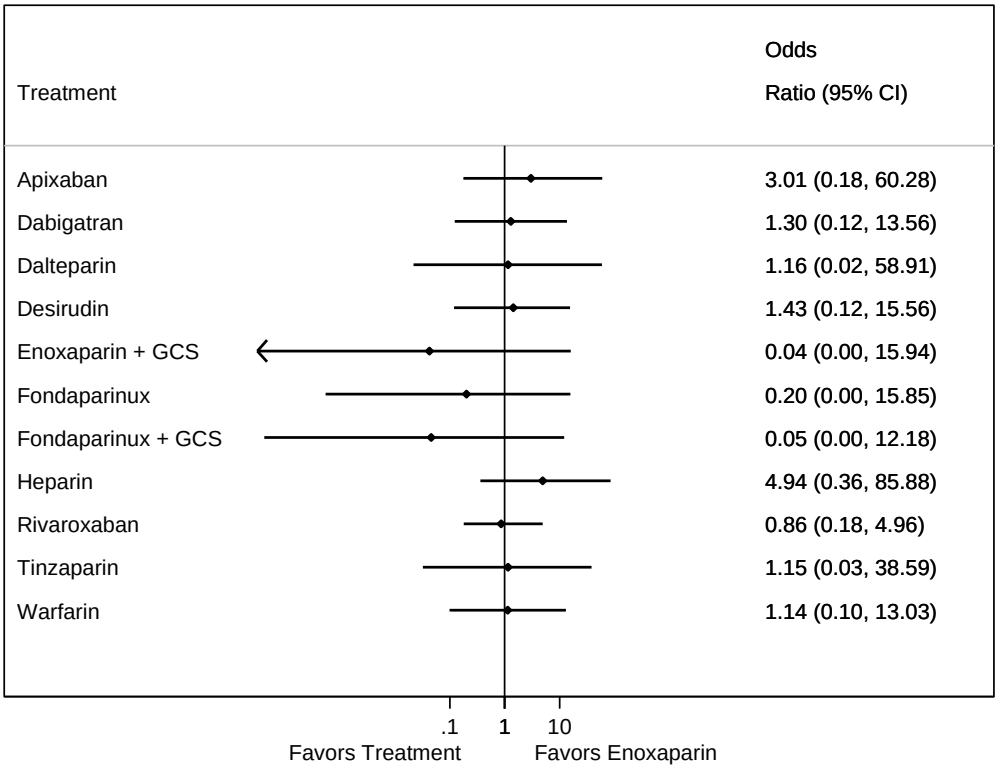


Figure 140. All Cause Mortality among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

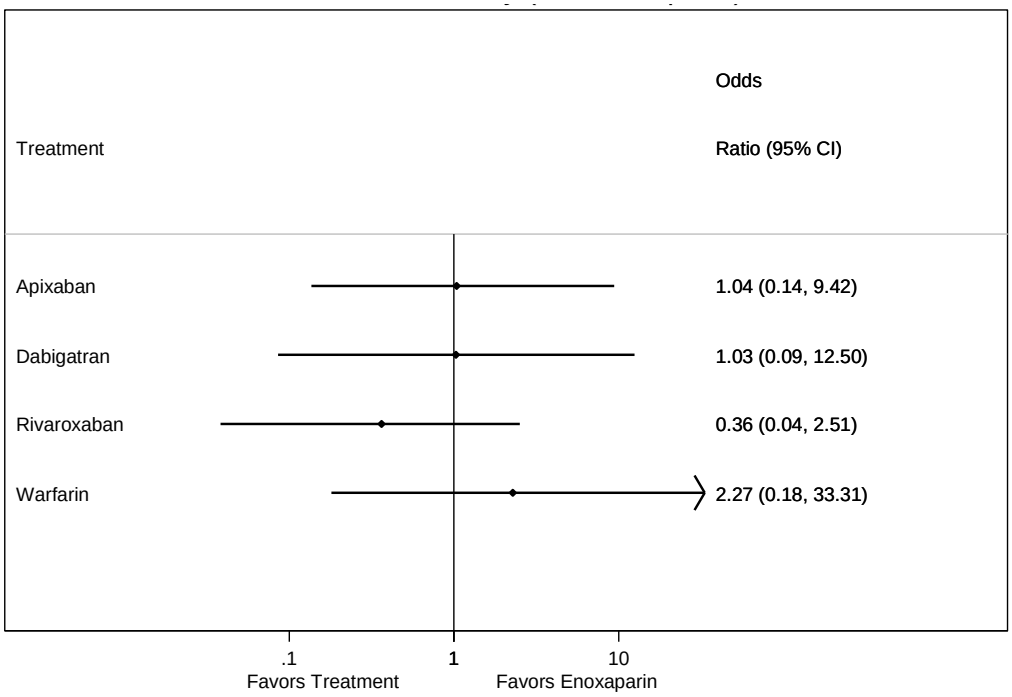


Figure 141. All Cause Mortality among Hip and Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

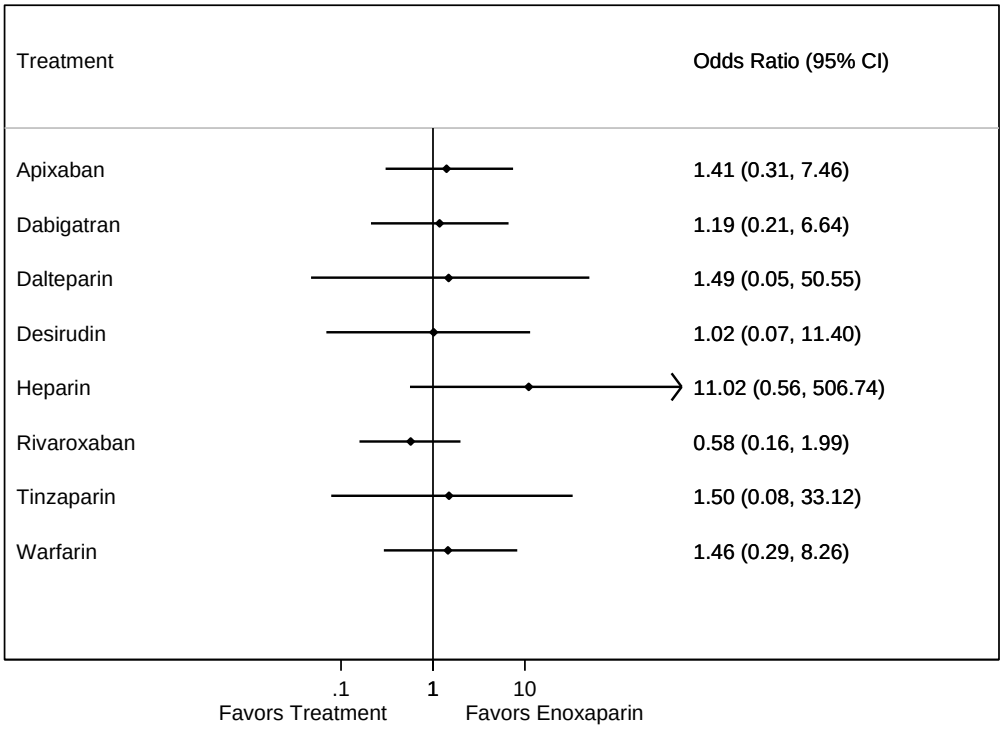


Figure 142. All Cause Mortality among Hip Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

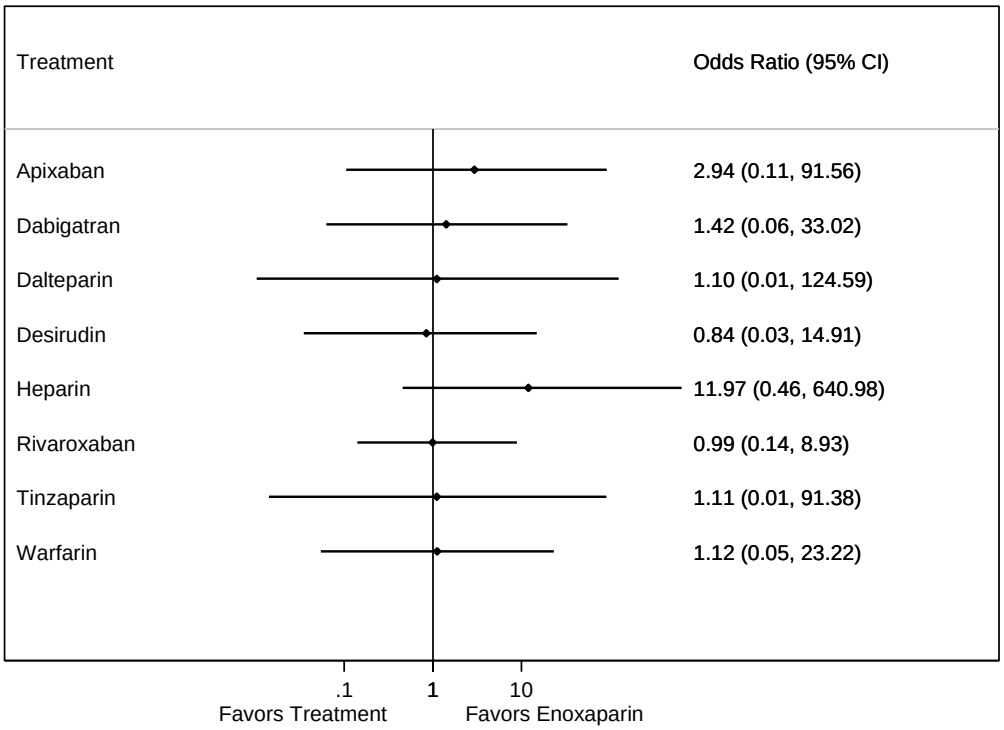


Figure 143. All Cause Mortality among Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

Same as prior model

Figure 144. All Cause Mortality among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

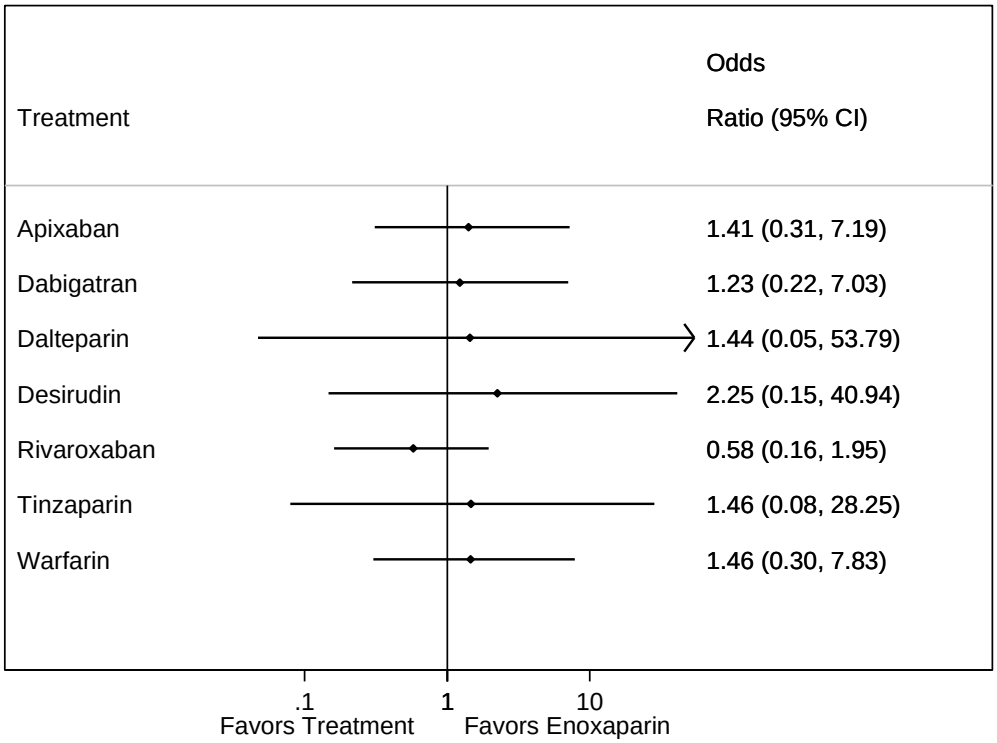


Figure 145. All Cause Mortality among Hip Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

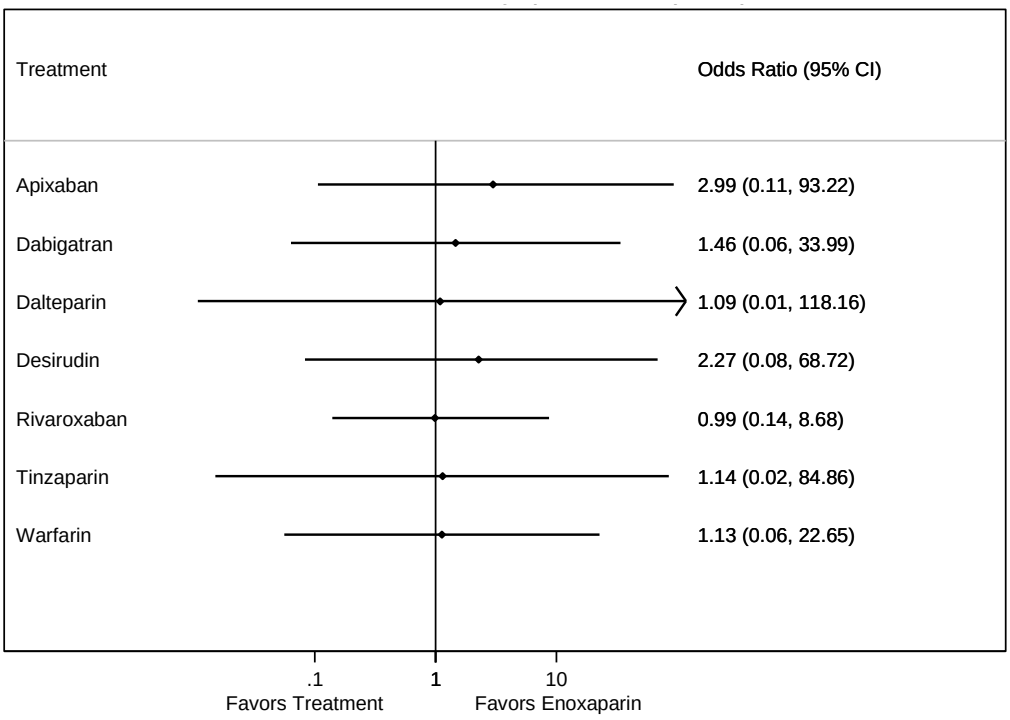


Figure 146. All Cause Mortality among Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

Same as prior model

Figure 147. All Cause Mortality among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 148. All Cause Mortality among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 149. All Cause Mortality among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

SYMPTOMATIC DEEP VEIN THROMBOSIS

Figure 150. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

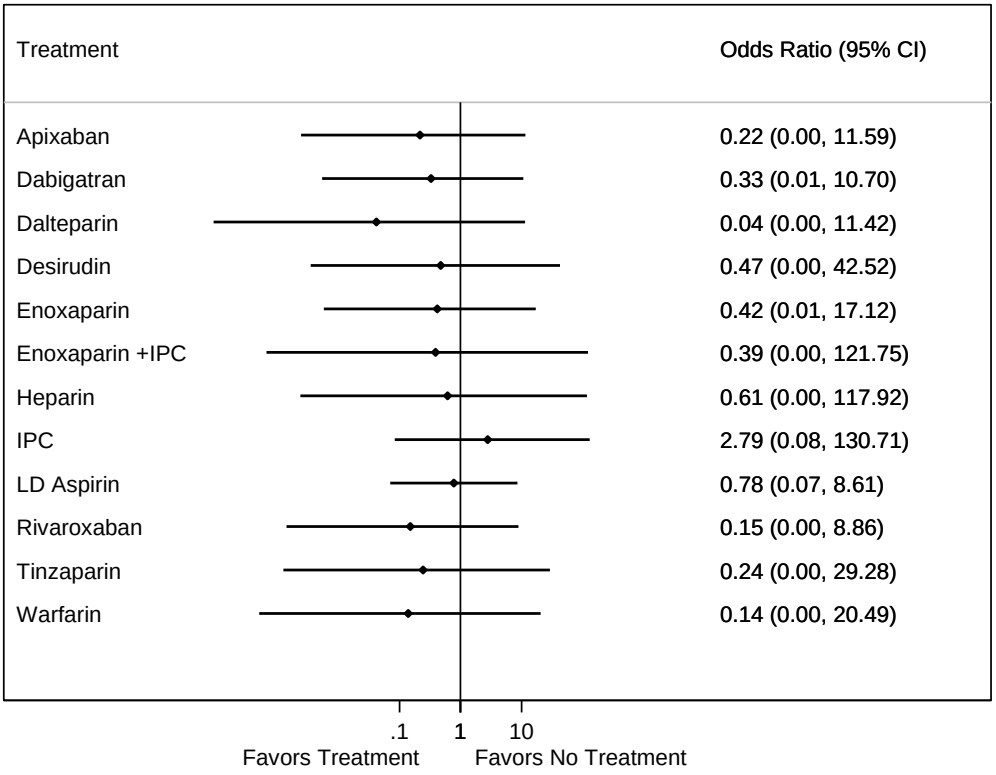


Figure 151. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

No studies in the model with no treatment as a comparator

Figure 152. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

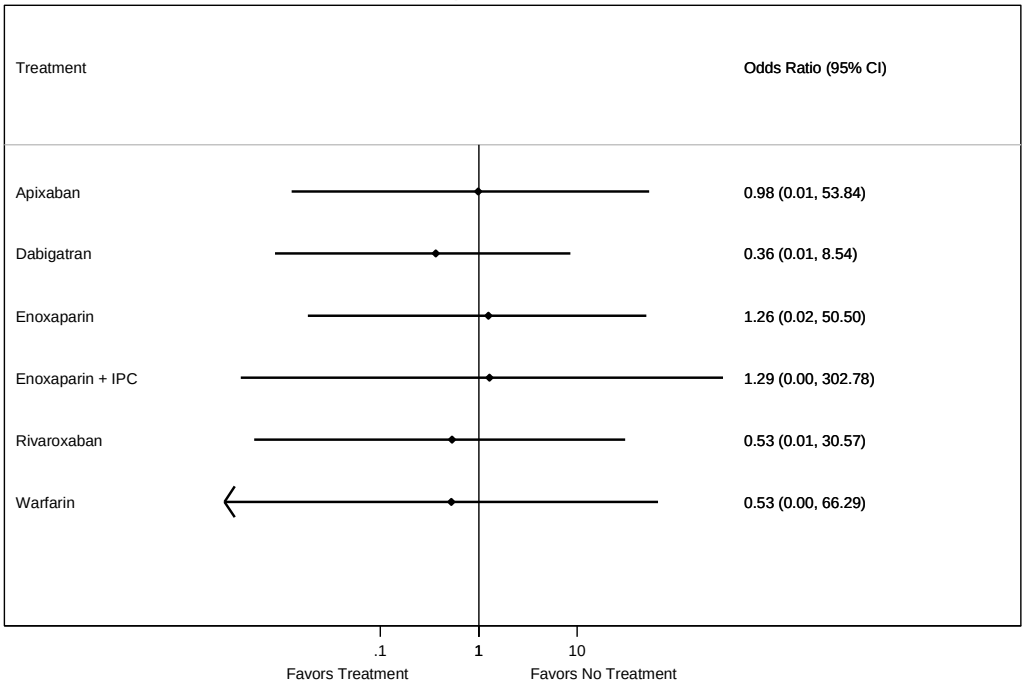


Figure 153. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

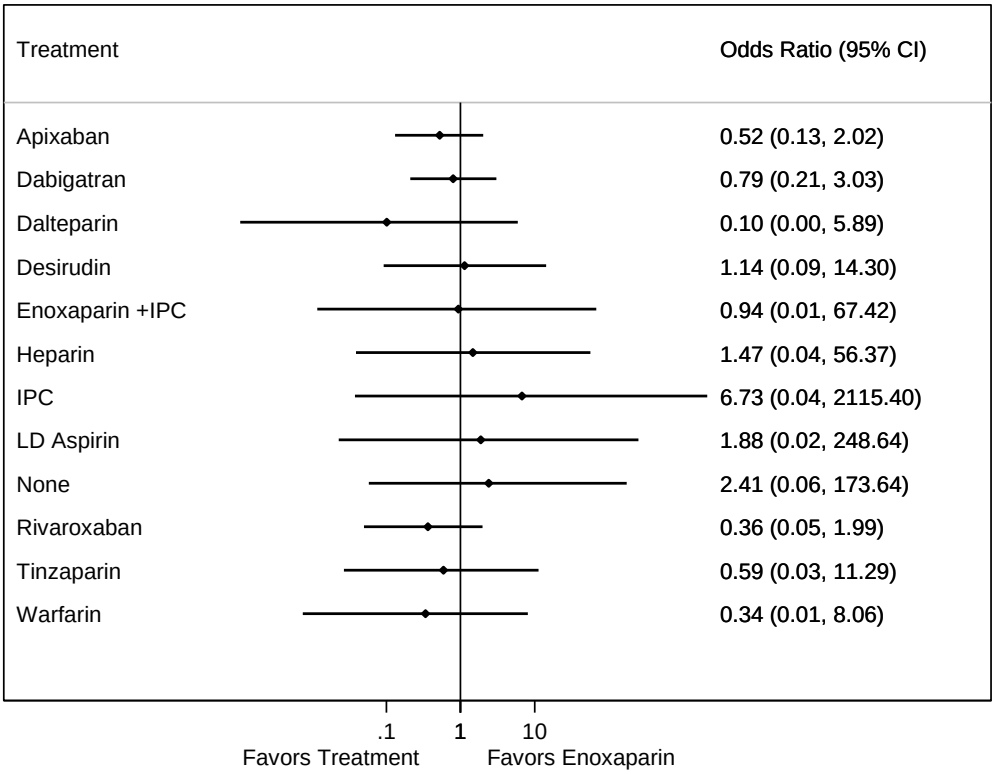


Figure 154. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

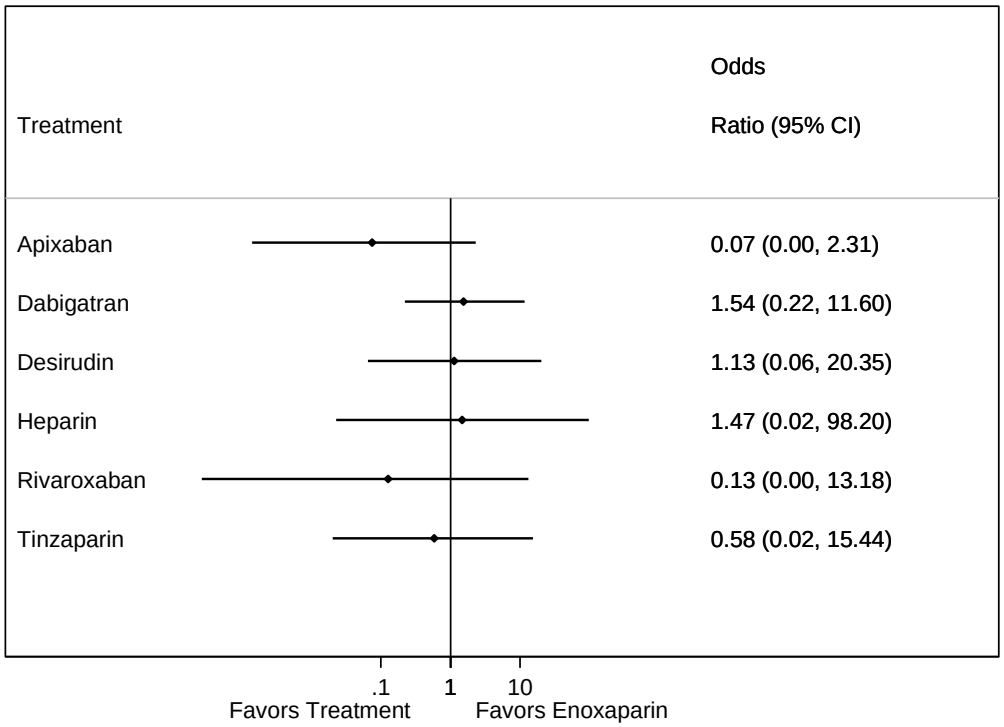


Figure 155. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

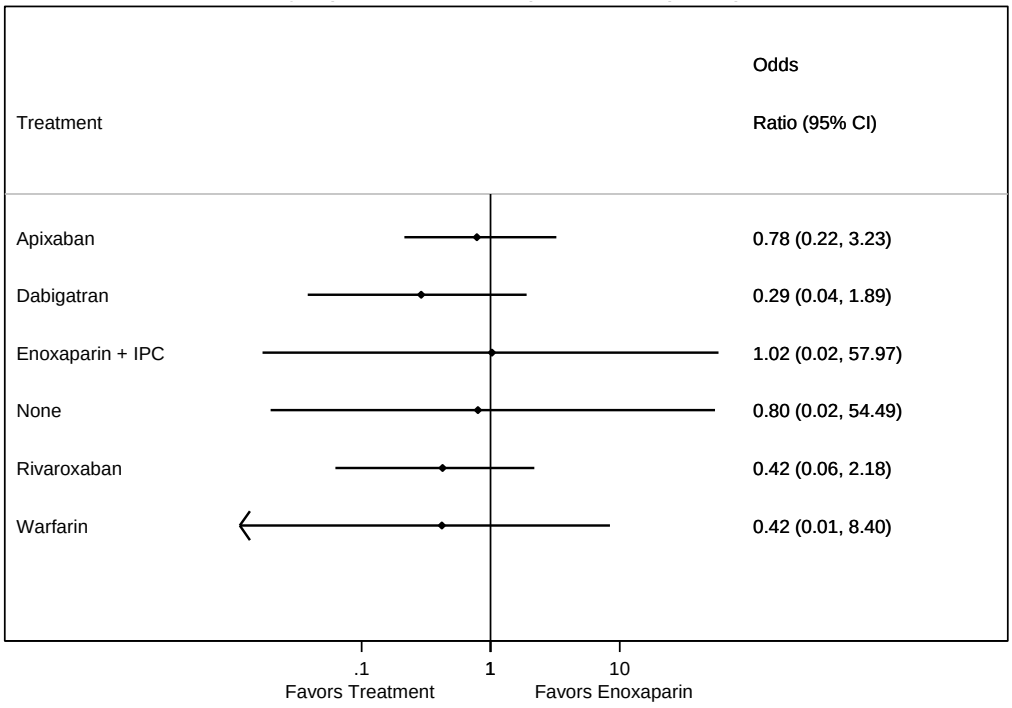


Figure 156. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

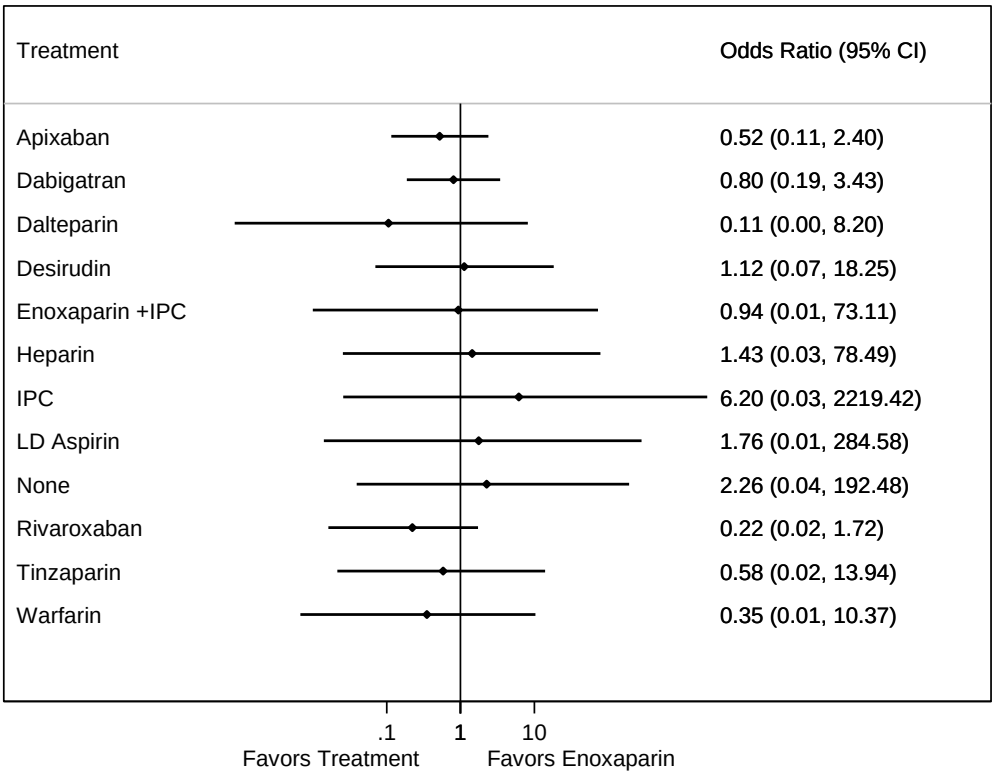


Figure 157. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

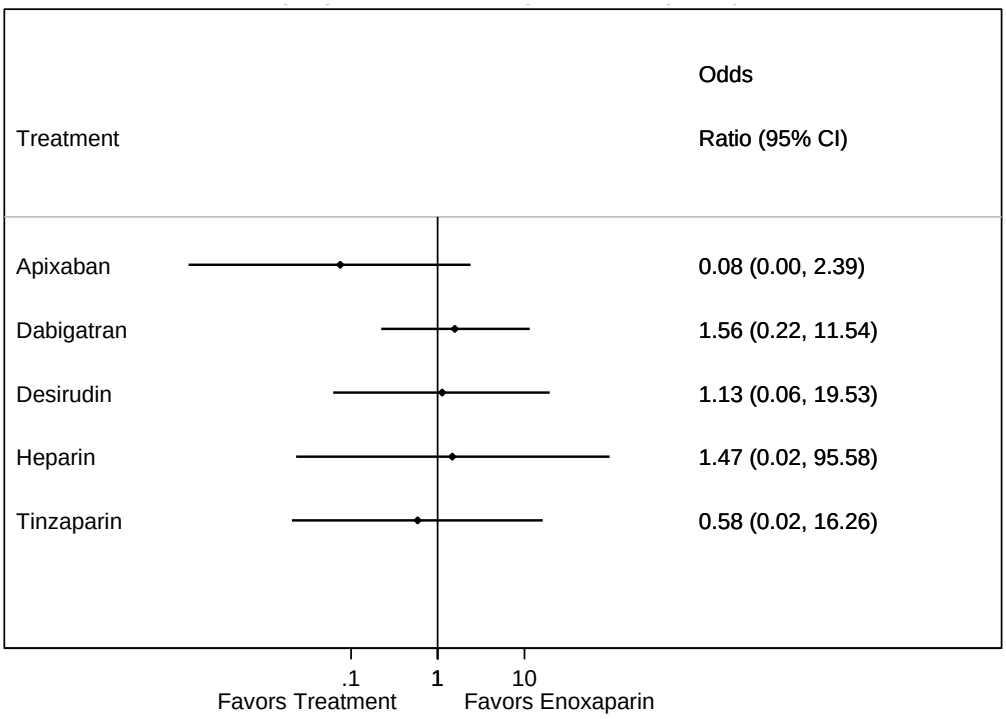


Figure 158. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

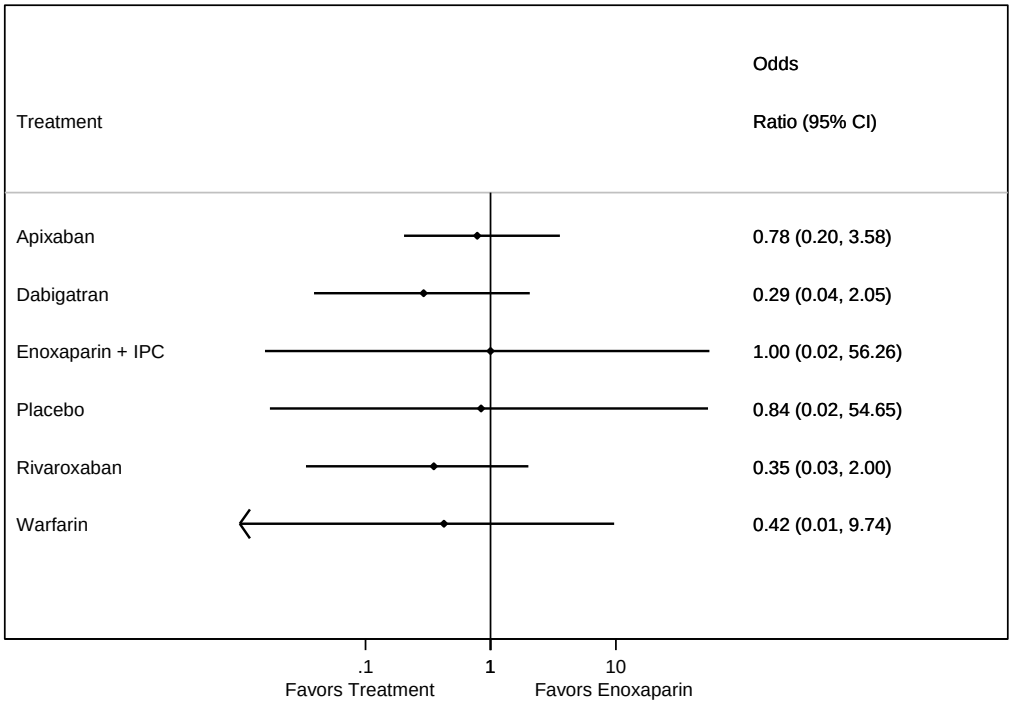


Figure 159. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

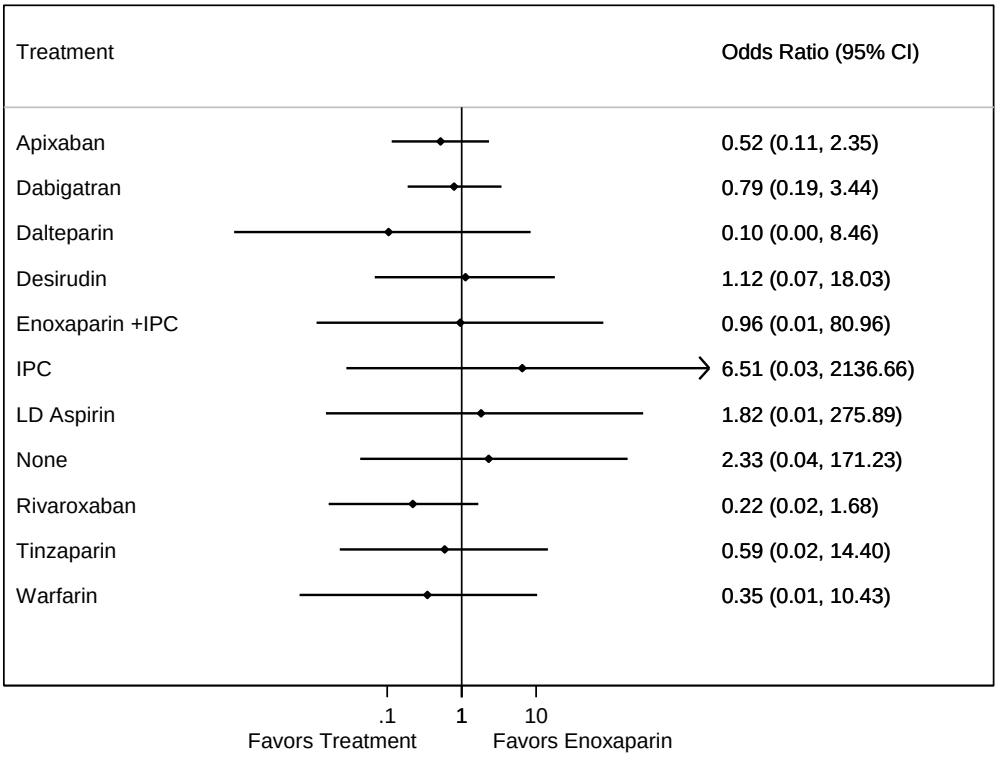


Figure 160. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

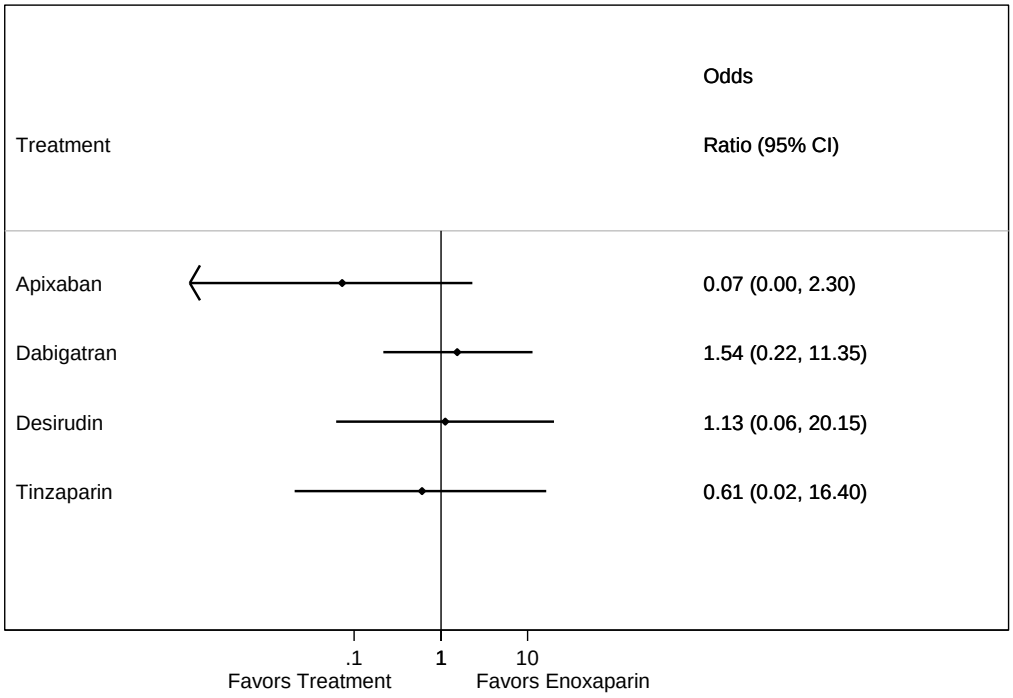


Figure 161. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

Same as prior model

Figure 162. Symptomatic Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

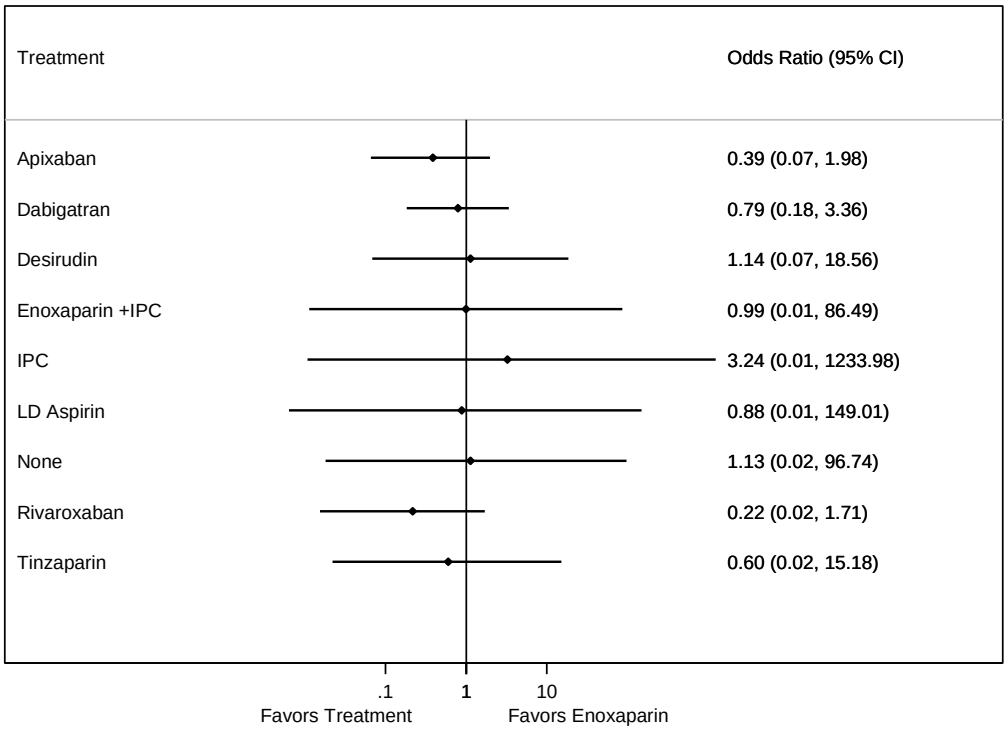


Figure 163. Symptomatic Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 164. Symptomatic Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

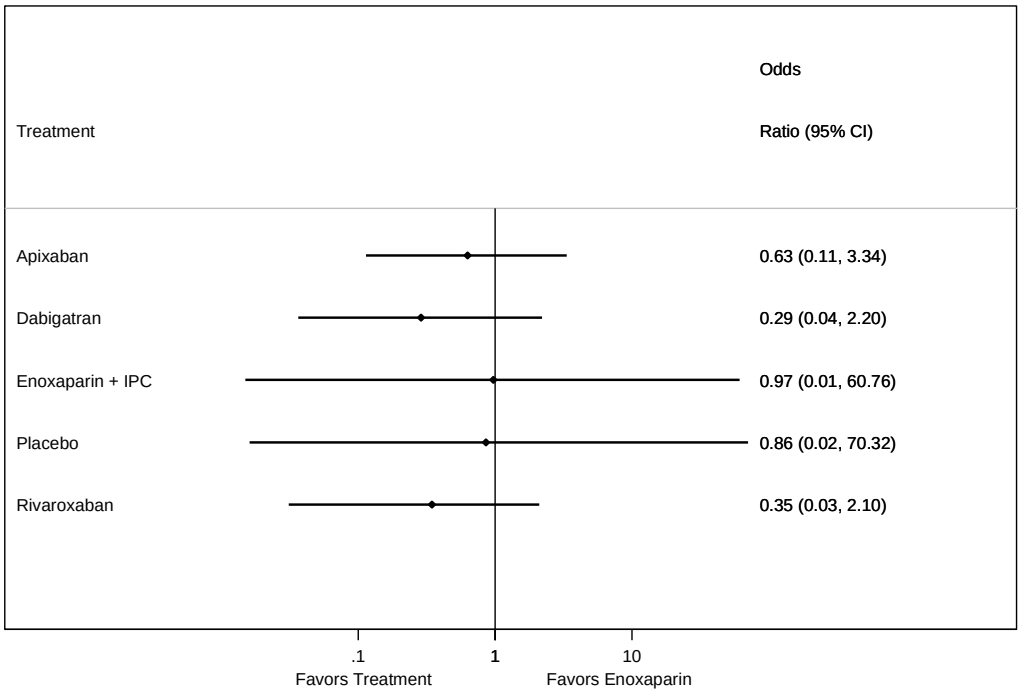


Table 97. Summary of Network Meta-Analysis Results - DVT

	Hip and Knee			Hip		Knee	
Agent	**All Trials**	**Without Heparin Trials**	**Without Heparin or Multi-Arm Trials (Final Model)**	**All Trials**	**Without Heparin or Multi-Arm Trials (Final Model)**	**All Trials**	**Without Heparin Trials**
Apixaban	●	●	○	●	●	●	●
Dabigatran	●	●	○	○	○	●	●
Dalteparin	●	○	○	○	○	n/a	n/a
Desirudin	●	●	○	○	○	n/a	n/a
Enoxaparin	●	●	○	○	○	●	●
Enoxaparin + IPC	●	●	○	n/a	n/a	●	●
Fondaparinux	●	●	●	●	●	n/a	n/a
GCS	○	○	n/a	n/a	n/a	○	○
HD Aspirin	○	○	○	n/a	n/a	n/a	n/a
Heparin	○	n/a	n/a	○	n/a	○	n/a
IPC	●	●	●	●	●	●	●
IPC + HD Aspirin	●	●	○	n/a	n/a	●	●
IPC + LD Aspirin	○	○	○	○	○	n/a	n/a
Rivaroxaban	●	●	●	●	●	●	●
Tinzaparin	○	○	○	○	○	n/a	n/a
Tinzaparin + GCS	○	○	n/a	n/a	n/a	n/a	n/a
Warfarin	○	○	○	○	○	○	○
YM150	○	○	○	○	○	n/a	n/a

● = significantly reduces DVT as compared to no treatment/placebo; ○ = no significant difference between agent and no treatment/placebo; n/a=agent not in model

Hip – model without heparin trials is the same as the final model

Knee – final model lacked a no treatment group

Figure 165. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

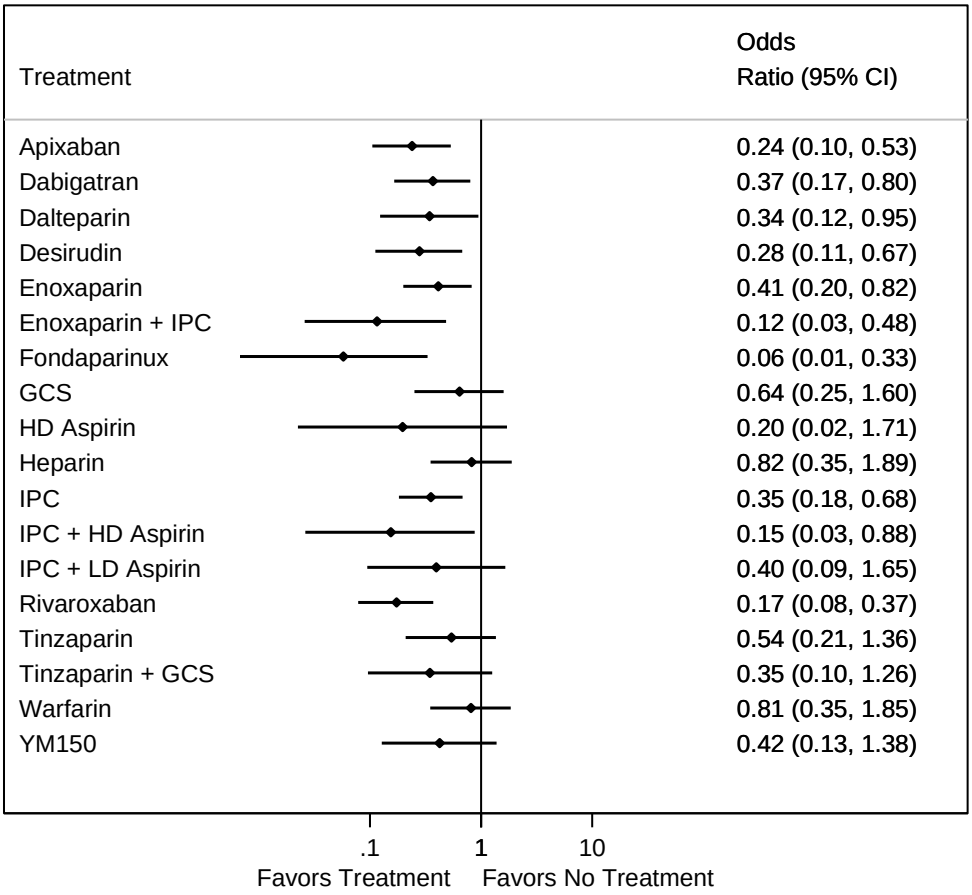


Figure 166. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

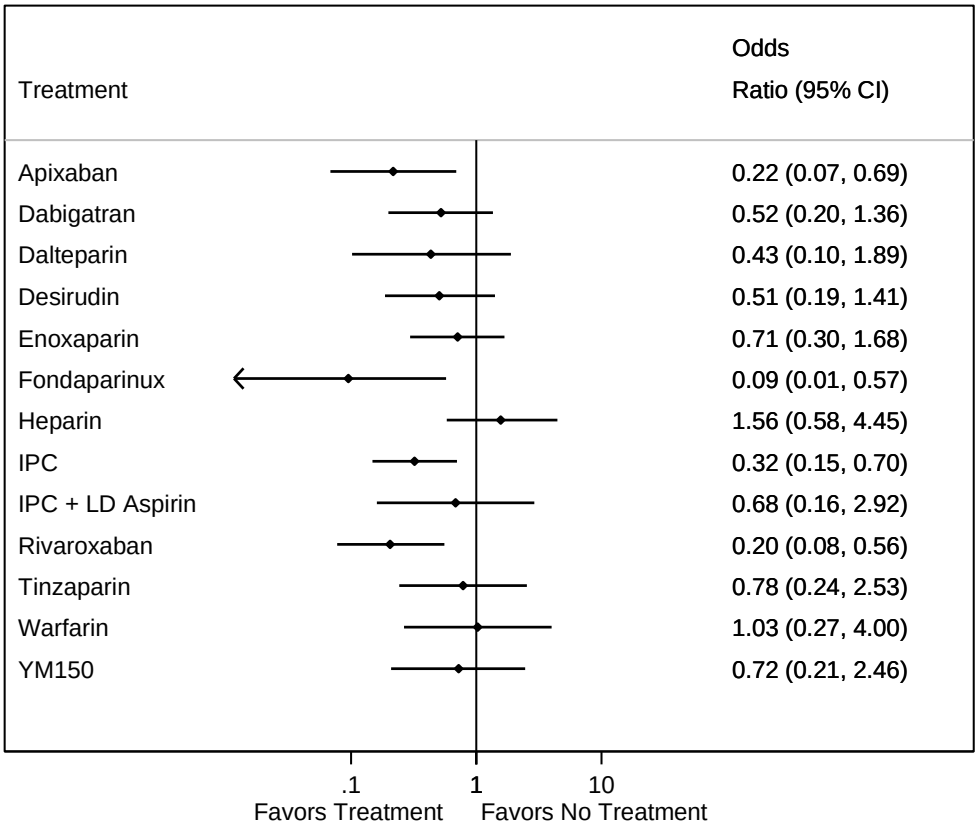


Figure 167. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

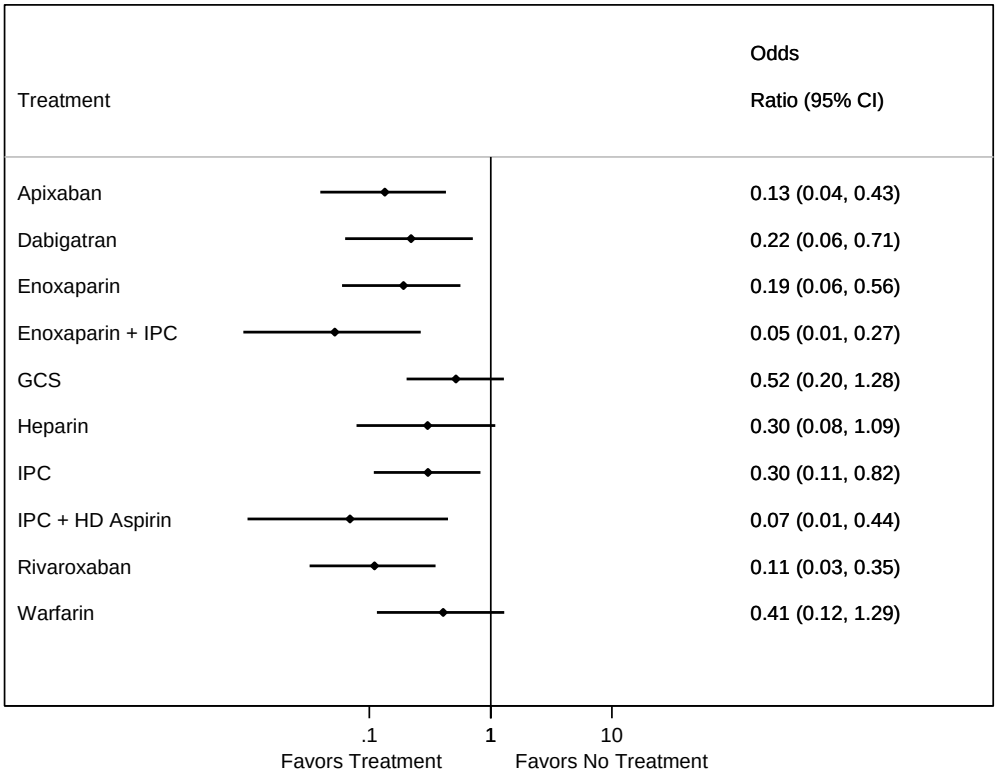


Figure 168. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

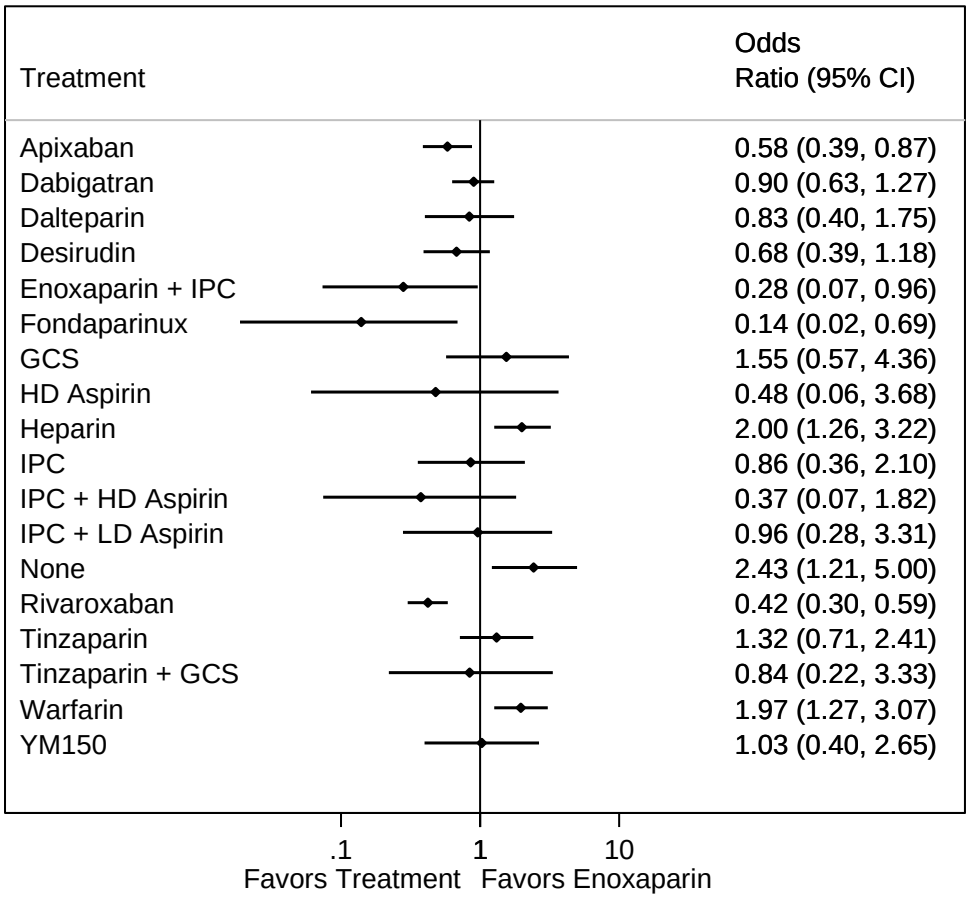


Figure 169. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

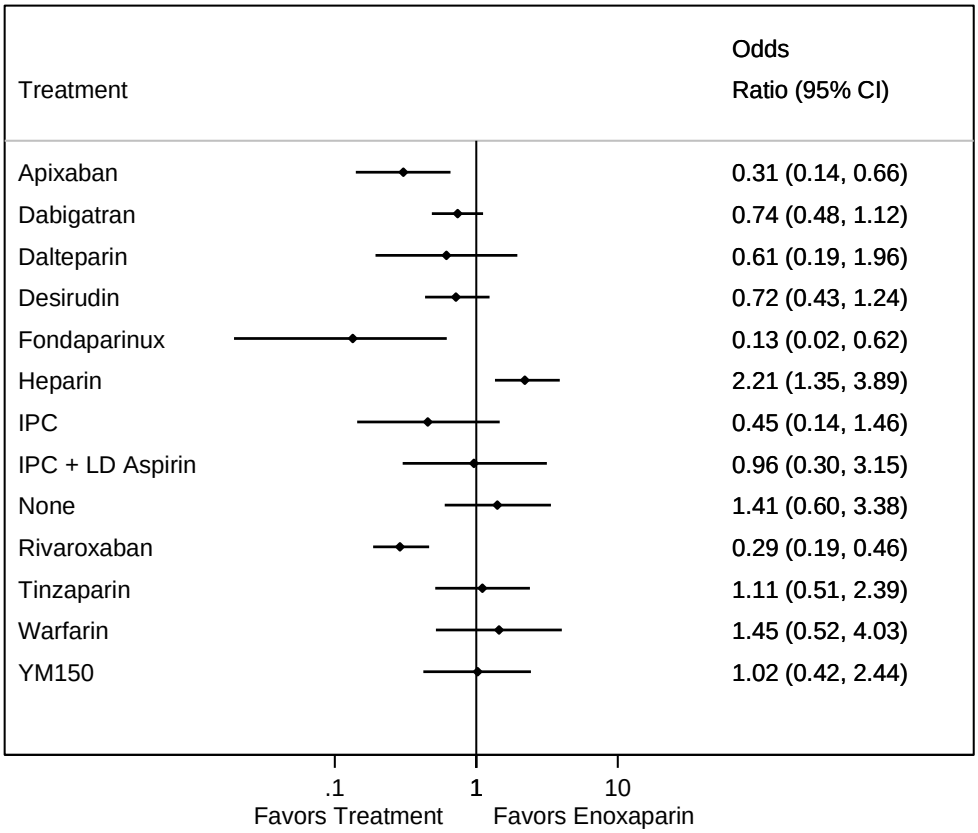


Figure 170. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

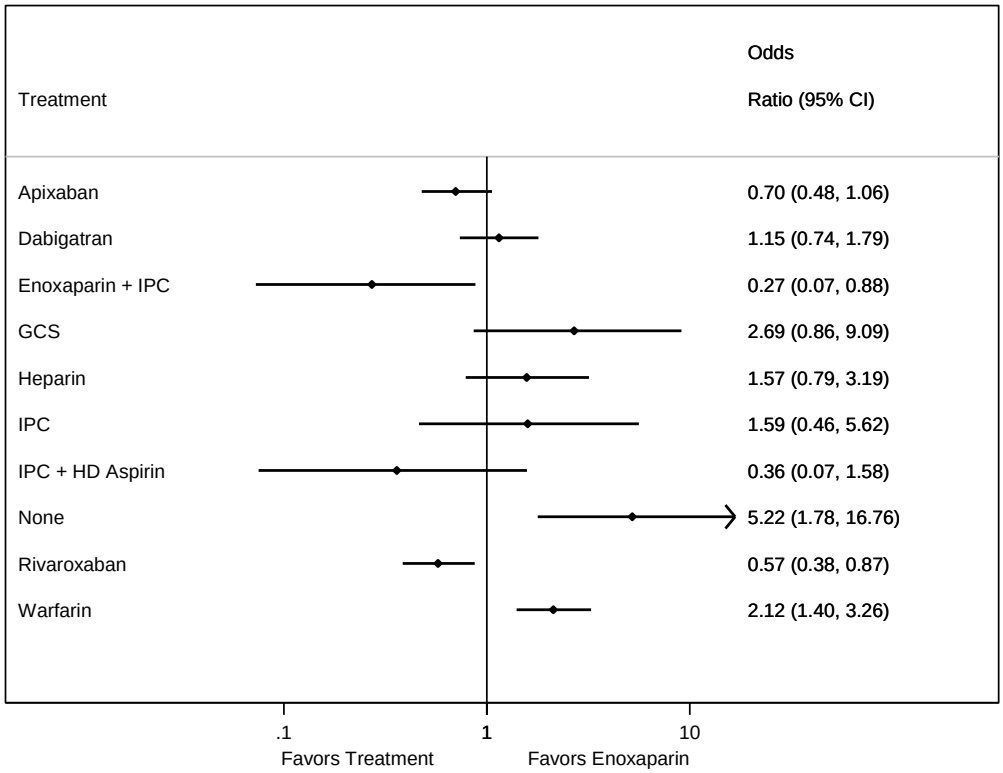


Figure 171. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

Same as prior model

Figure 172. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

Same as prior model

Figure 173. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials from Treatments with ≥ One Event (vs. Enoxaparin)

Same as prior model

Figure 174. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

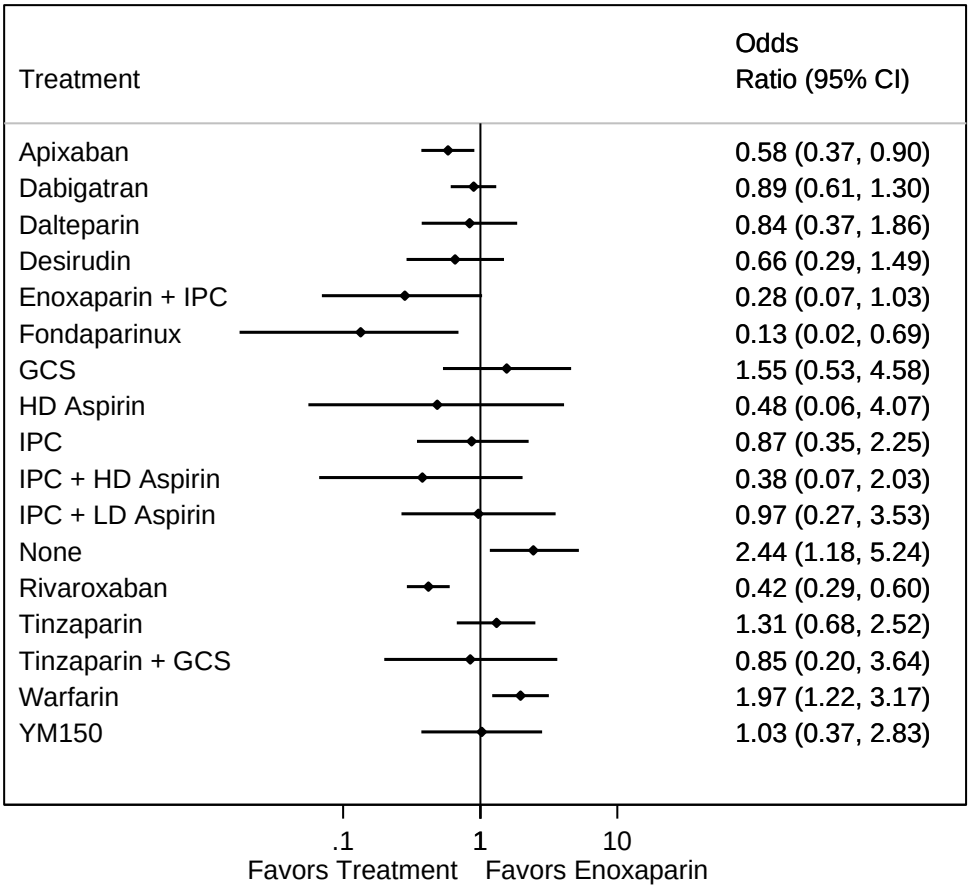


Figure 175. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

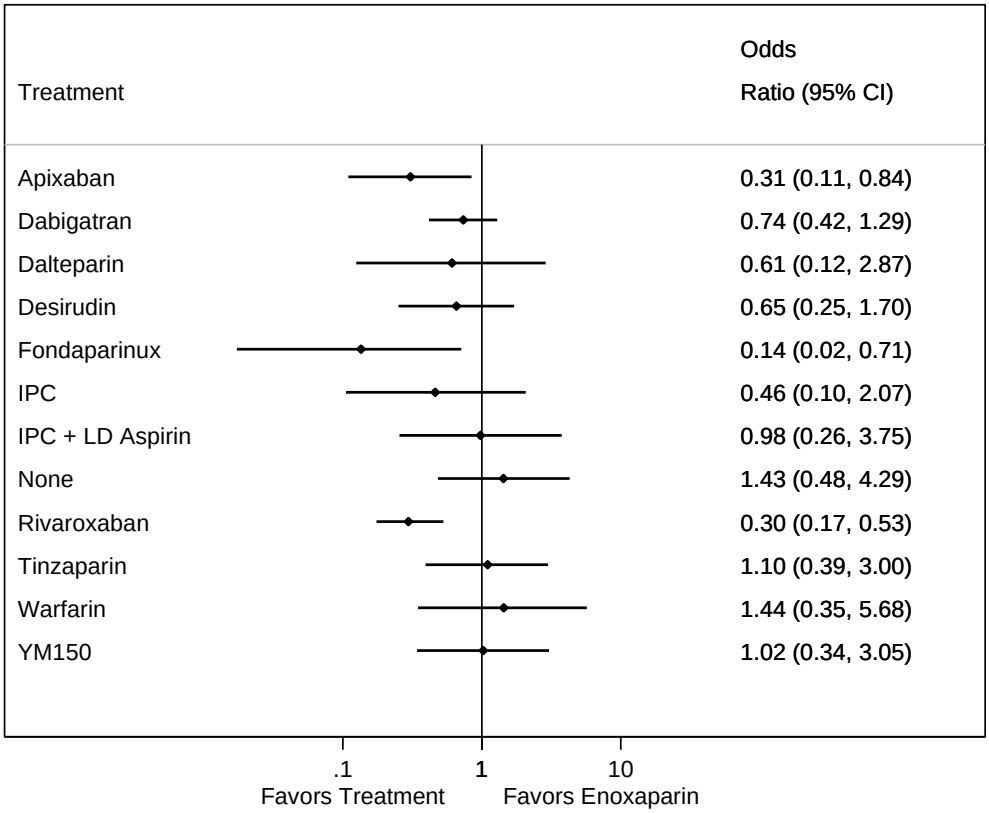


Figure 176. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials (vs. Enoxaparin)

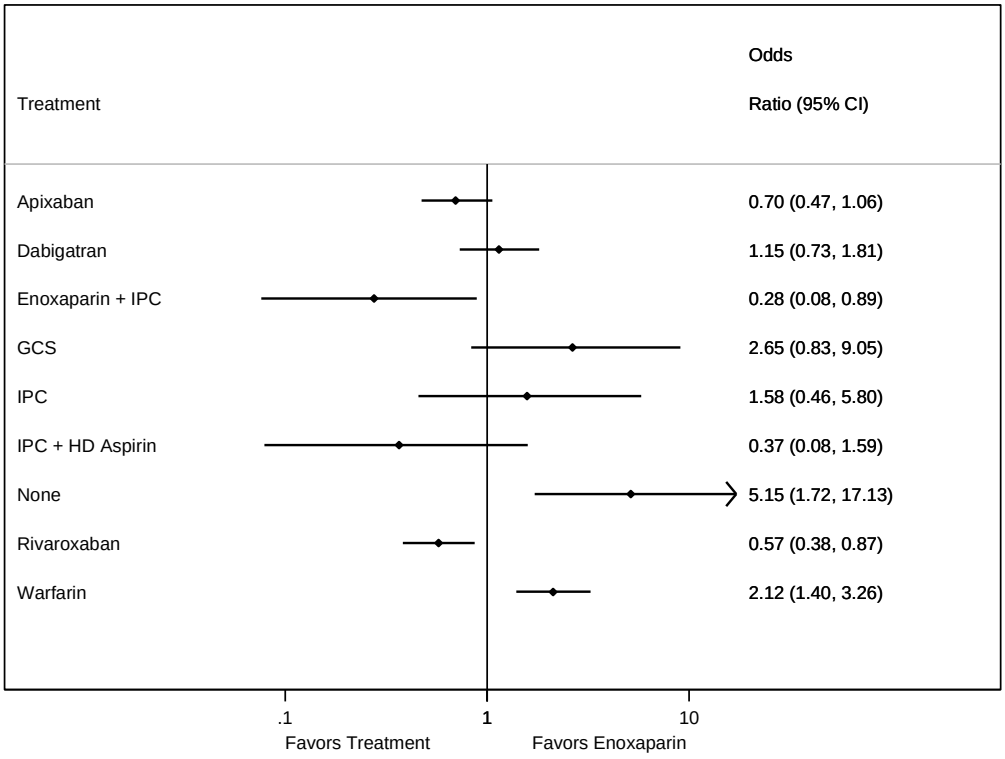


Figure 177. Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

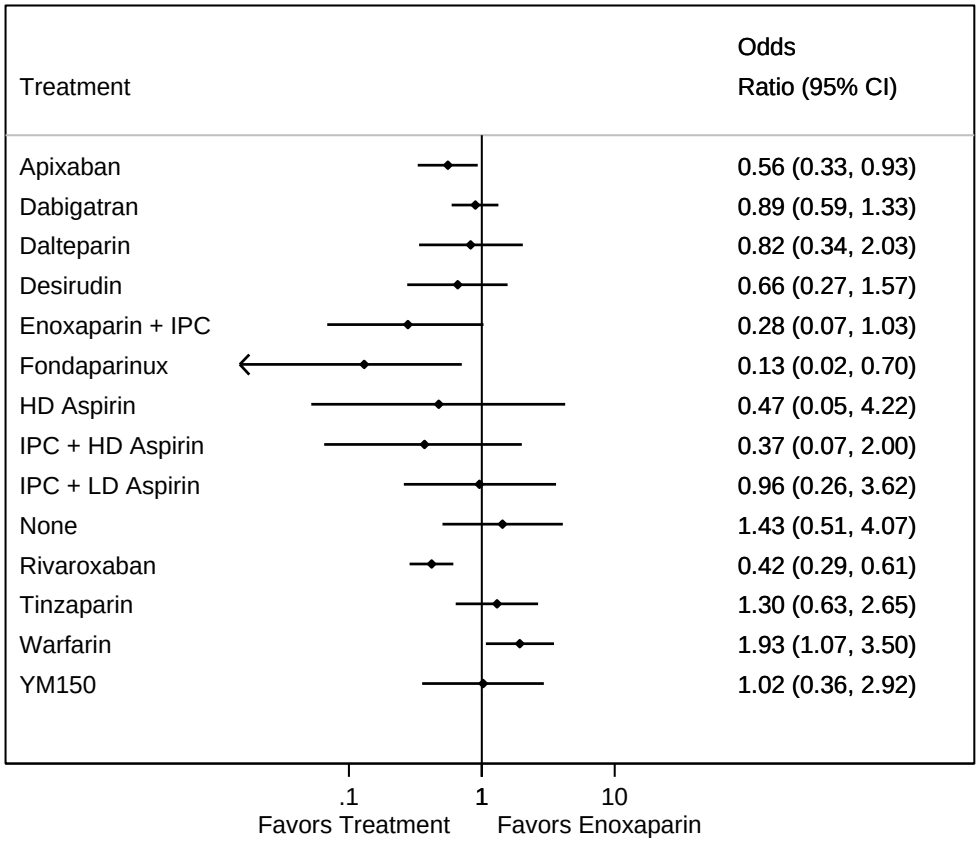
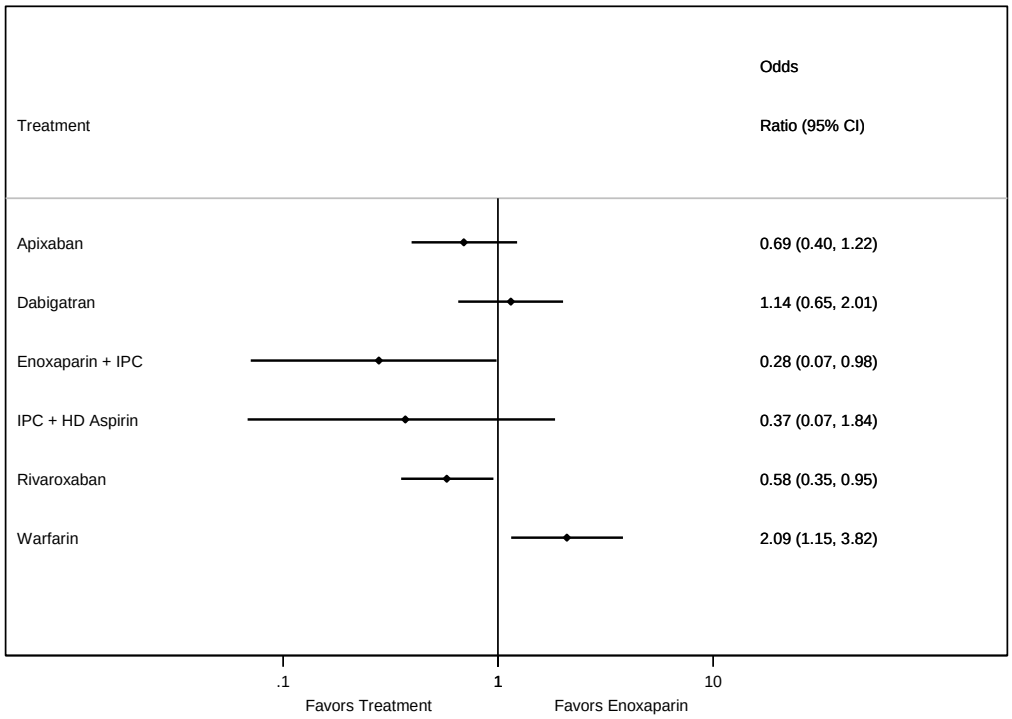


Figure 178. Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)

Same as prior model

Figure 179. Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



PROXIMAL DEEP VEIN THROMBOSIS

Figure 180. Proximal Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

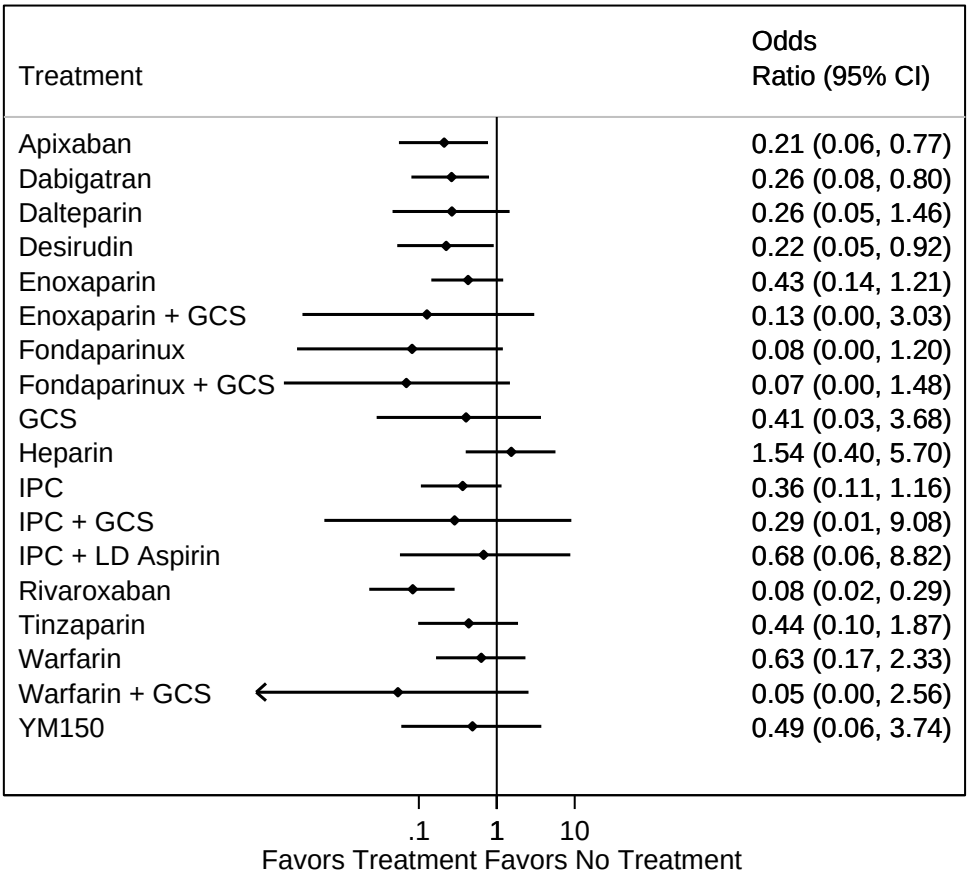


Figure 181. Proximal Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

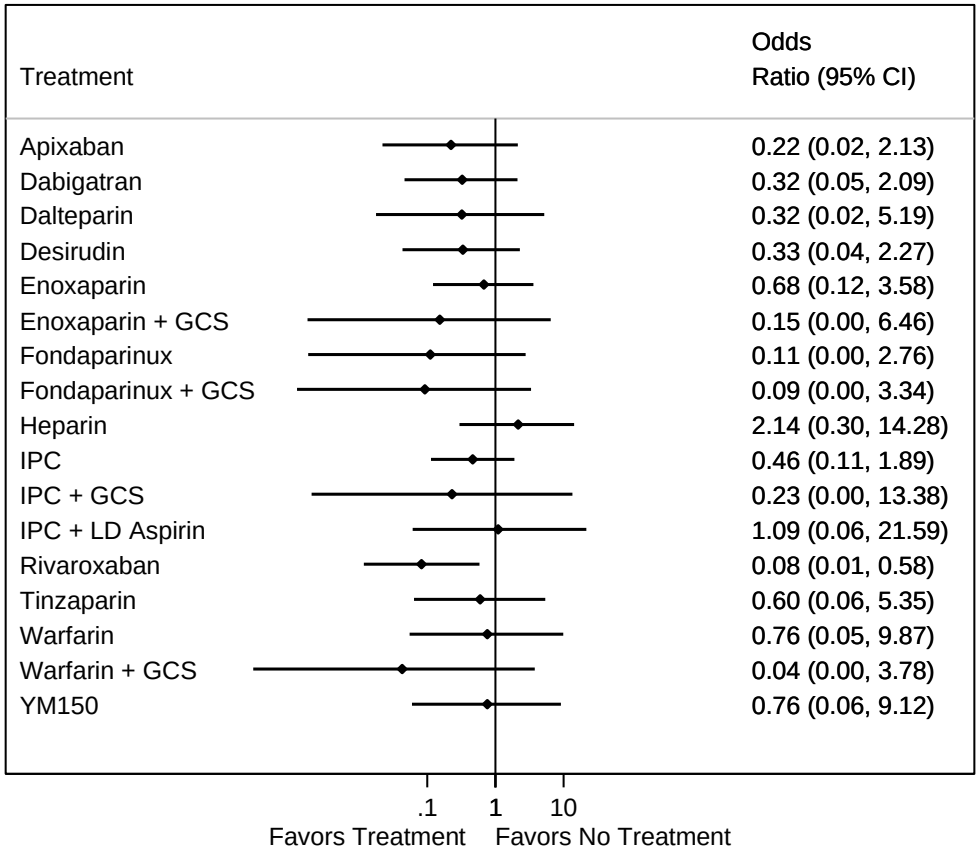


Figure 182. Proximal Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. No Treatment)

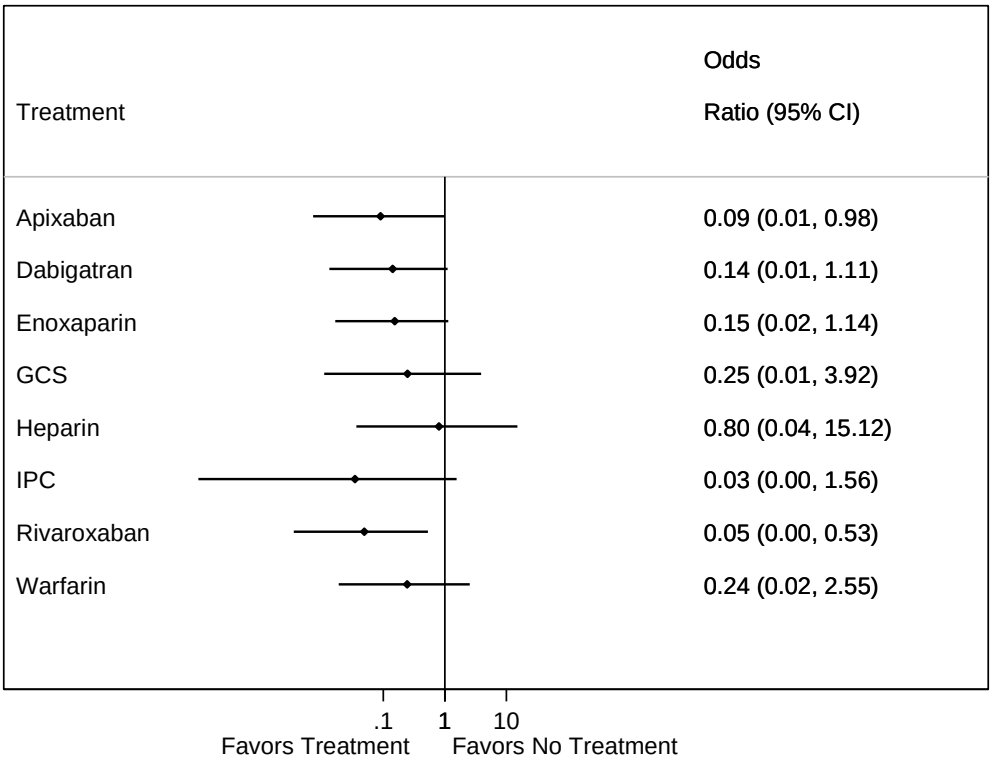


Figure 183. Proximal Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

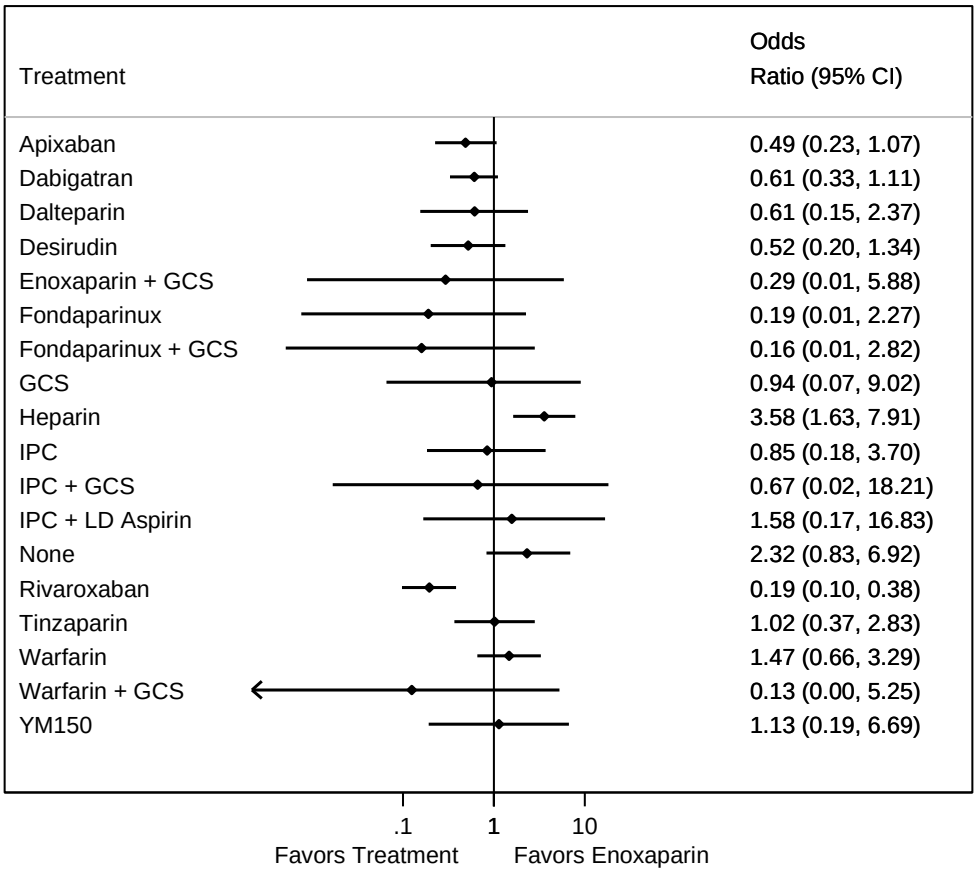


Figure 184. Proximal Deep Vein Thrombosis among Hip Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

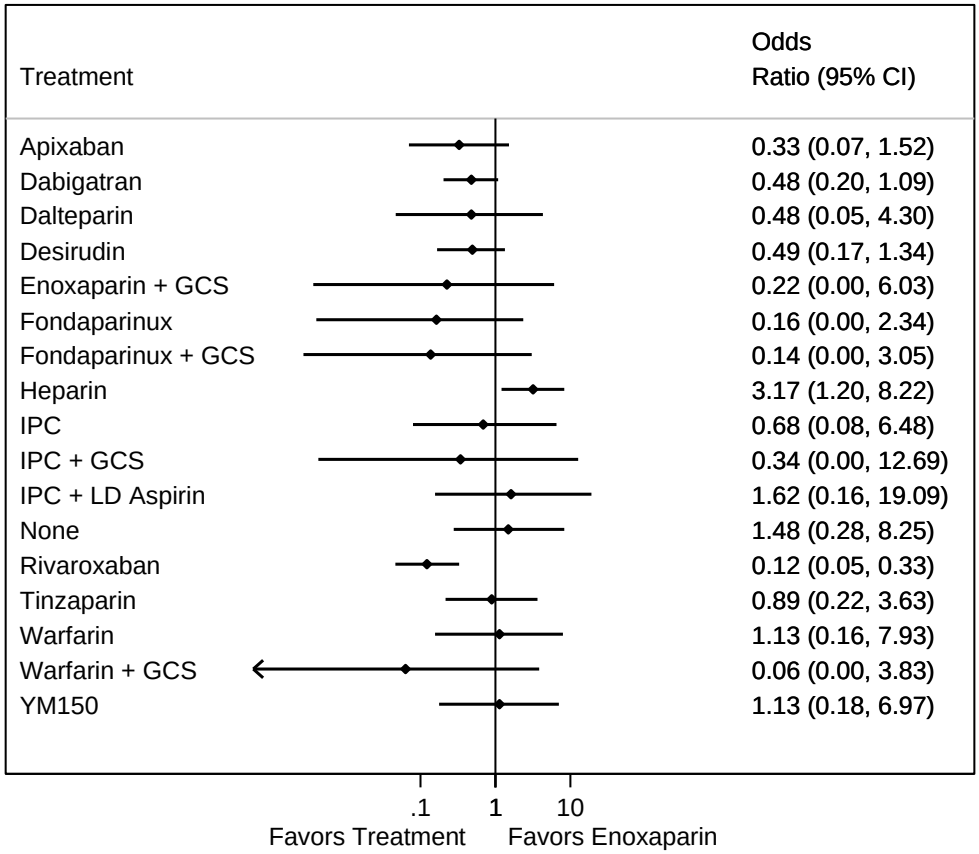


Figure 185. Proximal Deep Vein Thrombosis among Knee Patients - Network Meta-Analysis Results from All Trials (vs. Enoxaparin)

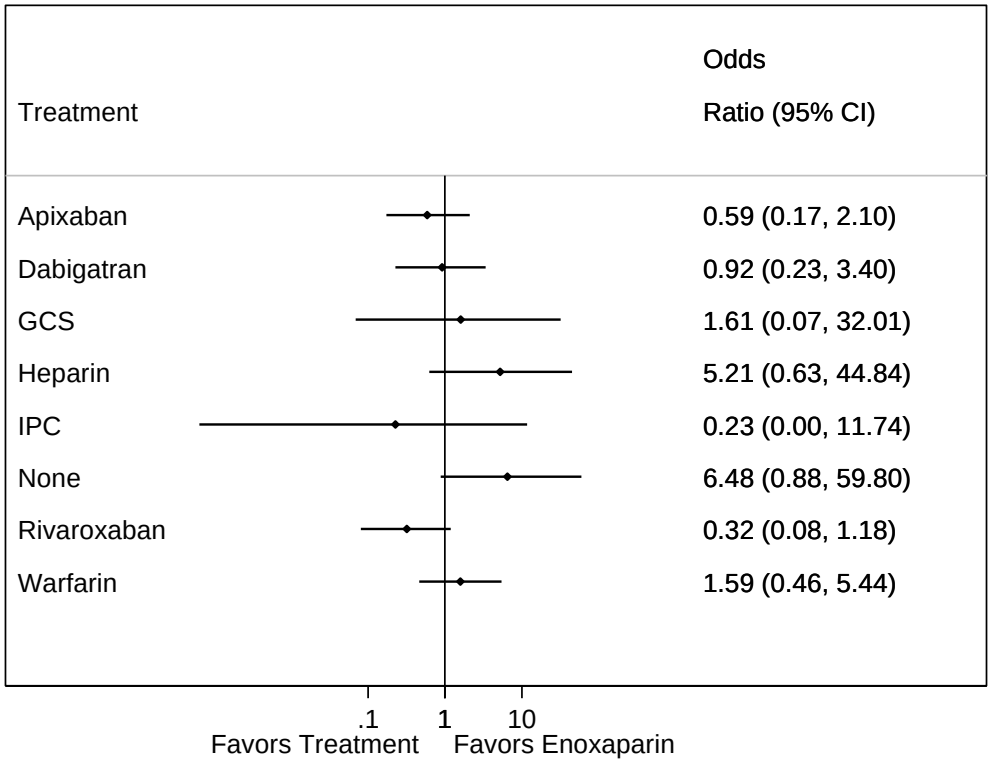
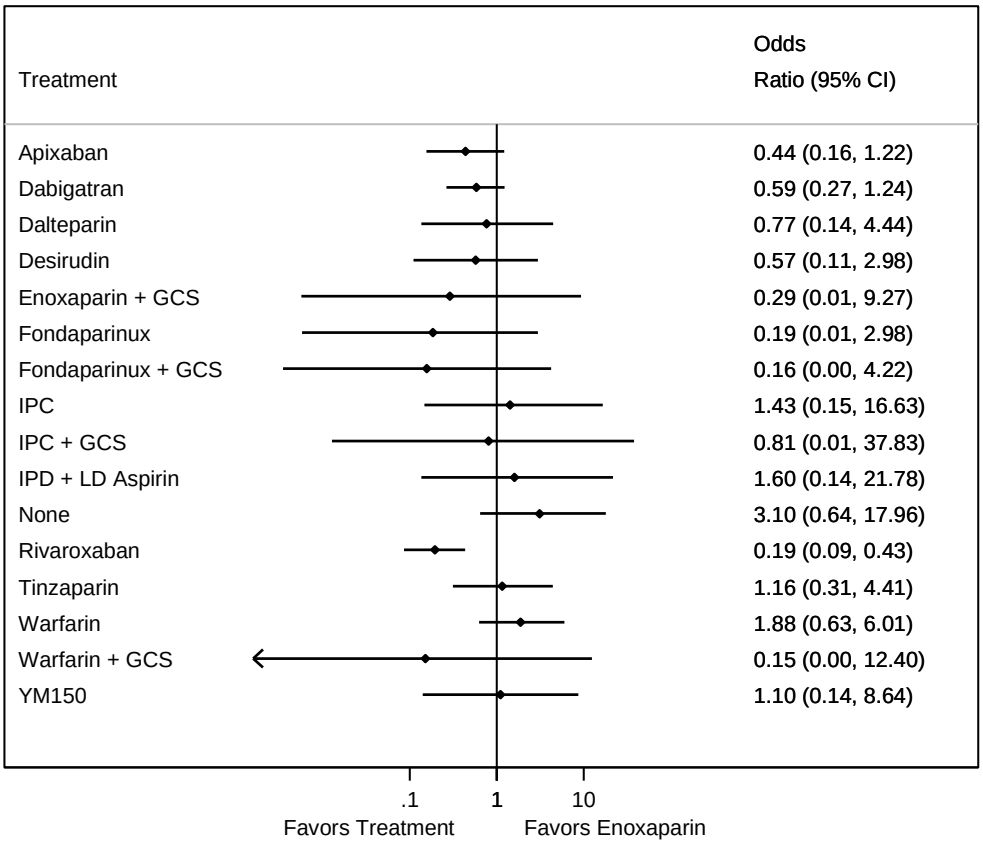


Figure 186. Proximal Deep Vein Thrombosis among Hip and Knee Patients - Network Meta-Analysis Results Without Heparin Trials and Without Trials with > 2 Arms (vs. Enoxaparin)



NETWORK META-ANALYSIS PAIRWISE COMPARISONS

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Desirudin	1.29 (0.15, 9.03)	0.83 (0.03, 12.29)	2.34 (0.11, 47.23)	2.97 (0.16, 61.13)	2.87 (0.22, 44.26)
Apixaban vs. Enoxaparin	1.10 (0.38, 3.15)	1.04 (0.22, 4.43)	1.05 (0.25, 4.01)	1.33 (0.33, 5.81)	1.29 (0.38, 4.78)
Apixaban vs. Heparin	0.25 (0.04, 1.37)	0.03 (0.00, 0.62)			
Apixaban vs. None	1.09 (0.07, 14.43)				10.55 (0.13, 5843)
Apixaban vs. Warfarin	1.03 (0.22, 4.49)	0.91 (0.10, 7.09)	0.95 (0.11, 6.60)	0.86 (0.08, 6.56)	0.98 (0.14, 5.77)
Dabigatran vs. Apixaban	0.86 (0.18, 3.88)	0.81 (0.09, 6.55)	0.82 (0.11, 5.91)	0.65 (0.08, 4.43)	0.75 (0.12, 3.98)
Dabigatran vs. Desirudin	1.11 (0.12, 7.99)	0.67 (0.02, 10.67)	1.92 (0.09, 38.05)	1.94 (0.09, 34.92)	2.15 (0.16, 29.55)
Dabigatran vs. Enoxaparin	0.95 (0.29, 2.80)	0.84 (0.16, 3.65)	0.86 (0.18, 3.33)	0.87 (0.19, 3.34)	0.97 (0.29, 3.03)
Dabigatran vs. Enoxaparin + IPC	0.99 (0.02, 60.58)	0.87 (0.01, 78.65)	0.85 (0.01, 72.75)	0.88 (0.01, 72.75)	0.96 (0.01, 68.03)
Dabigatran vs. GCS	0.61 (0.02, 17.03)				
Dabigatran vs. Heparin	0.21 (0.03, 1.23)	0.03 (0.00, 0.51)			
Dabigatran vs. IPC	3.31 (0.10, 190.38)				
Dabigatran vs. IPC + LD Aspirin	1.01 (0.05, 19.83)	0.86 (0.02, 30.05)	0.89 (0.03, 27.33)	0.88 (0.03, 24.39)	0.98 (0.04, 22.31)
Dabigatran vs. None	0.94 (0.06, 12.59)				7.90 (0.10, 4,647.11)
Dabigatran vs. Rivaroxaban	1.64 (0.33, 7.49)	1.56 (0.17, 12.30)	1.60 (0.20, 11.09)	1.63 (0.22, 11.18)	1.67 (0.32, 8.45)
Dabigatran vs. Tinzaparin	0.95 (0.05, 15.82)	0.78 (0.03, 20.80)	0.82 (0.03, 19.53)	0.71 (0.03, 15.26)	0.95 (0.01, 69.27)
Dabigatran vs. Warfarin	0.89 (0.16, 4.22)	0.73 (0.07, 6.16)	0.77 (0.08, 5.65)	0.56 (0.05, 4.06)	0.73 (0.12, 3.49)
Desirudin vs. Enoxaparin	0.86 (0.16, 5.01)	1.25 (0.12, 21.26)	0.45 (0.03, 6.32)	0.45 (0.03, 5.86)	0.45 (0.04, 4.44)
Desirudin vs. Heparin	0.19 (0.03, 1.07)	0.04 (0.00, 0.66)			
Desirudin vs. None	0.85 (0.04, 17.13)				3.68 (0.03, 2599)

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Desirudin vs. Warfarin	0.80 (0.11, 6.58)	1.09 (0.06, 27.06)	0.40 (0.02, 8.23)	0.29 (0.01, 5.38)	0.34 (0.02, 4.45)
Enoxaparin + IPC vs. Apixaban	0.87 (0.01, 49.16)	0.92 (0.01, 91.84)	0.96 (0.01, 82.68)	0.74 (0.01, 61.37)	0.78 (0.01, 55.92)
Enoxaparin + IPC vs. Desirudin	1.12 (0.01, 75.19)	0.77 (0.00, 101.49)	2.25 (0.01, 341.72)	2.20 (0.02, 301.57)	2.23 (0.02, 261.39)
Enoxaparin + IPC vs. Enoxaparin	0.96 (0.02, 49.01)	0.96 (0.01, 73.11)	1.01 (0.01, 68.24)	0.98 (0.01, 67.02)	1.00 (0.02, 62.43)
Enoxaparin + IPC vs. GCS	0.62 (0.00, 90.56)				
Enoxaparin + IPC vs. Heparin	0.21 (0.00, 13.38)	0.03 (0.00, 4.64)			
Enoxaparin + IPC vs. IPC	3.35 (0.02, 805.93)				
Enoxaparin + IPC vs. None	0.95 (0.01, 96.16)				8.19 (0.02, 12,835.88)
Enoxaparin + IPC vs. Rivaroxaban	1.67 (0.03, 93.50)	1.78 (0.02, 175.56)	1.88 (0.02, 165.17)	1.85 (0.02, 154.47)	1.73 (0.03, 126.72)
Enoxaparin + IPC vs. Tinzaparin	0.96 (0.01, 104.27)	0.90 (0.00, 172.09)	0.96 (0.01, 162.39)	0.81 (0.00, 123.10)	0.98 (0.00, 344.47)
Enoxaparin + IPC vs. Warfarin	0.90 (0.01, 52.72)	0.84 (0.01, 85.37)	0.91 (0.01, 81.70)	0.64 (0.01, 56.71)	0.76 (0.01, 55.59)
Enoxaparin vs. None	0.99 (0.08, 10.67)				8.18 (0.13, 4222)
GCS vs. Apixaban	1.41 (0.05, 38.02)				
GCS vs. Desirudin	1.82 (0.05, 60.40)				
GCS vs. Enoxaparin	1.56 (0.07, 35.41)				
GCS vs. Heparin	0.35 (0.01, 10.74)				
GCS vs. None	1.54 (0.08, 27.19)				
GCS vs. Rivaroxaban	2.70 (0.10, 74.29)				
GCS vs. Warfarin	1.46 (0.05, 39.69)				

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
HD Aspirin vs. Apixaban	7.30 (0.01, 38,177.44)				6.12 (0.00, 24,587.66)
HD Aspirin vs. Dabigatran	8.51 (0.01, 41,772.77)				8.17 (0.01, 32,859.63)
HD Aspirin vs. Desirudin	9.40 (0.01, 48,533.04)				17.57 (0.01, 90,219.42)
HD Aspirin vs. Enoxaparin	8.05 (0.01, 38,948.67)				7.89 (0.01, 28,853.89)
HD Aspirin vs. Enoxaparin + IPC	8.39 (0.02, 16,531.12)				7.89 (0.02, 10,593.54)
HD Aspirin vs. GCS	5.17 (0.00, 35,596.41)				
HD Aspirin vs. Heparin	1.79 (0.00, 9,395.63)				
HD Aspirin vs. IPC	28.13 (0.01, 240,385.70)				492.26 (0.03, 56,514,059.17)
HD Aspirin vs. IPC + HD Aspirin	1.00 (0.02, 53.30)				0.94 (0.01, 53.79)
HD Aspirin vs. IPC + LD Aspirin	8.60 (0.00, 56,954.05)				8.04 (0.00, 50,011.09)
HD Aspirin vs. None	7.98 (0.00, 56,954.05)				64.59 (0.01, 1,411,269.20)
HD Aspirin vs. Rivaroxaban	13.99 (0.01, 67,507.91)				13.63 (0.01, 52,575.21)
HD Aspirin vs. Tinzaparin	8.04 (0.00, 48,050.12)				7.76 (0.00, 83,283.02)
HD Aspirin vs. Tinzaparin + GCS	5.03 (0.00, 58,104.59)				

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
HD Aspirin vs. Warfarin	7.54 (0.01, 35,954.16)				5.99 (0.00, 24,343.01)
Heparin vs. Enoxaparin	4.50 (1.12, 21.28)	32.56 (2.42, 1,445.20)			
Heparin vs. None	4.46 (0.25, 78.96)				
Heparin vs. Warfarin	4.21 (0.68, 28.11)	28.45 (1.32, 1,589.22)			
IPC + HD Aspirin vs. Apixaban	7.32 (0.02, 14,228.47)				6.50 (0.01, 9,818.27)
IPC + HD Aspirin vs. Dabigatran	8.54 (0.02, 15,740.62)				8.69 (0.02, 12,900.22)
IPC + HD Aspirin vs. Desirudin	9.44 (0.02, 18,977.32)				18.65 (0.02, 37,049.12)
IPC + HD Aspirin vs. Enoxaparin	8.08 (0.02, 14,913.17)				8.39 (0.02, 11,778.13)
IPC + HD Aspirin vs. Enoxaparin + IPC	8.42 (0.13, 4,979.08)				8.38 (0.12, 4,411.63)
IPC + HD Aspirin vs. GCS	5.19 (0.01, 12,619.52)				
IPC + HD Aspirin vs. Heparin	1.80 (0.00, 3,206.71)				
IPC + HD Aspirin vs. IPC	28.25 (0.03, 88,432.96)				522.70 (0.06, 29,209,366.90)
IPC + HD Aspirin vs. IPC + LD Aspirin	8.63 (0.01, 25,848.30)				8.54 (0.01, 19,341.34)
IPC + HD Aspirin vs. None	8.01 (0.01, 21,396.87)				68.58 (0.03, 646,934.29)

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
IPC + HD Aspirin vs. Rivaroxaban	14.03 (0.04, 25,591.10)				14.47 (0.03, 21,290.15)
IPC + HD Aspirin vs. Tinzaparin	8.08 (0.01, 19,751.80)				8.25 (0.00, 41,357.13)
IPC + HD Aspirin vs. Tinzaparin + GCS	5.05 (0.00, 25,591.10)				
IPC + HD Aspirin vs. Warfarin	7.56 (0.02, 14,016.63)				6.37 (0.01, 9,330.09)
IPC + LD Aspirin vs. Apixaban	0.85 (0.04, 16.59)	0.93 (0.03, 35.02)	0.92 (0.03, 30.57)	0.74 (0.02, 21.78)	0.76 (0.03, 16.98)
IPC + LD Aspirin vs. Desirudin	1.09 (0.04, 27.36)	0.78 (0.01, 40.08)	2.15 (0.04, 145.62)	2.21 (0.04, 124.71)	2.19 (0.05, 92.94)
IPC + LD Aspirin vs. Enoxaparin	0.94 (0.06, 15.00)	0.97 (0.04, 26.47)	0.96 (0.04, 22.20)	0.99 (0.05, 22.04)	0.98 (0.05, 17.15)
IPC + LD Aspirin vs. Enoxaparin + IPC	0.98 (0.01, 121.75)	1.01 (0.00, 207.47)	0.95 (0.00, 192.48)	1.00 (0.01, 179.29)	0.98 (0.01, 141.46)
IPC + LD Aspirin vs. GCS	0.60 (0.01, 41.10)				
IPC + LD Aspirin vs. Heparin	0.21 (0.01, 4.69)	0.03 (0.00, 1.90)			
IPC + LD Aspirin vs. IPC	3.27 (0.04, 317.98)				
IPC + LD Aspirin vs. None	0.93 (0.02, 36.60)				8.04 (0.05, 6,142.58)
IPC + LD Aspirin vs. Rivaroxaban	1.63 (0.08, 31.44)	1.81 (0.05, 67.42)	1.79 (0.06, 56.26)	1.86 (0.07, 55.31)	1.70 (0.07, 37.56)
IPC + LD Aspirin vs. Tinzaparin	0.94 (0.02, 41.89)	0.91 (0.01, 73.92)	0.92 (0.01, 68.10)	0.81 (0.01, 50.55)	0.97 (0.01, 141.17)
IPC + LD Aspirin vs. Warfarin	0.88 (0.04, 17.71)	0.85 (0.02, 31.44)	0.87 (0.03, 28.11)	0.64 (0.02, 18.65)	0.75 (0.03, 16.20)
IPC vs. Apixaban	0.26 (0.00, 7.99)				0.01 (0.00, 6.21)
IPC vs. Dabigatran	0.30 (0.01, 10.00)				0.02 (0.00, 8.52)

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
IPC vs. Desirudin	0.33 (0.00, 13.64)				0.04 (0.00, 28.02)
IPC vs. Enoxaparin	0.29 (0.01, 7.43)				0.02 (0.00, 7.15)
IPC vs. Enoxaparin + IPC	0.30 (0.00, 50.00)				0.02 (0.00, 28.53)
IPC vs. GCS	0.18 (0.00, 5.86)				
IPC vs. Heparin	0.06 (0.00, 2.30)				
IPC vs. IPC + LD Aspirin	0.31 (0.00, 25.00)				0.02 (0.00, 15.72)
IPC vs. None	0.28 (0.01, 3.88)				0.13 (0.00, 9.63)
IPC vs. Rivaroxaban	0.50 (0.01, 15.66)				0.03 (0.00, 14.32)
IPC vs. Tinzaparin	0.29 (0.00, 20.00)				0.02 (0.00, 28.93)
IPC vs. Warfarin	0.27 (0.00, 8.36)				0.01 (0.00, 6.30)
LD Aspirin vs. Apixaban	0.90 (0.04, 24.02)				0.09 (0.00, 11.85)
LD Aspirin vs. Dabigatran	1.05 (0.04, 29.31)				0.12 (0.00, 16.30)
LD Aspirin vs. Desirudin	1.16 (0.03, 40.61)				0.27 (0.00, 53.79)
LD Aspirin vs. Enoxaparin	0.99 (0.05, 21.76)				0.12 (0.00, 12.83)
LD Aspirin vs. Enoxaparin + IPC	1.04 (0.01, 151.41)				0.12 (0.00, 66.09)
LD Aspirin vs. GCS	0.64 (0.02, 21.74)				
LD Aspirin vs. HD Aspirin	0.12 (0.00, 340.36)				0.02 (0.00, 102.10)
LD Aspirin vs. Heparin	0.22 (0.01, 6.80)				
LD Aspirin vs. IPC	3.47 (0.13, 152.93)				7.52 (0.06, 5,345.44)
LD Aspirin vs. IPC + HD Aspirin	0.12 (0.00, 92.57)				0.01 (0.00, 40.85)
LD Aspirin vs. IPC + LD Aspirin	1.06 (0.02, 66.89)				0.12 (0.00, 32.23)

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
LD Aspirin vs. None	0.99 (0.15, 6.53)				0.99 (0.12, 7.97)
LD Aspirin vs. Rivaroxaban	1.73 (0.07, 46.43)				0.21 (0.00, 27.63)
LD Aspirin vs. Tinzaparin	0.99 (0.02, 54.22)				0.12 (0.00, 74.74)
LD Aspirin vs. Tinzaparin + GCS	0.62 (0.00, 116.63)				
LD Aspirin vs. Warfarin	0.93 (0.04, 24.56)				0.09 (0.00, 11.61)
Rivaroxaban vs. Apixaban	0.52 (0.12, 2.34)	0.52 (0.06, 4.31)	0.51 (0.08, 3.69)	0.40 (0.05, 2.68)	0.45 (0.08, 2.37)
Rivaroxaban vs. Desirudin	0.67 (0.08, 4.66)	0.43 (0.02, 6.53)	1.20 (0.06, 24.98)	1.19 (0.06, 22.42)	1.29 (0.10, 17.78)
Rivaroxaban vs. Enoxaparin	0.58 (0.19, 1.67)	0.54 (0.12, 2.26)	0.53 (0.13, 2.06)	0.53 (0.13, 1.97)	0.58 (0.18, 1.81)
Rivaroxaban vs. Heparin	0.13 (0.02, 0.72)	0.02 (0.00, 0.32)			
Rivaroxaban vs. None	0.57 (0.04, 7.69)				4.74 (0.06, 2714)
Rivaroxaban vs. Warfarin	0.54 (0.11, 2.51)	0.47 (0.05, 3.92)	0.48 (0.06, 3.51)	0.34 (0.03, 2.45)	0.44 (0.07, 2.33)
Tinzaparin + GCS vs. Apixaban	1.45 (0.01, 241.53)				
Tinzaparin + GCS vs. Dabigatran	1.69 (0.01, 285.72)				
Tinzaparin + GCS vs. Desirudin	1.87 (0.01, 357.45)				
Tinzaparin + GCS vs. Enoxaparin	1.60 (0.01, 237.22)				
Tinzaparin + GCS vs. Enoxaparin + IPC	1.67 (0.00, 1,085.72)				
Tinzaparin + GCS vs. GCS	1.03 (0.02, 58.15)				
Tinzaparin + GCS vs. Heparin	0.36 (0.00, 65.56)				
Tinzaparin + GCS vs. IPC	5.60 (0.03, 1,647.48)				

Table 98. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients - Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Tinzaparin + GCS vs. IPC + LD Aspirin	1.71 (0.01, 584.64)				
Tinzaparin + GCS vs. None	1.59 (0.01, 230.90)				
Tinzaparin + GCS vs. Rivaroxaban	2.78 (0.02, 472.01)				
Tinzaparin + GCS vs. Tinzaparin	1.60 (0.01, 399.41)				
Tinzaparin + GCS vs. Warfarin	1.50 (0.01, 253.66)				
Tinzaparin vs. Apixaban	0.91 (0.06, 14.89)	1.03 (0.04, 28.67)	1.00 (0.04, 26.15)	0.92 (0.04, 22.81)	0.79 (0.01, 53.62)
Tinzaparin vs. Desirudin	1.17 (0.05, 25.56)	0.86 (0.01, 35.98)	2.34 (0.05, 128.25)	2.73 (0.06, 140.89)	2.26 (0.02, 247.89)
Tinzaparin vs. Enoxaparin	1.00 (0.07, 13.28)	1.07 (0.05, 21.24)	1.05 (0.06, 19.38)	1.22 (0.08, 22.35)	1.02 (0.02, 57.05)
Tinzaparin vs. GCS	0.64 (0.01, 38.17)				
Tinzaparin vs. Heparin	0.22 (0.01, 4.25)	0.03 (0.00, 1.77)			
Tinzaparin vs. IPC	3.50 (0.05, 326.69)				
Tinzaparin vs. None	0.99 (0.03, 35.23)				8.32 (0.02, 12,004.06)
Tinzaparin vs. Rivaroxaban	1.74 (0.10, 29.64)	1.99 (0.07, 55.15)	1.96 (0.08, 49.21)	2.29 (0.11, 57.40)	1.76 (0.02, 113.98)
Tinzaparin vs. Warfarin	0.94 (0.07, 12.34)	0.93 (0.05, 18.38)	0.95 (0.05, 17.05)	0.79 (0.04, 13.13)	0.77 (0.01, 53.57)
Warfarin vs. Enoxaparin	1.07 (0.35, 3.55)	1.14 (0.24, 6.25)	1.11 (0.25, 5.45)	1.55 (0.35, 10.01)	1.32 (0.37, 5.78)
Warfarin vs. None	1.06 (0.07, 15.52)				10.78 (0.13, 6349)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Enoxaparin	0.79 (0.45, 1.38)	0.79 (0.44, 1.43)	0.80 (0.45, 1.42)	0.75 (0.41, 1.33)	0.75 (0.41, 1.35)
Apixaban vs. Heparin	0.61 (0.28, 1.42)	0.60 (0.26, 1.48)			
Apixaban vs. None	1.46 (0.52, 4.26)	1.42 (0.46, 4.64)	0.86 (0.26, 3.07)	0.83 (0.25, 2.90)	0.83 (0.25, 2.82)
Apixaban vs. Warfarin	1.65 (0.69, 4.20)	1.71 (0.68, 4.47)	1.70 (0.69, 4.38)	1.56 (0.61, 4.03)	1.55 (0.59, 4.11)
Dabigatran vs. Apixaban	1.63 (0.77, 3.36)	1.62 (0.76, 3.46)	1.65 (0.78, 3.45)	1.75 (0.83, 3.76)	1.75 (0.82, 3.82)
Dabigatran vs. Enoxaparin	1.28 (0.80, 2.04)	1.29 (0.79, 2.09)	1.31 (0.82, 2.11)	1.32 (0.82, 2.10)	1.32 (0.81, 2.14)
Dabigatran vs. Heparin	1.00 (0.48, 2.16)	0.98 (0.46, 2.20)			
Dabigatran vs. None	2.37 (0.93, 6.47)	2.31 (0.82, 6.78)	1.42 (0.46, 4.56)	1.46 (0.48, 4.62)	1.45 (0.50, 4.46)
Dabigatran vs. Warfarin	2.68 (1.15, 6.42)	2.78 (1.16, 6.70)	2.81 (1.19, 6.90)	2.73 (1.15, 6.69)	2.72 (1.13, 6.86)
Dalteparin vs. Apixaban	1.18 (0.35, 3.76)	1.13 (0.33, 3.75)	1.15 (0.33, 3.69)	1.26 (0.37, 4.16)	1.26 (0.36, 4.31)
Dalteparin vs. Dabigatran	0.73 (0.23, 2.25)	0.70 (0.22, 2.23)	0.70 (0.21, 2.16)	0.72 (0.22, 2.28)	0.72 (0.22, 2.30)
Dalteparin vs. Desirudin	0.78 (0.19, 2.84)	0.75 (0.18, 2.87)	0.92 (0.21, 3.70)	0.97 (0.22, 3.99)	0.95 (0.22, 3.92)
Dalteparin vs. Enoxaparin	0.93 (0.32, 2.61)	0.90 (0.31, 2.61)	0.92 (0.30, 2.59)	0.95 (0.32, 2.74)	0.95 (0.31, 2.73)
Dalteparin vs. Fondaparinux	0.66 (0.14, 2.92)	0.63 (0.13, 2.92)	0.58 (0.12, 2.61)	0.61 (0.13, 2.76)	0.58 (0.12, 2.72)
Dalteparin vs. HD Aspirin	2.80 (0.40, 20.86)	2.78 (0.39, 21.71)	2.75 (0.39, 19.16)	2.83 (0.40, 21.50)	2.80 (0.40, 22.00)
Dalteparin vs. Heparin	0.72 (0.22, 2.43)	0.68 (0.20, 2.42)			
Dalteparin vs. IPC	11.60 (0.33, 5,580.31)				
Dalteparin vs. IPC + LD Aspirin	74.81 (2.90, 21,590.31)				63.82 (2.68, 5,931.31)
Dalteparin vs. LY517717	1.08 (0.03, 56.71)	1.02 (0.02, 54.11)	1.05 (0.03, 60.28)	1.01 (0.02, 39.25)	1.11 (0.03, 45.65)
Dalteparin vs. None	1.73 (0.44, 6.81)	1.62 (0.38, 6.96)	0.99 (0.22, 4.35)	1.05 (0.24, 4.61)	1.04 (0.23, 4.71)
Dalteparin vs. Rivaroxaban	0.60 (0.18, 2.01)	0.58 (0.17, 2.05)	0.59 (0.16, 2.02)	0.62 (0.17, 2.15)	0.61 (0.17, 2.12)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Dalteparin vs. Tinzaparin	1.02 (0.32, 3.38)	1.02 (0.30, 3.55)	1.03 (0.31, 3.39)	1.03 (0.31, 3.40)	1.05 (0.31, 3.59)
Dalteparin vs. Warfarin	1.95 (0.92, 4.10)	1.94 (0.90, 4.20)	1.96 (0.90, 4.16)	1.97 (0.91, 4.21)	1.96 (0.90, 4.21)
Dalteparin vs. YM150	6.30 (0.12, 2,038.56)				6.57 (0.12, 3,287.89)
Desirudin vs. Apixaban	1.53 (0.57, 4.28)	1.52 (0.55, 4.44)	1.26 (0.41, 3.82)	1.30 (0.43, 4.09)	1.32 (0.42, 4.21)
Desirudin vs. Dabigatran	0.94 (0.37, 2.54)	0.94 (0.36, 2.61)	0.76 (0.26, 2.21)	0.75 (0.26, 2.20)	0.76 (0.25, 2.24)
Desirudin vs. Enoxaparin	1.20 (0.54, 2.88)	1.21 (0.53, 2.96)	1.00 (0.38, 2.62)	0.98 (0.38, 2.59)	1.00 (0.38, 2.63)
Desirudin vs. Heparin	0.93 (0.37, 2.57)	0.92 (0.37, 2.63)			
Desirudin vs. None	2.22 (0.69, 7.80)	2.17 (0.63, 8.17)	1.08 (0.26, 4.60)	1.09 (0.26, 4.62)	1.10 (0.27, 4.68)
Desirudin vs. Warfarin	2.51 (0.87, 7.89)	2.60 (0.86, 8.41)	2.14 (0.65, 7.30)	2.03 (0.61, 7.05)	2.06 (0.62, 7.22)
Enoxaparin + GCS vs. Apixaban	0.18 (0.00, 3.68)				0.18 (0.00, 9.92)
Enoxaparin + GCS vs. Dabigatran	0.11 (0.00, 2.19)				0.10 (0.00, 5.59)
Enoxaparin + GCS vs. Dalteparin	0.16 (0.00, 3.65)				0.14 (0.00, 9.14)
Enoxaparin + GCS vs. Desirudin	0.12 (0.00, 2.56)				0.13 (0.00, 7.83)
Enoxaparin + GCS vs. Enoxaparin	0.14 (0.00, 2.72)				0.13 (0.00, 7.16)
Enoxaparin + GCS vs. Fondaparinux	0.10 (0.00, 1.85)				0.08 (0.00, 3.88)
Enoxaparin + GCS vs. Fondaparinux + GCS	0.49 (0.25, 0.85)				0.49 (0.24, 0.87)
Enoxaparin + GCS vs. HD Aspirin	0.43 (0.01, 15.77)				0.40 (0.00, 36.38)
Enoxaparin + GCS vs. Heparin	0.11 (0.00, 2.27)				
Enoxaparin + GCS vs. IPC	1.80 (0.01, 1,501.17)				
Enoxaparin + GCS vs. IPC + LD Aspirin	11.60 (0.08, 6,045.08)				9.05 (0.01, 4,750.48)
Enoxaparin + GCS vs. LY517717	0.17 (0.00, 20.78)				0.16 (0.00, 45.38)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Enoxaparin + GCS vs. None	0.27 (0.01, 5.53)				0.15 (0.00, 9.75)
Enoxaparin + GCS vs. Rivaroxaban	0.09 (0.00, 1.93)				0.09 (0.00, 4.77)
Enoxaparin + GCS vs. Tinzaparin	0.16 (0.00, 3.72)				0.15 (0.00, 9.65)
Enoxaparin + GCS vs. Warfarin	0.30 (0.01, 6.33)				0.28 (0.00, 16.14)
Enoxaparin + GCS vs. YM150	0.98 (0.00, 809.97)				0.93 (0.00, 1,584.46)
Enoxaparin vs. None	1.85 (0.78, 4.69)	1.79 (0.68, 4.87)	1.08 (0.37, 3.32)	1.11 (0.39, 3.32)	1.10 (0.39, 3.17)
Fondaparinux vs. Rivaroxaban	0.91 (0.27, 3.23)	0.92 (0.25, 3.45)	1.02 (0.29, 3.57)	1.01 (0.28, 3.57)	1.05 (0.30, 3.85)
Fondaparinux + GCS vs. Apixaban	0.37 (0.01, 7.49)				0.37 (0.00, 18.99)
Fondaparinux + GCS vs. Dabigatran	0.23 (0.01, 4.46)				0.21 (0.00, 10.55)
Fondaparinux + GCS vs. Dalteparin	0.31 (0.01, 7.40)				0.29 (0.00, 17.73)
Fondaparinux + GCS vs. Desirudin	0.24 (0.01, 5.14)				0.28 (0.00, 15.15)
Fondaparinux + GCS vs. Enoxaparin	0.29 (0.01, 5.53)				0.27 (0.00, 13.45)
Fondaparinux + GCS vs. Fondaparinux	0.21 (0.01, 3.75)				0.17 (0.00, 7.22)
Fondaparinux + GCS vs. HD Aspirin	0.88 (0.02, 32.27)				0.81 (0.00, 71.24)
Fondaparinux + GCS vs. Heparin	0.23 (0.01, 4.61)				
Fondaparinux + GCS vs. IPC	3.64 (0.03, 3,065.60)				
Fondaparinux + GCS vs. IPC + LD Aspirin	23.50 (0.18, 12,088.38)				18.52 (0.02, 9,528.09)
Fondaparinux + GCS vs. LY517717	0.34 (0.00, 41.80)				0.32 (0.00, 92.57)
Fondaparinux + GCS vs. None	0.54 (0.01, 11.30)				0.30 (0.00, 17.89)
Fondaparinux + GCS vs. Rivaroxaban	0.19 (0.00, 3.90)				0.18 (0.00, 9.28)
Fondaparinux + GCS vs. Tinzaparin	0.32 (0.01, 7.71)				0.30 (0.00, 19.14)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Fondaparinux + GCS vs. Warfarin	0.61 (0.02, 12.94)				0.57 (0.00, 31.19)
Fondaparinux + GCS vs. YM150	1.98 (0.01, 1,659.05)				1.91 (0.00, 3,108.82)
Fondaparinux vs. Apixaban	1.79 (0.54, 6.01)	1.79 (0.51, 6.28)	1.98 (0.58, 6.94)	2.06 (0.60, 7.29)	2.16 (0.63, 7.81)
Fondaparinux vs. Dabigatran	1.10 (0.34, 3.60)	1.10 (0.33, 3.74)	1.20 (0.37, 4.02)	1.18 (0.36, 3.90)	1.24 (0.38, 4.12)
Fondaparinux vs. Desirudin	1.18 (0.30, 4.56)	1.17 (0.28, 4.75)	1.58 (0.37, 7.03)	1.58 (0.37, 6.88)	1.63 (0.38, 7.32)
Fondaparinux vs. Enoxaparin	1.41 (0.48, 4.20)	1.42 (0.46, 4.34)	1.58 (0.53, 4.80)	1.56 (0.51, 4.84)	1.63 (0.55, 4.99)
Fondaparinux vs. Heparin	1.10 (0.33, 3.78)	1.08 (0.30, 3.96)			
Fondaparinux vs. IPC	17.55 (0.52, 8,266.78)				
Fondaparinux vs. None	2.61 (0.77, 9.57)	2.54 (0.69, 9.99)	1.71 (0.46, 6.82)	1.72 (0.46, 6.90)	1.79 (0.48, 6.99)
Fondaparinux vs. Tinzaparin	1.55 (0.36, 7.12)	1.60 (0.35, 7.67)	1.77 (0.40, 8.59)	1.68 (0.37, 8.14)	1.80 (0.39, 8.98)
Fondaparinux vs. Warfarin	2.95 (0.82, 10.84)	3.06 (0.81, 11.75)	3.37 (0.92, 13.04)	3.22 (0.87, 12.44)	3.36 (0.90, 13.40)
GCS vs. Apixaban	0.18 (0.00, 2.72)				0.21 (0.00, 74.51)
GCS vs. Dabigatran	0.11 (0.00, 1.65)				0.12 (0.00, 43.12)
GCS vs. Dalteparin	0.15 (0.00, 2.63)				0.17 (0.00, 65.04)
GCS vs. Desirudin	0.12 (0.00, 1.97)				0.16 (0.00, 57.45)
GCS vs. Enoxaparin	0.14 (0.00, 2.01)				0.16 (0.00, 54.93)
GCS vs. Enoxaparin + GCS	0.97 (0.05, 20.00)				1.18 (0.02, 82.85)
GCS vs. Fondaparinux	0.10 (0.00, 1.56)				0.10 (0.00, 30.39)
GCS vs. Fondaparinux + GCS	0.48 (0.03, 9.09)				0.57 (0.01, 43.03)
GCS vs. HD Aspirin	0.42 (0.01, 12.50)				0.47 (0.00, 211.03)
GCS vs. Heparin	0.11 (0.00, 1.68)				

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
GCS vs. IPC + LD Aspirin	11.11 (0.08, 100.00)				10.64 (0.01, 26,370.47)
GCS vs. LY517717	0.16 (0.00, 16.67)				0.19 (0.00, 219.64)
GCS vs. None	0.26 (0.01, 3.87)				0.17 (0.00, 66.55)
GCS vs. Rivaroxaban	0.09 (0.00, 1.41)				0.10 (0.00, 38.36)
GCS vs. Tinzaparin	0.15 (0.00, 2.86)				0.17 (0.00, 74.89)
GCS vs. Warfarin	0.29 (0.01, 4.57)				0.33 (0.00, 121.51)
GCS vs. YM150	0.94 (0.00, 100.00)				1.10 (0.00, 8,459.12)
HD Aspirin vs. Apixaban	0.42 (0.05, 3.14)	0.41 (0.05, 3.16)	0.42 (0.05, 3.26)	0.45 (0.05, 3.16)	0.45 (0.05, 3.42)
HD Aspirin vs. Dabigatran	0.26 (0.03, 1.89)	0.25 (0.03, 1.98)	0.25 (0.03, 1.97)	0.26 (0.03, 1.73)	0.26 (0.03, 1.90)
HD Aspirin vs. Desirudin	0.28 (0.03, 2.16)	0.27 (0.03, 2.29)	0.33 (0.04, 2.80)	0.34 (0.04, 2.81)	0.34 (0.04, 2.92)
HD Aspirin vs. Enoxaparin	0.33 (0.05, 2.26)	0.32 (0.04, 2.39)	0.33 (0.05, 2.40)	0.34 (0.04, 2.18)	0.34 (0.04, 2.34)
HD Aspirin vs. Fondaparinux	0.24 (0.03, 2.16)	0.23 (0.02, 2.21)	0.21 (0.02, 1.99)	0.22 (0.02, 1.84)	0.21 (0.02, 1.92)
HD Aspirin vs. Heparin	0.26 (0.03, 1.95)	0.25 (0.03, 2.02)			
HD Aspirin vs. IPC	4.14 (0.07, 2,363.74)				
HD Aspirin vs. IPC + LD Aspirin	26.71 (0.62, 8,450.66)				22.78 (0.62, 2,844.09)
HD Aspirin vs. LY517717	0.39 (0.01, 29.43)	0.37 (0.00, 25.89)	0.38 (0.01, 27.97)	0.36 (0.00, 18.88)	0.40 (0.01, 24.17)
HD Aspirin vs. None	0.62 (0.07, 5.17)	0.58 (0.06, 5.44)	0.36 (0.04, 3.33)	0.37 (0.04, 3.16)	0.37 (0.04, 3.42)
HD Aspirin vs. Rivaroxaban	0.22 (0.03, 1.58)	0.21 (0.02, 1.75)	0.22 (0.03, 1.77)	0.22 (0.03, 1.59)	0.22 (0.03, 1.67)
HD Aspirin vs. Tinzaparin	0.37 (0.05, 2.80)	0.37 (0.04, 2.94)	0.37 (0.05, 2.73)	0.36 (0.05, 2.62)	0.37 (0.05, 2.82)
HD Aspirin vs. Warfarin	0.70 (0.10, 4.17)	0.70 (0.10, 4.29)	0.71 (0.12, 4.37)	0.70 (0.11, 3.98)	0.70 (0.10, 4.16)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
HD Aspirin vs. YM150	2.25 (0.03, 832.97)				2.35 (0.03, 1,208.34)
Heparin vs. Enoxaparin	1.29 (0.70, 2.30)	1.32 (0.69, 2.39)			
Heparin vs. None	2.38 (0.88, 6.63)	2.36 (0.78, 7.3)			
Heparin vs. Warfarin	2.70 (1.06, 6.86)	2.83 (1.05, 7.41)			
IPC + LD Aspirin vs. Apixaban	0.02 (0.00, 0.35)				0.02 (0.00, 0.38)
IPC + LD Aspirin vs. Dabigatran	0.01 (0.00, 0.21)				0.01 (0.00, 0.21)
IPC + LD Aspirin vs. Desirudin	0.01 (0.00, 0.25)				0.01 (0.00, 0.32)
IPC + LD Aspirin vs. Enoxaparin	0.01 (0.00, 0.26)				0.01 (0.00, 0.26)
IPC + LD Aspirin vs. Fondaparinux	0.01 (0.00, 0.23)				0.01 (0.00, 0.21)
IPC + LD Aspirin vs. Heparin	0.01 (0.00, 0.22)				
IPC + LD Aspirin vs. IPC	0.16 (0.00, 153.39)				
IPC + LD Aspirin vs. None	0.02 (0.00, 0.56)				0.02 (0.00, 0.39)
IPC + LD Aspirin vs. Tinzaparin	0.01 (0.00, 0.36)				0.02 (0.00, 0.38)
IPC + LD Aspirin vs. Warfarin	0.03 (0.00, 0.60)				0.03 (0.00, 0.66)
IPC vs. Apixaban	0.10 (0.00, 3.15)				
IPC vs. Dabigatran	0.06 (0.00, 1.93)				
IPC vs. Desirudin	0.07 (0.00, 2.30)				
IPC vs. Enoxaparin	0.08 (0.00, 2.36)				
IPC vs. GCS	0.57 (0.00, 63.12)				
IPC vs. Heparin	0.06 (0.00, 1.98)				
IPC vs. None	0.15 (0.00, 4.51)				
IPC vs. Warfarin	0.17 (0.00, 5.45)				

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
LY517717 vs. Apixaban	1.10 (0.02, 42.95)	1.11 (0.02, 48.62)	1.10 (0.02, 38.28)	1.26 (0.04, 60.28)	1.13 (0.03, 42.18)
LY517717 vs. Dabigatran	0.67 (0.01, 25.92)	0.68 (0.01, 30.66)	0.67 (0.01, 23.78)	0.72 (0.02, 33.68)	0.65 (0.02, 24.12)
LY517717 vs. Desirudin	0.72 (0.01, 28.16)	0.73 (0.01, 35.20)	0.88 (0.02, 33.92)	0.96 (0.03, 50.05)	0.86 (0.02, 35.27)
LY517717 vs. Enoxaparin	0.86 (0.02, 31.41)	0.88 (0.02, 37.83)	0.88 (0.02, 29.64)	0.95 (0.03, 42.69)	0.85 (0.02, 31.19)
LY517717 vs. Fondaparinux	0.61 (0.01, 25.46)	0.62 (0.01, 31.47)	0.56 (0.01, 21.50)	0.61 (0.02, 31.94)	0.52 (0.01, 21.52)
LY517717 vs. Heparin	0.67 (0.01, 25.84)	0.67 (0.01, 30.85)			
LY517717 vs. IPC	10.75 (0.06, 11,114.44)				
LY517717 vs. IPC + LD Aspirin	69.34 (0.50, 37,421.47)				57.45 (0.48, 14,705.84)
LY517717 vs. None	1.60 (0.03, 67.15)	1.58 (0.03, 78.10)	0.95 (0.01, 37.41)	1.05 (0.03, 55.31)	0.94 (0.02, 38.82)
LY517717 vs. Tinzaparin	0.95 (0.02, 42.61)	0.99 (0.02, 48.57)	0.98 (0.02, 40.61)	1.02 (0.03, 51.57)	0.94 (0.02, 38.05)
LY517717 vs. Warfarin	1.81 (0.04, 71.16)	1.90 (0.04, 87.27)	1.87 (0.03, 70.74)	1.96 (0.06, 92.30)	1.76 (0.05, 67.63)
Rivaroxaban vs. Apixaban	1.96 (0.84, 4.54)	1.94 (0.80, 4.63)	1.95 (0.81, 4.59)	2.05 (0.85, 4.91)	2.05 (0.85, 4.95)
Rivaroxaban vs. Dabigatran	1.21 (0.55, 2.65)	1.20 (0.53, 2.74)	1.18 (0.54, 2.60)	1.18 (0.53, 2.58)	1.17 (0.52, 2.62)
Rivaroxaban vs. Desirudin	1.29 (0.44, 3.60)	1.28 (0.42, 3.61)	1.55 (0.49, 4.87)	1.58 (0.49, 4.95)	1.55 (0.48, 4.91)
Rivaroxaban vs. Enoxaparin	1.55 (0.82, 2.91)	1.54 (0.81, 2.97)	1.55 (0.81, 2.93)	1.55 (0.81, 2.92)	1.54 (0.81, 2.92)
Rivaroxaban vs. Heparin	1.20 (0.51, 2.90)	1.17 (0.48, 2.95)			
Rivaroxaban vs. IPC	19.24 (0.63, 9,499.55)				
Rivaroxaban vs. IPC + LD Aspirin	124.09 (5.55, 31,257.04)				103.86 (5.44, 8,217.32)
Rivaroxaban vs. LY517717	1.79 (0.05, 88.50)	1.75 (0.04, 86.23)	1.77 (0.05, 100.58)	1.63 (0.03, 54.00)	1.81 (0.05, 68.72)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Rivaroxaban vs. None	2.86 (0.98, 8.63)	2.76 (0.85, 9.57)	1.68 (0.47, 5.79)	1.71 (0.49, 6.10)	1.70 (0.50, 5.87)
Rivaroxaban vs. Tinzaparin	1.70 (0.50, 5.88)	1.74 (0.50, 6.11)	1.74 (0.51, 6.19)	1.68 (0.48, 6.04)	1.71 (0.50, 6.09)
Rivaroxaban vs. Warfarin	3.24 (1.26, 8.58)	3.32 (1.22, 8.94)	3.31 (1.25, 9.04)	3.21 (1.20, 8.77)	3.18 (1.19, 8.68)
Tinzaparin vs. Apixaban	1.16 (0.34, 3.70)	1.11 (0.32, 3.72)	1.12 (0.32, 3.68)	1.23 (0.35, 4.08)	1.20 (0.34, 4.04)
Tinzaparin vs. Dabigatran	0.71 (0.22, 2.18)	0.69 (0.21, 2.20)	0.68 (0.20, 2.11)	0.70 (0.21, 2.20)	0.69 (0.20, 2.18)
Tinzaparin vs. Desirudin	0.76 (0.19, 2.78)	0.73 (0.17, 2.80)	0.89 (0.20, 3.61)	0.94 (0.21, 3.95)	0.91 (0.20, 3.74)
Tinzaparin vs. Enoxaparin	0.91 (0.31, 2.54)	0.89 (0.30, 2.57)	0.89 (0.30, 2.51)	0.92 (0.30, 2.64)	0.90 (0.30, 2.64)
Tinzaparin vs. Heparin	0.71 (0.21, 2.33)	0.67 (0.19, 2.30)			
Tinzaparin vs. IPC	11.31 (0.30, 5,813.86)				
Tinzaparin vs. None	1.68 (0.43, 6.61)	1.59 (0.37, 6.81)	0.96 (0.21, 4.19)	1.02 (0.23, 4.78)	1.00 (0.21, 4.50)
Tinzaparin vs. Warfarin	1.91 (0.75, 4.80)	1.91 (0.72, 4.90)	1.90 (0.74, 4.79)	1.91 (0.73, 4.87)	1.87 (0.72, 4.77)
Warfarin vs. Enoxaparin	0.48 (0.23, 0.96)	0.46 (0.22, 0.98)	0.47 (0.22, 0.97)	0.48 (0.23, 1.00)	0.48 (0.22, 1.01)
Warfarin vs. None	0.88 (0.28, 2.81)	0.83 (0.24, 2.88)	0.51 (0.14, 1.85)	0.53 (0.15, 1.95)	0.53 (0.15, 1.97)
YM150 vs. Apixaban	0.19 (0.00, 8.43)				0.19 (0.00, 9.15)
YM150 vs. Dabigatran	0.12 (0.00, 5.13)				0.11 (0.00, 5.20)
YM150 vs. Desirudin	0.12 (0.00, 6.01)				0.14 (0.00, 7.39)
YM150 vs. Enoxaparin	0.15 (0.00, 6.37)				0.14 (0.00, 6.44)
YM150 vs. Fondaparinux	0.10 (0.00, 5.38)				0.09 (0.00, 4.81)
YM150 vs. Heparin	0.11 (0.00, 5.27)				
YM150 vs. IPC	1.84 (0.00, 2,069.37)				
YM150 vs. IPC + LD Aspirin	11.87 (0.02, 9,956.69)				9.71 (0.01, 4,105.16)

Table 99. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
YM150 vs. LY517717	0.17 (0.00, 37.00)				0.17 (0.00, 28.39)
YM150 vs. None	0.27 (0.00, 13.41)				0.16 (0.00, 8.52)
YM150 vs. Rivaroxaban	0.10 (0.00, 4.50)				0.09 (0.00, 4.38)
YM150 vs. Tinzaparin	0.16 (0.00, 8.37)				0.16 (0.00, 8.91)
YM150 vs. Warfarin	0.31 (0.00, 14.70)				0.30 (0.00, 14.75)

Table 100. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Apixaban vs. Dabigatran	1.12 (0.18, 7.64)	1.19 (0.12, 13.12)	1.15 (0.12, 12.58)	1.14 (0.18, 8.17)
Apixaban vs. Desirudin	0.90 (0.09, 10.05)	1.38 (0.08, 33.65)	0.63 (0.02, 15.17)	0.59 (0.04, 8.62)
Apixaban vs. Enoxaparin	1.33 (0.40, 4.95)	1.41 (0.31, 7.46)	1.41 (0.31, 7.19)	1.36 (0.39, 5.31)
Apixaban vs. Heparin	0.27 (0.02, 3.59)	0.13 (0.00, 4.00)		
Apixaban vs. Warfarin	0.95 (0.15, 5.64)	0.96 (0.10, 9.50)	0.97 (0.10, 9.22)	0.94 (0.15, 6.20)
Dabigatran vs. Enoxaparin	1.19 (0.31, 4.71)	1.19 (0.21, 6.64)	1.23 (0.22, 7.03)	1.19 (0.30, 4.86)
Dabigatran vs. Heparin	0.24 (0.01, 3.36)	0.11 (0.00, 3.30)		
Dabigatran vs. Warfarin	0.85 (0.12, 5.13)	0.81 (0.07, 8.26)	0.84 (0.08, 8.49)	0.83 (0.12, 5.60)
Dalteparin vs. Apixaban	1.05 (0.04, 25.84)	1.06 (0.02, 47.70)	1.02 (0.02, 48.33)	1.10 (0.04, 29.02)
Dalteparin vs. Dabigatran	1.17 (0.05, 32.69)	1.26 (0.03, 61.50)	1.18 (0.03, 65.96)	1.25 (0.04, 36.74)
Dalteparin vs. Desirudin	0.94 (0.03, 33.82)	1.45 (0.02, 131.24)	0.64 (0.01, 64.01)	0.65 (0.01, 28.99)
Dalteparin vs. Enoxaparin	1.39 (0.07, 27.72)	1.49 (0.05, 50.55)	1.44 (0.05, 53.79)	1.49 (0.07, 32.04)
Dalteparin vs. Fondaparinux	8.01 (0.05, 5,967.00)			6.88 (0.04, 8,928.47)
Dalteparin vs. Heparin	0.28 (0.01, 11.13)	0.13 (0.00, 13.60)		
Dalteparin vs. Rivaroxaban	2.28 (0.10, 50.81)	2.59 (0.07, 109.40)	2.50 (0.07, 114.32)	2.44 (0.10, 61.74)
Dalteparin vs. Tinzaparin	0.99 (0.04, 24.93)	0.99 (0.02, 52.51)	0.99 (0.02, 55.92)	1.02 (0.03, 28.96)
Dalteparin vs. Warfarin	0.99 (0.07, 13.83)	1.02 (0.05, 21.85)	0.99 (0.05, 23.36)	1.03 (0.07, 15.85)
Desirudin vs. Dabigatran	1.24 (0.11, 14.13)	0.86 (0.03, 16.05)	1.83 (0.07, 54.22)	1.92 (0.13, 34.47)
Desirudin vs. Enoxaparin	1.48 (0.20, 11.13)	1.02 (0.07, 11.40)	2.25 (0.15, 40.94)	2.29 (0.23, 29.11)
Desirudin vs. Heparin	0.30 (0.03, 2.09)	0.09 (0.00, 1.75)		
Desirudin vs. Warfarin	1.06 (0.09, 10.82)	0.70 (0.03, 12.15)	1.54 (0.06, 40.49)	1.59 (0.11, 26.82)
Enoxaparin + GCS vs. Apixaban	0.03 (0.00, 7.36)			0.04 (0.00, 8.02)
Enoxaparin + GCS vs. Dabigatran	0.03 (0.00, 8.95)			0.04 (0.00, 9.93)

Table 100. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Enoxaparin + GCS vs. Dalteparin	0.03 (0.00, 12.53)			0.03 (0.00, 14.54)
Enoxaparin + GCS vs. Desirudin	0.03 (0.00, 9.08)			0.02 (0.00, 7.33)
Enoxaparin + GCS vs. Enoxaparin	0.04 (0.00, 8.55)			0.05 (0.00, 9.08)
Enoxaparin + GCS vs. Fondaparinux	0.22 (0.01, 5.24)			0.24 (0.01, 5.61)
Enoxaparin + GCS vs. Fondaparinux + GCS	1.06 (0.31, 3.71)			1.06 (0.30, 3.89)
Enoxaparin + GCS vs. Heparin	0.01 (0.00, 3.13)			
Enoxaparin + GCS vs. Rivaroxaban	0.06 (0.00, 15.85)			0.08 (0.00, 16.68)
Enoxaparin + GCS vs. Tinzaparin	0.03 (0.00, 9.75)			0.04 (0.00, 11.30)
Enoxaparin + GCS vs. Warfarin	0.03 (0.00, 7.01)			0.04 (0.00, 7.86)
Fondaparinux + GCS vs. Apixaban	0.03 (0.00, 5.94)			0.04 (0.00, 6.29)
Fondaparinux + GCS vs. Dabigatran	0.03 (0.00, 7.19)			0.04 (0.00, 8.23)
Fondaparinux + GCS vs. Dalteparin	0.03 (0.00, 10.16)			0.03 (0.00, 12.18)
Fondaparinux + GCS vs. Desirudin	0.02 (0.00, 7.16)			0.02 (0.00, 5.74)
Fondaparinux + GCS vs. Enoxaparin	0.04 (0.00, 6.73)			0.05 (0.00, 7.34)
Fondaparinux + GCS vs. Fondaparinux	0.21 (0.01, 3.75)			0.23 (0.01, 3.95)
Fondaparinux + GCS vs. Heparin	0.01 (0.00, 2.50)			
Fondaparinux + GCS vs. Rivaroxaban	0.06 (0.00, 12.45)			0.08 (0.00, 13.38)
Fondaparinux + GCS vs. Tinzaparin	0.03 (0.00, 7.71)			0.03 (0.00, 9.35)
Fondaparinux + GCS vs. Warfarin	0.03 (0.00, 5.59)			0.03 (0.00, 6.24)
Fondaparinux vs. Apixaban	0.13 (0.00, 9.35)			0.16 (0.00, 10.73)
Fondaparinux vs. Dabigatran	0.15 (0.00, 11.78)			0.18 (0.00, 13.36)
Fondaparinux vs. Desirudin	0.12 (0.00, 12.86)			0.09 (0.00, 10.60)
Fondaparinux vs. Enoxaparin	0.17 (0.00, 10.92)			0.22 (0.00, 11.94)

Table 100. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Fondaparinux vs. Heparin	0.04 (0.00, 4.89)			
Fondaparinux vs. Warfarin	0.12 (0.00, 8.98)			0.15 (0.00, 10.61)
Heparin vs. Enoxaparin	4.95 (0.53, 59.86)	11.02 (0.56, 506.74)		
Heparin vs. Warfarin	3.53 (0.26, 56.32)	7.55 (0.26, 482.51)		
IPC + GCS vs. Apixaban	0.13 (0.00, 91.93)			0.16 (0.00, 74.37)
IPC + GCS vs. Dabigatran	0.14 (0.00, 102.31)			0.18 (0.00, 91.74)
IPC + GCS vs. Dalteparin	0.12 (0.00, 123.59)			0.14 (0.00, 141.32)
IPC + GCS vs. Desirudin	0.11 (0.00, 100.99)			0.09 (0.00, 61.99)
IPC + GCS vs. Enoxaparin	0.17 (0.00, 100.69)			0.22 (0.00, 94.82)
IPC + GCS vs. Enoxaparin + GCS	4.36 (0.27, 160.13)			4.17 (0.25, 142.02)
IPC + GCS vs. Fondaparinux	0.98 (0.01, 113.18)			1.00 (0.01, 102.41)
IPC + GCS vs. Fondaparinux + GCS	4.60 (0.22, 201.95)			4.42 (0.21, 186.79)
IPC + GCS vs. Heparin	0.03 (0.00, 35.95)			
IPC + GCS vs. Rivaroxaban	0.28 (0.00, 192.67)			0.35 (0.00, 167.00)
IPC + GCS vs. Tinzaparin	0.12 (0.00, 110.61)			0.15 (0.00, 97.71)
IPC + GCS vs. Warfarin	0.12 (0.00, 81.13)			0.15 (0.00, 72.31)
Rivaroxaban vs. Apixaban	0.46 (0.09, 2.07)	0.41 (0.05, 2.90)	0.41 (0.05, 2.80)	0.45 (0.08, 2.20)
Rivaroxaban vs. Dabigatran	0.51 (0.10, 2.72)	0.49 (0.06, 4.00)	0.47 (0.06, 3.95)	0.51 (0.09, 2.76)
Rivaroxaban vs. Desirudin	0.41 (0.04, 3.72)	0.56 (0.04, 10.76)	0.26 (0.01, 5.09)	0.27 (0.02, 3.18)
Rivaroxaban vs. Enoxaparin	0.61 (0.24, 1.54)	0.58 (0.16, 1.99)	0.58 (0.16, 1.95)	0.61 (0.22, 1.60)
Rivaroxaban vs. Fondaparinux	3.52 (0.05, 1,799)			2.82 (0.05, 2,219)
Rivaroxaban vs. Heparin	0.12 (0.01, 1.41)	0.05 (0.00, 1.29)		
Rivaroxaban vs. Warfarin	0.44 (0.08, 1.97)	0.39 (0.04, 2.91)	0.40 (0.05, 2.83)	0.42 (0.07, 2.10)

Table 100. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Tinzaparin vs. Apixaban	1.06 (0.08, 14.75)	1.07 (0.04, 31.85)	1.04 (0.04, 27.69)	1.07 (0.07, 15.80)
Tinzaparin vs. Dabigatran	1.18 (0.09, 17.99)	1.27 (0.04, 43.47)	1.19 (0.04, 37.04)	1.22 (0.08, 20.37)
Tinzaparin vs. Desirudin	0.95 (0.05, 21.05)	1.47 (0.04, 93.78)	0.65 (0.01, 36.34)	0.64 (0.02, 18.88)
Tinzaparin vs. Enoxaparin	1.41 (0.15, 15.10)	1.50 (0.08, 33.12)	1.46 (0.08, 28.25)	1.46 (0.14, 17.01)
Tinzaparin vs. Fondaparinux	8.08 (0.07, 5,234.36)			6.73 (0.06, 7,420.49)
Tinzaparin vs. Heparin	0.28 (0.01, 7.25)	0.14 (0.00, 9.78)		
Tinzaparin vs. Rivaroxaban	2.30 (0.21, 29.46)	2.61 (0.11, 75.19)	2.53 (0.11, 63.94)	2.39 (0.19, 34.71)
Tinzaparin vs. Warfarin	1.00 (0.15, 6.86)	1.03 (0.08, 12.83)	1.00 (0.08, 11.65)	1.01 (0.14, 7.46)
Warfarin + GCS vs. Apixaban	0.14 (0.00, 310.75)			0.16 (0.00, 220.08)
Warfarin + GCS vs. Dabigatran	0.15 (0.00, 391.11)			0.18 (0.00, 261.39)
Warfarin + GCS vs. Dalteparin	0.13 (0.00, 418.22)			0.15 (0.00, 383.37)
Warfarin + GCS vs. Desirudin	0.12 (0.00, 333.95)			0.09 (0.00, 171.57)
Warfarin + GCS vs. Enoxaparin	0.18 (0.00, 370.18)			0.22 (0.00, 273.96)
Warfarin + GCS vs. Enoxaparin + GCS	4.62 (0.04, 827.99)			4.21 (0.04, 634.60)
Warfarin + GCS vs. Fondaparinux	1.04 (0.00, 509.28)			1.00 (0.00, 352.13)
Warfarin + GCS vs. Fondaparinux + GCS	4.88 (0.04, 1,063.16)			4.46 (0.03, 763.57)
Warfarin + GCS vs. Heparin	0.04 (0.00, 111.94)			
Warfarin + GCS vs. IPC + GCS	1.06 (0.02, 60.22)			1.01 (0.02, 52.77)
Warfarin + GCS vs. Rivaroxaban	0.29 (0.00, 633.97)			0.36 (0.00, 460.82)
Warfarin + GCS vs. Tinzaparin	0.13 (0.00, 373.90)			0.15 (0.00, 256.21)
Warfarin + GCS vs. Warfarin	0.13 (0.00, 291.49)			0.15 (0.00, 209.14)
Warfarin vs. Enoxaparin	1.40 (0.42, 5.41)	1.46 (0.29, 8.26)	1.46 (0.30, 7.83)	1.44 (0.39, 5.80)

Table 101. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Dabigatran	0.66 (0.10, 4.38)	0.66 (0.08, 5.38)	0.66 (0.08, 5.22)	0.49 (0.05, 4.31)	0.50 (0.06, 3.79)
Apixaban vs. Desirudin	0.46 (0.03, 7.81)	0.47 (0.02, 10.78)	0.46 (0.02, 11.16)	0.34 (0.01, 8.69)	0.36 (0.02, 6.91)
Apixaban vs. Enoxaparin	0.52 (0.13, 2.02)	0.52 (0.11, 2.40)	0.52 (0.11, 2.35)	0.39 (0.07, 1.98)	0.40 (0.08, 1.79)
Apixaban vs. Heparin	0.35 (0.01, 17.13)	0.37 (0.01, 27.94)			
Apixaban vs. None	0.22 (0, 11.59)	0.23 (0, 17.8)	0.22 (0, 15.66)	0.34 (0.01, 14.17)	0.34 (0.01, 12.57)
Apixaban vs. Warfarin	1.56 (0.06, 69.13)	1.49 (0.05, 78.26)	1.51 (0.05, 77.01)		
Dabigatran vs. Desirudin	0.70 (0.04, 11.92)	0.71 (0.03, 16.23)	0.71 (0.03, 16.86)	0.69 (0.03, 16.36)	0.71 (0.04, 13.14)
Dabigatran vs. Enoxaparin	0.79 (0.21, 3.03)	0.80 (0.19, 3.43)	0.79 (0.19, 3.44)	0.79 (0.18, 3.36)	0.79 (0.20, 3.12)
Dabigatran vs. None	0.33 (0.01, 10.7)	0.35 (0.01, 15.23)	0.34 (0.01, 14.04)	0.70 (0.01, 57.69)	0.69 (0.01, 47.85)
Dabigatran vs. Warfarin	2.36 (0.07, 129.28)	2.28 (0.06, 146.94)	2.30 (0.06, 145.62)		
Dalteparin vs. Apixaban	0.19 (0.00, 11.16)	0.20 (0.00, 15.82)	0.20 (0.00, 16.01)		
Dalteparin vs. Dabigatran	0.13 (0.00, 9.13)	0.13 (0.00, 12.91)	0.13 (0.00, 13.56)		
Dalteparin vs. Desirudin	0.09 (0.00, 10.62)	0.09 (0.00, 17.08)	0.09 (0.00, 17.39)		
Dalteparin vs. Enoxaparin	0.10 (0.00, 5.89)	0.11 (0.00, 8.20)	0.10 (0.00, 8.46)		1.12 (0.08, 14.86)
Dalteparin vs. Enoxaparin +IPC	0.11 (0.00, 41.18)	0.11 (0.00, 57.57)	0.11 (0.00, 56.20)		
Dalteparin vs. Heparin	0.07 (0.00, 16.12)	0.07 (0.00, 29.99)			
Dalteparin vs. None	0.04 (0.00, 11.42)	0.05 (0.00, 18.19)	0.04 (0.00, 17.96)		
Dalteparin vs. Rivaroxaban	0.28 (0.00, 26.05)	0.48 (0.00, 84.52)	0.47 (0.00, 90.02)		
Dalteparin vs. Tinzaparin	0.17 (0.00, 27.06)	0.18 (0.00, 44.75)	0.18 (0.00, 42.18)		
Dalteparin vs. Warfarin	0.30 (0.02, 3.71)	0.30 (0.02, 4.80)	0.30 (0.02, 4.83)		
Desirudin vs. Enoxaparin	1.14 (0.09, 14.30)	1.12 (0.07, 18.25)	1.12 (0.07, 18.03)	1.14 (0.07, 18.56)	

Table 101. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Desirudin vs. None	0.47 (0.00, 42.52)	0.50 (0.00, 68.03)	0.48 (0.00, 64.01)	1.01 (0.01, 151.87)	0.97 (0.01, 117)
Desirudin vs. Warfarin	3.39 (0.06, 312.62)	3.20 (0.04, 369.81)	3.25 (0.04, 372.41)		
Enoxaparin +IPC vs. Apixaban	1.79 (0.02, 157.12)	1.79 (0.02, 184.75)	1.84 (0.02, 197.75)	2.58 (0.02, 316.08)	2.39 (0.03, 225.88)
Enoxaparin +IPC vs. Dabigatran	1.18 (0.01, 102.82)	1.17 (0.01, 116.75)	1.21 (0.01, 125.46)	1.26 (0.01, 135.64)	1.20 (0.01, 106.27)
Enoxaparin +IPC vs. Desirudin	0.82 (0.00, 111.39)	0.84 (0.00, 147.23)	0.85 (0.00, 148.56)	0.87 (0.00, 165.50)	0.85 (0.01, 118.75)
Enoxaparin +IPC vs. Enoxaparin	0.94 (0.01, 67.42)	0.94 (0.01, 73.11)	0.96 (0.01, 80.96)	0.99 (0.01, 86.49)	0.95 (0.01, 69.48)
Enoxaparin +IPC vs. Heparin	0.64 (0.00, 167.17)	0.66 (0.00, 243.96)			
Enoxaparin +IPC vs. None	0.39 (0.00, 121.75)	0.42 (0.00, 161.42)	0.41 (0.00, 171.74)	0.88 (0.00, 426.24)	0.82 (0.00, 280.90)
Enoxaparin +IPC vs. Rivaroxaban	2.58 (0.02, 288.59)	4.24 (0.03, 702.05)	4.35 (0.03, 738.04)	4.58 (0.03, 872.18)	2.67 (0.03, 303.69)
Enoxaparin +IPC vs. Warfarin	2.80 (0.01, 743.97)	2.67 (0.01, 930.76)	2.78 (0.01, 900.54)		
Enoxaparin vs. None	0.42 (0.01, 17.12)	0.44 (0.01, 25.64)	0.43 (0.01, 23.2)	0.89 (0.01, 55.48)	0.87 (0.01, 47.09)
Heparin vs. Dabigatran	1.86 (0.04, 90.02)	1.79 (0.02, 122.00)			
Heparin vs. Desirudin	1.29 (0.09, 18.71)	1.27 (0.07, 23.20)			
Heparin vs. Enoxaparin	1.47 (0.04, 56.37)	1.43 (0.03, 78.49)			
Heparin vs. None	0.61 (0.00, 118)	0.63 (0.00, 190)			
Heparin vs. Warfarin	4.39 (0.03, 810.78)	4.08 (0.02, 1,025.57)			
IPC vs. Apixaban	12.86 (0.06, 4,600.87)	11.82 (0.04, 5,244.84)	12.48 (0.04, 4,769.52)	8.41 (0.04, 2,581.17)	8.23 (0.05, 2,206.14)

Table 101. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
IPC vs. Dabigatran	8.48 (0.06, 2,497.39)	7.74 (0.04, 2,347.25)	8.19 (0.04, 2,316.93)	4.11 (0.01, 1,781.12)	4.12 (0.02, 1,540.71)
IPC vs. Dalteparin	66.29 (0.09, 76,114.95)	58.38 (0.05, 105,873.47)	62.68 (0.06, 103,777.04)		
IPC vs. Desirudin	5.90 (0.02, 2,670.44)	5.51 (0.01, 3,597.52)	5.80 (0.01, 3,547.51)	2.85 (0.00, 1,902.64)	2.93 (0.01, 1,587.63)
IPC vs. Enoxaparin	6.73 (0.04, 2,115.40)	6.20 (0.03, 2,219.42)	6.51 (0.03, 2,136.66)	3.24 (0.01, 1,233.98)	3.27 (0.02, 1,050.48)
IPC vs. Enoxaparin +IPC	7.16 (0.01, 12,951.93)	6.59 (0.01, 10,046.71)	6.79 (0.01, 9,976.62)	3.26 (0.00, 5,084.74)	3.45 (0.00, 4,019.85)
IPC vs. Heparin	4.56 (0.01, 3,604.72)	4.33 (0.01, 5,244.84)			
IPC vs. None	2.79 (0.08, 130.71)	2.74 (0.07, 156.80)	2.80 (0.07, 164.19)	2.87 (0.07, 178.04)	2.83 (0.08, 154.62)
IPC vs. Rivaroxaban	18.50 (0.08, 6,946.55)	27.97 (0.08, 18,196.78)	29.52 (0.09, 18,287.99)	14.97 (0.04, 10,604.14)	9.19 (0.03, 4,076.52)
IPC vs. Tinzaparin	11.43 (0.03, 6,939.60)	10.60 (0.02, 8,699.32)	10.98 (0.02, 8,308.21)	5.41 (0.01, 4,964.16)	5.52 (0.01, 3,812.35)
IPC vs. Warfarin	20.03 (0.04, 14,676.46)	17.64 (0.03, 19,633.65)	18.86 (0.03, 18,398.05)		
LD Aspirin vs. Apixaban	3.59 (0.03, 566.23)	3.36 (0.02, 675.87)	3.49 (0.02, 650.02)	2.29 (0.02, 313.25)	2.26 (0.03, 248.89)
LD Aspirin vs. Dabigatran	2.37 (0.04, 262.43)	2.20 (0.02, 291.20)	2.29 (0.02, 289.17)	1.12 (0.01, 222.74)	1.13 (0.01, 175.56)
LD Aspirin vs. Dalteparin	18.50 (0.04, 13,147.67)	16.58 (0.02, 16,564.22)	17.50 (0.03, 15,229.66)		

Table 101. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
LD Aspirin vs. Desirudin	1.65 (0.01, 376.53)	1.57 (0.01, 493.24)	1.62 (0.01, 520.61)	0.78 (0.00, 257.24)	0.80 (0.00, 197.55)
LD Aspirin vs. Enoxaparin	1.88 (0.02, 248.64)	1.76 (0.01, 284.58)	1.82 (0.01, 275.89)	0.88 (0.01, 149.01)	0.90 (0.01, 117.33)
LD Aspirin vs. Enoxaparin +IPC	2.00 (0.00, 1,775.79)	1.87 (0.00, 1,486.23)	1.89 (0.00, 1,508.69)	0.89 (0.00, 779.77)	0.94 (0.00, 512.35)
LD Aspirin vs. Heparin	1.27 (0.00, 528.48)	1.23 (0.00, 772.78)			
LD Aspirin vs. IPC	0.28 (0.00, 19.55)	0.28 (0.00, 27.39)	0.28 (0.00, 26.74)	0.27 (0.00, 27.36)	0.27 (0.00, 20.66)
LD Aspirin vs. None	0.78 (0.07, 8.61)	0.78 (0.05, 11.20)	0.78 (0.05, 11.22)	0.78 (0.05, 11.39)	0.78 (0.07, 9.13)
LD Aspirin vs. Rivaroxaban	5.17 (0.05, 1,021.47)	7.94 (0.04, 2,662.44)	8.25 (0.05, 2,614.95)	4.06 (0.02, 1,420.83)	2.52 (0.02, 492.26)
LD Aspirin vs. Tinzaparin	3.19 (0.01, 1,024.54)	3.01 (0.01, 1,256.39)	3.07 (0.01, 1,187.97)	1.47 (0.00, 657.21)	1.51 (0.01, 485.41)
LD Aspirin vs. Warfarin	5.59 (0.02, 2,487.42)	5.01 (0.01, 2,858.35)	5.26 (0.01, 2,576.02)		
Rivaroxaban vs. Apixaban	0.69 (0.06, 6.05)	0.42 (0.02, 5.11)	0.42 (0.02, 5.16)	0.56 (0.02, 7.90)	0.90 (0.07, 9.67)
Rivaroxaban vs. Dabigatran	0.46 (0.04, 3.88)	0.28 (0.01, 3.30)	0.28 (0.01, 3.32)	0.27 (0.01, 3.39)	0.45 (0.04, 4.15)
Rivaroxaban vs. Desirudin	0.32 (0.01, 6.33)	0.20 (0.00, 5.60)	0.20 (0.00, 5.63)	0.19 (0.00, 5.65)	0.32 (0.01, 6.92)
Rivaroxaban vs. Enoxaparin	0.36 (0.05, 1.99)	0.22 (0.02, 1.72)	0.22 (0.02, 1.68)	0.22 (0.02, 1.71)	0.36 (0.05, 2.06)
Rivaroxaban vs. Heparin	0.25 (0.00, 13.05)	0.15 (0.00, 12.57)			
Rivaroxaban vs. None	0.15 (0.00, 8.86)	0.10 (0.00, 8.94)	0.09 (0.00, 8.43)	0.19 (0.00, 18.80)	0.31 (0.00, 23.55)
Rivaroxaban vs. Warfarin	1.08 (0.03, 66.89)	0.63 (0.01, 50.30)	0.64 (0.01, 51.73)		
Tinzaparin vs. Apixaban	1.13 (0.04, 29.25)	1.12 (0.03, 37.86)	1.14 (0.03, 39.17)	1.55 (0.04, 60.95)	1.49 (0.05, 46.29)
Tinzaparin vs. Dabigatran	0.74 (0.03, 18.86)	0.73 (0.02, 23.76)	0.75 (0.02, 24.48)	0.76 (0.02, 25.79)	0.75 (0.02, 20.11)
Tinzaparin vs. Desirudin	0.52 (0.01, 24.05)	0.52 (0.01, 35.30)	0.53 (0.01, 36.86)	0.53 (0.01, 38.78)	0.53 (0.01, 27.97)

Table 101. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Tinzaparin vs. Enoxaparin	0.59 (0.03, 11.29)	0.58 (0.02, 13.94)	0.59 (0.02, 14.40)	0.60 (0.02, 15.18)	0.59 (0.03, 11.86)
Tinzaparin vs. Enoxaparin +IPC	0.63 (0.00, 112.39)	0.62 (0.00, 140.61)	0.62 (0.00, 141.17)	0.60 (0.00, 137.69)	0.62 (0.00, 111.50)
Tinzaparin vs. Heparin	0.40 (0.00, 42.69)	0.41 (0.00, 68.85)			
Tinzaparin vs. None	0.24 (0.00, 29.28)	0.26 (0.00, 45.56)	0.25 (0.00, 43.12)	0.53 (0.00, 102.51)	0.51 (0.00, 76.63)
Tinzaparin vs. Rivaroxaban	1.62 (0.05, 58.62)	2.64 (0.06, 172.43)	2.69 (0.06, 176.62)	2.76 (0.06, 189.24)	1.66 (0.05, 63.50)
Tinzaparin vs. Warfarin	1.75 (0.02, 211.66)	1.66 (0.01, 251.64)	1.72 (0.02, 257.24)		
Warfarin vs. Enoxaparin	0.34 (0.01, 8.06)	0.35 (0.01, 10.37)	0.35 (0.01, 10.43)		
Warfarin vs. None	0.14 (0.00, 20.49)	0.16 (0.00, 31.66)	0.15 (0.00, 29.9)		

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Apixaban vs. Desirudin	0.86 (0.43, 1.70)	0.89 (0.35, 2.24)	0.85 (0.31, 2.29)
Apixaban vs. Enoxaparin	0.58 (0.39, 0.87)	0.58 (0.37, 0.90)	0.55 (0.33, 0.92)
Apixaban vs. Heparin	0.29 (0.15, 0.54)		
Apixaban vs. None	0.24 (0.1, 0.53)	0.24 (0.1, 0.56)	0.39 (0.12, 1.25)
Apixaban vs. Tinzaparin	0.44 (0.22, 0.91)	0.44 (0.20, 0.97)	0.43 (0.18, 1.02)
Apixaban vs. Warfarin	0.30 (0.17, 0.52)	0.30 (0.16, 0.55)	0.29 (0.13, 0.62)
Dabigatran vs. Apixaban	1.54 (0.90, 2.64)	1.53 (0.85, 2.75)	1.61 (0.84, 3.11)
Dabigatran vs. Dalteparin	1.08 (0.47, 2.42)	1.07 (0.44, 2.59)	1.09 (0.40, 2.86)
Dabigatran vs. Desirudin	1.32 (0.68, 2.53)	1.36 (0.55, 3.35)	1.36 (0.52, 3.51)
Dabigatran vs. Enoxaparin	0.90 (0.63, 1.27)	0.89 (0.61, 1.30)	0.89 (0.60, 1.32)
Dabigatran vs. Enoxaparin + IPC	3.21 (0.89, 12.69)	3.16 (0.82, 13.36)	3.25 (0.82, 13.68)
Dabigatran vs. Heparin	0.45 (0.25, 0.80)		
Dabigatran vs. IPC + LD Aspirin	0.93 (0.26, 3.39)	0.92 (0.24, 3.54)	0.92 (0.23, 3.67)
Dabigatran vs. None	0.37 (0.17, 0.8)	0.37 (0.15, 0.83)	0.63 (0.21, 1.93)
Dabigatran vs. Rivaroxaban	2.13 (1.32, 3.46)	2.13 (1.26, 3.59)	2.13 (1.23, 3.66)
Dabigatran vs. Tinzaparin	0.68 (0.34, 1.37)	0.68 (0.32, 1.46)	0.69 (0.30, 1.55)
Dabigatran vs. Warfarin	0.46 (0.26, 0.80)	0.45 (0.24, 0.83)	0.46 (0.23, 0.93)
Dalteparin vs. Apixaban	1.43 (0.63, 3.28)	1.44 (0.59, 3.50)	1.48 (0.53, 4.18)
Dalteparin vs. Desirudin	1.23 (0.49, 3.10)	1.27 (0.41, 3.97)	1.26 (0.37, 4.41)
Dalteparin vs. Enoxaparin	0.83 (0.40, 1.75)	0.84 (0.37, 1.86)	0.82 (0.34, 2.00)
Dalteparin vs. Enoxaparin + IPC	2.98 (0.71, 13.65)	2.96 (0.64, 14.59)	2.99 (0.62, 15.38)
Dalteparin vs. Heparin	0.42 (0.17, 1.00)		

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Dalteparin vs. IPC	0.97 (0.3, 3.09)	0.97 (0.28, 3.22)	1.8 (0.34, 9.58)
Dalteparin vs. IPC + LD Aspirin	0.87 (0.20, 3.70)	0.86 (0.19, 3.99)	0.85 (0.17, 4.20)
Dalteparin vs. None	0.34 (0.12, 0.95)	0.34 (0.11, 1.01)	0.58 (0.15, 2.28)
Dalteparin vs. Rivaroxaban	1.98 (0.89, 4.49)	1.99 (0.83, 4.81)	1.96 (0.75, 5.14)
Dalteparin vs. Tinzaparin	0.63 (0.28, 1.47)	0.64 (0.26, 1.61)	0.63 (0.24, 1.67)
Dalteparin vs. Warfarin	0.42 (0.23, 0.77)	0.42 (0.22, 0.81)	0.43 (0.22, 0.84)
Dalteparin vs. YM150	0.81 (0.24, 2.7)	0.82 (0.22, 2.95)	0.8 (0.2, 3.22)
Desirudin vs. Enoxaparin	0.68 (0.39, 1.18)	0.66 (0.29, 1.49)	0.65 (0.28, 1.56)
Desirudin vs. Heparin	0.34 (0.20, 0.56)		
Desirudin vs. None	0.28 (0.11, 0.67)	0.27 (0.09, 0.8)	0.46 (0.12, 1.79)
Desirudin vs. Tinzaparin	0.51 (0.23, 1.18)	0.50 (0.18, 1.44)	0.50 (0.16, 1.55)
Desirudin vs. Warfarin	0.34 (0.17, 0.70)	0.33 (0.13, 0.86)	0.34 (0.12, 0.96)
Enoxaparin + IPC vs. Apixaban	0.48 (0.12, 1.77)	0.49 (0.11, 1.91)	0.50 (0.11, 2.07)
Enoxaparin + IPC vs. Desirudin	0.41 (0.10, 1.61)	0.43 (0.09, 1.99)	0.42 (0.08, 2.00)
Enoxaparin + IPC vs. Enoxaparin	0.28 (0.07, 0.96)	0.28 (0.07, 1.03)	0.27 (0.07, 1.03)
Enoxaparin + IPC vs. GCS	0.18 (0.03, 0.88)	0.18 (0.03, 0.97)	
Enoxaparin + IPC vs. Heparin	0.14 (0.03, 0.52)		
Enoxaparin + IPC vs. IPC	0.33 (0.07, 1.51)	0.33 (0.06, 1.59)	0.6 (0.08, 4.24)
Enoxaparin + IPC vs. None	0.12 (0.03, 0.48)	0.12 (0.02, 0.51)	0.19 (0.03, 1.05)
Enoxaparin + IPC vs. Rivaroxaban	0.67 (0.17, 2.41)	0.67 (0.16, 2.59)	0.65 (0.16, 2.59)
Enoxaparin + IPC vs. Tinzaparin	0.21 (0.05, 0.84)	0.22 (0.05, 0.93)	0.21 (0.04, 0.96)
Enoxaparin + IPC vs. Warfarin	0.14 (0.03, 0.53)	0.14 (0.03, 0.58)	0.14 (0.03, 0.60)

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Enoxaparin vs. None	0.41 (0.2, 0.82)	0.41 (0.19, 0.85)	0.71 (0.25, 2)
Fondaparinux vs. Apixaban	0.24 (0.03, 1.25)	0.23 (0.03, 1.26)	0.24 (0.03, 1.38)
Fondaparinux vs. Dabigatran	0.16 (0.02, 0.80)	0.15 (0.02, 0.81)	0.15 (0.02, 0.83)
Fondaparinux vs. Dalteparin	0.17 (0.02, 0.97)	0.16 (0.02, 1.00)	0.16 (0.02, 1.07)
Fondaparinux vs. Desirudin	0.21 (0.03, 1.12)	0.20 (0.02, 1.29)	0.20 (0.02, 1.34)
Fondaparinux vs. Enoxaparin	0.14 (0.02, 0.69)	0.13 (0.02, 0.69)	0.13 (0.02, 0.71)
Fondaparinux vs. Enoxaparin + IPC	0.50 (0.05, 3.93)	0.47 (0.04, 4.22)	0.48 (0.04, 4.31)
Fondaparinux vs. GCS	0.09 (0.01, 0.61)	0.09 (0.01, 0.63)	
Fondaparinux vs. HD Aspirin	0.29 (0.02, 3.99)	0.28 (0.01, 4.34)	0.28 (0.01, 4.64)
Fondaparinux vs. Heparin	0.07 (0.01, 0.37)		
Fondaparinux vs. IPC	0.16 (0.02, 1.01)	0.15 (0.02, 1.04)	0.29 (0.02, 2.66)
Fondaparinux vs. IPC + HD Aspirin	0.37 (0.03, 3.60)	0.35 (0.03, 3.99)	0.36 (0.02, 4.21)
Fondaparinux vs. IPC + LD Aspirin	0.15 (0.01, 1.14)	0.14 (0.01, 1.11)	0.14 (0.01, 1.20)
Fondaparinux vs. None	0.06 (0.01, 0.33)	0.05 (0.01, 0.34)	0.09 (0.01, 0.69)
Fondaparinux vs. Rivaroxaban	0.33 (0.04, 1.70)	0.32 (0.04, 1.71)	0.31 (0.04, 1.76)
Fondaparinux vs. Tinzaparin	0.11 (0.01, 0.58)	0.10 (0.01, 0.61)	0.10 (0.01, 0.63)
Fondaparinux vs. Tinzaparin + GCS	0.17 (0.01, 1.39)	0.16 (0.01, 1.46)	
Fondaparinux vs. Warfarin	0.07 (0.01, 0.37)	0.07 (0.01, 0.38)	0.07 (0.01, 0.40)
Fondaparinux vs. YM150	0.14 (0.02, 0.88)	0.13 (0.01, 0.93)	0.13 (0.01, 0.94)
GCS vs. Apixaban	2.66 (0.90, 8.18)	2.67 (0.85, 8.60)	
GCS vs. Dabigatran	1.73 (0.60, 5.13)	1.74 (0.56, 5.52)	
GCS vs. Dalteparin	1.86 (0.54, 6.54)	1.86 (0.49, 7.21)	

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
GCS vs. Desirudin	2.29 (0.72, 7.33)	2.37 (0.62, 9.26)	
GCS vs. Enoxaparin	1.55 (0.57, 4.36)	1.55 (0.53, 4.58)	
GCS vs. Heparin	0.77 (0.25, 2.37)		
GCS vs. IPC + LD Aspirin	1.61 (0.33, 8.08)	1.60 (0.30, 8.59)	
GCS vs. None	0.64 (0.25, 1.6)	0.64 (0.24, 1.68)	
GCS vs. Rivaroxaban	3.68 (1.28, 10.95)	3.70 (1.21, 11.66)	
GCS vs. Tinzaparin	1.18 (0.37, 3.88)	1.18 (0.34, 4.23)	
GCS vs. Warfarin	0.79 (0.26, 2.42)	0.79 (0.25, 2.57)	
HD Aspirin vs. Apixaban	0.82 (0.10, 6.57)	0.83 (0.09, 7.30)	0.84 (0.09, 7.71)
HD Aspirin vs. Dabigatran	0.53 (0.07, 4.25)	0.54 (0.06, 4.76)	0.52 (0.06, 4.71)
HD Aspirin vs. Dalteparin	0.57 (0.06, 5.00)	0.58 (0.06, 5.66)	0.56 (0.05, 5.77)
HD Aspirin vs. Desirudin	0.71 (0.08, 5.81)	0.74 (0.07, 7.25)	0.71 (0.07, 7.19)
HD Aspirin vs. Enoxaparin	0.48 (0.06, 3.68)	0.48 (0.06, 4.07)	0.46 (0.05, 3.97)
HD Aspirin vs. Enoxaparin + IPC	1.71 (0.35, 8.47)	1.72 (0.32, 9.22)	1.68 (0.31, 9.23)
HD Aspirin vs. GCS	0.31 (0.03, 2.99)	0.31 (0.03, 3.38)	
HD Aspirin vs. Heparin	0.24 (0.03, 1.91)		
HD Aspirin vs. IPC	0.56 (0.06, 5.16)	0.56 (0.05, 5.67)	1.01 (0.08, 13.48)
HD Aspirin vs. IPC + HD Aspirin	1.28 (0.36, 4.57)	1.28 (0.35, 4.83)	1.27 (0.34, 4.87)
HD Aspirin vs. IPC + LD Aspirin	0.50 (0.04, 5.32)	0.50 (0.04, 6.14)	0.48 (0.04, 6.04)
HD Aspirin vs. None	0.20 (0.02, 1.71)	0.20 (0.02, 1.90)	0.33 (0.03, 3.62)
HD Aspirin vs. Rivaroxaban	1.14 (0.14, 9.02)	1.15 (0.13, 10.06)	1.10 (0.12, 9.80)
HD Aspirin vs. Tinzaparin	0.36 (0.04, 3.06)	0.37 (0.04, 3.45)	0.36 (0.04, 3.44)

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
HD Aspirin vs. Tinzaparin + GCS	0.57 (0.05, 6.42)	0.57 (0.04, 7.46)	
HD Aspirin vs. Warfarin	0.24 (0.03, 1.97)	0.25 (0.03, 2.18)	0.24 (0.02, 2.21)
HD Aspirin vs. YM150	0.47 (0.05, 4.41)	0.47 (0.04, 5.04)	0.45 (0.04, 4.87)
Heparin vs. Enoxaparin	2.00 (1.26, 3.22)		
Heparin vs. None	0.82 (0.35, 1.89)		
Heparin vs. Warfarin	1.02 (0.54, 1.95)		
IPC + HD Aspirin vs. Apixaban	0.64 (0.12, 3.30)	0.65 (0.11, 3.71)	0.66 (0.11, 3.92)
IPC + HD Aspirin vs. Dabigatran	0.42 (0.08, 2.12)	0.42 (0.07, 2.38)	0.41 (0.07, 2.33)
IPC + HD Aspirin vs. Dalteparin	0.45 (0.08, 2.57)	0.45 (0.07, 2.96)	0.44 (0.06, 2.98)
IPC + HD Aspirin vs. Desirudin	0.55 (0.10, 2.95)	0.58 (0.08, 3.76)	0.56 (0.08, 3.74)
IPC + HD Aspirin vs. Enoxaparin	0.37 (0.07, 1.82)	0.38 (0.07, 2.03)	0.37 (0.06, 1.98)
IPC + HD Aspirin vs. Enoxaparin + IPC	1.34 (0.51, 3.51)	1.34 (0.48, 3.77)	1.33 (0.46, 3.85)
IPC + HD Aspirin vs. GCS	0.24 (0.04, 1.55)	0.24 (0.03, 1.77)	
IPC + HD Aspirin vs. Heparin	0.19 (0.03, 0.97)		
IPC + HD Aspirin vs. IPC	0.44 (0.07, 2.66)	0.44 (0.06, 2.97)	0.80 (0.09, 7.44)
IPC + HD Aspirin vs. IPC + LD Aspirin	0.39 (0.05, 2.91)	0.39 (0.05, 3.28)	0.38 (0.04, 3.28)
IPC + HD Aspirin vs. None	0.15 (0.03, 0.88)	0.16 (0.02, 0.97)	0.26 (0.03, 1.91)
IPC + HD Aspirin vs. Rivaroxaban	0.89 (0.17, 4.49)	0.90 (0.15, 5.01)	0.87 (0.14, 4.95)
IPC + HD Aspirin vs. Tinzaparin	0.28 (0.05, 1.57)	0.29 (0.05, 1.76)	0.28 (0.04, 1.78)
IPC + HD Aspirin vs. Tinzaparin + GCS	0.45 (0.05, 3.48)	0.45 (0.05, 4.07)	
IPC + HD Aspirin vs. Warfarin	0.19 (0.04, 0.99)	0.19 (0.03, 1.11)	0.19 (0.03, 1.13)
IPC + HD Aspirin vs. YM150	0.37 (0.06, 2.29)	0.37 (0.05, 2.63)	0.36 (0.05, 2.63)

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
IPC + LD Aspirin vs. Apixaban	1.65 (0.45, 6.09)	1.67 (0.43, 6.50)	1.75 (0.42, 7.32)
IPC + LD Aspirin vs. Desirudin	1.42 (0.37, 5.48)	1.48 (0.32, 6.79)	1.48 (0.30, 7.13)
IPC + LD Aspirin vs. Enoxaparin	0.96 (0.28, 3.31)	0.97 (0.27, 3.53)	0.97 (0.26, 3.66)
IPC + LD Aspirin vs. Enoxaparin + IPC	3.43 (0.60, 21.09)	3.43 (0.54, 22.67)	3.52 (0.54, 23.03)
IPC + LD Aspirin vs. Heparin	0.48 (0.13, 1.79)		
IPC + LD Aspirin vs. None	0.4 (0.09, 1.65)	0.4 (0.09, 1.74)	0.68 (0.13, 3.66)
IPC + LD Aspirin vs. Tinzaparin	0.73 (0.18, 2.91)	0.74 (0.17, 3.15)	0.74 (0.17, 3.36)
IPC + LD Aspirin vs. Warfarin	0.49 (0.13, 1.82)	0.49 (0.12, 1.96)	0.50 (0.12, 2.13)
IPC vs. Apixaban	1.47 (0.56, 3.96)	1.49 (0.54, 4.25)	0.83 (0.18, 3.74)
IPC vs. Dabigatran	0.96 (0.37, 2.51)	0.97 (0.36, 2.69)	0.51 (0.12, 2.23)
IPC vs. Desirudin	1.27 (0.45, 3.63)	1.32 (0.39, 4.65)	0.70 (0.13, 3.63)
IPC vs. Enoxaparin	0.86 (0.36, 2.10)	0.87 (0.35, 2.25)	0.46 (0.11, 1.86)
IPC vs. GCS	0.55 (0.20, 1.51)	0.56 (0.20, 1.61)	
IPC vs. Heparin	0.43 (0.16, 1.17)		
IPC vs. IPC + LD Aspirin	0.89 (0.20, 4.10)	0.89 (0.18, 4.47)	0.47 (0.07, 3.25)
IPC vs. None	0.35 (0.18, 0.68)	0.35 (0.18, 0.72)	0.32 (0.12, 0.84)
IPC vs. Rivaroxaban	2.04 (0.80, 5.34)	2.06 (0.77, 5.73)	1.09 (0.25, 4.67)
IPC vs. Tinzaparin	0.65 (0.23, 1.93)	0.66 (0.21, 2.12)	0.35 (0.07, 1.69)
IPC vs. Warfarin	0.44 (0.16, 1.19)	0.44 (0.16, 1.28)	0.24 (0.05, 1.08)
Rivaroxaban vs. Apixaban	0.72 (0.43, 1.23)	0.72 (0.41, 1.27)	0.76 (0.40, 1.44)
Rivaroxaban vs. Desirudin	0.62 (0.33, 1.17)	0.64 (0.26, 1.55)	0.64 (0.25, 1.64)
Rivaroxaban vs. Enoxaparin	0.42 (0.30, 0.59)	0.42 (0.29, 0.60)	0.42 (0.29, 0.61)

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Rivaroxaban vs. Heparin	0.21 (0.12, 0.37)		
Rivaroxaban vs. IPC + LD Aspirin	0.44 (0.12, 1.57)	0.43 (0.11, 1.65)	0.43 (0.11, 1.72)
Rivaroxaban vs. None	0.17 (0.08, 0.37)	0.17 (0.07, 0.39)	0.30 (0.10, 0.90)
Rivaroxaban vs. Tinzaparin	0.32 (0.16, 0.64)	0.32 (0.15, 0.68)	0.32 (0.14, 0.72)
Rivaroxaban vs. Warfarin	0.21 (0.12, 0.37)	0.21 (0.12, 0.39)	0.22 (0.11, 0.43)
Tinzaparin + GCS vs. Apixaban	1.45 (0.35, 6.13)	1.45 (0.32, 6.71)	
Tinzaparin + GCS vs. Dabigatran	0.94 (0.23, 3.89)	0.95 (0.21, 4.25)	
Tinzaparin + GCS vs. Dalteparin	1.01 (0.22, 4.79)	1.01 (0.19, 5.35)	
Tinzaparin + GCS vs. Desirudin	1.24 (0.29, 5.44)	1.29 (0.25, 6.89)	
Tinzaparin + GCS vs. Enoxaparin	0.84 (0.22, 3.33)	0.85 (0.20, 3.64)	
Tinzaparin + GCS vs. Enoxaparin + IPC	3.01 (0.49, 19.73)	2.99 (0.44, 22.33)	
Tinzaparin + GCS vs. GCS	0.54 (0.22, 1.35)	0.54 (0.20, 1.45)	
Tinzaparin + GCS vs. Heparin	0.42 (0.10, 1.79)		
Tinzaparin + GCS vs. IPC	0.98 (0.25, 3.76)	0.98 (0.23, 4.12)	
Tinzaparin + GCS vs. IPC + LD Aspirin	0.88 (0.14, 5.66)	0.87 (0.13, 6.05)	
Tinzaparin + GCS vs. None	0.35 (0.10, 1.26)	0.35 (0.09, 1.37)	
Tinzaparin + GCS vs. Rivaroxaban	2.00 (0.50, 8.28)	2.01 (0.46, 9.12)	
Tinzaparin + GCS vs. Tinzaparin	0.64 (0.15, 2.91)	0.64 (0.13, 3.21)	
Tinzaparin + GCS vs. Warfarin	0.43 (0.10, 1.82)	0.43 (0.09, 1.99)	
Tinzaparin vs. Enoxaparin	1.32 (0.71, 2.41)	1.31 (0.68, 2.52)	1.30 (0.64, 2.65)
Tinzaparin vs. Heparin	0.66 (0.30, 1.41)		
Tinzaparin vs. None	0.54 (0.21, 1.36)	0.54 (0.2, 1.43)	0.92 (0.26, 3.21)

Table 102. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Tinzaparin vs. Warfarin	0.67 (0.37, 1.20)	0.67 (0.35, 1.26)	0.67 (0.34, 1.34)
Warfarin vs. Enoxaparin	1.97 (1.27, 3.07)	1.97 (1.22, 3.17)	1.93 (1.08, 3.46)
Warfarin vs. None	0.81 (0.35, 1.85)	0.81 (0.33, 1.93)	1.37 (0.42, 4.51)
YM150 vs. Apixaban	1.76 (0.63, 4.97)	1.76 (0.59, 5.36)	1.85 (0.58, 5.96)
YM150 vs. Dabigatran	1.14 (0.42, 3.16)	1.15 (0.39, 3.40)	1.15 (0.38, 3.53)
YM150 vs. Desirudin	1.52 (0.50, 4.55)	1.56 (0.43, 5.75)	1.57 (0.40, 6.07)
YM150 vs. Enoxaparin	1.03 (0.40, 2.65)	1.03 (0.37, 2.83)	1.03 (0.36, 2.94)
YM150 vs. Enoxaparin + IPC	3.67 (0.77, 18.82)	3.63 (0.70, 20.35)	3.73 (0.69, 20.88)
YM150 vs. GCS	0.66 (0.16, 2.68)	0.66 (0.15, 2.86)	
YM150 vs. Heparin	0.51 (0.18, 1.48)		
YM150 vs. IPC	1.20 (0.32, 4.38)	1.18 (0.29, 4.65)	2.24 (0.39, 13.17)
YM150 vs. IPC + LD Aspirin	1.07 (0.22, 5.07)	1.06 (0.21, 5.50)	1.06 (0.20, 5.77)
YM150 vs. None	0.42 (0.13, 1.38)	0.42 (0.12, 1.46)	0.73 (0.17, 3.18)
YM150 vs. Rivaroxaban	2.44 (0.89, 6.70)	2.44 (0.84, 7.19)	2.44 (0.81, 7.46)
YM150 vs. Tinzaparin	0.78 (0.25, 2.40)	0.78 (0.24, 2.64)	0.79 (0.22, 2.82)
YM150 vs. Tinzaparin + GCS	1.22 (0.23, 6.34)	1.21 (0.21, 7.05)	
YM150 vs. Warfarin	0.52 (0.18, 1.49)	0.52 (0.17, 1.60)	0.53 (0.16, 1.76)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Enoxaparin	0.49 (0.23, 1.07)	0.44 (0.16, 1.22)	0.44 (0.16, 1.18)
Apixaban vs. None	0.21 (0.06, 0.77)	0.14 (0.02, 0.91)	0.17 (0.03, 0.97)
Apixaban vs. Warfarin	0.33 (0.11, 0.99)	0.23 (0.05, 1.05)	0.23 (0.05, 0.97)
Dabigatran vs. Apixaban	1.25 (0.46, 3.30)	1.34 (0.37, 4.74)	1.38 (0.40, 4.65)
Dabigatran vs. Enoxaparin	0.61 (0.33, 1.11)	0.59 (0.27, 1.24)	0.60 (0.29, 1.24)
Dabigatran vs. None	0.26 (0.08, 0.8)	0.19 (0.03, 0.96)	0.23 (0.04, 1.04)
Dabigatran vs. Warfarin	0.41 (0.15, 1.13)	0.31 (0.08, 1.15)	0.32 (0.08, 1.11)
Dalteparin vs. Apixaban	1.26 (0.26, 5.77)	1.75 (0.23, 13.34)	1.78 (0.26, 12.37)
Dalteparin vs. Dabigatran	1.01 (0.22, 4.40)	1.31 (0.20, 9.12)	1.29 (0.22, 8.05)
Dalteparin vs. Desirudin	1.18 (0.22, 6.13)	1.33 (0.12, 14.82)	1.35 (0.14, 13.25)
Dalteparin vs. Enoxaparin	0.61 (0.15, 2.37)	0.77 (0.14, 4.44)	0.78 (0.15, 4.15)
Dalteparin vs. Fondaparinux	3.23 (0.18, 102.82)	4.13 (0.15, 196.17)	4.27 (0.18, 202.35)
Dalteparin vs. IPC + LD Aspirin	0.39 (0.03, 5.27)	0.48 (0.02, 10.21)	0.48 (0.02, 9.43)
Dalteparin vs. None	0.26 (0.05, 1.46)	0.25 (0.02, 2.57)	0.29 (0.03, 2.70)
Dalteparin vs. Rivaroxaban	3.16 (0.68, 14.28)	3.92 (0.57, 27.47)	3.99 (0.65, 25.38)
Dalteparin vs. Tinzaparin	0.60 (0.13, 2.60)	0.66 (0.10, 4.27)	0.67 (0.11, 3.92)
Dalteparin vs. Warfarin	0.42 (0.14, 1.24)	0.41 (0.10, 1.52)	0.41 (0.11, 1.44)
Dalteparin vs. YM150	0.54 (0.06, 4.97)	0.70 (0.05, 10.54)	0.69 (0.05, 9.30)
Desirudin vs. Apixaban	1.07 (0.31, 3.57)	1.31 (0.19, 9.22)	1.31 (0.21, 8.20)
Desirudin vs. Dabigatran	0.86 (0.28, 2.67)	0.98 (0.16, 6.22)	0.95 (0.17, 5.34)
Desirudin vs. Enoxaparin	0.52 (0.20, 1.34)	0.57 (0.11, 2.98)	0.58 (0.12, 2.73)
Desirudin vs. IPC + LD Aspirin	0.33 (0.03, 3.79)	0.36 (0.02, 6.99)	0.36 (0.02, 6.48)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Desirudin vs. None	0.22 (0.05, 0.92)	0.19 (0.02, 1.77)	0.22 (0.02, 1.83)
Desirudin vs. Rivaroxaban	2.68 (0.84, 8.56)	2.94 (0.47, 18.60)	2.95 (0.53, 16.71)
Desirudin vs. Tinzaparin	0.51 (0.13, 2.05)	0.50 (0.06, 4.03)	0.50 (0.07, 3.55)
Desirudin vs. Warfarin	0.35 (0.10, 1.23)	0.31 (0.04, 2.16)	0.31 (0.04, 1.91)
Desirudin vs. YM150	0.46 (0.06, 3.43)	0.52 (0.04, 7.19)	0.51 (0.04, 6.13)
Enoxaparin + GCS vs. Apixaban	0.60 (0.02, 13.20)	0.66 (0.01, 24.85)	0.65 (0.01, 21.33)
Enoxaparin + GCS vs. Dabigatran	0.48 (0.01, 10.36)	0.50 (0.01, 17.39)	0.47 (0.01, 14.24)
Enoxaparin + GCS vs. Dalteparin	0.48 (0.01, 13.12)	0.38 (0.01, 18.36)	0.37 (0.01, 15.09)
Enoxaparin + GCS vs. Desirudin	0.57 (0.01, 13.30)	0.51 (0.01, 23.64)	0.50 (0.01, 19.63)
Enoxaparin + GCS vs. Enoxaparin	0.29 (0.01, 5.88)	0.29 (0.01, 9.27)	0.29 (0.01, 7.84)
Enoxaparin + GCS vs. Fondaparinux	1.55 (0.31, 7.74)	1.57 (0.21, 11.70)	1.56 (0.23, 10.64)
Enoxaparin + GCS vs. Fondaparinux + GCS	1.84 (0.80, 4.24)	1.85 (0.66, 5.20)	1.86 (0.70, 5.02)
Enoxaparin + GCS vs. IPC	0.35 (0.01, 9.97)	0.20 (0.00, 12.97)	0.23 (0.00, 12.22)
Enoxaparin + GCS vs. IPC + LD Aspirin	0.19 (0.00, 8.23)	0.18 (0.00, 13.28)	0.18 (0.00, 11.34)
Enoxaparin + GCS vs. None	0.13 (0.00, 3.03)	0.09 (0.00, 4.17)	0.11 (0.00, 4.12)
Enoxaparin + GCS vs. Rivaroxaban	1.52 (0.04, 32.56)	1.49 (0.03, 51.42)	1.46 (0.03, 44.08)
Enoxaparin + GCS vs. Tinzaparin	0.29 (0.01, 6.95)	0.25 (0.00, 10.32)	0.25 (0.00, 8.31)
Enoxaparin + GCS vs. Warfarin	0.20 (0.01, 4.45)	0.15 (0.00, 5.79)	0.15 (0.00, 4.88)
Enoxaparin + GCS vs. YM150	0.26 (0.01, 8.65)	0.26 (0.00, 14.95)	0.25 (0.00, 12.39)
Enoxaparin vs. None	0.43 (0.14, 1.21)	0.32 (0.06, 1.56)	0.38 (0.08, 1.66)
Fondaparinux + GCS vs. Apixaban	0.33 (0.01, 6.35)	0.36 (0.01, 11.40)	0.35 (0.01, 9.55)
Fondaparinux + GCS vs. Dabigatran	0.26 (0.01, 4.92)	0.27 (0.01, 8.04)	0.25 (0.01, 6.53)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Fondaparinux + GCS vs. Dalteparin	0.26 (0.01, 6.39)	0.20 (0.00, 8.76)	0.20 (0.00, 6.98)
Fondaparinux + GCS vs. Desirudin	0.31 (0.01, 6.46)	0.27 (0.00, 11.01)	0.27 (0.00, 9.08)
Fondaparinux + GCS vs. Enoxaparin	0.16 (0.01, 2.82)	0.16 (0.00, 4.22)	0.15 (0.00, 3.55)
Fondaparinux + GCS vs. Fondaparinux	0.84 (0.22, 3.31)	0.85 (0.15, 4.81)	0.84 (0.16, 4.36)
Fondaparinux + GCS vs. IPC	0.19 (0.00, 4.87)	0.11 (0.00, 6.14)	0.12 (0.00, 5.81)
Fondaparinux + GCS vs. IPC + LD Aspirin	0.10 (0.00, 4.03)	0.10 (0.00, 6.26)	0.10 (0.00, 5.40)
Fondaparinux + GCS vs. None	0.07 (0.00, 1.48)	0.05 (0.00, 1.97)	0.06 (0.00, 1.91)
Fondaparinux + GCS vs. Rivaroxaban	0.82 (0.02, 15.47)	0.80 (0.02, 23.93)	0.79 (0.02, 20.09)
Fondaparinux + GCS vs. Tinzaparin	0.16 (0.00, 3.36)	0.14 (0.00, 4.74)	0.13 (0.00, 3.87)
Fondaparinux + GCS vs. Warfarin	0.11 (0.00, 2.16)	0.08 (0.00, 2.68)	0.08 (0.00, 2.24)
Fondaparinux + GCS vs. YM150	0.14 (0.00, 4.13)	0.14 (0.00, 7.11)	0.14 (0.00, 5.74)
Fondaparinux vs. Apixaban	0.39 (0.01, 5.23)	0.42 (0.01, 8.13)	0.42 (0.01, 7.19)
Fondaparinux vs. Dabigatran	0.31 (0.01, 4.03)	0.32 (0.01, 5.77)	0.30 (0.01, 4.80)
Fondaparinux vs. Desirudin	0.36 (0.01, 5.30)	0.32 (0.01, 8.29)	0.32 (0.01, 7.04)
Fondaparinux vs. Enoxaparin	0.19 (0.01, 2.27)	0.19 (0.01, 2.98)	0.18 (0.01, 2.60)
Fondaparinux vs. IPC + LD Aspirin	0.12 (0.00, 3.72)	0.12 (0.00, 4.97)	0.11 (0.00, 4.46)
Fondaparinux vs. None	0.08 (0.00, 1.20)	0.06 (0.00, 1.48)	0.07 (0.00, 1.49)
Fondaparinux vs. Rivaroxaban	0.98 (0.04, 12.86)	0.95 (0.03, 17.00)	0.94 (0.03, 15.17)
Fondaparinux vs. Tinzaparin	0.19 (0.01, 2.81)	0.16 (0.00, 3.51)	0.16 (0.00, 2.96)
Fondaparinux vs. Warfarin	0.13 (0.00, 1.77)	0.10 (0.00, 1.98)	0.10 (0.00, 1.69)
Fondaparinux vs. YM150	0.17 (0.00, 3.69)	0.17 (0.00, 5.48)	0.16 (0.00, 4.66)
GCS vs. Apixaban	1.93 (0.12, 21.28)		

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
GCS vs. Dabigatran	1.55 (0.10, 15.89)		
GCS vs. Dalteparin	1.54 (0.08, 21.67)		
GCS vs. Desirudin	1.81 (0.11, 21.22)		
GCS vs. Enoxaparin	0.94 (0.07, 9.02)		
GCS vs. Enoxaparin + GCS	3.19 (0.06, 217.46)		
GCS vs. Fondaparinux	4.95 (0.13, 262.70)		
GCS vs. Fondaparinux + GCS	5.88 (0.12, 377.66)		
GCS vs. Heparin	0.26 (0.02, 2.92)		
GCS vs. IPC	1.11 (0.07, 11.70)		
GCS vs. IPC + GCS	1.41 (0.02, 109.84)		
GCS vs. IPC + LD Aspirin	0.60 (0.02, 14.98)		
GCS vs. None	0.41 (0.03, 3.68)		
GCS vs. Rivaroxaban	4.85 (0.31, 51.83)		
GCS vs. Tinzaparin	0.92 (0.05, 11.07)		
GCS vs. Warfarin	0.64 (0.04, 7.12)		
GCS vs. Warfarin + GCS	7.52 (0.08, 830.48)		
GCS vs. YM150	0.83 (0.04, 15.30)		
Heparin vs. Apixaban	7.32 (2.40, 22.09)		
Heparin vs. Dabigatran	5.88 (2.19, 15.99)		
Heparin vs. Dalteparin	5.83 (1.22, 28.67)		
Heparin vs. Desirudin	6.87 (2.80, 17.15)		
Heparin vs. Enoxaparin	3.58 (1.63, 7.91)		

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Heparin vs. Enoxaparin + GCS	12.13 (0.54, 447.20)		
Heparin vs. Fondaparinux	18.82 (1.38, 506.74)		
Heparin vs. Fondaparinux + GCS	22.35 (1.12, 755.21)		
Heparin vs. IPC	4.22 (0.79, 23.83)		
Heparin vs. IPC + GCS	5.37 (0.18, 229.75)		
Heparin vs. IPC + LD Aspirin	2.26 (0.19, 24.29)		
Heparin vs. None	1.54 (0.40, 5.70)		
Heparin vs. Rivaroxaban	18.41 (6.53, 52.56)		
Heparin vs. Tinzaparin	3.50 (0.97, 12.83)		
Heparin vs. Warfarin	2.44 (0.79, 7.53)		
Heparin vs. Warfarin + GCS	28.56 (0.61, 1,788.26)		
Heparin vs. YM150	3.16 (0.45, 22.07)		
IPC + GCS vs. Apixaban	1.36 (0.03, 39.81)	1.85 (0.03, 100.48)	1.56 (0.02, 71.16)
IPC + GCS vs. Dabigatran	1.09 (0.03, 31.53)	1.38 (0.02, 72.10)	1.13 (0.02, 48.76)
IPC + GCS vs. Dalteparin	1.09 (0.02, 39.45)	1.05 (0.01, 74.51)	0.88 (0.01, 50.15)
IPC + GCS vs. Desirudin	1.28 (0.03, 40.45)	1.41 (0.02, 95.49)	1.19 (0.01, 66.75)
IPC + GCS vs. Enoxaparin	0.67 (0.02, 18.21)	0.81 (0.01, 37.83)	0.68 (0.01, 27.30)
IPC + GCS vs. Enoxaparin + GCS	2.26 (0.69, 8.14)	2.78 (0.65, 14.85)	2.40 (0.62, 10.57)
IPC + GCS vs. Fondaparinux	3.50 (0.48, 27.83)	4.35 (0.39, 60.34)	3.75 (0.36, 44.04)
IPC + GCS vs. Fondaparinux + GCS	4.16 (0.98, 19.16)	5.14 (0.89, 37.68)	4.46 (0.83, 27.28)
IPC + GCS vs. IPC	0.79 (0.02, 29.70)	0.56 (0.00, 50.65)	0.55 (0.01, 39.88)
IPC + GCS vs. IPC + LD Aspirin	0.42 (0.01, 23.78)	0.50 (0.00, 50.91)	0.42 (0.00, 36.13)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
IPC + GCS vs. None	0.29 (0.01, 9.08)	0.26 (0.00, 16.58)	0.26 (0.00, 13.68)
IPC + GCS vs. Rivaroxaban	3.42 (0.08, 98.69)	4.14 (0.06, 208.51)	3.51 (0.05, 148.71)
IPC + GCS vs. Tinzaparin	0.65 (0.01, 20.86)	0.70 (0.01, 42.14)	0.59 (0.01, 28.47)
IPC + GCS vs. Warfarin	0.45 (0.01, 13.52)	0.43 (0.01, 23.52)	0.36 (0.00, 16.31)
IPC + GCS vs. YM150	0.59 (0.01, 25.41)	0.73 (0.01, 59.26)	0.61 (0.01, 39.77)
IPC + LD Aspirin vs. Apixaban	3.24 (0.30, 38.67)	3.67 (0.25, 60.64)	3.68 (0.26, 57.97)
IPC + LD Aspirin vs. Dabigatran	2.60 (0.25, 30.36)	2.74 (0.21, 41.68)	2.67 (0.21, 38.86)
IPC + LD Aspirin vs. Enoxaparin	1.58 (0.17, 16.83)	1.60 (0.14, 21.78)	1.61 (0.14, 21.50)
IPC + LD Aspirin vs. None	0.68 (0.06, 8.82)	0.52 (0.02, 10.57)	0.61 (0.03, 11.80)
IPC + LD Aspirin vs. Warfarin	1.08 (0.10, 13.07)	0.85 (0.05, 14.14)	0.86 (0.06, 13.68)
IPC vs. Apixaban	1.73 (0.31, 9.02)	3.27 (0.27, 47.61)	2.81 (0.27, 32.95)
IPC vs. Dabigatran	1.39 (0.28, 6.60)	2.44 (0.24, 30.57)	2.04 (0.23, 21.05)
IPC vs. Dalteparin	1.38 (0.18, 10.35)	1.87 (0.11, 37.04)	1.58 (0.10, 25.79)
IPC vs. Desirudin	1.63 (0.27, 9.25)	2.49 (0.15, 48.23)	2.14 (0.15, 34.47)
IPC vs. Enoxaparin	0.85 (0.18, 3.70)	1.43 (0.15, 16.63)	1.23 (0.14, 12.03)
IPC vs. Fondaparinux	4.45 (0.24, 154.78)	7.71 (0.21, 504.72)	6.75 (0.21, 413.23)
IPC vs. IPC + LD Aspirin	0.54 (0.03, 7.79)	0.89 (0.03, 30.20)	0.76 (0.03, 21.56)
IPC vs. None	0.36 (0.11, 1.16)	0.46 (0.09, 2.50)	0.47 (0.09, 2.30)
IPC vs. Rivaroxaban	4.36 (0.82, 21.80)	7.32 (0.65, 98.30)	6.32 (0.63, 70.11)
IPC vs. Tinzaparin	0.83 (0.13, 4.92)	1.23 (0.09, 20.01)	1.06 (0.09, 14.08)
IPC vs. Warfarin	0.58 (0.10, 3.05)	0.76 (0.06, 11.15)	0.66 (0.06, 7.78)
IPC vs. YM150	0.75 (0.07, 7.55)	1.30 (0.06, 32.52)	1.09 (0.06, 21.87)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Rivaroxaban vs. Apixaban	0.40 (0.14, 1.12)	0.45 (0.12, 1.65)	0.45 (0.13, 1.56)
Rivaroxaban vs. Dabigatran	0.32 (0.13, 0.80)	0.33 (0.11, 1.03)	0.32 (0.11, 0.93)
Rivaroxaban vs. Enoxaparin	0.19 (0.10, 0.38)	0.19 (0.09, 0.43)	0.20 (0.09, 0.42)
Rivaroxaban vs. IPC + LD Aspirin	0.12 (0.01, 1.31)	0.12 (0.01, 1.63)	0.12 (0.01, 1.56)
Rivaroxaban vs. None	0.08 (0.02, 0.29)	0.06 (0.01, 0.37)	0.07 (0.01, 0.39)
Rivaroxaban vs. Warfarin	0.13 (0.05, 0.38)	0.10 (0.02, 0.40)	0.10 (0.03, 0.38)
Tinzaparin vs. Apixaban	2.09 (0.58, 7.32)	2.65 (0.50, 14.34)	2.65 (0.54, 13.29)
Tinzaparin vs. Dabigatran	1.68 (0.51, 5.54)	1.98 (0.44, 9.58)	1.92 (0.47, 8.47)
Tinzaparin vs. Enoxaparin	1.02 (0.37, 2.83)	1.16 (0.31, 4.41)	1.16 (0.34, 4.11)
Tinzaparin vs. IPC + LD Aspirin	0.65 (0.05, 7.66)	0.72 (0.04, 11.94)	0.72 (0.04, 11.30)
Tinzaparin vs. None	0.44 (0.10, 1.87)	0.37 (0.04, 2.90)	0.44 (0.06, 3.04)
Tinzaparin vs. Rivaroxaban	5.25 (1.54, 17.78)	5.94 (1.29, 28.65)	5.95 (1.40, 26.29)
Tinzaparin vs. Warfarin	0.70 (0.25, 1.88)	0.62 (0.17, 2.21)	0.62 (0.18, 2.08)
Tinzaparin vs. YM150	0.90 (0.12, 6.96)	1.05 (0.09, 12.44)	1.03 (0.10, 10.69)
Warfarin + GCS vs. Apixaban	0.26 (0.00, 11.80)	0.35 (0.00, 32.01)	0.29 (0.00, 22.13)
Warfarin + GCS vs. Dabigatran	0.21 (0.00, 9.19)	0.26 (0.00, 23.38)	0.21 (0.00, 15.55)
Warfarin + GCS vs. Dalteparin	0.20 (0.00, 11.36)	0.20 (0.00, 23.13)	0.16 (0.00, 14.97)
Warfarin + GCS vs. Desirudin	0.24 (0.00, 11.75)	0.26 (0.00, 30.72)	0.22 (0.00, 20.43)
Warfarin + GCS vs. Enoxaparin	0.13 (0.00, 5.25)	0.15 (0.00, 12.40)	0.13 (0.00, 8.75)
Warfarin + GCS vs. Enoxaparin + GCS	0.42 (0.05, 3.78)	0.52 (0.04, 7.54)	0.45 (0.04, 5.49)
Warfarin + GCS vs. Fondaparinux	0.66 (0.04, 10.09)	0.82 (0.03, 24.22)	0.70 (0.03, 17.18)
Warfarin + GCS vs. Fondaparinux + GCS	0.78 (0.07, 8.10)	0.96 (0.06, 17.41)	0.83 (0.06, 12.47)

Table 103. Network Meta-Analysis - Pairwise Comparisons among Hip and Knee Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Warfarin + GCS vs. IPC	0.15 (0.00, 8.56)	0.11 (0.00, 14.91)	0.10 (0.00, 11.58)
Warfarin + GCS vs. IPC + GCS	0.19 (0.03, 1.08)	0.19 (0.02, 1.45)	0.19 (0.02, 1.35)
Warfarin + GCS vs. IPC + LD Aspirin	0.08 (0.00, 6.33)	0.09 (0.00, 15.21)	0.08 (0.00, 10.79)
Warfarin + GCS vs. None	0.05 (0.00, 2.56)	0.05 (0.00, 5.20)	0.05 (0.00, 4.17)
Warfarin + GCS vs. Rivaroxaban	0.64 (0.01, 28.99)	0.77 (0.01, 67.56)	0.66 (0.01, 47.23)
Warfarin + GCS vs. Tinzaparin	0.12 (0.00, 6.25)	0.13 (0.00, 13.22)	0.11 (0.00, 8.74)
Warfarin + GCS vs. Warfarin	0.09 (0.00, 3.95)	0.08 (0.00, 7.44)	0.07 (0.00, 5.11)
Warfarin + GCS vs. YM150	0.11 (0.00, 7.14)	0.14 (0.00, 17.76)	0.11 (0.00, 11.95)
Warfarin vs. Enoxaparin	1.47 (0.66, 3.29)	1.88 (0.63, 6.01)	1.88 (0.67, 5.66)
Warfarin vs. None	0.63 (0.17, 2.33)	0.61 (0.08, 4.21)	0.71 (0.11, 4.47)
YM150 vs. Apixaban	2.32 (0.33, 15.93)	2.52 (0.25, 25.33)	2.58 (0.29, 23.57)
YM150 vs. Dabigatran	1.86 (0.29, 12.17)	1.88 (0.21, 17.15)	1.87 (0.23, 15.58)
YM150 vs. Enoxaparin	1.13 (0.19, 6.69)	1.10 (0.14, 8.64)	1.13 (0.16, 8.25)
YM150 vs. IPC + LD Aspirin	0.72 (0.04, 12.54)	0.69 (0.02, 17.51)	0.70 (0.03, 16.46)
YM150 vs. None	0.49 (0.06, 3.74)	0.36 (0.02, 4.65)	0.43 (0.03, 5.11)
YM150 vs. Rivaroxaban	5.84 (0.88, 38.90)	5.65 (0.63, 51.83)	5.80 (0.70, 48.28)
YM150 vs. Warfarin	0.77 (0.11, 5.34)	0.59 (0.05, 6.03)	0.60 (0.06, 5.61)

Table 104. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Apixaban vs. Desirudin	0.33 (0.01, 7.16)	0.25 (0.00, 10.10)	0.66 (0.01, 31.94)	0.66 (0.02, 28.16)
Apixaban vs. Enoxaparin	0.29 (0.02, 3.62)	0.30 (0.01, 5.45)	0.29 (0.02, 4.25)	0.29 (0.02, 3.82)
Apixaban vs. Heparin	0.07 (0.00, 1.34)	0.01 (0.00, 0.60)		
Apixaban vs. None	2.45 (0.01, 2492)			2.44 (0.01, 1691)
Apixaban vs. Warfarin	0.36 (0.01, 9.18)	0.36 (0.01, 15.94)	0.35 (0.01, 11.63)	0.36 (0.01, 10.24)
Dabigatran vs. Apixaban	3.21 (0.14, 78.41)	3.17 (0.08, 122.36)	3.23 (0.11, 93.22)	3.19 (0.13, 82.93)
Dabigatran vs. Desirudin	1.05 (0.06, 14.14)	0.80 (0.02, 17.76)	2.12 (0.07, 62.99)	2.12 (0.08, 56.26)
Dabigatran vs. Enoxaparin	0.93 (0.14, 6.03)	0.94 (0.11, 7.84)	0.95 (0.13, 6.80)	0.94 (0.14, 6.38)
Dabigatran vs. Heparin	0.21 (0.01, 2.65)	0.04 (0.00, 1.16)		
Dabigatran vs. IPC + LD Aspirin	0.99 (0.03, 35.3)	0.96 (0.02, 51.9)	0.97 (0.02, 40.2)	0.99 (0.03, 35.6)
Dabigatran vs. None	7.86 (0.07, 6045)			7.79 (0.06, 3996)
Dabigatran vs. Rivaroxaban	1.00 (0.07, 12.13)	0.93 (0.04, 16.25)	0.96 (0.05, 13.45)	1.01 (0.07, 13.09)
Dabigatran vs. Tinzaparin	1.02 (0.03, 34.3)	1.04 (0.02, 48.5)	1.04 (0.03, 39.1)	1.02 (0.03, 34.6)
Dabigatran vs. Warfarin	1.14 (0.07, 18.05)	1.13 (0.04, 29.20)	1.14 (0.05, 22.07)	1.13 (0.06, 20.09)
Desirudin vs. Enoxaparin	0.88 (0.13, 7.68)	1.17 (0.10, 22.26)	0.45 (0.03, 6.98)	0.44 (0.03, 6.12)
Desirudin vs. Heparin	0.20 (0.03, 1.50)	0.05 (0.00, 0.84)		
Desirudin vs. None	7.47 (0.06, 6641)			3.68 (0.02, 2411)
Desirudin vs. Warfarin	1.08 (0.07, 22.65)	1.41 (0.05, 70.67)	0.54 (0.01, 18.60)	0.53 (0.02, 15.77)
Enoxaparin vs. None	8.46 (0.1, 6081)			8.31 (0.1, 3547)
Heparin vs. Enoxaparin	4.41 (0.80, 31.28)	25.43 (1.70, 1,032.77)		
Heparin vs. None	37.3 (0.33, 30946)			

Table 104. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Heparin vs. Warfarin	5.40 (0.38, 95.30)	30.72 (0.87, 2,573.44)		
IPC vs. Apixaban	0.06 (0.00, 51.32)			0.06 (0.00, 66.69)
IPC vs. Dabigatran	0.02 (0.00, 14.89)			0.02 (0.00, 17.48)
IPC vs. Desirudin	0.02 (0.00, 13.97)			0.04 (0.00, 46.11)
IPC vs. Enoxaparin	0.02 (0.00, 9.61)			0.02 (0.00, 12.40)
IPC vs. Heparin	0.00 (0.00, 2.87)			
IPC vs. IPC + LD Aspirin	0.02 (0.00, 20.15)			0.02 (0.00, 26.71)
IPC vs. None	0.14 (0.00, 10.05)			0.14 (0.00, 11.35)
IPC vs. Rivaroxaban	0.02 (0.00, 12.26)			0.02 (0.00, 16.58)
IPC vs. Tinzaparin	0.02 (0.00, 21.26)			0.02 (0.00, 26.55)
IPC vs. Warfarin	0.02 (0.00, 16.43)			0.02 (0.00, 20.27)
IPC + LD Aspirin vs. Tinzaparin	1.04 (0.02, 72.5)	1.08 (0.01, 109.4)	1.07 (0.01, 82.2)	1.03 (0.01, 75.9)
IPC + LD Aspirin vs. Apixaban	3.25 (0.06, 174.34)	3.29 (0.04, 296.49)	3.32 (0.05, 219.86)	3.23 (0.06, 181.64)
IPC + LD Aspirin vs. Desirudin	1.07 (0.03, 37.94)	0.83 (0.01, 51.83)	2.18 (0.03, 143.88)	2.14 (0.04, 127.23)
IPC + LD Aspirin vs. Enoxaparin	0.94 (0.05, 21.14)	0.97 (0.03, 29.73)	0.97 (0.04, 22.60)	0.95 (0.04, 21.05)
IPC + LD Aspirin vs. Heparin	0.21 (0.01, 6.90)	0.04 (0.00, 3.07)		
IPC + LD Aspirin vs. None	7.98 (0.04, 9,946.74)			7.89 (0.03, 5,931.31)
IPC + LD Aspirin vs. Rivaroxaban	1.01 (0.03, 35.23)	0.97 (0.02, 47.51)	0.99 (0.02, 35.87)	1.02 (0.03, 34.67)

Table 104. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
IPC + LD Aspirin vs. Warfarin	1.16 (0.03, 45.92)	1.18 (0.02, 74.00)	1.17 (0.02, 54.54)	1.15 (0.03, 47.66)
LD Aspirin vs. Apixaban	0.41 (0.00, 116.51)			0.41 (0.00, 129.15)
LD Aspirin vs. Dabigatran	0.13 (0.00, 26.15)			0.13 (0.00, 31.47)
LD Aspirin vs. Desirudin	0.13 (0.00, 26.21)			0.27 (0.00, 83.76)
LD Aspirin vs. Enoxaparin	0.12 (0.00, 17.48)			0.12 (0.00, 20.37)
LD Aspirin vs. Heparin	0.03 (0.00, 5.33)			
LD Aspirin vs. IPC	7.01 (0.05, 4,307.01)			7.21 (0.04, 5,014.05)
LD Aspirin vs. IPC + LD Aspirin	0.12 (0.00, 47.66)			0.13 (0.00, 47.70)
LD Aspirin vs. None	0.99 (0.09, 10.70)			1.00 (0.09, 11.67)
LD Aspirin vs. Rivaroxaban	0.13 (0.00, 24.95)			0.13 (0.00, 30.42)
LD Aspirin vs. Tinzaparin	0.13 (0.00, 42.39)			0.13 (0.00, 50.05)
LD Aspirin vs. Warfarin	0.14 (0.00, 33.05)			0.15 (0.00, 35.98)
Rivaroxaban vs. Apixaban	3.22 (0.16, 74.6)	3.41 (0.11, 145)	3.36 (0.14, 109.2)	3.15 (0.15,77.6)
Rivaroxaban vs. Desirudin	1.05 (0.07, 13.65)	0.86 (0.03, 20.13)	2.21 (0.08, 71.81)	2.09 (0.09, 52.93)
Rivaroxaban vs. Enoxaparin	0.93 (0.17, 5.48)	1.01 (0.14, 8.78)	0.99 (0.16, 7.52)	0.92 (0.16, 5.61)
Rivaroxaban vs. Heparin	0.21 (0.02, 2.45)	0.04 (0.00, 1.23)		
Rivaroxaban vs. None	7.89 (0.07, 6516)			7.69 (0.06, 4159)
Rivaroxaban vs. Warfarin	1.14 (0.08, 17.98)	1.22 (0.06, 34.30)	1.19 (0.07, 25.38)	1.12 (0.07, 18.60)
Tinzaparin vs. Apixaban	3.14 (0.07, 158.70)	3.05 (0.04, 236.75)	3.11 (0.06, 180.91)	3.13 (0.06, 154.78)
Tinzaparin vs. Desirudin	1.03 (0.03, 33.41)	0.77 (0.01, 37.68)	2.05 (0.03, 124.96)	2.08 (0.04, 106.80)
Tinzaparin vs. Enoxaparin	0.91 (0.05, 17.57)	0.90 (0.04, 22.11)	0.91 (0.04, 18.93)	0.92 (0.05, 16.66)

Table 104. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Tinzaparin vs. Heparin	0.21 (0.01, 6.30)	0.04 (0.00, 2.36)		
Tinzaparin vs. None	7.70 (0.04, 8,518.54)			7.66 (0.03, 5,558.04)
Tinzaparin vs. Rivaroxaban	0.98 (0.03, 29.52)	0.89 (0.02, 36.67)	0.93 (0.02, 29.64)	1.00 (0.03, 28.62)
Tinzaparin vs. Warfarin	1.12 (0.06, 21.31)	1.09 (0.04, 26.26)	1.10 (0.05, 22.35)	1.11 (0.06, 20.49)
Warfarin vs. Enoxaparin	0.82 (0.10, 6.75)	0.83 (0.07, 9.68)	0.83 (0.09, 7.94)	0.83 (0.10, 7.21)
Warfarin vs. None	6.9 (0.05, 6167)			6.88 (0.05, 3831)

Table 105. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event (No Heparin Trials)	Without Heparin or Multi-Arm Trials	Final Model
Apixaban vs. Enoxaparin	1.79 (0.35, 9.07)	1.68 (0.21, 12.00)	2.77 (0.38, 26.60)	2.60 (0.49, 19.34)
Apixaban vs. Heparin	0.13 (0.00, 11.20)			
Apixaban vs. None	0.21 (0, 26.79)			
Apixaban vs. Warfarin	1.09 (0.10, 12.21)	0.92 (0.04, 20.03)	0.34 (0.00, 15.04)	0.62 (0.02, 15.20)
Dabigatran vs. Apixaban	0.47 (0.03, 6.01)	0.38 (0.01, 9.77)	0.25 (0.01, 4.81)	0.33 (0.02, 3.91)
Dabigatran vs. Enoxaparin	0.84 (0.09, 6.17)	0.64 (0.03, 7.93)	0.68 (0.04, 6.81)	0.86 (0.10, 5.82)
Dabigatran vs. Enoxaparin + IPC	0.92 (0.01, 94)	0.65 (0.003, 112)	0.72 (0.004, 93.2)	0.91 (0.01, 85.7)
Dabigatran vs. GCS	0.1 (0.0001, 14.1)			
Dabigatran vs. Heparin	0.06 (0.00, 6.07)			
Dabigatran vs. None	0.1 (0.0001, 14.8)			
Dabigatran vs. Rivaroxaban	2.64 (0.14, 52.6)	3.04 (0.08, 134)	2.96 (0.09, 101)	2.66 (0.16, 47.4)
Dabigatran vs. Warfarin	0.51 (0.03, 8.46)	0.35 (0.01, 12.01)	0.08 (0.00, 3.84)	0.21 (0.01, 4.54)
Enoxaparin + IPC vs. Apixaban	0.51 (0.01, 48.72)	0.58 (0.00, 90.56)	0.34 (0.00, 37.83)	0.36 (0.00, 34.06)
Enoxaparin + IPC vs. Enoxaparin	0.92 (0.01, 64.07)	0.98 (0.01, 96.25)	0.95 (0.01, 71.52)	0.94 (0.01, 67.56)
Enoxaparin + IPC vs. GCS	0.11 (0.00, 66.42)			
Enoxaparin + IPC vs. Heparin	0.07 (0.00, 28.13)			
Enoxaparin + IPC vs. IPC	0.97 (0.00, 4,234.41)			
Enoxaparin + IPC vs. None	0.11 (0.00, 68.17)			
Enoxaparin + IPC vs. Rivaroxaban	2.88 (0.03, 357.45)	4.65 (0.03, 1,000.24)	4.12 (0.03, 697.85)	2.92 (0.03, 329.64)
Enoxaparin + IPC vs. Warfarin	0.56 (0.01, 61.93)	0.53 (0.00, 99.88)	0.12 (0.00, 23.95)	0.23 (0.00, 31.72)
Enoxaparin vs. None	0.12 (0, 11.05)			
GCS vs. Apixaban	4.58 (0.04, 3,733.12)			

Table 105. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event (No Heparin Trials)	Without Heparin or Multi-Arm Trials	Final Model
GCS vs. Enoxaparin	8.17 (0.09, 5,907.63)			
GCS vs. Heparin	0.61 (0.00, 1,307.67)			
GCS vs. None	0.97 (0.03, 33.48)			
GCS vs. Rivaroxaban	25.66 (0.19, 23,388.51)			
GCS vs. Warfarin	4.98 (0.04, 4,628.55)			
HD Aspirin + IPC vs. Apixaban	4.05 (0.01, 7,435.34)			2.87 (0.00, 5,597.08)
HD Aspirin + IPC vs. Dabigatran	8.60 (0.01, 18,251.45)			8.71 (0.01, 19,653.29)
HD Aspirin + IPC vs. Enoxaparin	7.24 (0.01, 11,418.61)			7.47 (0.02, 12,733.61)
HD Aspirin + IPC vs. Enoxaparin + IPC	7.90 (0.10, 3,648.24)			7.92 (0.09, 4,242.89)
HD Aspirin + IPC vs. GCS	0.89 (0.00, 5,161.59)			
HD Aspirin + IPC vs. Heparin	0.54 (0.00, 2,591.52)			
HD Aspirin + IPC vs. IPC	7.70 (0.00, 189,094.09)			
HD Aspirin + IPC vs. None	0.86 (0.00, 4,979.08)			
HD Aspirin + IPC vs. Rivaroxaban	22.74 (0.03, 52,052.08)			23.15 (0.04, 52,575.21)
HD Aspirin + IPC vs. Warfarin	4.41 (0.01, 8,982.20)			1.79 (0.00, 4,812.63)
Heparin vs. Enoxaparin	13.45 (0.22, 5,356.15)			
Heparin vs. None	1.6 (0, 2697)			
Heparin vs. Warfarin	8.20 (0.08, 4,345.95)			

Table 105. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Pulmonary Embolism

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event (No Heparin Trials)	Without Heparin or Multi-Arm Trials	Final Model
IPC vs. Apixaban	0.53 (0.00, 873.06)			
IPC vs. Dabigatran	1.12 (0.00, 2,102.75)			
IPC vs. Enoxaparin	0.94 (0.00, 1,371.97)			
IPC vs. GCS	0.12 (0.00, 10.72)			
IPC vs. Heparin	0.07 (0.00, 348.97)			
IPC vs. None	0.11 (0.00, 10.48)			
IPC vs. Rivaroxaban	2.95 (0.00, 5,630.76)			
IPC vs. Warfarin	0.57 (0.00, 1,166.78)			
Rivaroxaban vs. Apixaban	0.18 (0.01, 2.08)	0.13 (0.00, 2.74)	0.08 (0.00, 1.46)	0.12 (0.01, 1.36)
Rivaroxaban vs. Enoxaparin	0.32 (0.03, 2.10)	0.21 (0.01, 2.18)	0.23 (0.02, 1.98)	0.32 (0.04, 1.98)
Rivaroxaban vs. Heparin	0.02 (0.00, 2.27)			
Rivaroxaban vs. None	0.04 (0, 5.35)			
Rivaroxaban vs. Warfarin	0.19 (0.01, 2.90)	0.11 (0.00, 3.59)	0.03 (0.00, 1.23)	0.08 (0.00, 1.67)
Warfarin vs. Enoxaparin	1.64 (0.22, 11.87)	1.83 (0.14, 24.17)	8.09 (0.37, 390.33)	4.17 (0.35, 81.29)
Warfarin vs. None	0.19 (0, 28.9)			

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Apixaban vs. Enoxaparin	1.24 (0.51, 3.00)	1.22 (0.37, 3.96)	1.22 (0.37, 4.10)	1.23 (0.49, 3.13)
Apixaban vs. Heparin	0.98 (0.34, 2.97)	1.00 (0.27, 4.86)		
Apixaban vs. None	4.28 (0.91, 23.08)	7.98 (1.07, 108.31)	3.59 (0.40, 48.28)	2.45 (0.41, 16.54)
Apixaban vs. Warfarin	3.73 (0.89, 15.80)	3.71 (0.61, 22.49)	3.63 (0.63, 22.20)	3.63 (0.86, 17.25)
Dabigatran vs. Apixaban	1.31 (0.48, 3.83)	1.34 (0.34, 5.62)	1.34 (0.33, 5.67)	1.33 (0.45, 4.01)
Dabigatran vs. Enoxaparin	1.63 (0.94, 2.89)	1.63 (0.81, 3.50)	1.65 (0.80, 3.49)	1.63 (0.92, 2.99)
Dabigatran vs. Heparin	1.28 (0.57, 3.16)	1.35 (0.52, 4.66)		
Dabigatran vs. None	5.62 (1.35, 26.82)	10.71 (1.76, 121)	4.83 (0.67, 53.20)	3.26 (0.65, 18.73)
Dabigatran vs. Warfarin	4.89 (1.39, 17.67)	4.98 (1.13, 23.67)	4.88 (1.11, 23.43)	4.83 (1.34, 19.22)
Dalteparin vs. Apixaban	0.52 (0.11, 2.57)	0.52 (0.07, 3.79)	0.54 (0.07, 3.84)	0.54 (0.10, 2.76)
Dalteparin vs. Dabigatran	0.40 (0.09, 1.70)	0.39 (0.06, 2.17)	0.40 (0.06, 2.26)	0.41 (0.08, 1.76)
Dalteparin vs. Desirudin	0.55 (0.11, 2.55)	0.53 (0.07, 3.32)	0.65 (0.09, 4.79)	0.67 (0.12, 3.48)
Dalteparin vs. Enoxaparin	0.65 (0.17, 2.47)	0.64 (0.12, 3.06)	0.66 (0.12, 3.22)	0.67 (0.16, 2.55)
Dalteparin vs. Fondaparinux	0.46 (0.08, 2.63)	0.43 (0.05, 3.18)	0.41 (0.04, 3.10)	0.45 (0.07, 2.57)
Dalteparin vs. HD Aspirin	2.86 (0.43, 19.67)	2.73 (0.33, 23.97)	2.83 (0.33, 24.39)	2.76 (0.38, 19.24)
Dalteparin vs. Heparin	0.51 (0.12, 2.24)	0.52 (0.09, 3.40)		
Dalteparin vs. IPC + LD Aspirin	72.46 (1.84, 131,926)			51.52 (1.75, 11,743)
Dalteparin vs. LY517717	0.78 (0.02, 34.50)	0.75 (0.01, 41.14)	0.70 (0.01, 38.90)	0.77 (0.01, 46.15)
Dalteparin vs. None	2.23 (0.34, 16.01)	4.17 (0.42, 66.02)	1.93 (0.16, 29.61)	1.33 (0.16, 12.06)
Dalteparin vs. Rivaroxaban	0.36 (0.07, 1.85)	0.34 (0.05, 2.23)	0.36 (0.05, 2.35)	0.36 (0.07, 1.83)
Dalteparin vs. Tinzaparin	0.93 (0.30, 2.92)	0.94 (0.22, 4.09)	0.96 (0.22, 4.21)	0.96 (0.30, 3.13)
Dalteparin vs. Warfarin	1.94 (0.97, 3.85)	1.94 (0.76, 4.79)	1.96 (0.76, 4.84)	1.97 (0.94, 4.06)

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Dalteparin vs. YM150	4.73 (0.08, 1,588)			4.59 (0.07, 3,456)
Desirudin vs. Apixaban	0.95 (0.3, 3.23)	0.99 (0.22, 5.14)	0.83 (0.15, 4.46)	0.81 (0.22, 3.05)
Desirudin vs. Dabigatran	0.72 (0.28, 1.95)	0.74 (0.22, 2.66)	0.61 (0.15, 2.44)	0.61 (0.20, 1.81)
Desirudin vs. Enoxaparin	1.18 (0.54, 2.69)	1.20 (0.45, 3.54)	1.01 (0.30, 3.31)	1.00 (0.39, 2.54)
Desirudin vs. Heparin	0.93 (0.38, 2.54)	0.99 (0.35, 3.85)		
Desirudin vs. None	4.07 (0.95, 20.99)	7.89 (1.17, 93.88)	2.96 (0.33, 36.27)	2.00 (0.34, 13.63)
Desirudin vs. Warfarin	3.54 (0.89, 15.36)	3.67 (0.73, 20.80)	2.99 (0.51, 18.25)	2.96 (0.68, 13.94)
Enoxaparin + GCS vs. Apixaban	0.08 (0.00, 6.41)			0.08 (0.00, 6.26)
Enoxaparin + GCS vs. Dabigatran	0.06 (0.00, 4.36)			0.06 (0.00, 4.15)
Enoxaparin + GCS vs. Dalteparin	0.15 (0.00, 14.03)			0.16 (0.00, 13.07)
Enoxaparin + GCS vs. Desirudin	0.08 (0.00, 6.28)			0.10 (0.00, 7.71)
Enoxaparin + GCS vs. Enoxaparin	0.10 (0.00, 7.16)			0.10 (0.00, 6.71)
Enoxaparin + GCS vs. Fondaparinux	0.07 (0.00, 4.34)			0.07 (0.00, 3.60)
Enoxaparin + GCS vs. Fondaparinux + GCS	0.62 (0.33, 1.11)			0.62 (0.32, 1.17)
Enoxaparin + GCS vs. HD Aspirin	0.44 (0.00, 58.79)			0.43 (0.00, 54.43)
Enoxaparin + GCS vs. Heparin	0.08 (0.00, 5.79)			
Enoxaparin + GCS vs. IPC+LDAspirin	11.07 (0.01, 91,126)			8.01 (0.01, 6,816)
Enoxaparin + GCS vs. LY517717	0.12 (0.00, 35.62)			0.12 (0.00, 42.35)
Enoxaparin + GCS vs. None	0.34 (0.00, 25.51)			0.21 (0.00, 17.17)
Enoxaparin + GCS vs. Rivaroxaban	0.05 (0.00, 3.94)			0.06 (0.00, 4.11)
Enoxaparin + GCS vs. Tinzaparin	0.14 (0.00, 13.14)			0.15 (0.00, 11.92)
Enoxaparin + GCS vs. Warfarin	0.30 (0.00, 25.71)			0.31 (0.00, 24.26)

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Enoxaparin + GCS vs. YM150	0.72 (0.00, 750.70)			0.71 (0.00, 1,618.09)
Enoxaparin vs. None	3.46 (0.95, 14.53)	6.56 (1.21, 66.1)	2.93 (0.47, 28.88)	2.00 (0.44, 10.35)
Fondaparinux + GCS vs. Apixaban	0.13 (0.00, 9.68)			0.14 (0.00, 9.39)
Fondaparinux + GCS vs. Dabigatran	0.10 (0.00, 6.62)			0.10 (0.00, 6.45)
Fondaparinux + GCS vs. Dalteparin	0.25 (0.00, 21.82)			0.25 (0.00, 19.99)
Fondaparinux + GCS vs. Desirudin	0.13 (0.00, 9.56)			0.17 (0.00, 11.91)
Fondaparinux + GCS vs. Enoxaparin	0.16 (0.00, 11.09)			0.17 (0.00, 10.14)
Fondaparinux + GCS vs. Fondaparinux	0.11 (0.00, 6.61)			0.11 (0.00, 5.42)
Fondaparinux + GCS vs. HD Aspirin	0.70 (0.00, 91.29)			0.69 (0.00, 84.52)
Fondaparinux + GCS vs. Heparin	0.12 (0.00, 8.79)			
Fondaparinux + GCS vs. IPC + LD Aspirin	17.78 (0.01, 138,690)			12.85 (0.02, 10,446)
Fondaparinux + GCS vs. LY517717	0.19 (0.00, 55.53)			0.19 (0.00, 62.43)
Fondaparinux + GCS vs. None	0.55 (0.00, 39.25)			0.33 (0.00, 26.71)
Fondaparinux + GCS vs. Rivaroxaban	0.09 (0.00, 5.99)			0.09 (0.00, 6.36)
Fondaparinux + GCS vs. Tinzaparin	0.23 (0.00, 20.17)			0.24 (0.00, 18.32)
Fondaparinux + GCS vs. Warfarin	0.48 (0.00, 40.65)			0.49 (0.00, 37.37)
Fondaparinux + GCS vs. YM150	1.16 (0.00, 1,155)			1.15 (0.00, 2,507)
Fondaparinux vs. Apixaban	1.12 (0.26, 4.60)	1.21 (0.22, 8.03)	1.32 (0.23, 8.75)	1.22 (0.28, 5.28)
Fondaparinux vs. Dabigatran	0.86 (0.24, 2.97)	0.90 (0.20, 4.34)	0.98 (0.22, 4.82)	0.91 (0.25, 3.28)
Fondaparinux vs. Desirudin	1.18 (0.29, 4.49)	1.22 (0.23, 6.79)	1.60 (0.29, 10.98)	1.49 (0.35, 6.63)
Fondaparinux vs. Enoxaparin	1.39 (0.45, 4.24)	1.47 (0.40, 6.01)	1.62 (0.44, 6.61)	1.49 (0.48, 4.69)

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Fondaparinux vs. Heparin	1.10 (0.31, 3.94)	1.21 (0.30, 7.05)		
Fondaparinux vs. None	4.82 (1.07, 24.24)	9.65 (1.37, 124.59)	4.74 (0.62, 56.43)	2.98 (0.58, 19.22)
Fondaparinux vs. Rivaroxaban	0.77 (0.17, 3.13)	0.79 (0.15, 4.48)	0.88 (0.17, 5.01)	0.81 (0.19, 3.57)
Fondaparinux vs. Tinzaparin	2.00 (0.38, 11.29)	2.18 (0.34, 16.79)	2.34 (0.34, 18.63)	2.14 (0.40, 12.34)
Fondaparinux vs. Warfarin	4.19 (0.84, 21.16)	4.49 (0.74, 31.75)	4.79 (0.77, 34.88)	4.41 (0.90, 24.05)
GCS vs. Apixaban	0.08 (0.00, 24.46)			0.08 (0.00, 31.16)
GCS vs. Dabigatran	0.06 (0.00, 16.95)			0.06 (0.00, 20.88)
GCS vs. Dalteparin	0.15 (0.00, 46.43)			0.14 (0.00, 62.93)
GCS vs. Desirudin	0.08 (0.00, 23.90)			0.10 (0.00, 36.67)
GCS vs. Enoxaparin	0.10 (0.00, 26.02)			0.10 (0.00, 33.08)
GCS vs. Enoxaparin + GCS	0.99 (0.02, 35.34)			0.93 (0.02, 43.64)
GCS vs. Fondaparinux	0.07 (0.00, 14.92)			0.06 (0.00, 19.55)
GCS vs. Fondaparinux + GCS	0.62 (0.01, 22.53)			0.58 (0.01, 25.13)
GCS vs. HD Aspirin	0.43 (0.00, 178.22)			0.40 (0.00, 255.70)
GCS vs. Heparin	0.08 (0.00, 22.29)			
GCS vs. IPC + LD Aspirin	10.94 (0.00, 108,012)			7.46 (0.01, 13,643)
GCS vs. LY517717	0.12 (0.00, 78.65)			0.11 (0.00, 135.91)
GCS vs. None	0.34 (0.00, 99.58)			0.19 (0.00, 65.76)
GCS vs. Rivaroxaban	0.05 (0.00, 15.12)			0.05 (0.00, 19.61)
GCS vs. Tinzaparin	0.14 (0.00, 40.94)			0.14 (0.00, 64.33)
GCS vs. Warfarin	0.29 (0.00, 83.68)			0.29 (0.00, 121.15)
GCS vs. YM150	0.71 (0.00, 1,531.50)			0.66 (0.00, 3,428.92)

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
HD Aspirin vs. Apixaban	0.18 (0.02, 1.81)	0.19 (0.01, 2.64)	0.19 (0.01, 2.62)	0.20 (0.02, 2.04)
HD Aspirin vs. Dabigatran	0.14 (0.02, 1.24)	0.14 (0.01, 1.62)	0.14 (0.01, 1.61)	0.15 (0.02, 1.44)
HD Aspirin vs. Desirudin	0.19 (0.02, 1.89)	0.19 (0.01, 2.46)	0.23 (0.02, 3.23)	0.24 (0.02, 2.49)
HD Aspirin vs. Enoxaparin	0.23 (0.03, 1.89)	0.23 (0.02, 2.37)	0.23 (0.02, 2.37)	0.24 (0.03, 2.20)
HD Aspirin vs. Fondaparinux	0.16 (0.01, 1.87)	0.16 (0.01, 2.28)	0.14 (0.01, 2.05)	0.16 (0.01, 1.80)
HD Aspirin vs. Heparin	0.18 (0.02, 1.67)	0.19 (0.02, 2.40)		
HD Aspirin vs. IPC + LD Aspirin	25.33 (0.42, 46,630)			18.69 (0.40, 6,254)
HD Aspirin vs. LY517717	0.27 (0.00, 17.78)	0.27 (0.00, 20.37)	0.25 (0.00, 20.80)	0.28 (0.00, 22.69)
HD Aspirin vs. None	0.78 (0.06, 9.80)	1.52 (0.09, 39.21)	0.68 (0.04, 16.91)	0.48 (0.03, 7.59)
HD Aspirin vs. Rivaroxaban	0.12 (0.01, 1.31)	0.12 (0.01, 1.66)	0.13 (0.01, 1.65)	0.13 (0.01, 1.36)
HD Aspirin vs. Tinzaparin	0.32 (0.04, 2.39)	0.34 (0.04, 3.19)	0.34 (0.04, 3.36)	0.35 (0.04, 2.76)
HD Aspirin vs. Warfarin	0.68 (0.11, 3.94)	0.71 (0.10, 4.78)	0.69 (0.09, 4.63)	0.72 (0.11, 4.49)
HD Aspirin vs. YM150	1.65 (0.02, 614.62)			1.67 (0.02, 1,187.97)
Heparin vs. Enoxaparin	1.27 (0.66, 2.32)	1.21 (0.48, 2.47)		
Heparin vs. None	4.39 (1.19, 18.39)	7.96 (1.33, 80.4)		
Heparin vs. Warfarin	3.82 (1.03, 14.27)	3.70 (0.73, 16.69)		
IPC + LD Aspirin vs. Apixaban	0.01 (0.00, 0.23)			0.01 (0.00, 0.25)
IPC + LD Aspirin vs. Dabigatran	0.01 (0.00, 0.15)			0.01 (0.00, 0.17)
IPC + LD Aspirin vs. Desirudin	0.01 (0.00, 0.23)			0.01 (0.00, 0.32)
IPC + LD Aspirin vs. Enoxaparin	0.01 (0.00, 0.24)			0.01 (0.00, 0.26)
IPC + LD Aspirin vs. Fondaparinux	0.01 (0.00, 0.24)			0.01 (0.00, 0.24)
IPC + LD Aspirin vs. Heparin	0.01 (0.00, 0.21)			

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
IPC + LD Aspirin vs. None	0.03 (0.00, 1.21)			0.03 (0.00, 0.85)
IPC + LD Aspirin vs. Tinzaparin	0.01 (0.00, 0.48)			0.02 (0.00, 0.50)
IPC + LD Aspirin vs. Warfarin	0.03 (0.00, 0.95)			0.04 (0.00, 1.01)
LY517717 vs. Apixaban	0.67 (0.02, 23.20)	0.70 (0.02, 31.88)	0.77 (0.02, 44.04)	0.71 (0.01, 34.99)
LY517717 vs. Dabigatran	0.51 (0.01, 16.36)	0.52 (0.01, 19.81)	0.58 (0.01, 27.99)	0.53 (0.01, 25.10)
LY517717 vs. Desirudin	0.70 (0.02, 23.55)	0.71 (0.02, 28.47)	0.94 (0.02, 54.05)	0.87 (0.02, 44.30)
LY517717 vs. Enoxaparin	0.83 (0.02, 25.76)	0.85 (0.02, 30.05)	0.95 (0.02, 42.35)	0.87 (0.02, 38.74)
LY517717 vs. Fondaparinux	0.59 (0.01, 22.22)	0.58 (0.01, 25.51)	0.59 (0.01, 32.85)	0.58 (0.01, 29.64)
LY517717 vs. Heparin	0.65 (0.02, 22.11)	0.70 (0.02, 28.28)		
LY517717 vs. IPC + LD Aspirin	92.76 (0.58, 58,689)			66.89 (0.44, 34,544)
LY517717 vs. None	2.86 (0.07, 111.72)	5.56 (0.10, 331.62)	2.78 (0.04, 235.33)	1.73 (0.03, 108.64)
LY517717 vs. Tinzaparin	1.18 (0.03, 48.47)	1.25 (0.03, 67.69)	1.37 (0.03, 79.04)	1.25 (0.02, 69.13)
LY517717 vs. Warfarin	2.49 (0.06, 95.68)	2.59 (0.05, 118.87)	2.81 (0.05, 151.11)	2.56 (0.05, 136.18)
Rivaroxaban vs. Apixaban	1.46 (0.41, 5.35)	1.53 (0.32, 7.65)	1.5 (0.32, 7.67)	1.49 (0.41, 5.63)
Rivaroxaban vs. Dabigatran	1.11 (0.37, 3.37)	1.14 (0.31, 4.17)	1.11 (0.31, 4.08)	1.12 (0.35, 3.54)
Rivaroxaban vs. Desirudin	1.54 (0.45, 5.16)	1.55 (0.35, 6.53)	1.81 (0.39, 9.12)	1.83 (0.49, 7.06)
Rivaroxaban vs. Enoxaparin	1.81 (0.71, 4.73)	1.86 (0.65, 5.58)	1.83 (0.65, 5.43)	1.83 (0.72, 4.91)
Rivaroxaban vs. Heparin	1.43 (0.48, 4.49)	1.53 (0.43, 6.40)		
Rivaroxaban vs. IPC + LD Aspirin	203 (6.47, 245242)			141 (6.24, 42193)
Rivaroxaban vs. LY517717	2.19 (0.07, 89.3)	2.19 (0.06, 105)	1.93 (0.04, 89.1)	2.11 (0.04, 126.2)
Rivaroxaban vs. None	6.26 (1.35, 36.71)	12.19 (1.64, 152)	5.37 (0.64, 68.99)	3.66 (0.61, 26.76)
Rivaroxaban vs. Tinzaparin	2.6 (0.58, 12.7)	2.75 (0.49, 18)	2.65 (0.47, 16.9)	2.63 (0.53, 13.1)

Table 106. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Rivaroxaban vs. Warfarin	5.45 (1.25, 23.93)	5.67 (1.06, 32.43)	5.43 (1.04, 30.51)	5.42 (1.26, 25.58)
Tinzaparin vs. Apixaban	0.56 (0.12, 2.48)	0.56 (0.08, 3.49)	0.56 (0.08, 3.44)	0.57 (0.11, 2.60)
Tinzaparin vs. Dabigatran	0.43 (0.11, 1.63)	0.41 (0.08, 1.93)	0.42 (0.08, 1.99)	0.43 (0.10, 1.67)
Tinzaparin vs. Desirudin	0.59 (0.12, 2.62)	0.56 (0.09, 3.06)	0.68 (0.10, 4.25)	0.70 (0.14, 3.22)
Tinzaparin vs. Enoxaparin	0.70 (0.20, 2.41)	0.68 (0.16, 2.68)	0.69 (0.16, 2.77)	0.69 (0.18, 2.42)
Tinzaparin vs. Heparin	0.55 (0.13, 2.19)	0.56 (0.11, 3.03)		
Tinzaparin vs. None	2.41 (0.39, 15.72)	4.43 (0.48, 69.41)	2.02 (0.19, 27.39)	1.39 (0.19, 11.40)
Tinzaparin vs. Warfarin	2.10 (0.83, 5.16)	2.06 (0.64, 6.23)	2.05 (0.63, 6.28)	2.06 (0.80, 5.26)
Warfarin vs. Enoxaparin	0.33 (0.10, 1.03)	0.33 (0.08, 1.21)	0.34 (0.08, 1.23)	0.34 (0.10, 1.05)
Warfarin vs. None	1.15 (0.20, 7.07)	2.15 (0.26, 30.23)	0.99 (0.10, 12.67)	0.68 (0.10, 5.46)
YM150 vs. Apixaban	0.11 (0.00, 5.49)			0.12 (0.00, 6.93)
YM150 vs. Dabigatran	0.08 (0.00, 3.78)			0.09 (0.00, 4.87)
YM150 vs. Desirudin	0.12 (0.00, 5.67)			0.15 (0.00, 9.17)
YM150 vs. Enoxaparin	0.14 (0.00, 5.96)			0.15 (0.00, 7.77)
YM150 vs. Fondaparinux	0.10 (0.00, 5.07)			0.10 (0.00, 5.89)
YM150 vs. Heparin	0.11 (0.00, 5.10)			
YM150 vs. IPC + LD Aspirin	15.33 (0.01, 12,810)			11.22 (0.01, 7,738)
YM150 vs. LY517717	0.17 (0.0002, 29.1)			0.17 (0.0001, 58.8)
YM150 vs. None	0.47 (0.00, 27.63)			0.29 (0.00, 22.60)
YM150 vs. Rivaroxaban	0.08 (0.00, 3.59)			0.08 (0.00, 5.04)
YM150 vs. Tinzaparin	0.20 (0.00, 10.48)			0.21 (0.00, 13.46)
YM150 vs. Warfarin	0.41 (0.00, 21.65)			0.43 (0.00, 27.44)

Table 107. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Enoxaparin	0.65 (0.25, 2.05)	0.69 (0.23, 3.14)	0.69 (0.22, 3.15)	0.55 (0.15, 2.00)	0.55 (0.16, 1.87)
Apixaban vs. Heparin	0.63 (0.06, 7.92)	0.67 (0.05, 12.15)			
Apixaban vs. None	0.84 (0.15, 5.99)	0.53 (0.06, 6.61)	0.52 (0.05, 6.22)	0.42 (0.04, 4.14)	0.42 (0.04, 3.76)
Apixaban vs. Warfarin	1.16 (0.28, 5.89)	1.29 (0.25, 11.43)	1.29 (0.25, 11.57)	0.93 (0.14, 6.42)	0.92 (0.15, 5.71)
Dabigatran vs. Apixaban	1.39 (0.29, 6.09)	1.47 (0.21, 8.26)	1.47 (0.22, 8.43)	1.81 (0.34, 12.40)	1.81 (0.37, 11.00)
Dabigatran vs. Enoxaparin	0.90 (0.31, 2.85)	1.01 (0.31, 4.17)	1.01 (0.31, 4.15)	1.00 (0.32, 3.94)	0.99 (0.34, 3.55)
Dabigatran vs. Heparin	0.88 (0.08, 10.98)	0.98 (0.07, 16.74)			
Dabigatran vs. None	1.17 (0.25, 6.61)	0.78 (0.11, 6.06)	0.76 (0.11, 5.85)	0.77 (0.11, 5.9)	0.76 (0.11, 5.23)
Dabigatran vs. Warfarin	1.61 (0.34, 8.65)	1.89 (0.33, 16.04)	1.90 (0.34, 15.99)	1.69 (0.29, 12.55)	1.67 (0.31, 11.21)
Enoxaparin vs. None	1.31 (0.3, 6.04)	0.78 (0.1, 5.67)	0.75 (0.1, 5.16)	0.77 (0.11, 5.22)	0.77 (0.11, 4.87)
Fondaparinux vs. Apixaban	1.24 (0.02, 77.48)	1.94 (0.02, 187.35)	1.96 (0.02, 182.73)	2.45 (0.03, 256.72)	2.70 (0.04, 240.57)
Fondaparinux vs. Dabigatran	0.89 (0.01, 51.57)	1.32 (0.02, 105.85)	1.34 (0.02, 109.40)	1.36 (0.02, 111.94)	1.49 (0.02, 110.39)
Fondaparinux vs. Enoxaparin	0.80 (0.01, 45.74)	1.33 (0.02, 115.93)	1.35 (0.02, 114.21)	1.35 (0.02, 116.40)	1.48 (0.02, 113.41)
Fondaparinux vs. Heparin	0.79 (0.01, 80.16)	1.30 (0.01, 200.54)			
Fondaparinux vs. IPC	7.94 (0.03, 7,093.97)				
Fondaparinux vs. None	1.05 (0.02, 45.15)	1.04 (0.02, 57.11)	1.02 (0.02, 54.43)	1.04 (0.02, 55.59)	1.13 (0.03, 59.44)
Fondaparinux vs. Rivaroxaban	0.61 (0.01, 43.21)	1.10 (0.01, 122.85)	1.11 (0.01, 123.10)	1.10 (0.01, 124.21)	1.16 (0.02, 105.21)
Fondaparinux vs. Warfarin	1.44 (0.02, 96.83)	2.50 (0.03, 267.20)	2.54 (0.03, 279.78)	2.29 (0.02, 242.02)	2.49 (0.03, 225.65)
GCS vs. Apixaban	0.16 (0.00, 6.53)				
GCS vs. Dabigatran	0.12 (0.00, 4.71)				

Table 107. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
GCS vs. Enoxaparin	0.10 (0.00, 3.71)				
GCS vs. Fondaparinux	0.13 (0.0002, 32)				
GCS vs. Heparin	0.10 (0.00, 7.64)				
GCS vs. None	0.14 (0.00, 5.42)				
GCS vs. Rivaroxaban	0.08 (0.00, 3.74)				
GCS vs. Warfarin	0.19 (0.00, 8.22)				
Heparin vs. Enoxaparin	1.02 (0.11, 9.52)	1.03 (0.09, 11.51)			
Heparin vs. None	1.33 (0.09, 20.64)	0.41 (0.03, 4.19)			
Heparin vs. Warfarin	1.83 (0.15, 23.43)	1.93 (0.12, 35.06)			
IPC vs. Apixaban	0.16 (0.00, 7.33)				
IPC vs. Dabigatran	0.11 (0.00, 4.97)				
IPC vs. Enoxaparin	0.10 (0.00, 4.04)				
IPC vs. GCS	0.98 (0.00, 697.85)				
IPC vs. Heparin	0.10 (0.00, 8.11)				
IPC vs. None	0.13 (0.00, 5.49)				
IPC vs. Warfarin	0.18 (0.00, 9.66)				
Rivaroxaban vs. Apixaban	2.02 (0.34, 8.38)	1.76 (0.18, 9.04)	1.77 (0.18, 8.70)	2.22 (0.30, 11.48)	2.33 (0.37, 11.42)
Rivaroxaban vs. Dabigatran	1.45 (0.26, 6.26)	1.20 (0.14, 6.39)	1.21 (0.14, 6.23)	1.23 (0.15, 6.01)	1.29 (0.19, 5.91)
Rivaroxaban vs. Enoxaparin	1.30 (0.38, 3.85)	1.21 (0.26, 4.10)	1.22 (0.27, 4.05)	1.23 (0.29, 3.91)	1.28 (0.35, 3.88)
Rivaroxaban vs. Heparin	1.28 (0.10, 15.30)	1.18 (0.06, 16.91)			
Rivaroxaban vs. IPC	12.9 (0.25, 5094)				
Rivaroxaban vs. None	1.7 (0.25, 10.7)	0.94 (0.07, 9.14)	0.92 (0.07, 8.52)	0.94 (0.08, 8.69)	0.98 (0.09, 8.28)

Table 107. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Major Bleeding

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials	Final Model
Rivaroxaban vs. Warfarin	2.34 (0.43, 11.68)	2.28 (0.31, 14.70)	2.29 (0.31, 14.88)	2.08 (0.27, 12.33)	2.15 (0.32, 11.99)
Warfarin vs. Enoxaparin	0.56 (0.17, 1.76)	0.53 (0.12, 1.95)	0.53 (0.12, 1.97)	0.59 (0.14, 2.33)	0.60 (0.15, 2.24)
Warfarin vs. None	0.73 (0.11, 4.95)	0.8 (0.03, 18.1)	0.4 (0.03, 4.1)	0.45 (0.04, 4.69)	0.46 (0.04, 4.32)

Table 108. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Apixaban vs. Dabigatran	2.32 (0.06, 102)	2.08 (0.02, 206)	2.05 (0.02, 214)	2.22 (0.05, 112)
Apixaban vs. Desirudin	2.10 (0.05, 104.90)	3.49 (0.05, 393.86)	1.32 (0.01, 152.32)	1.29 (0.02, 95.11)
Apixaban vs. Enoxaparin	3.01 (0.18, 60.28)	2.94 (0.11, 91.56)	2.99 (0.11, 93.22)	2.86 (0.15, 64.01)
Apixaban vs. Heparin	0.61 (0.01, 31.25)	0.25 (0.00, 27.74)		
Apixaban vs. Warfarin	2.64 (0.06, 125.96)	2.64 (0.03, 254.68)	2.64 (0.03, 245.18)	2.51 (0.05, 143.74)
Dabigatran vs. Enoxaparin	1.30 (0.12, 13.56)	1.42 (0.06, 33.02)	1.46 (0.06, 33.99)	1.29 (0.11, 14.97)
Dabigatran vs. Heparin	0.26 (0.01, 8.72)	0.12 (0.00, 10.94)		
Dabigatran vs. Warfarin	1.14 (0.04, 33.58)	1.27 (0.02, 96.64)	1.29 (0.02, 96.35)	1.13 (0.03, 40.81)
Dalteparin vs. Apixaban	0.38 (0.00, 50.05)	0.37 (0.00, 120.06)	0.37 (0.00, 108.53)	0.41 (0.00, 65.76)
Dalteparin vs. Dabigatran	0.89 (0.01, 88.59)	0.78 (0.00, 214.86)	0.75 (0.00, 212.72)	0.91 (0.01, 113.07)
Dalteparin vs. Desirudin	0.81 (0.01, 89.48)	1.31 (0.01, 394.26)	0.48 (0.00, 144.75)	0.53 (0.00, 86.83)
Dalteparin vs. Enoxaparin	1.16 (0.02, 58.91)	1.10 (0.01, 124.59)	1.09 (0.01, 118.16)	1.17 (0.02, 76.25)
Dalteparin vs. Fondaparinux	5.77 (0.01, 6,581.38)			5.46 (0.01, 8,070.74)
Dalteparin vs. Heparin	0.23 (0.00, 26.79)	0.09 (0.00, 26.71)		
Dalteparin vs. Rivaroxaban	1.34 (0.02, 86.83)	1.11 (0.01, 166.50)	1.10 (0.01, 168.34)	1.34 (0.01, 116.16)
Dalteparin vs. Tinzaparin	1.01 (0.02, 56.4)	0.99 (0.01, 119)	0.96 (0.01, 108)	1.02 (0.01, 74.7)
Dalteparin vs. Warfarin	1.02 (0.04, 23.69)	0.99 (0.03, 37.00)	0.97 (0.03, 33.95)	1.03 (0.04, 27.44)
Desirudin vs. Dabigatran	1.1 (0.04, 30.5)	0.6 (0.01, 37.8)	1.56 (0.02, 157)	1.72 (0.04, 90.2)
Desirudin vs. Enoxaparin	1.43 (0.12, 15.56)	0.84 (0.03, 14.91)	2.27 (0.08, 68.72)	2.22 (0.11, 51.42)
Desirudin vs. Heparin	0.29 (0.02, 2.72)	0.07 (0.00, 1.83)		
Desirudin vs. Warfarin	1.26 (0.04, 36.23)	0.76 (0.01, 42.35)	2.01 (0.02, 182.91)	1.95 (0.04, 115.47)
Enoxaparin + GCS vs. Apixaban	0.01 (0.00, 11.23)			0.02 (0.00, 14.17)

Table 108. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Enoxaparin + GCS vs. Dabigatran	0.03 (0.00, 20.59)			0.04 (0.00, 26.29)
Enoxaparin + GCS vs. Dalteparin	0.04 (0.00, 50.20)			0.04 (0.00, 68.79)
Enoxaparin + GCS vs. Desirudin	0.03 (0.00, 18.56)			0.02 (0.00, 19.03)
Enoxaparin + GCS vs. Enoxaparin	0.04 (0.00, 15.94)			0.05 (0.00, 20.49)
Enoxaparin + GCS vs. Fondaparinux	0.21 (0.00, 9.79)			0.22 (0.00, 12.03)
Enoxaparin + GCS vs. Fondaparinux + GCS	0.93 (0.14, 6.71)			0.94 (0.13, 7.60)
Enoxaparin + GCS vs. Heparin	0.01 (0.00, 6.26)			
Enoxaparin + GCS vs. Rivaroxaban	0.05 (0.00, 22.78)			0.05 (0.00, 28.45)
Enoxaparin + GCS vs. Tinzaparin	0.04 (0.00, 36.78)			0.04 (0.00, 53.14)
Enoxaparin + GCS vs. Warfarin	0.04 (0.00, 23.59)			0.04 (0.00, 29.84)
Fondaparinux + GCS vs. Apixaban	0.02 (0.00, 8.76)			0.02 (0.00, 10.49)
Fondaparinux + GCS vs. Dabigatran	0.03 (0.00, 16.88)			0.04 (0.00, 19.38)
Fondaparinux + GCS vs. Dalteparin	0.04 (0.00, 40.21)			0.04 (0.00, 53.84)
Fondaparinux + GCS vs. Desirudin	0.03 (0.00, 14.45)			0.02 (0.00, 13.86)
Fondaparinux + GCS vs. Enoxaparin	0.05 (0.00, 12.18)			0.05 (0.00, 14.41)
Fondaparinux + GCS vs. Fondaparinux	0.23 (0.00, 6.00)			0.23 (0.00, 7.01)
Fondaparinux + GCS vs. Heparin	0.01 (0.00, 5.10)			
Fondaparinux + GCS vs. Rivaroxaban	0.05 (0.00, 17.73)			0.06 (0.00, 19.99)
Fondaparinux + GCS vs. Tinzaparin	0.04 (0.00, 30.69)			0.04 (0.00, 41.14)
Fondaparinux + GCS vs. Warfarin	0.04 (0.00, 18.36)			0.04 (0.00, 22.58)
Fondaparinux vs. Apixaban	0.07 (0.0001, 14.2)			0.08 (0.0001, 16.7)
Fondaparinux vs. Dabigatran	0.15 (0.0003, 25)			0.17 (0.0002, 27.4)

Table 108. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Fondaparinux vs. Desirudin	0.14 (0.00, 23.17)			0.10 (0.00, 20.70)
Fondaparinux vs. Enoxaparin	0.20 (0.00, 15.85)			0.21 (0.00, 17.98)
Fondaparinux vs. Heparin	0.04 (0.00, 7.57)			
Fondaparinux vs. Warfarin	0.18 (0.00, 28.22)			0.19 (0.00, 33.25)
Heparin vs. Enoxaparin	4.94 (0.36, 85.88)	11.97 (0.46, 640.98)		
Heparin vs. Warfarin	4.35 (0.12, 181.27)	10.72 (0.13, 1,506)		
Rivaroxaban vs. Apixaban	0.29 (0.01, 8.44)	0.34 (0.01, 20)	0.33 (0.01, 18.7)	0.31 (0.01, 10.2)
Rivaroxaban vs. Dabigatran	0.66 (0.04, 13)	0.7 (0.02, 32.5)	0.68 (0.02, 32.3)	0.68 (0.04, 15.2)
Rivaroxaban vs. Desirudin	0.60 (0.04, 13.33)	1.18 (0.04, 61.37)	0.44 (0.01, 24.17)	0.39 (0.01, 13.44)
Rivaroxaban vs. Enoxaparin	0.86 (0.18, 4.96)	0.99 (0.14, 8.93)	0.99 (0.14, 8.68)	0.87 (0.16, 5.40)
Rivaroxaban vs. Fondaparinux	4.31 (0.04, 2,069.37)			4.07 (0.04, 2,591.52)
Rivaroxaban vs. Heparin	0.17 (0.01, 4.13)	0.08 (0.00, 4.31)		
Rivaroxaban vs. Warfarin	0.76 (0.04, 16.01)	0.89 (0.03, 39.21)	0.87 (0.03, 37.23)	0.77 (0.03, 19.73)
Tinzaparin vs. Apixaban	0.38 (0.00, 35.80)	0.38 (0.00, 97.13)	0.38 (0.00, 91.74)	0.40 (0.00, 48.47)
Tinzaparin vs. Dabigatran	0.88 (0.01, 63.69)	0.78 (0.00, 172.26)	0.78 (0.00, 158.38)	0.89 (0.01, 80.88)
Tinzaparin vs. Desirudin	0.80 (0.01, 64.59)	1.32 (0.01, 328.98)	0.50 (0.00, 117.92)	0.52 (0.00, 65.56)
Tinzaparin vs. Enoxaparin	1.15 (0.03, 38.59)	1.11 (0.01, 91.38)	1.14 (0.02, 84.86)	1.15 (0.03, 50.96)
Tinzaparin vs. Fondaparinux	5.72 (0.02, 5,059.38)			5.36 (0.01, 7,030.41)
Tinzaparin vs. Heparin	0.23 (0.00, 19.22)	0.09 (0.00, 20.97)		
Tinzaparin vs. Rivaroxaban	1.33 (0.02, 61.81)	1.12 (0.01, 132.82)	1.15 (0.01, 122.36)	1.32 (0.02, 80.64)
Tinzaparin vs. Warfarin	1.01 (0.07, 13.86)	1.00 (0.04, 22.87)	1.01 (0.04, 22.69)	1.01 (0.06, 15.91)
Warfarin vs. Enoxaparin	1.14 (0.10, 13.03)	1.12 (0.05, 23.22)	1.13 (0.06, 22.65)	1.14 (0.08, 15.88)

Table 109. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – All Cause Mortality

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials (without Continuity Correction)
Apixaban vs. Dabigatran	1.01 (0.04, 27.8)	1.01 (0.03, 33)
Apixaban vs. Enoxaparin	1.04 (0.14, 9.42)	1.06 (0.12, 10.62)
Apixaban vs. Warfarin	0.46 (0.02, 13.5)	0.49 (0.02, 16.4)
Dabigatran vs. Enoxaparin	1.03 (0.09, 12.50)	1.04 (0.08, 14.53)
Dabigatran vs. Warfarin	0.45 (0.01, 16)	0.48 (0.01, 20)
Rivaroxaban vs. Apixaban	0.35 (0.01, 5.60)	0.26 (0.01, 4.88)
Rivaroxaban vs. Dabigatran	0.35 (0.01, 8.31)	0.26 (0.01, 6.90)
Rivaroxaban vs. Enoxaparin	0.36 (0.04, 2.51)	0.27 (0.02, 2.18)
Rivaroxaban vs. Warfarin	0.16 (0.00, 3.78)	0.13 (0.00, 3.54)
Warfarin vs. Enoxaparin	2.27 (0.18, 33.31)	2.18 (0.15, 33.58)

Table 110. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials (with Continuity Correction)	All Trials from Treatments with ≥1 Event	Without Heparin Trials (No Multi-Arm Trials)	Final Model
Apixaban vs. Dabigatran	0.05 (0.00, 2.62)	0.05 (0.00, 2.59)	0.05 (0.00, 2.51)	0.05 (0.00, 2.52)
Apixaban vs. Desirudin	0.07 (0.00, 6.09)	0.07 (0.00, 6.12)	0.06 (0.00, 6.31)	0.06 (0.00, 5.93)
Apixaban vs. Enoxaparin	0.07 (0.00, 2.31)	0.08 (0.00, 2.39)	0.07 (0.00, 2.30)	0.07 (0.00, 2.32)
Apixaban vs. Heparin	0.05 (0.0002, 11.7)	0.05 (0.0002, 11.6)		
Dabigatran vs. Desirudin	1.36 (0.04, 45.24)	1.39 (0.04, 47.09)	1.37 (0.04, 47.37)	1.40 (0.04, 46.90)
Dabigatran vs. Enoxaparin	1.54 (0.22, 11.60)	1.56 (0.22, 11.54)	1.54 (0.22, 11.35)	1.57 (0.22, 11.72)
Desirudin vs. Enoxaparin	1.13 (0.06, 20.35)	1.13 (0.06, 19.53)	1.13 (0.06, 20.15)	1.12 (0.06, 20.11)
Heparin vs. Dabigatran	0.95 (0.01, 93.88)	0.94 (0.01, 91.29)		
Heparin vs. Desirudin	1.30 (0.06, 26.23)	1.30 (0.06, 27.11)		
Heparin vs. Enoxaparin	1.47 (0.02, 98.20)	1.47 (0.02, 95.58)		
Rivaroxaban vs. Apixaban	1.70 (0.00, 795.52)			1.80 (0.00, 921.50)
Rivaroxaban vs. Dabigatran	0.08 (0.00, 13.20)			0.08 (0.00, 13.69)
Rivaroxaban vs. Desirudin	0.11 (0.00, 27.83)			0.12 (0.00, 30.45)
Rivaroxaban vs. Enoxaparin	0.13 (0.00, 13.18)			0.13 (0.00, 14.30)
Rivaroxaban vs. Heparin	0.09 (0.00, 47.6)			
Tinzaparin vs. Apixaban	7.85 (0.06, 1,283)	7.77 (0.06, 1,342)	8.36 (0.07, 1,519.29)	8.22 (0.07, 1,369.22)
Tinzaparin vs. Dabigatran	0.38 (0.01, 17.39)	0.37 (0.01, 18.25)	0.39 (0.01, 18.39)	0.38 (0.01, 17.76)
Tinzaparin vs. Desirudin	0.52 (0.01, 39.49)	0.52 (0.01, 42.35)	0.54 (0.01, 42.31)	0.53 (0.01, 41.55)
Tinzaparin vs. Enoxaparin	0.58 (0.02, 15.44)	0.58 (0.02, 16.26)	0.61 (0.02, 16.40)	0.59 (0.02, 16.17)
Tinzaparin vs. Heparin	0.4 (0.002, 80.6)	0.4 (0.002, 80.8)		
Tinzaparin vs. Rivaroxaban	4.62 (0.01, 4523)			4.57 (0.01, 4420)

Table 111. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Symptomatic DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	All Trials from Treatments with ≥1 Event (No Heparin Trials)	Without Heparin Trials or Multi-Arm Trials	Final Model
Apixaban vs. Dabigatran	2.7 (0.28, 30.7)	2.67 (0.25, 33.3)	2.19 (0.16, 30.1)	2.22 (0.18, 29.1)
Apixaban vs. Enoxaparin	0.78 (0.22, 3.23)	0.78 (0.20, 3.58)	0.63 (0.11, 3.34)	0.63 (0.13, 3.00)
Apixaban vs. None	0.98 (0.01, 53.8)	0.93 (0.01, 62.05)	0.74 (0.01, 52.67)	0.80 (0.01, 50.81)
Apixaban vs. Warfarin	1.87 (0.09, 68.92)	1.85 (0.09, 82.43)		
Dabigatran vs. Enoxaparin	0.29 (0.04, 1.89)	0.29 (0.04, 2.05)	0.29 (0.04, 2.20)	0.28 (0.04, 1.96)
Dabigatran vs. None	0.36 (0.01, 8.54)	0.35 (0.01, 9.74)	0.34 (0.01, 10.17)	0.36 (0.01, 9.32)
Dabigatran vs. Warfarin	0.69 (0.02, 38.98)	0.69 (0.02, 49.30)		
Enoxaparin + IPC vs. Apixaban	1.31 (0.02, 87.36)	1.28 (0.02, 88.23)	1.54 (0.02, 133.75)	1.51 (0.02, 108.31)
Enoxaparin + IPC vs. Dabigatran	3.53 (0.04, 324.41)	3.41 (0.03, 299.17)	3.38 (0.03, 330.30)	3.36 (0.04, 297.97)
Enoxaparin + IPC vs. Enoxaparin	1.02 (0.02, 57.97)	1.00 (0.02, 56.26)	0.97 (0.01, 60.76)	0.95 (0.02, 53.68)
Enoxaparin + IPC vs. None	1.29 (0.00, 303)	1.19 (0.00, 307)	1.14 (0.00, 334)	1.21 (0.00, 307)
Enoxaparin + IPC vs. Rivaroxaban	2.41 (0.03, 208.93)	2.84 (0.03, 311.38)	2.81 (0.03, 330.96)	2.26 (0.03, 195.00)
Enoxaparin + IPC vs. Warfarin	2.45 (0.01, 535.93)	2.36 (0.01, 536.46)		
Enoxaparin vs. None	1.26 (0.02, 50.5)	1.19 (0.02, 58.21)	1.17 (0.01, 62.12)	1.27 (0.02, 60.58)
Rivaroxaban vs. Apixaban	0.54 (0.05, 4.13)	0.45 (0.02, 3.82)	0.55 (0.03, 6.10)	0.67 (0.05, 6.44)
Rivaroxaban vs. Dabigatran	1.46 (0.10, 19.18)	1.20 (0.05, 18.21)	1.21 (0.05, 18.05)	1.48 (0.09, 20.29)
Rivaroxaban vs. Enoxaparin	0.42 (0.06, 2.18)	0.35 (0.03, 2.00)	0.35 (0.03, 2.10)	0.42 (0.06, 2.28)
Rivaroxaban vs. None	0.53 (0.01, 30.6)	0.42 (0.00, 29.2)	0.40 (0.00, 30.5)	0.54 (0.00, 33.4)
Rivaroxaban vs. Warfarin	1.01 (0.03, 52.61)	0.83 (0.02, 47.66)		
Warfarin vs. Enoxaparin	0.42 (0.01, 8.40)	0.42 (0.01, 9.74)		
Warfarin vs. None	0.53 (0.00, 66.29)	0.50 (0.00, 81.53)		

Table 112. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials – Final Model (No Multi-Arm Trials)
Apixaban vs. Desirudin	0.43 (0.16, 1.06)	0.47 (0.11, 1.89)
Apixaban vs. Enoxaparin	0.31 (0.14, 0.66)	0.31 (0.11, 0.84)
Apixaban vs. Heparin	0.14 (0.05, 0.34)	
Apixaban vs. None	0.22 (0.07, 0.69)	0.21 (0.05, 0.95)
Apixaban vs. Tinzaparin	0.28 (0.09, 0.82)	0.28 (0.07, 1.19)
Apixaban vs. Warfarin	0.21 (0.06, 0.76)	0.21 (0.04, 1.21)
Dabigatran vs. Apixaban	2.42 (1.00, 5.79)	2.41 (0.75, 7.79)
Dabigatran vs. Dalteparin	1.21 (0.35, 4.12)	1.21 (0.23, 6.48)
Dabigatran vs. Desirudin	1.03 (0.51, 1.96)	1.13 (0.37, 3.39)
Dabigatran vs. Enoxaparin	0.74 (0.48, 1.12)	0.74 (0.42, 1.29)
Dabigatran vs. Heparin	0.33 (0.16, 0.63)	
Dabigatran vs. IPC + LD Aspirin	0.77 (0.22, 2.64)	0.75 (0.18, 3.25)
Dabigatran vs. None	0.52 (0.2, 1.36)	0.52 (0.15, 1.74)
Dabigatran vs. Rivaroxaban	2.56 (1.34, 4.57)	2.49 (1.08, 5.28)
Dabigatran vs. Tinzaparin	0.67 (0.28, 1.61)	0.67 (0.21, 2.15)
Dabigatran vs. Warfarin	0.51 (0.17, 1.55)	0.51 (0.12, 2.34)
Dalteparin vs. Apixaban	2.01 (0.50, 8.04)	2.00 (0.30, 12.88)
Dalteparin vs. Desirudin	0.86 (0.24, 2.98)	0.93 (0.15, 5.86)
Dalteparin vs. Enoxaparin	0.61 (0.19, 1.96)	0.61 (0.12, 2.87)
Dalteparin vs. Heparin	0.28 (0.08, 0.95)	
Dalteparin vs. IPC	1.35 (0.26, 7.02)	1.32 (0.15, 11.38)
Dalteparin vs. IPC + LD Aspirin	0.64 (0.12, 3.20)	0.63 (0.08, 4.81)

Table 112. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials – Final Model (No Multi-Arm Trials)
Dalteparin vs. None	0.43 (0.10, 1.89)	0.43 (0.06, 2.89)
Dalteparin vs. Rivaroxaban	2.12 (0.60, 7.11)	2.06 (0.37, 10.34)
Dalteparin vs. Tinzaparin	0.55 (0.24, 1.31)	0.56 (0.17, 1.83)
Dalteparin vs. Warfarin	0.42 (0.25, 0.73)	0.42 (0.21, 0.87)
Dalteparin vs. YM150	0.60 (0.14, 2.57)	0.60 (0.09, 3.99)
Desirudin vs. Enoxaparin	0.72 (0.43, 1.24)	0.65 (0.25, 1.70)
Desirudin vs. Heparin	0.32 (0.20, 0.52)	
Desirudin vs. None	0.51 (0.19, 1.41)	0.46 (0.11, 1.95)
Desirudin vs. Tinzaparin	0.65 (0.26, 1.69)	0.59 (0.15, 2.43)
Desirudin vs. Warfarin	0.49 (0.16, 1.58)	0.45 (0.09, 2.54)
Enoxaparin vs. None	0.71 (0.3, 1.68)	0.70 (0.23, 2.08)
Fondaparinux vs. Apixaban	0.44 (0.05, 2.50)	0.44 (0.05, 3.17)
Fondaparinux vs. Dabigatran	0.18 (0.03, 0.89)	0.18 (0.02, 1.08)
Fondaparinux vs. Dalteparin	0.22 (0.02, 1.49)	0.22 (0.02, 2.24)
Fondaparinux vs. Desirudin	0.19 (0.03, 0.95)	0.21 (0.02, 1.39)
Fondaparinux vs. Enoxaparin	0.13 (0.02, 0.62)	0.14 (0.02, 0.71)
Fondaparinux vs. Heparin	0.06 (0.01, 0.31)	
Fondaparinux vs. IPC	0.29 (0.03, 2.07)	0.29 (0.02, 2.78)
Fondaparinux vs. IPC + LD Aspirin	0.14 (0.01, 0.97)	0.14 (0.01, 1.20)
Fondaparinux vs. None	0.09 (0.01, 0.57)	0.09 (0.01, 0.71)
Fondaparinux vs. Rivaroxaban	0.46 (0.06, 2.29)	0.46 (0.05, 2.62)
Fondaparinux vs. Tinzaparin	0.12 (0.02, 0.68)	0.12 (0.01, 0.90)

Table 112. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials – Final Model (No Multi-Arm Trials)
Fondaparinux vs. Warfarin	0.09 (0.01, 0.58)	0.09 (0.01, 0.84)
Fondaparinux vs. YM150	0.13 (0.02, 0.80)	0.13 (0.01, 0.98)
Heparin vs. Enoxaparin	2.21 (1.35, 3.89)	
Heparin vs. None	1.56 (0.58, 4.45)	
Heparin vs. Warfarin	1.52 (0.50, 5.00)	
IPC + LD Aspirin vs. Apixaban	3.16 (0.79, 12.83)	3.19 (0.60, 17.08)
IPC + LD Aspirin vs. Desirudin	1.35 (0.37, 4.81)	1.49 (0.29, 7.68)
IPC + LD Aspirin vs. Enoxaparin	0.96 (0.30, 3.15)	0.98 (0.26, 3.75)
IPC + LD Aspirin vs. Heparin	0.44 (0.12, 1.55)	
IPC + LD Aspirin vs. None	0.68 (0.16, 2.92)	0.68 (0.12, 3.85)
IPC + LD Aspirin vs. Tinzaparin	0.87 (0.22, 3.56)	0.89 (0.17, 4.84)
IPC + LD Aspirin vs. Warfarin	0.67 (0.15, 3.13)	0.68 (0.1, 4.7)
IPC vs. Apixaban	1.49 (0.37, 6.00)	1.51 (0.25, 9.35)
IPC vs. Dabigatran	0.61 (0.18, 2.12)	0.63 (0.13, 3.15)
IPC vs. Desirudin	0.63 (0.18, 2.24)	0.71 (0.12, 4.17)
IPC vs. Enoxaparin	0.45 (0.14, 1.46)	0.46 (0.10, 2.07)
IPC vs. Heparin	0.21 (0.06, 0.71)	
IPC vs. IPC + LD Aspirin	0.47 (0.09, 2.38)	0.47 (0.06, 3.45)
IPC vs. None	0.32 (0.15, 0.70)	0.32 (0.12, 0.91)
IPC vs. Rivaroxaban	1.57 (0.44, 5.29)	1.56 (0.31, 7.42)
IPC vs. Tinzaparin	0.41 (0.10, 1.67)	0.42 (0.07, 2.61)
IPC vs. Warfarin	0.31 (0.07, 1.5)	0.32 (0.04, 2.52)

Table 112. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials – Final Model (No Multi-Arm Trials)
Rivaroxaban vs. Apixaban	0.95 (0.40, 2.39)	0.97 (0.31, 3.23)
Rivaroxaban vs. Desirudin	0.40 (0.21, 0.81)	0.45 (0.16, 1.42)
Rivaroxaban vs. Enoxaparin	0.29 (0.19, 0.46)	0.30 (0.17, 0.53)
Rivaroxaban vs. Heparin	0.13 (0.07, 0.26)	
Rivaroxaban vs. IPC + LD Aspirin	0.3 (0.09, 1.07)	0.3 (0.07, 1.32)
Rivaroxaban vs. None	0.20 (0.08, 0.56)	0.21 (0.06, 0.72)
Rivaroxaban vs. Tinzaparin	0.26 (0.11, 0.66)	0.27 (0.09, 0.9)
Rivaroxaban vs. Warfarin	0.20 (0.07, 0.63)	0.21 (0.05, 0.97)
Tinzaparin vs. Enoxaparin	1.11 (0.51, 2.39)	1.10 (0.39, 3.00)
Tinzaparin vs. Heparin	0.50 (0.19, 1.23)	
Tinzaparin vs. None	0.78 (0.24, 2.53)	0.77 (0.17, 3.39)
Tinzaparin vs. Warfarin	0.76 (0.39, 1.49)	0.76 (0.3, 1.97)
Warfarin vs. Enoxaparin	1.45 (0.52, 4.03)	1.44 (0.35, 5.68)
Warfarin vs. None	1.03 (0.27, 4.00)	1.01 (0.17, 5.88)
YM150 vs. Apixaban	3.35 (1.03, 10.71)	3.34 (0.76, 14.92)
YM150 vs. Dabigatran	1.38 (0.53, 3.62)	1.39 (0.41, 4.77)
YM150 vs. Desirudin	1.43 (0.50, 3.88)	1.56 (0.37, 6.65)
YM150 vs. Enoxaparin	1.02 (0.42, 2.44)	1.02 (0.34, 3.05)
YM150 vs. Heparin	0.46 (0.16, 1.24)	
YM150 vs. IPC	2.25 (0.52, 9.41)	2.21 (0.35, 13.9)
YM150 vs. IPC + LD Aspirin	1.06 (0.24, 4.55)	1.05 (0.19, 5.91)
YM150 vs. None	0.72 (0.21, 2.46)	0.72 (0.15, 3.32)

Table 112. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials – Final Model (No Multi-Arm Trials)
YM150 vs. Rivaroxaban	3.54 (1.29, 9.29)	3.45 (0.98, 11.50)
YM150 vs. Tinzaparin	0.93 (0.29, 2.98)	0.93 (0.21, 4.17)
YM150 vs. Warfarin	0.71 (0.18, 2.73)	0.71 (0.12, 4.21)

Table 113. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Apixaban vs. Enoxaparin	0.70 (0.48, 1.06)	0.70 (0.47, 1.06)	0.69 (0.40, 1.22)
Apixaban vs. Heparin	0.45 (0.20, 1.01)		
Apixaban vs. None	0.13 (0.04, 0.43)	0.14 (0.04, 0.44)	
Apixaban vs. Warfarin	0.33 (0.19, 0.57)	0.33 (0.19, 0.57)	0.33 (0.15, 0.75)
Dabigatran vs. Apixaban	1.64 (0.89, 2.94)	1.64 (0.88, 2.94)	1.65 (0.74, 3.62)
Dabigatran vs. Enoxaparin	1.15 (0.74, 1.79)	1.15 (0.73, 1.81)	1.14 (0.65, 2.01)
Dabigatran vs. Enoxaparin + IPC	4.24 (1.21, 16.78)	4.17 (1.18, 16.3)	4.10 (1.04, 17.96)
Dabigatran vs. Heparin	0.73 (0.32, 1.68)		
Dabigatran vs. None	0.22 (0.06, 0.71)	0.22 (0.06, 0.73)	
Dabigatran vs. Rivaroxaban	2.00 (1.08, 3.62)	1.99 (1.08, 3.66)	1.99 (0.93, 4.15)
Dabigatran vs. Warfarin	0.54 (0.29, 0.99)	0.54 (0.29, 1.00)	0.55 (0.24, 1.24)
Enoxaparin + IPC vs. Apixaban	0.39 (0.10, 1.32)	0.39 (0.10, 1.35)	0.40 (0.09, 1.58)
Enoxaparin + IPC vs. Enoxaparin	0.27 (0.07, 0.88)	0.28 (0.08, 0.89)	0.28 (0.07, 0.98)
Enoxaparin + IPC vs. GCS	0.10 (0.02, 0.55)	0.10 (0.02, 0.55)	
Enoxaparin + IPC vs. Heparin	0.17 (0.04, 0.68)		
Enoxaparin + IPC vs. IPC	0.17 (0.03, 0.99)	0.17 (0.03, 0.97)	
Enoxaparin + IPC vs. None	0.05 (0.01, 0.27)	0.05 (0.01, 0.27)	
Enoxaparin + IPC vs. Rivaroxaban	0.47 (0.12, 1.63)	0.48 (0.12, 1.65)	0.48 (0.11, 1.85)
Enoxaparin + IPC vs. Warfarin	0.13 (0.03, 0.44)	0.13 (0.03, 0.45)	0.13 (0.03, 0.54)
Enoxaparin vs. None	0.19 (0.06, 0.56)	0.19 (0.06, 0.58)	
GCS vs. Apixaban	3.83 (1.13, 13.71)	3.79 (1.10, 13.74)	

Table 113. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
GCS vs. Dabigatran	2.34 (0.69, 8.53)	2.31 (0.67, 8.52)	
GCS vs. Enoxaparin	2.69 (0.86, 9.09)	2.65 (0.83, 9.05)	
GCS vs. Heparin	1.71 (0.45, 6.90)		
GCS vs. None	0.52 (0.20, 1.28)	0.51 (0.20, 1.29)	
GCS vs. Rivaroxaban	4.68 (1.39, 16.88)	4.61 (1.34, 16.74)	
GCS vs. Warfarin	1.27 (0.37, 4.60)	1.25 (0.37, 4.55)	
HD Aspirin + IPC vs. Apixaban	0.51 (0.10, 2.35)	0.52 (0.11, 2.37)	0.53 (0.09, 2.90)
HD Aspirin + IPC vs. Dabigatran	0.31 (0.06, 1.47)	0.32 (0.06, 1.48)	0.32 (0.05, 1.76)
HD Aspirin + IPC vs. Enoxaparin	0.36 (0.07, 1.58)	0.37 (0.08, 1.59)	0.37 (0.07, 1.84)
HD Aspirin + IPC vs. Enoxaparin + IPC	1.33 (0.55, 3.20)	1.33 (0.56, 3.20)	1.33 (0.49, 3.56)
HD Aspirin + IPC vs. GCS	0.13 (0.02, 0.91)	0.14 (0.02, 0.91)	
HD Aspirin + IPC vs. Heparin	0.23 (0.04, 1.19)		
HD Aspirin + IPC vs. IPC	0.23 (0.03, 1.61)	0.23 (0.03, 1.60)	
HD Aspirin + IPC vs. None	0.07 (0.01, 0.44)	0.07 (0.01, 0.45)	
HD Aspirin + IPC vs. Rivaroxaban	0.63 (0.12, 2.90)	0.64 (0.13, 2.93)	0.64 (0.11, 3.41)
HD Aspirin + IPC vs. Warfarin	0.17 (0.03, 0.77)	0.17 (0.03, 0.81)	0.18 (0.03, 0.98)
Heparin vs. Enoxaparin	1.57 (0.79, 3.19)		
Heparin vs. None	0.30 (0.08, 1.09)		
Heparin vs. Warfarin	0.74 (0.33, 1.68)		
IPC vs. Apixaban	2.27 (0.62, 8.51)	2.25 (0.61, 8.78)	
IPC vs. Dabigatran	1.38 (0.37, 5.32)	1.38 (0.37, 5.42)	

Table 113. Network Meta-Analysis – Pairwise Comparisons among Knee Patients – Deep Vein Thrombosis

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
IPC vs. Enoxaparin	1.59 (0.46, 5.62)	1.58 (0.46, 5.80)	
IPC vs. GCS	0.59 (0.20, 1.70)	0.60 (0.20, 1.69)	
IPC vs. Heparin	1.01 (0.24, 4.30)		
IPC vs. None	0.30 (0.11, 0.82)	0.31 (0.11, 0.82)	
IPC vs. Rivaroxaban	2.76 (0.75, 10.37)	2.74 (0.74, 10.69)	
IPC vs. Warfarin	0.75 (0.20, 2.86)	0.74 (0.20, 2.91)	
Rivaroxaban vs. Apixaban	0.82 (0.46, 1.44)	0.82 (0.46, 1.44)	0.83 (0.39, 1.77)
Rivaroxaban vs. Enoxaparin	0.57 (0.38, 0.87)	0.57 (0.38, 0.87)	0.58 (0.35, 0.95)
Rivaroxaban vs. Heparin	0.37 (0.16, 0.83)		
Rivaroxaban vs. None	0.11 (0.03, 0.35)	0.11 (0.03, 0.36)	
Rivaroxaban vs. Warfarin	0.27 (0.15, 0.49)	0.27 (0.15, 0.49)	0.28 (0.13, 0.60)
Warfarin vs. Enoxaparin	2.12 (1.40, 3.26)	2.12 (1.40, 3.26)	2.09 (1.15, 3.82)
Warfarin vs. None	0.41 (0.12, 1.29)	0.41 (0.12, 1.34)	

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Apixaban vs. Enoxaparin	0.33 (0.07, 1.52)	0.33 (0.04, 2.87)
Apixaban vs. None	0.22 (0.02, 2.13)	0.22 (0.01, 5.02)
Apixaban vs. Warfarin	0.29 (0.02, 3.61)	0.29 (0.01, 10.78)
Dabigatran vs. Apixaban	1.45 (0.25, 8.47)	1.44 (0.12, 16.66)
Dabigatran vs. Enoxaparin	0.48 (0.20, 1.09)	0.47 (0.14, 1.56)
Dabigatran vs. None	0.32 (0.05, 2.09)	0.31 (0.02, 3.94)
Dabigatran vs. Warfarin	0.43 (0.05, 3.59)	0.42 (0.02, 9.66)
Dalteparin vs. Apixaban	1.44 (0.09, 20.99)	1.41 (0.03, 68.31)
Dalteparin vs. Dabigatran	0.99 (0.09, 10.70)	0.98 (0.03, 31.66)
Dalteparin vs. Desirudin	0.97 (0.08, 11.37)	0.81 (0.02, 37.94)
Dalteparin vs. Enoxaparin	0.48 (0.05, 4.30)	0.46 (0.02, 12.26)
Dalteparin vs. Fondaparinux	2.91 (0.08, 196.37)	2.47 (0.03, 304.90)
Dalteparin vs. IPC + LD Aspirin	0.29 (0.01, 6.99)	0.29 (0.00, 20.70)
Dalteparin vs. None	0.32 (0.02, 5.19)	0.31 (0.01, 16.10)
Dalteparin vs. Rivaroxaban	3.90 (0.30, 40.85)	3.68 (0.10, 116.63)
Dalteparin vs. Tinzaparin	0.54 (0.09, 3.01)	0.52 (0.04, 6.51)
Dalteparin vs. Warfarin	0.42 (0.13, 1.28)	0.41 (0.08, 1.88)
Dalteparin vs. YM150	0.42 (0.02, 7.52)	0.42 (0.01, 23.08)
Desirudin vs. Apixaban	1.49 (0.23, 9.46)	1.75 (0.09, 33.68)
Desirudin vs. Dabigatran	1.03 (0.27, 3.87)	1.22 (0.12, 13.26)
Desirudin vs. Enoxaparin	0.49 (0.17, 1.34)	0.58 (0.08, 4.38)
Desirudin vs. IPC + LD Aspirin	0.30 (0.02, 3.78)	0.36 (0.01, 10.69)

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Desirudin vs. None	0.33 (0.04, 2.27)	0.38 (0.02, 7.91)
Desirudin vs. Rivaroxaban	4.04 (0.9, 15.89)	4.55 (0.41, 47.75)
Desirudin vs. Tinzaparin	0.56 (0.09, 3.1)	0.65 (0.04, 11.82)
Desirudin vs. Warfarin	0.44 (0.05, 3.97)	0.51 (0.01, 17.34)
Desirudin vs. YM150	0.44 (0.05, 3.53)	0.52 (0.02, 11.08)
Enoxaparin + GCS vs. Apixaban	0.68 (0.01, 26.26)	0.80 (0.01, 76.55)
Enoxaparin + GCS vs. Dabigatran	0.47 (0.01, 14.28)	0.56 (0.01, 36.49)
Enoxaparin + GCS vs. Dalteparin	0.47 (0.00, 28.53)	0.57 (0.00, 102.10)
Enoxaparin + GCS vs. Desirudin	0.46 (0.01, 14.94)	0.46 (0.00, 39.69)
Enoxaparin + GCS vs. Enoxaparin	0.22 (0.00, 6.03)	0.26 (0.00, 14.21)
Enoxaparin + GCS vs. Fondaparinux	1.37 (0.23, 8.48)	1.40 (0.11, 18.77)
Enoxaparin + GCS vs. Fondaparinux + GCS	1.64 (0.56, 4.75)	1.65 (0.37, 7.55)
Enoxaparin + GCS vs. IPC	0.33 (0.00, 18.19)	0.38 (0.00, 56.60)
Enoxaparin + GCS vs. IPC + LD Aspirin	0.14 (0.00, 8.15)	0.17 (0.00, 21.93)
Enoxaparin + GCS vs. None	0.15 (0.00, 6.46)	0.17 (0.00, 17.65)
Enoxaparin + GCS vs. Rivaroxaban	1.84 (0.03, 56.71)	2.08 (0.02, 135.78)
Enoxaparin + GCS vs. Tinzaparin	0.25 (0.00, 9.19)	0.29 (0.00, 26.05)
Enoxaparin + GCS vs. Warfarin	0.20 (0.00, 9.48)	0.23 (0.00, 32.46)
Enoxaparin + GCS vs. YM150	0.20 (0.00, 8.77)	0.24 (0.00, 24.73)
Enoxaparin vs. None	0.68 (0.12, 3.58)	0.66 (0.07, 6.26)
Fondaparinux + GCS vs. Apixaban	0.42 (0.01, 13.45)	0.48 (0.00, 34.43)
Fondaparinux + GCS vs. Dabigatran	0.29 (0.01, 7.19)	0.34 (0.00, 16.04)

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Fondaparinux + GCS vs. Dalteparin	0.29 (0, 14.53)	0.34 (0, 50.2)
Fondaparinux + GCS vs. Desirudin	0.28 (0.01, 7.52)	0.28 (0.00, 17.92)
Fondaparinux + GCS vs. Enoxaparin	0.14 (0.00, 3.05)	0.16 (0.00, 6.16)
Fondaparinux + GCS vs. Fondaparinux	0.84 (0.20, 3.59)	0.85 (0.10, 6.86)
Fondaparinux + GCS vs. IPC	0.20 (0.00, 9.30)	0.23 (0.00, 27.47)
Fondaparinux + GCS vs. IPC + LD Aspirin	0.08 (0.00, 4.31)	0.10 (0.00, 10.25)
Fondaparinux + GCS vs. None	0.09 (0.00, 3.34)	0.11 (0.00, 8.10)
Fondaparinux + GCS vs. Rivaroxaban	1.12 (0.02, 28.08)	1.26 (0.02, 60.82)
Fondaparinux + GCS vs. Tinzaparin	0.15 (0.00, 4.60)	0.18 (0.00, 12.07)
Fondaparinux + GCS vs. Warfarin	0.12 (0.00, 4.79)	0.14 (0.00, 15.29)
Fondaparinux + GCS vs. YM150	0.12 (0.00, 4.42)	0.14 (0.00, 11.44)
Fondaparinux vs. Apixaban	0.50 (0.01, 11.11)	0.57 (0.01, 22.62)
Fondaparinux vs. Dabigatran	0.34 (0.01, 5.74)	0.40 (0.01, 9.93)
Fondaparinux vs. Desirudin	0.33 (0.01, 5.98)	0.33 (0.01, 11.91)
Fondaparinux vs. Enoxaparin	0.16 (0.00, 2.34)	0.19 (0.00, 3.67)
Fondaparinux vs. IPC + LD Aspirin	0.10 (0.00, 3.81)	0.12 (0.00, 7.11)
Fondaparinux vs. None	0.11 (0.00, 2.76)	0.12 (0.00, 5.57)
Fondaparinux vs. Rivaroxaban	1.34 (0.03, 23.27)	1.49 (0.03, 37.30)
Fondaparinux vs. Tinzaparin	0.18 (0.00, 3.86)	0.21 (0.00, 7.98)
Fondaparinux vs. Warfarin	0.15 (0, 4.15)	0.17 (0, 10.63)
Heparin vs. Apixaban	9.60 (1.57, 58.62)	
Heparin vs. Dabigatran	6.60 (1.83, 23.52)	

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Heparin vs. Dalteparin	6.65 (0.59, 81.45)	
Heparin vs. Desirudin	6.42 (2.52, 17.37)	
Heparin vs. Enoxaparin	3.17 (1.20, 8.22)	
Heparin vs. Enoxaparin + GCS	14.1 (0.45, 950)	
Heparin vs. Fondaparinux	19.34 (1.12, 852.35)	
Heparin vs. Fondaparinux + GCS	23.1 (0.9, 1269)	
Heparin vs. IPC	4.63 (0.4, 48.3)	
Heparin vs. IPC + GCS	9.31 (0.22, 778)	
Heparin vs. IPC + LD Aspirin	1.96 (0.14, 23.95)	
Heparin vs. None	2.14 (0.30, 14.28)	
Heparin vs. Rivaroxaban	25.95 (6.30, 99.98)	
Heparin vs. Tinzaparin	3.57 (0.63, 19.43)	
Heparin vs. Warfarin	2.81 (0.32, 24.95)	
Heparin vs. Warfarin + GCS	49.85 (0.71, 5814)	
Heparin vs. YM150	2.81 (0.35, 22.24)	
IPC + GCS vs. Apixaban	1.03 (0.01, 54.05)	1.22 (0.01, 182.91)
IPC + GCS vs. Dabigatran	0.71 (0.01, 29.99)	0.85 (0.01, 94.07)
IPC + GCS vs. Dalteparin	0.72 (0.01, 56.04)	0.86 (0.00, 236.28)
IPC + GCS vs. Desirudin	0.69 (0.01, 30.36)	0.70 (0.00, 97.91)
IPC + GCS vs. Enoxaparin	0.34 (0.00, 12.69)	0.40 (0.00, 36.67)
IPC + GCS vs. Enoxaparin + GCS	1.51 (0.34, 6.80)	1.53 (0.18, 12.81)
IPC + GCS vs. Fondaparinux	2.08 (0.20, 21.98)	2.14 (0.08, 61.01)

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
IPC + GCS vs. Fondaparinux + GCS	2.48 (0.40, 15.46)	2.52 (0.19, 35.48)
IPC + GCS vs. IPC	0.50 (0.00, 36.86)	0.57 (0.00, 137.96)
IPC + GCS vs. IPC + LD Aspirin	0.21 (0.00, 16.49)	0.25 (0.00, 52.04)
IPC + GCS vs. None	0.23 (0.00, 13.38)	0.27 (0.00, 42.73)
IPC + GCS vs. Rivaroxaban	2.79 (0.03, 117.10)	3.17 (0.02, 345.16)
IPC + GCS vs. Tinzaparin	0.38 (0.00, 19.09)	0.45 (0.00, 63.75)
IPC + GCS vs. Warfarin	0.30 (0.00, 18.80)	0.35 (0.00, 79.12)
IPC + GCS vs. YM150	0.30 (0.00, 18.23)	0.36 (0.00, 58.32)
IPC + LD Aspirin vs. Apixaban	4.90 (0.30, 88.32)	4.83 (0.15, 166.50)
IPC + LD Aspirin vs. Dabigatran	3.37 (0.29, 44.66)	3.35 (0.17, 72.75)
IPC + LD Aspirin vs. Enoxaparin	1.62 (0.16, 19.09)	1.59 (0.10, 27.09)
IPC + LD Aspirin vs. None	1.09 (0.06, 21.59)	1.05 (0.03, 39.53)
IPC + LD Aspirin vs. Warfarin	1.43 (0.07, 32.72)	1.40 (0.03, 76.94)
IPC vs. Apixaban	2.07 (0.15, 31.44)	2.13 (0.05, 90.29)
IPC vs. Dabigatran	1.42 (0.14, 15.94)	1.48 (0.06, 39.17)
IPC vs. Dalteparin	1.44 (0.06, 36.86)	1.51 (0.02, 144.5)
IPC vs. Desirudin	1.39 (0.13, 16.76)	1.22 (0.03, 47.70)
IPC vs. Enoxaparin	0.68 (0.08, 6.48)	0.70 (0.03, 14.64)
IPC vs. Fondaparinux	4.17 (0.13, 292.36)	3.73 (0.05, 410.76)
IPC vs. IPC + LD Aspirin	0.42 (0.02, 10.39)	0.44 (0.01, 26.15)
IPC vs. None	0.46 (0.11, 1.89)	0.47 (0.06, 3.67)
IPC vs. Rivaroxaban	5.60 (0.51, 61.74)	5.55 (0.20, 146.64)

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
IPC vs. Tinzaparin	0.77 (0.06, 11.25)	0.79 (0.02, 31.19)
IPC vs. Warfarin	0.61 (0.03, 12.33)	0.62 (0.01, 42.35)
IPC vs. YM150	0.61 (0.04, 11.35)	0.63 (0.01, 29.34)
Rivaroxaban vs. Apixaban	0.37 (0.06, 2.36)	0.38 (0.03, 4.81)
Rivaroxaban vs. Dabigatran	0.25 (0.07, 0.97)	0.27 (0.05, 1.58)
Rivaroxaban vs. Enoxaparin	0.12 (0.05, 0.33)	0.13 (0.04, 0.45)
Rivaroxaban vs. IPC + LD Aspirin	0.08 (0.01, 0.96)	0.08 (0.00, 1.67)
Rivaroxaban vs. None	0.08 (0.01, 0.58)	0.08 (0.01, 1.11)
Rivaroxaban vs. Warfarin	0.11 (0.01, 1.02)	0.11 (0, 2.73)
Tinzaparin vs. Apixaban	2.69 (0.34, 21.76)	2.71 (0.14, 55.26)
Tinzaparin vs. Dabigatran	1.85 (0.36, 9.66)	1.88 (0.17, 21.52)
Tinzaparin vs. Enoxaparin	0.89 (0.22, 3.63)	0.89 (0.11, 7.21)
Tinzaparin vs. IPC + LD Aspirin	0.55 (0.03, 8.36)	0.56 (0.02, 17.39)
Tinzaparin vs. None	0.60 (0.06, 5.35)	0.59 (0.03, 12.63)
Tinzaparin vs. Rivaroxaban	7.27 (1.24, 38.3)	7.06 (0.6, 78.34)
Tinzaparin vs. Warfarin	0.79 (0.2, 3.11)	0.79 (0.1, 6.12)
Tinzaparin vs. YM150	0.79 (0.08, 7.85)	0.81 (0.04, 18.58)
Warfarin + GCS vs. Apixaban	0.19 (0.00, 15.12)	0.23 (0.00, 59.86)
Warfarin + GCS vs. Dabigatran	0.13 (0.00, 8.99)	0.16 (0.00, 31.03)
Warfarin + GCS vs. Dalteparin	0.13 (0.00, 15.61)	0.16 (0.00, 73.55)
Warfarin + GCS vs. Desirudin	0.13 (0.00, 9.06)	0.13 (0.00, 32.33)
Warfarin + GCS vs. Enoxaparin	0.06 (0.00, 3.83)	0.08 (0.00, 12.47)

Table 114. Network Meta-Analysis – Pairwise Comparisons among Hip Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Warfarin + GCS vs. Enoxaparin + GCS	0.28 (0.02, 2.95)	0.29 (0.01, 6.83)
Warfarin + GCS vs. Fondaparinux	0.39 (0.02, 7.47)	0.40 (0.01, 24.12)
Warfarin + GCS vs. Fondaparinux + GCS	0.46 (0.03, 6.01)	0.48 (0.01, 16.31)
Warfarin + GCS vs. IPC	0.09 (0.00, 10.21)	0.11 (0.00, 41.72)
Warfarin + GCS vs. IPC + GCS	0.19 (0.03, 1.15)	0.19 (0.02, 1.92)
Warfarin + GCS vs. IPC + LD Aspirin	0.04 (0.00, 4.76)	0.05 (0.00, 15.89)
Warfarin + GCS vs. None	0.04 (0.00, 3.78)	0.05 (0.00, 13.44)
Warfarin + GCS vs. Rivaroxaban	0.52 (0.00, 34.12)	0.60 (0.00, 113.41)
Warfarin + GCS vs. Tinzaparin	0.07 (0.00, 5.42)	0.08 (0.00, 20.70)
Warfarin + GCS vs. Warfarin	0.06 (0.00, 5.37)	0.07 (0.00, 24.39)
Warfarin + GCS vs. YM150	0.06 (0.00, 5.16)	0.07 (0.00, 18.73)
Warfarin vs. Enoxaparin	1.13 (0.16, 7.93)	1.14 (0.06, 20.74)
Warfarin vs. None	0.76 (0.05, 9.87)	0.75 (0.02, 30.02)
YM150 vs. Apixaban	3.41 (0.31, 36.16)	3.37 (0.14, 81.04)
YM150 vs. Dabigatran	2.35 (0.31, 17.48)	2.34 (0.17, 32.79)
YM150 vs. Enoxaparin	1.13 (0.18, 6.97)	1.11 (0.11, 11.55)
YM150 vs. Fondaparinux	0.15 (0.00, 3.94)	0.17 (0.00, 7.61)
YM150 vs. IPC + LD Aspirin	0.70 (0.03, 13.32)	0.70 (0.02, 25.87)
YM150 vs. None	0.76 (0.06, 9.12)	0.74 (0.03, 19.20)
YM150 vs. Rivaroxaban	9.23 (1.13, 71.95)	8.76 (0.61, 122.36)
YM150 vs. Warfarin	1.00 (0.07, 13.99)	0.97 (0.02, 41.22)

Table 115. Network Meta-Analysis – Pairwise Comparisons among Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Apixaban vs. Enoxaparin	0.59 (0.17, 2.10)	0.50 (0.10, 2.44)
Apixaban vs. None	0.09 (0.01, 0.98)	0.01 (0.00, 0.88)
Apixaban vs. Warfarin	0.37 (0.08, 1.93)	0.22 (0.02, 1.94)
Dabigatran vs. Apixaban	1.57 (0.22, 9.30)	2.21 (0.24, 20.11)
Dabigatran vs. Enoxaparin	0.92 (0.23, 3.40)	1.10 (0.23, 5.27)
Dabigatran vs. None	0.14 (0.01, 1.11)	0.02 (0.00, 1.00)
Dabigatran vs. Warfarin	0.58 (0.09, 3.42)	0.49 (0.05, 4.22)
Enoxaparin vs. None	0.15 (0.02, 1.14)	0.02 (0.00, 1.30)
GCS vs. Apixaban	2.74 (0.09, 67.76)	
GCS vs. Dabigatran	1.75 (0.07, 40.89)	
GCS vs. Enoxaparin	1.61 (0.07, 32.01)	
GCS vs. Heparin	0.31 (0.01, 12.26)	
GCS vs. IPC	7.13 (0.10, 3,130.66)	
GCS vs. None	0.25 (0.01, 3.92)	
GCS vs. Rivaroxaban	5.03 (0.17, 137.00)	
GCS vs. Warfarin	1.02 (0.03, 25.89)	
Heparin vs. Apixaban	8.84 (0.74, 103.54)	
Heparin vs. Dabigatran	5.64 (0.48, 75.94)	
Heparin vs. Enoxaparin	5.21 (0.63, 44.84)	
Heparin vs. IPC	22.99 (0.25, 11305)	

Table 115. Network Meta-Analysis – Pairwise Comparisons among Patients – Proximal DVT

Results expressed as Odds Ratio (95% CI) Comparison	All Trials	Without Heparin Trials or Multi-Arm Trials (Final Model)
Heparin vs. None	0.80 (0.04, 15.12)	
Heparin vs. Rivaroxaban	16.23 (1.37, 210.19)	
Heparin vs. Warfarin	3.28 (0.28, 39.49)	
IPC vs. Apixaban	0.38 (0.00, 23.95)	
IPC vs. Dabigatran	0.25 (0.00, 14.94)	
IPC vs. Enoxaparin	0.23 (0.00, 11.74)	
IPC vs. None	0.03 (0.00, 1.56)	
IPC vs. Rivaroxaban	0.71 (0.00, 48.57)	
IPC vs. Warfarin	0.14 (0.00, 9.29)	
Rivaroxaban vs. Apixaban	0.54 (0.08, 3.17)	0.63 (0.07, 5.02)
Rivaroxaban vs. Dabigatran	0.35 (0.05, 2.38)	0.29 (0.03, 2.29)
Rivaroxaban vs. Enoxaparin	0.32 (0.08, 1.18)	0.32 (0.07, 1.26)
Rivaroxaban vs. None	0.05 (0.00, 0.53)	0.01 (0.00, 0.51)
Rivaroxaban vs. Warfarin	0.20 (0.03, 1.19)	0.14 (0.01, 1.06)
Warfarin vs. Enoxaparin	1.59 (0.46, 5.44)	2.25 (0.49, 11.88)
Warfarin vs. None	0.24 (0.02, 2.55)	0.04 (0, 4.22)

CONSISTENCY CHECKS

The table below summarizes the results of the network meta-analysis consistency checks. See Table 116 through Table 137 for details of the results of these consistency checks.

SUMMARY OF CONSISTENCY CHECKS

All Trials Except Those That Did Not Observe Any Events

Inconsistency was noted in the following comparisons:

All Trials	
Ln OR (with continuity correction)	
Major Bleed	No Inconsistencies
PE	No Inconsistencies
DVT	No Inconsistencies
Symptomatic DVT	No Inconsistencies
All Cause Mortality	No Inconsistencies
Proximal DVT	No Inconsistencies
All Trials from Treatments with ≥ One Event	
Ln OR (no continuity correction)	
Major Bleed	Enoxaparin vs None
PE	No Inconsistencies
DVT	No Inconsistencies
Symptomatic DVT	No Inconsistencies
All Cause Mortality	No Inconsistencies
Without Heparin Trials	
Major Bleed	No Inconsistencies
PE	No Inconsistencies
	Enoxaparin vs IPC
DVT	Warfarin vs Apixaban
Symptomatic DVT	No Inconsistencies
All Cause Mortality	Test Not Possible (No Closed Loops)
Without Heparin Trials and Without Trials with > 2 Arms	
Major Bleed	No Inconsistencies
PE	No Inconsistencies
DVT	No Inconsistencies
Symptomatic DVT	Test Not Possible (No Closed Loops)
All Cause Mortality	Test Not Possible (No Closed Loops)
Proximal DVT	No Inconsistencies
Without Heparin Trials and Without Trials with > 2 Arms With Continuity Correction	
Major Bleed	No Inconsistencies
PE	No Inconsistencies
DVT	No Inconsistencies
Symptomatic DVT	Test Not Possible (No Closed Loops)
All Cause Mortality	Test Not Possible (No Closed Loops)
Proximal DVT	No Inconsistencies

Table 116. Model 1 (all trials) PE Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.099	0.667	-0.108	0.344	0.075	0.000	0.000	1.000
Heparin	1.534	0.828	1.994	0.668	-0.860	0.000	0.000	1.000
Desirudin	-0.092	0.969	-0.691	0.668	0.542	0.000	0.000	1.000
Apixaban	0.094	0.605	0.118	0.281	-0.006	0.000	0.000	1.000
Tinzaparin	0.040	1.397	-0.009	1.416	-1.878	8.722	0.215	0.829
GCS	0.450	1.681	2.002	1.942	6.190	3.878	1.596	0.110
IPC	-1.298	1.882						
None	0.008	1.321	-0.036	1.413	-0.351	3.979	0.088	0.930
Warfarin vs:								
Tinzaparin	-0.059	1.397	0.008	1.415	2.654	8.923	0.297	0.766
Heparin vs:								
Desirudin	-1.627	0.973	-1.184	0.898	-2.548	0.000	0.000	1.000
GCS vs:								
IPC	-1.747	1.979	-2.002	2.001	-11.650	13.525	0.861	0.389
None	-0.442	1.585	0.000	1.417	-1.763	0.000	0.000	1.000
IPC vs:								
None	1.306	1.592	1.981	1.393	-2.203	0.000	0.000	1.000

Table 117. Model 1 (all trials) Major Bleed Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-0.747	0.383	-0.574	0.323	-0.424	0.000	0.000	1.000
Heparin	0.239	0.313	0.289	0.262	-0.115	0.000	0.000	1.000
None	-0.615	0.465	0.011	0.582	1.729	0.968	1.787	0.074
Apixaban	-0.230	0.300	-0.232	0.204	0.002	0.000	0.000	1.000
Dabigatran	0.250	0.248	0.251	0.179	-0.001	0.000	0.000	1.000
Desirudin	0.190	0.443	-0.005	0.319	0.211	0.000	0.000	1.000
GCS	-1.949	1.613	-2.009	1.418	0.205	0.000	0.000	1.000
IPC	-2.415	2.243	-2.009	1.418	-0.270	0.000	0.000	1.000
Tinzaparin	-0.113	0.556	-0.683	0.821	-1.053	1.116	0.944	0.345
Fondaparinux	0.358	0.577	0.282	0.504	0.244	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.517	0.480	1.974	2.000	1.546	2.060	0.750	0.453
Tinzaparin	0.634	0.486	0.782	0.375	-0.218	0.000	0.000	1.000
Heparin vs:								
None	-0.854	0.515	-2.227	0.916	-2.006	1.107	1.812	0.070
Desirudin	-0.050	0.507	0.673	0.820	1.170	1.043	1.122	0.262
None vs:								
Dabigatran	0.865	0.512	0.972	1.007	0.144	1.169	0.124	0.902
Fondaparinux	0.973	0.672	1.034	1.004	0.111	1.351	0.082	0.934
GCS vs:								
Enoxaparin + GCS	0.030	1.571	0.000	1.418	0.131	0.000	0.000	1.000
Fondaparinux vs:								
Fondaparinux + GCS	-1.560	1.674	-1.966	1.999	-1.358	3.656	0.371	0.710
Enoxaparin + GCS vs:								
Fondaparinux + GCS	0.718	0.325	0.569	0.184	0.070	0.000	0.000	1.000

Table 118. Model 1 (all trials) All Cause Mortality Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Heparin	2.435	1.758	0.601	-0.546	0.196	0.000	0.000	1.000
Desirudin	-0.045	1.366	0.647	-0.157	-0.009	0.000	0.000	1.000
Heparin vs:								
Desirudin	-2.480	1.859	-2.002	-3.200	0.721	3.931	0.183	0.855

Table 119. Model 1 (all trials) Symptomatic DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-1.032	1.674	0.000	1.417	-2.614	0.000	0.000	1.000
Apixaban	-0.644	0.617	-0.601	0.317	-0.015	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.388	1.685	0.711	1.160	-0.291	0.000	0.000	1.000

Table 120. Model 1 (all trials) DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.673	0.227	0.725	0.136	-0.029	0.000	0.000	1.000
Heparin	0.693	0.240	0.619	0.159	0.058	0.000	0.000	1.000
Tinzaparin	0.276	0.312	0.098	0.234	0.229	0.000	0.000	1.000
Desirudin	-0.389	0.280	-0.417	0.123	0.007	0.000	0.000	1.000
Apixaban	-0.543	0.207	-0.511	0.082	-0.006	0.000	0.000	1.000
None	0.886	0.340	0.757	0.247	0.145	0.000	0.000	1.000
IPC	-0.152	0.435	0.428	0.534	1.725	0.921	1.873	0.061
GCS	0.439	0.510	0.877	0.469	-2.361	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.398	0.301	-0.269	0.121	-0.025	0.000	0.000	1.000
Apixaban	-1.216	0.291	-1.016	0.354	0.616	0.621	0.993	0.321
Heparin vs:								
Desirudin	-1.081	0.264	-0.949	0.176	-0.105	0.000	0.000	1.000
None vs:								
IPC	-1.038	0.348	-1.073	0.199	0.017	0.000	0.000	1.000
GCS	-0.447	0.489	-0.633	0.356	0.209	0.000	0.000	1.000
IPC vs:								
GCS	0.590	0.519	0.483	0.439	0.271	0.000	0.000	1.000

Table 121. Model 1 (all trials) Proximal DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.378	0.357	0.393	0.244	-0.013	0.000	0.000	1.000
Apixaban	-0.740	0.355	-0.740	0.214	0.000	0.000	0.000	1.000
Dabigatran	-0.485	0.271	-0.423	0.149	-0.027	0.000	0.000	1.000
None	0.812	0.486	0.504	0.477	8.007	0.000	0.000	1.000
Tinzaparin	0.027	0.440	-0.111	0.317	0.149	0.000	0.000	1.000
Desirudin	-0.644	0.415	-0.538	0.212	-0.037	0.000	0.000	1.000
IPC	-0.156	0.682	-2.000	1.999	-2.087	2.126	0.981	0.326
Heparin	1.272	0.361	1.097	0.249	0.159	0.000	0.000	1.000
GCS	-0.091	1.190	0.000	1.419	0.308	2.606	0.118	0.906
Warfarin vs:								
Apixaban	-1.118	0.486	0.038	1.007	1.507	1.150	1.311	0.190
Tinzaparin	-0.351	0.431	-0.237	0.228	-0.044	0.000	0.000	1.000
Dabigatran vs:								
None	1.297	0.527	2.033	0.825	1.244	1.073	1.159	0.246
None vs:								
IPC	-0.968	0.537	-0.807	0.273	-0.056	0.000	0.000	1.000
GCS	-0.904	1.176	-1.013	1.007	0.301	0.000	0.000	1.000
Desirudin vs:								
Heparin	1.916	0.408	1.551	0.253	0.229	0.000	0.000	1.000
IPC vs:								
GCS	0.065	1.218	2.002	1.942	3.194	2.493	1.281	0.200

Table 122. Model 2 (all trials from treatments with ≥ one event) PE Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.160	0.897	-0.108	0.344	0.046	0.000	0.000	1.000
Heparin	3.720	1.709	1.994	0.668	0.312	0.000	0.000	1.000
Desirudin	0.401	1.433	-0.691	0.668	0.303	0.000	0.000	1.000
Apixaban	0.018	0.820	0.118	0.281	-0.013	0.000	0.000	1.000
Tinzaparin	0.088	1.601	-0.009	1.416	0.348	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.072	1.599	0.008	1.415	-0.290	0.000	0.000	1.000
Heparin vs:								
Desirudin	-3.320	1.717	-1.184	0.898	-0.804	0.000	0.000	1.000

Table 123. Model 2 (all trials from treatments with ≥ one event) Major Bleeding Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-0.776	0.394	-0.574	0.323	-0.413	0.000	0.000	1.000
Heparin	0.258	0.336	0.289	0.262	-0.047	0.000	0.000	1.000
None	-0.601	0.519	0.011	0.582	2.967	1.282	2.316	0.021
Desirudin	0.206	0.478	-0.005	0.319	0.169	0.000	0.000	1.000
Tinzaparin	-0.123	0.577	-0.683	0.821	-1.106	1.153	0.959	0.338
Fondaparinux	0.352	0.596	0.282	0.503	0.172	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.555	0.506	1.974	2.000	1.516	2.067	0.733	0.463
Tinzaparin	0.653	0.511	0.782	0.375	-0.152	0.000	0.000	1.000
Heparin vs:								
None	-0.860	0.578	-2.227	0.916	-2.273	1.181	1.925	0.054
Desirudin	-0.053	0.539	0.673	0.820	1.277	1.088	1.174	0.240
None vs:								
Dabigatran	0.847	0.555	0.972	1.006	0.180	1.207	0.149	0.881
Fondaparinux	0.953	0.713	1.034	1.005	0.163	1.427	0.114	0.909

Table 124. Model 2 (all trials from treatments with ≥ one event) All Cause Mortality Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Heparin	2.435	1.758	0.601	-0.546	0.196	0.000	0.000	1.000
Desirudin	-0.045	1.366	0.647	-0.157	-0.009	0.000	0.000	1.000
Heparin vs:								
Desirudin	-2.480	1.859	-2.002	-3.200	0.721	3.931	0.183	0.855

Table 125. Model 2 (all trials from treatments with ≥ one event) Symptomatic DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-1.032	1.674	0.000	1.417	-2.614	0.000	0.000	1.000
Apixaban	-0.644	0.617	-0.601	0.317	-0.015	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.388	1.685	0.711	1.160	-0.291	0.000	0.000	1.000

Table 126. Model 2 (all trials from treatments with ≥ one event) DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.673	0.227	0.725	0.136	-0.029	0.000	0.000	1.000
Heparin	0.693	0.240	0.619	0.159	0.058	0.000	0.000	1.000
Tinzaparin	0.276	0.312	0.098	0.234	0.229	0.000	0.000	1.000
Desirudin	-0.389	0.280	-0.417	0.123	0.007	0.000	0.000	1.000
Apixaban	-0.543	0.207	-0.511	0.082	-0.006	0.000	0.000	1.000
None	0.886	0.340	0.757	0.247	0.145	0.000	0.000	1.000
IPC	-0.152	0.435	0.428	0.534	1.725	0.921	1.873	0.061
GCS	0.439	0.510	0.877	0.469	-2.361	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.398	0.301	-0.269	0.121	-0.025	0.000	0.000	1.000
Apixaban	-1.216	0.291	-1.016	0.354	0.616	0.621	0.993	0.321
Heparin vs:								
Desirudin	-1.081	0.264	-0.949	0.176	-0.105	0.000	0.000	1.000
None vs:								
IPC	-1.038	0.348	-1.073	0.199	0.017	0.000	0.000	1.000
GCS	-0.447	0.489	-0.633	0.356	0.209	0.000	0.000	1.000
IPC vs:								
GCS	0.590	0.519	0.483	0.439	0.271	0.000	0.000	1.000

Table 127. Model 3 (without heparin trials) PE Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.128	0.824	-0.108	0.344	0.050	0.000	0.000	1.000
Apixaban	0.037	0.751	0.118	0.281	-0.013	0.000	0.000	1.000
Tinzaparin	0.068	1.521	-0.009	1.416	0.498	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.060	1.525	0.008	1.415	-0.422	0.000	0.000	1.000

Table 128. Model 3 (without heparin trials) Major Bleeding Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-0.764	0.386	-0.574	0.323	-0.522	0.000	0.000	1.000
None	-0.100	0.558	0.011	0.582	1.362	2.035	0.669	0.503
Tinzaparin	-0.120	0.567	-0.683	0.821	-1.077	1.135	0.948	0.343
Fondaparinux	0.445	0.577	0.282	0.503	0.524	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.530	0.501	1.974	2.000	1.541	2.066	0.746	0.456
Tinzaparin	0.644	0.503	0.782	0.375	-0.172	0.000	0.000	1.000
None vs:								
Dabigatran	0.378	0.588	0.972	1.006	0.903	1.240	0.728	0.466
Fondaparinux	0.546	0.716	1.034	1.005	0.993	1.433	0.693	0.488

Table 129. Model 3 (without heparin trials) Symptomatic DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-1.032	1.674	0.000	1.417	-2.614	0.000	0.000	1.000
Apixaban	-0.644	0.617	-0.601	0.317	-0.015	0.000	0.000	1.000
Warfarin vs:								
Apixaban	0.388	1.685	0.711	1.160	-0.291	0.000	0.000	1.000

Table 130. Model 3 (without heparin trials) DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.676	0.277	0.725	0.136	-0.016	0.000	0.000	1.000
Tinzaparin	0.270	0.387	0.098	0.234	0.100	0.000	0.000	1.000
Apixaban	-0.544	0.258	-0.511	0.082	-0.004	0.000	0.000	1.000
None	0.911	0.402	0.757	0.247	0.093	0.000	0.000	1.000
IPC	-0.118	0.506	0.428	0.534	5.333	1.669	3.195	0.001
GCS	0.470	0.591	0.877	0.469	-0.689	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.406	0.380	-0.269	0.121	-0.016	0.000	0.000	1.000
Apixaban	-1.220	0.353	-1.016	0.354	42.640	5.114	8.337	0.000
None vs:								
IPC	-1.029	0.409	-1.073	0.199	0.014	0.000	0.000	1.000
GCS	-0.441	0.566	-0.633	0.356	0.125	0.000	0.000	1.000
IPC vs:								
GCS	0.588	0.592	0.483	0.439	0.128	0.000	0.000	1.000

Table 131. Model 4 (without heparin or trials with >2 arms) PE Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.386	0.835	-0.108	0.345	0.102	0.000	0.000	1.000
Tinzaparin	0.212	1.447	-0.009	1.416	4.959	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.174	1.452	0.008	1.415	-3.419	0.000	0.000	1.000

Table 132. Model 4 (without heparin or trials with >2 arms) Major Bleeding Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-0.732	0.406	-0.574	0.323	-0.427	0.000	0.000	1.000
None	-0.129	0.573	0.011	0.582	4.704	3.376	1.393	0.163
Tinzaparin	-0.104	0.583	-0.683	0.821	-1.169	1.166	1.002	0.316
Fondaparinux	0.442	0.605	0.282	0.503	0.361	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	0.628	0.525	0.782	0.375	-0.161	0.000	0.000	1.000
None vs:								
Dabigatran	0.403	0.605	0.972	1.006	0.892	1.259	0.708	0.479
Fondaparinux	0.571	0.731	1.034	1.005	0.983	1.464	0.671	0.502

Table 133. Model 4 (without heparin or trials with >2 arms) DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.653	0.396	0.725	0.136	-0.010	0.000	0.000	1.000
Tinzaparin	0.273	0.484	0.098	0.234	0.054	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.380	0.473	-0.269	0.121	-0.008	0.000	0.000	1.000

Table 134. Model 4 (without heparin or trials with >2 arms) Proximal DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.633	0.634	0.393	0.244	0.042	0.000	0.000	1.000
Dabigatran	-0.544	0.431	-0.423	0.149	-0.016	0.000	0.000	1.000
None	1.168	0.935	0.504	0.477	0.234	0.000	0.000	1.000
Tinzaparin	0.152	0.744	-0.111	0.317	0.058	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	-0.482	0.735	-0.237	0.228	-0.026	0.000	0.000	1.000
Dabigatran vs:								
None	1.712	0.989	2.033	0.825	-0.733	0.000	0.000	1.000

Table 135. Model 5 (without heparin or trials with >2 arms, with continuity correction) PE Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.300	0.748	-0.108	0.345	0.110	0.000	0.000	1.000
Tinzaparin	0.148	1.407	-0.009	1.416	-12.718	12.750	0.997	0.319
Warfarin vs:								
Tinzaparin	-0.152	1.394	0.008	1.415	5.456	8.265	0.660	0.509

Table 136. Model 5 (without heparin or trials with >2 arms, with continuity correction) Major Bleeding Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	-0.739	0.411	-0.574	0.323	-0.418	0.000	0.000	1.000
None	-0.099	0.559	0.011	0.582	1.381	2.065	0.669	0.504
Tinzaparin	-0.098	0.591	-0.683	0.821	-1.213	1.183	1.026	0.305
Fondaparinux	0.460	0.612	0.282	0.503	0.372	0.000	0.000	1.000
Warfarin vs:								
Tinzaparin	0.640	0.524	0.782	0.375	-0.150	0.000	0.000	1.000
None vs:								
Dabigatran	0.373	0.592	0.972	1.006	0.917	1.245	0.737	0.461
Fondaparinux	0.558	0.729	1.034	1.005	1.002	1.459	0.687	0.492

Table 137. Model 5 (without heparin or trials with >2 arms, with continuity correction) Proximal DVT Consistency Check on Ln Odds Ratio

Comparison	MC Mean	MC SD	Direct Ln OR	Direct SD (Ln OR)	Omega	SD Omega	Z	p
Enoxaparin vs:								
Warfarin	0.619	0.592	0.393	0.244	0.046	0.000	0.000	1.000
Dabigatran	-0.508	0.397	-0.423	0.149	-0.014	0.000	0.000	1.000
None	0.975	0.837	0.504	0.477	0.226	0.000	0.000	1.000
Tinzaparin	0.143	0.693	-0.111	0.317	0.067	0.000	0.000	1.000
Warfarin vs:								
Dabigatran	-1.126	0.715						
None	0.356	1.014						
Tinzaparin	-0.475	0.686	-0.237	0.228	-0.030	0.000	0.000	1.000
Dabigatran vs:								
None	1.482	0.871	2.033	0.825	-4.790	0.000	0.000	1.000

MODEL FIT

Table 138. Network Meta-Analysis Model Fit

Outcome	Joint	Model	Data Points	Residual Deviance
Pulmonary Embolism	Both Hip and Knee	All Trials	71	72.96
Pulmonary Embolism	Hip	All Trials	38	39.28
Pulmonary Embolism	Knee	All Trials	29	31.17
Pulmonary Embolism	Both Hip and Knee	All Trials from Treatments with ≥ 1 Event	55	61.5
Pulmonary Embolism	Hip	All Trials from Treatments with ≥ 1 Event	32	35.06
Pulmonary Embolism	Knee	All Trials from Treatments with ≥ 1 Event	21	23.95
Pulmonary Embolism	Both Hip and Knee	Without Heparin Trials	43	48.41
Pulmonary Embolism	Hip	Without Heparin Trials	22	23.2
Pulmonary Embolism	Knee	Without Heparin Trials	21	23.95
Pulmonary Embolism	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	40	43.66
Pulmonary Embolism	Hip	Without Heparin Trials and Without Multi-Arm Trials	22	23.2
Pulmonary Embolism	Knee	Without Heparin Trials and Without Multi-Arm Trials	18	19.23
Pulmonary Embolism	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	50	53.23
Pulmonary Embolism	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	28	29.32
Pulmonary Embolism	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	20	20.33
Major Bleeding	Both Hip and Knee	All Trials	99	103.9
Major Bleeding	Hip	All Trials	66	68.13
Major Bleeding	Knee	All Trials	33	34.88
Major Bleeding	Both Hip and Knee	All Trials from Treatments with ≥ 1 Event	81	93.23
Major Bleeding	Hip	All Trials from Treatments with ≥ 1 Event	54	61.71
Major Bleeding	Knee	All Trials from Treatments with ≥ 1 Event	29	32.16
Major Bleeding	Both Hip and Knee	Without Heparin Trials	67	72.33
Major Bleeding	Hip	Without Heparin Trials	42	44.66
Major Bleeding	Knee	Without Heparin Trials	27	30.07
Major Bleeding	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	64	69.28
Major Bleeding	Hip	Without Heparin Trials and Without Multi-Arm Trials	42	44.66
Major Bleeding	Knee	Without Heparin Trials and Without Multi-Arm Trials	24	26.84

Table 138. Network Meta-Analysis Model Fit

Outcome	Joint	Model	Data Points	Residual Deviance
Major Bleeding	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	78	82.43
Major Bleeding	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	54	54.33
Major Bleeding	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	24	25.71
All Cause Mortality	Both Hip and Knee	All Trials	56	57.18
All Cause Mortality	Hip	All Trials	34	35.37
All Cause Mortality	Knee	All Trials	16	16.09
All Cause Mortality	Both Hip and Knee	All Trials from Treatments with ≥ 1 Event	42	46.99
All Cause Mortality	Hip	All Trials from Treatments with ≥ 1 Event	26	29.13
All Cause Mortality	Knee	All Trials from Treatments with ≥ 1 Event	16	16.94
All Cause Mortality	Both Hip and Knee	Without Heparin Trials	36	40.95
All Cause Mortality	Hip	Without Heparin Trials	20	23.38
All Cause Mortality	Knee	Without Heparin Trials	16	16.94
All Cause Mortality	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	36	40.95
All Cause Mortality	Hip	Without Heparin Trials and Without Multi-Arm Trials	20	23.38
All Cause Mortality	Knee	Without Heparin Trials and Without Multi-Arm Trials	16	16.94
All Cause Mortality	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	50	51.62
All Cause Mortality	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	28	29.96
All Cause Mortality	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	16	16.09
Symptomatic DVT	Both Hip and Knee	All Trials	41	42.78
Symptomatic DVT	Hip	All Trials	16	17.26
Symptomatic DVT	Knee	All Trials	19	19.38
Symptomatic DVT	Both Hip and Knee	All Trials from Treatments with ≥ 1 Event	41	42.7
Symptomatic DVT	Hip	All Trials from Treatments with ≥ 1 Event	14	14.96
Symptomatic DVT	Knee	All Trials from Treatments with ≥ 1 Event	19	20.22
Symptomatic DVT	Both Hip and Knee	Without Heparin Trials	39	40.57

Table 138. Network Meta-Analysis Model Fit

Outcome	Joint	Model	Data Points	Residual Deviance
Symptomatic DVT	Hip	Without Heparin Trials	12	12.86
Symptomatic DVT	Knee	Without Heparin Trials	19	20.22
Symptomatic DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	34	35.28
Symptomatic DVT	Hip	Without Heparin Trials and Without Multi-Arm Trials	12	12.86
Symptomatic DVT	Knee	Without Heparin Trials and Without Multi-Arm Trials	16	17.12
Symptomatic DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	34	35.03
Symptomatic DVT	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	14	15.26
Symptomatic DVT	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	16	16.36
DVT	Both Hip and Knee	All Trials	79	80.28
DVT	Hip	All Trials	44	45.94
DVT	Knee	All Trials	31	30.21
DVT	Both Hip and Knee	All Trials from Treatments with ≥ 1 Event	79	80.28
DVT	Hip	All Trials from Treatments with ≥ 1 Event	44	45.94
DVT	Knee	All Trials from Treatments with ≥ 1 Event	31	30.21
DVT	Both Hip and Knee	Without Heparin Trials	69	70.15
DVT	Hip	Without Heparin Trials	36	37.78
DVT	Knee	Without Heparin Trials	29	28.16
DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	58	59.12
DVT	Hip	Without Heparin Trials and Without Multi-Arm Trials	36	37.78
DVT	Knee	Without Heparin Trials and Without Multi-Arm Trials	22	21.95
DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	58	59.12
DVT	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	36	37.78
DVT	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	22	21.95
Proximal DVT	Both Hip and Knee	All Trials	87	87.91
Proximal DVT	Hip	All Trials	54	57.22

Table 138. Network Meta-Analysis Model Fit

Outcome	Joint	Model	Data Points	Residual Deviance
Proximal DVT	Knee	All Trials	29	29.37
Proximal DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials	70	73.31
Proximal DVT	Both Hip and Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	70	71.45
Proximal DVT	Hip	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	46	48.03
Proximal DVT	Knee	Without Heparin Trials and Without Multi-Arm Trials (with continuity correction)	20	20.33

INDIVIDUAL STUDY RESULTS

Table 139. Individual Study Results - Fatal PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 months	1599	1596	0.10%	0.10%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2.5 months	1528	1529	0.10%	0.00%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	95 days	2708	2699	0.00%	0.00%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	105	109; n3:109	0.00%	0.00% g3:0%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	35 days	2047	2041	0.00%	0.10%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	3 months	113	118	0.00%	0.00%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.00%	0.00%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	5 weeks	283	300	0.00%	0.00%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	17 days	604	643	0.00%	0.00%	No

Table 139. Individual Study Results - Fatal PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	0.00%	0.00%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	6 weeks	802	785	0.10%	0.00%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	10 days	202	229	0.00%	0.00%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	10 days	180	180	0.00%	0.00%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	NR	195	209	0.00%	0.00%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	14 days	333	332	0.00%	0.00%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	0.00%	0.00%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	~14 days	336	334	0.00%	0.00%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	NR	138	136	0.00%	0.00%	No
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	High	NR	112	117	0.00%	1.70%	No
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	Moderate	NR	141	136	0.00%	0.00%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	0.10%	0.10%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	High	6 weeks	177	260	0.00%	0.40%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	NR	400	395	0.00%	0.00%	No

Table 139. Individual Study Results - Fatal PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	49 days	517	517	0.20%	0.20%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	49 days	1129	1123	0.10%	0.00%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	49 days	1126	1128	0.10%	0.20%	No
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	Both	High	NR	116	130	0.00%	0.00%	No
Hull et al. 1990	IPC	None	Hip	Moderate	3 months	152	158	0.70%	0.00%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	1-2 months, not including 1st 6-10 days	142	157	0.00%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	2 months	1595	1558	0.00%	0.10%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	10 weeks	1228	1229	0.00%	0.20%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.10%	0.00%	No

Table 139. Individual Study Results - Fatal PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	the month after 1st week (also 0 in 1st week)	102	104	0.00%	0.00%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	0.00%	0.00%	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	Moderate	NR	105	105	1.00%	0.00%	No

Table 140. Individual Study Results - Fatal Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 weeks	1596	1588	0.00%	0.10%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	35 days	2673	2659	0.00%	0.00%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	105	109; n3:109	0.00%	0.00% g3:0%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	3 months	113	118	0.00%	0.00%	No
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC (Rapid Inflation Asymmetrical Compression Device)	Aspirin (≥300mg/Day) + IPC (Sequential Compression Device)	Knee	High	in-hospital	206	217	0.00%	0.00%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.00%	0.00%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	679	694	0.00%	0.00%	No

Table 140. Individual Study Results - Fatal Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1146	1154	0.10%	0.00%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	17 days	857	868	0.00%	0.00%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	6 weeks	802	785	0.10%	0.00%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	NR	223	220	0.00%	0.00%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	14 days	333	332	0.00%	0.00%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	0.00%	0.00%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	~14 days	336	334	0.00%	0.00%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	NR	138	136	0.00%	0.00%	No
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	Moderate	NR	141	136	0.00%	0.00%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	0.00%	0.60%	No

Table 140. Individual Study Results - Fatal Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	11 days	517	517	0.00%	0.00%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1140	1133	0.00%	0.00%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1128	1129	0.00%	0.00%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	7-11 days	142	157	0.00%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	38 days	2209	2224	0.00%	0.00%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	1228	1229	0.00%	0.00%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	~2 weeks	1220	1239	0.00%	0.00%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.10%	0.00%	No
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	11 days	136	132	0.00%	0.00%	No
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	7-11 days	80	162	0.00%	0.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	9 days	102	104	0.00%	0.00%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	0.00%	0.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	9 days	156	166	0.00%	0.00%	No

Table 141. Individual Study Results - Symptomatic PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 months	1599	1596	1.10%	0.80%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2.5 months	1528	1529	0.50%	0.10%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	95 days	2708	2699	0.10%	0.30%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	105	109 n3:109	0.00%	1.80% g3:0%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	35 days	2047	2041	0.40%	0.40%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	3 months	113	118	0.90%	0.80%	No
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + IPC	Knee	Moderate	NR	129	135	0.80%	0.00%	No
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC (Rapid Inflation Asymmetrical Compression Device)	Aspirin (≥300mg/Day) + IPC (Sequential Compression Device)	Knee	High	6 months	206	217	0.00%	0.50%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	High	3 months	1001	992	0.20%	0.40%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.00%	0.00%	No

Table 141. Individual Study Results - Symptomatic PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	5 weeks	283	300	0.00%	0.00%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	675	685	0.00%	0.10%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1137	1142	0.40%	0.30%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	3 months	604	643	1.30%	1.10%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	NR	271	279	0.00%	0.00%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	0.00%	0.00%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	6 weeks	802	785	0.40%	0.80%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	Moderate	10 days	202	229	0.50%	0.00%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	44 days	180	180	0.00%	2.20%	Yes

Table 141. Individual Study Results - Symptomatic PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	High	NR	110	110 n3:110 n4:110	0.00%	0.90% g3:0.0% g4:0.9%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	7 days	195	209	0.00%	1.90%	Yes
Colwell et al. 1995	Enoxaparin	Heparin	Knee	High	NR	228	225	0.00%	0.90%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	NR	333	332	0.00%	0.60%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	0.00%	0.90%	No
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	0.50%	0.50%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	~14 days	336	334	0.30%	0.90%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	NR	138	136	0.00%	0.70%	No
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	Moderate	NR	141	136	0.70%	0.70%	No
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	Moderate	NR	80	86	1.30%	0.00%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	1.00%	0.80%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	0.00%	0.60%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	Moderate	~10 days	115	171	0.00%	0.00%	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	49 days	517	517	0.60%	1.00%	No

Table 141. Individual Study Results - Symptomatic PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	49 days	1129	1123	0.40%	0.30%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	49 days	1126	1128	1.10%	0.40%	No
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	Both	High	NR	116	130	0.00%	0.00%	No
Hull et al. 1990	IPC	None	Hip	Moderate	~14 days	152	158	0.00%	0.60%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	10 weeks	196	190	1.00%	1.10%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	1-2 months	142	157	0.70%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	36 days	1595	1558	0.30%	0.10%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	864	869	0.10%	0.60%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	day 17	1201	1217	0.00%	0.30%	Yes
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.30%	0.50%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	~ 1 week	102	104	0.00%	0.00%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	3 months	715	721	0.10%	0.10%	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	Moderate	NR	105	105	1.00%	1.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	9 days	114	127	0.00%	0.00%	No

Table 142. Individual Study Results - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 weeks	1596	1588	0.70%	1.40%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2 weeks	1501	1508	0.60%	0.90%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	35 days	2673	2659	0.80%	0.70%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	155	149; n3:151	0.60%	0.00% g3:0%	No
Kim et al. 1998	Aspirin (≥300mg/Day)	None	Hip	Moderate	NR	50	50	0.00%	0.00%	No
Harris et al. 1977	Aspirin (≥300mg/Day)	Placebo	Hip	High	NR	44	51	0.00%	0.00%	No
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	High	NR	43	43	7.00%	9.30%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	High	4-5 weeks	1010	1003	1.40%	0.90%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	2.30%	0.80%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	NR	385	392	4.70%	2.00%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	679	694	1.50%	1.30%	No

Table 142. Individual Study Results - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1146	1154	2.00%	1.60%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	3 months	857	868	0.70%	1.40%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	NR	271	279	2.20%	1.40%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	day0-1	496	489	8.90%	4.50%	Yes
Eriksson et al. 1997(b) †	Desirudin	Enoxaparin	Hip	High	10 days	1028	1023	1.90%	2.00%	No
Eriksson et al. 1997†	Desirudin	Heparin	Hip	High	NR	223	220	0.00%	0.00%	No
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	High	NR	110	110 n3:110 n4:110	1.80%	0.00% g3:0% g4:0%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	NR	195	209	4.10%	6.20%	No
Colwell et al. 1995	Enoxaparin	Heparin	Knee	High	NR	228	225	1.30%	1.30%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	14 days	333	332	3.30%	5.70%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	1.60%	0.00%	No

Table 142. Individual Study Results - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Turpie et al. 1986	Enoxaparin	Placebo	Hip	High	14 days or until discharge	50	50	2.00%	4.00%	No
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	1.80%	0.90%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	~14 days	336	334	2.10%	1.80%	No
Samama et al. 1997	Enoxaparin + GCS	Placebo + GCS	Hip	High	10 days	85	85	1.20%	1.20%	No
Senaran et al. 2006	Enoxaparin; GCS Allowed	Heparin; GCS Allowed	Hip	High	NR	50	50	4.00%	0.00%	No
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	High	NR	102	101	2.00%	0.00%	No
Fuji et al. 2008 (knee)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Knee	High	NR	91	89	1.10%	4.50%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	0.60%	0.30%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	5.20%	2.30%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	High	~10 days	177	260	4.50%	3.50%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	NR	404	391	0.20%	0.00%	No
Yokote et al. 2011	Fondaparinux + IPC	Enoxaparin + IPC; Group 3: Placebo + IPC	Hip	High	12 weeks	85	86; n3:85	0.00%	0.00% g3:0%	No
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Both	High	NR	165	169	1.80%	0.60%	No

Table 142. Individual Study Results - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	NR	517	517	2.10%	0.20%	Yes
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	NR	1140	1133	4.10%	2.80%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	NR	1128	1129	1.80%	1.00%	No
Fordyce et al. 1992†	Foot Pump + GCS	GCS	Hip	High	NR	39	40	0.00%	0.00%	No
Mannucci et al. 1976†	Heparin	None	Hip	Moderate	NR	45	51	11.10%	0.00%	Yes
Hampson et al. 1974†	Heparin	Placebo	Hip	Moderate	NR	48	52	0.00%	0.00%	No
Paiement et al. 1987	IPC	Warfarin	Hip	Moderate	NR	66	72	0.00%	0.00%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	10 weeks	198	194	0.00%	5.70%	Yes
Agnelli et al. 2007	LY517717	Enoxaparin	Both	High	1 month	106	90	0.90%	1.10%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	7-11 days	142	157	0.70%	1.90%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	38 days	2209	2224	0.30%	0.10%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	1228	1229	0.10%	0.10%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	~2 weeks	1220	1239	0.60%	0.50%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.70%	0.30%	No

Table 142. Individual Study Results - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	11 days	136	132	2.20%	1.50%	No
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	7-11 days	80	162	2.50%	0.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	9 days	102	104	0.00%	1.90%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	2.80%	1.20%	No
Poller et al. 1995	Warfarin	Heparin	Both	High	NR	31	37	0.00%	0.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	6 weeks	156	166	0.00%	0.60%	No
Eriksson et al. 2007d	YM150; Mechanical Allowed (Used In 1/3)	Enoxaparin; Mechanical Allowed (Used In 1/3)	Hip	High	~5 weeks	36	36	0.00%	0.00%	No

†: These studies used the term severe or serious instead of major

Table 143. Individual Study Results - All Cause Mortality

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 months	1599	1596	0.20%	0.40%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2.5 months	1528	1529	0.20%	0.10%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	95 days	2708	2699	0.20%	0.10%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	105	109; n3:109	0.00%	0.00%; %g3:0%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	35 days	2047	2041	0.40%	0.50%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	3 months	113	118	0.90%	0.00%	No
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC (Rapid Inflation Asymmetrical Compression Device)	Aspirin (≥300mg/Day) + IPC (Sequential Compression Device)	Knee	High	in-hospital	206	217	0.00%	0.50%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	High	5-6 weeks	1001	992	0.00%	0.20%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.00%	0.00%	No

Table 143. Individual Study Results - All Cause Mortality

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	675	685	0.10%	0.10%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1137	1142	0.30%	0.00%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	3 months	604	643	0.30%	0.30%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	0.40%	0.40%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	6 weeks	802	785	0.50%	0.30%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	6 weeks	277	277	0.00%	0.40%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	44 days	180	180	0.00%	1.10%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	NR	195	209	0.50%	1.00%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	14 days	333	332	0.00%	0.00%	No

Table 143. Individual Study Results - All Cause Mortality

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	0.00%	0.00%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	6 months	336	334	0.30%	0.30%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	NR	143	147	0.00%	0.00%	No
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	High	NR	112	117	0.90%	2.60%	No
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	Moderate	NR	141	136	0.00%	0.00%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	0.60%	0.70%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	0.60%	1.70%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	High	1 month from discharge to discharge	177	260	0.00%	0.40%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	+ 18-19 days	404	391	0.70%	0.30%	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	1 month	517	517	0.40%	0.60%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	NR	1140	1133	0.20%	0.40%	No

Table 143. Individual Study Results - All Cause Mortality

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	~14 days	1128	1129	0.50%	0.30%	No
Hull et al. 1990	IPC	None	Hip	Moderate	NR	152	158	1.30%	0.00%	No
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	High	NR	110	110	0.90%	0.90%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	~10 days	142	157	0.00%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	49 days	1595	1558	0.30%	0.30%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	49 days	1228	1229	0.20%	0.70%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	6 weeks	1201	1217	0.00%	0.50%	Yes
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	6 weeks	1526	1508	0.40%	0.40%	No
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	49 days	109	106	0.90%	0.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	6 weeks	102	104	0.00%	0.00%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	0.70%	0.70%	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	Moderate	~14 days	105	105	1.00%	1.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	36 days	114	127	0.00%	0.00%	No

Table 144. Individual Study Results - Reoperation due to Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	35 days	2673	2659	0.00%	0.00%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	155	149 n3:151	0.00%	0.00% g3:0%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.80%	0.00%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	NR	385	392	0.30%	0.30%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	679	694	0.40%	0.10%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1146	1154	0.20%	0.30%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	17 days	857	868	0.00%	0.10%	No
Eriksson et al. 1991	Dalteparin	Heparin	Hip	High	NR	67	69	0.00%	0.00%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	10 days	277	277	1.40%	0.70%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	NR	223	220	0.00%	0.00%	No

Table 144. Individual Study Results - Reoperation due to Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	11 days	517	517	0.40%	0.20%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1140	1133	0.40%	0.30%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1128	1129	0.20%	0.20%	No
Windisch et al. 2010	Foot Pump + Enoxaparin + GCS	Enoxaparin + GCS	Knee	Moderate	NR	40	40	0.00%	0.00%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	7-11 days	128	157	0.00%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	38 days	2209	2224	0.10%	0.00%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	1228	1229	0.00%	0.00%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	~2 weeks	1220	1239	0.40%	0.30%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.30%	0.10%	No
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	11 days	136	132	1.50%	0.00%	No
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	7-11 days	80	162	1.30%	0.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	9 days	102	104	0.00%	0.00%	No

Table 145. Individual Study Results - Clinically Important Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	Clinically relevant nonmajor bleeding	2 weeks	1596	1588	2.20%	3.00%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	Clinically relevant nonmajor bleeding	2 weeks	1501	1508	2.90%	3.80%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	35 days	2673	2659	4.10%	4.50%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	Clinically relevant bleeding	2 weeks	129	124	1.60%	2.40%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	Clinically significant bleeding	NR	385	392	4.90%	2.60%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	Composite major or clinically significant bleeding	NR	385	392	8.30%	4.60%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	Clinically relevant nonmajor bleeding	11 days	679	694	5.90%	5.30%	No

Table 145. Individual Study Results - Clinically Important Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	Clinically relevant nonmajor bleeding	5 weeks	1146	1154	4.20%	3.50%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	Clinically relevant nonmajor bleeding	17 days	857	868	2.70%	2.40%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	Clinically relevant nonmajor bleeding	3 months (not including 1st 17 days)	857	868	0.70%	0.30%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	Any Clinically Important Bleeding	NR	173	176	33.50%	23.30%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	Clinically significant minor bleeding	NR	404	391	5.00%	4.10%	No
Bailey et al. 1991	IPC + GCS	Warfarin + GCS	Hip	Moderate	Clinically important bleeding	NR	50	45	0.00%	0.00%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	7-11 days	128	157	1.60%	3.20%	No

Table 145. Individual Study Results - Clinically Important Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	38 days	2209	2224	2.90%	2.40%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	5-6 weeks	1228	1229	3.30%	2.70%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	Clinically relevant nonmajor bleeding	~2 weeks	1220	1239	2.70%	2.30%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	Clinically relevant nonmajor bleeding	day 17	1526	1508	2.60%	2.00%	No
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	Clinically relevant nonmajor bleeding	11 days	136	132	5.90%	0.00%	Yes
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	Clinically relevant nonmajor bleeding	7-11 days	80	162	1.30%	1.90%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	Clinically relevant nonmajor bleeding	9 days	102	104	2.90%	2.90%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	6 weeks	156	166	3.20%	2.40%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Clinically relevant nonmajor bleeding	9 days	156	166	2.60%	2.40%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Major or clinically relevant nonmajor bleeding	6 weeks	156	166	3.20%	3.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Major or clinically relevant nonmajor bleeding	9 days	156	166	2.60%	3.00%	No
Eriksson et al. 2007d	YM150; Mechanical Allowed (Used In 1/3)	Enoxaparin; Mechanical Allowed (Used In 1/3)	Hip	High	Clinically relevant nonmajor bleeding	~5 weeks	36	36	0.00%	0.00%	No

Table 146. Individual Study Results - Minor Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 weeks	1596	1588	2.40%	2.50%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2 weeks	1501	1508	3.40%	3.60%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	35 days	2673	2659	6.90%	7.50%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	155	149 n3:151	5.80%	4.00% g3:5.3%	No
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	High	NR	43	43	9.30%	9.30%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	7.00%	4.80%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	NR	385	392	9.60%	6.40%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	679	694	8.80%	9.90%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1146	1154	6.10%	6.40%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	day0-1	496	489	0.60%	0.40%	No

Table 146. Individual Study Results - Minor Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	day2-8	496	489	1.20%	1.60%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	NR	195	209	8.20%	5.70%	No
Colwell et al. 1995	Enoxaparin	Heparin	Knee	High	NR	228	225	18.90%	21.80%	No
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	14 days	333	332	1.80%	3.60%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	High	NR	124	112	0.80%	1.80%	No
Turpie et al. 1986	Enoxaparin	Placebo	Hip	High	14 days or until discharge	50	50	2.00%	0.00%	No
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	9.60%	5.90%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	~14 days	336	334	28.00%	24.90%	No
Samama et al. 1997	Enoxaparin + GCS	Placebo + GCS	Hip	High	10 days	85	85	38.80%	23.50%	No
Senaran et al. 2006	Enoxaparin; GCS Allowed	Heparin; GCS Allowed	Hip	High	NR	50	50	2.00%	8.00%	No
Fuji et al. 2008 (knee)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Knee	High	NR	91	89	6.60%	4.50%	No
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	High	NR	102	101	6.90%	2.00%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	8.80%	6.80%	No

Table 146. Individual Study Results - Minor Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	28.30%	21.00%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	High	~10 days	177	260	3.40%	3.10%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	NR	404	391	7.20%	6.40%	No
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Hip	High	NR	81	82	2.50%	0.00%	No
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Knee	High	NR	84	87	2.40%	3.40%	No
Paiement et al. 1987	IPC	Warfarin	Hip	Moderate	NR	66	72	4.50%	4.20%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	10 weeks	198	194	37.40%	40.20%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	7-11 days	128	157	3.90%	3.80%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	38 days	2209	2224	5.80%	5.80%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	~2 weeks	1220	1239	4.30%	4.40%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	10.20%	9.20%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	1228	1229	6.50%	5.50%	No
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	11 days	136	132	4.40%	4.50%	No
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	High	7-11 days	80	162	5.00%	4.90%	No

Table 146. Individual Study Results - Minor Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	9 days	102	104	5.90%	2.90%	No
Hull et al. 1993	Tinzaparin	Warfarin	Knee	High	NR	317	324	1.60%	1.50%	No
Hull et al. 1993	Tinzaparin	Warfarin	Hip	High	NR	398	397	1.30%	2.30%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	1.40%	1.90%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	6 weeks	156	166	3.80%	3.00%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	9 days	156	166	3.80%	3.00%	No
Eriksson et al. 2007d	YM150; Mechanical Allowed (Used In 1/3)	Enoxaparin; Mechanical Allowed (Used In 1/3)	Hip	High	~5 weeks	36	36	19.40%	22.20%	No

Table 147. Individual Study Results - Any Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
McKenna et al. 1980	Aspirin (≥300mg/Day)	IPC; Group 3: Placebo	Knee	Moderate	Active bleeding	NR	12	10; n3:12	8.30%	0.00%; g3: 0%	No
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	All bleeding	2 weeks	1596	1588	5.30%	6.80%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	All bleeding	2 weeks	1501	1508	6.90%	8.40%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	All bleeding	35 days	2673	2659	11.70%	12.60%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	All bleeding	6 weeks	155	149; n3:151	7.10%	5.40%; g3:5.3%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	Any bleeding	2 weeks	129	124	10.90%	8.10%	No
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Hip	High	Any bleeding	NR	81	82	4.90%	0.00%	Yes
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Knee	High	Any bleeding	NR	84	87	3.60%	4.60%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	Any bleeding	38 days	2209	2224	6.00%	5.90%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	Any bleeding	~2 weeks	1220	1239	4.90%	4.80%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	Any bleeding	day 17	1526	1508	10.50%	9.40%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Any bleeding	6 weeks	156	166	7.10%	5.40%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	Any bleeding	9 days	156	166	6.40%	5.40%	No
Colwell et al. 1995	Enoxaparin	Heparin	Knee	High	Bleeding at nonoperative site	NR	228	225	17.10%	20.90%	No

Table 147. Individual Study Results - Any Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 1995	Enoxaparin	Heparin	Knee	High	Bleeding at operative site	NR	228	225	3.90%	2.20%	No
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	Moderate	Bleeding complications	NR	166	146	3.60%	5.50%	No
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	High	Bleeding complications	NR	110	110; n3:110 n4:110	8.20%	2.7%; g3:3.6% g4:2.7%	No
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	High	Bleeding complications	NR	108	111	3.70%	0.00%	Yes
Moskovitz et al. 1978	Heparin + GCS	GCS	Hip	High	Bleeding complications	NR	35	32	54.30%	28.10%	No
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	High	Bleeding complications	NR	110	110	3.60%	3.60%	No
Agnelli et al. 2007	LY517717	Enoxaparin	Both	High	Bleeding events (major and minor)	~1 week	106	90	0.90%	2.20%	No
Santori et al. 1994	Heparin	Foot Pump	Hip	Moderate	Bleeding problems or wound hematoma	NR	65	67	13.80%	0.00%	Yes
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	Both Major and Minor Bleeding	NR	1516	1495	0.60%	0.30%	No
Eriksson et al. 1991	Dalteparin	Heparin	Hip	High	Excessive bleeding (>3000 ml)	NR	67	69	1.50%	7.20%	No
Mannucci et al. 1976	Heparin	None	Hip	Moderate	Excessive operative bleeding	NR	45	51	20.00%	21.60%	No
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + Ipc	Knee	Moderate	Internal bleeding complication	NR	129	135	0.80%	0.00%	No

Table 147. Individual Study Results - Any Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	Operative site bleeding	NR	271	279	4.40%	1.10%	No
Bauer et al. 2001	GCS Recommended Fondaparinux;	GCS Recommended Enoxaparin;	Knee	High	Other bleeding	11 days	517	517	2.70%	3.70%	No
Lassen et al. 2002	GCS Recommended Fondaparinux;	GCS Recommended Enoxaparin;	Hip	High	Other bleeding	11 days	1140	1133	3.90%	3.40%	No
Turpie et al. 2002	GCS Recommended	GCS Recommended	Hip	High	Other bleeding	11 days	1128	1129	1.50%	2.10%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	Other bleeding complications	NR	271	279	5.90%	3.60%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	Potentially significant non-overt bleeding	6 weeks	155	149; n3:151	0.60%	1.30%; g3:0%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	Surgical bleeding complications	10 days	277	277	2.90%	2.50%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	Trivial bleeding	day0-1	496	489	1.20%	1.80%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	Trivial bleeding	day2-8	496	489	3.80%	2.70%	No

Table 147. Individual Study Results - Any Bleeding

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Urinary bleeding requiring rehospitalization	10 weeks	198	194	0.00%	0.50%	No
Harris et al. 1974	Aspirin (≥300mg/Day) + GCS	Warfarin + GCS; Group 3: Heparin + GCS	Hip	High	Wound-bleeding complications	NR	51	55; n3:20	2.00%	18.2%; g3:20%	Yes

Table 148. Individual Study Results - Transfusion

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	Bleed requiring transfusion: hematemesis or melena	35 days	2047	2041	0.30%	0.10%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	Bleed requiring transfusion: other bleed	35 days	2047	2041	2.30%	2.90%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	Bleed requiring transfusion: wound bleed >=4 days	35 days	2047	2041	0.50%	0.60%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	Need for transfusion	NR	404	391	33.20%	36.10%	No
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	High	Patients Requiring Transfusion in 1st Postoperative Week	NR	43	43	48.80%	20.90%	Yes
Bonneux et al. 2006	Fondaparinux + GCS	Enoxaparin + GCS	Knee	High	Postoperative Transfusions	NR	55	54	12.70%	9.30%	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	Postoperative Transfusions	11 days	517	517	42.90%	38.10%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	Postoperative Transfusions	11 days	1140	1133	62.60%	60.90%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	Postoperative Transfusions	11 days	1128	1129	52.60%	49.20%	No
Avikainen et al. 1995	Enoxaparin	Heparin	Hip	High	Postoperative Transfusions	NR	83	84	31.30%	26.20%	No

Table 148. Individual Study Results - Transfusion

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	Moderate	Transfusion after 48h	NR	166	146	0.00%	0.00%	No
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	High	Transfusion of >2 units	NR	60	61	48.30%	55.70%	No
Stone et al. 1996	IPC	Enoxaparin	Hip	Moderate	Transfusion of at least 2 units	NR	25	25	12.00%	28.00%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	Transfusions after recovery room	~14 days	336	334	42.00%	32.30%	Yes
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	High	Transfusions during surgery or in recovery room	~14 days	336	334	9.20%	9.60%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	Transfusions for replacement of operative blood loss	NR	1516	1495	66.90%	62.10%	Yes
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	Transfusions for replacement of postoperative blood loss	NR	1516	1495	2.80%	1.50%	Yes
Poller et al. 1995	Warfarin	Heparin	Both	High	Patients requiring at least 3 units of red cells during surgery	NR	31	37	9.70%	8.10%	No

Table 149. Individual Study Results - Wound Hematoma – Severe/Complicated/Requiring Intervention

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Sharrock et al. 1990	Heparin + Aspirin (≥300mg/Day) + GCS	Aspirin (≥300mg/Day) + GCS	Hip	Moderate	Deep hematoma	NR	60	66	3.30%	1.50%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	Evacuation of hematoma	35 days	2047	2041	0.80%	0.40%	No
Eriksson et al. 1991	Dalteparin	Heparin	Hip	High	Evacuation of hematoma	NR	67	69	0.00%	0.00%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	Hematoma necessitating treatment	NR	138	136	0.00%	0.00%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Hematoma requiring prolonged hospitalization	10 weeks	198	194	0.00%	0.50%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Hematoma requiring rehospitalization	10 weeks	198	194	0.00%	0.50%	No
Avikainen et al. 1995	Enoxaparin	Heparin	Hip	High	Revisions due to wound hematomas	NR	83	84	0.00%	0.00%	No
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	Both	High	Surgical intervention due to hematoma or infection	NR	116	130	0.00%	0.00%	No

Table 149. Individual Study Results - Wound Hematoma – Severe/Complicated/Requiring Intervention

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	Wound hematoma, Complicated	NR	496	489	0.40%	0.20%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	Wound hematoma, Complicated	NR	715	721	0.40%	0.40%	No
Hume et al. 1973	Heparin + GCS	GCS; Group 3: Warfarin + GCS	Hip	Moderate	Wound hematoma, major	NR	18	19; n3:17	38.90%	5.30% g3:5.9%	Yes
Torholm et al. 1991	Dalteparin	Placebo	Hip	High	Wound hematoma, severe	NR	58	54	0.00%	0.00%	No

Table 150. Individual Study Results - Wound Hematoma

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Kim et al. 1998	Aspirin (≥300mg/Day)	None	Hip	Moderate	NR	50	50	0.00%	2.00%	No
Harris et al. 1977	Aspirin (≥300mg/Day)	Placebo	Hip	High	NR	44	51	6.80%	2.00%	No
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	High	NR	43	43	9.30%	16.30%	No
Woolson et al. 1991	Aspirin (≥300Mg/Day) + GCS + IPC	GCS + IPC; Group 3: Warfarin + GCS + IPC	Hip	Moderate	NR	70	73; n3:69	1.40%	1.40%; g3:1.4%	No
Dechavanne et al. 1989	Dalteparin	Heparin	Hip	High	NR	41	40	9.80%	10.00%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	2.00%	3.30%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	10.30%	9.20%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	NR	1028	1023	8.30%	7.90%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	NR	277	277	5.10%	5.40%	No
Warwick et al. 1995	Enoxaparin + GCS	GCS	Hip	High	NR	78	78	0.00%	3.80%	No
Fauno et al. 1994	Enoxaparin + GCS	Heparin + GCS	Knee	High	NR	92	93	8.70%	12.90%	No
Mannucci et al. 1976	Heparin	None	Hip	Moderate	NR	45	51	20.00%	0.00%	Yes
VTCSG 1975	Heparin	None	Hip	Moderate	NR	30	30	13.30%	10.00%	No

Table 150. Individual Study Results - Wound Hematoma

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Sharrock et al. 1990	Heparin + Aspirin (≥300mg/Day) + GCS	Aspirin (≥300mg/Day) + GCS	Hip	Moderate	NR	60	66	1.70%	0.00%	No
Hume et al. 1973	Heparin + GCS	GCS; Group 3: Warfarin + GCS	Hip	Moderate	NR	18	19; n3:17	16.70%	0.00% g3:29.4%	Yes
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	6.70%	3.60%	Yes
Hull et al. 1993	Tinzaparin	Warfarin	Knee	High	NR	317	324	8.80%	5.90%	No
Hull et al. 1993	Tinzaparin	Warfarin	Hip	High	NR	398	397	5.80%	2.50%	No
Barber et al. 1977	Warfarin	Heparin	Hip	Moderate	NR	58	19	24.10%	15.80%	No
Fordyce et al. 1991	Warfarin	Placebo	Hip	High	NR	74	74	8.10%	10.80%	No

Table 151. Individual Study Results - Deep Wound Infection

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	Deep wound infection	10 days	1028	1023	0.20%	0.20%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	Deep infection	NR	223	220	0.00%	0.00%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	Reoperation due to infection	10 days	277	277	0.70%	0.00%	No
Barber et al. 1977	Warfarin	Heparin	Hip	Moderate	Deep wound infection	NR	58	19	0.00%	0.00%	No

Table 152. Individual Study Results - Wound Infection

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	155	149; n3:151	1.90%	0.70%; g3:2.0%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	High	35 days	2047	2041	0.60%	0.90%	No
Dechavanne et al. 1989	Dalteparin	Heparin	Hip	High	NR	41	40	0.00%	5.00%	No
Torholm et al. 1991	Dalteparin	Placebo	Hip	High	NR	58	54	3.40%	0.00%	No
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	High	NR	60	61	0.00%	0.00%	No
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	High	1 month	110	110 n3:110 n4:110	0.00%	1.80% g3:0.9% g4:1.8%	No
Avikainen et al. 1995	Enoxaparin	Heparin	Hip	High	NR	83	84	0.00%	0.00%	No
Fauno et al. 1994	Enoxaparin + GCS	Heparin + GCS	Knee	High	NR	92	93	1.10%	3.20%	No
Moskovitz et al. 1978	Heparin + GCS	GCS	Hip	High	NR	35	32	0.00%	0.00%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	38 days	2209	2224	0.40%	0.40%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	High	5-6 weeks	1228	1229	0.70%	0.50%	No
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	High	~2 weeks	1220	1239	0.60%	0.90%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	1526	1508	0.30%	0.20%	No

Table 152. Individual Study Results - Wound Infection

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Fordyce et al. 1991	Warfarin	Placebo	Hip	High	NR	74	74	0.00%	1.40%	No

Table 153. Individual Study Results - GI Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Haas et al. 1990	Aspirin (≥300mg/Day)	IPC	Knee	Moderate	NR	58	61	0.00%	0.00%	No
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	High	NR	43	43	7.00%	2.30%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	3 months	113	118	0.00%	0.80%	No
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	High	NR	60	61	0.00%	0.00%	No

Table 154. Individual Study Results - Injection-Site Hematoma

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 1991	Dalteparin	Heparin	Hip	High	NR	67	69	3.00%	10.10%	No
Torholm et al. 1991	Dalteparin	Placebo	Hip	High	NR	58	54	0.00%	0.00%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	10 days	1028	1023	2.80%	0.60%	Yes
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	10 days	277	277	9.70%	10.80%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	NR	223	220	1.80%	1.80%	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	Moderate	NR	105	105	62.90%	19.00%	Yes

Table 155. Individual Study Results - Other Wound or Bleeding Complications

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Anemia requiring prolonged hospitalization	10 weeks	198	194	0.00%	2.60%	Yes
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Anemia with hypotension requiring intervention	10 weeks	198	194	0.00%	1.00%	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	High	Dehiscence	10 days	277	277	0.40%	0.40%	No
Warwick et al. 1995	Enoxaparin + GCS	GCS	Hip	High	Discharge from drain sites which persisted beyond the 6th postop day	NR	78	78	21.80%	10.30%	No
Harris et al. 1974	Aspirin (≥300mg/Day) + GCS	Warfarin + GCS; Group 3: Heparin + GCS	Hip	High	Distant complications	NR	51	55; n3:20	2.00%	10.90% g3:0%	Yes
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	Hemoglobin decreased	NR	404	391	11.90%	11.00%	No
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	High	Low Hemoglobin (<9 g/dL)	NR	60	61	6.70%	11.50%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	High	Major complications	NR	113	118	1.80%	0.80%	No
Haas et al. 1990	Aspirin (≥300mg/Day)	IPC	Knee	Moderate	Wound complications	NR	58	61	8.60%	9.80%	No

Table 155. Individual Study Results - Other Wound or Bleeding Complications

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	Wound Dehiscence	10 days	1028	1023	0.60%	0.50%	No
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	High	Wound drainage over 500ml in 72h	NR	60	61	13.30%	16.40%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Wound drainage requiring rehospitalization	10 weeks	198	194	0.00%	0.50%	No
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Moderate	Wound drainage requiring rehospitalization	NR	198	194	0.00%	0.50%	No
Westrich et al. 2005	Heparin + Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	Hip	High	Wound or bleeding complications	NR	69	65	0.00%	0.00%	No
Bonneux et al. 2006	Fondaparinux + GCS	Enoxaparin + GCS	Knee	High	Wound problems	NR	55	54	7.30%	7.40%	No
Stone et al. 1996	IPC	Enoxaparin	Hip	Moderate	Wound problems	NR	25	25	4.00%	0.00%	No
Torholm et al. 1991	Dalteparin	Placebo	Hip	High	Wound rupture	NR	58	54	0.00%	1.90%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	Wound rupture	NR	223	220	0.00%	0.00%	No

Table 156. Individual Study Results - Symptomatic DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	2 months	1599	1596	0.40%	0.60%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	2.5 months	1528	1529	0.30%	0.50%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	95 days	2708	2699	0.00%	0.30%	Yes
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	High	6 weeks	105	109 n3:109	1.90%	0.90% g3:0.9%	No
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	Moderate	35 days	2047	2041	0.70%	0.90%	No
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC (Rapid Inflation Asymmetrical Compression Device)	Aspirin (≥300mg/Day) + IPC (Sequential Compression Device)	Knee	High	NR	206	217	0.00%	0.00%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	High	3 months	1001	992	0.10%	0.40%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	High	2 weeks	129	124	0.80%	1.60%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	5 weeks	283	300	0.70%	0.30%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	11 days	675	685	0.10%	1.20%	Yes

Table 156. Individual Study Results - Symptomatic DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	High	5 weeks	1137	1142	0.50%	0.10%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	High	3 months (not including 1st 17 days)	604	643	0.30%	0.30%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	337	338	1.50%	4.40%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	High	6 weeks	802	785	1.00%	0.90%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	44 days	180	180	2.20%	2.80%	No
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	1.40%	0.90%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	High	NR	138	136	1.40%	0.70%	No
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	Moderate	3 months	141	136	0.70%	0.70%	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	High	11 days	517	517	0.60%	0.80%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1129	1123	0.30%	0.10%	No
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	High	11 days	1126	1128	0.40%	0.00%	Yes

Table 156. Individual Study Results - Symptomatic DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Hull et al. 1990	IPC	None	Hip	Moderate	3 months	152	158	1.30%	0.60%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	High	1-2 months	113	107	0.00%	0.90%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	High	day 17	965	959	0.60%	1.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	~ 1 week	102	104	0.00%	1.90%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	High	9 days	114	127	0.00%	0.00%	No

Table 157. Individual Study Results - DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	Low	2 weeks	971	997	14.60%	24.40%	Yes
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	Moderate	2 weeks	1142	1122	7.80%	8.20%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	Low	35 days	1944	1911	1.10%	3.60%	Yes
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	Moderate	12 days	105	109; n3:109	10.50%	12.80% g3:25.7%	Yes
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	Moderate	7-9 days	166	146	56.60%	53.40%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	Moderate	7 days	113	118	6.20%	7.60%	No
Westrich et al. 2006†	Aspirin (≥300mg/Day) + IPC	Enoxaparin + IPC	Knee	Moderate	4-6 weeks	129	135	17.80%	14.10%	No
Lachiewicz et al. 2004†	Aspirin (≥300mg/Day) + IPC (Rapid Inflation Asymmetrical Compression Device)	Aspirin (≥300mg/Day) + IPC (Sequential Compression Device)	Knee	Moderate	NR	206	217	7.30%	15.70%	Yes
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	Low	NR	791	783	7.60%	8.60%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	Moderate	7 days	283	300	16.60%	24.00%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	17 days	604	643	30.00%	24.60%	No

Table 157. Individual Study Results - DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	11 days	503	511	36.00%	36.00%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	Moderate	5 weeks	874	894	4.60%	6.30%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	NR	192	190	14.60%	25.80%	Yes
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	Moderate	day 6	337	338	10.70%	24.00%	Yes
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	Moderate	10 days	773	768	18.40%	25.50%	Yes
Eriksson et al. 1996	Desirudin	Heparin	Hip	Moderate	10 days	202	229	18.30%	33.60%	Yes
Eriksson et al. 1997	Desirudin	Heparin	Hip	Moderate	10 days	180	180	7.20%	23.30%	Yes
Chin et al. 2009†	Enoxaparin	Group 3: GCS; Group 4: IPC; Group 5: No Treatment	Knee	Moderate	NR	110	n3:110 n4:110	5.50%	12.70% g3:8.2% g4:21.8%	Yes
Colwell et al. 1994	Enoxaparin	Heparin	Hip	Moderate	7 days	194	207	4.60%	11.60%	Yes
Colwell et al. 1995	Enoxaparin	Heparin	Knee	Moderate	NR	228	225	24.60%	33.80%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	Moderate	12 days	120	108	12.50%	25.00%	No

Table 157. Individual Study Results - DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	20.10%	21.70%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	Moderate	~14 days	206	211	36.90%	51.70%	Yes
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	Low	NR	89	99	53.90%	57.60%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	Moderate	NR	138	136	13.00%	17.60%	No
Edwards et al. 2008†	Enoxaparin + IPC	Enoxaparin	Both	Low	discharge	141	136	3.50%	11.00%	No
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	Moderate	NR	80	86	33.80%	41.90%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	Moderate	NR	173	176	25.40%	44.90%	Yes
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	Moderate	4-5 weeks	115	171	1.70%	9.40%	Yes
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	Moderate	11 days	361	361	12.50%	27.10%	Yes
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	908	918	4.00%	9.00%	Yes
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	784	796	5.60%	8.20%	No
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	Both	Moderate	NR	116	130	1.70%	6.20%	No
Hull et al. 1990	IPC	None	Hip	Moderate	~14 days	152	158	23.70%	48.70%	Yes
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	Moderate	NR	98	103	26.50%	31.10%	No

Table 157. Individual Study Results - DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2010†	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Low	10 days	196	190	4.10%	4.20%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	965	959	5.70%	7.90%	No
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	Moderate	6-10 days	113	107	10.60%	25.20%	Yes
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	36 days	1595	1558	0.80%	3.40%	Yes
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	5-6 weeks	864	869	1.60%	8.20%	Yes
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	824	878	9.60%	18.20%	Yes
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	Moderate	9 days	109	106	13.80%	17.00%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	Moderate	~ 1 week	102	104	20.60%	29.80%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	Moderate	NR	590	617	31.40%	37.40%	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	Moderate	NR	93	97	31.20%	45.40%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	Moderate	9 days	114	127	19.30%	18.90%	No

†: these studies used ultrasound rather than venography

Table 158. Individual Study Results - Proximal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	Low	2 weeks	1192	1199	0.80%	2.20%	Yes
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	Low	35 days	2196	2190	0.30%	0.90%	Yes
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	Moderate	2 weeks	1254	1207	0.70%	0.90%	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	Moderate	12 days	105	109; n3:109	1.90%	2.80% g3:1.8%	No
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	Moderate	NR	166	146	9.60%	12.30%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	Moderate	7 days	113	118	0.00%	0.80%	No
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + IPC	Knee	Moderate	4-6 weeks	129	135	2.30%	3.70%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	Low	4-5 weeks	804	792	2.10%	3.90%	No
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	Moderate	2 weeks	102	104	0.00%	5.80%	Yes
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	Moderate	7 days	283	300	2.10%	5.70%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	11 days	506	510	2.60%	3.10%	No

Table 158. Individual Study Results - Proximal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	Moderate	5 weeks	905	914	2.00%	3.50%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	17 days	604	643	2.30%	1.60%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	NR	192	190	5.20%	8.40%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	Moderate	day 6	354	363	0.80%	3.00%	No
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	Moderate	10 days	802	785	4.50%	7.50%	Yes
Eriksson et al. 1996	Desirudin	Heparin	Hip	Moderate	10 days	202	229	3.00%	19.70%	Yes
Eriksson et al. 1997	Desirudin	Heparin	Hip	Moderate	10 days	180	180	1.70%	8.90%	Yes
Chin et al. 2009	Enoxaparin	GCS; Group 3:IPC; Group 4: No Treatment	Knee	Moderate	NR	110	110 n3:110 n4:110	0.90%	0.90% g3:0.0% g4:2.7%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	Moderate	7 days	194	207	2.10%	4.80%	No
Colwell et al. 1995	Enoxaparin	Heparin	Knee	Moderate	NR	228	225	2.20%	9.80%	Yes
Planes et al. 1988	Enoxaparin	Heparin	Hip	Moderate	12 days	120	108	7.50%	18.50%	No

Table 158. Individual Study Results - Proximal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	10.50%	9.50%	No
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	Moderate	~14 days	206	211	11.70%	10.40%	No
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	Low	NR	89	99	0.00%	4.00%	Yes
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	Moderate	NR	138	136	8.70%	12.50%	No
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	Moderate	NR	80	86	7.50%	10.50%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	Moderate	NR	173	176	1.70%	11.40%	Yes
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	Moderate	10 days	115	171	0.90%	2.90%	No
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	High	42 days	400	395	4.80%	4.10%	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	Moderate	11 days	368	372	2.40%	5.40%	No
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	922	927	0.70%	2.50%	Yes
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	816	830	1.70%	1.20%	No
Hull et al. 1990	IPC	None	Hip	Moderate	~14 days	152	158	14.50%	26.60%	Yes
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	Moderate	NR	98	103	12.20%	2.90%	Yes
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Low	10 days	196	190	1.50%	1.10%	No

Table 158. Individual Study Results - Proximal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	Moderate	6-10 days	113	107	2.70%	2.80%	No
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	36 days	1595	1558	0.10%	2.00%	Yes
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	5-6 weeks	864	869	0.60%	5.10%	Yes
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	824	878	1.10%	2.30%	No
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	965	959	0.30%	1.40%	Yes
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	Moderate	9 days	109	106	0.90%	4.70%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	Moderate	~ 1 week	102	104	1.00%	2.90%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	Moderate	NR	590	617	6.10%	7.60%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	Moderate	9 days	114	127	4.40%	3.90%	No

Table 159. Individual Study Results - Distal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	Moderate	NR	166	146	47.00%	41.10%	No
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	Moderate	7 days	113	118	6.20%	6.80%	No
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + IPC	Knee	Moderate	4-6 weeks	129	135	15.50%	10.40%	No
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	Low	4-5 weeks	792	785	5.40%	4.50%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	Moderate	7 days	283	300	15.20%	22.30%	No
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	11 days	503	511	33.40%	32.90%	No
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	Moderate	5 weeks	874	894	2.50%	2.70%	No
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	Moderate	17 days	604	643	27.60%	23.00%	No
Francis et al. 1997	Dalteparin	Warfarin	Hip	Moderate	NR	192	190	10.90%	22.60%	Yes

Table 159. Individual Study Results - Distal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	Moderate	NR	110	110; n3:110 n4:110	4.50%	11.80% g3:8.2% g4:19.1%	Yes
Colwell et al. 1994	Enoxaparin	Heparin	Hip	Moderate	7 days	194	207	2.10%	5.30%	No
Colwell et al. 1995	Enoxaparin	Heparin	Knee	Moderate	NR	228	225	22.40%	24.00%	No
Planes et al. 1988	Enoxaparin	Heparin	Hip	Moderate	12 days	120	108	5.00%	6.50%	No
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	Low	NR	89	99	53.90%	53.50%	No
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	Moderate	NR	138	136	4.30%	5.10%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	Moderate	NR	173	176	23.70%	33.50%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	Moderate	10 days	115	171	0.90%	7.60%	Yes
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	Moderate	11 days	372	366	9.40%	21.30%	Yes
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	909	917	3.30%	7.30%	Yes
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	Moderate	11 days	796	800	4.30%	6.80%	No
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	Moderate	NR	98	103	6.10%	19.40%	Yes
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	Low	10 days	196	190	2.60%	3.20%	No

Table 159. Individual Study Results - Distal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	Moderate	6-10 days	113	107	8.00%	22.40%	Yes
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	36 days	1595	1558	0.70%	1.40%	No
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	Moderate	5-6 weeks	864	869	1.00%	3.10%	Yes
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	824	878	8.50%	15.90%	Yes
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	Moderate	day 17	965	959	5.40%	6.60%	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	Moderate	~ 1 week	102	104	19.60%	26.90%	No
Eriksson et al. 2010	YM150	Enoxaparin	Hip	Moderate	9 days	114	127	14.90%	15.00%	No

Table 160. Individual Study Results - Thrombocytopenia

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	High	NR	102	104	0.00%	0.00%	No
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	High	NR	385	392	0.30%	0.30%	No
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	High	NR	177	260	0.00%	0.00%	No
Senaran et al. 2006	Enoxaparin; GCS Allowed	Heparin; GCS Allowed	Hip	High	NR	50	50	0.00%	2.00%	No
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	High	NR	219	221	0.00%	0.00%	No
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	High	NR	1516	1495	0.10%	0.00%	No
Colwell et al. 1994	Enoxaparin	Heparin	Hip	High	NR	195	209	0.00%	1.00%	No
Eriksson et al. 1997	Desirudin	Heparin	Hip	High	NR	223	220	0.00%	0.90%	No
Sharrock et al. 1990	Heparin + Aspirin (≥300mg/Day) + GCS	Aspirin (≥300mg/Day) + GCS	Hip	Moderate	NR	60	66	0.00%	0.00%	No
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	High	NR	1596	1588	0.20%	0.30%	No
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	High	NR	1501	1508	0.00%	0.10%	No
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	High	NR	2673	2659	0.00%	0.10%	No
Dechavanne et al. 1989	Dalteparin	Heparin	Hip	High	NR	41	40	0.00%	0.00%	No
Eriksson et al. 1991	Dalteparin	Heparin	Hip	High	NR	67	69	0.00%	0.00%	No

Table 160. Individual Study Results - Thrombocytopenia

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Levine et al. 1991	Enoxaparin	Heparin	Hip	High	NR	333	332	0.00%	0.00%	No
Hull et al. 1993	Tinzaparin	Warfarin	Both	High	NR	715	721	0.00%	0.00%	No
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	High	NR	173	176	0.00%	0.00%	No
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	High	NR	496	489	0.00%	0.00%	No

Table 161. Duration of Prophylaxis Studies - Fatal Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	NR	117	110	0.00%	0.00%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	from discharge to discharge + 3months	117	116	0.00%	0.00%	No
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	day 35	422	420	0.00%	0.00%	No
Prandoni et al. 2002	Warfarin for 28 days after discharge	Warfarin until discharge (~9 days)	Hip	Moderate	2 months following 1st 4 weeks	184	176	0.00%	0.00%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	day6-day35 (i.e. not including day0-6)	199	180	0.00%	0.00%	No

Table 162. Duration of Prophylaxis Studies - Symptomatic PE

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	day7-35	111	106	0.00%	2.80%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	High	1 month	217	221	0.00%	0.90%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	High	1 month	224	211	0.00%	0.50%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	1 month	441	432	0.00%	0.70%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	from discharge to discharge + 18-19 days	117	116	0.00%	1.70%	No
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	day 35	422	420	0.20%	0.50%	No
Prandoni et al. 2002	Warfarin for 28 days after discharge	Warfarin until discharge (~9 days)	Hip	Moderate	4 weeks	184	176	0.00%	0.60%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	day6-day35 (i.e. not including day0-6)	152	133	0.00%	0.00%	No

Table 163. Duration of Prophylaxis Studies - Major Bleeding

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	1 month	441	432	0.00%	0.20%	No
Planes et al. 1996	Enoxaparin for 21 days after discharge; GCS Recommended	Enoxaparin until discharge, then Placebo for 21 days; GCS Recommended	Hip	High	NR	90	89	0.00%	0.00%	No
Manganelli et al. 1998	Heparin for 30 days	Heparin until discharge	Hip	Moderate	discharge-day45	28	33	0.00%	0.00%	No
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	day 35	422	420	0.70%	0.50%	No
Prandoni et al. 2002	Warfarin for 28 days after discharge	Warfarin until discharge (~9 days)	Hip	Moderate	4 weeks	184	176	0.50%	0.00%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	day6-day35 (i.e. not including day0-6)	199	180	0.00%	0.00%	No
Lassen et al. 1998	Dalteparin for 35 days; GCS Allowed	Dalteparin for 7 days, then Placebo for 28 days; GCS Allowed	Hip	High	35 days	140	141	0.00%	0.70%	No
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	NR	117	110	0.00%	0.00%	No

Table 164. Duration of Prophylaxis Studies - All Cause Mortality

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	day7-35	117	110	0.90%	0.90%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	1 month	441	432	0.00%	0.20%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	3 months from randomization, not including hospitalization (~1st week postop)	117	116	0.00%	0.00%	No
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	NR	422	420	0.00%	0.00%	No
Prandoni et al. 2002	Warfarin for 28 days after discharge	Warfarin until discharge (~9 days)	Hip	Moderate	day 35	184	176	0.00%	0.00%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	day6-day35 (i.e. not including day0-6)	152	133	0.00%	0.80%	No

Table 165. Duration of Prophylaxis Studies - Symptomatic DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	from discharge to discharge + 18-19 days	117	116	1.70%	6.90%	No
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	day 35	422	420	0.50%	1.70%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	day6-day35 (i.e. not including day0-6)	152	133	2.00%	2.30%	No

Table 166. Duration of Prophylaxis Studies - Rehospitalization due to DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	NR	117	116	9.40%	27.60%	Yes

Table 167. Duration of Prophylaxis Studies - Deep Vein Thrombosis

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	Moderate	day 35 (not including day 0-7)	278	279	3.60%	12.50%	Yes
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	Moderate	1 month	217	221	17.5%	20.8%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	Moderate	1 month	224	221	8.0%	23.2%	Yes
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	Moderate	1 month	441	432	12.7%	22.0%	Yes
Lassen et al. 1998	Dalteparin for 35 days; GCS Allowed	Dalteparin for 7 days, then Placebo for 28 days; GCS Allowed	Hip	Low	day 35	113	102	4.40%	11.80%	No
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	day 35 (not including day0-7)	114	104	19.30%	31.70%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	Moderate	from discharge to discharge + 18-19 days	117	116	17.90%	38.80%	Yes
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	Moderate	day0-35	174	188	17.20%	36.70%	Yes

Table 168. Duration of Prophylaxis Studies - Proximal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Lassen et al. 1998	Dalteparin for 35 days; GCS Allowed	Dalteparin for 7 days, then Placebo for 28 days; GCS Allowed	Hip	Low	day 35	113	102	0.90%	4.90%	No
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	day 35 (not including day0-7)	114	104	8.80%	13.50%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	Moderate	1 month	217	221	4.10%	7.70%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	Moderate	1 month	224	221	2.70%	12.20%	Yes
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	Moderate	1 month	441	432	3.40%	10.20%	Yes
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	Moderate	from discharge to discharge + 18-19 days	117	116	6.80%	24.10%	Yes
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	Moderate	day 35	422	420	0.90%	1.40%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	Moderate	day0-35	162	153	3.10%	9.20%	No

Table 169. Duration of Prophylaxis Studies - Distal DVT

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	Moderate	1 month	217	221	13.40%	12.20%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	Moderate	1 month	224	211	5.40%	10.40%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	Moderate	1 month	441	432	9.30%	11.30%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	Moderate	from discharge to discharge + 18-19 days	117	116	11.10%	12.90%	No

Table 170. Duration of Prophylaxis Studies - Wound Hematoma

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Planes et al. 1996	Enoxaparin for 21 days after discharge; GCS Recommended	Enoxaparin until discharge, then Placebo for 21 days; GCS Recommended	Hip	High	Wound hematoma	NR	90	89	1.10%	1.10%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	Wound hematoma, complicated	NR	199	180	0.50%	1.10%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	Wound hematoma, uncomplicated	NR	199	180	2.50%	2.80%	No

Table 171. Duration of Prophylaxis Studies - Injection-Site Hematoma

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	NR	117	110	0.90%	0.90%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	NR	131	131	4.60%	0.80%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	High	1 month	217	221	0.50%	0.90%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	High	1 month	224	211	1.80%	1.40%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	1 month	441	432	1.10%	1.20%	No

Table 172. Duration of Prophylaxis Studies - Other Bleeding Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	High	Bleeding	1 month	217	221	3.70%	2.70%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	High	Bleeding	1 month	224	211	0.90%	2.40%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	Bleeding	1 month	441	432	2.30%	2.50%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	Trivial bleeding	day6-day35 (i.e. not including day0-6)	199	180	17.60%	8.90%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	Minor bleeding	day6-day35 (i.e. not including day0-6)	199	180	1.50%	2.80%	No
Lassen et al. 1998	Dalteparin for 35 days; GCS Allowed	Dalteparin for 7 days, then Placebo for 28 days; GCS Allowed	Hip	High	Minor Bleeding Complications	35 days	140	141	12.90%	7.80%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Knee	High	Ecchymosis	NR	217	221	0.50%	0.50%	No
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Hip	High	Ecchymosis	NR	224	211	2.70%	0.90%	No

Table 172. Duration of Prophylaxis Studies - Other Bleeding Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Comp et al. 2001	Enoxaparin for 28 days	Enoxaparin for 7 days, then Placebo for 21 days	Both	High	Ecchymosis	NR	441	432	1.60%	0.70%	No
Planes et al. 1996	Enoxaparin for 21 days after discharge; GCS Recommended	Enoxaparin until discharge, then Placebo for 21 days; GCS Recommended	Hip	High	Epistaxis	NR	90	89	1.10%	0.00%	No
Bergqvist et al. 1996	Enoxaparin for 21 days after discharge	Enoxaparin until discharge, then Placebo for 21 days	Hip	High	Hemoglobin decrease of 2g/dL	NR	131	131	1.50%	3.10%	No
Planes et al. 1996	Enoxaparin for 21 days after discharge; GCS Recommended	Enoxaparin until discharge, then Placebo for 21 days; GCS Recommended	Hip	High	Hematemesis	NR	90	89	1.10%	0.00%	No

Table 173. Duration of Prophylaxis Studies - Thrombocytopenia

Author	Group1	Group2	Joint	Strength	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Barrellier et al. 2010	LMWH for 35 days	LMWH for 10 days	Knee	High	NR	422	420	0.00%	0.00%	No
Dahl et al. 1997	Dalteparin, GCS, Dextran for 7 days, then Dalteparin for 28 more days	Dalteparin, GCS, Dextran for 7 days, then Placebo for 28 days	Hip	High	NR	117	110	0.00%	0.00%	No
Hull et al. 2000b	Dalteparin for 35 days; GCS Allowed (Used In <10%)	Warfarin until discharge, then Placebo; GCS Allowed (Used In <10%)	Hip	High	NR	199	180	3.00%	5.60%	No

Table 174. Prophylaxis Starting Time Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	All Cause Mortality	1 month	1003	997	0.40%	0.10%	No
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	High	Symptomatic PE	NR	95	101	0.00%	0.00%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Hip	High	Symptomatic PE	6 weeks	384	383	0.80%	0.50%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Knee	High	Symptomatic PE	6 weeks	619	614	1.00%	1.10%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Symptomatic PE	6 weeks	1003	997	0.90%	1.00%	No

Table 174. Prophylaxis Starting Time Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Fatal Bleeding	6 weeks	1003	997	0.00%	0.00%	No
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	High	Major bleeding	NR	103	105	4.90%	1.90%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Major bleeding	NR	65	61	1.50%	1.60%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Major Bleeding	6 weeks	1003	997	1.40%	0.70%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Wound Hematoma Requiring Reoperation	NR	65	61	0.00%	0.00%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Reoperation due to Bleeding	6 weeks	1003	997	1.10%	0.50%	No

Table 174. Prophylaxis Starting Time Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	High	Bleeding Complications	NR	103	105	10.70%	8.60%	No
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	High	Minor Bleeding	NR	103	105	5.80%	6.70%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Wound Hematoma	NR	65	61	1.50%	6.60%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Minor Bleeding	NR	65	61	0.00%	0.00%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Minor Bleeding	6 weeks	1003	997	1.40%	2.00%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Wound Infection	NR	65	61	0.00%	0.00%	No

Table 174. Prophylaxis Starting Time Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Hip	High	Symptomatic DVT	6 weeks	384	383	0.00%	0.30%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Knee	High	Symptomatic DVT	6 weeks	619	614	1.60%	1.60%	No
Colwell et al. 2006	Fondaparinux Starting 8 hours after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux starting morning of first day after surgery; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	High	Symptomatic DVT	6 weeks	1003	997	1.10%	1.10%	No
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	Moderate	Venographic DVT	1 week	95	101	38.90%	37.60%	No
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	Moderate	Proximal DVT	NR	95	101	5.30%	6.90%	No

Table 174. Prophylaxis Starting Time Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Francis et al. 1996	Adjusted-dose Warfarin starting 10-14 days preoperatively + GCS	Adjusted-dose Warfarin starting night before surgery (initial dose based on body weight) + GCS	Knee	Moderate	Distal DVT	NR	95	101	33.70%	30.70%	No
Planes et al. 1991	Enoxaparin, starting 12 hours after surgery	Enoxaparin, starting with half-dose one hour after anesthesia, then full dose 12 hours after surgery	Hip	High	Thrombocytopenia	NR	65	61	0.00%	0.00%	No
Lassen et al. 2000	Tinzaparin starting 12 hours before surgery (dosage by weight: 3500-6500IU/day)	Tinzaparin starting 2 hours before surgery (dosage by weight: 2500-4500IU/day)	Hip	Moderate	Heparin-associated Thrombocytopenia	NR	96	94	0.00%	0.00%	No

Table 175. Prophylaxis Dosage and Route of Administration Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	All Cause Mortality	10 weeks	113	109	0.00%	0.00%	No
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	Symptomatic PE	6 weeks	113	109	0.90%	0.90%	No
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	Fatal Bleeding	6 months	113	109	0.00%	0.00%	No
Wilson et al. 1994	Adjusted-dose Warfarin continued for 1 month after discharge: IPC allowed (used in 73%)	Adjusted-dose Warfarin until discharge, then 2 mg/day for 1 month; IPC allowed (used in 73%)	Both	High	Major Bleeding	NR	47	49	0.00%	0.00%	No
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	Major Bleeding	6 weeks	113	109	0.00%	0.00%	No
Feller et al. 1992	Adjusted-dose Warfarin	Warfarin 1mg/day	Hip	High	Bleeding complications		100	100	3.00%	0.00%	No
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	Hematoma	6 weeks	113	109	0.90%	0.00%	No
Wilson et al. 1994	Adjusted-dose Warfarin continued for 1 month after discharge: IPC allowed (used in 73%)	Adjusted-dose Warfarin until discharge, then 2 mg/day for 1 month; IPC allowed (used in 73%)	Both	High	Minor Bleeding	NR	47	49	2.10%	4.10%	No

Table 175. Prophylaxis Dosage and Route of Administration Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Vives et al. 2001	Adjusted-dose Warfarin for 6 weeks	Adjusted-dose Warfarin until discharge, then 2 mg/day	Both	Moderate	Symptomatic DVT	6 weeks	113	109	7.10%	4.60%	No
Feller et al. 1992	Adjusted-dose Warfarin	Warfarin 1mg/day	Hip	Moderate	Venographic DVT	NR	91	98	17.60%	30.60%	No
Feller et al. 1992	Adjusted-dose Warfarin	Warfarin 1mg/day	Hip	Moderate	Proximal DVT	NR	91	98	4.40%	11.20%	No
Feller et al. 1992	Adjusted-dose Warfarin	Warfarin 1mg/day	Hip	Moderate	Distal DVT	NR	91	98	13.20%	19.40%	No
Harris et al. 1985	Aspirin (1200mg/Day)	Aspirin (300mg/Day)	Hip	High	Major Bleeding Complications	NR	48	43	0.00%	0.00%	No
Harris et al. 1982	Aspirin (3600mg/Day)	Aspirin (1200mg/Day)	Hip	Moderate	Bleeding Complications	NR	90	92	1.10%	0.00%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	High	All Cause Mortality	NR	199	208	1.00%	0.00%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	High	Major Bleeding	7 days	199	208	3.50%	5.30%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	High	Minor Bleeding	7 days	199	208	7.00%	7.20%	No
Leyvraz et al. 1983	Heparin 3500IU every 8 hours	Adjusted-dose Heparin	Hip	High	Wound hematoma	NR	41	38	12.20%	7.90%	No

Table 175. Prophylaxis Dosage and Route of Administration Studies - All Outcomes

Author	Group1	Group2	Joint	Strength	Outcome	Duration	n1	n2	% Group 1	% Group 2	Significant Difference
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin, SC; IPC (Used In 82%) Allowed	Hip	High	Major bleeding	NR	43	41	2.30%	2.40%	No
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin, SC; IPC (Used In 82%) Allowed	Hip	High	Minor bleeding	NR	43	41	4.70%	9.80%	No
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin, SC; IPC (Used In 82%) Allowed	Hip	High	Patients receiving any postop transfusions	NR	43	41	27.90%	26.80%	No
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin, SC; IPC (Used In 82%) Allowed	Hip	High	Patients receiving 2+ transfusions	NR	43	41	16.30%	17.10%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	Moderate	Any DVT	7 days	199	208	3.00%	2.90%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	Moderate	Proximal DVT	7 days	199	208	4.50%	3.80%	No
Spiro et al. 1994	Enoxaparin 40mg once daily; GCS Allowed (Used In 57%)	Enoxaparin 30mg twice daily; GCS Allowed (Used In 57%)	Hip	Moderate	Distal DVT	7 days	199	208	6.00%	3.80%	No

INDIVIDUAL STUDY DETAILS

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Agnelli et al. 2007	LY517717	Enoxaparin	several dose groups: 25, 50, 75, 100, 125, 150; once daily, starting 6-8h after surgery, total of 6-10 doses	40mg once daily, starting evening before surgery, total of 6-10 doses	ipc devices, muscle stimulators prohibited, use of antiplatelet or anticoagulant agents discouraged
Avikainen et al. 1995	Enoxaparin	Heparin	40mg daily starting 12h preoperatively for 10 days	5000IU starting 2h before operation, second dose 12h postop	n.r.
Bailey et al. 1991	IPC + GCS	Warfarin + GCS	SCDs (6 chambers (2 thigh, 4 calf), peak pressure 40mmHg) started immediately after surgery, worn continuously except for bathing and physical therapy	10mg (7.5 for women over 70 and patients with minor liver function test abnormalities) night before surgery, 5 mg night of surgery if prothrombin time <15 sec, then maintained dose at 14-16sec (also monitored partial thromboplastin times)	graded elastic compression stockings (TED hose) used in both groups before and after surgery
Barber et al. 1977	Warfarin	Heparin	15mg loading dose 36h after surgery, none next day, 5mg day after that, then adjusted dose to maintain PR time 10-20% continued for 3 weeks	5000 units at 12h intervals starting evening before surgery for 3 weeks	n.r.
Barrellier et al. 2010	LMWH + LMWH	LMWH	continue prophylactic anticoagulant drug up to day35 (almost all used enoxaparin)	stop prophylactic therapy at day10	anticoagulant up to day7, other methods employed according to each center's usual practice

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
					after venography, investigators could extend prophylaxis with any currently available therapy; use of intermittent pneumatic compression, dextran, and any other anticoagulant, thrombolytic, or antiplatelet agent was prohibited; use of graduated-compression stockings and physiotherapy was recommended
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	2.5mg once daily and a placebo once daily, starting 6+-2h after surgery, continued until day 5-9	30mg twice daily, starting 12-24h after surgery, continued until day 5-9	
Bergqvist et al. 1996	Enoxaparin + Enoxaparin	Enoxaparin +Placebo	40mg enoxaparin once daily, starting 12h preop, continued thru hospital discharge, then 21 more days	40mg enoxaparin once daily, starting 12h preop, continued thru hospital discharge, then placebo for 21 days	n.r.
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin; IPC (Used In 82%) Allowed	heparin/SNAC 10mL (1.5g SNAC/60000 U heparin), plus s.c. saline injections every 6h for 12 doses starting 10h postop	5000U heparin s.c. plus 10 or 15mL oral control syrup (SNAC and vehicle without heparin) every 8h for 12 doses, starting 10h postop	~82% of each group used external pneumatic compression
Bonneux et al. 2006	Fondaparinux + GCS	Enoxaparin + GCS	1st injection 6-12h after operation, 2nd 18-24h after 1st, continued for 6 weeks; dosage not specified	1st injection evening before surgery, 2nd 12-24h after operation, continued for 6 weeks; dosage not specified	graduated compression stockings

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	40mg once daily until day 5-7	grp2: graduated compression stockings applied directly to both legs; grp3 intermittent pneumatic compression, 45-52mmHg; grp4: no prophylaxis	n.r.
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Fondaparinux only	Fondaparinux + graduated compression stockings for 35-49 days applied preoperatively and worn until last follow up visit; long leg stockings used unless thigh circumference necessitated use of short leg stockings	fondaparinux 2.5 mg daily for 5-9 days starting 6h after closure of the surgical wound, 2nd dose 18-24h later
Colwell et al. 1994	Enoxaparin	Heparin	30mg every 12h in grp1; 40mg once daily in grp2; 1st dose within 24h postoperative, continued a maximum of 7 days	5000 units every 8h, starting within 24h postoperatively for maximum of 7 days	n.r.
Colwell et al. 1995	Enoxaparin	Heparin	30mg every 12h, starting within 8h after surgery after adequate hemostasis, continued for 4-14 days	5000 units every 8h, starting within 8h after surgery after adequate hemostasis, continued for 4-14 days	n.r.
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	30mg every 12h starting within 24h postop, after hemostasis established, until discharge	starting dose 7.5mg, adjusted for INR 2-3, starting as early as 48h preop at investigator's discretion, definitely started within 24h postop, until discharge	no anticoagulatnts, antithrobotics, or aspirin allowed, nor pneumatic compression devices; elastic compression stockings allowed

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Colwell et al. 2006	Fondaparinux; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux; GCS (Used In 68%), IPC (Used In 54%) Allowed	2.5mg 8h after surgery and not less than 4h after removal of indwelling catheters, 2nd dose of 2.5mg at least 12h later, then continued once daily for total of 7-10 days	2.5mg on morning of 1st day after surgery, continued once daily for 7-10 days	intermittent pneumatic compression or plantar compression pump was allowed (68% used elastic compression stockings, 54% ipc); use of aspirin, nsaids, and other anti-inflammatory agents was discouraged, dextran, antiplatelet drugs other than aspirin, thrombolytic treatment, and fibrinolytic agents were prohibited
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	CECT+SFT intermittent sequential compression device, on both calves immediately after induction of anesthesia (max pressure 50mmHg), continued for 10 days, plus option of 81mg aspirin daily (at discretion of treating surgeon; used in 63% of cases)	enoxaparin 30mg every 12h until discharge (avg discharge ~3 days) and then 40mg once daily, starting morning after surgery and continued for 10 days	n.r.
Comp et al. 2001	Enoxaparin + Enoxaparin; GCS Allowed (Used In 70%)	Enoxaparin +Placebo; GCS Allowed (Used In 70%)	30mg 2x/day for 7-10 days, then 40mg once daily for 3 weeks	30mg enoxaparin 2x/day for 7-10 days, then placebo once daily for 3 weeks	70% reported use of graduated compression stockings

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Dahl et al. 1997	Dalteparin, GCS, Dextran + Dalteparin	Dalteparin, GCS, Dextran + Placebo	continue 5000IU dalteparin daily for 4 additional weeks (total of 5 weeks)	placebo	evening before operation and for the next 7 days, all patients received single dose of dalteparin 000IU, dextran-70 given day of surgery and day after, all patients wore below-knee graded elastic stockings on both legs, before operation and for first week after
Dechavanne et al. 1989	Dalteparin	Heparin	2500antiXa U every 12h for 2 days postop, then 5000 U once daily, started 2h before surgery, continued for 10-13 days	5000IU calcium heparin 2x/day for 2 days postoperatively, then dose adjusted according to APTT, continued for 10-13 days; 1st dose 2h before surgery	n.r.
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	cect device (intermittent sequential compression device, max pressure 50mmHg), starting at operation on worn for length of hospitalization	no cect device	30mg every 12h for 7-8 days after surgery starting morning after surgery
Eriksson et al. 1991	Dalteparin	Heparin	5000IU daily for 10 days, starting evening before operation	5000IU 3x/day for 10 days, starting 2h preop	n.r.
Eriksson et al. 1996	Desirudin	Heparin	15mg 2x/day for 8-11 days, starting after induction of anesthesia	5000IU heparin 3x/day for 8-11 days, starting 2h before surgery	list of prohibited drugs
Eriksson et al. 1997	Desirudin	Heparin	15mg 2x/day for 8-11 days, starting 30min before operation	5000IU sodium heparin 3x/day for 8-11 days, starting 2h before operation	list of prohibited drugs

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	15mg 2x/day for 8-12 days, starting 30min before operation	40mg once daily for 8-12 days, starting evening before surgery	n.r.
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	300mg once daily; 1st dose 1-4h after surgery	40mg once daily starting evening before surgery, continued until venography (6-10 days)	elastic compression stockings and nsaids, including low-dose aspirin, were allowed, pneumatic compression devices not allowed
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	5mg every 12h, starting 6-8h after surgery and continuing for 5-9 days	40mg once daily for 5-9 days, starting evening before surgery	elastic compression stockings were allowed, ipc not
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	5mg every 12h, starting 6-8h after surgery and continuing for 5-9 days	40mg once daily for 5-9 days, starting evening before surgery	intermittent pneumatic compression not allowed
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	5mg every 12h, starting 6-8h after surgery and continuing for 5-9 days	40mg once daily for 5-9 days, starting evening before surgery	elastic compression stockings were allowed, ipc not
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	220 mg, once daily for 6-10 days, starting with half dose 1-4h after surgery	40mg once daily starting evening before surgery, continued for 6-10 days	elastic compression stockings and low-dose aspirin and cox2 inhibitors, were allowed, pneumatic compression devices not allowed
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	220mg, once daily for 28-35 days, starting with half dose 1-4h after surgery	40mg once daily starting evening before surgery, continued for 28-35 days	elastic compression stockings and low-dose aspirin and cox2 inhibitors, were allowed, pneumatic compression devices not allowed

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Eriksson et al. 2007d	YM150; Mechanical Allowed (Used In 1/3)	Enoxaparin; Mechanical Allowed (Used In 1/3)	several dose groups of ym150: 3, 10, 30, 60mg once daily, starting 6-10h postop, continued for 7-10 days	40mg once daily, starting 12h before surgery, continued for 7-10 days	about 1/3 used nonpharmacological prophylaxis; after venography, patients could continue on nonstudy drug prophylaxis
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	10mg once daily for 31-39 days, starting 6-8h after surgery	40mg once daily for 31-39 days, starting 12h before surgery	n.r.
Eriksson et al. 2010	YM150	Enoxaparin	several dose groups of ym150: 5, 10, 30, 60, or 120mg once daily, starting 6-10h after wound closure, continued for 5 weeks	40mg once daily, starting 12h before surgery, continued for 5 weeks	n.r.
Eriksson et al. 2011	Dabigatran	Enoxaparin	220mg once daily, starting 1-4h after surgery, continued for 28-35 days	40mg once daily, starting the evening before surgery, continued for 28-35 days	no ipc or high dose aspirin allowed
Fauno et al. 1994	Enoxaparin + GCS	Heparin + GCS	40mg once daily starting evening before operation, continuing for 7-10 days	5000IU 3x daily starting evening before operation, continuing for 7-10 days	compression stockings
Feller et al. 1992	Warfarin	Warfarin	1mg daily starting night before surgery and continued for 14 days	adjusted dose with target INR 2-4	n.r.
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	30mg every 12h starting as soon as hemostasis achieved and within 8h after surgical wound closure, continued for 4-14 days	7.5mg initial dose (as soon as hemostasis achieved and within 8h after surgical wound closure), then INR 2-3, continued for 4-14 days	graduated compression stockings were allowed

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Fordyce et al. 1991	Warfarin	Placebo	1mg warfarin daily for 1 week before and 3 weeks after surgery	placebo	n.r.
Fordyce et al. 1992	Foot Pump + GCS	GCS	A-V Impulse System (foot pump) used when patient in bed or sitting at rest	no foot pump	graduated compression stockings for both legs applied in recovery room
Francis et al. 1992	IPC + GCS	Warfarin + GCS	external pneumatic compression (6 chambers, 2 thigh, 4 calf) pressure 35-55mmHg, starting immediately before surgery and worn at all times while in bed, continued until venography at 6-8 days postop	starting 10-14 days preoperatively, with dose adjusted to acieve PT index on day of surgery of 1.14-1.28, and 1.5 postop (corresponding to INR of 1.5 and 2.5 respectively), ,continued until venography	graduated elastic stockings (TED)
Francis et al. 1996	Warfarin + GCS	Warfarin + GCS	starting 10-14 days preoperatively, 2.5mg alternating with 5mg daily, adjusted dose to achieve INR of 1.5 on day of surgery followed by increase to target INR of 2.2-3.0, continued until venography day 5-9	starting night before surgery with initial dose based on body weight (5, 7.5, or 10mg), same dose on night of surgery, then target INR of 2.2, continued until venography postop day 5-9	thigh-high graduated elastic stockings on both legs
Francis et al. 1997	Dalteparin	Warfarin	2500IU 2h before operation, then 2500IU on evening of operation at least 6h after preoperative dose, then 5000IU once daily until venography performed ~7 days postoperatively	5-7.5mg (based on weight) for the 1st dose the evening before the operation, 2nd dose same as 1st, given evening of operation, then INR ~2.5 until venography	n.r.

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	40mg qd starting 24-36h after surgery, continued for 14 days	placebo	only compression bandages and stockings were allowed
Fuji et al. 2008 (knee)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	40mg qd starting 24-36h after surgery, continued for 14 days	placebo	only compression bandages and stockings were allowed
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	2.5mg once daily dose from day2 to days11-15 (i.e. starting 24h after surgery)	placebo syringe	see article for prohibited items; stockings allowed
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	220mg once daily, starting as early as possible on day after surgery or at least 2h after removing indwelling catheter and confirming absence of abnormal bleeding from the drainage sites, continued for 11-14 days	placebo	elastic compression stockings and dressing allowed; ipc and other anticoagulants/antiplateletsnot permitted

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
				mechanical started immdiately after induction of anesthesia; for THA, used sequential pnuematic calf sleeves, for TKA operated leg was fitted with a foot sleeve for the operation and then switched to the calf sleeve, as in the other leg (device called WizAir continuous enhanced circulation therapy); advised that pump should be activated continuously without activity restrictions; also had 100mg	
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	40mg once daily starting within 12h after operation	aspirin once daily starting 12h after operation	n.r.
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	220mg, once daily for 12-15 days, starting with half dose 6-12h after surgery	30mg 2x/day for 12-15 days, starting 12-24h after surgery	elastic compression stockings and low-dose aspirin and cox2 inhibitors, were allowed, pneumatic compression devices not allowed

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Haas et al. 1990	Aspirin (≥300mg/Day)	IPC	650mg 2x/day, starting day before operation, continuing until discharge	pneumatic sequential compression boots (6 chambers (2 thigh, 4 calf), presure 35-55mmHg), starting on uninvolved extremity just before operation, and on affected extremity immediately postoperatively, worn continuously except for washing and walking, worn until lung scan at 5-7 days postop	n.r.
Hampson et al. 1974	Heparin	Placebo	5000 units calcium heparin with their preoperative medication, continued 3x/day for 7-10 days (7 days for 1st half of patients, 10 days for 2nd half)	placebo	n.r.
Harris et al. 1974	Aspirin (≥300mg/Day) + GCS	Warfarin + GCS; Group 3: Heparin + GCS	600mg starting day before surgery, 600mg twice daily postop until patients ready for discharge	warfarin: 1st dose 10mg night before operation, 5mg night of operation, then 1.5x the control value of prothrombin time, continued until patient ready for discharge; group 3: heparin: 1st 12 patients, 5000 units subcutaneously 2h before surgery and every 12h thereafter, other 8 patients switched interval to every 8h	elastic stockings used during and after the operation continuously until patient out of bed and walking 5-6 times daily, foot and ankle exercises started in recovery room and continued throughout postop period

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Harris et al. 1977	Aspirin (≥300mg/Day)	Placebo	0.6g aspirin twice daily starting the day before operation and continued until venogram and usually for additional 2 weeks	placebo	all aspirin containing compounds were discontinued at least 2 weeks before admission and prohibited throughout the study
Harris et al. 1982	Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	900mg 4x/day, starting 24h preop, continued until venography (7-10 days) with pause from night before operation until postop oral intake of food was tolerated (total of 36-48h pause)	300mg 4x/day, starting 24h preop, continued until venography (7-10 days) with pause from night before operation until postop oral intake of food was tolerated (total of 36-48h pause)	n.r.
Harris et al. 1985	Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	600mg aspirin 2x/day starting one day preoperatively, resuming when patient able to take pills by mouth (24-36h postop), continuing 10-14 days (until venography)	150mg aspirin 2x/day starting one day preoperatively, resuming when patient able to take pills by mouth (24-36h postop), continuing 10-14 days (until venography)	n.r.
Hull et al. 1990	IPC	None	sequential calf and thigh intermittent compression begun postoperatively in the recovery room (6 chambers: 2 thigh, 4 calf) max pressure 50-65mmHg, continued until discharge or for 14 days, worn continuously except while walking	no prophylaxis	n.r.

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Hull et al. 1993	Tinzaparin	Warfarin	75 Xa units per kg body weight once daily, starting 18-24h after surgery if no evident bleeding or excessive wound discharge, continued until 14th postop day or until discharge (also placebo capsule)	10mg warfarin postop on evening of surgery, then adjusted for INR 2-3, for 14 days or until discharge (also placebo injection)	n.r.
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	2500IU within 2h before surgery, then 2500IU 4h postop, then 5000IU once daily while in hospital (~6 days)	initial 10mg dose postoperatively on evening of surgery (age70+ or weight<57kg had 5mg dose), then adjusted dose for INR 2-3	25-30% used graduated compression stockings
Hull et al. 2000b	Dalteparin; Gcs Allowed (Used In <10%)	Warfarin; GCS Allowed (Used In <10%)	2500IU within 2h before surgery, then 2500IU 4h postop, then 5000IU once daily for 35 days	warfarin in hospital (see dosage in corresponding study), placebo out of hospital	<10% used graduated compression stockings; pneumatic compression and other drugs not allowed
Hume et al. 1973	Heparin + GCS	GCS; Group 3: Warfarin + GCS	heparin: 5000IU 2h preop and every 8h postop	none; group 3: warfarin, 1st dose (timing not specified) usually 10mg, then adjusted for prothrombin time at 1.5x control value	no aspirin allowed; elastic stockings were worn
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	10mg once daily for 31-39 days, starting 6-8h after surgery	40mg once daily for 10-14 days, starting 12h before surgery	n.r.
Kim et al. 1998	Aspirin (≥300mg/Day)	None	1.2 g aspirin daily in 3 doses, starting 48h before operation and ending 14 days after	no prophylaxis	n.r.

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day) + IPC	rapid inflation asymmetrical compression device (knee high sleeve with 2 chambers (45-52mmHg)	sequential compression device (knee-high sleeve with 3 chambers (45mmHg)	aspirin 325 night before surgery and 2x/day while eigher in hospital or rehab unit, either knee or thigh high compression stockings beneath the pneumatic compression devices recommended to continue at home both aspirin and compression stockings
Lassen et al. 1991	Tinzaparin + GCS	GCS	50 units anti_xa per kg body weight once daily, started 2h preop, continued for 7 days	saline once daily	thigh length graded compression stockings for both legs, applied 1h before operation, used until venography at day8-10
Lassen et al. 1998	Dalteparin + Dalteparin; GCS Allowed	Dalteparin + Placebo; GCS Allowed	dalteparin 5000 units once daily, starting 12h before operation and continuing for 7 days; then continued until day 35	dalteparin 5000 units once daily, starting 12h before operation and continuing for 7 days; then placebo until day 35	compression stockings were allowed
Lassen et al. 2000	Tinzaparin	Tinzaparin	dosage stratified by body weight: 3500, 5000, 6500IU, starting 12h before surgery, continued once daily for 8 days	dosage stratified by body weight: 2500, 3500, 4500IU, starting 2h before surgery, continued once daily for 8 days	n.r.

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
					after venography, investigators could extend prophylaxis with any currently available therapy; use of intermittent pneumatic compression, dextran, and any other anticoagulant, thrombolytic, or antiplatelet agent was prohibited; use of graduated-compression stockings and physiotherapy was recommended
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	2.5mg once daily and placebo, starting a mean of 6h after operation, continued till days 5-9	40mg enoxaparin and a placebo, starting 12h before surgery, second 12-24h after operation, continued to days 5-9	
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	2.5mg bid, started 12-24h after surgery, continued for 12 days (until venography)	enox: 30 mg 2x/day, timing same as apixaban; group 3: warfarin: INR 1.8-3, starting with 5mg on evening of day of surgery, continued for 12 days	n.r.
Lassen et al. 2008	Rivaroxaban	Enoxaparin	10mg once daily for 10-14 days, starting 6-8h after surgery	40mg once daily, starting 12h before surgery, for 10-14 days	n.r.
Lassen et al. 2009	Apixaban	Enoxaparin	2.5mg orally 2x/day and placebo injection, starting 12-24h after surgery, continued for 10-14 days	30mg s.c. every 12h and placebo tablets, starting 12-24h after surgery, continued for 10-14 days	n.r.
Lassen et al. 2010	Apixaban	Enoxaparin	2.5mg orally 2x/day and placebo injection, starting 12-24h after surgery, continued for 10-14 days	40mg/day for 10-14 days, starting 12h before surgery	n.r.

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Lassen et al. 2010b	Apixaban	Enoxaparin	2.5mg orally 2x/day and placebo injection, starting 12-24h after surgery, continued for 32-38 days	40mg/day for 32-38 days, starting 12h before surgery	n.r.
Leclerc et al. 1996	Enoxaparin	Warfarin	30mg every 12h starting morning of 1st day after surgery until 14 days or discharge, whichever first	warfarin goal of INR 2-3 using a prespecified nomogram; oral medications started evening of day of surgery, continued for 14 days or until discharge, whichever 1st	no other agents or stocking used
Levine et al. 1991	Enoxaparin	Heparin	30mg twice daily beginggin 12-24h postop and continued for 14 days or until discharge if earlier	calcium heparin 7500 units twice daily, beginning 12-24h postop and continued for 14 days or until discharge if earlier	n.r.
Leyvraz et al. 1983	Heparin	Heparin	3500IU heparin every 8h	started with 3500IU, then adjusted dose based on APTT	n.r.
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	aspirin + thigh high external pneumatic compression boots applied in recovery room, worn continously except when bathing or walking until venogram performed on postop day 6-8 (6 chambers 2 thigh, 4 calf, 35-55mmHg)	aspirin only, no boots	aspirin 325 mg 2x/day starting on day of operation continuing for 3 weeks

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	325 mg aspirin twice daily begun on day of admission for 6 weeks after surgery	10mg warfarin on night of surgery, none the next day, then daily doses adjusted to maintain the prothrombin time between 1.2-1.5 control value; convestion to aspirin prophylaxis after 7-10? days	use of aspirin-containing drugs prohibited during study; all NSAIDs discontinued 7 days before admission
Manganelli et al. 1998	Heparin	Heparin	5000IU every 8h until discharge	5000IU every 8h until discharge and continued until 30th postop day	n.r.
Mannucci et al. 1976	Heparin	None	5000 units calcium heparin 2h preop and every 8h postop until fully ambulatory on crutches	no treatment	none
McKenna et al. 1980	Aspirin (≥300mg/Day)	IPC; Group 3: Placebo	1300mg 3x/day until discharge	compression: intermittent low-pressure pneumatic compression device (2 thigh and calf cuffs that inflate alternately, max pressure 30mmHg), applied to nonoperated limb before anesthesia, and operated limb at end of operation; group 3: placebo: 1 tablet 3x/day	n.r.
Moskovitz et al. 1978	Heparin + GCS	GCS	sodium heparin, 5000 units every 8h starting morning of day of surgery continued for 7 days	placebo	compressive stockings

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Paiement et al. 1987	IPC	Warfarin	intermittent external pneumatic compression boots (6 chambers (2 thigh, 4 calf), 45-55mmHg), worn bilaterally continuosly except when washing and walking)	10mg night before operation, 5mg night of operation, then adjusted dose to maintain prothrombin time at 15 sec, continued 2 until 2 days after venogram (10th day postop)	n.r.
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	5 week of 160 mg daily enteric-coated aspirin or matching placebo started immediately after randomization (before surgery) with 1st dose chewed or broken; recommended that non-study aspirin and other NSAIDs be avoided unless specifically indicated during study	5 week of 160 mg daily enteric-coated aspirin or matching placebo started immediately after randomization (before surgery) with 1st dose chewed or broken; recommended that non-study aspirin and other NSAIDs be avoided unless specifically indicated during study	non-study aspirin taken in hospital by 5%, other NSAIDs 27%, unfractionated heparin 2%, lmwh 35%
Planes et al. 1988	Enoxaparin	Heparin	40mg daily starting 12h preoperatively and continued for 14 days or until discharge if earlier	5000IU 3x daily starting 2h before operation, continuing for 14 days or discharge if earlier	elastic bandaging of the legs
Planes et al. 1991	Enoxaparin	Enoxaparin	40mg daily starting 12h postop, continuing for ? Days (venography was performed 12-15 days)	20mg 1h after anesthesia, then 40mg daily starting 12h postop, continuing for ? Days (venography was performed 12-15 days)	elastic bandaging of the legs

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Planes et al. 1996	Enoxaparin + Enoxaparin; GCS Recommended	Enoxaparin +Placebo; GCS Recommended	40mg enoxaparin once daily, continued thru discharge, then continued for 21 more days	40mg enoxaparin once daily, continued thru discharge, then placebo for 21 more days	advised to wear compression stockings on legs during day, to avoid nsaids, other selected treatments allowed when necessary; anticoagulant agents, antiplatelet agents, and intramuscular injections not allowed
Planes et al. 1999	Enoxaparin	Tinzaparin	40mg (4000 anti-Factor IU Xa) starting 12h preoperatively, then 12h postop, then once daily	4500 anti-Factor IU Xa starting 12h preoperatively, then 12h postop, then once daily	elastic bandaging of the legs, elevation of the foot of the bed recommended but not universally applied (~70% in each group)
Poller et al. 1995	Warfarin	Heparin	1mg daily starting 7 days before surgery continued until venography (day 9-14)	5000IU 3x/day starting 2h before operation continued until venography (day 9-14)	n.r.
Prandoni et al. 2002	Warfarin + Warfarin	Warfarin + None	continue warfarin 4 more weeks, INR 2-3	discontinue warfarin at hospital discharge (~day9)	all received 5mg/d starting on 2nd preoperative day, after surgery dosage adjusted for INR 2-3
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	3x 5000 IU heparin sodium for 3 days after surgery; as the PTT did not reach 40 seconds, the dosage was increased to 3x 7500 IU on the fourth day (goal of 40 sec PTT)	40mg enoxaparin once daily as long as hospitalized (~16 days)	5000IU heparin sodium night before operation as well as in the morning and evening of the operation day; antithrombosis stockings

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	0.6g aspirin twice daily starting when able to take oral medicines, usually in the recovery room or on the morning after operation and continued until fully ambulatory, usually 3-5 weeks after operation; contraindication to aspirin: active peptic ulceration or allergy to aspirin	warfarin doses to achieve 1.5-2x prothrombin time, starting the evening after operation and continued until fully ambulatory; contraindication to warfarin: active peptic ulcer, severe diastolic hypertension, bleeding diathesis, GI bleeding, or gross hematuria	n.r.
Samama et al. 1997	Enoxaparin + GCS	Placebo + GCS	40mg once daily for 10+-2 days	placebo	gradual compression stockings
Santori et al. 1994	Heparin	Foot Pump	5000IU of calcium heparin 3x/day for 10 days, starting day before operation	AV Impulse System to both feet starting immediately after operation for 7-10 days	n.r.
Senaran et al. 2006	Enoxaparin; GCS Allowed	Heparin; GCS Allowed	40mg daily starting 12h preoperatively for 7-10 days (until discharge)	5000IU starting 8h preoperatively and continued 3x a day for 7-10 days	elastic compression stockings allowed
Sharrock et al. 1990	Heparin + Aspirin (≥300mg/Day) + GCS	Aspirin (≥300mg/Day) + GCS	1000 units of heparin 5 minutes before operation, 500 units given every 30 minutes under end of operation	placebo	650mg aspirin daily during hospitalization, elastic stockings on both limbs when pateint arrived in recovery room
Spiro et al. 1994	Enoxaparin; GCS Allowed (Used In 57%)	Enoxaparin; GCS Allowed (Used In 57%)	40mg once daily; starting within 24h after surgery, continued for as long as 7 days	30mg every 12h, starting within 24h after surgery, continued for as long as 7 days	57% used graduated compression stockings

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Stone et al. 1996	IPC	Enoxaparin	Flowtron DVT garment worn on oppposite leg during operation, second garment applied at end of procedure (Flowtron = intermittent pneumatic calf compression garment)	40mg daily beginning evening before operation coninued until discharge, usually 10 days	n.r.
Torholm et al. 1991	Dalteparin	Placebo	2500IU for 1st 2 doses (at 2h preop and 12h postop), then 5000IU once daily for 6 days	placebo	n.r.
Turpie et al. 1986	Enoxaparin	Placebo	30mg twice daily starting 12-24h after surgery continued for 14 days or until discharge	placebo twice daily starting 12-24h after surgery continued for 14 days or until discharge	n.r.
Turpie et al. 2001	Fondaparinux	Enoxaparin	once daily starting 6h after end of surgery (dose 3 mg) for 5-10 days	30mg enoxaparin every 12h starting 12-24h after end of surgery, for 5-10 days	n.r.
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	2.5mg once daily and placebo, starting 4-8h after operation, continued till days 5-9	30mg enoxaparin twice daily, starting 12-24h after surgery, for 5-9 days	after venography, investigators could extend prophylaxis with any currently available therapy; use of intermittent pneumatic compression, dextran, and any other anticoagulant, thrombolytic, or antiplatelet agent was prohibited; use of graduated-compression stockings and physiotherapy was recommended

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	5mg every 12h, starting 6-8h after surgery and continuing for 5-9 days	30mg 2x/day for 5-9 days, starting morning after surgery	elastic compression stockings were allowed, ipc not
Turpie et al. 2009	Rivaroxaban	Enoxaparin	10mg once daily for 11-15 days, starting 6-8h after surgery	30mg 2x/day for 11-15 days, starting 12-24h after surgery	n.r.
Vives et al. 2001	Warfarin	Warfarin	target PT 14-16 seconds, continued for total of 6 weeks	2mg/d during outpatient period, continued for total of 6 weeks	adjusted dose warfarin before discharge; no elastic supportive stockings were used
VTCSG 1975	Heparin	None	5000IU 2h preop and then every 8h for 10 days	none	n.r.
Warwick et al. 1995	Enoxaparin + GCS	GCS	40mg at 12h before operation, and 12 and 36h postop	no enox	bilateral thigh-length graduated compression stockings
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	40mg 12h before surgery and every 24h thereafter until 8th postop day	foot pump slippers applied in recovery room and used whenever patient was not weight-bearing (130mmHg)	graduated compression stockings for 6 weeks
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	40mg 12h before surgery and every 24h thereafter until discharge	foot pump slippers applied in recovery room and used whenever patient was not weight-bearing until discharge (130mmHg)	graduated compression stockings (below-knee)
Westrich et al. 2005	Heparin + Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	intraoperative dose of unfractionated heparin 15 U/kg	placebo	325mg 2x/day for 1 month; intermittent pneumatic compression was not used

Table 176. Individual Study Data - Treatment Details

Author	Group 1	Group 2	Group 1 Details (onset, duration, dosing)	Group 2 Details (onset, duration, dosing)	Adjuvant Interventions
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + Ipc	325 mg enteric-coated aspirin twice daily, starting on night of surgery in recovery room, and continued for 4 weeks postop	30mg twice daily starting 2h after epidural catheter removal (~48h postop) until discharge; upon discharge 40mg once daily for 3 weeks	pneumatic compression device: VenaFlow highi-flow calf compression device, used upon arrival in recovery until discharge
Wilson et al. 1994	Warfarin; IPC Allowed (Used In 73%)	Warfarin; IPC Allowed (Used In 73%)	fixed dose 2mg/d warfarin during outpatient period, continued for 1 month after discharge	adjusted dose with target PT range of 15-17 seconds, continued for 1 month after discharge	both groups had same adjusted dose warfarin before discharge; 73% used ipc
Windisch et al. 2010	Foot Pump + Enoxaparin + GCS	Enoxaparin + GCS	A-V Impulse System (foot pump), enoxaparin, stockings	no foot pump; enoxaparin and stockings	enoxaparin (40mg once daily), thigh-length anti-embolic or compression stockings
Woolson et al. 1991	Aspirin (≥300Mg/Day) + GCS + IPC	GCS + IPC; Group 3: Warfarin + GCS + IPC	650mg aspirin 2x/day starting evening before operation, and thigh-high elastic stockings and intermittent pneumatic compression boots (thigh high, 6 chambers 35-55mmHg) worn during operation and continuously until day before discharge (~7 days) except when bathed or walked	mechanical only: same as grp1 except no aspirin; group 3: mechanical and 7.5 or 10mg warfarin evening before operation, then dose to maintain prothrombin time at 1.2-1.3x control (14-16 sec)	n.r.
Yokote et al. 2011	Fondaparinux + IPC	Enoxaparin + IPC; Group 3: Placebo + IPC	2.5mg once daily for 10 days, starting 18h postop + IPC device for 2 days	20mg 2x/day for 10 days, starting 17h postop + ipc for 2 days;group 3: placebo + ipc for 2 days	ipc

Table 177. Study Data - Patient and Funding Details

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Agnelli et al. 2007	LY517717	Enoxaparin	Both	106	90	63	Yes	Yes
Avikainen et al. 1995	Enoxaparin	Heparin	Hip	83	84	66	NR	NR
Bailey et al. 1991	IPC + GCS	Warfarin + GCS	Hip	50	45	65	Yes	NR
Barber et al. 1977	Warfarin	Heparin	Hip	58	19	66	NR	NR
Barrellier et al. 2010	LMWH + LMWH	LMWH	Knee	422	420	71	No	No
Bauer et al. 2001	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Knee	517	517	68	Yes	Yes
Bergqvist et al. 1996	Enoxaparin + Enoxaparin	Enoxaparin +Placebo	Hip	131	131	70	Yes	Yes
Berkowitz et al. 2003	Heparin, Oral; IPC (Used In 82%) Allowed	Heparin; IPC (Used In 82%) Allowed	Hip	43	41	63	Yes	Yes
Bonneux et al. 2006	Fondaparinux + GCS	Enoxaparin + GCS	Knee	55	54	66	No	No
Chin et al. 2009	Enoxaparin	GCS; Group 3: IPC; Group 4: No Treatment	Knee	110	110; N3:110; N4:110	67	NR	NR
Cohen et al. 2007	Fondaparinux	Fondaparinux + GCS	Hip	404	391	65	NR	Yes
Colwell et al. 1994	Enoxaparin	Heparin	Hip	195	209	65	Yes	Yes
Colwell et al. 1995	Enoxaparin	Heparin	Knee	228	225	68	NR	NR
Colwell et al. 1999	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Hip	1516	1495	64	Yes	Yes
Colwell et al. 2006	Fondaparinux; GCS (Used In 68%), IPC (Used In 54%) Allowed	Fondaparinux; GCS (Used In 68%), IPC (Used In 54%) Allowed	Both	1003	997	67	Yes	NR

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Colwell et al. 2010	IPC; Low Dose Aspirin Allowed (Used In 63%)	Enoxaparin	Hip	198	194	63	Yes	Yes
Comp et al. 2001	Enoxaparin + Enoxaparin; GCS Allowed (Used In 70%)	Enoxaparin +Placebo; GCS Allowed (Used In 70%)	Both	441	432	65	Yes	Yes
Dahl et al. 1997	Dalteparin, GCS, Dextran + Dalteparin	Dalteparin, GCS, Dextran + Placebo	Hip	117	110	71	NR	NR
Dechavanne et al. 1989	Dalteparin	Heparin	Hip	41	40	64	Yes	Yes
Edwards et al. 2008	Enoxaparin + IPC	Enoxaparin	Both	141	136	67	Yes	NR
Eriksson et al. 1991	Dalteparin	Heparin	Hip	67	69	69	No	No
Eriksson et al. 1996	Desirudin	Heparin	Hip	277	277	66	Yes	Yes
Eriksson et al. 1997	Desirudin	Heparin	Hip	223	220	68	Yes	Yes
Eriksson et al. 1997(b)	Desirudin	Enoxaparin	Hip	1028	1023	66	Yes	Yes
Eriksson et al. 2005	Dabigatran; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Enoxaparin; GCS And Nsaids (Inc. Low Dose Aspirin) Allowed	Both	385	392	65	Yes	Yes
Eriksson et al. 2006	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	136	132	65	Yes	Yes
Eriksson et al. 2006b	Rivaroxaban	Enoxaparin	Hip	142	157	65	Yes	Yes
Eriksson et al. 2007	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Hip	80	162	65	Yes	Yes
Eriksson et al. 2007b	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	679	694	68	Yes	Yes

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Eriksson et al. 2007c	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Hip	1146	1154	64	Yes	Yes
Eriksson et al. 2007d	YM150; Mechanical Allowed (Used In 1/3)	Enoxaparin; Mechanical Allowed (Used In 1/3)	Hip	36	36	63	Yes	Yes
Eriksson et al. 2008	Rivaroxaban	Enoxaparin	Hip	2209	2224	63	Yes	Yes
Eriksson et al. 2010	YM150	Enoxaparin	Hip	156	166	59	Yes	Yes
Eriksson et al. 2011	Dabigatran	Enoxaparin	Hip	1010	1003	62	Yes	Yes
Fauno et al. 1994	Enoxaparin + GCS	Heparin + GCS	Knee	92	93	70	Yes	Yes
Feller et al. 1992	Warfarin	Warfarin	Hip	100	100	NR	NR	NR
Fitzgerald et al. 2001	Enoxaparin; GCS Allowed	Warfarin; GCS Allowed	Knee	173	176	68	Yes	Yes
Fordyce et al. 1991	Warfarin	Placebo	Hip	74	74	68	NR	NR
Fordyce et al. 1992	Foot Pump + GCS	GCS	Hip	39	40	70	NR	No
Francis et al. 1992	IPC + GCS	Warfarin + GCS	Hip	110	110	64	No	NR
Francis et al. 1996	Warfarin + GCS	Warfarin + GCS	Knee	103	105	69	No	NR
Francis et al. 1997	Dalteparin	Warfarin	Hip	271	279	63	Yes	Indirect
Fuji et al. 2008 (hip)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Hip	102	101	63	Yes	Yes
Fuji et al. 2008 (knee)	Enoxaparin; GCS Allowed	Placebo; GCS Allowed	Knee	91	89	69	Yes	Yes
Fuji et al. 2008b	Fondaparinux; GCS Allowed	Placebo; GCS Allowed	Both	165	169	66	Yes	NR
Fuji et al. 2010	Dabigatran; GCS Allowed	Placebo; GCS Allowed	Knee	129	124	71	Yes	Yes
Gelfer et al. 2006	Enoxaparin	Aspirin (<300mg/Day) + IPC	Both	60	61	68	No	NR

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Ginsberg et al. 2009	Dabigatran; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Enoxaparin; GCS, Low Dose Aspirin And Cox-2 Inhibitors Allowed	Knee	857	868	66	Yes	Yes
Haas et al. 1990	Aspirin (≥300mg/Day)	IPC	Knee	58	61	69	No	NR
Hampson et al. 1974	Heparin	Placebo	Hip	48	52	68	NR	NR
Harris et al. 1974	Aspirin (≥300mg/Day) + GCS	Warfarin + GCS; Group 3: Heparin + GCS	Hip	51	55; N3:20	NR	Yes	NR
Harris et al. 1977	Aspirin (≥300mg/Day)	Placebo	Hip	44	51	NR	Yes	NR
Harris et al. 1982	Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	Hip	90	92	NR	No	NR
Harris et al. 1985	Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	Hip	48	43	NR	Yes	NR
Hull et al. 1990	IPC	None	Hip	152	158	65	No	NR
Hull et al. 1993	Tinzaparin	Warfarin	Both	715	721	66	Yes	NR
Hull et al. 2000	Dalteparin; GCS Allowed (Used In 25-30%)	Warfarin; GCS Allowed (Used In 25-30%)	Hip	496	489	63	Yes	Yes
Hull et al. 2000b	Dalteparin; Gcs Allowed (Used In <10%)	Warfarin; GCS Allowed (Used In <10%)	Hip	199	180	63	Yes	Yes
Hume et al. 1973	Heparin + GCS	GCS; Group 3: Warfarin + GCS	Hip	18	19; N3:17	NR	Yes	NR
Kakkar et al. 2008	Rivaroxaban	Enoxaparin	Hip	1228	1229	62	Yes	Yes
Kim et al. 1998	Aspirin (≥300mg/Day)	None	Hip	50	50	NR	NR	NR
Lachiewicz et al. 2004	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day) + IPC	Knee	206	217	67	Yes	No
Lassen et al. 1991	Tinzaparin + GCS	GCS	Hip	105	105	67	NR	NR

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Lassen et al. 1998	Dalteparin + Dalteparin; GCS Allowed	Dalteparin + Placebo; GCS Allowed	Hip	140	141	69	NR	NR
Lassen et al. 2000	Tinzaparin	Tinzaparin	Hip	96	94	67	NR	NR
Lassen et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	1140	1133	66	Yes	No
Lassen et al. 2007	Apixaban	Enoxaparin; Group 3: Warfarin	Knee	155	149; N3:151	67	Yes	Yes
Lassen et al. 2008	Rivaroxaban	Enoxaparin	Knee	1220	1239	68	Yes	Yes
Lassen et al. 2009	Apixaban	Enoxaparin	Knee	1599	1596	66	Yes	Yes
Lassen et al. 2010	Apixaban	Enoxaparin	Knee	1528	1529	67	Yes	Yes
Lassen et al. 2010b	Apixaban	Enoxaparin	Hip	2708	2699	61	Yes	Yes
Leclerc et al. 1996	Enoxaparin	Warfarin	Knee	336	334	69	Yes	Yes
Levine et al. 1991	Enoxaparin	Heparin	Hip	333	332	66	Yes	NR
Leyvraz et al. 1983	Heparin	Heparin	Hip	41	38	69	NR	NR
Lieberman et al. 1994	Aspirin (≥300mg/Day) + IPC	Aspirin (≥300mg/Day)	Hip	113	118	66	No	No
Lotke et al. 1996	Aspirin (≥300mg/Day)	Warfarin, Then Aspirin	Both	166	146	67	No	NR
Manganelli et al. 1998	Heparin	Heparin	Hip	28	33	66	NR	NR
Mannucci et al. 1976	Heparin	None	Hip	45	51	60	No	NR
McKenna et al. 1980	Aspirin (≥300mg/Day)	IPC; Group 3: Placebo	Knee	12	10; N3:12	65	NR	NR
Moskovitz et al. 1978	Heparin + GCS	GCS	Hip	35	32	NR	No	NR
Paiement et al. 1987	IPC	Warfarin	Hip	66	72	NR	Yes	NR
PEP Trial Collaborative Group 2000	Aspirin (<300mg/Day)	Placebo	Both	2047	2041	67	Yes	NR
Planes et al. 1988	Enoxaparin	Heparin	Hip	124	112	66	NR	NR

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Planes et al. 1991	Enoxaparin	Enoxaparin	Hip	65	61	67	NR	Indirect
Planes et al. 1996	Enoxaparin + Enoxaparin; GCS Recommended	Enoxaparin +Placebo; GCS Recommended	Hip	90	89	69	Yes	Yes
Planes et al. 1999	Enoxaparin	Tinzaparin	Hip	219	221	65	Yes	Yes
Poller et al. 1995	Warfarin	Heparin	Both	31	37	67	NR	NR
Prandoni et al. 2002	Warfarin + Warfarin	Warfarin + None	Hip	184	176	68	NR	NR
Rader et al. 1998	Heparin + GCS + Heparin	Heparin + GCS + Enoxaparin	Both	116	130	NR	NR	NR
Salzman et al. 1971	Aspirin (≥300mg/Day)	Warfarin	Hip	43	43	50	Yes	NR
Samama et al. 1997	Enoxaparin + GCS	Placebo + GCS	Hip	85	85	67	Yes	Yes
Santori et al. 1994	Heparin	Foot Pump	Hip	65	67	71	No	No
Senaran et al. 2006	Enoxaparin; GCS Allowed	Heparin; GCS Allowed	Hip	50	50	54	Yes	NR
Sharrock et al. 1990	Heparin + Aspirin (≥300mg/Day) + GCS	Aspirin (≥300mg/Day) + GCS	Hip	60	66	64	No	No
Spiro et al. 1994	Enoxaparin; GCS Allowed (Used In 57%)	Enoxaparin; GCS Allowed (Used In 57%)	Hip	199	208	65	Yes	Yes
Stone et al. 1996	IPC	Enoxaparin	Hip	25	25	64	NR	NR
Torholm et al. 1991	Dalteparin	Placebo	Hip	58	54	66	NR	No
Turpie et al. 1986	Enoxaparin	Placebo	Hip	50	50	67	No	NR
Turpie et al. 2001	Fondaparinux	Enoxaparin	Hip	177	260	67	Yes	Yes
Turpie et al. 2002	Fondaparinux; GCS Recommended	Enoxaparin; GCS Recommended	Hip	1128	1129	67	Yes	No
Turpie et al. 2005	Rivaroxaban; GCS Allowed	Enoxaparin; GCS Allowed	Knee	102	104	66	Yes	Yes
Turpie et al. 2009	Rivaroxaban	Enoxaparin	Knee	1526	1508	65	Yes	Yes

Author	Group1	Group2	Joint	N1	N2	Mean Age	Industry Funding	Any Author Conflict of Interest
Vives et al. 2001	Warfarin	Warfarin	Both	113	109	64	No	NR
VTCSG 1975	Heparin	None	Hip	30	30	64	Yes	NR
Warwick et al. 1995	Enoxaparin + GCS	GCS	Hip	78	78	NR	No	Indirect
Warwick et al. 1998	Enoxaparin + GCS	Foot Pump + GCS	Hip	143	147	68	No	Yes
Warwick et al. 2002	Enoxaparin + GCS	Foot Pump + GCS	Knee	112	117	72	NR	Yes
Westrich et al. 2005	Heparin + Aspirin (≥300mg/Day)	Aspirin (≥300mg/Day)	Hip	69	65	73	No	NR
Westrich et al. 2006	Aspirin (≥300mg/Day) + IPC	Enoxaparin + Ipc	Knee	136	139	69	Yes	NR
Wilson et al. 1994	Warfarin; IPC Allowed (Used In 73%)	Warfarin; IPC Allowed (Used In 73%)	Both	49	47	58	No	NR
Windisch et al. 2010	Foot Pump + Enoxaparin + GCS	Enoxaparin + GCS	Knee	40	40	69	NR	NR
Woolson et al. 1991	Aspirin (≥300Mg/Day) + GCS + IPC	GCS + IPC; Group 3: Warfarin + GCS + IPC	Hip	70	73; N3:69	65	No	No
Yokote et al. 2011	Fondaparinux + IPC	Enoxaparin + IPC; Group 3: Placebo + IPC	Hip	85	86; N3:85	63	No	No

APPENDIX XVI
CONCLUSIONS OF OTHER SYSTEMATIC REVIEWS

Table 178. Systematic Review Conclusions - Prophylaxis

Author	Title	Summary	Quality Evaluation
Dranitsaris 2011	Meta regression analysis to indirectly compare dalteparin to enoxaparin for the prevention of venous thromboembolic events following total hip replacement	The findings suggested comparable safety and efficacy between dalteparin and enoxaparin in TKR patients.	No
Huang 2011	Apixaban versus enoxaparin in patients with total knee arthroplasty	Apixaban in non-inferior to subcutaneous enoxaparin when used for the same duration, with considerable advantage regarding safety profile of major bleeding after TKA.	Yes
Cao 2010	Rivaroxaban versus enoxaparin for thromboprophylaxis after total hip or knee arthroplasty: a meta-analysis of randomized controlled trials	Rivaroxaban was more effective than the recommended dose of enoxaparin and had a similar safety profile for thromboprophylaxis after hip and knee arthroplasty	Yes
Kurmis 2010	Review article: thromboprophylaxis after total hip replacement	There is robust evidence to support an extended course (>14 days) of thromboprophylaxis after THR.	No
Melillo 2010	Rivaroxaban for thromboprophylaxis in patients undergoing major orthopedic surgery	Rivaroxaban has demonstrated comparable safety and superior efficacy to enoxaparin.	No
Salazar 2010	Direct thrombin inhibitors versus vitamin K antagonists or low molecular weight heparins for prevention of venous thromboembolism following total hip or knee replacement (Review)	Direct thrombin inhibitors are as effective in the prevention of major venous thromboembolism in THR or TKR as LMWH and vitamin K antagonists. However, they show higher mortality and cause more bleeding than LMWH. No severe hepatic complications were reported in the analysed studies. Use of ximelagatran is not recommended for VTE prevention in patients who have undergone orthopedic surgery. More studies are necessary regarding dabigatran.	Yes

Table 178. Systematic Review Conclusions - Prophylaxis

Tasker 2010	Meta-analysis of low molecular weight heparin versus placebo in patients undergoing total hip replacement and post-operative morbidity and mortality since their introduction	Clinically relevant VTEs are a rare complication following THR. The lower risk of VTE narrows the risk benefit of potent pharmacological thromboprophylaxis. We do not support their use in patients undergoing THR without additional thromboembolic risk factors.	No
Brown 2009	Venous Thromboembolism Prophylaxis After Major Orthopaedic Surgery: A Pooled Analysis of Randomized Controlled Trials	The VTE rates with aspirin were not significantly different than the rates for vitamin K antagonists (VKA), low molecular weight heparins (LMWH), and pentasaccharides. The operative site bleeding relative risks of VKA, LMWH, and pentasaccharides versus aspirin, are 4.9, 6.4, and 4.2, respectively. A pooled analysis of RCTs supports the use of aspirin for VTE prophylaxis after major orthopaedic surgery.	No
Holmes 2009	Dabigatran etexilate for the prevention of venous thromboembolism in patients undergoing elective hip and knee surgery: a single technology appraisal	DBG (220 mg and 150 mg once daily) is not inferior to enoxaparin (40 mg once daily and 30 mg twice daily) in terms of major VTE or VTE-related events (secondary outcome). Meta-analysis shows that 220 mg DBG is not inferior to enoxaparin (40 mg once daily or 30 mg twice daily) in reducing total VTE and all-cause mortality (primary outcome) in total hip or knee replacement, whereas there is uncertainty around the clinical effectiveness of 150 mg DBG for this outcome. In the MTC analysis DBG compared favourably with the other interventions, with the exception of extended enoxaparin and fondaparinux. The adverse event profile was not significantly different in those receiving DBG and those receiving enoxaparin.	Yes

Table 178. Systematic Review Conclusions - Prophylaxis

Hull 2009	Assessing the Safety Profiles of New Anticoagulants for Major Orthopedic Surgery Thromboprophylaxis	The definitions of bleeding events that clinical trials of thromboprophylaxis use in their assessment of new anticoagulants strongly influences each drug's perceived safety profile and may underestimate bleeding risks. Clinical studies of new anticoagulants urgently need standardization of bleeding definitions to allow intertrial comparability and to ensure consistent reporting of clinically relevant outcomes.	No
Lazo-Langner 2009	Lessons From Ximelagatran: Issues for Future Studies Evaluating New Oral Direct Thrombin Inhibitors for Venous Thromboembolism Prophylaxis in Orthopedic Surgery	This study suggested that the risk-benefit profile of ximelagatran—and probably other similar agents— depends on the type of surgery, the initial timing of administration, and probably the dose. These issues should be explicitly explored in future trials evaluating new direct thrombin inhibitors.	Yes
Kakkos 2008	Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients (Review)	Combined modalities should be used in the prevention of venous thromboembolism in the types of high risk groups studied in the current systematic review.	Yes
Sharrock 2008	Potent Anticoagulants are Associated with a Higher All-Cause Mortality Rate After Hip and Knee Arthroplasty	The recommendations from the Chest Physicians Consensus Statement advocate low-molecular-weight heparin or warfarin for prophylaxis after THA and TKA. These recommendations often result in physicians feeling compelled to prescribe these anticoagulants to avoid potential litigation. The increased risk of bleeding complications has encouraged several experienced surgeons who perform joint arthroplasty to emphasize caution in the use of these anticoagulants. We believe the American College of Chest Physicians should reconsider their guidelines to reflect the fact that PE occurs despite the use of potent anticoagulants and may, in fact, expose patients to increased mortality after surgery.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Xing 2008	Has the incidence of deep vein thrombosis in patients undergoing total hip/knee arthroplasty changed over time? A systematic review of randomized controlled trials	The incidence of DVT in patients undergoing elective TKA appears to have declined in patients receiving warfarin thromboprophylaxis. We identified potential contributors to the observed decline including reduced operative time, reduced tourniquet time and potentially changes in the way that warfarin was administered for prophylaxis. Our results suggest that when studies which use warfarin for DVT prophylaxis are designed, they should use contemporary estimates of the rate of DVT after TKA.	Yes
Ivanovic 2007	Thromboprophylaxis in total hip-replacement surgery in Europe: acenocoumarol, fondaparinux, dabigatran and rivaroxban	Studies have shown that during the first 10 days, low molecular heparins started preoperatively or fondaparinux commenced postoperatively are preferred over the vitamin K antagonists. Clinical results included in the new Dutch CBO evidence based guidelines have shown that LMWHs, VKA and fondaparinux are equally effective in the extended period.	No
Chan 2006	Role for Aspirin after Total Hip Replacement?	No large trials of acceptable quality which specifically compared aspirin with placebo following total hip replacement were identified. Clinical practice guidelines, meta-analyses and one clinical trial assessed aspirin against placebo or other agents used in thrornboprophylaxis in major orthopaedic surgery, including elective total hip replacement. There is insufficient evidence to support the use of aspirin alone as thromboprophylaxis following elective total hip replacement.	No
Mismetti 2004	Prevention of venous thromboembolism in orthopedic surgery with vitamin K antagonists: a meta-analysis	In patients undergoing major orthopedic surgery, VKAs are less effective than LMWH, without any significant difference in the bleeding risk.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Deitelzweig 2003	Venous Thromboembolism Prevention with LMWHs in Medical and Orthopedic Surgery Patients	Enoxaparin has demonstrated efficacy and safety in VTE prevention in medical patients, whereas information is limited or lacking for dalteparin and tinzaparin. Total hip replacement (THR) trials have been conducted with all US-marketed LMWHs and have demonstrated the efficacy and safety of each agent. Trials specifically establishing the efficacy of an LMWH in total knee replacement surgery (TKR) have been published for enoxaparin. One combination THR and TKR trial has been published for tinzaparin. These trial outcomes have positioned the LMWHs as key alternatives to adjusted-dose warfarin for VTE prophylaxis in orthopedic surgery. Inherent differences between LMWHs prevent the extrapolation of clinical outcomes from 1 trial to another.	No
Nutescu 2003	Tinzaparin: Considerations for Use in Clinical Practice	Tinzaparin is safe and effective for prevention and treatment of DVT. Consistent once-daily dosing may facilitate self-administration of tinzaparin in the outpatient setting.	No
O'Donnell 2003	Reduction of Out-of-Hospital Symptomatic Venous Thromboembolism by Extended Thromboprophylaxis With Low-Molecular-Weight Heparin Following Elective Hip Arthroplasty	The absolute reduction in symptomatic venous thromboembolism attributed to extended prophylaxis in some studies and meta-analyses seems to have been overestimated.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Tran 2003	Fondaparinux for Prevention of Venous Thromboembolism in Major Orthopedic Surgery	Fondaparinux is the first of a new class of synthetic factor Xa inhibitors that demonstrated greater efficacy compared with enoxaparin for the prevention of VTE in rnajor orthopedic surgery without an increase in clinically relevant bleeding. Given the favorable cost-effectiveness analysis and improved efficacy profile, fondaparinux should be considered for formula addition for DVT prophylaxis in patients undergoing hip and knee replacement surgery. in patients undergoing hip fracture surgery, fondaparinux should be considered the DVT prophylaxis of choice. Extended thromboprophylaxis up to 28dais resulted in additional reduction in VTE (both symptomatic and venography-proven DVT) in patients with hip fracture surgery.	No
Zufferey 2003	Optimal low-molecular-weight heparin regimen in major orthopaedic surgery	Our results support the hypothesis that with LMWH there is a relationship between dose and reduction of risk of asymptomatic total or proximal DVT. We found no convincing evidence that starting prophylaxis preoperatively in major orthopaedic surgery is associated with a better benefit-risk ratio than starting postoperatively	No
Cheng 2002	Fondaparinux: A New Antithrombotic Agent	Fondaparinux has shown efficacy in the prevention of venous thromboembolism in patients undergoing hip or knee replacement surgery. Largescale clinical trials of its potential efficacy in deep vein thrombosis and acute coronary syndromes are ongoing. Use of fondaparinux may be associated with an increased bleeding risk, and patients should be assessed individually to ensure that the possible benefits outweigh the risks. Routine use of fondaparinux as a replacement for low-molecular-weight heparin is not recommended at this time.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Douketis 2002	Short-Duration Prophylaxis Against Venous Thromboembolism After Total Hip or Knee Replacement	In patients who undergo hip or knee replacement and receive short-duration anticoagulant prophylaxis, symptomatic nonfatal venous thromboembolism will occur in about 1 of 32 patients and fatal pulmonary embolism will occur in about 1 of 1000 patients within 3 months of the surgery. Although the prevalence of asymptomatic deep vein thrombosis is more than 2-fold higher after knee replacement than after hip replacement 7 to 10 days after surgery, in the subsequent 3 months, symptomatic venous thromboembolism is more likely to occur after hip replacement.	No
Strebel 2002	Preoperative or Postoperative Start of Prophylaxis for Venous Thromboembolism With Low-Molecular-Weight Heparin in Elective Hip Surgery?	We find no convincing evidence that starting prophylaxis preoperatively is associated with a lower incidence of venous thromboembolism than starting postoperatively. Perioperative regimens may lower the risk of postoperative thrombosis, but if so, this positive effect is offset by an increase in postoperative major bleeding.	No
Brookenthal 2001	A Meta-Analysis of Thromboembolic Prophylaxis in Total Knee Arthroplasty	For total DVT, all agents except dextran and aspirin protected significantly better than placebo (P .0001). For proximal DVT rates, low-molecular-weight heparin was significantly better than warfarin (P .0002). There was a trend that aspirin was better than warfarin (P .0106). No significant difference was found for symptomatic pulmonary embolism, fatal pulmonary embolism, major hemorrhage, or total mortality.	No
Eikelboom 2001	Extended duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials	Among patients undergoing total hip or knee replacement, extended-duration prophylaxis significantly reduces the frequency of symptomatic venous thromboembolism. The reduction in risk is equivalent to about 20 symptomatic events per 1000 patients treated.	Yes

Table 178. Systematic Review Conclusions - Prophylaxis

Hull 2001	Extended Out-of-Hospital Low-Molecular-Weight Heparin Prophylaxis against Deep Venous Thrombosis in Patients after Elective Hip Arthroplasty: A Systematic Review	Extended LMWH prophylaxis showed consistent effectiveness and safety in the trials (regardless of study variations in clinical practice and length of hospital stay) for venographic deep venous thrombosis and symptomatic venous thromboembolism. The aggregate findings support the need for extended outof-hospital prophylaxis in patients undergoing hip arthroplasty surgery.	Yes
Hull 2001	Timing of Initial Administration of Low-Molecular-Weight Heparin Prophylaxis Against Deep Vein Thrombosis in Patients Following Elective Hip Arthroplasty	The timing of initiating low-molecular weight heparin significantly influences antithrombotic effectiveness. The practice of delayed initiation of low molecular-weight heparin prophylaxis results in suboptimal antithrombotic effectiveness without a substantive safety advantage.	Yes
Freedman 2000	A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty	The best prophylactic agent in terms of both efficacy and safety was warfarin, followed by pneumatic compression, and the least effective and safe was low-dose heparin. Warfarin provided the lowest risk of both proximal deep venous thrombosis and symptomatic pulmonary embolism. However, there were no identifiable significant differences in the rates of fatal pulmonary embolism or death among the agents. Significant risks of minor and major bleeding complications were observed with greater frequency with certain prophylactic agents, particularly low-molecular-weight heparin (minor bleeding) and low-dose heparin (both major and minor bleeding).	No

Table 178. Systematic Review Conclusions - Prophylaxis

Westrich 2000	Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty	Our findings have shown that pneumatic compression had the lowest incidence of thromboembolism and is an acceptable form of prophylaxis in TKA. Aspirin alone was inadequate. Warfarin alone is used routinely in many institutions, but it too had a greater incidence of associated thromboembolism than LMWH and pneumatic compression. Although the LMWHs appear to give a reduction in thromboembolism, complications are ubiquitous in all published studies and included haemorrhagic problems as well as thrombocytopenia. No statistically significant difference was noted between the above prophylactic regimes due to the very small incidence of symptomatic PE.	Yes
Agu 1999	Graduated compression stockings in the prevention of venous thromboembolism	Graduated compression stockings reduce the overall cross-sectional area of the limb, increase the linear velocity of venous flow, reduce venous wall distension and improve valvular function. Fifteen randomized controlled trials of graduated compression stockings alone were reviewed. Stockings reduced the relative risk of DVT by 64 per cent in general surgical patients and 57 per cent following total hip replacement. The effect of stockings was enhanced by combination with pharmacological agents such as heparin; the combination is recommended in patients at moderate or high risk of DVT. Knee-length stockings are as effective and should replace above-knee stockings. Complications are rare and avoidable.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Hull 1999	Preoperative vs Postoperative Initiation of Low-Molecular-Weight Heparin Prophylaxis Against Venous Thromboembolism in Patients Undergoing Elective Hip Replacement	Our findings support the need for a randomized comparison of preoperative and postoperative initiation of pharmacological prophylaxis of DVT. Such a trial would resolve the divergent practices for DVT prophylaxis between Europe and the North American countries, the United States and Canada, and would affect the treatment for thousands of patients on both continents.	No
Howard 1998	Low molecular weight heparin decreases	Low molecular weight heparin is more efficacious than either adjusted dose heparin or adjusted dose warfarin, when used to prevent DVT and proximal DVT following total knee arthroplasty.	Yes
Vanek 1998	Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves	IPC devices significantly decreased the relative risk of DVT compared with placebo among major orthopedic surgery patients; compared with warfarin, the incidence of DVT was similar overall, but IPC was better at preventing calf DVT while warfarin was better at preventing proximal DVT	No
Howard 1997	Dalteparin: a low-molecular-weight heparin	Dalteparin is the second LMWH to receive approval by the Food and Drug Administration. Dalteparin is indicated for prophylaxis against DVT in patients undergoing abdominal surgery. Clinical studies have shown that single daily doses of dalteparin provide a safe and effective alternative to fixed-dose UH therapy.	No
Skoutakis 1997	Danaparoid in the prevention of thromboembolic complications	Danaparoid is an antithrombotic agent with characteristics that distinguish it from heparin and LMWHs. Based on the efficacy and safety data reviewed, danaparoid should be considered one of the drugs of choice for the prevention of thromboembolic complications in patients undergoing orthopedic hip procedures and the drug of choice for the management of any patient with heparin-induced thrombocytopenia who requires anticoagulant therapy.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Murray 1996	Thromboprophylaxis and death after total hip replacement	Our study demonstrates that there is not enough evidence in the literature to conclude that any form of pharmacological thromboprophylaxis decreases the death rate after total hip replacement. For this reason guidelines which recommend their routine use to prevent death after hip replacement are not justified.	No
Borris 1994	Perioperative thrombosis prophylaxis with low molecular weight heparins in elective hip surgery	Thromboprophylaxis with recommended dosages of LMWH was significantly more effective than both placebo (no prophylaxis), dextran 70 and low-dose unfractionated heparin (UH) (5,000 [U thrice daily) in terms of protection against objectively diagnosed deep vein thrombosis (DVT), which is the main source of postoperative pulmonary embolism. The efficacy of LMWH was similar to that of adjusted-dose UH but only 2 studies have been conducted with this regimen so far. When combined with 0.5 mp dihydroergotanine (DHE), UH was as effective as LMWH but DHE bears a definite risk of circulatory disturbances in the lower limbs. In all studies LMWH prophylaxis was side under the clinical conditions.	No
Imperiale 1994	A meta-analysis of methods to prevent venous thromboembolism following total hip replacement	The results suggest that low-molecular-weight heparin and compression stockings have the greatest relative efficacy in preventing venous thromboembolism following total hip replacement. Low-molecular-weight heparin may be more effective, though at a small risk of clinically important bleeding.	Yes
Anderson 1993	Efficacy and Cost of Low-Molecular-Weight Heparin Compared with Standard Heparin for the Prevention of Deep Vein Thrombosis after Total Hip Arthroplasty	Low-molecular-weight heparin is more effective and is at least as safe as standard heparin for the prevention of deep vein thrombosis after total hip arthroplasty.	No

Table 178. Systematic Review Conclusions - Prophylaxis

Carter 1993	Enoxaparin: the low-molecular-weight heparin for prevention of postoperative thromboembolic complications	Clinical studies performed throughout the world have shown that enoxaparin is superior or equivalent to other antithrombotic agents, including heparin, n preventing the formation of venous thromboembolism. In addition, enoxaparin appears to possess an equivalent or lower incidence of bleeding complications when compared with heparin prophylaxis.	No
Mohr 1993	Prophylactic agents for venous thrombosis in elective hip surgery	Multiple agents or combinations are effective prophylaxis for deep venous thrombosis, but none decreases the rate to zero, There was overlap in the 95% confidence intervals for the probability of deep venous thrombosis for various agents and especially for the probabilities for proximal thrombi. Many agents have not been compared directly with each other, but low-molecular weight heparin consistently performed well.	Yes
Leizorovicz 1992	Low molecular weight heparin in prevention of perioperative thrombosis	Low molecular weight heparins seem to have a higher benefit to risk ratio than unfractionated heparin in preventing perioperative thrombosis. However, it remains to be shown in a suitably powered clinical trial whether low molecular weight heparin reduces the risk of fatal pulmonary embolism compared with heparin.	No

Table 179. Systematic Review Conclusions – Neuraxial Anesthesia

Author	Title	Summary	Quality Evaluation
Hu 2009	A comparison of regional and general anaesthesia for total replacement of the hip or knee	In conclusion, our data support the recent trend towards the increased use of regional anaesthesia. Furthermore, epidural anaesthesia/analgesia has been shown to improve the post-operative outcomes by relieving pain, reducing pulmonary complications, allowing early mobilisation and shortening the length of hospital stay	No
Macfarlane 2009	Does Regional Anesthesia Improve Outcome After Total Knee Arthroplasty?	There was insufficient evidence from RCTs alone to conclude if anesthetic technique influenced mortality, cardiovascular morbidity other than postoperative hypotension, or the incidence of DVT and PE in the setting of routine thromboprophylaxis. Our systematic review does not suggest a difference in blood loss or duration of surgery in patients receiving GA and/or systemic analgesia versus RA and/or RA for TKA. However, RA does reduce postoperative pain and opioid-related adverse effects for TKA. Length of stay also may be reduced and rehabilitation facilitated by RA compared with GA.	Yes
Macfarlane 2009	Does Regional Anaesthesia Improve Outcome After Total Hip Arthroplasty? A Systematic Review	There is insufficient evidence from RCTs alone to conclude if anaesthetic technique influenced mortality, cardiovascular morbidity, or the incidence of DVT and PE when using thromboprophylaxis. Blood loss may be reduced in patients receiving RA rather than GA for THA. Compared with systemic analgesia, regional analgesia can reduce postoperative pain, morphine consumption, and nausea and vomiting. Length of stay is not reduced and rehabilitation does not appear to be facilitated by RA or analgesia for THA.	Yes
Guay 2006	The effect of neuraxial blocks on surgical blood loss and blood transfusion requirements: a meta-analysis	In summary neuraxial blocks have a clear and definite effect on surgical blood loss, but this effect do not usually lead to a reduction in the number of transfused patients except for patients undergoing total hip replacement and spinal fusion.	No

Author	Title	Summary	Quality Evaluation
Mauermann 2006	A Comparison of Neuraxial Block Versus General Anesthesia for Elective Total Hip Replacement: A Meta-Analysis	Patients undergoing elective THR under neuraxial anesthesia seem to have better outcomes than those under GA. Our data indicate that neuraxial block is associated with a decrease in intraoperative blood loss and the number of patients requiring blood transfusions. It is not known whether some of the beneficial effects such as reduced incidence of DVT and PE provided by neuraxial block are applicable to today's practice when compared with investigations performed 20 years ago. However, our findings indicate that neuraxial block should be considered as a valid and potentially beneficial technique for elective THR.	No

Table 180. Systematic Review Conclusions – Ultrasound Screening

Author	Title	Summary	Quality Evaluation
Berry 2001	Surveillance for venous thromboembolic disease after total knee arthroplasty	Several studies have shown a low VTED rate when compression ultrasound is used for screening as part of a clinical algorithm after knee arthroplasty. However, the only large RCT evaluating ultrasound screening failed to show a reduction in morbidity. The benefits of surveillance depend on practice-specific factors, including the type and duration of prophylaxis, the rate of VTED associated with that protocol, and the accuracy of screening tests used for that surveillance.	No

APPENDIX XVII
BIBLIOGRAPHIES
INCLUDED STUDIES

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