

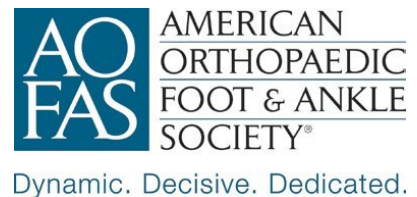
Prevention of Surgical Site Infections After Major Extremity Trauma

Evidence-Based Clinical Practice Guideline

Adapted by:

The American Academy of Orthopaedic Surgeons Board of Directors
March 21, 2022

Endorsed by:



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Disclaimer

This clinical practice guideline (CPG) was developed by a physician volunteer clinical practice guideline development group based on a formal systematic review of the available scientific and clinical information and accepted approaches to treatment and/or diagnosis. This clinical practice guideline is not intended to be a fixed protocol, as some patients may require more or less treatment or different means of diagnosis. Clinical patients may not necessarily 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 patient's specific clinical circumstances.

Disclosure Requirement

In accordance with AAOS policy, all individuals whose names appear as authors or contributors to the 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 voting on the recommendations contained within this clinical practice guideline.

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FDA Clearance

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SUMMARY OF RECOMMENDATIONS

Recommendations are formed when there is sufficient evidence by which to create a directional statement. This is defined as evidence from two or more high quality studies (i.e., a strong recommendation), two or more moderate quality studies (i.e., a moderate recommendation), or statements resulting in a strong or moderate strength following Evidence to Decision Framework upgrading and/or downgrading.

Initial Antibiotics

Early delivery of antibiotics is suggested to lower the risk of deep infection in the setting of open fracture in major extremity trauma.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Preoperative Antibiotics

Utilization of preoperative antibiotics is suggested to prevent SSI in operative treatment of open fractures.

Strength of Evidence: Limited

Strength of Recommendation: Moderate  (Upgraded)

Evidence from one or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, lower strength evidence can be upgraded to moderate due to major concerns addressed in the EtD Framework.

Surgery Timing

It is suggested that patients with open fractures are brought to the OR for debridement and irrigation as soon as reasonable, and ideally before 24 hours post injury.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Perioperative and Postoperative Antibiotics - Systemic

In patients with major extremity trauma undergoing surgery, it is recommended that antibiotic prophylaxis with systemic cefazolin or

clindamycin be administered, except for Type III (and possibly Type II) open fractures, for which additional Gram-negative coverage is preferred.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Perioperative and Postoperative Antibiotics – Local

In patients with major extremity trauma undergoing surgery, local antibiotic prophylactic strategies, such as vancomycin powder, tobramycin-impregnated beads, or gentamicin-covered nails, may be beneficial.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★★★★

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Initial Wound Management - Irrigation

Irrigation with saline (without additives) is recommended for management of open wounds in major extremity trauma.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Initial Wound Management - Fixation

Definitive fixation of fractures at initial debridement and primary closure of wounds in selected patients may be considered when appropriate, however no favored treatment was observed.

Temporizing external fixation remains a viable option for the treatment of open fractures in major extremity trauma

Strength of Evidence: Strong

Strength of Recommendation: Moderate ★★★★★ (Downgraded)

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Wound Coverage

Wound coverage fewer than 7 days from injury date is suggested.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Negative Pressure Wound Therapy – Open and Closed Fractures

After closed fracture fixation, negative pressure wound therapy may mitigate the risk of revision surgery or SSIs; however, after open fracture fixation, negative pressure wound therapy does not appear to offer an advantage when compared to sealed dressings as it does not decrease wound complications or amputations.

Strength of Evidence: Strong

Strength of Recommendation: Strong 

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Open Wound Closure

Closing an open wound when it is feasible, without any gross contamination is recommended.

Strength of Evidence: Strong

Strength of Recommendation: Strong 

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Silver Coated Dressings

Silver coated dressings are not suggested to improve outcomes or decrease pin site infections.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Modifiable Risk Factors

In patients undergoing surgery for major extremity trauma, patients should be counseled that:

- There may be an increased risk for SSI in patients who smoke or who are diabetic.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

- There may be an increased risk for SSI in obese patients
- Significant alcohol use (>14 units per week) increases the risk of infection postoperatively.
- High flow perioperative FIO₂ has not been shown to alter the risk of postoperative infection.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★★★☆

Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

- Low albumin (<36g/L) increases the risk of infection postoperatively.
- Elevated postoperative glucose levels (>125 mg/dL) increase the risk for infection.
- Preoperative transfusion, intraoperative evaluation by a vascular service in patients with grade 3a, 3b open fractures with well perfused limbs, and preoperative MRSA positivity has not been shown to alter the risk of postoperative infection.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★★☆☆

Evidence from two or more "Low" quality studies with consistent findings or evidence from a single "Moderate" quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Administrative Risk Factors

In patients undergoing surgery for major extremity trauma, patients should be counseled that:

- **There is minimal evidence that race, or socioeconomic status affects risk of SSI.**

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

- **There is no significant difference in risk of SSI when being treated as an inpatient or outpatient.**

Strength of Evidence: Limited

Strength of Recommendation: Limited 

Evidence from two or more "Low" quality studies with consistent findings or evidence from a single "Moderate" quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

SUMMARY OF OPTIONS

Options are formed when there is little or no evidence on a topic. This is defined as low quality evidence or a single moderate quality study (i.e., a limited strength option), no evidence or only conflicting evidence (i.e., a consensus option), or statements resulting in a limited or consensus strength following Evidence to Decision Framework upgrading and/or downgrading.

Negative Pressure Wound Therapy - High Risk Surgical Incisions

It is suggested to use an incisional negative pressure wound therapy for high- risk surgical incisions (e.g., pilon, plateau, or calcaneus fractures) to reduce the risk of deep surgical site infection.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Orthoplastic Team

Implementation of an orthoplastic team may decrease length of stay, deep infection, and additional operations to bone, and also may help improve time to wound healing and time to union.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Hyperbaric O₂

In patients with open fracture, hyperbaric O₂ may not benefit patient outcomes.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Preoperative Skin Preparation

In the absence of reliable evidence, it is the opinion of the workgroup that:

1. Providers may consider perioperative nasal and skin (full body) decolonization of patients, when possible.
2. Patients should shower or bathe (full body) with soap (anti-microbial or non-anti-microbial) or an antiseptic agent before surgery, when possible.
3. Surgical skin preparation should be performed with an alcohol-based antiseptic agent, unless contraindicated.

Strength of Evidence: Consensus

Strength of Option: Consensus ★★★★★

There is no supporting evidence, or limited level evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion.

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INTRODUCTION

OVERVIEW

This Clinical Practice Guideline (CPG) is one of six funded by a Department of Defense grant to the METRC collaborative to evaluate the evidence regarding various aspects of recovery from injury to determine the most helpful recommendations for treatment. The CPG herein is based on a systematic review of published studies examining the prevention of surgical site infection (SSI) after major extremity trauma in adults. It provides recommendations that will help practitioners to integrate the current evidence and clinical practice, and it highlights gaps in the literature in need of future research. This guideline is intended to be used by appropriately trained physicians and clinicians who manage the treatment of major extremity trauma. It also serves as an information resource for developers and applied users of clinical practice guidelines.

GOALS AND RATIONALE

The purpose of this clinical practice guideline is to evaluate the current best evidence associated with treatment. Evidence-based medicine (EBM) standards advocate for use of empirical evidence by physicians in their clinical decision making. To assist with access to the large resources of information, a systematic review of the literature in publication was conducted between November 2020 and August 2021. It highlights where there is good evidence, where evidence is lacking, and what topics future research will need to target in order to help facilitate evidence-based decision making in the prevention of SSI in patients with major extremity trauma. AAOS staff methodologists assisted the physician/clinician work group in evaluating the existing literature so that they could formulate the following recommendations based on a rigorous systematic process. Musculoskeletal care is provided in many different settings and by a variety of providers. We created this guideline as an educational tool to guide qualified physicians and clinicians in making treatment decisions that improve the quality and efficacy

of care. This guideline should not be construed as including all possible methods of care or excluding acceptable interventions similarly directed at obtaining favorable outcomes. The final decision to use a specific procedure must be made after assessing all concerns presented by the patient and consideration of locality-specific resources.

INTENDED USERS

This guideline is intended to be used by orthopaedic surgeons and other healthcare providers managing adults with major extremity trauma. It serves as an information resource for medical practitioners. In general, individual practicing physicians and clinicians do not have the resources required to complete a project of comparable scope and duration involving the evaluation of an extensive literature base. In April 2019, the AAOS adopted the use of the GRADE Evidence-to-Decision Framework into its clinical practice guideline development methodology. This Framework enables work group members to incorporate additional factors into the strength of each recommendation and move away from the rigidity of previous AAOS recommendation language stems. The AAOS intends for this guideline to assist treatment providers not only in making shared clinical decisions with their patients, but also in describing to patients and their loved ones why a selected intervention represents the best available course of treatment. This guideline is not intended for use as a benefits determination document. It does not cover allocation of resources, business and ethical considerations, and other factors needed to determine the material value of orthopaedic care. Users of this guideline may also want to consider the appropriate use criteria (AUC) related to the prevention of SSI in major extremity trauma.

PATIENT POPULATION

This guideline is intended for use with adults (≥ 18 yrs) who have sustained a major extremity trauma. Major extremity trauma was defined by the working group.

The population included all injury types limited to the context of an extremity fracture:

1. Open fracture
2. Major/High energy closed fracture
3. Degloving injury
4. Morel lesions
5. Gunshot injury (low and high velocity)
6. Crush injury
7. Blast injury
8. Moderate to high energy force

SCOPE

The scope of this guideline includes preoperative, perioperative, and postoperative interventions in addition to an evaluation of risk factors to decrease surgical site infection following major extremity trauma. This guideline does not provide recommendations for patients with a current surgical site infection at the site of orthopaedic trauma, for patients undergoing secondary surgeries (i.e., non-union or malunion), or for patients with injuries isolated to their fingers or toes. Furthermore, literature before 1985 was not considered.

ETIOLOGY

Major Extremity Trauma can result from numerous mechanisms. These injuries include those occurring in combat arenas as well as those presenting to civilian trauma centers. Consideration of the etiology, mechanism of injury, soft tissue envelope, neurovascular structures, bony integrity, and comorbidities need to be considered when treating these injuries.

INCIDENCE AND PREVALENCE

Major extremity trauma combines multiple injury types with varying degrees of incidence and prevalence. For this reason, there are significant limitations in accurately determining the true incidence and prevalence of major extremity trauma. Within this limitation, open fractures have an incidence between 11.5 - 13 per 100,000 persons.^{1,2} In the United States in 2013, there were 27,900 and 2,700 hospital discharges due to firearm and explosive injuries, respectively.³

Between 2001-2017, U.S. military data demonstrates over 1,700 combat-related amputations, with 31% of patients having multiple amputations. Over 70% of these amputations resulted from an improvised

explosive device, and 84% involved a lower limb.⁴ In the U.S., the 2020 prevalence of traumatic amputation is estimated at 906,000 and is expected to rise to 1.3 million by 2050.⁵

BURDEN OF DISEASE

More than 50,000 US military personnel have been wounded in combat while serving in Iraq and Afghanistan since 2001, and approximately 50% of these injuries were musculoskeletal in nature.⁶ It has been estimated that 70% of all orthopaedic injuries sustained in these conflicts involved significant trauma to the extremities, often resulting in complete or partial limb amputation.⁷ Traumatic segmental bone loss is a complex clinical problem, one that often requires extreme solutions.⁸ Many alternatives, including Ilizarov bone transport,^{9,10} microvascular free fibular transfer,¹¹ massive bone grafts,^{12,13} amputation,^{14,15} the Masquelet induced membrane technique,^{16,17} arthroplasty with mega-prostheses,¹⁸ implantable devices such as telescopic nails,¹⁹ and biologics such as recombinant human bone morphogenetic protein-2 (rhBMP-2) have also been trialed.^{20,21} However, all of these treatment options have their own sets of problems and complications.

Fracture-related infections (FRIs) and SSI following trauma occur more frequently compared to elective orthopaedic procedures. These infections can have a huge economic impact, often negatively influence long-term functional outcomes, and can potentially lead to amputation or death. Surgical stabilization of fractures sometimes results in conditions with a damaged and contaminated local environment. This may then require prolonged procedures with extensive soft tissue dissection and insertion of metal implants, frequently in patients with significant comorbidities that cannot be optimized prior to surgery. Recent research has provided guidance on treatment decisions based on high-level evidence, but many questions remain, with little or no supporting evidence.

EMOTIONAL AND PHYSICAL IMPACT

High-energy injuries can be associated with military warfare and training, or with civilian

View background material via the SSI Trauma CPG [eAppendix 1](#)

View data summaries via the SSI Trauma CPG [eAppendix 2](#)

injuries often related to automobile or motorcycle accidents. These can cause severe trauma to the extremities, often resulting in segmental or open fractures, with or without bone loss. The importance of improving clinicians' ability to successfully manage these injuries cannot be overemphasized, as these devastating injuries can result in permanent disability with delayed returns to military duties or other employment. This in turn results in a decreased quality of life and high costs associated with treatment, and most importantly, it may lead to the inability of the affected individuals to return to active duty or gainful employment early in their careers. These individuals and their families then face a protracted course of continued medical care that is inevitably costly, with a significant risk of failure that may conceivably lead to eventual amputation. The most compelling military benefits for the successful completion of this project will be allowing severely injured troops to initiate rehabilitation more quickly, to resume weight bearing early, and return to duty faster and more reliably by providing effective interventions that limit the risks associated with this challenging clinical problem.

POTENTIAL BENEFITS, HARM, AND CONTRAINDICATIONS

Although many interventions have been advocated to reduce the risk of infection when managing orthopaedic trauma and fractures, all surgical procedures have an increased probability of surgical site infection following trauma. Infection of the surgical site is independently associated with an increased risk of nonunion, increased risk of the need for further surgery, increased risk of implant failure, and a prolonged Length of Stay (LOS), as well as the greater cost associated with these complications. This project should lead to a reduction in the rate of these complications when compared to current expected outcomes, while also substantially reducing the time required to complete successful treatment. This approach has a high probability of more effectively managing trauma and fractures by mitigating the risk of infection associated with surgical intervention in this vulnerable population, potentially

expediting care and theoretically leading to enhanced outcomes.

METHODS

The methods used to perform this systematic review were employed to minimize bias and enhance transparency in the selection, appraisal, and analysis of the available evidence. These processes are vital to the development of reliable, transparent, and accurate clinical recommendations. To view the full AAOS clinical practice guideline methodology please visit <https://www.aaos.org/quality/research-resources/methodology/>.

This clinical practice guideline evaluates the prevention of SSI after major extremity trauma in adults. The AAOS approach incorporates practicing physicians (clinical experts) and methodologists who are free of potential conflicts of interest relevant to the topic under study, as recommended by clinical practice guideline development experts.¹

This CPG was prepared by the AAOS/METRC Prevention of Surgical Site Infection after Major Extremity Trauma Guideline physician development group (clinical experts) with the assistance of the AAOS Clinical Quality and Value (CQV) Department (methodologists). To develop this CPG, the clinical practice guideline development group held an introductory meeting on August 29, 2020, to establish the scope of the clinical practice guideline. As physician experts, the clinical practice guideline development group defined the scope of the clinical practice guideline by creating PICO Questions (i.e., population, intervention, comparison, and outcome) that directed the literature search. The AAOS Medical Librarian created and executed the search (see eAppendix I for search strategy).

LITERATURE SEARCHES

The systematic review begins with a comprehensive search of the literature. Articles considered were published prior to the start date of the search in a minimum of three electronic databases; PubMed, EMBASE, and the Cochrane Central Register of Controlled

Trials. The medical librarian conducts the search using key terms determined from the guideline development group's PICO questions.

A CQV methodologist reviews/includes only primary literature but supplements the electronic search with a manual search of the bibliographies of secondary literature sources, such as systematic reviews, as available. The methodologist then evaluates all recalled articles for possible inclusion based on the study selection criteria and summarizes the evidence for the guideline work group who assist with reconciling possible errors and omissions.

A study attrition diagram is provided in the appendix of each document that details the numbers of identified abstracts, recalled and selected studies, and excluded studies that were evaluated in the CPG. The search strategies used to identify the abstracts is also included in the appendix of each CPG document.

DEFINING THE STRENGTH OF RECOMMENDATION

Judging the quality of evidence is only a steppingstone towards arriving at the strength of a CPG recommendation. The strength of recommendation also takes into account the quality, quantity, and the trade-off between the benefits and harms of a treatment, the magnitude of a treatment's effect, and whether data exists on critical outcomes.

INTERPRETING THE STRENGTH OF EVIDENCE

Strength of recommendation expresses the degree of confidence one can have in a recommendation. As such, the strength expresses how possible it is that a

recommendation will be overturned by future evidence. It is very difficult for future evidence to overturn a recommendation that is based on many high quality randomized controlled trials that show a large effect. It is much more likely that future evidence will overturn recommendations derived from a few small retrospective comparative studies. Consequently, recommendations based on the former kind of evidence are given a "strong" strength of recommendation and statement based on the latter kind of evidence are presented as options to the practicing clinician, rather than a directional recommendation, with either a "limited" strength or, in the event of no supporting or only conflicting evidence, a "consensus" strength.

VOTING ON THE RECOMMENDATIONS

The recommendations and their strength are voted on by the guideline development group members during the final meeting. If a disagreement between the group members occurs, there is further discussion to see whether the disagreement(s) could be resolved. Recommendations are approved and adopted in instances where a simple majority (60%) of the guideline development group votes to approve; the guideline development group had consensus (100% approval) when voting on every recommendation for this guideline with one group member abstaining from voting on the wound coverage recommendation. Any recommendation strength upgrade or downgrade based on the Evidence-to-Decision Framework requires a super majority (75%) approval of the work group.

Table I. Level of Evidence Descriptions





Strength	Overall Strength of Evidence	Description of Evidence Quality	Strength Visual
Strong	Strong or Moderate	Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Or Rec is upgraded from Moderate using the EtD framework.	
Moderate	Strong, Moderate or Limited	Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Or Rec is upgraded or downgraded from Limited or Strong using the EtD framework.	
Limited	Limited or Moderate	Evidence from one or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Or Rec is downgraded from Strong or Moderate using the EtD Framework.	
Consensus*	No Evidence	There is no supporting evidence, or higher quality evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion.	

Table II. Interpreting the Strength of a Recommendation or Option

Strength of Recommendation	Patient Counseling (Time)	Decision Aids	Impact of Future Research
Strong	Least	Least Important, unless the evidence supports no difference between two alternative interventions	Not likely to change
Moderate	Less	Less Important	Less likely to change
Limited	More	Important	Change possible/anticipated
Consensus	Most	Most Important	Impact unknown

REVIEW PERIOD

Following the final meeting, the CPG draft undergoes a 3-week review period for additional input from external content experts. Written comments are provided on the structured review form. All reviewers are required to disclose their conflicts of interest.

Specialty societies relevant to the topic are solicited for nominations of individual reviewers approximately six weeks before the final meeting. The review period is announced as it approaches, and others interested can volunteer to review the draft. The chairs of the guideline work group review the draft of the guideline prior to dissemination.

Some specialty societies (both orthopaedic and non-orthopaedic) ask their evidence-based practice (EBP) committee to provide review of the guideline. The organization is responsible for coordinating the distribution of our materials and consolidating their comments onto one form. The chair of the external EBP committees provides disclosure of their conflicts of interest (COI) and manages the potential conflicts of their members.

The review stage gives external stakeholders an opportunity to provide evidence-based direction for modifications that they believe have been overlooked. Since the draft is subject to revisions until its approval by the AAOS Board of Directors as the final step in the guideline development process, confidentiality of all working drafts is essential.

The CPG is also provided to members of the AAOS Board of Directors (BOD), members of the Research and Quality Council (RQC), members of the Board of Councilors (BOC), members of the Board of Specialty Societies (BOS), and members of the Committee on Evidence-Based Quality and Value (EBQV) for review and comment. Based on these bodies, over 200 commentators have the opportunity to provide input into each CPG.

The chairs of the guideline work group, the manager of the guideline, and the Director of the AAOS Department of Clinical Quality and Value draft the initial responses to comments that address methodology. These responses are then reviewed by the chair and co-chair, who respond to questions concerning clinical practice and techniques. Comments received and the initial drafts of the responses are also reviewed by members of the guideline development group. Proposed changes to recommendation language as a result of the review period are based on the evidence. Final revisions are summarized in a report that is provided alongside the guideline document throughout the remainder of the approval processes and final publication.

The AAOS believes in the importance of demonstrating responsiveness to input received during the review process and welcomes the critiques of external specialty societies. Following final approval of the guideline, all individual responses are posted on our website

<http://www.aaos.org/quality> with a point-by-point reply to each non-editorial comment. Reviewers who wish to remain anonymous notify the AAOS to have their names de-identified; their comments, our responses, and their COI disclosures are still posted.

THE AAOS CPG APPROVAL PROCESS

This final clinical practice guideline draft must be approved by the AAOS Committee on Evidence Based Quality and Value, the AAOS Research and Quality Council, and the AAOS Board of Directors. These decision-making bodies are described in the SSI CPG eAppendix 1. Their charge is to approve or reject its publication by majority vote.

REVISION PLANS

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

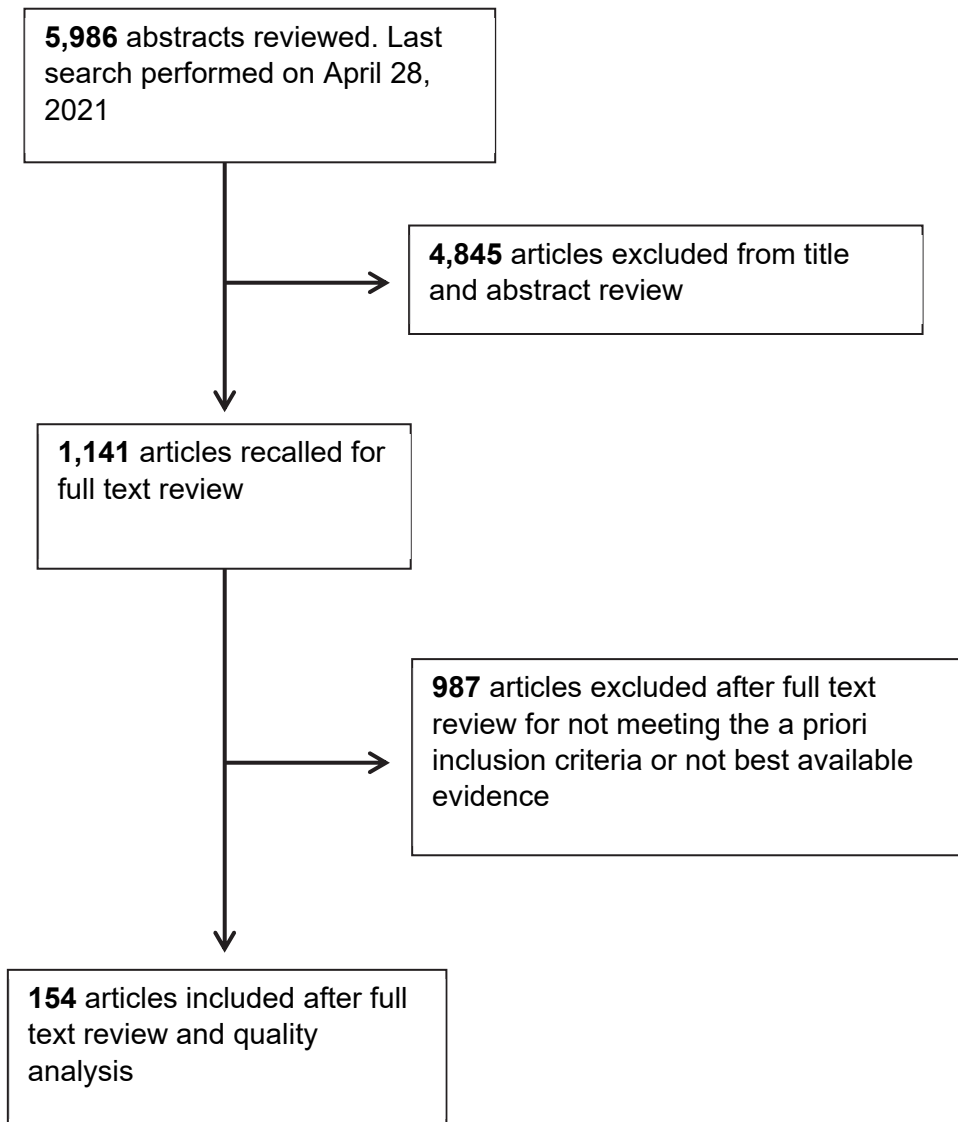
CPG DISSEMINATION PLANS

The primary purpose of the present document is to provide interested readers with full documentation of the best available evidence for various procedures associated with the topic of this review. Publication of most clinical practice guidelines is announced by an Academy press release. Additionally, articles are authored by the clinical practice guideline development group members and published in the *Journal of the American Academy of Orthopaedic Surgeons* and in *AAOS Now*. Most clinical practice guidelines are distributed at the AAOS Annual Meeting in the Resource Center. The final guideline recommendations and their supporting rationales will be hosted on www.OrthoGuidelines.org.

Selected clinical practice guidelines are disseminated by webinar, the AAOS Learning Management Systems (LMS), Media Briefings, and by distributing them at relevant Continuing Medical Education (CME) courses and at the AAOS Resource Center during Annual Meeting.

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STUDY ATTRITION FLOWCHART



RECOMMENDATIONS

Recommendations are formed when there is sufficient evidence by which to create a directional statement. This is defined as evidence from two or more high quality studies (i.e., a strong recommendation), two or more moderate quality studies (i.e., a moderate recommendation), or statements resulting in a strong or moderate strength following Evidence to Decision Framework upgrading and/or downgrading.

Initial Antibiotics

Early delivery of antibiotics is suggested to lower the risk of deep infection in the setting of open fracture in major extremity trauma.

Strength of Evidence: Moderate 

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Rationale

Three moderate quality studies (Hendrickson 2020, Weber 2014, Westgeest 2016) have examined the effectiveness of early antibiotics in the setting of open fracture for prevention of deep infection. Two moderate studies (Lack 2015 and Roddy 2020) compared time from arrival to the emergency department, while one moderate study (Zuelzer 2020) compared time from injury to antibiotic delivery. While the timing was somewhat different between these studies, all three demonstrated that the earliest feasible timing of antibiotic administration reduced the risk of deep infection. Investigation of the effectiveness of early antibiotics for the prevention of other adverse events in the setting of open fracture, such as nonunion or wound complications, has been limited to date, without any significant differences seen in one moderate quality study (Westgeest 2016).

Benefits & Harms

The potential benefit of early antibiotic treatment is prevention of deep infection. The potential harms of antibiotic administration include allergy (including anaphylaxis), microbiome disturbances, Clostridioides difficile infection and selection of antibiotic resistance.

Outcome Importance

Development of deep infection after major extremity trauma can lead to severe morbidity, prolonged hospitalization, and significantly increased utilization of healthcare resources.

Cost Effectiveness/Resource Utilization

The cost of prophylactic antibiotic dosing is significantly less than what is required for treatment of deep infection.

Feasibility

While seemingly feasible, the treatment of major extremity trauma is frequently not an isolated entity and may not always be the most pressing issue in the setting of severe trauma. It is important that the

healthcare professionals responsible for the musculoskeletal care of patients with major lower extremity trauma be aware of and advocate for the earliest feasible timing for administration of antibiotics in this setting.

Future Research

Future research is needed to further refine the threshold on timing of early antibiotic treatment for the prevention of deep infections following open fracture with major extremity trauma, as well as to determine if early antibiotic treatment is associated with lower risk of other adverse events, such as nonunion or wound complications.

Preoperative Antibiotics

Utilization of preoperative antibiotics is suggested to prevent SSI in operative treatment of open fractures.

Strength of Evidence: Limited

Strength of Recommendation: Moderate  (Upgraded)

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Rationale

Prophylactic antibiotics prior to fracture surgery has become the standard of care for several decades. Surprisingly the data supporting prophylactic antibiotic use in such procedures is at best scarce. In 1970s and 1980s a handful of studies provided support for preoperative antibiotic use in both closed and open fractures (Boyd 1973, Patzakis 1974, Burnett 1980, Gatell 1984, Braun 1987, Buckley 1990).

Notably there are only two studies in open fracture patients (Patzakis 1974, Braun 1987). The study by Braun (1987) is a moderate quality study that compared administration of cloxacillin for 10 days versus placebo for 10 days in only 100 patients with open fractures. This study demonstrated a decrease in combined group of both superficial and deep infections in the cloxacillin arm ($p < 0.05$). If each subgroup deep and superficial infections) is individually compared, the decrease was not significant.

The additional studies available support the use of prophylactic antibiotics and provide additional evidence for upgrading the level of recommendation, on the other hand, they largely fall outside of the scope of this CPG.

Benefits & Harms

Prevention of SSIs is extremely important in open fractures. Use of initial antibiotics can decrease the bioburden of organisms in the wound. On the other hand, indiscriminate use of antibiotics can lead to significant cost, adverse events and emergence of resistant bacteria.

Outcome Importance

Inappropriate use of antibiotics can lead to an increase in antibiotic related adverse events, emergence of resistance and increased morbidity and mortality. However, post traumatic bone infections can cause suffering and disability in the patient and result in higher medical costs. Therefore, prevention of such infections is crucial.

Cost Effectiveness/Resource Utilization

Antibiotic use must consider cost of the drug, pharmacy time for drug preparation, and nursing time for administration of the drug. Additionally, if there are adverse events or emergence of resistance related to antibiotics, it can lead to prolongation of hospital stay and worse clinical outcomes.

Acceptability

Antibiotics are indicated for prevention of fracture related infections (FRI) and are currently the standard of care.

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Feasibility

Intervention has been extensively used and is feasible.

Future Research

Initial antibiotic therapy for prevention of infections in open fractures is the current standard of care. This data has been derived from small scale studies which have shown marginal benefit. A large-scale research study is needed to address the efficacy of antibiotics for prevention of infection in open fractures and the impact of this therapy on emergence of resistance and antibiotic related adverse events.

Additional References Cited in Rationale

1. Boyd, Robert J.; Burke, John F.; Colton, Theodore A Double-Blind Clinical Trial of Prophylactic Antibiotics in Hip Fractures, *The Journal of Bone & Joint Surgery*: September 1973 - Volume 55 - Issue 6 - p 1251-1255
2. Burnett JW, Gustilo RB, Williams DN, Kind AC. Prophylactic antibiotics in hip fractures. A double-blind, prospective study. *The Journal of Bone and Joint surgery. American Volume*. 1980 Apr;62(3):457-462. PMID: 7364818.
3. Gatell JM, Riba J, Lozano ML, et al. Prophylactic cefamandole in orthopaedic surgery. *The Journal of Bone and Joint surgery. American Volume*. 1984 Oct;66(8):1219-1222. PMID: 6386819.
4. Buckley R, Hughes GN, Snodgrass T, Huchcroft SA. Perioperative cefazolin prophylaxis in hip fracture surgery. *Canadian Journal of surgery. Journal Canadien de Chirurgie*. 1990 Apr;33(2):122-127. PMID: 2268811
5. Patzakis, Michael J.; Harvey, J. Paul JR.; Ivler, Daniel The Role of Antibiotics in the Management of Open Fractures, *The Journal of Bone & Joint Surgery*: April 1974 - Volume 56 - Issue 3 - p 532-541

Surgery Timing

It is suggested that patients with open fractures are brought to the OR for debridement and irrigation as soon as reasonable, and ideally before 24 hours post injury.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Rationale

There are many articles comparing the proportion of patients with surgical site infection in open fractures whose surgical debridement took place either before or after 6 hours. One high quality study (Konbaz 2019), nine moderate quality studies (Albright 2020, Enninghorst 2011, Harley 2002, Hendrickson 2020, Hull 2014, Noumi 2005, Olinger 2018, Weber 2014, Westgeest 2016), and twenty low quality studies (Whiting 2019, Pollak 2010, Sagar 1987, Srouf 2015, Campbell 2020, Wei 2014, Nibert 2016, Al-Arabi 2007, Hendrickson 2018, Malhotra 2014, Spencer 2004, Arti 2012, Joseph 2020, Fernandes 2015, Reuss 2007, Tripuraneni 2008, Al-Hilli 2010, Charalambous 2005, Crowe 2017, Townley 2010) were reviewed. One high quality (Konbaz 2019) study did not support the 6-hour rule for performing the debridement but demonstrated a correlation of infection with the Gustillo classification, use of external fixation and not closing the wound primarily at the first debridement. Six moderate quality studies did not support the 6-hour rule (Albright 24 hours, Harley no correlation with time to surgery, Hendrickson no correlation with time to antibiotics, Noumi no correlation, Weber no correlation, Westgeest no correlation).

Benefits/Harms of Implementation

The current evidence is insufficient to definitively confirm the importance of early surgical intervention for open fractures, although this might not be true for certain fractures such as tongue-type calcaneus fractures. In some fractures, such as pilon fracture, waiting for final surgical intervention might be more appropriate. More studies are required.

Outcome Importance

This data suggests waiting a few extra hours to perform surgery in most but not all open fractures might have advantages in terms of preparation for surgery, marshalling the necessary resources, staffing, and equipment. However, more evidence is needed.

Cost Effectiveness/Resource Utilization

The current insufficient evidence indicates urgent surgical care might not be necessary for most but not all open fractures. Timely surgical care would be expected to improve the resource allocation and potentially enhance outcomes post-surgery if and when the operative team is better prepared and adequately staffed.

Acceptability

More timely surgery as opposed to urgent surgical care can potentially improve preparation of the surgical team as well as allow for better patient optimization. In certain cases, access to comprehensive
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medical care is simply not possible within the proposed 6-hour surgery window, particularly in under resourced rural and geographically isolated areas.

Future Research

Most of the current evidence comes from retrospective case series with small cohorts. In many instances, the study population has more than one type of fracture or includes fractures in different anatomical regions. Future studies require larger cohorts, concentration on specific fracture types or anatomical regions, and greater specificity in the operative and postoperative protocols. Prospective randomized studies, particularly if done through multicenter design, are required to more definitively address this issue and establish a widely recognized standard of care.

Perioperative and Postoperative Antibiotics – Systemic and Local

In patients with major extremity trauma undergoing surgery, it is recommended that antibiotic prophylaxis with systemic cefazolin or clindamycin be administered, except for Type III (and possibly Type II) open fractures, for which additional Gram-negative coverage is preferred.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

In patients with major extremity trauma undergoing surgery, local antibiotic prophylactic strategies, such as vancomycin powder, tobramycin-impregnated beads, or gentamicin-covered nails, may be beneficial.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★★★☆

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Rationale

In patients with major extremity trauma undergoing surgery, antibiotic prophylaxis with systemic cefazolin or clindamycin is recommended over expanded Gram-negative coverage, although for Type III fractures, piperacillin-tazobactam is preferred. The addition of gentamicin or vancomycin to cefazolin does not appear to be helpful. In closed and open fractures (except Type III and possibly Type II open fractures), there is no need to continue antibiotic prophylaxis longer than a day. Local antibiotic delivery prophylaxis appears to be promising, with one high quality study (O’Toole 2021) finding that peri-operative vancomycin powder may be useful for decreasing Gram-positive infections in closed fractures. Implant protection was also identified as being promising for prevention of surgical site infection, with one study (Pinto 2019) demonstrating a benefit for gentamicin coated nails; tobramycin-impregnated beads (Osterman 1995) also appeared promising.

Three high (Mathur 2013, Vasenius 1998, Carsenti-Etesse 1999), five moderate (Crist 2018, Dunkel 2013, Janmohammadi 2011, Saveli 2013, Sorger 1999), and seven low quality articles (Lloyd 2017, Frantz 2020, Bankhead-Kendall 2019, Lachman 2018, Pannell 2016, Patanwala 2019, Stennett 2020) informed the recommendation for antibiotic prophylaxis, and one high (O’Toole 2021), two moderate (Moehring 2000, Pinto 2019) and four low quality articles (Qadir 2020, Singh 2015, Vaida 2020, Osterman 1995) informed the recommendation for local prophylactic strategies. Lloyd (2017) evaluated narrow spectrum (cefazolin, clindamycin or amoxicillin-clavulanate) compared to expanded Gram-negative coverage (included fluoroquinolone and/or aminoglycoside) for combat-related open fracture injuries reporting a beneficial effect of the latter for skin and soft-tissue infections, with no difference in osteomyelitis, length of hospitalization, or operating room visits. A higher proportion of patients in the expanded Gram-negative coverage group had Gram-negative organisms isolated that

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were not susceptible to fluoroquinolones and/or aminoglycosides. The authors concluded that their results support the use of cefazolin or clindamycin with open fractures.

Sorger (1999) evaluated the response to either gentamicin 5 mg/kg divided into two daily doses or gentamicin 6 mg/kg once daily, both in combination with cefazolin 1g/8hours for open tibial, ankle, forearm, femur, humerus, foot, and patella fracture, revealing no differences in infection rates.

Vasenius (1998) evaluated the response to peri-operative clindamycin versus cloxacillin for open clavicle, upper arm, elbow, forearm, wrist/hand, finger, femur, knee, lower leg, ankle, foot, toe, talus or calcaneus fracture, with the former being more beneficial with regards to total infection rates. Neither clindamycin nor cloxacillin demonstrated high efficacy in Type III open fractures.

Frantz (2020) compared intravenous cefazolin and aminoglycoside to piperacillin-tazobactam for Gustilo type II or III open fractures of the extremities. Compared to piperacillin-tazobactam, both cefazolin-based regimens had higher risks of delayed wound healing or superficial infection. Compared to piperacillin-tazobactam, cefazolin alone had higher independent odds of deep infection requiring return to the operating room.

Janmohammadi (2011) compared cefazolin with gentamicin to cefazolin with ciprofloxacin for open type IIIA open humerus, radius, ulnar, femur, tibia, and fibula fractures, reporting no difference in efficacy for infection prevention.

Dunkel (2013) evaluated reduced versus extended post-operative antibiotic durations in open fractures (Gustilo and Anderson grade I, II and III and unclassifiable). Overall, compared with one day of antibiotic treatment, two to three days, four to five days or > five days did not exhibit any significant differences in the infection risk. Cefuroxime was the most frequently prescribed antibiotic in this study, although 40 different antibiotic regimens were used.

Saveli (2013) performed a pilot randomized clinical safety study evaluating prophylactic antibiotics in open fractures. Patients were randomized to receive cefazolin alone or vancomycin and cefazolin from presentation to the emergency department until 24 hours after the surgical intervention. There was no difference in the rates of surgical site infections between the study arms.

Mathur (2013) randomly allocated patients to receive three doses of intravenous cefuroxime perioperatively versus 5 days of intravenous cefuroxime with amikacin followed by oral cefuroxime until suture removal for open reduction and internal fixation of closed fractures of limbs reporting no difference in surgical site infection rates.

Lachman (2018) evaluated intravenous cefazolin or vancomycin compared to oral cephalexin or clindamycin for closed ankle fractures with no differences noted.

Crist (2018) performed a randomized study of 23 hours of prophylactic post-operative cefazolin compared to placebo after open reduction internal fixation of closed extremity fractures with no differences in surgical site infections between the two groups.

One open label randomized clinical trial (O'Toole 2021) evaluated intrawound vancomycin powder compared controls for adults with an operatively treated tibial plateau or pilon fracture. The probability of deep infection was lower in the vancomycin powder than the control group with the effect of vancomycin powder attributed to its reduction against Gram-positive but not Gram-negative infections.

Osterman (1995) evaluated tobramycin-impregnated beads compared to no tobramycin-impregnated beads for patients with severe open fractures, with all patients receiving intravenous tobramycin, penicillin and cefazolin, to prevent surgical site infection post-surgery reporting a reduced overall infection rate with the use of tobramycin-impregnated beads. Both acute infection and local osteomyelitis

were decreased with the use of tobramycin-impregnated beads, but this was statistically significant only in Gustilo type-3B and type-3C fractures for acute infection, and only in type-II and type-IIIB fractures for chronic osteomyelitis.

Moehring (2000) performed a randomized prospective clinical trial in patients with open fractures comparing tobramycin-impregnated beads versus intravenous antibiotics demonstrating no differences between the groups. Pinto (2019) evaluated gentamicin-impregnated intramedullary interlocking nails versus controls in Gustilo type I and II open tibia fractures reporting a beneficial effect in terms of reduced surgical site infection.

A limitation is that data on several possible alternative antibiotics, that might be considered for prophylaxis, was unavailable. Clindamycin is not favored by some guidelines.

Benefits/Harms of Implementation

The potential benefit is prevention of infection. The potential harms of antibiotic administration include allergy (including anaphylaxis), microbiome disturbances, Clostridioides difficile infection and selection for antibiotic resistance.

Outcome Importance

Development of infection after major extremity trauma can lead to severe morbidity, prolonged hospitalization and results in significantly increased utilization of healthcare resources.

Cost Effectiveness/Resource Utilization

The cost of peri-operative and post-operative, prophylactic antibiotic(s) is significantly less than what is required for subsequent treatment of infection should it occur.

Future Research

Future research is needed to further refine the ideal peri-operative and post-operative, prophylactic antibiotic(s) best prevent SSI post-surgery.

Initial Wound Management – Irrigation and Fixation

Irrigation with saline (without additives) is recommended for management of open wounds in major extremity trauma.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reasons to downgrade from the EtD framework

Definitive fixation of fractures at initial debridement and primary closure of wounds in selected patients may be considered when appropriate, however no favored treatment was observed.

Temporizing external fixation remains a viable option for the treatment of open fractures in major extremity trauma.

Strength of Evidence: Strong

Strength of Recommendation: Moderate ★★★★★ (downgrade)

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Rationale

Four high (Bhandari 2015, Petrisor 2011, Anglen 2005, Gao 2019)) and three moderate (Olufemi 2017, Ovsaka 2016, Pinto 2019) quality articles informed the recommendation on wound irrigation and five high (Garg 2019, Mohseni 2011, Galal 2018, Keating 1997, Konbaz 2019), fifteen moderate (Antich-Adrover 1997, Henley 1998, Tornetta 1994, Tu 1995, Holbrook 1989, Bali 2011, Avilucea 2016, Zhang 2016, Bach 1989, Pal 2015, Nuomi 2005, Finkemeier 2000, Ma 2006, Pinto 2019, Al-Hourani 2019), and twenty-four low quality (Nikolic 2018, D’Alleyrand 2014, Sun 2021, Ganji 2011, Memon 2014, Erturk 2013, Pollak 2010, Alberts 1999, Rohde 2007, Inan 2007, Zhao 2019, Wei 2014, Yokoyama 1995, Revak 2021, Stoddart 2020, Kayali 2009, Danoff 2015, Lee 2009, Ziran 2004, Tareen 2019, Gupta 2015, Williams 1995, Yokoyama 1999, Uchiyama 2016) articles informed the fixation statements. While there is a plethora of evidence seeking to answer questions surrounding appropriate management of the soft tissue injuries associated with major extremity trauma, the majority of evidence is of lower quality or not generalizable to this entire population.

There has been work to attempt to address the important questions regarding what solution is best for initial management and irrigation of open wounds in the setting of major trauma. Work by Anglen (2005) has shown with convincing evidence that there is little help and potential harm to additives such as soap and antibiotics. Saline alone is sufficient for initial irrigation of these wounds. The FLOW group and others have shown that there is no significant difference in outcomes when looking at very low, low, or high-pressure irrigation in the management of these wounds. There are also initial cost considerations regarding these different treatment options. Using saline and very low-pressure devices for the delivery in initial management of open wounds is not only appropriate but has the added advantage of saving cost in an environment where this is often a consideration.

When surgeons are faced with decisions regarding initial management of open wounds and fractures in patients who suffer major extremity trauma, there is no algorithm that fits all patients and injuries. A

significant body of research has attempted to answer this question. We can safely say that, in appropriate settings, definitive fixation of fractures and closure of traumatic wounds is appropriate. If, in a treating surgeon's opinion, the wounds are not amenable to immediate closure, temporizing fixation (of which there are many different possibilities) and wound management until such time that definitive management is feasible is a prudent course of action. While there are some high-quality studies that assist us in making this recommendation, our group decided to downgrade from a strong to moderate strength of recommendation because of the large differences among studies that discuss outcomes in these settings. No patient and injury combination are ever the same. Every factor must be taken into consideration when making these decisions.

Benefits & Harms

The benefits of appropriate management of the soft tissue injury associated with major extremity trauma far outweigh the potential harms. Soft tissue integrity is essential for appropriate extremity function and protection of the underlying structures. The harm of inappropriate or inadequate soft tissue management can be significant.

Outcome Importance

Favorable outcomes of soft tissue injury associated with major extremity trauma allows for significant secondary benefits including decreased initial hospital length of stay and fewer operative interventions, both freeing resources to address additional patients. By diminishing the risk of deep infection, the economic burden of care for these patients can potentially be reduced, again increasing the opportunity to utilize valuable healthcare resources more efficiently. Treatment failure as a result of infection almost invariably results in additional procedures, rehospitalization, and prolonged antibiotics, delaying rehabilitation and frequently eliminating affected individuals from the workforce. The specter of late amputation after failed limb-salvage is often a very real consideration and may sometimes be the preferred definitive reconstructive option. These important issues can clearly have dramatic socio-economic implications, not only with regards to the necessary health care but also in terms of lost wages, possible divorce, dissolution of the nuclear family, depression, social isolation, and workers compensation claims.

Cost Effectiveness/Resource Utilization

While the costs associated with appropriate soft tissue management in major extremity trauma can be great, the initial cost of management can be far outpaced by the potential cost of management of the sequela of complications.

Acceptability

Appropriate soft tissue management is generally accepted as important although specific details regarding the most appropriate management continues to be a topic of important scholarly work.

Feasibility

Appropriate management of these soft tissue injuries is highly feasible, and an important facet of existing trauma systems that will continue to be further refined moving forward.

Future Research

Further research is required to definitively answer important questions surrounding the appropriate management of soft tissue injuries associated with major extremity trauma.

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- What is the most appropriate initial management of extremities in the setting of major soft tissue injury with and without fracture?
- What irrigation solutions are most appropriate and at what pressure?
- When is temporizing fixation and delayed coverage more appropriate than definitive fixation and primary soft tissue closure?

Wound Coverage

Wound coverage fewer than 7 days from injury date is suggested.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate 

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework

Rationale

Four moderate quality (Lack 2015, Clegg 2019, Olinger 2018, Hendrickson 2020) and thirteen low quality (Vandenberg 2017, Chua 2014, Hou 2011, Rinker 2008, Arslan 2019, Liu 2012, Whiting 2019, Hohmann 2007, Scharfenberger 2017, Pollak 2000, D’Alleyrand 2014, Philandrianos 2018, Yazar 2006) studies have investigated the risk of deep infection or need for late amputation as a function of the time necessary to achieve definitive wound coverage. However, almost all of these investigations only analyzed the time to coverage data as a secondary outcome within a broader study. There are no Level 1 studies that serve as the basis for this recommendation, with no randomized controlled trials available. Three of the four moderate-quality studies (Lack 2015, Clegg 2019, Olinger 2018) only evaluated timing of definitive coverage as a secondary outcome, limiting their value with respect to the gravitas they carry specific to this recommendation. Regardless, all three fully support the concept of early definitive coverage of open fracture wounds with flaps, local or distant, when necessary. These three studies all report better outcomes when coverage is achieved on or before the 7th day.

The fourth moderate quality study (Hendrickson 2020) and all thirteen of the low quality (Vandenberg 2017, Chua 2014, Hou 2011, Rinker 2008, Arslan 2019, Liu 2012, Whiting 2019, Hohmann 2007, Scharfenberger 2017, Pollak 2000, D’Alleyrand 2014, Philandrianos 2018, Yazar 2006) studies were observational longitudinal cohort studies, and although completed retrospectively they collectively further inform this recommendation. They are all therefore inevitably susceptible to potential confounding and multiple biases, particularly selection bias. The most severe injuries would in fact be less likely suitable for early coverage, and therefore at increased risk of treatment failure independent of the timing of definitive coverage. Nevertheless, almost all these studies support and promote the general principle of early definitive coverage of open fracture wounds with local rotational myoplasties or microvascular free tissue transfers when necessary. The majority of these studies specify 7 days as the defined limit, with worse outcomes consistently reported when coverage is delayed beyond 7 days for any reason.

Benefits & Harms

The available studies consistently demonstrate, with few exceptions, that early coverage of open fractures very likely decreases the risk of deep infection, with a resulting decreased length of stay, fewer procedures during the initial hospitalization, and a diminished risk of later developing both skeletal and soft-tissue specific complications.

Outcome Importance

These injuries are often devastating in severity and are generally at tremendous risk of permanent disability or amputation; minimizing the possibility of deep infection is certainly of paramount importance. Infection almost inevitably results in additional surgery, prolonged hospitalization, and independently increases the probability of treatment failure or late amputation. This potentially condemns the affected individual to a protracted course of further limb-salvage procedures, additional hospitalizations, and prolonged antibiotics, all of which can dramatically delay the rehabilitation process and in many instances

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permanently remove them from the active workforce. All these considerations have tremendous economic implications, not only for the necessary health care but also additional substantial societal costs in terms of lost wages and workers' compensation.

Cost Effectiveness/Resource Utilization

This timeframe allows for coordination of care with other specialties, including plastic surgeons or other surgeons and nursing staff with microvascular expertise. This definitive procedure can then be scheduled electively, when clinical and logistical conditions have been optimized. This also provides time to complete angiography if necessary to better define the local vascular anatomy, to aid in preoperative planning, selection of donor tissue, and surgical decision-making processes such as choice of anastomotic technique.

Acceptability

Early wound coverage is preferable, and within 7 days appears to strike a reasonable balance between clinical urgency and practicality. The current literature supports this timeframe, and this recommendation should be considered highly acceptable.

Feasibility

Delay of definitive coverage for several days has certain benefits regarding better patient optimization in poly-trauma scenarios, as well as allowing for transfer from rural or regional medical facilities that may lack the necessary resources or expertise. Under most circumstances, the seven-day limit for securing soft-tissue coverage provides the necessary balance between satisfying the dual demands of clinical exigency and what are often complex superimposed logistical issues.

Future Research

Most of the current evidence consists of uncontrolled retrospective longitudinal cohort studies with only small or moderate sample size. These studies are limited by inherent selection bias and other confounding factors, limiting their intrinsic value and generalizability. In some cases, the study population has more than one type of fracture or includes fractures in different anatomical regions. Future studies require a larger sample size, concentration on specific fracture types or anatomical regions, and adherence to strict protocols in the pre-operative, operative, and postoperative periods. Given the wide spectrum of pathology often encountered, the probability of concomitant poly trauma in many cases, and the likelihood of confounding factors characteristic of the trauma population, large prospective randomized studies with a multicenter design would prove difficult to coordinate, but ultimately will be required to answer this question definitively and establish the standard of care.

Negative Pressure Wound Therapy – Open and Closed Fractures

After closed fracture fixation, negative pressure wound therapy may mitigate the risk of revision surgery or SSIs; however, after open fracture fixation, negative pressure wound therapy does not appear to offer an advantage when compared to sealed dressings as it does not decrease wound complications or amputations.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reason to downgrade from the EtD framework.

Rationale

Four high quality (Costa 2018, Virani 2016, Arti 2006, Stannard 2006) and five low quality (Rinker 2008, Labler 2004, Burt 2020, Blum 2012, Joethy 2013) studies have evaluated the role of negative pressure wound therapy for wound management after high-energy trauma. This includes both open fracture care as well as for the management of post-operative incisions following stabilization of at-risk fractures. The higher quality studies included 2 large multicenter RCTs, as well as 3 small single center RCTs. The large multicenter studies concluded NPWT did not provide any benefit compared to standard wound care with sterile gauze dressings. The use of NPWT did not improve patient self-rated disability at 12 months, and rates of deep infection were not reduced with NPWT compared to standard dressings. Although the three smaller single center RCTs demonstrated better outcomes with NPWT, these findings were not confirmed. Although several low-quality studies demonstrated more favorable outcomes with NPWT, this more likely reflects elements of selection bias and other confounding variables often associated with uncontrolled retrospective studies.

Benefits & Harms

The large high-level study demonstrated that NPWT does not appear to have any significant influence on the risk of deep infection, the length of hospitalization, or the risk of later developing either skeletal or soft-tissue specific complications. At least one recent low-quality study (Burt 2020) suggests NPWT may be associated with a dramatically increased risk of one or more complications, and its continued use for this clinical situation should be considered recognizing the decision is difficult to justify with respect to the increased costs associated.

Outcome Importance

Routine wound care with sterile gauze dressing changed regularly appears to be equally efficacious in comparison to NPWT, as demonstrated in the highest quality study to evaluate these two treatment alternatives. While this suggests that either treatment could be employed with complete confidence at the discretion of treating clinicians, the financial implications and burden on the healthcare system cannot support the continued use of NPWT for this particular application.

Cost Effectiveness/Resource Utilization

The lack of any genuine benefit resulting from NPWT does not at this time justify the increased costs associated. Despite the outcomes reported in earlier uncontrolled retrospective studies, as epitomized by Blum (2012), high quality studies reveal the convenience and potential theoretical advantages of NPWT

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do not warrant the increased costs that inevitably accrue. This likely reflects inherent biases and confounding factors characteristic of many retrospective clinical studies.

Acceptability

Standard wound care with sterile gauze dressings changed regularly has proven to be equally effective when compared to NPWT. The current literature fully supports this conclusion, and this recommendation should be considered highly acceptable.

Feasibility

Despite the attraction of convenience with respect to nursing staff and dressings used, the potential benefits of NPWT for wound care related to major extremity trauma have not yet been realized. While highly feasible in many clinical situations, the inability to demonstrate any tangible benefits has failed to justify the increased costs associated.

Future Research

Although large multicenter randomized trials have failed to demonstrate any advantage of NPWT for the early management of open fractures, the potential benefit of this type of treatment for post-operative wounds following stabilization of complex high-energy at-risk fractures has not been evaluated with as much rigor. Similarly, the role of intermittent irrigation with antibiotics or other wound cleansing agents as an adjunct to standard NPWT has also not been adequately explored with any high-level studies.

Open Wound Closure

Closing an open wound when it is feasible to without any gross contamination is recommended.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reasons to downgrade from the EtD framework

Rationale

Two high quality (Jenkinson 2014, Konbaz 2019) and four low quality (Wei 2014, Peterson 2020, Russell 1990, Hohman 2007) studies have addressed the topic of primary closure of an open fracture, and all have concluded the practice is safe in selected wounds after adequate formal operative debridement by an experienced surgeon(s). Jenkinson (2014) investigated the risk of developing deep infection after primary closure of the open fracture site in a series of 349 Type 1/2/3A lower extremity injuries treated at a North American academic Level 1 trauma center. Using a propensity-matched cohort model, and after carefully controlling for a number of other confounding variables, they demonstrated the rate of infection was more than four times higher in those managed with delayed primary closure compared to those closed immediately. The remaining four low quality studies were observational longitudinal cohort studies, and they are all therefore inevitably susceptible to potential confounding and multiple biases, particularly selection bias. More severe injuries would generally be less suitable for primary closure, and therefore are at increased risk of infection independent of the timing of closure. The Hohmann (2007) study from South Africa used a different model, where open fractures at one hospital were closed primarily and open fractures at another hospital underwent delayed primary closure. Although they observed no meaningful difference in infection rates and this result is favorable for advocates of immediate early primary wound closure, in this context it also can be considered equally favorable for delayed wound closure protocols. Nevertheless, most of these low quality studies further support and promote the general principle of early primary closure of open fracture wounds whenever possible. Only the Russell (1990) study reported the risk of infection following primary closure of Type 1/2/3A injuries resulted in a higher risk of deep infection (14%) compared to delayed closure of similar wounds (0%). However, this particular cohort was treated between 1981 and 1985, and perhaps does not adhere to current standards for surgical debridement or antibiotic options.

Benefits & Harms

The contemporary literature consistently indicates that, after thorough operative debridement by an experienced surgeon, primary closure of many open fractures can be considered safe and effective. This action very likely decreases the risk of deep infection, and is associated with a shorter length of stay, fewer procedures during the initial hospitalization, and a reduced risk of later developing further complications.

Outcome Importance

Minimizing the possibility of infection is extremely important because infection almost always leads to additional surgery and prolonged hospitalization. Deep infection may result in chronic osteomyelitis or an infected non-union, and treatment failure may ultimately lead to amputation. These factors all have significant economic implications, including not only the greater health care costs that might accrue but also the substantial additional societal costs in terms of lost wages and workers' compensation. There

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are additional complex implications regarding the affected individual's social status, the risk of divorce and disruption of the family unit, and the possibility of depression and isolation.

Cost Effectiveness/Resource Utilization

Primary wound closure for selected open fractures is the more cost-effective approach, and one that utilizes fewer resources. Fewer operative procedures and a decreased length of initial hospitalization inevitably results in more efficient allocation of hospital beds, theatre time, theatre space, and clinical consumables.

Acceptability

Early primary wound closure is preferable, and current literature informs us this can be safely done in selected cases following meticulous operative debridement by an experienced surgeon. Considering the reduction in length of stay and more efficient resource utilization, this recommendation should be considered highly acceptable.

Feasibility

Primary wound closure for selected open fractures is an easily implemented and more cost-effective alternative. It requires an experienced trauma surgeon to make the decision, and this is perhaps not always convenient. However, surgeons can choose this course of action with confidence when the wound is carefully assessed and considered appropriate.

Future Research

This recommendation is largely based on uncontrolled retrospective studies with inadequate sample size, studies that may be diminished by the substantial risk of selection bias and other confounding factors. Future research will require a larger sample size, concentration on specific fracture types or anatomical regions, and adherence to strict protocols in the pre-operative, operative, and postoperative periods. Given the tremendous variety of pathology encountered, the probability of additional severe injuries in many cases, and the likelihood of confounding factors typical of the trauma population, large prospective randomized studies with a multicenter design would prove difficult to coordinate, but ultimately will be required to answer this question definitively.

Silver Coated Dressings

Silver coated dressings are not suggested to improve outcomes or decrease pin site infections.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★☆☆

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework

Rationale

One high quality study (Yuenyongviwat 2011) investigated the use of silver coated dressings which was a prospective randomized controlled study among 30 patients who had an open tibial fracture treated with debridement and external fixation. It compared the outcome of pin dressing using silver sulfadiazine (study group = 15) with dry dressing (control = 15). It should be noted that these patients had a silver dressing of their external fixator pin sites and not the tibial open wound or closure itself. The study group had daily pin-site dressing with normal saline and applied 0.5 ml of 1% silver sulfadiazine. The control group had daily dry dressings.

The authors considered a pin tract infection present if erythema, cellulitis, serous or purulent discharge occurred around a pin site and deep infection of osteolysis around the pin, and sequestrum.

The prevalence of pin-site infection reports ranges from 10-42% depending on the study site, study subject and follow-up period. The consequence of pin-site infection is pain, pin loosening and increased risk of peri-implant infection.

In this study cohort at least 80% were Gustilo Type 3 classification of open fracture (in 13 and 12 patients, respectively). In the silver-coated dressing arm, 46.7% developed infected pin sites, while 40% developed it in the control group. There was no significant difference between these groups.

Benefits & Harms

There appears to be neither any benefit nor harm in using silver-impregnated dressings for this application. No patients had an adverse reaction to the silver dressing.

Cost Effectiveness/Resource Utilization

Silver-coated dressings using materials such as silver sulfadiazine are a marginal cost in the initial context of major extremity trauma.

Acceptability

Appropriate soft tissue management is generally accepted as important although the specific details of this management continues to be a topic of important scholarly work.

Feasibility

Appropriate management of soft tissue injuries is highly feasible, and an important facet of existing trauma systems that will continue to be further refined moving forward.

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Future Research

There is a need for future studies which utilize silver coated dressings on the closed wound itself, both in the setting of operative stabilization of closed fractures and following debridement and closure of open fracture sites.

Modifiable Risk Factors

In patients undergoing surgery for major extremity trauma, patients should be counseled that:

- There may be an increased risk for SSI in patients who smoke or who are diabetic.

Strength of Evidence: Strong

Strength of Recommendation: Strong ★★★★★

Evidence from two or more “High” quality studies with consistent findings for recommending for or against the intervention. Also requires no reasons to downgrade from the EtD framework

- There may be an increased risk for SSI in obese patients.
- Significant alcohol use (>14 units per week) increases the risk of infection postoperatively.
- High flow perioperative FIO2 has not been shown to alter the risk of postoperative infection.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★★★☆

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework

- Low albumin (<36g/L) increases the risk of infection postoperatively.
- Elevated postoperative glucose levels (>125 mg/dL) increase the risk for infection.
- Preoperative transfusion, intraoperative evaluation by a vascular service in patients with grade 3a, 3b open fractures with well perfused limbs, and preoperative MRSA positivity has not been shown to alter the risk of postoperative infection.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Rationale

Three high (Molina 2015, Chan 2019, Esposito (2019), ten moderate (Enninghost 2011, Su 2017, Li 2020, Olson 2021, Bai 2019, Morris 2013, Clegg 2019, Sagi 2017, Hendrickson 2020, Castillo 2005), and two low quality studies (Pollak 2010, Adams 2001) investigated the effect of smoking on SSI. There were mixed findings with 40% of these papers finding an increased risk of SSI in smokers and 60% finding no difference in SSI between smokers and non-smokers. However, some of these studies that did not identify a difference in the two groups were likely underpowered to be able to discern a difference.

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Two high (Chan 2019, Molina 2015), four moderate (Hendrickson 2020, Li 2020, Bai 2019, Clegg 2019), and two low quality studies (Kline 2009, Ricci 2014) investigated the effect of diabetes on SSI. Again, there were mixed findings with 62.5% of the studies finding an increased risk for SSI in patients with diabetes and 37.5% of the studies finding no difference.

One high (Chan 2019) and three moderate quality studies (Olson 2021, Bai 2019, Su 2017) investigated the effect of obesity on SSI. Chan (2019) and Olson (2021) observed no increase in risk for SSI following ORIF of tibial plafond and tibial plateau fractures in obese patients as compared to patients who were not obese whereas Bai (2019) and Su (2017) noted an increased risk for SSI in obese patients with femoral and calcaneal fractures.

One high quality study (Chan 2019) investigated the effect of alcohol on SSI and reported that alcohol use >14 units per week significantly increased the likelihood of surgical site infection.

One high quality study (Stall 2013) investigated the effect of high flow perioperative O₂ on the risk for SSI but observed no difference in risk for infection in patients with high (80%) or low (30%) FIO₂ perioperative oxygen.

One moderate quality study (Bai 2019) investigated the effect of low albumin on SSI and noted a higher risk for deep infection in patients with preop albumin <36g/L as compared to those with preoperative albumin >36g/L.

One moderate quality study (Ren 2015) investigated the effect of blood glucose on SSI and reported an increased risk for infection in patients with elevated postoperative glucose levels when compared to patients with glucose <125 mg/dL.

One moderate quality study (Weber 2014) investigated the effect of transfusion on SSI but failed to identify any significant difference in the risk of deep infection in patients who received a transfusion as compared to those that did not.

One moderate quality study (Waikukul 1998) investigated the need for intraoperative vascular surgery consultation for Gustilo type 3A/3B open lower extremity fractures and reported that although this exploration did improve chronic swelling, decrease paresthesias and decrease the risk for re-grafting, it did not alter the risk for SSI.

One moderate quality study (Saveli 2013) observed no increased risk of superficial SSI, MSSA/MRSA deep infection or any deep infection when patients were noted to have preoperative MRSA colonization as compared to those that were not.

Benefits & Harms

Modification of these risk factors, when possible, has the potential to significantly decrease postoperative infection in patients with major extremity trauma.

Outcome Importance

This data provides information that may improve patient counseling in the perioperative period. While these risk factors are modifiable, surgical treatment of these fractures is generally performed on an urgent basis with a timeline that generally does not allow preoperative alteration of these risk factors. Although some of these risk factors can be modified in the immediate postoperative period, it is unclear how this may or may not influence outcomes.

Cost Effectiveness/Resource Utilization

This recommendation allows physicians, hospitals and payors to better counsel patients and align expectations with respect to the increased risk factors for SSI.

Acceptability

Medical optimization is performed when possible perioperatively. This information can help inform clinicians as to what modifiable risk factors should be targeted in the immediate perioperative period.

Feasibility

Medical optimization can be undertaken while a patient is still in the hospital for their injury. Other modifiable risk factors such as alcohol use, smoking and glycemic control require patient comprehension and compliance to have any reasonable expectation of positively influencing outcomes.

Future Research

Many of these studies are retrospective in nature and may not be powered to fully describe the various risk factors for SSI after major lower extremity trauma. Therefore, further prospective research with larger cohorts, perhaps in a trauma registry, would assist in further elucidating these risk factors.

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Administrative Risk Factors

In patients undergoing surgery for major extremity trauma, patients should be counseled that:

- There is minimal evidence that race, or socioeconomic status affects risk of SSI.

Strength of Evidence: Moderate

Strength of Recommendation: Moderate ★★★★★

Evidence from two or more “Moderate” quality studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

- There was no significant difference in risk of SSI when being treated as an inpatient or outpatient.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★★★★

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Rationale

Two high (Driesman 2017, Molina 2015) and one moderate quality study (Morris 2013) investigated the effect of race and socio-economic status (SES) on SSI, and these demonstrated that race and SES do not alter one’s risk for SSI. It is beyond the scope of this PICO to discuss the effect of race and SES on other surgical outcomes.

One moderate (Backes 2014) and one low quality study (Bergin 2012) discussed the effect of inpatient and outpatient treatment of major extremity trauma as it relates to SSI, and both demonstrated that there was no significant difference in risk of SSI between these two groups.

Benefits & Harms

There are no specific harms to be expected with implementing this recommendation.

Outcome Importance

While there are many other factors that affect the risk for surgical site infection, this allows for discussion with patients that their demographics do not seem to significantly influence their risk of infection.

Cost Effectiveness/Resource Utilization

This recommendation requires minimal resources and there is no cost associated with implementation.

Acceptability

While there is excellent evidence that patient demographics affect other measurable peri and post-operative outcomes, there is no evidence that it specifically affects their risk of surgical site infection in major extremity trauma.

Feasibility

Implementation of this PICO is quite feasible. However, again, patients should be counseled that this recommendation specifically addresses surgical site infection alone and does not address other outcome measures.

Future Research

There is minimal evidence to better inform surgeons regarding the impact of external risk factors for surgical site infection. Furthermore, many of the studies were specific to certain fracture types and therefore could not be generalized to other types of fracture. Future trauma registries may be able to address these issues more definitively, if they include these particular types of external factors in their data sets.

OPTIONS

Low quality evidence, no evidence, or conflicting supporting evidence have resulted in the following statements for patient interventions to be listed as options for the specified condition. Future research may eventually cause these statements to be upgraded to strong or moderate recommendations for treatment.

Negative Pressure Wound Therapy - High Risk Surgical Incisions

It is suggested to use an incisional negative pressure wound therapy for high- risk surgical incisions (e.g., pilon, plateau, or calcaneus fractures) to reduce the risk of deep surgical site infection.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.

Rationale

There is one moderate quality prospective randomized trial (Stannard 2012) on this topic that demonstrated reduced deep surgical site infection using NPWT. A second earlier study by the same group also reported reduced drainage using this technique.

Benefits & Harms

There are no reported harms.

Outcome Importance

If the rate of infection can be decreased with negative pressure wound therapy, then patients’ outcomes will be improved and there is potential for health care cost savings

Cost Effectiveness/Resource Utilization

Although the overall cost-benefit analysis is currently unknown, utilization of negative pressure wound therapy invariably adds cost to the standard treatment, however, surgical site infections are associated with worse patient outcomes, and both high healthcare and associated societal costs.

Acceptability

Negative pressure wound therapy is used for many applications, so this practice is likely to be acceptable to many clinicians if it does not delay discharge or is not too expensive to implement.

Feasibility

While certainly feasible in this clinical scenario, the inability to demonstrate any benefit has failed to justify the increased costs associated. Although NPWT for post-operative wound care following ORIF for high risk closed fractures after major extremity trauma is an attractive option in selected cases, implementation will likely continue to be influenced by cost considerations

Future Research

There is only one high quality study available, and a larger multicenter trial on this topic would provide more compelling data.

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Orthoplastic Team

Implementation of an orthoplastic team may decrease length of stay, deep infection, and additional operations to bone and also may help improve time to wound healing and time to union.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework

Rationale

Two low quality studies (Vandenberg 2017, Boriani 2017) investigated implementation of an orthoplastic team when treating patients with open tibial fractures. Boriani (2017) was a multi-center prospective study assessing the effect of an integrated orthoplastic unit compared to an independent orthopaedic only approach. After 12 months follow-up, the authors reported the orthoplastic approach resulted in significantly less cases of deep infection/osteomyelitis than the orthopaedic only approach. Furthermore, the orthoplastic approach had significantly better results in all other assessed outcomes, including bone healing, length of stay, and soft-tissue healing. However, the study as designed was simply not a valid comparison of an integrated orthoplastic unit to an independent orthopaedic unit; this was instead a comparison to a unit without any plastic surgery or microvascular support of any kind. Boriani (2017) presented no data demonstrating their multidisciplinary unit achieved better outcomes compared to results obtained prior to its introduction. Vandenberg (2017) was a smaller, single-center study determining patient outcomes after introducing a combined/integrated orthopaedic trauma and plastics microsurgical team to their institution. They compared a pre-integration cohort to a post-integration cohort to measure changes in post-operative complications. The authors observed no difference in infection or other complication outcomes between the two groups. Although Vandenberg (2017) found no difference between the integrated orthoplastic unit and independent orthopaedic only approaches, Boriani (2017) with a larger sample size and a multi-center design, suggests that the implementation of an orthoplastic approach may improve patient outcomes in certain health care settings. Nevertheless, plastic surgical or microvascular technical expertise are an essential component of contemporary wound management and open fracture treatment, regardless of whether it is integrated into a formal multi-disciplinary unit.

Cost Effectiveness/Resource Utilization

Within major trauma centers that already provide expert orthopaedic services and have the capacity for sophisticated wound care using plastic surgery and microvascular techniques, there is some potential to reduce costs by optimizing resource allocation. Limited data suggests more timely surgery and earlier wound closure can reduce the length of stay and number of surgical procedures required. Coordinating the delivery of care through an integrated orthoplastic unit will probably provide a more cost-effective and efficient model of care for open major extremity trauma.

Acceptability

While gathering momentum in hospitals throughout the United Kingdom and Europe, it remains to be seen whether this practice gains acceptance more widely in North America. Although conceptually attractive, its benefit has not yet been convincingly demonstrated. Nevertheless, there is at this time no reason to believe this approach would encounter resistance if it were to be introduced.

Feasibility

Major trauma centers in contemporary healthcare systems already have the capacity to deliver expert orthopaedic care and use state of the art skeletal stabilization methods, as well as providing sophisticated wound care using plastic surgery and advanced microvascular techniques. Coordinating the delivery of this care as an orthoplastic unit, to optimize resource allocation and ultimately enhance patient outcomes, is not only very feasible, but also a laudable goal that could ultimately improve care. However, in those healthcare systems without plastic surgical support for wound coverage following open major extremity trauma, this remains an unrealistic expectation.

Future Research

The role of an integrated orthoplastic unit, with shared decision-making as part of a coordinated strategy, has simply not been adequately evaluated to date. At this time, it is not possible to make a recommendation here with any confidence regarding the potential benefit of multi-disciplinary management of major extremity trauma. Further prospective evaluation of this approach at the same institution both before and after implementation of an orthoplastic team would be of great interest.

Hyperbaric O₂

In patients with open fracture, hyperbaric O₂ may not benefit patient outcomes.

Strength of Evidence: Limited

Strength of Recommendation: Limited ★★☆☆

Evidence from two or more “Low” quality studies with consistent findings or evidence from a single “Moderate” quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework

Rationale

One moderate quality study (Bouachour 1996) regarding hyperbaric treatment investigated the presence of wound healing following crushing injuries. In crush injuries to the extremities, ischemia can occur on the macro (arterial disruption) or micro (microcirculatory insufficiency) level. The concept behind hyperbaric oxygen therapy is to increase the amount of dissolved oxygen in the plasma, enhancing local tissue oxygen delivery to attempt to preserve tissue viability and improve the wound-healing process.

In the Bouachour (1996) study, subjects (n=36) were randomly assigned to treatment with either hyperbaric oxygen (HBO, session of 100% O₂ at 2.5atm for 90 minutes twice daily over 6 days) versus a placebo chamber (atmospheric conditions) in patients who had a crush injury that required an irrigation and debridement and then tension-free wound closure. Transcutaneous oxygen levels were measured during the trial. Complete healing was obtained in 17 patients in the HBO group versus 10 patients in the placebo group (p<0.01). There was a significantly smaller number of patients requiring skin grafts/flaps, vascular procedures or amputations in the HBO group relative to the control group (p<0.05). In the subgroup of patients who were older than 40 and had a Gustilo type III soft-tissue injury, wound healing was obtained in 87.5% of patients in the HBO group versus 30% in the placebo group.

Benefits & Harms

The potential benefits of enhancing the wound-healing process are profound. Hyperbaric treatment is contraindicated in some patients with certain neurologic, pulmonary, or otorhinolaryngologic diseases.

Outcome Importance

In the small subset of patients who are fortunate to receive care in a facility with a hyperbaric chamber, it may benefit some patients with a crush injury to an extremity.

Cost Effectiveness/Resource Utilization

In the Bouachour (1996) study, the length of hospital stay was similar in the two study arms: 22.4 in the HBO group and 22.9 in the placebo group. Although the cost of hyperbaric treatment may be great (the chamber itself, and the expense necessary to fund a qualified medical officer as well as, staffing with skilled technicians) the total investment may be less (amortized over time) than the potential cost of management of the sequela of the potential complications associated with crush injuries. However, formal cost/benefit analysis has not been completed.

Acceptability

Clinical studies indicating the use of hyperbaric treatment in the surgical management of open traumatic fractures or crush injuries are limited.

Feasibility

Management of crush injuries incorporating hyperbaric oxygen is feasible but would be difficult to implement without substantial investment in infrastructure that is currently available on a very limited basis.

Future Research

- What is the correct algorithm for patient selection and hyperbaric oxygen therapy?
- What is the preferred duration of treatment for injuries of this type?
- How soon or how late can therapy be initiated for any meaningful clinical difference? Is there a role for outpatient HBO₂?
- Which patient populations are best served with HBO₂, if any?
- Is there a role for transcutaneous oxygen pressure monitoring while managing those with limb ischemia due to crush injuries or open fractures?

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Preoperative Skin Preparation

In the absence of reliable evidence, it is the opinion of the workgroup that:

1. Providers may consider perioperative nasal and skin (full body) decolonization of patients, when possible.
2. Patients should shower or bathe (full body) with soap (anti-microbial or non-anti-microbial) or an antiseptic agent before surgery, when possible.
3. Surgical skin preparation should be performed with an alcohol-based antiseptic agent, unless contraindicated.

Strength of Evidence: Consensus

Strength of Option: Consensus ★★★★★

Description: There is no supporting evidence, or limited level evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion.

Rationale

No literature met our inclusion criteria for this PICO, therefore, recommendations from other groups and areas of orthopaedic surgery were reviewed.

1. Perioperative nasal and skin (full body) decolonization

S. aureus nasal carriage is associated with subsequent infection in surgical patients. Mupirocin nasal ointment is an effective treatment for the eradication of *S. aureus* carriage. Some studies have shown benefit with mupirocin nasal application for reducing *S. aureus* related SSIs in orthopedic surgeries, but the efficacy of eradication has not been definitively demonstrated, as study samples were too small. The positive trend reported, however, should encourage further studies with sufficient power. Until such time, the risk/benefit should be assessed individually on a case-by-case basis.

In the one low quality study in the trauma literature (Urias 2018), a retrospective comparative review was performed of patients undergoing repair of lower extremity fractures who received either (1) a chlorhexidine gluconate (CHG) washcloth bath or solution shower preoperatively alone (pre-intervention group) or (2) nasal painting using povidone-iodine skin and nasal antiseptic (PI-SNA) in addition to the CHG washcloth bath or solution shower preoperatively (intervention group). The pre-intervention group consisted of 930 cases with a 1.1% infection rate (10 SSIs) and the intervention group consisted of 962 cases with a 0.2% infection rate (2 SSIs). This observed difference was statistically significant, $p=0.020$.

In the General Assembly of the 2nd International Consensus Meeting on Musculoskeletal Infection, a strong consensus (super majority) statement was made that no definitive recommendation can be given regarding the routine implementation of pre-operative *S. aureus* screening and nasal decolonization protocols because of conflicting literature. In addition, no definitive recommendation can be made as to the role of selective versus universal treatment, although the universal treatment strategy seems to be the most cost-effective approach and easiest to implement (Akesson 2019). This consensus statement was based on moderate evidence.

In the WHO evidence-based recommendations for the prevention of SSIs, the panel made a conditional recommendation based on moderate quality evidence that patients undergoing orthopaedic surgery who are known nasal carriers of *S. aureus* should receive perioperative intranasal applications of mupirocin 2% ointment with or without a combination of chlorhexidine gluconate body wash (Allegranzi 2016).

2. Preoperative showering or bathing

Preoperative whole-body bathing is a good clinical practice to ensure that the skin is clean before surgery and to decrease the bacterial burden. Either a plain or antiseptic soap can be used for preoperative bathing, however, current evidence is insufficient to provide a recommendation on the use of CHG for the purpose of reducing SSIs.

In the General Assembly of the 2nd International Consensus Meeting on Musculoskeletal Infection, a strong consensus (super majority) statement was also made that pre-operative skin cleansing at home prior to orthopedic surgery does have a role in the reduction of subsequent SSIs and periprosthetic joint infections (PJIs). Specifically, CHG bathing/wipes have been shown to have excellent results in preventing PJIs/SSIs (Atkins 2019). This consensus statement was based on moderate evidence.

In the 2017 Centers for Disease Control and Prevention Guideline for the prevention of SSIs, a strong recommendation was made based on accepted practice (Category IB) to advise patients to shower or bathe (full body) with soap (anti-microbial or non-anti-microbial) or an antiseptic agent on at least the night before the procedure (Berrios-Torres 2017).

In the WHO evidence-based recommendations for the prevention of SSIs, the panel made a conditional recommendation based on moderate quality evidence that good clinical practice requires that patients bathe or shower before surgery, and that either a plain or anti-microbial soap can be used for this purpose (Allegranzi 2016).

3. Surgical skin preparation

Standard practice in the management of extremity fractures includes sterile technique and surgical skin preparation with an antiseptic solution. The antiseptic solutions kill bacteria and decrease the quantity of native skin flora, thereby reducing the risk of SSI. Although use of antiseptics for surgical skin cleaning is recommended, the type of antiseptic agent is disputed. Therefore, the only consistent consensus recommendation in the literature has been the inclusion of an alcohol-based antiseptic agent in any skin preparation.

In the General Assembly of the 2nd International Consensus Meeting on Musculoskeletal Infection, a strong consensus (super majority) statement was made that there appears to be no differences between various surgical skin preparation agents (CHG versus povidine-iodine) in reducing the risk of SSI in patients undergoing orthopaedic procedures, as long as isopropyl alcohol is part of the preparation (Atkins et al. 2019). This consensus statement was based on limited evidence. The authors noted that an ideal solution has yet to be identified for surgical site skin preparations, but there is an overall consensus that the skin preparation solution should contain alcohol.

In the 2017 Centers for Disease Control and Prevention Guideline for the prevention of SSIs, a strong recommendation was made based on high-quality evidence (Category IA) that pre-operative skin preparation should be performed with an alcohol-based antiseptic agent, unless contraindicated (Berrios-Torres 2017).

In the WHO evidence-based recommendations for the prevention of SSIs, the panel made a strong recommendation for use of alcohol-based antiseptic solutions that are based on CHG for pre-operative surgical site skin preparation in patients undergoing surgical procedures, based on low to moderate quality of evidence (Allegranzi 2016).

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Benefits & Harms

The potential benefit of pre-operative skin preparations is prevention of surgical site and deep infection. The potential harms of pre-operative skin preparations include skin reactions or allergies (including anaphylaxis), mupirocin resistance, and microbiome disturbances. More specifically, alcohol-based solutions should not be used on neonates or come into contact with mucosa or eyes, and caution should be exercised because of their flammable nature. CHG solutions can cause skin irritation and must not be allowed to come into contact with the brain, meninges, eye, or middle ear. Alcohol based antiseptics are not recommended for open wounds or those with related allergy.

Outcome Importance

Prevention of SSIs is of primary importance. Development of surgical site or deep infection after major extremity trauma can lead to severe morbidity, prolonged hospitalization and significantly increased utilization of healthcare resources.

Cost Effectiveness/Resource Utilization

Skin preparation with an antiseptic and preoperative bathing with soap are simple, inexpensive and widely available measures. Mupirocin is readily available and although it is a relatively expensive drug, application is easy. The cost of nasal decolonization, pre-operative skin cleansing prior to surgery, or surgical skin preparation is significantly less than what is required for treatment of surgical site or deep infection.

Acceptability

Highly acceptable with very few contraindications.

Feasibility

While seemingly feasible, the treatment of major extremity trauma is frequently not an isolated entity and may not always be the most pressing issue in the setting of severe trauma. It is important that the healthcare professionals responsible for the musculoskeletal care of patients with major lower extremity trauma be aware of and advocates for the appropriate use of pre-operative skin preparation techniques, including nasal decolonization, pre-operative skin cleansing prior to surgery, and surgical skin preparation. Preoperative skin cleansing and surgical skin preparation are widely used and are well accepted. Nasal decolonization is not universally practiced but is acceptable to most clinicians.

Future Research

Future research is needed to determine what the optimal approach is for nasal decolonization, pre-operative skin cleansing prior to surgery, and surgical skin preparation in the prevention of deep infections following open fracture with major extremity trauma. Further studies are needed to determine how these choices may vary within orthopaedic surgery, including based on the type of surgical procedure (urgent trauma versus semi-elective) or in the presence of an open fracture. Examples of questions to further explore in future, large scale studies include:

1. Which antiseptic agent is superior for prevention of SSIs in fracture patients?
2. Is CHG bathing more effective than soap? What is the optimal timing of bathing and number of baths?

3. Is mupirocin ointment effective in preventing infection with *S. aureus* in open fracture patients, especially when the standard 5 days application prior to surgery is not a feasible option? Will a different dosing and shorter application period (1-2 days) be of benefit in a subset of patients who have a delay in fracture surgery?
4. Would the combination of bathing with an antiseptic agent and application of mupirocin be more effective than either intervention alone?

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APPENDICES

Appendix I: References

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Appendix II: PICO Questions Used to Define Literature Search

1. In patients with major extremity trauma who are undergoing surgery for an open fracture, what is the timing of antibiotic administration that best prevents SSI post-surgery?
2. In patients with major extremity trauma who are undergoing surgery, what pre-operative, prophylactic antibiotic(s) best prevent SSI post-surgery?
3. In patients with major extremity trauma who are undergoing surgery, what is the timing of surgery post-injury, that best prevents SSI post-surgery?
4. In patients with major extremity trauma who are undergoing surgery, what peri-operative and post-operative, prophylactic antibiotic(s) best prevent SSI post-surgery?
5. In patients with major extremity trauma who are undergoing surgery, what pre-operative skin preparations best prevent SSI post-surgery?
6. In patients with major extremity trauma who are undergoing surgery, what is the best initial wound management strategy to prevent SSI post-surgery?
7. In patients with closed major extremity trauma who are undergoing surgery, what wound closure management strategies best prevent SSI post-surgery?
8. In patients with open major extremity trauma who are undergoing surgery, what wound closure management strategies best prevent SSI post-surgery?
9. In patients with major extremity trauma who are undergoing surgery, what perioperative modifiable risk factors affect rates of SSI post-surgery?
10. In patients with major extremity trauma who are undergoing surgery, what perioperative administrative risk factors affect rates of SSI post-surgery?

Appendix III: PICO Inclusion Criteria

- Study must be of patients with major extremity trauma, who do not currently have a documented surgical site infection at the site of the orthopaedic trauma
- Study must be published in or after <Minimum: 1985>
- Study should have <10> or more patients per group
- Outcome Follow-up Time: <all follow-up times>

Standard Criteria for all CPGs

- Article must be a full article report of a clinical study (studies using registry data can be included in a guideline if it is published in a peer-reviewed journal and meets all other inclusion criteria/quality standards).
- Retrospective non-comparative case series, medical records review, meeting abstracts, historical articles, editorials, letters, and commentaries are excluded.
- Confounded studies (i.e., studies that give patients the treatment of interest AND another treatment) are excluded.
- Case series studies that have non-consecutive enrollment of patients are excluded.
- Controlled trials in which patients were not stochastically assigned to groups AND in which there was either a difference in patient characteristics or outcomes at baseline AND where the authors did not statistically adjust for these differences when analyzing the results are excluded.
- All studies of “Very Weak” strength of evidence are excluded.
- All studies evaluated as Level V will be excluded.
- Composite measures or outcomes are excluded even if they are patient oriented.
- Study must appear in a peer-reviewed publication
- For any included study that uses “paper-and-pencil” outcome measures (e.g., SF-36), only those outcome measures that have been validated will be included
- For any given follow-up time point in any included study, there must be $\geq 50\%$ patient follow-up (if the follow-up is $>50\%$ but $<80\%$, the study quality will be downgraded by one Level)
- Study must be of humans
- Study must be published in English
- Study results must be quantitatively presented
- Study must not be an in vitro study
- Study must not be a biomechanical study
- Study must not have been performed on cadavers

*We will only evaluate surrogate outcomes when no patient-oriented outcomes are available.

Best Available Evidence

When examining primary studies, we will analyze the best available evidence regardless of study design. We will first consider randomized controlled trials identified by the search strategy. In the absence of two or more RCTs, we will sequentially search for prospective controlled trials, prospective comparative studies, retrospective comparative studies, and prospective case-series studies. Only studies of the highest level of available evidence are included, assuming that there were 2 or more studies of that higher level. For example, if there are two high quality studies that address the recommendation, moderate and low studies addressing the same procedure and outcomes are not included.

Definitions:

- *Definitions of project specific terms*

▪ Major Extremity Trauma:

- Limit population to only include high energy extremity fractures
- All Injury types listed below are limited to the context of extremity fractures
 1. Open fracture
 2. Major/High energy closed fracture
 3. Degloving injury
 4. Morel lesions

5. Gunshot injury (low and high velocity)

6. Crush injury
7. Blast injury
8. Moderate to high energy force

• Infection:

- Deep Infection: CDC guidelines/definition
 - <https://www.cdc.gov/nhsn/pdfs/pscManual/9pscSSIcurrent.pdf>
- Fracture Related Infection
 - <https://www.sciencedirect.com/science/article/pii/S0020138317305636>

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Appendix IV: Guideline Development Group Disclosures

Prior to the development of this clinical practice guideline, clinical practice guideline development group members disclose conflicts of interest (COI). They disclose COIs in writing to 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 = Royalties from a company or supplier; 2 = Speakers bureau/paid presentations for a company or supplier; 3A = Paid employee for a company or supplier; 3B = Paid consultant for a company or supplier; 3C = Unpaid consultant for a company or supplier; 4 = Stock or stock options in a company or supplier; 5 = Research support from a company or supplier as a PI; 6 = Other financial or material support from a company or supplier; 7 = Royalties, financial or material support from publishers; 8 = Medical/Orthopaedic publications editorial/governing board; 9 = Board member/committee appointments for a society.

Voting Members' and Non-Voting Oversight Chairs' Disclosures

Voting: 1 workgroup member abstained from voting on the Wound Coverage recommendation.

Antonia Chen, MD, MBA, FAAOS

Submitted on: 12/02/2021

3M: Paid consultant

AAOS: Board or committee member

Adaptive Phage Therapeutics: Paid consultant

AJRR: Board or committee member

American Association of Hip and Knee Surgeons: Board or committee member

Avanos: Paid consultant

BICMD: Paid consultant

bOne: Paid consultant; Stock or stock Options

Clinical Orthopaedics and Related Research: Editorial or governing board

Convatec: Paid consultant

Ethicon: Paid consultant

European Knee Association: Board or committee member

GLG: Paid consultant

Graftworx: Stock or stock Options

Guidepoint: Paid consultant

Heraeus: Paid consultant

Hyalex: Stock or stock Options

Irrimax: Paid consultant; Stock or stock Options

Joint Purification Systems: Stock or stock Options

Journal of Arthroplasty: Editorial or governing board

Journal of Bone & Joint Infection: Editorial or governing board

Journal of Bone and Joint Surgery - American: Editorial or governing board

Journal of Orthopaedic Research: Editorial or governing board

Knee Surgery, Sports Traumatology, Arthroscopy: Editorial or governing board

Pfizer: Paid consultant

Sectra: Research support

SLACK Incorporated: Publishing royalties, financial or material support

Sonoran: Stock or stock Options

Stryker: Paid consultant

UpToDate: Publishing royalties, financial or material support

Ashton Goldman, MD

(This individual reported nothing to disclose); Submitted on: 04/15/2020

Kevin Tetsworth, MD

Submitted on: 03/06/2020

4Web Medical: Paid presenter or speaker (\$0) Number of Presentations: 0

Australasian Limb Lengthening and Reconstruction Society (President): Board or committee member (\$0)

BioConsultancy Pty Ltd: Stock or stock Options Number of Shares: 0

Extremos Medical: Unpaid consultant

Journal of Limb Lengthening and Reconstruction: Editorial or governing board (\$0)

LifeHealthcare: Paid presenter or speaker (\$0) Number of Presentations: 0

Smith & Nephew: Paid presenter or speaker (\$0) Number of Presentations: 0

Smith & Nephew: Paid consultant (\$0)

Stryker: Paid presenter or speaker (\$0) Number of Presentations: 0

Stryker: Paid consultant (\$0)

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(This individual reported nothing to disclose); Submitted on: 04/14/2020

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Submitted on: 04/14/2020

AAOS: Board or committee member (\$0)

American Board of Orthopaedic Surgery, Inc.: Board or committee member (\$0)

American Shoulder and Elbow Surgeons: Board or committee member (\$0)

DJ Orthopaedics: IP royalties (\$0)

DJ Orthopaedics: Paid presenter or speaker (\$0) Number of Presentations: 0

DJ Orthopaedics: Paid consultant (\$0)

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Accelerate Diagnostics: Research support (\$0)

Allergan: Research support (\$0) N/A(Self)

American Society of Microbiology: Board or committee member (\$0)

CD Diagnostics: Research support (\$0) Research grant(Self)

Clinical Infectious Diseases: Editorial or governing board (\$0)

ContraFect: Research support (\$0) N/A(Self)

Curetis: Research support (\$0)

HBMS: Research support (\$0)

Infectious Diseases Board Review (Faculty): Board or committee member (\$0)

Journal of Clinical Microbiology: Editorial or governing board (\$0)

Mayo Clinic, Rochester MN (my employer): Employee (\$0)

Merck: Research support (\$0) N/A(Self)

Shionogi: Research support (\$0) N/A(Self)

Up-to-Date: Editorial or governing board (\$50) Royalties(Self)

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USMLE: Board or committee member (\$0)

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American Academy of Pediatrics: Board or committee member (\$0)

Pediatric Orthopaedic Society of North America: Board or committee member (\$0)

Ruth Jackson Orthopaedic Society: Board or committee member (\$0) Committee member(Self)

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American Orthopaedic Foot and Ankle Society: Board or committee member (\$0) Committee member(Self)

Medshape: Paid consultant (\$0) n/a(Self)

Wright Medical Technology, Inc.: Research support (\$0)

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Submitted on: 05/06/2020

AAOS: Board or committee member (\$0)

American College of Surgeons: Board or committee member (\$0)

American Orthopaedic Association: Board or committee member (\$0) N/A(Self)

AOTrauma: Board or committee member (\$0) Committee member(Self)

Geriatric Orthopaedic Surgery and Rehabilitation: Editorial or governing board (\$0) N/A(Self)

Journal of Orthopaedic Trauma: Editorial or governing board (\$0) n/a(Self)

Mergenet: Stock or stock Options Number of Shares: 14,500 N/A(Self)

Orthopaedic Trauma Association: Board or committee member (\$0)

The Orthopaedic Implant Company: Stock or stock Options Number of Shares: 25,000 N/A(Self)

Wright Medical Technology, Inc.: IP royalties (\$1,100) N/A(Self)

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DePuy, A Johnson & Johnson Company: Paid presenter or speaker (\$0) Number of Presentations: 0

Orthopaedic Trauma Association: Board or committee member (\$0) Education Committee Member(Self)

Stryker: Paid presenter or speaker (\$0) Number of Presentations: 0

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Submitted on: 09/15/2020

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Journal of Orthopaedic Trauma: Editorial or governing board (\$0) reviewer(Self)

Journal of the American Academy of Orthopaedic Surgeons: Editorial or governing board (\$0)

Reviewer(Self)

Southeastern Fracture Consortium: Board or committee member (\$0) N/A(Self)

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Submitted on: 09/17/2020

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Imagen: Paid consultant; Stock or stock Options

lincotek (formerly Coorstek): IP royalties

Smith & Nephew: Paid consultant

Zimmer: Paid presenter or speaker"

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(This individual reported nothing to disclose); Submitted on: 01/22/2020