

# Review Period Report

## **Evidence-Based Clinical Practice Guideline for the Prevention of Surgical Site Infections Following Major Extremity Trauma**

# Table of Contents

Overview of the Review Period .....	3
Reviewer Key .....	4
Table 1. Reviewer Key.....	4
Reviewer Demographics.....	5
Table 2: Reviewer Demographics .....	5
Reviewers' Disclosure Information.....	6
Table 3. Disclosure Question Key.....	6
Table 4. Reviewer's Disclosure Information .....	7
Reviewer Responses to Structured Review Form Questions.....	8
Table 5. Reviewer Responses to Structured Review Questions 1-4 .....	8
Table 6. Reviewer Responses to Structured Review Questions 5-8 .....	10
Table 7. Reviewer Responses to Structured Review Questions 9-12.....	11
Table 8. Reviewer Responses to Structured Review Questions 13-16 .....	12
Reviewer Detailed Responses and Editorial Suggestions.....	14
Reviewer #1, Lynne Jones, M.D.....	14
<i>Workgroup Response to Reviewer #1</i> .....	15
Reviewer #2, Matthew Grosso, M.D.....	16
<i>Workgroup Response to Reviewer #2</i> .....	17
Reviewer #3, Flutura Hasa, M.D. ....	18
<i>Workgroup Response to Reviewer #3</i> .....	25
Reviewer #4, Mihail Radulescu, M.D.....	26
<i>Workgroup Response to Reviewer #4</i> .....	27
Reviewer #5, Ronald Delanois, M.D.....	28
<i>Workgroup Response to Reviewer #5</i> .....	29
Reviewer #6, Krishna Reddy, M.D.....	30
<i>Workgroup Response to Reviewer #6</i> .....	31
Reviewer #7, Matthew Houdek, M.D. ....	32
<i>Workgroup Response to Reviewer #7</i> .....	33
Reviewer #8, Shari Jawetz, M.D. ....	34
<i>Workgroup Response to Reviewer #8</i> .....	36
Reviewer #9, Louis Lewandowski, M.D. ....	37
<i>Workgroup Response to Reviewer #9</i> .....	38
Reviewer #10, Christopher Souder, M.D.....	39

*Workgroup Response to Reviewer #10* ..... 40  
Reviewer #11, Matthew Abdel, M.D. .... 41  
*Workgroup Response to Reviewer #11* ..... 42  
Reviewer #12, Roman Natoli, M.D. .... 43  
*Workgroup Response to Reviewer #12* ..... 45  
Reviewer #13, Nicholas Tedesco, M.D. .... 46  
*Workgroup Response to Reviewer #13* ..... 48  
Reviewer #14, F. Scott Gray, M.D. .... 49  
*Workgroup Response to Reviewer #14* ..... 50  
Reviewer #15, Michelle Ghert, M.D. .... 51  
*Workgroup Response to Reviewer #15* ..... 52  
Appendix A – Structured Review Form ..... 53

# **Prevention of Surgical Site Infections Following Major Extremity Trauma**

## **Overview of the Review Period**

The reviews and comments related to this clinical practice guideline are reprinted in this document and posted on the AAOS website. All reviewers are required to disclose their conflict of interests.

### **Review Process:**

AAOS contacted 12 organizations with content expertise to review a draft of the clinical practice guideline during the four-week peer review period that began in December 2021.

Additionally, the draft was 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.

- Fifteen (15) individuals provided comments via the electronic structured peer review form. No reviewers asked to remain anonymous.
- All fifteen reviews were on behalf of a society and/or committee.
- The work group considered all comments and made some modifications when they were consistent with the evidence.

## Reviewer Key

Each reviewer was assigned a number (see below). All responses in this document are listed by the assigned peer reviewer's number.

**Table 1. Reviewer Key**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>Society/ Committee Being Represented</b>
1	Lynne Jones	
2	Matthew Grosso	American Association of Hip and Knee Surgeons
3	Flutura Hasa	3M Company
4	Mihail Radulescu	American Academy of Orthopaedic Surgeons
5	Ronald Delanois	The Knee Society
6	Krishna Reddy	American Academy of Orthopaedic Surgeons, Key Informants Panel
7	Matthew Houdek	American Academy of Orthopaedic Surgeons, Key Informants Panel
8	Shari Jawetz	American College of Radiology
9	Louis Lewandowski	Society of Military Orthopaedic Surgeons
10	Christopher Souder	Pediatric Orthopaedic Society of North America
11	Matthew Abdel	American Academy of Orthopaedic Surgeons, Board of Directors
12	Roman Natoli	American Academy of Orthopaedic Surgeons, Key Informants Panel
13	Nicholas Tedesco	Musculoskeletal Tumor Society

## Reviewer Demographics

**Table 2: Reviewer Demographics**

Reviewer Number	Name of Reviewer	Primary Specialty	Work Setting
1	Lynne Jones	Other	Academic Practice
2	Matthew Grosso	Total Joint	Private Group or Practice
3	Flutura Hasa	Other	Other
4	Mihail Radulescu	Total Joint	Private Group or Practice
5	Ronald Delanois	Adult Knee	Academic Practice
6	Krishna Reddy	Sports Medicine	Non-Military Government or Public
7	Matthew Houdek	Ortho/Oncology	Academic Practice
8	Shari Jawetz	Other	Academic Practice
9	Louis Lewandowski	Trauma	Military
10	Christopher Souder	Pediatric Orthopaedics	Private Group or Practice
11	Matthew Abdel	Adult Hip	Academic Practice
12	Roman Natoli	Trauma	Academic Practice
13	Nicholas Tedesco	Ortho/Oncology	Academic Practice
14	F Scott Gray	Foot and Ankle	Private Group or Practice
15	Michelle Ghert	Ortho/Oncology	Academic Practice

## Reviewers' Disclosure Information

All reviewers are required to disclose any possible conflicts that would bias their review via a series of 10 questions (see Table 3). For any positive responses to the questions (i.e. "Yes"), the reviewer was asked to provide details on their possible conflict.

**Table 3. Disclosure Question Key**

<b>Disclosure Question</b>	<b>Disclosure Question Details</b>
<b>A</b>	A) Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device?
<b>B</b>	B) Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company?
<b>C</b>	C) Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
<b>D</b>	D) Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
<b>E</b>	E) Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
<b>F</b>	F) Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds)
<b>G</b>	G) Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
<b>H</b>	H) Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier?
<b>I</b>	I) Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers?
<b>J</b>	J) Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication?

**Table 4. Reviewer’s Disclosure Information**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>Disclosure Available via AAOS Disclosure System</b>	<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>	<b>E</b>	<b>F</b>	<b>G</b>	<b>H</b>	<b>I</b>	<b>J</b>
1	Lynne Jones	Yes										
2	Matthew Grosso	Yes										
3	Flutura Hasa	No	No	No	No	No	No	Yes	No	No	No	No
4	Mihail Radulescu	Yes										
5	Ronald Delanois	Yes										
6	Krishna Reddy	Yes										
7	Matthew Houdek	Yes										
8	Shari Jawetz	No										
9	Louis Lewandowski	Yes	No	No	No	No	No	No	No	No	No	No
10	Christopher Souder	Yes										
11	Matthew Abdel	Yes										
12	Roman Natoli	Yes										
13	Nicholas Tedesco	Yes										
14	F Scott Gray	Yes										
15	Michelle Ghert	Yes										



## Reviewer Responses to Structured Review Form Questions

All reviewers are asked 16 structured review questions which have been adapted from the Appraisal of Guidelines for Research and Evaluation (AGREE) II Criteria\*. Their responses to these questions are listed on the next few pages.

**Table 5. Reviewer Responses to Structured Review Questions 1-4**

Reviewer Number	Name of Reviewer	1. The overall objective(s) of the guideline is (are) specifically described.	2. The health question(s) covered by the guideline is (are) specifically described.	3. The guideline's target audience is clearly described.	4. There is an explicit link between the recommendations and the supporting evidence.
1	Lynne Jones	Strongly Agree	Agree	Strongly Agree	Agree
2	Matthew Grosso	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
3	Flutura Hasa	Agree	Agree	Agree	Agree
4	Mihail Radulescu	Strongly Agree	Strongly Agree	Agree	Agree
5	Ronald Delanois	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Krishna Reddy	Agree	Strongly Agree	Agree	Agree
7	Matthew Houdek	Agree	Strongly Agree	Agree	Strongly Agree
8	Shari Jawetz	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
9	Louis Lewandowski	Strongly Agree	Agree	Strongly Agree	Agree
10	Christopher Souder	Strongly Agree	Agree	Strongly Agree	Agree
11	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
12	Roman Natoli	Strongly Agree	Strongly Agree	Agree	Strongly Agree
13	Nicholas Tedesco	Strongly Agree	Strongly Agree	Strongly Agree	Agree
14	F Scott Gray	Strongly Agree	Strongly Agree	Strongly Agree	Agree
15	Michelle Ghert	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>1. The overall objective(s) of the guideline is (are) specifically described.</b>	<b>2. The health question(s) covered by the guideline is (are) specifically described.</b>	<b>3. The guideline's target audience is clearly described.</b>	<b>4. There is an explicit link between the recommendations and the supporting evidence.</b>
1	Lynne Jones	Strongly Agree	Agree	Strongly Agree	Agree
2	Matthew Grosso	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
3	Flutura Hasa	Agree	Agree	Agree	Agree
4	Mihail Radulescu	Strongly Agree	Strongly Agree	Agree	Agree
5	Ronald Delanois	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Krishna Reddy	Agree	Strongly Agree	Agree	Agree
7	Matthew Houdek	Agree	Strongly Agree	Agree	Strongly Agree
8	Shari Jawetz	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
9	Louis Lewandowski	Strongly Agree	Agree	Strongly Agree	Agree
10	Christopher Souder	Strongly Agree	Agree	Strongly Agree	Agree
11	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
12	Roman Natoli	Strongly Agree	Strongly Agree	Agree	Strongly Agree
13	Nicholas Tedesco	Strongly Agree	Strongly Agree	Strongly Agree	Agree

**Table 6. Reviewer Responses to Structured Review Questions 5-8**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>5. Given the nature of the topic and the data, all clinically important outcomes are considered.</b>	<b>6. The patients to whom this guideline is meant to apply are specifically described.</b>	<b>7. The criteria used to select articles for inclusion are appropriate.</b>	<b>8. The reasons why some studies were excluded are clearly described.</b>
1	Lynne Jones	Strongly Agree	Strongly Agree	Agree	Strongly Agree
2	Matthew Grosso	Strongly Agree	Strongly Agree	Strongly Agree	Agree
3	Flutura Hasa	Agree	Agree	Agree	Agree
4	Mihail Radulescu	Strongly Agree	Agree	Strongly Agree	Agree
5	Ronald Delanois	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Krishna Reddy	Strongly Agree	Strongly Agree	Agree	Neutral
7	Matthew Houdek	Disagree	Agree	Agree	Neutral
8	Shari Jawetz	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
9	Louis Lewandowski	Agree	Agree	Strongly Agree	Agree
10	Christopher Souder	Agree	Strongly Agree	Agree	Agree
11	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
12	Roman Natoli	Agree	Neutral	Agree	Agree
13	Nicholas Tedesco	Strongly Agree	Strongly Agree	Agree	Neutral
14	F Scott Gray	Strongly Agree	Strongly Agree	Strongly Agree	Agree
15	Michelle Ghert	Strongly Agree	Strongly Agree	Strongly Agree	Agree

**Table 7. Reviewer Responses to Structured Review Questions 9-12**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>9. All important studies that met the article inclusion criteria are included</b>	<b>10. The validity of the studies is appropriately appraised.</b>	<b>11. The methods are described in such a way as to be reproducible</b>	<b>12. The statistical methods are appropriate to the material and the objectives of this guideline</b>
1	Lynne Jones	Strongly Agree	Strongly Agree	Strongly Agree	Neutral
2	Matthew Grosso	Strongly Agree	Agree	Strongly Agree	Strongly Agree
3	Flutura Hasa	Agree	Agree	Agree	Agree
4	Mihail Radulescu	Agree	Agree	Agree	Agree
5	Ronald Delanois	Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Krishna Reddy	Strongly Agree	Agree	Agree	Neutral
7	Matthew Houdek	Disagree	Agree	Agree	Agree
8	Shari Jawetz	Strongly Agree	Strongly Agree	Strongly Agree	Agree
9	Louis Lewandowski	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
10	Christopher Souder	Agree	Neutral	Agree	Agree
11	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
12	Roman Natoli	Agree	Strongly Agree	Strongly Agree	Strongly Agree
13	Nicholas Tedesco	Agree	Agree	Strongly Agree	Strongly Agree
14	F Scott Gray	Strongly Agree	Agree	Agree	Agree
15	Michelle Ghert	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

**Table 8. Reviewer Responses to Structured Review Questions 13-16**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>13. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed.</b>	<b>14. Health benefits, side effects, and risks are adequately addressed.</b>	<b>15. The writing style is appropriate for health care professionals.</b>	<b>16. The grades assigned to each recommendation are appropriate.</b>
1	Lynne Jones	Agree	Strongly Agree	Strongly Agree	Disagree
2	Matthew Grosso	Agree	Strongly Agree	Strongly Agree	Agree
3	Flutura Hasa	Agree	Agree	Agree	Agree
4	Mihail Radulescu	Agree	Agree	Strongly Agree	Agree
5	Ronald Delanois	Strongly Agree	Strongly Agree	Strongly Agree	Agree
6	Krishna Reddy	Agree	Agree	Agree	Strongly Agree
7	Matthew Houdek	Agree	Agree	Agree	Agree
8	Shari Jawetz	Strongly Agree	Strongly Agree	Strongly Agree	Agree
9	Louis Lewandowski	Strongly Agree	Strongly Agree	Agree	Strongly Agree
10	Christopher Souder	Agree	Strongly Agree	Strongly Agree	Strongly Agree
11	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
12	Roman Natoli	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
13	Nicholas Tedesco	Strongly Agree	Strongly Agree	Strongly Agree	Agree
14	F Scott Gray	Strongly Agree	Agree	Strongly Agree	Disagree
15	Michelle Ghert	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

Reviewers' Recommendation for Use of this Guideline in Clinical Practice

**Would you recommend these guidelines for use in clinical practice?**

<b>Reviewer Number</b>	<b>Name of Reviewer</b>	<b>Would you recommend these guidelines for use in clinical practice?</b>
1	Lynne Jones	Recommend
2	Matthew Grosso	Strongly Recommend
3	Flutura Hasa	Recommend
4	Mihail Radulescu	Strongly Recommend
5	Ronald Delanois	Strongly Recommend
6	Krishna Reddy	Strongly Recommend
7	Matthew Houdek	Recommend
8	Shari Jawetz	Strongly Recommend
9	Louis Lewandowski	Strongly Recommend
10	Christopher Souder	Recommend
11	Matthew Abdel	Strongly Recommend
12	Roman Natoli	Recommend
13	Nicholas Tedesco	Strongly Recommend
14	F Scott Gray	Strongly Recommend
15	Michelle Ghert	Recommend

## Reviewer Detailed Responses and Editorial Suggestions

### Reviewer #1, Lynne Jones, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p><b>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</b></p>
1	Lynne Jones, M.D.		<p>A. Pg 6 lines 2-6 This should include the definition of limited.</p> <p>B. Pg 16,17 Why is this section in future tense?</p> <p>C. Pg 27 line 38 and pg 28 line 12 In one place it states “operation room” and the other “operating room”. One should be selected for consistency.</p> <p>D. Pg 35 line 12 The study by Tahir, 2020 has been retracted. Removal of this article will result in the reclassification of strengths of evidence and recommendation.</p> <p>E. Pg 38 line 17 The reviewers state that this is strong evidence but then later state that the recommendation is “based on uncontrolled retrospective studies with inadequate sample size”. This statement does not appear to support the recommendation.</p> <p>F. Pg 40 line 5 This section should begin on its own page.</p> <p>G. Pg 41 line 12 The word “us” should probably be “has”.</p> <p>H. Pg 43 line 5 Why is this rated moderate when there are two high quality studies to support this?</p> <p>I. Pg 51 line 12 This sentence needs copyediting: “Evidence there is no supporting evidence.”</p> <p>J. I did not have access to e-Appendix 2 to review.</p> <p>K. The CPG would benefit from grammar-check and copy-editing for spacing.</p>

***Workgroup Response to Reviewer #1***

Dear Lynne Jones, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Information on interpreting the strength of evidence can be found in the "Methodology" section.
- B. Thank you for your feedback. The guideline has been modified.
- C. Thank you for the feedback. The sentence has been modified to state, "operating room".
- D. The Tahir study was removed from our evidence list. After removal, 4 high quality articles remained supporting the recommendation.
- E. Thank you for your feedback. We believe the future research statement is a fair critique of the literature. There are still 2 "high-level" studies. Furthermore, the text was edited to replace "are generally" with "may be".
- F. Thank you for your feedback. The guideline has been modified.
- G. Thank you for your feedback. The guideline has been modified.
- H. Thank you for your feedback. This typo has been corrected on the manuscript.
- I. Thank you for your feedback. The guideline has been modified.
- J. All relevant tables and appendices were made available to reviewers when the review period opened.
- K. Thank you for your feedback. The guideline has been reviewed for grammar and formatting errors.



**Reviewer #2, Matthew Grosso, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
2	Matthew Grosso, M.D.	American Association of Hip and Knee Surgeons	<p>A. The AAHKS evidence based medicine committee and AAHKS leadership approves this CPG, with minor recommendations below.</p> <p>B. Page 6 and Page 27. “Perioperative and Postoperative Antibiotics- Systemic” To help with potential confusion, consider rewording the recommendation. The current recommendation reads. “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.” Changing to, ... “for which an additional antibiotic with Gram-negative coverage is preferred”. This could potentially help clarify that the intention is for a second antibiotic rather than an alternative antibiotic with some gram-negative coverage.</p> <p>C. Page 35. “Negative Pressure Wound Therapy – Open and Closed Fractures” For this recommendation, the higher quality multi-center studies listed do not seem to support the use of NPWT for open or even closed fracture wound care. There were three smaller single center RCTs which demonstrated better outcomes with NPWT. However, the CPG authors acknowledge that the findings of these smaller studies may have been confounded by selection bias and the retrospective nature of the studies. As such, the authors may want to re-consider the strength of the evidence description from "strong" to "moderate."</p> <p>D. Page 39. “Silver Coated Dressings” For this recommendation, there is one High Quality Study. There appears to be an error in the reporting of the outcome measures. “In the silver-coated dressing arm, 7% developed infected pin sites, while 40% developed it in the control group.” Reviewing the article, the actual number is 46.7% in the treatment arm (7/15) versus 40% in the control arm (6/15). In addition, the “High Quality” label of this study could potentially be downgraded given the very low power of this study to detect differences due to small sample size.</p>

***Workgroup Response to Reviewer #2***

Dear Matthew Grosso, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for your feedback. The rationale addresses this point. Zosyn alone would be adequate for gram - coverage. (Please see lines 1084-1086). We specifically removed Zosyn from the recommendation and decided to place it in the rationale instead as other antibiotics may be appropriate as well.
- C. Thank you for your feedback. The work group reviewed the recommendation after the Tahir study was removed and determined no edits were necessary.
- D. Thank you for your feedback. The manuscript has been updated to include "pin site infections." Additionally, the typographical errors concerning the reported percentages have been modified.

**Reviewer #3, Flutura Hasa, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
3	Flutura Hasa, M.D.	3M Company	<p>A. Thank you for the opportunity to review and comment on this draft guideline. Overall, the document is well-done, is based on current evidence and well evaluated. The statements are prospectively correct. However, there are some aspects of guidance not included in this guideline and it is important to include the surgical site infections in the scope of the patient perioperative journey period-intraop-postop journey.</p> <p>B. The following comments provide the scientific rationale and references supporting suggested additions for consideration by the AAOS Guideline authoring committee. This recommendation covers preventing and treating site infections who are having a surgical procedure involving a cut through the skin. It focuses on methods used before, during and after surgery to minimize the risk of infection. To help reduce surgical site infection, trauma related surgical therapies should employ a care bundle that includes incision management, topical intranasal therapies, preoperative bathing, hair removal, and appropriate timing and stewardship of perioperative prophylactic antibiotics combined with smoking cessation, glycemic control and perioperative normothermia. This topic has been described extensively with strong level of evidence in an expert consensus review by J. Parvizi et al.<sup>1</sup></p> <p>C. Comment #1.            -Recommendation: Add new text for incision management along with strong supporting evidence.            -Proposed new text: Supporting Rationale for proposed add text to Recommendation related to Negative Wound Pressure Therapy, High Risk Incisions:            Foam-based closed incisional negative pressure therapy has demonstrated significant reduction in superficial SSI in high-risk patients with Class I and Class II wounds including those with diabetes, obesity, and renal disease. Suggesting that if wounds are significantly soiled and left open technology is developing to provide Negative Pressure debridement level instillation. Appropriate use of Negative Wound Pressure Therapy requires coverage of critical structures like underlined blood vessels before application consistent with IFU.            -Citations that support this proposed new text/ guideline recommendation are provided including a meta-analysis used for US FDA de novo clearance of this type of incisional therapy technology and high-quality evidence for recommending specific patients undergoing high-risk procedures<sup>1-7</sup>            The following additional information details the scientific basis for the improved outcomes achieved by closed incision negative pressure as compared with traditional wound dressings:            -1. Barrier function: Even though not unique to ciNPT, the drape component of the dressing presents a barrier to microbial organisms (per ASTM 1671-07; Internal report 0000021109).            -2. Biomechanics: Direct impact of negative pressure: If the incision is relatively loosely approximated, fluids can be directly evacuated from the incisional space within the tissue into the canister via the dressing and associated tubing. There is a vacuum-induced tendency to reduce the volume of this relative dead space. This results in the pulling together (from within) of incisional faces of tissue, thereby off-loading the incision line,</p>

and increasing resistance to dehiscence (Wilkes RP, Kilpadi DV, Zhao Y et al, Closed incision management with negative pressure wound therapy (CIM): Biomechanics. *Surgical Innov*, 2012;19:67-75; Loveluck J, Copeland T, Hill J et al. Biomechanical modelling of the forces applied to closed incisions during single-use negative pressure wound therapy. *ePlasty*, 2016;16:183-195; both utilized computer and bench models). Indirect impact of negative pressure: If the superficial incision is relatively well-closed and the incisional space within the tissue is isolated from the dressing, i.e., there is no direct fluid communication between it and the dressing, dressing design plays a more significant role in the effect of negative pressure on the underlying tissue. Specifically, the extent of change in shape of the foam-based dressing under negative pressure matters (as compared with non-foam-based dressings). When air is evacuated from the foam dressing, the foam shrinks and in doing so pulls the tissue to which the dressing is adhered to the midline of the dressing –in effect, pulling together (from the outside) the incisional edges/faces (Kilpadi DV and Olivie M. Evaluation of closed incision negative pressure therapy systems on the closure of incisional space model. *J Wound Care*, 2019;28:850-860; bench model).

-3. Fluid management: Foam-based ciNPT has been shown to impact fluid in the underlying tissues directly, as described above, and/or via endogenous mechanisms, e.g., lymphatic drainage, as indicated by edema reduction in a porcine model (Glaser DA, Farnsworth CL, Varley ES et al. Negative pressure therapy for closed spine incisions: a pilot study. *WOUNDS*, 2012;24:308-316) and hematoma/seroma reduction (Kilpadi DV and Cunningham MR. Evaluation of closed incision management with negative pressure wound therapy (CIM); hematoma/seroma and involvement of the lymphatic system. *Wound Repair Regen.*, 2011;19: 588-596 - porcine model; Pachowsky M, Gusinde J, Klein A et al. Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty. *Int Orthop.*, 2012;36:719-722 - human clinical trial). Additional animal study suggests that stimulation of lymphatic angiogenesis may also contribute.

-4. Quality of Healing: Porcine incisions treated with foam-based ciNPT for 5 days were tougher (required more energy to cause incisional dehiscence) than gauze-control treated incisions, 35 days after cessation of therapy. The energy required to induce incision separation is a representative gauge of clinically relevant impact loading such as experienced when coughing. This may be explained, in part, by histomorphometry data related to the mechanism of wound healing indicating that the foam-based ciNPT treated porcine incisions had narrower scar/healed areas in the deep dermis compared to the controls (Kilpadi DV, Lessing C, Derrik K. Healed porcine incisions previously treated with a surgical incision management system: mechanical, histomorphometry, and gene expression properties. *Aesthetic Plast Surg.*, 2014;38:767-778).

-5. Cost Implications: Economic modelling utilizing published clinical outcomes data illustrates the cost effectiveness of ciNPWT as compared with standard of care: primary outcomes demonstrated a 12% reduction in SSI post-sternotomy in obese patients. (Grauhan O, Navasardyan A, Hofmann M et al. Prevention of post sternotomy wound infections in obese patients by negative pressure wound therapy. *J Thorac Cardiovasc Surg* 2013;145:1387-1392. Grauhan O, Navasardyan A, Tutkun B et al. Effect of surgical incision management on wound infections in a post sternotomy patient population. *Int Wound J* 2014;11:6-9) DeLissovoy et al. reported a 67% reduction in SSI cost per cardiovascular incision with a per incision saving of \$4,025. (De Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. *Am J Infect Control*. 2009 Jun;37(5):387-97). In addition to cardiac applications, SSI reduction has been observed in studies across various specialties and surgical procedures. Use of foam-based ciNPT has been shown to beneficially impact health economics

			<p>and/or quality of life (QOL. (Singh D, Gabriel A, Parvizi J et al. Meta-analysis of comparative trials evaluating a single use closed incision negative pressure therapy system. <i>Plast Reconstr Surg</i> 2019; 143:41S-46S). Orthopaedic: Revision arthroplasties: A study of revision total knee (TKA) and total hip (THA) arthroplasties showed decreased complications and reoperations (Newman JM, Siqueira MBP, Klika AK et al. Use of closed incisional negative pressure wound therapy after revision total hip and knee arthroplasty in patients at high risk for infection – A prospective, randomized clinical trial. <i>J Arthroplasty</i>, 2019;34:554-559). In a revision TKA study, foam-based ciNPT reduced the likelihood of surgical site complications, readmission, and length of stay (Higuera-Rueda C, Cooper H, Cross M et al. Decreased 90-day surgical site complication rates with closed incision negative pressure therapy after revision knee arthroplasty: A randomized trial, presented at AAHKS 2020) in high-risk total knee arthroplasty). THERAPY UNITS</p> <ul style="list-style-type: none"> <li>○ Parvizi J, Shohat N, Gehrke T. Prevention of periprosthetic joint infection: new guidelines. <i>Bone Joint J.</i> 2017;99-B (4 Supple B):3–10.</li> <li>○ Pachowsky M, Gusinde J, Klein A, Lehl S, Schulz-Drost S, Schlechtweg P, Pauser J, Gelse K, Brem MH. Negative pressure wound therapy to prevent seromas and treat surgical incisions after total hip arthroplasty, <i>Int Orthop.</i>, 2012;36:719-722.</li> <li>○ Pauser J, Nordmeyer M, Biber R, Jantsch J, Kopschina C, Bail HJ, Brem MH. Incisional negative pressure wound therapy after hemiarthroplasty for femoral neck fractures – reduction of wound complications. <i>Int Wound J.</i>, 2016;13:663-667.</li> <li>○ Newman JM, Siqueira MBP, Klika A.K, Molloy, R. M., Barsoum, W.K, &amp;Higuera, C.A(2019). Use of closed incisional negative pressure wound therapy after revision Total Hip and Knee arthroplasty in patients at high risk for infection. <i>J Arthroplasty</i>, 2019;34:554-559).</li> <li>○ Cooper HJ, Bas MA. Closed-Incision Negative-Pressure Therapy Versus Antimicrobial Dressings After Revision Hip and Knee Surgery: A Comparative Study.<i>J Arthroplasty</i>2016;31:1047–1052.</li> <li>○ Redfern RE, Cameron-Ruetz C, O'Drobinak S, Chen J, Beer KJ. Closed incision negative pressure therapy effects on postoperative infection and surgical site complication after total hip and knee arthroplasty. <i>J Arthroplasty</i> 2017; 32:3333-3339.</li> <li>○ FDA De Novo Summary (DEN180013) DE NOVO CLASSIFICATION REQUEST FOR PREVENA 125 AND PREVENA PLUS 125 THERAPY UNITS. <a href="https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180013.pdf">https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180013.pdf</a></li> </ul> <p>D. Comment #2. Recommendation: Include what current guidelines indicate that using an antimicrobial incise drape is more effective at reducing contamination than using a standard clear incise drape as a recommendation along with current interdisciplinary care. Supporting Rationale to add this recommendation: References (to cite):</p> <ul style="list-style-type: none"> <li>○ Association of perioperative Registered Nurses (AORN). Guideline for sterile technique [DRAFT 2021].</li> <li>○ Asia Pacific Society of Infection Control. The APSIC guidelines for the prevention of surgical site infections. <a href="http://apsic-apac.org/wp-content/uploads/2018/05/APSIC-SSI-Preventionguideline-March-2018.pdf">http://apsic-apac.org/wp-content/uploads/2018/05/APSIC-SSI-Preventionguideline-March-2018.pdf</a>. Published March 2018. Accessed August 23, 2018</li> </ul>
--	--	--	---

			<ul style="list-style-type: none"> <li>○ National Institute for Health and Clinical Excellence. Prevention and treatment of surgical site infection. Clinical Guideline. <a href="https://www.nice.org.uk/guidance/cg74/evidence/fullguideline-242005933">https://www.nice.org.uk/guidance/cg74/evidence/fullguideline-242005933</a>. Published October 22, 2008. Updated February 2017. Accessed August 23, 2018</li> <li>○ National Health and Medical Research Council. Australian guidelines for the prevention and control of infection in healthcare. <a href="https://www.nhmrc.gov.au/book/australian-guidelinesprevention-and-control-infection-healthcare-2010/b4-3-4-considerations-du">https://www.nhmrc.gov.au/book/australian-guidelinesprevention-and-control-infection-healthcare-2010/b4-3-4-considerations-du</a>. Published 2010. Updated January 10, 2010. Accessed August 23, 2018.</li> <li>○ Commission for Hospital Hygiene and Infection Prevention (KRINKO) at RKI, Prevention of postoperative wound infections. 2018.</li> <li>○ Bejko J, Tasia V, Carrozzini M, et al. Comparison of efficacy and cost of iodine impregnated drape vs. standard drape in cardiac surgery; study in 5100 patients. <i>J Cardiovasc Transl Res.</i> 2015; 8:431-7</li> </ul> <p>E. Comment #3. Recommendation: Proposed new text for the recommendation for the Preoperative Skin Preparation in the guideline of the use of nasal decolonization for all patients that will require surgical therapy/ as a recommendation along with current interdisciplinary care.</p> <p>The suggested text discusses limitations of mupirocin and considerations related to povidone-iodine formulations and a universal (bathing see above recommendation and decolonization all patients) approach to other Healthcare Acquired Infections<sup>1-14</sup></p> <p>Supporting Rationale and Citations:</p> <ul style="list-style-type: none"> <li>-Evidence supports topical intranasal therapies to eradicate staphylococcal colonization. From 18% to 30% of all patients undergoing surgery are carriers of <i>Staphylococcus aureus</i>, and they have 3 times the risk of <i>S. aureus</i> surgical site infection and bacteraemia. Specifically, for patients undergoing high risk surgeries (e.g., cardiothoracic, orthopedic, and neurosurgery), use an intranasal anti staphylococcal antibiotic/antiseptic (e.g., mupirocin or iodophor) and chlorhexidine wash or wipes prior to surgery.</li> <li>-It is recommended that topical nasal therapy be applied universally<sup>1</sup></li> <li>-Evidence supports the use of an intranasal iodophor antiseptic of at least 5% as an alternative to mupirocin<sup>4</sup> and association of a bundled intervention<sup>11,12</sup> with surgical site infections among patients undergoing hip surgeries,<sup>11</sup> addresses as well as the concerns with mupirocin resistance,<sup>7,8,9,10</sup></li> </ul> <p>References (to cite):</p> <ul style="list-style-type: none"> <li>○ Centers for Disease Control. Strategies to Prevent Hospital-onset <i>Staphylococcus aureus</i> Bloodstream Infections in Acute Care Facilities. <a href="https://www.cdc.gov/hai/prevent/staph-prevention-strategies.html">https://www.cdc.gov/hai/prevent/staph-prevention-strategies.html</a> Accessed January. 3, 2022</li> <li>○ Weiser, M. C., and C. S. Moucha (2015). "The Current State of Screening and Decolonization for the Prevention of <i>Staphylococcus aureus</i> Surgical Site Infection After Total Hip and Knee Arthroplasty." <i>J Bone Joint Surg Am</i> 97(17): 1449-1458.</li> <li>○ Torres, E. G., et al. (2016). "Is Preoperative Nasal Povidone-Iodine as Efficient and Cost-Effective as Standard Methicillin-Resistant <i>Staphylococcus aureus</i> Screening Protocol in Total Joint Arthroplasty?" <i>J Arthroplasty</i> 31(1): 215-218.</li> <li>○ Phillips M, Rosenberg A, Shopsin B, et al. Preventing surgical site infections: A randomized, open-label trial of nasal mupirocin ointment and nasal povidone-iodine solution. <i>Infect Control Hosp Epidemiol</i> 2014;35(7):826–832.</li> </ul>
--	--	--	--

- Loftus RW, Dexter F, Goodheart MJ, et al. The Effect of Improving Basic Preventive Measures in the Perioperative Arena on Staphylococcus aureus Transmission and Surgical Site Infections: A Randomized Clinical Trial. JAMA Netw Open. 2020;3(3): e201934. doi:10.1001/jamanetworkopen.2020.1934.
- Bebko SP, Green DM, Awad SS. Effect of a preoperative decontamination protocol on surgical site infections in patients undergoing elective orthopaedic surgery with hardware implantation. JAMA Surg. Published online March 04, 2015. doi:10.1001/jamasurg.2014.3480.
- Bathoorn E, Hetem DJ, Alphenaar J, Kusters JG, Bonten MJM. Emergence of high-level mupirocin resistance in coagulase-negative staphylococci associated with increased short-term mupirocin use. J Clin Microbiol. 2012;50(9):2947-2950
- Lepainteur M, Royer G, Bourrel AS, et al. Prevalence of resistance to antiseptics and mupirocin among invasive coagulase-negative staphylococci from very preterm neonates in NICU: the creeping threat? J Hosp Infect. 2013;83(4):333-336
- Orrett FA. The emergence of mupirocin resistance among clinical isolates of methicillin-resistant Staphylococcus aureus in Trinidad: a first report. Jpn J Infect Dis. 2008;61(2):107-110
- Rossney A, O'Connell S. Emerging high-level mupirocin resistance among MRSA isolates in Ireland. Euro Surveill. 2008;13(14).
- Schweizer ML, Chiang HY, Septimus E, et al. Association of a bundled intervention with surgical site infections among patients undergoing cardiac, hip, or knee surgery. JAMA. 2015;313(21):2162-71.
- Ramos N, Skeete F, Haas JP, et al. Surgical site infection prevention initiative patient attitude and compliance. Bull NYU Hosp Jt Dis. 2011;69(4):312-5.
- Maslow J. et al. Patient Experience with Mupirocin or Povidone-Iodine Nasal Decolonization | Orthopedics. 2014;37(6): e576-581. Doi.org. <https://doi.org/10.3928/01477447-20140528-59>.
- Surgical Site Infections, International Nosocomial Infection Control Consortium (INICC) Report, Data Summary of 30 Countries, 2005-2010. DOI:10.1086/670626

-Proposed new text for the recommendation for the Preoperative Skin Preparation in the guideline of the use of antiseptic, base the selection on patient and procedure consideration. 1-5

-Baseline considerations should include patient factors, the active ingredients such as: aqueous solution or dual active solution, and size of the area being prepped.

- World Health Organization: WHO Global Guidelines for the Prevention of Surgical Site Infection 2016. Retrieved from <http://www.who.org>
- CDC HICPAC Guideline for the Prevention of Surgical Site Infection. JAMA, May 2017. <http://jamanetwork.com/journals/jamasurgery/fullarticle/2623725>
- AORN. Guideline for Perioperative Practice: Patient Skin Antisepsis. Guidelines for Perioperative Practices. Denver, Colorado: AORN, Inc. 2021.
- Anderson, D.J. et al. Strategies to Prevent Surgical Site Infection in Acute Care Hospitals: 2014 Update. Retrieved from [www.jstor.org](http://www.jstor.org) DOI: 10.1086/676022
- National Quality Forum 2010 safe practice #22 on surgical site infection.

F. Comment 4#. Recommendation: Include hair removal as a recommendation along with current interdisciplinary care.

			<p>Supporting Rationale to add hair removal recommendation: Do not use hair removal routinely to reduce the risk of surgical site infection. If hair has to be removed, use electric clippers with a single-use head on the day of surgery. Do not use razors for hair removal, because they increase the risk of surgical site infection.)<sup>1</sup> Health Agencies and Professional Society Hair Removal Recommendations. 1-5</p> <p>References (to cite):</p> <ul style="list-style-type: none"> <li>○ Preoperative hair removal to reduce surgical site infection, November 2011, Cochrane database of systematic reviews, DOI:10.1002/14651858</li> <li>○ Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20: 250-278.</li> <li>○ Gaynes R, Richards C, Edwards J, et al. The National Nosocomial Infections Surveillance (NNIS) System Hospitals. Feeding back surveillance data to prevent hospital-acquired infections. Emerg Infect Dis 2001; 7:295-298.</li> <li>○ Guidelines for Perioperative Practice, AORN, 2021</li> <li>○ Guideline for the prevention of surgical site infection, CDC, 2021</li> </ul> <p>G. Comment #5. Recommendation: Include perioperative normothermia as a recommendation along with current interdisciplinary care. 1-10</p> <p>Multiple organizations support maintaining normothermia during the perioperative period<sup>1-7</sup> and some elaborate on that recommendation by endorsing prewarming specifically. 1,2,3, 7 Forced air warming has a positive effect on patients’ thermal comfort and overall patient satisfaction. 9</p> <p>Supporting Rationale to add perioperative normothermia: Maintaining perioperative normothermia is supported in literature as well as recommended in multiple other guidelines as hypothermia is associated with significant negative outcomes. Prewarming is recommended by NICE, AORN, ASPAN. Monitoring core temperature on a reliable device is an important first step in temperature management. NICE and AORN recommend continuously monitoring the patient’s core temperature through all phases of perioperative care. The importance of pre-operative, intra-operative, and post-operative warming techniques to maintain perioperative normothermia should be noted for all hip fractures surgical therapy needed patients.</p> <p>References (to cite):</p> <ul style="list-style-type: none"> <li>○ National Institute for Health and Care Excellence. Hypothermia: Prevention and management in adults having surgery. 2008. Updated 2016. <a href="https://www.nice.org.uk/guidance/cg65/chapter/recommendations">https://www.nice.org.uk/guidance/cg65/chapter/recommendations</a></li> <li>○ World Health Organization: WHO Guidelines for the prevention of Surgical Site Infection. 2016. Retrieved from <a href="http://www.who.org">http://www.who.org</a></li> <li>○ American Society of Perianesthesia Nurses. ASPAN’s Evidence-based Clinical Practice Guideline for the Promotion of Perioperative Normothermia. 2010. <a href="https://www.aspan.org/Portals/6/docs/ClinicalPractice/Guidelines/Normothermia_Guideline_12-10_JoPAN.pdf">https://www.aspan.org/Portals/6/docs/ClinicalPractice/Guidelines/Normothermia_Guideline_12-10_JoPAN.pdf</a></li> <li>○ American College of Surgeons: Surgical Site Infection Guidelines, 2016 Update.</li> </ul>
--	--	--	--



			<ul style="list-style-type: none"><li>○ Society for Healthcare Epidemiology of America. Strategies to Prevent Surgical Site Infections in Acute Care Hospitals. 2014 Update.</li><li>○ AORN 2019 Guidelines for Perioperative Practices. Denver, Guideline for Hypothermia. Colorado: AORN, Inc.</li><li>○ Surgical site infections: prevention and treatment NICE guideline [NG125] <a href="https://www.nice.org.uk/guidance/ng125">https://www.nice.org.uk/guidance/ng125</a> Published date: 11 April 2019</li><li>○ Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996;334:1209–1215.</li><li>○ Wagner, D.P., M.J. Byrne, and K.L. Kolcaba, Effects of Comfort Warming on Preoperative Patients. AORN J, 2006. 84(3): p. 427-448.</li><li>○ Putzu M, Casati A, Berti M, Pagliarini G, Fanelli G. Clinical complications, monitoring, and management of perioperative mild hypothermia: anesthesiologic features. Acta Biomed 2007; 78:163–169.</li></ul> <p>H. Thank you for consideration of these comments. Feel free to contact me with any questions or for further discussion as needed.</p>
--	--	--	---

***Workgroup Response to Reviewer #3***

Dear Flutura Hasa, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for your feedback. The separate specific comments that were listed after this note were reviewed individually.
- C. Thank you for your feedback. The work group reviewed the recommendation after the Tahir study was removed and determined no additional edits were necessary.
- D. Thank you for your feedback. This topic was not evaluated within this CPG but can be considered for inclusion in a future update.
- E. Thank you for your feedback. The section was reviewed and determined to be adequate. These additions can potentially be considered in a future update.
- F. Thank you for your feedback. This topic was not evaluated within this CPG but can be considered for inclusion in a future update.
- G. Thank you for your feedback. No literature was found meeting our inclusion criteria for this topic, but it can be reevaluated when the CPG is updated in the future.
- H. Thank you.

**Reviewer #4, Mihail Radulescu, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
4	Mihail Radulescu, M.D.	American Academy of Orthopaedic Surgeons	<p>A. "Silver coated dressings are not suggested to improve outcomes or decrease infections."                      -It is debatable... 7 vs 40                      -In the silver-coated dressing arm, 7% developed infected pin sites, while 40% developed it in the control group. There was no significant difference between these groups.</p> <p>B. "There may be an increased risk for SSI in patients who smoke or who are diabetic"                      -well controlled/ uncontrolled diabetes                      -vasculopathy present or not make a difference</p> <p>C. "Surgical skin preparation should be performed with an alcohol-based antiseptic agent, unless contraindicated" 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).                      -which are the contraindications? open wound, allergy?</p> <p>D. Great job.</p>

***Workgroup Response to Reviewer #4***

Dear Mihail Radulescu, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your feedback. The manuscript has been updated to include "pin site infections." Additionally, the typographical errors concerning the reported percentages have been modified.
- B. Thank you for your feedback. Vasculopathies were not evaluated. For diabetes mellitus- most studies use binary (present/not) rather than stratification by perioperative glucose, a1c, etc. More granularities would have been helpful with the data.
- C. Thank you for your feedback. Rationale reviewed and text added to mention that alcohol-based antiseptics are not recommended for open wounds or those with related allergy. There are other contraindications, but they do not apply for the current topic.
- D. Thank you for the positive feedback.

**Reviewer #5, Ronald Delanois, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
5	Ronald Delanois, M.D.	The Knee Society	<p>A. My only concern regarding this clinical guideline is the section that refers to race and socioeconomic standing not impacting the risk for SSI. As more data is becoming available regarding the lack of information specific to social determinants of health and their impact on outcomes, most importantly race, this reviewer is concerned regarding these recommendations. This reviewer would either recommend the ratings being changed to a two star or simply eliminating it from the clinical guideline.</p>

***Workgroup Response to Reviewer #5***

Dear Ronald Delanois, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your feedback. Current data suggests there is minimal evidence for risk of SSI. We simply need more data on this very important topic in order to change the recommendation.

**Reviewer #6, Krishna Reddy, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	<b>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</b>
6	Krishna Reddy, M.D.	American Academy of Orthopaedic Surgeons, Key Informants Panel	A. Having reviewed the guidelines, I feel it is well structured, precise, and covered all the key and relevant areas of the topic.

***Workgroup Response to Reviewer #6***

Dear Krishna Reddy, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for your positive feedback.



**Reviewer #7, Matthew Houdek, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
7	Matthew Houdek, M.D.	American Academy of Orthopaedic Surgeons, Key Informants Panel	<p>A. I think the structure of the guidelines are good, but for SSI shouldn't we also be looking at how wounds are closed? You included the information on the VAC dressing and silver ion dressings, however this nothing on the use of different closure techniques. Should we be using staples, sutures or a glue dressing? This impacts wound healing, and subsequent SSI. It may be a good idea to include this as it could provide some guidance.</p> <p>B. Table 2 seems odd. The Decision Aids Column seems backwards. Wouldn't a Strong recommendation be the most important in counseling a patient?</p>

***Workgroup Response to Reviewer #7***

Dear Matthew Houdek, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your feedback. PICO's which included the topic of wound closure were investigated, however not all aspects of the questions had literature fitting our inclusion criteria. The closure topics with literature were included in the recommendations as able.
- B. Thank you for your feedback. Methodology suggests that topics with limited evidence should be viewed with less certainty of the effectiveness of a given intervention as compared to a strong recommendation, and therefore more counseling may be necessary to discuss the lack of evidence and all options available. However, patient counseling is still an important aspect of care at all levels of evidence.

**Reviewer #8, Shari Jawetz, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
8	Shari Jawetz, M.D.	American College of Radiology	<p>A. Thank you for the invitation to review and comment on this clearly written guideline which addresses many considerations for preventing SSI in trauma patients. I do have a few specific comments which I have outlined below.</p> <p>B. Page 23 – section on Cost Effectiveness/Resource Utilization  “Antibiotic use is associated with higher cost of the drug...” Please clarify the first section of the statement. I’m not sure if the phrase “Antibiotic use is associated with higher cost of the drug” was a mistake here, because this part of the sentence is confusing. I understand how antibiotic use is associated with increased pharmacy time for prep and antibiotic resistance etc., but I’m not sure what you mean that antibiotic use is associated with higher cost of the drug. Did you mean antibiotic use is associated with higher cost of hospitalization or perhaps something else?</p> <p>C. Page 41 – paragraph 4 which begins “Two moderate quality studies (Bhandari 2003, Giannoudis 2000)...”  I have issues with the statement: “However, neither paper attempted to correlate the risk of anti-inflammatory use with SSI.” These 2 references are insufficient to make a moderate level recommendation that anti-inflammatory use does not alter the risk of postoperative infection. Neither the Bhandari nor the Giannoudis papers address the impact of anti-inflammatory use on postoperative infection, so I don’t believe that you can utilize these references to support or refute this recommendation at all. If there are no other references that address the impact of anti-inflammatory use on post-operative infection, then I don’t think you can make an evidence based recommendation at all, and this should be a subject for expert consensus and/or future study.</p> <p>D. Page 43 – Rationale section, paragraph 1, sentence 1  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. By the level of evidence descriptions in Table 1, this recommendation should be a strong recommendation, not moderate, given that 1 moderate and 2 high quality studies demonstrate that race and SES don’t alter the risk of SSI.</p> <p>E. Page 49 - Cost Effectiveness/Resource Utilization section</p>

			<p>What is the reference you cite for Bouachour 2017? Such a reference is not included in your bibliography. I believe, from looking at the Bouachour 1996 reference and that data that you cite, this probably just represents a typo that should instead be Bouachour 1996. Given the data provided in this Bouachour 1996 reference, wouldn't this reference support a statement such as: "In patients with open fracture, hyperbaric O2 may benefit patient outcomes"? Why would you use this reference to support a recommendation against hyperbaric O2 when the data from this manuscript shows a statistically significant benefit to the use of hyperbaric O2 in patients with crush injuries? It's still a recommendation of limited strength, but I believe the reference supports the opposite of your recommendation. Please clarify.</p>
--	--	--	--

***Workgroup Response to Reviewer #8***

Dear Shari Jawetz, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for providing feedback.
- B. Thank you for your feedback. The manuscript has been edited for clarity.
- C. Thank you for your feedback. Articles were reviewed and determined to not appropriately address question of interest. Furthermore, the articles were excluded, and corresponding recommendation statement removed.
- D. Thank you for your feedback. The manuscript has been modified.
- E. Thank you for your feedback. This typographical error has been edited on the manuscript.

**Reviewer #9, Louis Lewandowski, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
9	Louis Lewandowski, M.D.	Society of Military Orthopaedic Surgeons	<p>A. The authors of "Prevention of Surgical Site Infections (SSI) Following Major Extremity Trauma" provide a concise CPG in which to find clear evidence-based recommendation in order to decrease the risk of infections in these complex injuries. The parameter in which articles were selected by was clearly defined as well as the differentiation of the strength of the evidence utilized for the recommendations contained within the CPG. The inclusion of modifiable risk factor provides critical information when discussing patient behaviors associated with post-operative infection with patients and possible lifestyle changes that can be performed to decrease the likelihood of SSI.</p>

***Workgroup Response to Reviewer #9***

Dear Louis Lewandowski, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

**Reviewer #10, Christopher Souder, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
10	Christopher Souder, M.D.	Pediatric Orthopaedic Society of North America	<p>A. Pg 24--the discussion regarding preop antibiotics for open fractures seems to be based off of dated literature. Pg 15 mentions that literature prior to 1985 was not considered. With that guiding the discussion, only 1 moderate at best article would be included in the review and would presumably lower the recommendation.</p> <p>B. Pg 33--on the 2nd bullet point--has this not already be addressed within the studies listed above?</p> <p>C. Pg 36--the heading of this recommendation seems misleading. The statement suggests that 'After closed fracture fixation, negative pressure wound therapy may mitigate the risk of revision surgery or SSIs'. But the explanation following this does not support the statement. The larger, higher quality trials did not find this. Sure, it may not have been researched fully (as suggested by Future Research statement) but that would not be enough of a reason to state the entry statement of this guideline with that statement. A reader would be expected for a study to suggest it is beneficial in the setting of closed fractures if the opening line read in the way it is currently written.</p> <p>D. Pg 40-- The title of this statement is misleading as well. The single article is one describing silver dressings around ex-fix pins not the wound. In addition, it is underpowered to show any reasonable result. This fact that this is a study regarding ex-fix pin sites is clear in the discussion but is insufficient to limit confusion when a reader quickly reads the bolded statements. Personally, I believe this statement provides no significant value as it is merely a statement about pin site care of which there are numerous pathways. It does not address the injury itself. If it is to remain included, the bolded title should more clearly state that this is evaluating silver dressings about ex-fix pin sites.</p> <p>E. Pg50--the title would suggest there is a reference that would not support the use of HBO yet the only referenced article suggested it was beneficial. Constructing the statement in a negative manner is misleading that there is evidence to suggest it does not help but that is not the direction of the information used to formulate this guideline</p>



***Workgroup Response to Reviewer #10***

Dear Christopher Souder, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your feedback. Only one moderate quality article was included in our evidence pool, which informed our strength designations. However, the authors felt it was also important to reference additional literature in the rationale that did not fit our inclusion criteria. This literature is not included as part of the evidence for this recommendation.
- B. Thank you for your feedback. The workgroup listed areas of study they felt they were important to continue studying.
- C. Thank you for your feedback. The work group reviewed the recommendation after the Tahir study was removed and determined no edits were necessary.
- D. Thank you for your feedback. The manuscript has been updated to include "pin site infections."
- E. Thank you for your feedback. 1 study with 36 patients is limited. "May not benefit" is a reflection of the lack of evidence.

**Reviewer #11, Matthew Abdel, M.D.**

<b>Reviewer Number</b>	<b>Reviewer Name</b>	<b>Society or committee you are representing</b>	<b>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</b>
11	Matthew Abdel M.D..	American Academy of Orthopaedic Surgeons, Board of Directors	A. See above.

***Workgroup Response to Reviewer #11***

Dear Matthew Abdel, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. No comment.

**Reviewer #12, Roman Natoli, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
12	Roman Natoli, M.D.	American Academy of Orthopaedic Surgeons, Key Informants Panel	<p>A. This CPG draft is excellently done, as come to be expected of Academy guidelines. I rated one neutral, "patients to whom this guideline is meant to apply are specifically described." This should not be perceived as negative, rather it a result of looking at Major Extremity Trauma. While the populations are enumerated to 8 injury types, the spectrum within these injury types still makes the entire population heterogenous. I see no good wat around this given the current lack of granularity in clinical research on these topics.</p> <p>B. Re: Silver Coated Dressings. It seems the recommendation is made from 1 study on pin tract infections. But the language of the recommendation "Silver coated dressings are not suggested to improve outcomes or decrease infections" seems broad. I went into it thinking I would be reading about Silver and wounds or incisions. Can it be more focused on pin sites? Further, the Acceptability &amp; Feasibility sections then talk about 'Appropriate soft tissue management'. I agree with the statements but, again, feel like they are reaching to far from what I gather is a discussion about external fixator pin sites.</p> <p>C. Small correction in that increase should be made plural in the statement "• Low albumin (&lt;36g/L) increases the risk of infection postoperatively"</p> <p>D. Small correction in Cost Effectiveness/Resource Utilization for Administrative Risk Factors. The t should be deleted in the statement "This recommendation requires minimal resources and there is not cost associated with implementation."</p> <p>E. Small correction in Acceptability for Negative Pressure Wound Therapy - High Risk Surgical Incisions. The word 'not' should go before 'too' in the statement "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 too expensive to implement." Also, period needs added at end of Feasibility statement.</p> <p>F. In Preoperative Skin Preparation, was there any information uncovered for nasal decolonization for either</p> <ol style="list-style-type: none"> <li>1) one-time application of povidone-iodine (5% or 10%) on the morning of surgery</li> <li>2) one-time application of antiseptic alcohol nasal decolonization on the morning of surgery</li> </ol>

			G. Finally, in Appendix III, Definitions, the injury types are listed as 9 through 16. They should be 1 through 8.
--	--	--	---

***Workgroup Response to Reviewer #12***

Dear Roman Natoli, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for your feedback. The manuscript has been updated to include "pin site infections."
- C. Thank you for your feedback. The guideline has been modified.
- D. Thank you for your feedback. The guideline has been modified.
- E. Thank you for your feedback. The guideline has been modified.
- F. Thank you for your feedback. All literature meeting our inclusion criteria was included as evidence for this Recommendation. If a topic is not reported on, it typically means no evidence on the topic was found in our literature search.
- G. Thank you for the feedback. The guideline manuscript has been modified.

**Reviewer #13, Nicholas Tedesco, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
13	Nicholas Tedesco, M.D.	Musculoskeletal Tumor Society	<p>A. Unfortunately, line numbers did not come through in the word document for me (perhaps a Mac incompatibility thing?), so I have done my best to point to specific points of the document without the use of line numbers:</p> <p>B. Top of page 8 (and page 31), for the "Initial Wound Management - Fixation" heading, It discusses why this was a downgraded recommendation on page 31. However, the italicized text states, "Also requires no reason to downgrade from the EtD framework". These seem to be contradictory.</p> <p>C. Page 24, for "utilization of preoperative antibiotics is suggested to prevent SSI in operative treatment of open fractures", depending on the specific criterion for selecting papers in this topic, the classic Gustilo and Anderson paper specifically addresses this topic and is not listed in the narrative review for this recommendation. It provides strong support for this recommendation (reduction in infections from 44% to 9% once abx were routinely employed).</p> <p>D. Another thing is at the end of the document to answer PICO questions, only studies after 1985 were included yet the G&amp;A paper (as well as most cited n this age) were before that. Perhaps the study inclusion criteria on page 67, 2nd bullet point, should be changed? <a href="https://pubmed.ncbi.nlm.nih.gov/773941/">https://pubmed.ncbi.nlm.nih.gov/773941/</a></p> <p>E. Page 36, for "After closed fracture fixation, negative pressure wound therapy may mitigate the risk of revision surgery or SSIs...et al", one of the "high quality" RCT's (Tahir 2020) has been retracted. I'm unclear why but this should be investigated, reviewed, and the narrative text changed to reflect that. <a href="https://pubmed.ncbi.nlm.nih.gov/32600140/">https://pubmed.ncbi.nlm.nih.gov/32600140/</a></p> <p>F. Page 40, for "Silver coated dressings are not suggested to improve outcomes or decrease infections", something seems majorly disconnected here from the available evidence and the recommendation. First, in the second to last sentence under "rationale", the numbers are not correct. 7 patients (46%), not 7% had an infection in the study group. Second, and more importantly, this recommendation should be downgraded, or really, inconclusive. A single study from 10 years ago with an N of 15 in its 2 arms should in no way tell us that there is moderate evidence silver dressings are useless. That is a very underpowered study, and the treatment group comes nowhere near to treating the breadth of pathologies the scope of this guideline is trying to address. In fact, this only looked at pin tract</p>

			<p>infections and not wound infections from the open injury or definitive fracture surgery at all. This topic needs way more data before a statement like the above can be made. Perhaps the recommendation should be more like, "there is limited evidence to suggest that silver coated dressings are not helpful for external fixators to prevent pin tract infections.</p> <p>G. Excellent work and collaborative effort!</p>
--	--	--	---



### ***Workgroup Response to Reviewer #13***

Dear Nicholas Tedesco, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. No comment.
- B. Thank you for your feedback. The definitions describe the strength of evidence. Here the italicized is defining "strong evidence" as evidence from 2 or more high quality studies and no reasons to downgrade. Because this recommendation had more than 2 high quality studies supporting it, but the workgroup determined there were reasons to downgrade, the strength of recommendation was then downgraded to "Moderate" quality even though the strength of evidence was "Strong".
- C. Thank you for your feedback. Only literature published after 1985 were considered for inclusion in our evidence pool. (Other literature not fitting this criteria could be discussed by the workgroup as necessary in the rationale, but this literature cannot be included in the final strength assessments).
- D. Thank you for your feedback. Additional references not fitting our inclusion criteria and not considered for final strength assessment were discussed in the rationale. Text has been added to the manuscript citing this literature more clearly.
- E. Thank you for your feedback. The Tahir study was removed, and edits were made as necessary.
- F. Thank you for your feedback. The manuscript has been updated to include "pin site infections." Additionally, the typographical errors concerning the reported percentages have been modified.
- G. Thank you for the positive feedback.

**Reviewer #14, F. Scott Gray, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
14	F. Scott Gray, M.D.	American Academy of Orthopaedic Surgeons, Board of Councilors	<p>A. I think my agree and strongly agree comments are self-explanatory, subtle differences not real relevant. However, I have a disagreement on page 40 under the section of Modifiable Risk Factors with respect to a limited grade.</p> <ul style="list-style-type: none"> <li>• Low albumin (&lt;36g/L) increase the risk of infection postoperatively.</li> <li>• Elevated postoperative glucose levels (&gt;125 mg/dL) increases the risk for infection.</li> </ul> <p>These items were given a limited two-star grade for recommendations. I think there is evidence in the literature indicating that these two items are much more correlated with SSI control when these items are "under better control." Here are just two stand outs and they fall in line with what I think is traditional evidence-based thinking. It is my opinion that it matters not whether the setting is elective joint surgery or trauma. Trauma is of course impossible to control preoperatively, but not post operatively.</p> <ul style="list-style-type: none"> <li>• <a href="https://pubmed.ncbi.nlm.nih.gov/30106824/">https://pubmed.ncbi.nlm.nih.gov/30106824/</a></li> <li>• <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5238522/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5238522/</a></li> </ul> <p>B. Other than what I have opined about with respect to Modifiable factors of low albumin and blood sugar control.</p>

***Workgroup Response to Reviewer #14***

Dear F. Scott Gray, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your feedback. We were limited in the scope of the CPG to only including articles focused on trauma patients; While other literature may exist on these RFs, they could not be included for this recommendation because they did not meet our inclusion criteria.
- B. Thank you for your feedback.

**Reviewer #15, Michelle Ghert, M.D.**

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
15	Michelle Ghert, M.D.	American Academy of Orthopaedic Surgeons, Key Informants Panel	<ul style="list-style-type: none"> <li>A. Methodology is transparent and thorough. The recommendations are supported by the evidence. The composition of the guideline development group is not described in sufficient detail.</li> <li>B. The recommendations for NPWT are confusing (not recommended, yes recommended). Can those 2 sections be combined?</li> </ul>

***Workgroup Response to Reviewer #15***

Dear Michelle Ghert, M.D.,

Thank you for your expert review of the Prevention of Surgical Site Infections Following Major Extremity Trauma Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

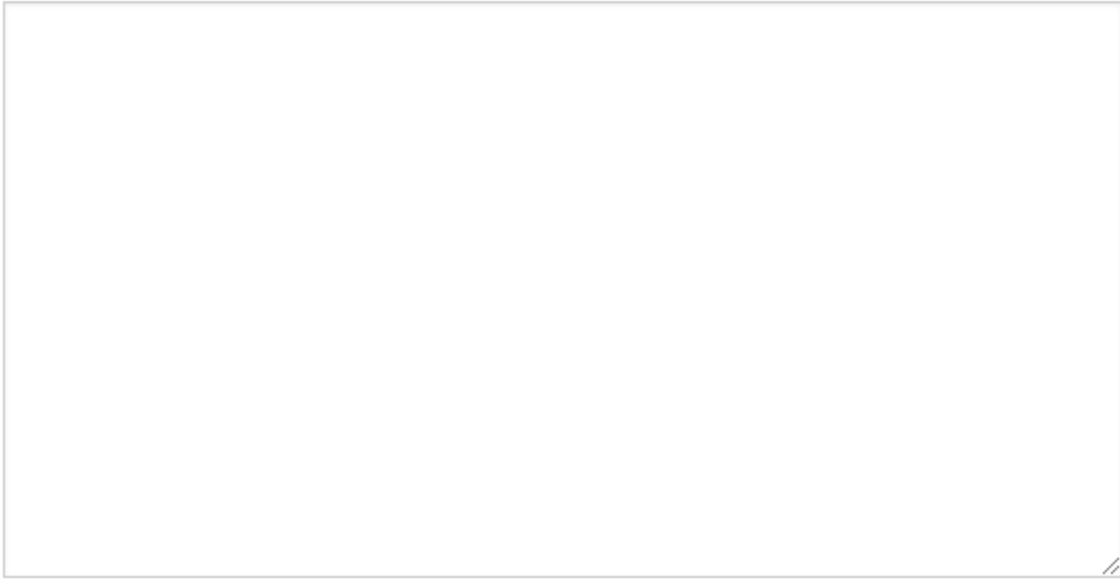
- A. Thank you for your feedback. The names of the guideline development work group members are blinded during the duration of the review period.
- B. Thank you for your feedback. The workgroup reviewed the recommendation after the Tahir study was removed and determined no edits were necessary.

## Appendix A – Structured Review Form

### Review Questions (REQUIRED)

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

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



**Would you recommend these guidelines for use in clinical practice? (REQUIRED)**

- Strongly Recommend
- Recommend
- Would Not Recommend
- Unsure

**Additional Comments regarding this clinical practice guideline?**

