Quality evaluation of clinical practice guidelines for thromboprophylaxis in orthopaedic trauma based on AGREE II and AGREE-REX: a systematic review protocol

Ling-Xiao He,1,2 Jing-Ying Xie,1,3 Juan Lv,1,4 Huan Liu,1,5 Deng-Bin Liao,1,2 Guang-Lin Wang,2,6 Ning Ning,1,7 Zong-Ke Zhou6,7

ABSTRACT
Introduction Orthopaedic trauma patients are at high risk of venous thromboembolism (VTE). As VTE prophylaxis has gradually raised public concerns, guidelines related to this topic have increased over time. However, the existing recommendations of thromboprophylaxis guidelines in orthopaedic trauma patients are still inconsistent, and the quality of the guidelines and recommendations for the topic still lacks comprehensive assessments. This review aims to critically appraise clinical practice guidelines for thromboprophylaxis in orthopaedic trauma patients.

Methods and analysis We will conduct a comprehensive literature search up to 31 October 2022 in databases (PubMed, EMBASE, CINAHL, Web of Science, the Cochrane Library, etc.), academic websites and guideline repositories. The quality of the guidelines and recommendations will be assessed by five reviewers independently using the Appraisal of Guidelines Research and Evaluation II instrument (AGREE-II) and the AGREE - Recommendation Excellence (AGREE-REX). We will summarise the characteristics of the guidelines and compare the differences between these recommendations.

Ethics and dissemination This study will follow the Declaration of Helsinki and has received approval from the Ethics Committee on Biomedical Research, West China Hospital, Sichuan University (ethics approval no. 2021-009). The results will be summarised as a paper, disseminated through peer-reviewed journals, and will help guide further research in the future.

Protocol registration number CRD42021273405.

STRENGTHS AND LIMITATIONS OF THIS STUDY
⇒ We will evaluate the quality of clinical practice guidelines and the applicability of the recommendations in guidelines related to venous thromboembolism prevention in orthopaedic trauma patients to guide evidence-based clinical practice.
⇒ We will conduct a comprehensive literature search and use the widely recognised Appraisal of Guidelines Research and Evaluation II (AGREE-II) and AGREE-Recommendation Excellence tools for rigorous quality evaluation.
⇒ All the members will not participate in the quality appraisal until received systematic review training.
⇒ This study will be limited to guidelines written in Chinese and English, which could be a limiting factor.
⇒ This study might be included in guidelines that were developed earlier or not updated in time. Thus, more cautious interpretations of the study results should be needed.

INTRODUCTION
Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), is the third most common cause of cardiovascular-related death and results in a mass of disability-adjusted life-years lost in hospitalised patients.1 More than 500 000 VTE-related deaths occur in the USA1 and cost US$7–US$10 billion for healthcare annually.2 As an avoidable in-hospital complication, each case of VTE will take an excess of 5.4 hospitalisation days and increase the mortality rate by 6.6 times.3 About 6% of patients with DVT and 12% of patients with PE die within 1 month after diagnosis.4 Various factors can lead to the occurrence of VTE, such as major surgery, trauma, plaster fixation, tumours, etc.5 Orthopaedic trauma patients are at high risk of VTE due to multiple risk factors. The incidence of VTE in orthopaedic trauma patients can vary from 4.78% to 40.25%,6–9 depending on the location of the injury, VTE monitoring method, ethnicity, etc.

Thromboprophylaxis has been proven able to reduce the occurrence of VTE effectively.10 Both chemical and mechanical prophylaxis strategies have shown their effects in orthopaedic trauma patients. At present, the most widely used VTE prevention clinical practice...
guideline (CPG) in orthopaedic surgery is the ninth edition of the VTE prevention guideline presented by the American College of Chest Physicians (ACCP) in 2012. However, its recommendations for patients with orthopaedic trauma are insufficient, covering only patients with hip fractures, isolated lower leg injuries and knee arthroscopy. And no specific recommendations for the dose and frequency of chemoprophylaxis are mentioned in the above ACCP guideline. Recently, several updated CPGs for VTE prevention have been published, but many have been formed based on expert consensus. In addition, there are still many issues to be determined, such as the timing, duration and best practice protocol for VTE prevention in patients with different types of orthopaedic trauma. It is still necessary to explore further construction of a VTE prevention programme that fits the clinical situation of orthopaedic trauma patients based on guidelines.

Currently, the Appraisal of Guidelines for Research & Evaluation II instrument (AGREE-II) is widely accepted to evaluate the methodological quality of the guidelines. However, this tool does not assess the specific recommendations provided in the guidelines and cannot guarantee their applicability in clinical practice. The AGREE-Recommendation EXcellence (AGREE-REX) tool mainly evaluates the quality and applicability of the guideline recommendations, which is a powerful supplement to AGREE-II. We hope to use the AGREE-II and AGREE-REX tools to critically appraise the current CPGs for VTE prevention in orthopaedic trauma and understand both the methodological and recommendation quality of the current guidelines, which help guide the selection of reliable recommendations following the clinical situation.

**METHODS AND ANALYSIS**

**Objectives**

We plan to systematically collect VTE prophylaxis CPGs in the field of orthopaedic trauma and use AGREE-II and AGREE-REX tools to conduct a rigorous quality appraisal to answer the following questions:

1. What is the methodological quality of the VTE prophylaxis CPGs in orthopaedic trauma?
2. What similarities and differences are the recommendations provided in the current CPGs for VTE prophylaxis in orthopaedic trauma?
3. What is the strength and quality of the evidence provided in the current CPGs for VTE prophylaxis in orthopaedic trauma?

**Protocol and registration**

This report follows the Preferred Reporting Items for Systematic Review and Meta-Analysis statement (see online supplemental appendix 1) and has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42021273405.

**Patient and public involvement**

Patients and/or the public will not be involved in the design, conduct, reporting or dissemination plans of this research.

**Eligibility criteria**

See details in table 1. We will only include openly published literature in the study and grey literature will be excluded.

**SELECTION OF STUDIES**

**Data sources**

The following databases and websites from inception to 31 October 2022 will be searched:


**Seamless Table 1 Inclusion and exclusion criteria**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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</thead>
<tbody>
<tr>
<td>1. Guidelines published in English or Chinese.</td>
<td>1. Evidence summary, editorials, letters, consensus statements, policy statements or standards, or just a quick reference guide which do not involve the evaluation of evidence and the description of the method of forming recommendations.</td>
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<tr>
<td>2. The guideline has clearly stated that it is a ‘guideline’ in the context.</td>
<td>2. The previous version of the updated guideline.</td>
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<tr>
<td>3. The content includes statements and recommendations for the prevention of VTE in orthopaedic trauma patients.</td>
<td>3. Repeated publication.</td>
</tr>
<tr>
<td>5. The latest complete version of the guideline and any partial revisions or updates published afterward.</td>
<td>5. Only included one or more of the following: spinal fractures, craniofacial or maxillofacial fractures, rib fractures, or skin and soft tissue injuries.</td>
</tr>
</tbody>
</table>

VTE, venous thromboembolism.
Box 1  Sample research strategy for PubMed

#1 (((orthopedics[MeSH Terms]) OR (traumatology[MeSH Terms])) OR (wounds and injuries[MeSH Terms]))
#2 ((((fracture[Title/Abstract]) OR (limb trauma[Title/Abstract])) OR (extremity trauma[Title/Abstract])) OR (musculoskeletal injury[Title/Abstract])) OR (musculoskeletal trauma[Title/Abstract])) OR (limb immobilization[Title/Abstract])) OR (skeletal fixation[Title/Abstract])) OR ("orthopedic trauma"[Title/Abstract] AND "trauma"[Title/Abstract]))
#3 ((venous thromboembolism[MeSH Terms]) OR (venous thrombosis[MeSH Terms]) OR (pulmonary embolism[MeSH Terms]))
#4 (((venous thromboembolism[Title/Abstract]) OR (venothromboembolism[Title/Abstract])) OR (venous thrombosis[Title/Abstract])) OR (vein thrombosis[Title/Abstract]) OR (DVT[Title/Abstract]) OR (VTE[Title/Abstract])) OR (pulmonary embolism[Title/Abstract])) OR (lung embolism[Title/Abstract])) OR (PE[Title/Abstract])) OR (thromboembolism[Title/Abstract])) OR (embolism[Title/Abstract])) OR (blood clot[Title/Abstract]))
#5 ((thromboprophylaxis[Title/Abstract]) OR (prophylaxis[Title/Abstract])) OR (prevent*[Title/Abstract]))
#6 ((((heparin[MeSH Terms]) OR (heparin, low-molecular-weight[MeSH Terms])) OR (anticoagulants[MeSH Terms])) OR (warfarin[MeSH Terms])) OR (aspirin[MeSH Terms])) OR (vena cava filters[MeSH Terms])) OR (stockings, compression[MeSH Terms])) OR (intermittent pneumatic compression devices[MeSH Terms]))
#7 ((pentasaccharide[Title/Abstract]) OR (fondaparinux[Title/Abstract])) OR (LMWH[Title/Abstract]))
#8 (guideline[Publication Type]) OR (consensus development conference[Publication Type]))
#9 ((guidelines as topic[MeSH Terms]) OR (consensus[MeSH Terms])) OR (consensus development conferences as topic[MeSH Terms]))
#10 (((guideline[Title/Abstract]) OR (guidance[Title/Abstract])) OR (recommendation[Title/Abstract])) OR (consensus[Title/Abstract])) OR (best practice[Title/Abstract]))
#11 #1 OR #2
#12 #3 OR #4
#13 #5 OR #6 OR #7
#14 #8 OR #9 OR #10
#15 #11 AND #12 AND #13 AND #14


4. Others: any additional guidelines identified from references of eligible guidelines.

Search strategies
Terms related to “orthopedic trauma”, “VTE”, “prevention” and “guideline” will be adopted for the search in each database. Detailed search strategies are listed in online supplemental appendix 2. An example of a database search strategy is shown in box 1.

Determination of eligibility
Two reviewers (LH and J-YX) will independently screen and select the literature. First, they will determine whether the documents meet the inclusion criteria based on the titles and abstracts. After that, the reviewers will obtain the full texts of the documents, then read and filter out the eligible guidelines. Any disagreement between the two reviewers will be resolved through consensus or by the third reviewer (Z-KZ).

DATA EXTRACTION
We will extract the following information of CPGs: (1) title; (2) year of publication; (3) authors; (4) country of development; (5) objective of CPG; (6) target users; (7) method used to collect the evidence; (8) grading methods for the evidence; (9) recommendation formulation method; (10) guideline validation methods; (11) intended users and (12) the specific content of the recommendations given, including the method of thromboprophylaxis, the timing of initiation, dose and duration, and target patients. In addition, we will record each score of items in AGREE-II and AGREE-REX with their reasons.

QUALITY ASSESSMENT OF CPGS
We will assess the quality of CPGs by AGREE-II. The tool was released in 2009 and includes 23 items in 6 domains (scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability and editorial independence), with two additional assessments for the guideline’s overall quality and whether it is recommended to use.

The quality of recommendations is evaluated using AGREE-REX. The tool was released in 2019 and included nine items in three domains (clinical applicability, values and preferences, and implementability). Each item has two assessment questions, one for quality evaluation (required) and another for suitability for use (optional). Overall judgement for all recommendations in CPG has two additional assessments: (1) I would recommend these recommendations for use in the appropriate context (required) and (2) I would recommend these recommendations for use in my context (optional).

Both AGREE-II and AGREE-REX quality evaluation items adopt a Likert scale of one to seven scores. The standardised scores for each domain are calculated according to the user manual, ranging from 0% to 100%. The higher the score obtained, the better the quality of the guideline in the relevant field. Considering that the method for evaluating the overall quality of the guideline remains controversial, we will not use a cut-off value to rate the overall quality but directly present the reviewers’ subjective judgement results.

Five reviewers (LH, J-YX, JL, HL and NN) conducted quality appraisals after systematically learning how to use AGREE-II and AGREE-REX. Reviewers use the online platform MY AGREE PLUS to use AGREE-II independently.
and blindly (https://www.agreetrust.org/my-agree/), while the AGREE-REX assessment is performed offline.

DESCRIPTION AND COMPARISON OF THE RECOMMENDATIONS

We plan to compare the recommendations included in the CPG, which will be extracted independently by two reviewers (D-BL and GL-W). The recommendations will be expectedly classified according to risk assessment, screening strategies, mechanical prophylaxis, chemical prophylaxis and other interventions to evaluate their scopes and differences in different CPGs. Discrepancies will be highlighted when there are conflicts between some recommendations.

DATA ANALYSIS AND PRESENTATION

All the data will be saved with Excel (Microsoft 365, Microsoft, Redmond, Washington, USA) and analysed with SPSS statistical software (.26, IBM). For each domain of AGREE II and AGREE-REX, we will calculate the score by the following formula:

\[
\text{The scaled domain score} = \frac{\text{Obtained score} - \text{Minimum possible score}}{\text{Maximum possible score} - \text{Minimum possible score}}
\]

Scores for guidelines and recommendations will be described using the mean (SD) and median (IQR) (if needed). The intraclass correlation coefficient (ICC) will be used to evaluate the degree of agreement between reviewers. Based on Landis and Koch, an ICC value of 0.00–0.20 indicates slight agreement, 0.21–0.40 indicates fair agreement, 0.41–0.61 indicates moderate agreement, 0.61–0.80 indicates substantial agreement, 0.81–1.00 indicates almost perfect agreement. Differences in domain scores between CPGs will be compared using the Kruskal-Wallis H test. Significance level \(\alpha=0.05\) (two tailed).

Our study is expected to begin in November 2022 and complete in April 2023. We will explain any methodological changes in the study. The results are intended to be published in a peer-reviewed open journal.

DISCUSSION

Thromboprophylaxis in orthopaedic trauma patients is complicated due diverse risk factors. It is challenging to choose appropriate prevention methods for patients with coagulation abnormalities, lower limb injuries, etc. The use of anticoagulants may increase the risk of bleeding and wound complications in trauma patients, especially in the early postoperative period. Research in this field is scattered and controversial, and more work is needed to draw conclusions.

There is still no consensus on evaluating evidence and recommendations between different guidelines, which increases the uncertainty of clinical decision making. Even in the relatively large number of hip fracture patients studied, physicians still believe that there is a lack of adequate clinical guidelines. We hope to evaluate the relevant guidelines for VTE prevention in orthopaedic trauma and critically appraise the quality of the guidelines and recommendations. To the best of our knowledge, there is currently no systematic review on the quality of English and Chinese orthopaedic trauma thromboprophylaxis guidelines.

It is a long process that costs plenty of workforce and resources for planning, formulating and disseminating a CPG, especially for high-quality CPGs. Rigorous methodology and regular updates play essential roles in maintaining the quality of the guidelines and practical application. Identifying high-quality recommendations will help us to prescribe appropriate thromboprophylaxis in the trauma population. It will also help discover knowledge gaps and new points for further research. We plan to summarise the divergent recommendations in such guidelines, which will be the main focus of future thromboprophylaxis research.

Our research may still have shortcomings. First, although we will adopted a comprehensive search strategy, only openly published documents will be obtained, and some grey literature may miss during the process. Second, we will only include CPGs published in Chinese and English, which may lead to an underestimation of the overall number of guidelines. Third, to obtain as comprehensive information as possible, we will not limit the start time for the publication of the guidelines. Those recommendations from earlier CPGs may not be consistent with current evidence.

Author affiliations
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Acknowledgements The authors gratefully acknowledge the suggestions given by Mr. Lei Luo on the manuscript language editing.

Contributors Study design: LH, J-YX, NN and Z-KZ. Protocol drafting: LH, J-YX, JY, JL, HL and D-BL. Manuscript reviewing and editing: LH, G-LW, NN and Z-KZ. All the authors have read, discussed, and approved the final version of the manuscript. NN and Z-KZ contributed equally to the manuscript.

Funding This research is supported by West China Nursing Discipline Development Special Fund Project, Sichuan University (No. XKH202003).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES


33. Cosgrove L, Shaunhnessey AF, Shanefield T. When is a guideline not a guideline? The devil is in the details. BMJ Evid Based Med 2018;23:33–6.

# PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

<table>
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<th>Section/topic</th>
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<th>Checklist item</th>
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<td><strong>Authors</strong></td>
<td></td>
<td>Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author</td>
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<td><strong>Support</strong></td>
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<td>Provide name for the review funder and/or sponsor</td>
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<td>Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol</td>
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<td><strong>INTRODUCTION</strong></td>
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<td>Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)</td>
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<td>Eligibility criteria</td>
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<td>Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>Information sources</td>
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<td>Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage</td>
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<td>Search strategy</td>
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<td>Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated</td>
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<td>STUDY RECORDS</td>
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<td>Data management</td>
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<td>Describe the mechanism(s) that will be used to manage records and data throughout the review</td>
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<td>Selection process</td>
<td>11b</td>
<td>State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)</td>
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<td>Data collection process</td>
<td>11c</td>
<td>Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators</td>
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<td>Data items</td>
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<td>List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications</td>
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<td>Outcomes and prioritization</td>
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<td>List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale</td>
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<td>Risk of bias in individual studies</td>
<td>14</td>
<td>Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis</td>
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<td>Synthesis</td>
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<td>Describe criteria under which study data will be quantitatively synthesized</td>
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<td>If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$, Kendall’s tau)</td>
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<td>Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)</td>
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<td>If quantitative synthesis is not appropriate, describe the type of summary planned</td>
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<td>Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective</td>
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<td>#6 ((((((heparin&gt;[MeSH Terms]) OR (heparin, low-molecular-weight[MeSH Terms])) OR (anticoagulants[MeSH Terms])) OR (warfarin[MeSH Terms])) OR (aspirin[MeSH Terms])) OR (vena cava filters[MeSH Terms])) OR (stockings, compression[MeSH Terms])) OR (intermittent pneumatic compression devices[MeSH Terms]))</td>
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<td>#7 ((pentasaccharide&gt;Title/Abstract)) OR (fondaparinux&gt;Title/Abstract)) OR (LMWH&gt;Title/Abstract))</td>
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<td>#8 (guideline$Publication Type)) OR (consensus development conference$Publication Type))</td>
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<td>#10 (((guideline&gt;Title/Abstract)) OR (guidance&gt;Title/Abstract)) OR (recommendation&gt;Title/Abstract)) OR (consensus&gt;Title/Abstract)) OR (best practice&gt;Title/Abstract))</td>
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<td>#14 #8 OR #9 OR #10</td>
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<td>#15 #11 AND #12 AND #13 AND #14</td>
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1. exp orthopedics/
2. exp traumatology/
3. exp musculoskeletal injury/
4. fracture.ab,ti.
5. limb trauma.ab,ti.
6. extremity trauma.ab,ti.
7. musculoskeletal injury$ab,ti.
8. musculoskeletal trauma.ab,ti.
9. limb immobilization.ab,ti.
10. skeletal fixation.ab,ti.
11. (orthop$ adj3 trauma).ab,ti.
12. exp venous thromboembolism/
13. exp lung embolism/
14. venous thromboembolism.ab,ti.
15. venothromboembolism.ab,ti.
I6 venous thrombosis.ab,ti.
I7 vein thrombosis.ab,ti.
I8 DVT.ab,ti.
I9 VTE.ab,ti.
I20 pulmonary embolism.ab,ti.
I21 lung embolism.ab,ti.
I22 PE.ab,ti.
I23 thromboembolism.ab,ti.
I24 embolism.ab,ti.
I25 blood clot.ab,ti.
I26 exp heparin/ or exp low molecular weight heparin/
I27 exp anticoagulant agent/
I28 exp warfarin/
I29 exp acetylsalicylic acid/
I30 exp vena cava filter/
I31 exp compression stocking/
I32 exp intermittent pneumatic compression device/
I33 thromboprophylaxis.ab,ti.
I34 prophyla$.ab,ti.
I35 prevent$.ab,ti.
I36 pentasaccharide$.ab,ti.
I37 fondaparinux.ab,ti.
I38 LMWH.ab,ti.
I39 exp practice guideline/
I40 exp consensus/ or exp consensus development/
I41 guideline.ab,ti.
I42 guidance.ab,ti.
I43 recommendation.ab,ti.
I44 consensus.ab,ti.
I45 best practice.ab,ti.
I46 1 or 2 or 3 or 4 or 5 or 7 or 8 or 9 or 10 or 11
I47 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or
I48 24 or 25
I49 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or
I38
I49 39 or 40 or 41 or 42 or 43 or 44 or 45
I50 46 and 47 and 48 and 49

EBSCO- CINAHL
S1 MH Orthopedic Surgery OR MH Trauma OR MH (Wounds and Injuries)
S2 AB fracture OR AB limb trauma OR AB extremity trauma OR AB
musculoskeletal injur* OR AB musculoskeletal trauma OR AB limb immobili*
OR AB skeletal fixation OR AB orthop#dic trauma
S3 MH Venous Thromboembolism OR MH Pulmonary Embolism
S4 AB venous thromboembolism OR AB veno thromboembolism OR AB
venous thrombosis OR AB vein thrombosis OR AB (DVT OR VTE OR PE)
OR AB pulmonary embolism OR AB lung embolism OR AB
thromboembolism OR AB embolism OR AB blood clot
S5 MH Heparin, Low-Molecular-Weight OR MH Heparin OR MH
Anticoagulants OR MH Warfarin OR MH Aspirin OR MH Vena Cava Filters
OR MH Compression Garments
S6 AB thromboprophylaxis OR AB prophyla* OR AB prevent* OR AB
pentassacharide* OR AB fondaparinux OR AB compression stocking* OR AB
intermittent pneumatic compression
S7 MH Practice Guidelines OR MH Consensus
S8 AB guideline OR AB guidance OR AB consensus OR AB recommendation
OR AB best practice
<table>
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<tr>
<th>Term 1</th>
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<tr>
<td>S9 S1 OR S2</td>
<td>S10 S3 OR S4</td>
<td>S11 S5 OR S6</td>
<td>S12 S7 OR S8</td>
<td>S13 S9 AND S10 AND S11 AND S12</td>
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</table>

**Web of Science**

1. TS=(fracture OR "limb trauma" OR "extremity trauma" OR "musculoskeletal injur*" OR "musculoskeletal trauma" OR "limb immobili*" OR "skeletal fixation" OR "orthop* NEAR/3 trauma")
2. TS=("venous thromboembolism" OR venothromboembolism OR "venous thrombosis" OR "vein thrombosis" OR DVT OR VTE OR "pulmonary embolism" OR "lung embolism" OR PE OR thromboembolism OR embolism OR "blood clot")
3. TS=(thromboprophylaxis OR prophyla* OR prevent* OR heparin OR LMWH OR anticoagulants OR warfarin OR aspirin OR "vena cava filters" OR "compression stocking" OR "intermittent pneumatic compression devices" OR IPC OR pentassacharide* OR fondaparinux)
4. TS=(guideline OR guidance OR consensus OR recommendation OR "best practice")
5. #4 AND #3 AND #2 AND #1

**Cochrane Library (via Ovid)**

1. exp orthopedics/
2. exp traumatology/
3. exp "wounds and injuries"/
4. fracture.ab,ti.
5. limb trauma.ab,ti.
6. extremity trauma.ab,ti.
7. musculoskeletal injur$.ab,ti.
8. musculoskeletal trauma.ab,ti.
9. limb immobili$.ab,ti.
10. skeletal fixation.ab,ti.
11. (orthop$ adj3 trauma).ab,ti.
12. exp venous thromboembolism/
13. exp venous thrombosis/
14. exp pulmonary embolism/
15. venous thromboembolism.ab,ti.
16. venothromboembolism.ab,ti.
17. venous thrombosis.ab,ti.
18. vein thrombosis.ab,ti.
19. DVT.ab,ti.
20. VTE.ab,ti.
21. pulmonary embolism.ab,ti.
22. lung embolism.ab,ti.
23. PE.ab,ti.
24. thromboembolism.ab,ti.
25. embolism.ab,ti.
26. blood clot.ab,ti.
27. exp heparin/
28. exp heparin, low-molecular-weight/
29. exp anticoagulants/
30. exp warfarin/
31. exp aspirin/
32. exp vena cava filters/
33. exp stockings, compression/
34. exp intermittent pneumatic compression devices/
35. thromboprophylaxis.ab,ti.
36. prophyla$.ab,ti.
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<td>1 (( &quot;矫形外科学&quot;[加权:扩展] OR &quot;创伤和损伤&quot;[加权:扩展] OR &quot;创伤学&quot;[加权:扩展]) OR &quot;骨折&quot;[常用字段] OR &quot;创伤&quot;[常用字段] OR &quot;肌肉骨骼损伤&quot;[常用字段] OR &quot;肢体制动&quot;[常用字段] OR &quot;内固定&quot;[常用字段] OR &quot;外固定&quot;[常用字段]) AND ( 人类[特征词])</td>
<td>SU=‘骨折 + 骨科 + 创伤 + 肌肉骨骼损伤 + 内固定 + 外固定’ AND SU=‘静脉血栓 + 肺栓塞 + 肺梗死 + DVT + VTE + PE’ AND SU=‘肝素 + 低分子肝素 + 阿司匹林 + 华法林 + 抗凝药 + 血栓预防 + 血栓预防 + 机械预防 + 腔静脉滤器 + 间歇加压 + 弹力袜 + 间歇加压装置 + LMWH + 戊糖 + 磺达肝癸’</td>
<td>主题:(骨折 OR 骨科 OR 创伤 OR 肌肉骨骼损伤 OR 内固定 OR 外固定) and 主题:(静脉血栓 OR 肺栓塞 OR 肺梗死 OR DVT OR VTE OR PE) and 主题:(肝素 OR 低分子肝素 OR 阿司匹林 OR 华法林 OR 抗凝药 OR 血栓预防 OR 化学预防 OR 机械预防 OR 腔静脉滤器 OR 间歇加压 OR 弹力袜 OR LMWH OR 戊糖 OR 磺达肝癸)</td>
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Guideline repositories: thromboembolism OR deep vein thrombosis OR pulmonary embolism OR VTE OR 静脉血栓 OR 肺栓塞 OR 肺梗死