# ASH, ABHH, ACHO, Grupo CAHT, Grupo CLAHT, SAH, SBHH, SHU, SOCHIHEM, SOMETH, Sociedad Panameña de Hematología, SPH, SVH, 2021 Guidelines for Prevention of Venous Thromboembolism in Latin America

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# Abstract

**Background:** Venous thromboembolism (VTE) is a common disease in Latin American settings. Implementation of international guidelines in Latin American settings requires additional considerations.

**Objective:** To provide evidence-based guidelines about VTE prevention for Latin American patients, clinicians, and decision makers.

**Methods:** We used the GRADE ADOLOPMENT method to adapt recommendations from two American Society of Hematology (ASH) VTE guidelines (Prevention of VTE in Surgical Patients and Prophylaxis for Medical Patients). ASH and 12 local hematology societies formed a guideline panel composed of medical professionals from 10 countries in Latin America. Panelists prioritized 20 questions relevant to the Latin American context. A knowledge synthesis team updated evidence reviews of health effects conducted for the original ASH guidelines and summarized information about factors specific to the Latin American context, i.e., values and preferences, resources, accessibility, feasibility, and impact on health equity.

**Results:** The panel agreed on 21 recommendations. In comparison with the original guideline, 6 recommendations changed direction and 4 changed strength.

**Conclusions:** This guideline ADOLOPMENT project highlighted the importance of contextualization of recommendations in other settings, based on differences in values, resources, feasibility, and health equity impact.



# Keywords

venous thromboembolism prophylaxis; anticoagulation; hematology; practice guidelines; GRADE; DVT; PE

# Introduction

## Aim of these guidelines and specific objectives

The purpose of this guideline is to provide evidence-based recommendations for the Latin American context about the prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE) in surgical and medical patients, as well in long-distance travelers. The recommendations included in this document were adapted from the already-published American Society of Hematology (ASH) Clinical Practice Guidelines on Venous Thromboembolism (VTE).

The target audience includes patients, hematologists, general practitioners, internists, hospitalists, vascular interventionalists, intensivists, other clinicians, pharmacists, and decision makers.

Current evidence-based recommendations are informed by different evidence sources, such as randomized trials evaluating the health effects of interventions, but also by studies assessing patients' values and preferences, resource use, accessibility, feasibility, and impact on health equity.[1-3] Some of these factors are likely variable in different settings (e.g., costs). Although the ASH Clinical Guidelines on Venous Thromboembolism were developed for a global audience, recommendations were influenced by high-income-country perspectives. Therefore, implementation of some of these recommendations may not be straightforward in other contexts and may require additional considerations. Also, developing evidence-based recommendations is a lengthy and resource-intensive process. This is mainly due to the difficulty of identifying and synthetizing the relevant evidence necessary to develop trustworthy recommendations. Thus, the whole process cannot be easily replicated when local recommendations are needed, and adaptation is an efficient approach.

The model we used in this guideline, GRADE ADOLOPMENT,[4] allowed us to take advantage of the enormous effort made in the development of the original ASH VTE Guidelines but at the same time to generate recommendations specifically tailored for the Latin American setting.

## Description of the health problem

In the absence of prophylaxis, the risk of DVT and PE in hospitalized surgical and medical patients can be considerable.[5,6] Additionally, numerous studies conducted in Latin America showed that a significant proportion of patients do not receive appropriate prophylaxis. In one Brazilian cohort, 25% of high-risk inpatients and 45% of moderate-risk inpatients did not receive any prophylaxis, while in one Argentinian cohort, although most medical inpatients received some form of thromboprophylaxis, compliance with guidelines was poor and resulted in underuse in 25% of patients and overuse in 15%.[7] Typically, a significant proportion of high-risk patients are undertreated and low-risk patients are overtreated.[8]

An important socioeconomic gap exists in Latin America. Persons in lower socioeconomic strata are disadvantaged, as they have less access to medical health care services, medications, and education.[9-23] This is relevant to the use of thromboprophylaxis, because where public and private health care systems coexist, the adequacy of thromboprophylaxis exhibits an important breach: patients treated at public hospitals, which generally provide care for disadvantaged populations, receive appropriate thromboprophylaxis less often than patients treated at private hospitals.[24]

# Methods

The recommendations presented in this guideline were adapted to the context of Latin America following the GRADE ADOLOPMENT method[4] (GRADE: Grading of Recommendations, Assessment, Development and Evaluation) and according to the principles outlined by the Institute of Medicine[3] and the Guideline International Network.[2]

The detailed methods used in this effort are described elsewhere [CITATION TO BE ADDED].

## Organization, panel composition, planning, and coordination

This project was a collaboration of ASH and 12 hematology societies in Latin America: Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular (ABHH); Asociación Colombiana de Hematología y Oncología (ACHO); Grupo Cooperativo Argentino de Hemostasia y Trombosis (Grupo CAHT); Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis (Grupo CLAHT); Sociedad Argentina de Hematología (SAH); Sociedad Boliviana de Hematología y Hemoterapia (SBHH); Sociedad Chilena de Hematología (SOCHIHEM); Sociedad de Hematología del Uruguay (SHU); Sociedad Mexicana de Trombosis y Hemostasia (SOMETH); Sociedad Panameña de Hematología; Sociedad Peruana de Hematología (SPH); and Sociedad Venezolana de Hematología (SVH). Project coordination was provided by ASH. Project oversight was provided by the ASH Guideline Oversight Subcommittee, which reported to the ASH Committee on Quality, and by the executive boards of the Latin American partner societies. The partner societies nominated individuals to serve on the guideline panel.

The McMaster University GRADE Centre recommended methodologists to conduct systematic evidence reviews and facilitate the GRADE ADOLOPMENT process. ASH vetted all nominated individuals, including for conflicts of interest, and formed the panel to include 2 methodologists (I.N. and A.I.) and 11 hematologists from 10 countries: Argentina, Bolivia, Brazil, Chile, Colombia, Mexico, Panamá, Perú, Uruguay, and Venezuela. The partner societies were represented as follows: Dr. Suely Meireles Rezende represented ABHH, Dr. Guillermo León Basantes represented ACHO, Dr. Patricia Casais represented Grupo CAHT and Grupo CLAHT, Dr. Cecilia C. Colorio represented SHA, Dr. Mario L. Tejerina Valle represented SBHH, Dr. Jaime Pereira represented SOCHIHEM, Dr. Ricardo Aguilar represented the Sociedad Panameña de Hematología, Dr. Pedro P. García Lázaro represented SPH, Dr. María Cecilia Guillermo Esposito represented SHU, and Dr. Juan Carlos Serrano represented SVH. In October 2019, representation of Grupo CLAHT was transferred from Dr. Casais to Dr. Guillermo Esposito.

The McMaster University GRADE Centre formed a knowledge synthesis team that included individuals based in Chile and Argentina. The team determined methods; prepared meeting materials; updated the evidence reviews conducted for the source ASH guidelines; and searched for regional information about values and preferences, resources, accessibility, feasibility, and impact on health equity. Methodologists from the knowledge synthesis team (I.N. and A.I.) facilitated discussions and guided the panel through decision making.

The panel's work was done using web-based tools (www.surveymonkey.com and www.gradepro.org) and face-to-face and online meetings. These meetings were mostly conducted in Spanish.

The membership of the panel and the knowledge synthesis team is described in supplement 1.

## Guideline funding and management of conflicts of interest

The source guidelines and these adapted guidelines were wholly funded by ASH, a nonprofit medical specialty society that represents hematologists, and the ASH Foundation. ASH staff supported panel appointments and coordinated meetings but had no role in choosing the guideline questions or determining the recommendations. Staff and members of the partner Latin American societies who did not serve on the guideline panel also had no such role. Members of the guideline panel received travel reimbursement for attendance at in-person meetings but received no other payments. Through the McMaster GRADE Centre, some researchers who contributed to the systematic evidence reviews received salary or grant support. Other researchers participated to fulfill requirements of an academic degree or program.

Conflicts of interest of all participants were managed according to ASH policies based on recommendations of the Institute of Medicine (IOM 2009) and the Guidelines International Network.[25] On appointment, all panelists agreed to avoid direct conflicts of interest with companies that could be affected by the guidelines. Participants disclosed all financial and nonfinancial interests relevant to the guideline topic. ASH staff reviewed the disclosures and made judgments about conflicts. Greatest attention was given to direct financial conflicts with

for-profit companies that could be directly affected by the guidelines. At the time these recommendations were made, none of the panelists had such conflicts. In consideration of regional economic factors in Latin America, ASH adjusted the conflict-of-interest policy for this panel to allow direct payment from affected companies to panelists for travel to attend educational meetings only. Four panelists reported travel support to attend educational meetings from companies that could be affected by the guidelines. ASH and the partner societies agreed to manage such support through disclosure. None of the researchers who contributed to the systematic evidence reviews or who supported the guideline development process had any direct financial conflicts with for-profit companies that could be affected by the guidelines. Recusal was not implemented, because at the time the recommendations were made, the panel members did not have any direct financial conflicts with companies that could be affected by the guidelines. In August 2020, one panelist disclosed that during the guideline development process he received a direct payment from a company that could be affected by the guidelines and in march 2021, one panelist disclosed that during the guideline development process he received a direct payment from a company that could be affected by the guidelines. These conflicts might have triggered recusal at the time the recommendations were made; however, the activities and disclosures occurred after the panel had agreed on recommendations, and therefore, no panelists were recused. Members of the Guideline Oversight Subcommittee reviewed the guidelines in relation to these late disclosures and agreed that conflict was unlikely to have influenced any of the recommendations. Supplement 2 provides the complete disclosure-of-interest forms of all panel members. In part A of the forms, individuals disclosed direct financial interests for 2 years prior to appointment; in part B, indirect financial interests; and in part C, not mainly financial interests. Part D describes new interests disclosed by individuals after appointment. Part E summarizes ASH decisions about which interests were judged to be conflicts and how they were managed. Supplement 3 provides the complete disclosure-of-interest forms of researchers who contributed to these guidelines.

## Selecting clinical questions for adaptation

The guideline panel selected the following guidelines to be adapted from the original ASH VTE guidelines: prevention of venous thromboembolism in surgical hospitalized patients[26] and prophylaxis for hospitalized and nonhospitalized medical patients.[27] This decision was informed by priorities expressed by the Latin American partner societies. The panel also considered the development status and publication time frames of the source guidelines.

From all the clinical questions addressed by the two above-mentioned source guidelines, the guideline panel prioritized those most relevant for the Latin American setting. First, through an on-line survey, panelists rated the clinical questions using a 9-point scale ranging from not relevant to highly relevant. Then, clinical questions were ranked based on the median score from all the panelists. Finally, in an in-person meeting, panelists reviewed the scores and selected the final clinical questions based on the results of the survey, while also ensuring consistency and comprehensiveness of the guideline as a whole (Table 1).

Table 1. Clinical questions adapted

| |
|---|
| Prevention of venous thromboembolism in surgical patients |
| VTE prophylaxis vs. no prophylaxis in patients undergoing major general surgery |
| VTE prophylaxis vs. no prophylaxis in patients undergoing surgery following major trauma |
| VTE prophylaxis vs. no prophylaxis in patients undergoing laparoscopic cholecystectomy |
| VTE prophylaxis vs. no prophylaxis in patients undergoing transurethral resection of the prostate |
| VTE prophylaxis vs. no prophylaxis in patients undergoing radical prostatectomy |
| VTE pharmacological prophylaxis vs. no prophylaxis in patients undergoing major neurosurgical procedures |
| Mechanical vs. pharmacological prophylaxis |
| Short-term (7 to 10 days) vs extended prophylaxis (30 days) |
| Delayed initiation vs. early administration of pharmacological prophylaxis |
| Mechanical compression devices vs. compression stockings |
| Prevention of venous thromboembolism in medical patients |
| Unfractionated heparin vs. low-molecular-weight heparin in critically and acutely ill patients |
| Prophylaxis vs. no prophylaxis in acutely ill patients |
| Direct oral anticoagulants vs. no prophylaxis |
| Short period vs. extended prophylaxis |
| Prophylaxis vs. no prophylaxis in chronically ill patients |
| Mechanical prophylaxis vs. no prophylaxis in patients who cannot receive pharmacological prophylaxis |
| Compression stockings vs. mechanical compression devices |
| Prevention of vein thromboembolism in long-distance travelers |
| Prophylaxis with low-molecular-weight heparin vs. no prophylaxis |
| Prophylaxis with compression stockings vs. no prophylaxis |

VTE, venous thromboembolism

# Evidence reviews and inclusion of local data

The original ASH VTE guidelines included an Evidence-to-Decision (EtD) framework for each of the questions addressed.[1] The knowledge synthesis team updated the electronic search of

randomized trials and observational studies of the original guidelines and conducted a comprehensive search of regional evidence about patients' values and preferences, resource use, accessibility, feasibility, and impact on health equity (supplement 4). For each EtD framework, researchers for the knowledge synthesis team summarized the data used on the original guideline as well as all relevant regional information identified using the GRADEpro guideline development tool (McMaster University, Hamilton, Ontario, Canada, and Evidence Prime, Inc., Kraków, Poland). To estimate the absolute effect of the interventions, we calculated the risk difference by multiplying the pooled risk ratio and the baseline risk of each outcome. We used as baseline risk the median of the risks observed in control groups of the included trials. Additionally, when possible, the researchers used the baseline risk observed in large observational studies.

We assessed certainty of the body of evidence (also known as quality of the evidence or confidence in the estimated effects) following the GRADE approach.[28,29] We made judgments regarding risk of bias, precision, consistency, directness, and likelihood of publication bias and categorized the certainty in the evidence into four levels ranging from very low to high.

## Development of recommendations

During an in-person meeting that took place in Rio de Janeiro, Brazil, from April 23 to 26, 2018, the panel developed recommendations based on the evidence summarized in the EtD tables. The panel agreed on the direction and strength of recommendations through group discussion and deliberation. In rare instances, when consensus was not reached, voting took place. In such circumstances, the result of the voting was recorded on the respective EtD table. The direction of the recommendation was decided by simple majority, whereas an 80% majority was required to issue a strong recommendation.

Although in the case of the original VTE guidelines, panels defined the direction and strength of every recommendation and made judgments on every relevant domain included in the EtD, Latin American panelists were not aware of those decisions and judgments.

## Document review

Draft recommendations were reviewed by all members of the panel, revised, and then made available online from March 7 through April 12, 2019, for external review by stakeholders, including members of the Latin American partner societies, allied organizations, medical professionals, patients, and the general public. Notifications were made via email and social media and at in-person meetings. There were 385 views of the draft recommendations, 78% from Latin America. Five individuals submitted comments. The document was revised to address pertinent comments, but no changes were made to recommendations. On XXXX the ASH Guideline Oversight Subcommittee and the ASH Committee on Quality agreed that the defined guideline development process was followed, and on XXXX the officers of the ASH Executive Committee approved submission of the guidelines for publication under the imprimatur of ASH. Starting on XXXX and through XXXX, the partner societies approved the guidelines. The guidelines were then subjected to peer review by *Blood Advances*.

## How to use these guidelines

The recommendations are labeled as “strong” or “conditional” according to the GRADE approach. The words “the ASH Latin American guideline panel recommends” are used for strong recommendations and “the ASH Latin American guideline panel suggests” for conditional recommendations. Table 2 provides GRADE’s interpretation of strong and conditional recommendations by patients, clinicians, health care policy makers, and researchers.

These guidelines are primarily intended to help clinicians make decisions about diagnostic and treatment alternatives. Other purposes are to inform policy, education, and advocacy and to state future research needs. They may also be used by patients. These guidelines are not intended to serve or be construed as a standard of care. Clinicians must make decisions on the basis of the clinical presentation of each individual patient, ideally through a shared process that considers the patient's values and preferences with respect to the anticipated outcomes of the chosen option. Decisions may be constrained by the realities of a specific clinical setting and local resources, including but not limited to institutional policies, time limitations, and availability of treatments. These guidelines may not include all appropriate methods of care for the clinical scenarios described. As science advances and new evidence becomes available, recommendations may become outdated. Following these guidelines cannot guarantee successful outcomes. ASH and the partner societies do not warrant or guarantee any products described in these guidelines.

Statements about the underlying values and preferences as well as qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines. The use of these guidelines is also facilitated by the links to the EtD frameworks and interactive summary-of-findings tables in each section.

# Search results

In our comprehensive search for the Latin America setting, we did not identify any additional randomized trials providing additional evidence on the efficacy or safety of the interventions of interest. Neither did we find studies reporting on patients´ values and preferences. We did find information about the cost of the interventions in different countries of the region as well evidence of accessibility and potential impact on health equity. This information is summarized for each question in the adapted Evidence-to-Decision tables.

# Recommendations

## Interpretation of strong and conditional recommendations

The strength of a recommendation is expressed as either strong ("the guideline panel recommends...") or conditional ("the guideline panel suggests…") and has the interpretation described in Table 2.

Table 2. Interpretation of strong and conditional recommendations

| Implications for: | Strong recommendation | Conditional recommendation |
|---|---|---|
| **Patients** | Most individuals in this situation would want the recommended course of action, and only a small proportion would not. | The majority of individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences. |
| **Clinicians** | Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences. | Different choices will be appropriate for individual patients, and clinicians must help each patient arrive at a management decision consistent with the patient's values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences. |
| **Policy makers** | The recommendation can be adopted as policy in most situations. Adherence to | Policy-making will require substantial debate and involvement of various |

| | | |
|---|---|---|
| | this recommendation according to the guideline could be used as a quality criterion or performance indicator. | stakeholders. Performance measures should assess whether decision-making is appropriate. |
| **Researchers** | The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations. | The recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help to identify possible research gaps. |

# Prevention of venous thromboembolism in surgical patients

*In patients undergoing major general surgery, should we use thromboprophylaxis?*

**Recommendation 1**

For patients undergoing major general surgery, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on low certainty in the evidence about effects ⊕⊕◯◯).

**Remarks:**

The panel considered that for patients undergoing major general surgery at average risk of bleeding, pharmacological and mechanical prophylaxis are reasonable alternatives. However, pharmacological prophylaxis is probably easier to implement.

Recommendations 7 to 10 address the alternatives, period of administration, and time of initiation.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/QP-9jk-Ih5Y

## Justification

This recommendation did not change its direction or its strength. The panel considered that the recommendation is feasible to implement in the region, given the general availability of pharmacological prophylaxis, especially unfractionated heparin.

## Conclusion

Predicting the individual risk of VTE and bleeding remains a challenge. The most extensively studied quantitative risk assessment model for nonorthopedic surgical patients is the Caprini score.[30] However, no trial has evaluated to what extent the use of a prognostic model in guiding decisions about thromboprophylaxis may lead to an improvement of patients´ outcomes. Although prognostic models are a useful guide, they do not replace the careful consideration of the clinical circumstances. Given the relatively high risk of VTE in patients undergoing general major surgery, the use of pharmacological prophylaxis seems to be the better alternative.

*In patients undergoing surgery following major trauma, should we use thromboprophylaxis?*

**Recommendation 2**

In patients undergoing surgery following major trauma, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on very low certainty in the evidence about effects ⊕◯◯◯).

**Remarks:**

In patients who are actively bleeding or at high risk of bleeding, mechanical prophylaxis may be preferable over pharmacological prophylaxis.

It is important to consider that patients who remain hospitalized after surgery may have an increased risk of thrombosis due to the lack of ambulation (see recommendations about thromboprophylaxis in acutely and critically ill patients).

> Recommendations 7 to 10 address the alternatives, period of administration, and time of initiation.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/s5NYjofhp3Q

## Justification

This recommendation changed its direction. The original guideline panel made a conditional recommendation in favor of prophylaxis in individuals who are at low to moderate risk for bleeding and against prophylaxis in patients at high risk of bleeding. The Latin American panel, using indirect evidence, considered that mechanical prophylaxis could be an appropriate alternative for individuals who are actively bleeding or at high risk of bleeding. Thus, the panel suggested using pharmacological prophylaxis when the risk of bleeding is considered low or moderate and mechanical prophylaxis when this risk is high. The panel acknowledged that access to mechanical prophylaxis, especially compression devices, may be limited within the region. Therefore, barriers to the implementation of this recommendation may exist in some settings.

## Conclusion

Patients who undergo surgery after major trauma are a heterogeneous population. However, the panel considered that the majority of patients will have an increased risk of thrombosis due to prolonged bed rest and immobilization. Therefore, thromboprophylaxis should be considered in all the patients with major trauma. Patients with moderate or low risk of bleeding may be managed with pharmacological prophylaxis, which is generally available and accessible within the region. However, for patients at high risk of bleeding, mechanical prophylaxis may be a better alternative. It is important to note that bleeding risk may change over time; thus, different

modalities of thromboprophylaxis may be needed. Additionally, patients with major trauma may experience medical complications which may extend hospitalization. In such situations, the recommendations for acutely and critically ill medical patients may apply.

*In patients undergoing laparoscopic cholecystectomy, should we use thromboprophylaxis?*

**Recommendation 3.**

In patients undergoing laparoscopic cholecystectomy, the ASH Latin American Guideline Panel suggests against thromboprophylaxis (conditional recommendation based on very low certainty in the evidence about effects ⨁◯◯◯).

**Remarks:**

Patients who are not admitted to hospital or stay just one or two nights likely do not benefit from thromboprophylaxis. However, patients who remain hospitalized after the surgery may benefit from prophylaxis, especially if they are at high risk of VTE.

For such patients, recommendations 7 to 10 address the alternatives, period of administration, and time of initiation.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at

https://guidelines.ash.gradepro.org/staging/profiles/KhVQXtb41GE

## Justification

This recommendation did not change its direction or its strength. The implementation of the recommendation was considered feasible across the different settings of the region.

## Conclusion

In many settings in the region, elective laparoscopic cholecystectomy is conducted without hospital admission or with a very short stay. In such circumstances, the VTE risk is very low and probably does not justify the inconvenience or the risk of bleeding associated with pharmacological thromboprophylaxis. Patients with acute cholecystitis may stay longer in the hospital, but in general, they are able to ambulate relatively soon, and the risk of VTE probably remains low. However, in cases of complicated cholecystitis, patients who experience medical complications, patients with previous VTE, and patients who are diagnosed with gallbladder cancer during the hospitalization may have a higher risk of VTE. In these situations, thromboprophylaxis may be needed.

*In patients undergoing transurethral resection of the prostate or radical prostatectomy, should we use thromboprophylaxis?*

**Recommendations 4 and 5**

In patients undergoing transurethral resection of the prostate or radical prostatectomy, the ASH Latin American Guideline Panel suggests against thromboprophylaxis (both conditional recommendations based on very low certainty in the evidence about effects ⨁◯◯◯).

**Remarks:**

The risk of bleeding after a transurethral resection or radical prostatectomy is likely higher than after major general surgery. Therefore, for a patient at an average risk of VTE, the undesirable consequences of pharmacological thromboprophylaxis likely outweigh its potential benefits.

If VTE risk remains as an important concern, mechanical prophylaxis may be an appropriate alternative.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD frameworks are shown online at https://guidelines.ash.gradepro.org/staging/profiles/i-aKrVRFPVE and https://guidelines.ash.gradepro.org/staging/profiles/SSop4y0g3FM

## Justification

These recommendations did not change their direction or their strength. The implementation of the recommendations was considered feasible across the different settings of the region.

## Conclusion

Patients who undergo transurethral resection or radical prostatectomy may have a higher risk of bleeding than average surgical patients. On the other hand, in individuals with benign prostatic hyperplasia without risk factors for VTE, the risk of thrombosis may be small. Therefore, thromboprophylaxis may not be needed. However, patient with prostate cancer or those with previous VTE events may benefit from prophylaxis. If the bleeding risk is an important concern, mechanical prophylaxis may be a good alternative for such patients.

*In patients undergoing major neurosurgical procedures, should we use thromboprophylaxis?*

**Recommendation 6**

In patients undergoing major neurosurgical procedures, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on very low certainty in the evidence about effects ⨁◯◯◯).

**Remarks:**

Most patients undergoing major neurosurgical procedures are likely at high risk of VTE and simultaneously at high risk of bleeding. Thus, decisions regarding the use of prophylaxis and its modality should be done on an individual basis.

If the risk of bleeding is considered high, mechanical prophylaxis may be a better initial alternative. It is important to consider that bleeding risk will change over time; thus, the decision regarding the use of pharmacological or mechanical prophylaxis should be evaluated periodically.

## Summary of the evidence

No additional evidence the efficacy or safety of the intervention was identified. The EtD framework is shown online at

https://guidelines.ash.gradepro.org/staging/profiles/eT7F_MIH5NY

## Justification

This recommendation changed direction. The original guideline panel made a conditional recommendation against prophylaxis. The Latin American panel, using indirect evidence, considered that mechanical prophylaxis could be an appropriate alternative for patients at high risk of bleeding, especially early after surgery. Thus, the panel suggested using prophylaxis and deciding on the specific modality according to the risk of bleeding. The panel acknowledged that access to mechanical prophylaxis, especially compression devices, may be limited within the region. Therefore, barriers to the implementation of this recommendation may exist in some settings.

## Conclusion

Typically, patients who undergo major neurosurgical procedures have simultaneously a high risk of VTE and a high risk of bleeding. Additionally, these risks may change over time during hospitalization, according to mobility conditions and complications or reinterventions. Therefore, the optimal strategy for each individual patient may be different and need to be decided taking into consideration the individual risk factors.

The panel considered that when the risk of bleeding is high, for example, on the initial days after surgery, mechanical prophylaxis may be a better alternative. However, once the risk of bleeding decreases, pharmacological prophylaxis, which is generally more accessible, may be used.

*In surgical patients in whom thromboprophylaxis is preferred, should we use mechanical or pharmacological thromboprophylaxis?*

**Recommendation 7**

In surgical patients in whom thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests either mechanical or pharmacological prophylaxis (conditional recommendation based on low certainty in the evidence about effects ⨁⨁◯◯).

**Remarks:**

This recommendation applies to the populations discussed in recommendations 1 to 6.

Pharmacological prophylaxis might be a better alternative for patients at high risk of VTE. However, patients with an increased risk of bleeding may be better off with mechanical prophylaxis. The individual decision should be made considering the specific clinical circumstances (i.e., risk of VTE and bleeding), the patient´s values and preferences, and the availability of the options. Also, given that the risks of VTE and bleeding may change over time, the decision should be reassessed frequently.

## Summary of the evidence

## Justification

This recommendation did not change its direction or its strength. The panel considered that within the region, pharmacological prophylaxis, especially unfractionated heparin, is more generally available and accessible. Thus, this was the preferred option for the majority of patients. However, in patients with high risk of bleeding, efforts should be made to provide mechanical prophylaxis.

## Conclusion

For surgical patients at average risk of bleeding (e.g., major general surgery), pharmacological prophylaxis may be the preferred alternative, given that is typically available and accessible within the region. However, in patients with an increased risk of bleeding (e.g., transurethral resection of the prostate) or in patients in whom bleeding may result in a very unfavorable outcome (e.g., major neurosurgical procedures), mechanical prophylaxis seems to be a better alternative.

*In surgical patients in whom mechanical thromboprophylaxis is preferred, should we use compression devices or compression stockings?*

**Recommendation 8**

For surgical patients in whom mechanical thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests mechanical compression devices over compression stockings (conditional recommendation based on low certainty in the evidence about effects ⊕⊕◯◯).

**Remarks:**

> This recommendation applies to the populations discussed in recommendations 1 to 6.
>
> Mechanical devices may not be available in all settings in Latin America. However, since the difference between mechanical devices and compression stockings is likely small, compression stockings are a reasonable alternative for patients for whom mechanical prophylaxis is preferred and where there is limited availability of devices.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/lXRaHfHLe6A

## Justification

This recommendation did not change its direction or its strength. The panel considered that mechanical compression devices may not be available in some settings within the region. In this situation, compression stockings are a reasonable alternative.

## Conclusion

As discussed in recommendation 7, mechanical prophylaxis may be preferred in individuals at high risk of bleeding in whom pharmacological prophylaxis may be considered risky. The decision regarding the use of compression devices or compression stockings, when both are available, may be guided by the risk of VTE. In patients with risk factors for VTE or previous VTE events, compression devices may have a larger benefit. Nevertheless, for the majority of patients at average risk of VTE, the difference between compression devices and stockings is likely small, and therefore, both are reasonable alternatives.

*In surgical patients in whom pharmacological thromboprophylaxis is preferred, should we use short or extended prophylaxis?*

**Recommendation 9**

In surgical patients in whom pharmacological thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests short prophylaxis (7 to 10 days) over extended prophylaxis (30 days) (conditional recommendation based on very low certainty in the evidence about effects ⨁◯◯◯).

**Remarks:**

This recommendation applies to the populations discussed in recommendations 1 to 6.

For patients at average risk of VTE, a short prophylaxis likely will be enough. However, patients with an increased risk of VTE, such as patients undergoing cancer or orthopedic surgery, may benefit from extended prophylaxis. Furthermore, patients requiring longer immobilization might need extended thromboprophylaxis as well.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/epECz42IU9I

## Justification

This recommendation changed its direction. The original guideline panel made a recommendation in favor of extended prophylaxis, basing their judgment mainly on individuals at high risk of VTE, such as patients undergoing to cancer surgery or orthopedic surgery. The Latin American panel considered that although extended prophylaxis may be an appropriate alternative for such patients, the VTE risk is likely lower in typical patients undergoing major surgery. Also, extended prophylaxis is an expensive intervention. Within the region, drugs and

devices used outside the hospital are not generally reimbursed by health insurances. Thus, extended prophylaxis may be associated with an important out-of-pocket expenditure and health inequities.

## Conclusion

As discussed in recommendation 7, pharmacological prophylaxis may be preferred in individuals at average or low risk of bleeding. As with the previous recommendation, the decision regarding the use of a short or extended scheme may be guided by the risk of VTE. In patients with risk factors for VTE or previous VTE events, extended schemes may be appropriate; also, in patients in whom the surgery will be associated with a long period of immobilization, such immobilization or the surgery itself may lead to a significant increase of the risk of VTE (e.g., orthopedic surgery). However, most patients undergoing general surgery have no significant VTE risk factors. In those patients, extended prophylaxis may increase the cost and the burden of treatment unnecessarily.

*In surgical patients in whom pharmacological thromboprophylaxis is preferred, should we use delayed or early prophylaxis?*

**Recommendation 10**

In surgical patients in whom pharmacological thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests delayed prophylaxis (12 hours after surgery) over early administration (before surgery or within 12 hours post-surgery) (conditional recommendation based on very low certainty in the evidence about effects ⊕◯◯◯).

**Remarks:**

The time of initiation should be assessed on an individual basis, with the surgical team considering the risk of VTE and risk of bleeding.

> Patients who need hospitalization for a significant period of time before surgery might benefit from prophylaxis (see recommendations about thromboprophylaxis in acutely and critically ill patients).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/DZQrUWF2RtU

## Justification

This recommendation changed its direction. The original guideline panel made a recommendation in favor of either alternative: delayed prophylaxis and early administration. The Latin American panel judged that for the majority of patients undergoing surgery, the risk of VTE before the procedure was very small. Also, the use of early prophylaxis might slightly increase the risk of bleeding during surgery, it adds cost, and it may be impractical for surgical teams.

## Conclusion

The decision whether to use pharmacological prophylaxis before or after surgery will largely depend on the clinical circumstances before the procedure. For bedridden patients or those who have an increased risk of VTE (e.g., previous events or risk factors), the use of prophylaxis before surgery may be justified. In contrast, for patients undergoing elective procedures, those who are able to walk, or, in general, patients at low risk of VTE, the use of prophylaxis before surgery probably has little or no impact.

Table 3 summarizes the recommendations for the prevention of VTE in surgical patients.

618 Table 3. Summary of recommendations for prevention of VTE in surgical patients.

<table>
<tr><th>Population</th><th>Preferred alternative</th><th>Proposed treatment</th><th>Specific strategy</th></tr>
<tr><td>Patients undergoing major general surgery</td><td rowspan="3">Use thromboprophylaxis (recommendations 1, 2, and 6)</td><td rowspan="3">High risk of bleeding: Mechanical prophylaxis<br><br>Average risk of bleeding: Pharmacological prophylaxis</td><td rowspan="3">If pharmacological prophylaxis is preferred: A short scheme (7–10 days) initiated 12 hours after surgery (recommendations 9 and 10)</td></tr>
<tr><td>Patients undergoing surgery following major trauma</td></tr>
<tr><td>Patients undergoing major neurosurgical procedures</td></tr>
<tr><td>Patients undergoing laparoscopic cholecystectomy</td><td rowspan="3">No thromboprophylaxis (recommendations 3–5)</td><td rowspan="3">High risk of VTE: Mechanical prophylaxis<br><br>Average risk of VTE: No prophylaxis</td><td rowspan="3">If mechanical prophylaxis Is preferred: mechanical compression devices when available. Compression stockings may be a reasonable alternative if there are barriers to access compression devices (recommendation 8)</td></tr>
<tr><td>Patients undergoing transurethral resection of the prostate</td></tr>
<tr><td>Patients undergoing radical prostatectomy</td></tr>
</table>

619 VTE, venous thromboembolism.

620

621 # Prevention of venous thromboembolism in medical patients

622 # and long-distance travelers.

623 *In medically ill patients, should we use heparins as thromboprophylaxis?*

624 **Recommendation 11**

625 In acutely medically ill patients, the ASH Latin American Guideline Panel suggests against

626 routinely use of heparins (unfractionated heparin or low-molecular-weight heparin)

(conditional recommendation based on low certainty in the evidence about effects ⨁⨁◯◯).

**Remarks:**

In the majority of patients admitted to hospital for noncritical medical conditions, the risk of VTE is likely small, especially if they are able to walk or perform physical therapy. In those cases, the benefit of prophylaxis with heparins may be very small. In contrast, pharmacological prophylaxis may be appropriate for individuals at increased risk of VTE, such as bedridden patients or those with previous VTE events or major risk factors.

The panel emphasizes that the risk of VTE and bleeding may change over time. Thus, a frequent assessment of the potential benefits and harms of thromboprophylaxis is needed.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/0AITXwIQxrE

## Justification

This recommendation changed its direction. The original panel made a recommendation in favor of prophylaxis with heparins, while the Latin American panel made a recommendation against. This change of direction had to do with the baseline risk of VTE in average medical patients. The Latin American guideline panel considered that the majority of patients admitted to hospital for noncritical medical conditions have a low risk of VTE, especially if they retain their mobility.

## Conclusion

Predicting the individual risk of VTE and bleeding remains a challenge. The two most extensively studied quantitative risk assessment models are the empirically derived Padua score (link) and

the database-derived IMPROVE score (link). However, no trial has evaluated to what extent the use of a prognostic model in guiding decisions about thromboprophylaxis may lead to an improvement of patients´ outcomes.

For the majority of patients admitted to hospital with noncritical conditions, especially if they are able to walk or perform physical therapy, the use of heparins probably adds cost and inconvenience without a significant impact on VTE prevention. Therefore, in such patients, nonpharmacological interventions, such as active mobilization and encouragement to walk, may be the best alternative. In contrast, in individuals at high risk of VTE, such as bedridden patients and individuals with risk factors such as cancer or previous VTE events, the use of heparins may be justified.

*In critically ill patients, should we use heparins as thromboprophylaxis?*

**Recommendation 12**

In acutely critically ill patients, the ASH Latin American Guideline Panel suggests the use of heparins (unfractionated heparin or low-molecular-weight heparin) over no use (conditional recommendation based on moderate certainty in the evidence about effects ⊕⊕⊕◯).

**Remarks:**

It is important to consider that the risk of VTE or risk of bleeding may change during a hospital stay. Thus, a frequent assessment is needed.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at

https://guidelines.ash.gradepro.org/staging/profiles/IjOB2yeS6mU

## Justification

This recommendation changed its strength. The original panel made a strong recommendation in favor of prophylaxis with heparins, while the Latin American panel made a conditional recommendation. The panel considered that for the majority of critically ill patients, the benefits of thromboprophylaxis (moderate reduction of VTE risk) probably outweigh the potential harms (small increase of bleeding). However, a proportion of individuals, for example, neurosurgical or trauma patients, may not obtain a net benefit from thromboprophylaxis, given their increased risk of bleeding. Thus, a conditional recommendation was considered more appropriate, emphasizing a careful assessment of each individual's clinical circumstances.

## Conclusion

For most critical patients, the benefits of using of heparins probably outweighs its potential harms, cost, and inconvenience. Therefore, in general, critically ill patients should receive prophylactic-dose heparins as part of their standard management. However, not all critically ill patients are equal. Some may have a bleeding risk several times higher than that of average patients. For example, neurosurgical and trauma patients, especially early in the evolution of the disease, are at high risk of bleeding and may not benefit from the routine use of heparins. Once the bleeding risk decreases, however, they should receive prophylactic heparins, as the increased risk of VTE remains high while patients are in a critical condition.

*In critically and medically ill patients who require pharmacologic prophylaxis, should we use LMWH or UFH?*

**Recommendation 13**

In acutely critically and medically ill patients who require pharmacologic prophylaxis, the ASH Latin American Guideline Panel suggests either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) (conditional recommendation based on low certainty in the evidence about effects ⊕⊕◯◯).

**Remarks:**

The difference between LMWH and UFH in patient-important outcomes (thrombotic events and bleeding) is very small in magnitude. Therefore, UFH may be a reasonable alternative in settings where the price of LMWH is a barrier. In situations where access to LMWH is not a concern, this option probably represents a more convenient alternative for patients and providers.

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/10btxfG5oBU

## Justification

This recommendation changed its direction. The original panel made a conditional recommendation in favor of LMWH, while the Latin American panel made a conditional recommendation in favor of either. The absolute differences between the effects of LMWH and UFH in patient-important outcomes (thrombotic events and bleeding) are very small, i.e., less than 1%. Additionally, LMWH is significantly more expensive in Latin America, and there are important access barriers within the region. Therefore, both options are reasonable management alternatives, and the final decision likely will depend on contextual factors such as affordability and availability.

## Conclusion

In terms of prevention of VTE events, both LMWH and UFH have very similar effects. The same is true for their bleeding risk. However, in settings where the price of LMWH and its availability

are not concerns, this option probably represents a more convenient alternative for patients and providers, since it requires only a single subcutaneous injection every day.

*In critically and medically ill patients who cannot receive pharmacological prophylaxis, should we use mechanical prophylaxis?*

> **Recommendation 14**
>
> In acutely critically and medically ill patients who cannot receive pharmacological prophylaxis, the ASH Latin American Guideline Panel suggests using mechanical prophylaxis over no prophylaxis (conditional recommendation based on moderate certainty in the evidence about effects ⊕⊕⊕◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/ZDxQZbsAxl8

## Justification

This recommendation did not change its direction or its strength. The panel considered that mechanical prophylaxis, especially compression stockings, is generally available within the region.

## Conclusion

From a clinical standpoint, the most frequent reason to not be able to receive pharmacologic prophylaxis (heparins) is an increased risk of bleeding. In those scenarios, mechanical prophylaxis offers a small reduction of the VTE risk with no increase in the risk of bleeding. However, it is important to acknowledge that the risk of bleeding changes during the evolution

of the disease. The risk typically decreases during hospitalization once the underlying factors or conditions are stabilized or resolved. The same is true with the risk of VTE. Once patients improve their condition and they can ambulate, the baseline risk of VTE sharply decreases. Therefore, clinicians should periodically reassess the decision regarding the use of mechanical prophylaxis and decide whether to switch to pharmacological prophylaxis or discontinue prophylaxis according to the clinical circumstances and patients´ preferences.

*In critically and medically ill patients who need mechanical prophylaxis, should we use pneumatic compression devices or graduated compression stockings?*

**Recommendation 15**

In acutely critically and medically ill patients who need mechanical prophylaxis, the ASH Latin American Guideline Panel suggests using either pneumatic compression devices or graduated compression stockings (conditional recommendation based on very low certainty in the evidence about effects ⊕◯◯◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/lp0Bzf3bd6g

## Justification

This recommendation did not change its direction or its strength. The panel considered that, in general, compression stockings are more generally available than compression devices within the region.

## Conclusion

The absolute differences in the effects of compression devices and stockings in patient-important outcomes (thrombotic events and bleeding) are likely small. Thus, the final decision should consider contextual factors such as the cost of the options and their availability. Also, some patients may prefer one option over the other, since compression devices use intermittent pression but are typically noisy and may interrupt sleep. On the other hand, stockings apply a continuous pressure that may be uncomfortable for some patients.

*In critically and medically ill patients who require pharmacological thromboprophylaxis, should we use a short period of prophylaxis or an extended period?*

**Recommendation 16**

In acutely critically and medically ill patients who require pharmacological thromboprophylaxis, the ASH Latin American Guideline Panel suggests using a short period of prophylaxis (inpatients) over an extended period (inpatients and extended-duration outpatients) (conditional recommendation based on moderate certainty in the evidence about effects ⊕⊕⊕◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/2KPmq0bxrpc

## Justification

This recommendation changed its strength. The original panel made a strong recommendation in favor of a short prophylaxis, while the Latin American panel made a conditional recommendation in the same direction. The panel considered that there was some uncertainty

regarding the baseline risk of VTE. While for most patient the baseline risk of VTE is small, and thus, an extended prophylaxis will not result in a significant benefit, there are some patients with a higher baseline risk of VTE who maintain this risk after discharge, especially if they need a long rehabilitation and are not able to ambulate. Those patients may benefit from a longer prophylaxis.

## Conclusion

For the majority of patients, the risk of VTE during the hospitalization is small and decreases sharply after discharge. In those circumstances, maintaining extended pharmacological prophylaxis likely will result in more harms (i.e., bleeding) than benefits. However, there are some critically ill patients that are discharged after a prolonged hospitalization and need a longer period of rehabilitation in order to ambulate and perform basic daily life activities (such being able to eat or dress by themselves). Those patients are at higher risk of VTE and may benefit from an extended pharmacological prophylaxis. It is important, however, to discontinue it once immobility resolves (see recommendation 16).

*In chronically ill patients, should we use thromboprophylaxis?*

> **Recommendation 17**
>
> In chronically ill patients, the ASH Latin American Guideline Panel suggests against using thromboprophylaxis (conditional recommendation based on very low certainty in the evidence about effects ⨁◯◯◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/Ib3kIhxhbJg

## Justification

This recommendation did not change its direction or its strength.

## Conclusion

In chronically ill medical patients, including nursing home patients, the harms of thromboprophylaxis (i.e., bleeding) likely outweighs its benefits. Also, it adds cost and inconvenience for patients and caregivers. In chronically ill patients, early mobilization, rehabilitation, and physical therapy may be used along other nonpharmacological strategies to decrease VTE risk.

*In acutely ill patients who require pharmacological thromboprophylaxis, should we use LMWH or DOACs?*

> **Recommendation 18 and 19**
>
> In acutely ill patients who require pharmacological thromboprophylaxis, the ASH Latin American Guideline Panel suggests using LMWH over direct oral anticoagulants (DOACs) (conditional recommendation based on moderate certainty in the evidence about effects ⊕⊕⊕◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/ilxhQm9kubk and https://guidelines.ash.gradepro.org/staging/profiles/eFavpAWyGmA

## Justification

This recommendation changed its strength. The original panel made a strong recommendation in favor of LMWH (over DOACs), while the Latin American panel made a conditional recommendation in the same direction. The evidence from 3 clinical trials showed that, compared with a short period of LMWH, both short and extended courses of DOAC increase bleeding without a significant impact on VTE reduction. This led the original panel to formulate a strong recommendation against DOACs. However, the absolute increase in bleeding is small: between 0.2 and 1.2% (see the summary-of-findings table). The Latin American panel considered that some patients may be willing to trade the small increment in bleeding for the convenience of an oral medication. Therefore, the panel issued a conditional recommendation.

## Conclusion

In terms of preventing VTE events, in medical patients DOAC and LMWH seem to be equivalent from a clinical perspective. This contrasts with what has been observed in surgical patients, where the use of DOACs offers a small additional protection in comparison to LMWH. What we did find in the meta-analysis was an increase of the risk of bleeding with DOAC. This was observed with a short course and with an extended prophylaxis with DOAC. Therefore, the current evidence suggests that in medical patients, in contrast with surgical patients, DOACs increase bleeding with no additional benefit on VTE prevention. However, the difference is of small absolute magnitude. In settings where DOACs are available, some patients may place more value on the convenience of an oral medication than the small increase of the risk of bleeding, especially if the baseline risk of bleeding is small.

*In long-distance travelers, should we use thromboprophylaxis?*

> **Recommendation 20 and 21**
>
> In long-distance travelers (>4 hours) with low risk of VTE, the ASH Latin American Guideline Panel suggests against thromboprophylaxis. However, for long-distance travelers with high risk of VTE, the ASH Latin American Guideline Panel suggests thromboprophylaxis with compression stockings or LMWH (both conditional recommendations based on very low certainty in the evidence about effects ⨁◯◯◯).

## Summary of the evidence

No additional evidence on the efficacy or safety of the intervention was identified. The EtD framework is shown online at https://guidelines.ash.gradepro.org/staging/profiles/GVAxJF3R_qQ, https://guidelines.ash.gradepro.org/staging/profiles/DDOVtb6rIBk, and https://guidelines.ash.gradepro.org/staging/profiles/idMG2TWPCFw

## Justification

This recommendation did not change its direction or its strength.

## Conclusion

The large majority of long-distance travelers have a minimal risk of VTE. Hence, harms, cost, and inconvenience likely outweigh any potential benefit.

In contrast, patients with an increased risk of VTE, for example, individuals with a recent surgery or history of VTE, postpartum women, and individuals with an active malignancy, may experience a thrombotic event as consequence of the travel. Therefore, the use of thromboprophylaxis may be justified.

Regarding the options for thromboprophylaxis, plenty of indirect evidence supports the use of LMWH or compression stockings. The evidence with aspirin is very limited, and there is no evidence of the potential effect of DOACs.

Table 4 summarizes the recommendations for the prevention of VTE in acutely and critically ill medical patients.

Table 4. Summary of recommendations for prevention of VTE in medical patients.

| Population | Preferred alternative | Proposed treatment |
|---|---|---|
| **Critically ill inpatients** | **Use thromboprophylaxis** (recommendation 12) | **If prophylaxis is preferred:** Short scheme (inpatient only) of LMWH or UFH. (recommendations 13, 16, 17, and 18)<br><br>**Patients who cannot receive pharmacological prophylaxis:** Mechanical prophylaxis with either compression devices or compression stockings (recommendations 14 and 15) |
| **Acutely ill inpatients** | **No thromboprophylaxis** (recommendation 11) | |
| **Chronically ill patients** | **No thromboprophylaxis** (recommendation 16) | |
| **Long-distance travelers** | **Average risk of VTE:** No prophylaxis<br>**High risk of VTE:** Use thromboprophylaxis (recommendations 19 and 20) | **If prophylaxis is preferred:** Either compression stockings or LMWH |

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# Authorship contributions

I.N. and H.J.S. developed the methods for this adaptation. I.N. and A.I. wrote the first draft of the manuscript and revised the manuscript based on authors' suggestions; guideline panel members (I.N., A.I., R.A., G.L.B., P.C., C.C.C., M.C.G.E., P.P.G.L., J.P., L.A.M.-G., S.M.R., J.C.S., and M.L.T.V.) critically reviewed the manuscript and provided suggestions for improvement; members of the knowledge synthesis team (I.N., A.I., F.V., L.K., G.R., and H.J.S.) contributed with evidence summaries to the guidelines. All authors approved the content. I.N. and A.I. led panel meetings.

# Disclosures of conflicts of interest

See supplements 2 and 3.

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