Prophylaxis for Hospitalized and Non-Hospitalized Medical Patients

An Educational Slide Set

American Society of Hematology 2018 Guidelines for Management of Venous Thromboembolism

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American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and non-hospitalized medical patients

Holger J. Schünemann, Mary Cushman, Allison E. Burnett, Susan R. Kahn, Jan Beyer-Westendorf, Frederick A. Spencer, Suely M. Rezende, Neil A. Zakai, Kenneth A. Bauer, Francesco Dentali, Jill Lansing, Sara Balduzzi, Andrea Darzi, Gian Paolo Morgano, Ignacio Neumann, Robby Nieuwlaat, Juan J. Yepes-Nuñez, Yuan Zhang, and Wojtek Wiercioch
ASH Clinical Practice Guidelines on VTE

1. Prevention of VTE in Surgical Hospitalized Patients
2. **Prophylaxis in Hospitalized and Non-Hospitalized Medical Patients**
3. Treatment of Acute VTE (DVT and PE)
4. Optimal Management of Anticoagulation Therapy
5. Prevention and Treatment of VTE in Patients with Cancer
6. Heparin-Induced Thrombocytopenia (HIT)
7. Thrombophilia
8. Pediatric VTE
9. VTE in the Context of Pregnancy
10. Diagnosis of VTE
### How were these ASH guidelines developed?

#### PANEL FORMATION
Each guideline panel was formed following these key criteria:
- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of COI

#### CLINICAL QUESTIONS
10 to 20 clinically-relevant questions generated in PICO format (population, intervention, comparison, outcome)

Example: PICO question “Should LMWH versus UFH be used for VTE prophylaxis in critically ill patients?”

#### EVIDENCE SYNTHESIS
Evidence summary generated for each PICO question via systematic review of health effects plus:
- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

#### MAKING RECOMMENDATIONS
Recommendations made by guideline panel members based on evidence for all factors.
How patients and clinicians should use these recommendations

<table>
<thead>
<tr>
<th></th>
<th>STRONG Recommendation</th>
<th>CONDITIONAL Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients</strong></td>
<td>Most individuals would want the intervention.</td>
<td>A majority would want the intervention, but many would not.</td>
</tr>
<tr>
<td><strong>For clinicians</strong></td>
<td>Most individuals should receive the intervention.</td>
<td>Different choices will be appropriate for different patients, depending on their values and preferences. Use <strong>shared decision making</strong>.</td>
</tr>
</tbody>
</table>
VTE in medical inpatients is common

**Half** of VTE events occur due to hospital admission for surgery (24%) or medical illness (22%)

**40%** of hospitalized patients have 3 or more risk factors for VTE

**Risk factors for VTE in hospital** include cancer, older age, prior VTE, central lines, immobility

Increase in thrombosis risk in medical inpatients persists **45 to 60 days** after discharge
Patient groups addressed in this chapter

**Acutely Ill Medical Patient**
Patients hospitalized for medical illness

**Critically Ill Patient**
Patients suffering from immediately life-threatening illness requiring admission to intensive care unit

**Chronically Ill Medical Patient**
Those with medical conditions who may be cared for in long-term care facilities

**Long-distance Traveler**
Those traveling by air for ≥ 4 hours
Who is at risk for VTE in hospital?

• Risk Assessment Models (RAMs) can identify inpatients at high risk
• **Examples:** Padua, IMPROVE-VTE Scores

**Padua RAM: Factors**
- Previous VTE
- Thrombophilia
- Active cancer
- Age > 70 years
- Reduced mobility
- Recent trauma/surgery
- Heart or respiratory failure
- Acute MI or stroke
- Hormonal treatment
- Obesity (BMI > 30)
- Infection/rheumatologic

**IMPROVE-VTE RAM: Factors**
- Previous VTE
- Thrombophilia
- Active cancer
- Age > 60 years
- Immobilization of ≥ 7 days
- Lower limb paralysis
- ICU/CCU stay

These RAMs are not extensively validated for guiding decisions about prophylaxis.
The following outcomes were rated by the panel as critical to decision-making:

• High value was placed on avoiding these outcomes
• Asymptomatic VTE were not considered critical outcomes

Mortality
Pulmonary Embolism (PE)
Moderate to Severe Deep Vein Thrombosis (DVT)
Major Bleeding
Case: Medical Inpatient Admission

82 year old male

Past Medical History: Emphysema, type 2 diabetes, obesity (body mass index [BMI] of 42 kg/m²), provoked DVT 15 years ago (after appendectomy)

Medications: Tiotropium, metformin, amlodipine, ramipril

Admitted to: Internal Medicine Ward with pneumonia

Treated with: antibiotics, supplemental oxygen

He is not ambulating on the ward due to dyspnea and generalized weakness.
Which ONE of the following options would you suggest for thromboprophylaxis during this medical inpatient’s hospital admission?

A. Subcutaneous low molecular weight heparin (LMWH)
B. Direct oral anticoagulant (Betrixaban, Rivaroxaban, or Apixaban)
C. Graduated compression stockings
D. No prophylaxis because patient is low thrombosis risk
Our patient’s risk factors for VTE

<table>
<thead>
<tr>
<th>Padua RAM: Factors</th>
<th>IMPROVE-VTE RAM: Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>Previous VTE</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>Thrombophilia</td>
</tr>
<tr>
<td>Active cancer</td>
<td>Active cancer</td>
</tr>
<tr>
<td>Age &gt; 70 years</td>
<td>Age &gt; 60 years</td>
</tr>
<tr>
<td>Reduced mobility</td>
<td>Immobilization of ≥ 7 days</td>
</tr>
<tr>
<td>Recent trauma/surgery</td>
<td>Lower limb paralysis</td>
</tr>
<tr>
<td>Heart or respiratory failure</td>
<td>ICU/CCU stay</td>
</tr>
<tr>
<td>Acute MI or stroke</td>
<td></td>
</tr>
<tr>
<td>Hormonal treatment</td>
<td></td>
</tr>
<tr>
<td>Obesity (BMI &gt; 30)</td>
<td></td>
</tr>
<tr>
<td>Infection/rheumatologic</td>
<td></td>
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</tbody>
</table>
**Recommendation**

- In **acutely ill medical patients**, the panel suggests using **UFH, LMWH, or fondaparinux** rather than no parenteral anticoagulant (conditional recommendation, low certainty)

- The panel suggests using **LMWH (low certainty)** or **fondaparinux (very low certainty)** rather than UFH (conditional recommendation)

**Parenteral anticoagulant compared with no parenteral anticoagulant:**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with no parenteral anticoagulant</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.97 (0.91 to 1.04)</td>
<td>69 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.59 (0.45 to 0.78)</td>
<td>10 per 1,000</td>
</tr>
<tr>
<td>Symptomatic proximal DVT</td>
<td>0.28 (0.06 to 1.37)</td>
<td>4 per 1,000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.48 (0.81 to 2.71)</td>
<td>7 per 1,000</td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low ▼ Moderate ▼ Strong ▼
### Recommendation

In **acutely or critically ill medical patients**, the panel suggests using **pharmacological VTE prophylaxis over mechanical prophylaxis** *(conditional recommendation, very low certainty)*

**Pharmacologic prophylaxis** compared with **mechanical prophylaxis** *(graduated compression stockings or pneumatic compression devices):*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Risk with pharmacologic prophylaxis</th>
<th>Risk difference with mechanical prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>0.95 (0.42 to 1.13)</td>
<td>18 per 1,000</td>
<td>1 fewer death per 1,000</td>
<td>(11 fewer to 21 more)</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>1.54 (0.48 to 4.93)</td>
<td>1 per 1,000</td>
<td>1 more PE per 1,000</td>
<td>(1 fewer to 4 more)</td>
</tr>
<tr>
<td><strong>Symptomatic proximal DVT</strong></td>
<td>2.20 (0.22 to 22.09)</td>
<td>2 per 1,000</td>
<td>2 more DVT per 1,000</td>
<td>(1 fewer to 38 more)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>0.87 (0.25 to 3.08)</td>
<td>28 per 1,000</td>
<td>4 fewer bleeds per 1,000</td>
<td>(21 fewer to 58 more)</td>
</tr>
</tbody>
</table>

**Quality of Evidence (GRADE):**
- Low
- Moderate
- Strong
**Recommendation**

In acutely ill hospitalized **medical patients**, the panel recommends using **LMWH over DOACs** for VTE prophylaxis (strong recommendation, moderate certainty)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality of Evidence (GRADE): Low Moderate Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>0.64 (0.21 to 1.98)</td>
<td>1 per 1,000</td>
<td>Low</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>1.01 (0.29 to 3.53)</td>
<td>1 per 1,000</td>
<td>Moderate</td>
</tr>
<tr>
<td>Symptomatic proximal DVT</td>
<td>1.03 (0.34 to 3.08)</td>
<td>2 per 1,000</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>1.70 (1.02 to 2.82)</td>
<td>2 per 1,000</td>
<td></td>
</tr>
</tbody>
</table>

*these estimates apply to low baseline bleeding risk*
You start VTE prophylaxis with **prophylactic LMWH** for this internal medicine admission.

Two days into the hospital admission, your patient is admitted to the **critical care unit** with respiratory failure and septic shock:

- He is intubated and started on vasopressors
- His labs:

<table>
<thead>
<tr>
<th>Labs on Transfer to ICU</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>12.0 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>103 x 10^9/L</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>15.6 x 10^9/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.47 mg/dL (eGFR 49 mL/min/1.73 m^2)</td>
</tr>
</tbody>
</table>
Your patient has been transferred to the intensive care unit (ICU), and has mild thrombocytopenia and acute kidney injury.

Which ONE of the following options would you recommend for thromboprophylaxis now?

A. Subcutaneous LMWH
B. Subcutaneous Unfractionated Heparin (UFH)
C. Graduated Compression Stockings
D. Graduated Compression Stockings combined with LMWH
### Recommendation

In **critically ill medical patients**, the panel suggests using **LMWH over UFH** *(conditional recommendation, moderate certainty)*

LMWH compared with UFH in critically ill patients:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>0.90 (0.75 to 1.08)</td>
<td>Risk with UFH: 243 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk difference with LMWH: 24 fewer deaths per 1,000 (61 fewer to 19 more)</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>0.80 (0.44 to 1.46)</td>
<td>Risk with UFH: 11 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk difference with LMWH: 2 fewer PE per 1,000 (6 fewer to 5 more)</td>
</tr>
<tr>
<td><strong>Symptomatic proximal DVT</strong></td>
<td>0.87 (0.60 to 1.25)</td>
<td>Risk with UFH: 25 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk difference with LMWH: 3 fewer DVT per 1,000 (10 fewer to 6 more)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>0.98 (0.76 to 1.27)</td>
<td>Risk with UFH: 53 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk difference with LMWH: 1 fewer bleeds per 1,000 (13 fewer to 14 more)</td>
</tr>
<tr>
<td><strong>Heparin-induced thrombocytopenia</strong></td>
<td>0.42 (0.15 to 1.18)</td>
<td>Risk with UFH: 6 per 1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Risk difference with LMWH: 4 fewer episodes per 1,000 (5 fewer to 1 more)</td>
</tr>
</tbody>
</table>

**Critically ill patients may require other prophylaxis options due to hepatic or renal dysfunction.**

Quality of Evidence (GRADE): Low - Moderate - Strong
**Recommendation**

In **acutely and critically ill medical patients**, the panel suggests **pharmacological VTE prophylaxis alone** over mechanical combined with pharmacological VTE prophylaxis (**conditional recommendation, very low certainty**)

### Mechanical combined with pharmacologic compared with pharmacologic alone:

<table>
<thead>
<tr>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with pharmacologic prophylaxis alone</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>0.50 (0.05 to 5.30)</td>
<td>8 per 1,000</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>0.35 (0.05 to 2.22)</td>
<td>1 per 1,000</td>
</tr>
<tr>
<td><strong>Symptomatic proximal DVT</strong></td>
<td>0.13 (0.04 to 0.40)</td>
<td>2 per 1,000</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>2.83 (0.30 to 26.70)</td>
<td>28 per 1,000</td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low 🔴, Moderate 🔴, Strong 🔴
Case: Back to our patient

• You decide to continue prophylactic LMWH without mechanical prophylaxis after your patient’s transfer to the ICU

• Three days into his ICU admission, he develops upper GI bleeding

• Gastroscopy reveals a small gastric ulcer with a visible bleeding vessel; this vessel is clipped

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>7.5 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>88 x 10^9/L</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>13.0 x 10^9/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.47 mg/dL (eGFR 49 mL/min/1.73 m^2)</td>
</tr>
</tbody>
</table>
Your patient has had recent upper GI bleeding. You decide to withhold pharmacologic prophylaxis to ensure hemostasis.

Which of the following options for thromboprophylaxis would you suggest at this time?

A. Graduated Compression Stockings
B. Pneumatic Compression Devices
C. Calf exercises
D. No mechanical prophylaxis is needed
Recommendation

In **acutely and critically ill medical patients** who are not receiving pharmacological VTE prophylaxis, the panel suggests either pneumatic compression devices or graduated compression stockings for VTE prophylaxis (conditional recommendation, very low certainty)

**Pneumatic compression devices** compared with **graduated compression stockings**:

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with graduated compression stockings</td>
</tr>
<tr>
<td>Mortality</td>
<td>3.43 (0.15 to 79.74)</td>
<td>0 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.38 (0.02 to 8.86)</td>
<td>43 per 1,000</td>
</tr>
<tr>
<td>Symptomatic proximal DVT</td>
<td>0.16 (0.01 to 2.98)</td>
<td>130 per 1,000</td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low ▼ Moderate ▼ Strong ▼
Case continued: Discharge from hospital

• Your patient recovers from his upper GI bleed and septic shock, and is transferred back to the internal medicine ward.

• Within a few days he is started back on LMWH for pharmacologic VTE prophylaxis.

• He has been in hospital for a total of 9 days and is being discharged back to his home, as his pneumonia has resolved.
You are discharging your patient after an acute medical illness. He has received prophylaxis with LMWH in hospital for 9 days. He is ambulatory and back on his usual medications.

What would you recommend on discharge for VTE prophylaxis?

A. Stop LMWH on the day of discharge
B. Extend LMWH for 3 weeks post-discharge
C. Switch LMWH on discharge to a DOAC, and continue the DOAC for 3 weeks post-discharge
D. Graduated compression stockings for 3 weeks post-discharge
What is the rationale for extending VTE prophylaxis beyond hospital discharge?

• Most hospital-related VTE events occur **out of hospital**, in the first month after discharge

• VTE risk in medical patients is elevated for 45-60 days post-discharge

• Duration of inpatient prophylaxis is shortening as the average hospital length of stay decreases

Huang Am J Med 2014
Cohen NEJM 2016
Cohen NEJM 2014
Goldhaber NEJM 2011
Recommendation

In acutely ill hospitalized medical patients, the panel recommends **inpatient over inpatient plus extended duration outpatient VTE prophylaxis** (strong recommendation, moderate certainty).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.00 (0.89 to 1.12)</td>
<td>0 fewer deaths per 1,000 (5 fewer to 5 fewer)</td>
</tr>
<tr>
<td>PE</td>
<td>0.63 (0.39 to 1.03)</td>
<td>1 fewer PE per 1,000 (3 fewer to 0 fewer)</td>
</tr>
<tr>
<td>Symptomatic proximal DVT</td>
<td>0.54 (0.32 to 0.91)</td>
<td>3 fewer DVT per 1,000 (4 fewer to 1 fewer)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>2.09 (1.33 to 3.27)</td>
<td>4 more bleeds per 1,000 (1 more to 8 more)</td>
</tr>
</tbody>
</table>

Extended prophylaxis (30-40 days) compared with in-hospital prophylaxis (any agent):
**Recommendation**

In acutely ill hospitalized medical patients, the panel recommends inpatient VTE prophylaxis with LMWH only, rather than inpatient and extended duration outpatient VTE prophylaxis with DOACs (strong recommendation, moderate certainty).

**Extended DOAC prophylaxis (30-40 days) compared with shorter LMWH prophylaxis:**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative effect: RR (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk with shorter duration non-DOAC inpatient prophylaxis</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.01 (0.89 to 1.14)</td>
<td>49 per 1,000</td>
</tr>
<tr>
<td>PE</td>
<td>0.67 (0.41 to 1.09)</td>
<td>4 per 1,000</td>
</tr>
<tr>
<td>Symptomatic proximal DVT</td>
<td>0.62 (0.36 to 1.05)</td>
<td>6 per 1,000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.99 (1.08 to 3.65)</td>
<td>4 per 1,000</td>
</tr>
</tbody>
</table>

**Quality of Evidence (GRADE): Low Moderate Strong**
In summary, why is routine post-discharge extended prophylaxis currently not recommended?

- Extended prophylaxis *may* reduce PE and DVT, but absolute impact on VTE reduction is very small (1 to 3 fewer VTE per 1,000 patients treated), and is similar to number of bleeding events caused

- Extended prophylaxis does not impact mortality

- Possible that the three included RCTs (APEX, MAGELLAN, ADOPT) did not select patients at sufficiently high risk for VTE
  - However, the recent MARINER trial *(Spyropoulos NEJM 2018)* also did not show significant reduction in VTE despite use of a modified IMPROVE VTE risk score to select high-risk medical inpatients for extended prophylaxis with rivaroxaban
Case Conclusion and a Visitor

• On discharge you stop LMWH, and he does not receive extended VTE prophylaxis out of hospital. He recovers and does not develop VTE.

• Two months later, the patient’s 50 year old niece decides to visit him from England (7 hour flight to Baltimore).

• She is has a history of unprovoked DVT 4 years ago, and her BMI is 38 kg/m². She is currently not on anticoagulant or antiplatelet therapy.
This patient’s niece has a history of unprovoked VTE, and her BMI is 38. She is boarding a long-distance flight (> 4 hours).

What would you suggest for VTE prophylaxis during her flight?

A. LMWH
B. Graduated compression stockings
C. Aspirin
D. No prophylaxis is needed
Air Travel and VTE

- **Long-distance travelers:** 4-hour flight or longer

- Air travel associated with 2.8-fold increase in risk of VTE; risk increases with flight duration

- Several risk factors increase risk of VTE multiplicatively with risk of prolonged air travel
  - Pregnancy, cancer, plaster casts, hormonal therapy, oral contraception
Recommendation

- In people at **increased VTE risk** the panel suggests using **graduated compression stockings or prophylactic LMWH** for long-distance travel *(conditional recommendation, very low certainty)*

- If compression stockings or LMWH are not used, aspirin should be used instead of no prophylaxis *(conditional recommendation, very low certainty)*

<table>
<thead>
<tr>
<th>Who is at increased risk?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Recent surgery</td>
</tr>
<tr>
<td>• Prior VTE</td>
</tr>
<tr>
<td>• Postpartum women</td>
</tr>
<tr>
<td>• Active malignancy</td>
</tr>
<tr>
<td>• 2+ risk factors including combinations of the above with hormonal replacement therapy, obesity, or pregnancy</td>
</tr>
</tbody>
</table>

- LMWH, stockings, and ASA have small, uncertain benefit
- There is no evidence regarding use of DOACs for prophylaxis during air travel
Stockings, LMWH, and aspirin have small, very uncertain effects on VTE prevention – and the estimated absolute benefits are very small

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Relative Effects (RR, 95% CI) on VTE Prevention (compared with no intervention)</th>
<th>Absolute Risk Difference with each intervention (compared with no prophylaxis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graduated Compression Stockings</td>
<td>• 0.10 (0.04 to 0.25)</td>
<td>• 3 fewer PE per 1,000,000 (3 fewer to 3 fewer)</td>
</tr>
<tr>
<td></td>
<td>• 1.8 fewer asymptomatic DVT per 10,000 (1.9 fewer to 1.5 fewer)</td>
<td></td>
</tr>
<tr>
<td>LMWH</td>
<td>• 0.10 (0.10 to 2.11)</td>
<td>• 3 fewer PE per 1,000,000 (3 fewer to 4 more)</td>
</tr>
<tr>
<td></td>
<td>• 17.8 fewer asymptomatic DVT per 10,000 (1.9 fewer to 2.2 more)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>• 0.75 (0.13 to 4.32)</td>
<td>• 1 fewer PE per 1,000,000 (3 fewer to 12 more)</td>
</tr>
<tr>
<td></td>
<td>• 0.5 fewer asymptomatic DVT per 10,000 (1.7 fewer to 6.5 more)</td>
<td></td>
</tr>
</tbody>
</table>

Quality of Evidence (GRADE): Low • Moderate • Strong
Applying these guidelines to our patient: why are these recommendations “conditional?”

50 year old female with prior unprovoked VTE and obesity

What is her approximate risk of VTE in association with her flight?

Baseline annual risk ≈ 1 in 1000 (age) x 2 (obesity) x 5 (prior VTE) ≈ 1 in 100 per year

Daily VTE risk ≈ 1 in 100 x 1 in 365 days per year ≈ 1 in 3,650

VTE risk per flight ≈ 1 in 3,650 (daily risk) x 30 days of risk x 3 (RR with flight) ≈ 3%

What is the benefit of LMWH prophylaxis?

RR 0.10 (95% CI 0.01-2.11) compared with no intervention

Approximate VTE risk per flight with LMWH = 3% x 0.10 = 0.3% (high uncertainty, 95% CI 0.03% to 6.3%)

There is very low certainty and small absolute effect size in these estimates

Physicians must take patient-centered factors into account

Eichinger Arch Int Med 2008
Silverstein Arch Int Med 1998
However, patients without VTE risk factors do not merit prophylaxis for air travel

Recommendation

In long-distance travelers **without risk factors for VTE**, the panel suggests **not using graduated compression stockings, LMWH, or aspirin** for VTE prophylaxis (**conditional recommendation, very low certainty**)
Case: Conclusion

• Given her history of previous VTE and obesity, you feel that she merits VTE prophylaxis either with graduated compression stockings or LMWH during her flight.

• She receives prophylactic LMWH on the morning of her 7-hour flight, and does not develop VTE.
Other guideline recommendations that were not covered in this presentation

For these topics, conditional recommendations were made based on weak or very weak quality of evidence

• Medical outpatients with **minor provoking risk factors** for VTE (immobility, minor injury, illness, infection)

• **Chronically ill** medical patients or **nursing home** patients
Some of the 29 identified future priorities for research

• Optimal prophylaxis dosing for obese, underweight, renal patients
• Utility of mechanical prophylaxis in medical outpatients at high risk
• Bleeding and thrombosis risk estimation in medical and critically ill patients
• More study of post discharge measures to prevent VTE
• Comparison of different forms of mechanical prophylaxis to each other
• Comparison of combined approaches (mechanical plus pharmacologic) versus pharmacologic prophylaxis alone
• Utility of prophylaxis in high-risk chronically ill/nursing home patients
• Effectiveness and safety of DOACs for prophylaxis during air travel
In Summary: Back to our Objectives

1. Describe VTE prophylaxis recommendations for patients hospitalized with a medical illness or critical illness
   • Risk assessment models, LMWH compared with DOACs

2. Describe VTE prophylaxis recommendations for patients discharged from hospital after an acute medical illness
   • Extended versus in-hospital prophylaxis, LMWH compared with DOACs

3. Identify when long-distance travelers may benefit from receiving VTE prophylaxis
   • Graduated compression stockings or LMWH for those with strong VTE risk factors
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See more about the ASH VTE guidelines at www.hematology.org/VTEguidelines