Prevention of VTE in Orthopedic Surgery Patients: A Norwegian adaptation of the 9th ed. of the ACCP Antithrombotic Therapy and Prevention of Thrombosis Evidence-based Clinical Practice Guidelines

Main Editor
Lars-Petter Granan

Publishing Info
v0.2 published on 04.08.2015
Sections

1 - Orthopedic surgery and prevention of venous thromboembolism
2 - Patients at moderate to high risk of thrombosis: All surgery of the lower extremities
3 - Major orthopedic surgery: patients at low risk of thrombosis
4 - Other interventions and screening
Summary of recommendations

1 - Orthopedic surgery and prevention of venous thromboembolism

Overarching modifications made to the original guideline:

Certain drugs and mechanical devices (vena cava filter, intermittent pneumatic compression devices - IPCD) are excluded, either because they are not readily available (off-label) or because they are seldom used in clinical practice in Norway. In the latter case, we justify the exclusion of the interventions as there are alternative, frequently used and equally effective treatment options. We have decided to exclude IPCDs from the guideline as they are infrequently used in Norway and have insufficient documentation for isolated use. They should be used for a minimum of 18 hours per day and thus compliance is potentially low. No studies have adequately assessed potential skin problems. Furthermore, we do not believe it to be financially justifiable to suggest use of a new technical tool with limited documentation and expected compliance issues.

There were inconsistencies in the baseline risk estimates for DVT and pulmonary embolism applied in AT9, and the authors of the original chapter recognized that the incidence rates of venous thromboembolism (VTE) have fallen over the past decade due to improved surgical techniques and postoperative care. Moreover, earlier studies on thromboprophylaxis usually included screening for DVT and thus reported both asymptomatic and symptomatic cases. Asymptomatic DVT is considered to have little clinical relevance, i.e. that it is not considered a patient important outcome. Due to the uncertainty regarding the validity of the baseline estimates used in AT9, we have chosen to replace these with data from the control arm (LMWH) in a recent meta-analysis on new oral anticoagulants (NOAC). We have also collected data on the incidence rates of VTE following total hip arthroplasty, total knee arthroplasty and hip fracture surgery from the National Patient Registry (NPR) in Norway, from January 2008 to December 2011. These risk estimates correspond well with incidence data found in the control arm in the meta-analysis on NOAC vs low-molecular-weight heparin.

The use of aspirin as a thromboprophylactic agent from the first postoperative day is controversial. There has recently been published efficacy studies that provide better documentation. The Norwegian guideline panel plans to add a recommendation regarding aspirin as thromboprophylaxis during the coming months.

2 - Patients at moderate to high risk of thrombosis: All surgery of the lower extremities

Strong Recommendation
We recommend thromboprophylaxis with low molecular weight heparin, low-dose direct factor Xa inhibitor (apixaban, rivaroxaban) or dabigatran for the first 10 postoperative days.

*High risk: previous symptomatic VTE.
Moderate risk: age > 80 years or multiple comorbidities.
Patient risk can be assessed using the Charlson Comorbidity index or ASA classification. Please see under "practical information".*

Weak Recommendation

We suggest extending thromboprophylaxis for up to 35 days after surgery.

3 - Major orthopedic surgery: patients at low risk of thrombosis

Total Hip and Knee Arthroplasty

Weak Recommendation

We suggest thromboprophylaxis with low molecular weight heparin, low-dose direct factor Xa inhibitor (apixaban, rivaroxaban) or dabigatran for the first 10 postoperative days.
We suggest against extending thromboprophylaxis beyond 10 days.

Fast-track general joint replacement surgery

Weak Recommendation

We suggest thromboprophylaxis with low-molecular-weight heparin until discharge (1-4 days).
We suggest against extending thromboprophylaxis beyond discharge.

Fractures of the proximal femur: surgery with prosthesis or osteosynthesis

Strong Recommendation

We recommend thromboprophylaxis with low-molecular-weight heparin (LMWH) for the first 10 postoperative days.

Weak Recommendation

We suggest extending thromboprophylaxis for up to 35 days following surgery.
4 - Other interventions and screening

Extremity injuries distal to the knee, including those that require immobilization

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend against thromboprophylaxis.</td>
</tr>
</tbody>
</table>

Arthroscopic surgery of the knee and ankle

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend against thromboprophylaxis.</td>
</tr>
</tbody>
</table>

DVT screening

<table>
<thead>
<tr>
<th>Strong Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>In asymptomatic patients, we recommend against DVT screening with ultrasound or venography.</td>
</tr>
</tbody>
</table>
1 - Orthopedic surgery and prevention of venous thromboembolism

Overarching modifications made to the original guideline:

Certain drugs and mechanical devices (vena cava filter, intermittent pneumatic compression devices - IPCD) are excluded, either because they are not readily available (off-label) or because they are seldom used in clinical practice in Norway. In the latter case, we justify the exclusion of the interventions as there are alternative, frequently used and equally effective treatment options. We have decided to exclude IPCDs from the guideline as they are infrequently used in Norway and have insufficient documentation for isolated use. They should be used for a minimum of 18 hours per day and thus compliance is potentially low. No studies have adequately assessed potential skin problems. Furthermore, we do not believe it to be financially justifiable to suggest use of a new technical tool with limited documentation and expected compliance issues.

There were inconsistencies in the baseline risk estimates for DVT and pulmonary embolism applied in AT9, and the authors of the original chapter recognized that the incidence rates of venous thromboembolism (VTE) have fallen over the past decade due to improved surgical techniques and postoperative care. Moreover, earlier studies on thromboprophylaxis usually included screening for DVT and thus reported both asymptomatic and symptomatic cases. Asymptomatic DVT is considered to have little clinical relevance, i.e. that it is not considered a patient important outcome. Due to the uncertainty regarding the validity of the baseline estimates used in AT9, we have chosen to replace these with data from the control arm (LMWH) in a recent meta-analysis on new oral anticoagulants (NOAC). We have also collected data on the incidence rates of VTE following total hip arthroplasty, total knee arthroplasty and hip fracture surgery from the National Patient Registry (NPR) in Norway, from January 2008 to December 2011. These risk estimates correspond well with incidence data found in the control arm in the meta-analysis on NOAC vs low-molecular-weight heparin.

The use of aspirin as a thromboprophylactic agent from the first postoperative day is controversial. There has recently been published efficacy studies that provide better documentation. The Norwegian guideline panel plans to add a recommendation regarding aspirin as thromboprophylaxis during the coming months.

Practical Advice

Key Info

<table>
<thead>
<tr>
<th>Benefits and harms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of evidence</td>
</tr>
<tr>
<td>Preference and values</td>
</tr>
</tbody>
</table>
Resources and other considerations

Rationale

References
2 - Patients at moderate to high risk of thrombosis: All surgery of the lower extremities

**Strong Recommendation**

We recommend thromboprophylaxis with low molecular weight heparin, low-dose direct factor Xa inhibitor (apixaban, rivaroxaban) or dabigatran for the first 10 postoperative days.

*High risk: previous symptomatic VTE.*
*Moderate risk: age > 80 years or multiple comorbidities.*

Patient risk can be assessed using the Charlson Comorbidity index or ASA classification. Please see under "practical information".

**Practical Advice**

For patients with liver or kidney disease, low body weight, age over 75 years or patients on drugs with the possibility of interactions with the new oral anticoagulants, we recommend to adjust the dose according to the drug information or to choose an alternative drug.

**Risk factors for thromboembolic events (VTE)**

In the absence of validated risk scores we have identified the following risk factors:

- Previous VTE (relative risk increase of 5.3)
- Age 80 years or older (relative risk increase of 1.58)
- High degree of comorbidities (at least 3 points on the Charlson Comorbidity index. Relative risk increase of 1.73)

**Suggested dosage** (patients with a hip fracture should only use LMWH)

- **Sc LMWH:** either dalteparin 5000 IU, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 12 hours before or after surgery
- Apixaban 2.5 mg x 2 started 12 hours after surgery
- Dabigatran 110 mg for the first dose, followed by 220 mg x 1 started 1-4 hours after surgery
- Rivaroxaban 10 mg x 1 started 6-10 hours after surgery

**Charlson comorbidity index:**

- 0 points = low risk. 1-2 points = moderate risk. 3 points or higher = high risk

<table>
<thead>
<tr>
<th>6 points</th>
<th>Metastatic solid tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AIDS</td>
</tr>
<tr>
<td>3 points</td>
<td>Moderat to serious liver disease</td>
</tr>
<tr>
<td>2 points</td>
<td>Diabetes with end-organ damage</td>
</tr>
<tr>
<td></td>
<td>Moderat to serious kidney disease</td>
</tr>
<tr>
<td></td>
<td>Malignant tumor</td>
</tr>
</tbody>
</table>
Leukemia or lymphoma
Hemiplegia

| 1 point       | Chronic heart failure
|               | Cardiovascular disease: Previous myocardial infarction, peripheral artery disease, stroke or TIA
|               | Chronic pulmonary disease
|               | Mild liver disease
|               | Stomach ulcer
|               | Diabetes without complications
|               | Connective tissue disease
|               | Dementia

**ASA physical status classification system**

| ASA1 | Healthy patient. No organic, physiological, biochemical or psychiatric disorder. The condition to be treated is localised and does not cause any systemic disturbances. Less than 5 cigarettes per day. The patient is under 80 years of age. |
| ASA2 | Moderate organic disease or disturbance not causing functional limitations, but might result in specific precautions being made or certain anesthetic measures. The disease(s) can either be caused by the condition that is to be treated or by another pathological process. Age over 80 or newborns younger than 3 months. More than 5 cigarettes per day. |
| ASA3 | Serious organic disease or disturbance that causes defined functional limitations. |
| ASA4 | Life threatening organic disease that is not necessarily related to the condition that is to be treated or will be improved by the surgical procedure. |
| ASA5 | Moribund patient not expected to survive the next 24 hours, with or without surgery. |

**Key Info**

**Benefits and harms**
Patients with one or more patient-specific risk factors for thrombosis have an up to 6-fold increased risk of venous thromboembolism.  
For 1000 patients not receiving thromboprophylaxis we expect (worst case scenario):  
139 DVTs and 69 pulmonary emboli during the first 5 weeks following surgery.  
With prophylaxis (LMWH/UFH) the incidence is substantially reduced to 61 and 30 per 1000 patients, respectively.  
Approximately 2/3 of VTE cases occur during the first two weeks following surgery.  
We do not anticipate any effect of thromboprophylaxis on the rate of fatal pulmonary emboli.  
For absolute risks of major bleeding we refer to the specific recommendations for the each surgery.
**Quality of evidence**

Overall the quality of the evidence is moderate, with relative effect estimates derived from a meta-analysis with possible risk of bias in the included studies. The baseline risk of VTE is derived from the National Patient Registry (NPR) for the period 2008-11 and a Danish registry study (for high-risk patients).

**Preference and values**

Given the high risk of VTE we believe all or nearly all patients will elect to use short-term prophylaxis provided that they do not have contraindications such as an increased risk of bleeding.

**Resources and other considerations**

Apixaban, rivaroxaban and dabigatran have labeled use and pre-approved reimbursement for elective total hip or knee arthroplasty.

**Rationale**

We give a strong recommendation in favor of short-term thromboprophylaxis to patients with moderate to high risk of thromboembolic events given a significant risk reduction of VTE at the cost of a marginally increased risk of bleeding.

We have derived the baseline risk estimates from the National Patient Registry (NPR) in Norway, applying VTE incidence rates in patients following surgery for hip fractures, and recognize the resulting inherent uncertainty for our absolute effect estimates. We have assumed that all patients registered in the NPR received extended thromboprophylaxis and have taken into account the relative risk increase due to various patient specific factors. All in all, this results in a conservative calculation that rather over- than underestimates the risk of not using thromboprophylaxis.

We believe it to be important that patients are mobilized as soon as possible after surgery, but the evidence that this affects the incidence rates of VTE is lacking.

From studies on major hip or knee arthroplasty we have evidence that thromboprophylaxis does not affect the incidence of fatal pulmonary emboli. However, studies have shown that thromboprophylaxis might effect all-cause mortality in patients with hip fractures. We are uncertain whether the positive effect on mortality is due to the orthopedic condition itself or to the patient's age and number of comorbidities. For more information, we refer to the specific recommendations for each type of surgery.

**References**


Gomez-Outes et al. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis. BMJ 2012;344:e3675 22700784 10.1136/bmj.e3675

**PICO (2.1)**

**Population:** Thromboprophylaxis in patients at moderate risk of VTE  
**Intervention:** Heparin  
**Comparator:** No prophylaxis  
**Outcomes:** DVT, non-fatal pulmonary embolism

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>45 per 1000</td>
<td>20 per 1000</td>
<td>25 fewer (CI 31 fewer - 17 fewer)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>22 per 1000</td>
<td>10 per 1000</td>
<td>12 fewer (CI 15 fewer - 8 fewer)</td>
</tr>
<tr>
<td>Major bleed (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>4 per 1000</td>
<td>6 per 1000</td>
<td>2 more (CI 1 more - 3 more)</td>
</tr>
</tbody>
</table>

**PICO References**

**PICO Summary**


**Baseline risk:** The risk of VTE without prophylaxis is based on partially indirect data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rate is adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. The baseline risks for high-risk patients are then calculated by using the adjusted NPR data and applying relative estimates from Pedersen et al, who found a relative risk increase of VTE of 5.3 (95% CI 3.99 to 7.05) in patients with previous venous thrombosis. For other patient categories they found a relative risk increase of 1.58 (1.01 to 2.47) in patients >80 years and RR 1.73 (1.24 to 2.41) in patients with three or more points on the Charlson comorbidity index. The baseline risk of major bleeding is based on indirect data from a population undergoing total hip or knee arthroplasty: Neumann et al. Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 (10):710-9. It is thus possible that the real absolute incidence of major bleeding is somewhat higher than what we use here.

**Quality of the documentation:** For all outcomes except mortality, the quality is downgraded to moderate as several of the studies included in Collins' meta-analysis were not blinded and there was an inadequate description of the allocation procedures. A certain degree of heterogeneity was observed across studies for the effect on non-fatal pulmonary emboli. The included studies were on patients undergoing general surgery, but adding Collins' studies on orthopedic surgeries did not significantly change the relative effect estimate.

**PICO (2.1)**

**Population:** Thromboprophylaxis in total hip or knee arthroplasty

**Intervention:** Heparin

**Comparator:** No prophylaxis

**Outcomes:** Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds, bleeds that require reoperation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Imprecise estimates and use of indirect data</td>
<td>RR: 1.01 (CI 0.68 - 1.48)</td>
<td>1 per 1000</td>
<td>0 per 1000</td>
<td>0 more (CI 0 fewer - 0 more)</td>
<td>9252 (10 studies)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Confidence in effect estimates</td>
<td>Relative effect</td>
<td>No prophylaxis</td>
<td>Heparin</td>
<td>Difference with</td>
<td>Participants (studies), Follow-up</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------------------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>---------</td>
<td>----------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate</td>
<td>RR: 0.44</td>
<td>13 per 1000</td>
<td>6 per 1000</td>
<td>7 fewer</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td></td>
<td>Risk of bias and partly indirect data</td>
<td>(CI 0.31 - 0.63)</td>
<td></td>
<td></td>
<td>(CI 9 fewer - 5 fewer)</td>
<td></td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate</td>
<td>RR: 0.44</td>
<td>6 per 1000</td>
<td>3 per 1000</td>
<td>3 fewer</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td></td>
<td>Risk of bias and partly indirect data</td>
<td>(CI 0.31 - 0.63)</td>
<td></td>
<td></td>
<td>(CI 4 fewer - 2 fewer)</td>
<td></td>
</tr>
<tr>
<td>Major bleeds (5 weeks)</td>
<td>Moderate</td>
<td>RR: 1.57</td>
<td>4 per 1000</td>
<td>6 per 1000</td>
<td>2 more</td>
<td>12.929 (44 studies)</td>
</tr>
<tr>
<td></td>
<td>Risk of bias and partly indirect data</td>
<td>(CI 1.32 - 1.87)</td>
<td></td>
<td></td>
<td>(CI 1 more - 3 more)</td>
<td></td>
</tr>
<tr>
<td>Bleeds requiring reoperation (5 weeks)</td>
<td>Moderate</td>
<td>RR: 1.57</td>
<td>0 per 1000</td>
<td>0 per 1000</td>
<td>0 more</td>
<td>12.929 (44 studies)</td>
</tr>
<tr>
<td></td>
<td>Risk of bias and partly indirect data</td>
<td>(CI 1.32 - 1.87)</td>
<td></td>
<td></td>
<td>(CI 0 more - 0 more)</td>
<td></td>
</tr>
</tbody>
</table>

PICO References


PICO Summary


**Baseline risk:** The baseline risk of mortality is derived from: Poultsides et al. Meta-analysis of cause of death following total joint replacement using different thromboprophylaxis regimens. J Bone Joint Surg...
In the included studies there were only two deaths 0-42 days postoperatively, both of unknown cause. The study showed no effect of thromboprophylaxis on either all cause mortality or fatal pulmonary embolism. 

The baseline risk of VTE and major bleeding are derived from: Neumann et al. Oral direct Factor Xa inhibitors versus low- molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 ( 10):710 -9. We have applied the incidence rates in the LMWH arm of the included studies and adjusted for the effects of LMWH.

**Quality of the evidence:** Of the studies included in the systematic review by Collins et al there were several studies that were not blinded and allocation procedure were not sufficiently described. There was a certain degree of heterogeneity across studies on the effect on non-fatal pulmonary embolism, but this is not significant. The included population underwent general surgery. We however believe that the relative effect is similar for orthopedic patients, which is supported by other findings in Collins extended meta-analysis. The relative effect on symptomatic DVTs is believed to be the same as for non-fatal pulmonary embolism.

**Mortality:** As the meta-analysis by Poultsides et al did not include enough patients to demonstrate any effect of thromboprophylaxis on mortality, we derived the relative effect estimates of thromboprophylaxis on mortality using indirect data from a recent large meta-analysis on internal medicine patients (Lederle et al).

**Wound complications, including infection:** Jameson et al found that of a total of 85,642 patients with hip arthroplasty recorded in the National Joint Registry for England and Wales, 312 (0.36 %) were re-operated due to wound complications.

**PICO (2.2)**

**Population:** Thromboprophylaxis in patients at high risk of VTE  
**Intervention:** Heparin  
**Comparator:** No prophylaxis  
**Outcomes:** DVT, non-fatal pulmonary embolism

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
</table>
| DVT (5 weeks)                         | Moderate

**Risk of bias and indirectness of borderline importance.**

RR: 0.44  
( CI 0.31 - 0.63)

138 per 1000  
61 per 1000  
77 fewer  
( CI 95 fewer - 51 fewer )

12,698 (22)

| Non-fatal pulmonary embolism (5 weeks) | Moderate

**Risk of bias and indirectness of borderline importance.**

RR: 0.44  
( CI 0.31 - 0.63)

69 per 1000  
30 per 1000  
39 fewer  
( CI 48 fewer - 28 fewer )

12,698 (22)
Outcomes | Confidence in effect estimates | Relative effect | No prophylaxis | Heparin | Difference with | Participants (studies), Follow-up
---|---|---|---|---|---|---
Major bleed (5 weeks) | Moderate | RR: 1.57 (CI 1.32 - 1.87) | 4 per 1000 | 6 per 1000 | 2 more (CI 1 more - 3 more) | 12,929 (44)

PICO References

PICO Summary

Baseline risk: The risk of VTE without prophylaxis is based on partially indirect data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rate is adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. The baseline risks for high-risk patients are then calculated by using the adjusted NPR data and applying relative estimates from Pedersen et al, who found a relative risk increase of VTE of 5.3 (95% CI 3.99 to 7.05) in patients with previous venous thrombosis. For other patient categories they found a relative risk increase of 1.58 (1.01 to 2.47) in patients > 80 years and RR 1.73 (1.24 to 2.41) in patients with three or more points on the Charlson comorbidity index.
The baseline risk of major bleeding is based on indirect data from a population undergoing total hip or knee arthroplasty: Neumann et al. Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 ( 10):710 -9. It is thus possible that the real absolute incidence of major bleeding is somewhat higher than what we use here.

Quality of the documentation: For all outcomes except mortality, the quality is downgraded to moderate as several of the studies included in Collins’ meta-analysis were not blinded and there was an inadequate description of the allocation procedures. A certain degree of heterogeneity was
observed across studies for the effect on non-fatal pulmonary emboli. The included studies were on patients undergoing general surgery, but adding Collins’ studies on orthopedic surgeries did not significantly change the relative effect estimate.

**Weak Recommendation**

We suggest extending thromboprophylaxis for up to 35 days after surgery.

**Practical Advice**

For patients with liver or kidney disease, low body weight, age over 75 years or patients on drugs with the possibility of interactions with the new oral anticoagulants, we recommend to adjust the dose according to the drug information or to choose an alternative drug.

**Risk factors for thromboembolic events (VTE)**

In the absence of validated risk scores we have identified the following risk factors:

- Previous VTE (relative risk increase of 5.3)
- Age 80 years or older (relative risk increase of 1.58)
- High degree of comorbidities (at least 3 points on the Charlson Comorbidity index. Relative risk increase of 1.73)

**Suggested dosage** (patients with a hip fracture should only use LMWH)

- **Sc LMWH:** either dalteparin 5000 IU, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 12 hours before or after surgery
- Apixaban 2.5 mg x 2 started 12 hours after surgery
- Dabigatran 110 mg for the first dose, followed by 220 mg x 1 started 1-4 hours after surgery
- Rivaroxaban 10 mg x 1 started 6-10 hours after surgery

**Charlson comorbidity index:**

- 0 points = low risk. 1-2 points = moderate risk. 3 points or higher = high risk

<table>
<thead>
<tr>
<th>Points</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Metastatic solid tumor</td>
</tr>
<tr>
<td></td>
<td>AIDS</td>
</tr>
<tr>
<td>3</td>
<td>Moderate to serious liver disease</td>
</tr>
<tr>
<td>2</td>
<td>Diabetes with end-organ damage</td>
</tr>
<tr>
<td></td>
<td>Moderate to serious kidney disease</td>
</tr>
<tr>
<td></td>
<td>Malignant tumor</td>
</tr>
<tr>
<td></td>
<td>Leukemia or lymphoma</td>
</tr>
<tr>
<td></td>
<td>Hemiplegia</td>
</tr>
<tr>
<td>1</td>
<td>Chronic heart failure</td>
</tr>
</tbody>
</table>

6 points

6 points

3 points

3 points

2 points

2 points

1 point
Cardiovascular disease: Previous myocardial infarction, peripheral artery disease, stroke or TIA
Chronic pulmonary disease
Mild liver disease
Stomach ulcer
Diabetes without complications
Connective tissue disease
Dementia

ASA physical status classification system

<table>
<thead>
<tr>
<th>ASA</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA1</td>
<td>Healthy patient. No organic, physiological, biochemical or psychiatric disorder. The condition to be treated is localised and does not cause any systemic disturbances. Less than 5 cigarettes per day. The patient is under 80 years of age.</td>
</tr>
<tr>
<td>ASA2</td>
<td>Moderate organic disease or disturbance not causing functional limitations, but might result in specific precautions being made or certain anesthetic measures. The disease(s) can either be caused by the condition that is to be treated or by another pathological process. Age over 80 or newborns younger than 3 months. More than 5 cigarettes per day.</td>
</tr>
<tr>
<td>ASA3</td>
<td>Serious organic disease or disturbance that causes defined functional limitations.</td>
</tr>
<tr>
<td>ASA4</td>
<td>Life threatening organic disease that is not necessarily related to the condition that is to be treated or will be improved by the surgical procedure.</td>
</tr>
<tr>
<td>ASA5</td>
<td>Moribund patient not expected to survive the next 24 hours, with or without surgery.</td>
</tr>
</tbody>
</table>

Key Info

Benefits and harms
Patients with one or more patient-specific risk factors for thrombosis have an up to 6-fold increased risk of venous thromboembolism.
For 1000 patients not receiving thromboprophylaxis we expect (worst case scenario):
139 DVTs and 69 pulmonary emboli during the first 5 weeks following surgery.
With prophylaxis (LMWH/UFH) the incidence is substantially reduced to 61 and 30 per 1000 patients, respectively.

Approximately 2/3 of VTE cases occur during the first two weeks following surgery.

We do not anticipate any effect of thromboprophylaxis on the rate of fatal pulmonary emboli. For absolute risks of major bleeding we refer to the specific recommendations for the each surgery.

Quality of evidence
Overall the quality of the evidence is moderate, with relative effect estimates derived from a meta-analysis with possible risk of bias in the included studies. The baseline risk of VTE is
derived from the National Patient Registry (NPR) for the period 2008-11 and a Danish registry study (for high-risk patients).

Preference and values
Given the high risk of VTE we believe all or nearly all patients will elect to use short-term prophylaxis provided that they do not have contraindications such as an increased risk of bleeding. The burden of self-injecting with LMWH over weeks may result in some patients not wanting extended prophylaxis and clinicians should be sensitive to patient preferences in this case.

Resources and other considerations
Apixaban, rivaroxaban and dabigatran have labeled use and pre-approved reimbursement for elective total hip or knee arthroplasty.

Rationale
Our weak recommendation for extended thromboprophylaxis in moderate to high risk patients takes into consideration the anticipated modest absolute effects in reducing thromboembolic events weighed against the increased risk of bleeds and burden of treatment, particularly with LMWH self-injections. Clinicians should consider individual patient factors (e.g. mobilization capability and bleeding risk) and preferences when applying this recommendation in practice.

We have derived the baseline risk estimates from the National Patient Registry (NPR) in Norway, applying VTE incidence rates in patients following surgery for hip fractures, and recognize the resulting inherent uncertainty for our absolute effect estimates. We have assumed that all patients registered in the NPR received extended thromboprophylaxis and have taken into account the relative risk increase due to various patient specific factors. All in all, this results in a conservative calculation that rather over- than underestimates the risk of not using thromboprophylaxis.

We believe it to be important that patients are mobilized as soon as possible after surgery, but the evidence that this affects the incidence rates of VTE is lacking.

From studies on major hip or knee arthroplasty we have evidence that thromboprophylaxis does not affect the incidence of fatal pulmonary emboli. However, studies have shown that thromboprophylaxis might effect all-cause mortality in patients with hip fractures. We are uncertain whether the positive effect on mortality is due to the orthopedic condition itself or to the patient's age and number of comorbidities.
For more information, we refer to the specific recommendations for each type of surgery.

References

Gomez-Outes et al. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis. BMJ 2012;344:e3675 22700784 10.1136/bmj.e3675


PICO (2.1)

Population: Thromboprophylaxis in patients at moderate risk of VTE

Intervention: Heparin

Comparator: No prophylaxis

Outcomes: DVT, non-fatal pulmonary embolism

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with (participants, follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>45 per 1000</td>
<td>20 per 1000</td>
<td>25 fewer (CI 31 fewer - 17 fewer) (22)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>22 per 1000</td>
<td>10 per 1000</td>
<td>12 fewer (CI 15 fewer - 8 fewer) (22)</td>
</tr>
<tr>
<td>Major bleed (5 weeks)</td>
<td>Moderate risk of bias and indirectness of borderline importance</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>4 per 1000</td>
<td>6 per 1000</td>
<td>2 more (CI 1 more - 3 more) (44)</td>
</tr>
</tbody>
</table>

PICO References


**PICO Summary**


**Baseline risk:** The risk of VTE without prophylaxis is based on partially indirect data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rate is adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. The baseline risks for high-risk patients are then calculated by using the adjusted NPR data and applying relative estimates from Pedersen et al, who found a relative risk increase of VTE of 5.3 (95% CI 3.99 to 7.05) in patients with previous venous thrombosis. For other patient categories they found a relative risk increase of 1.58 (1.01 to 2.47) in patients > 80 years and RR 1.73 (1.24 to 2.41) in patients with three or more points on the Charlson comorbidity index.

The baseline risk of major bleeding is based on indirect data from a population undergoing total hip or knee arthroplasty: Neumann et al. Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 (10):710-9. It is thus possible that the real absolute incidence of major bleeding is somewhat higher than what we use here.

**Quality of the documentation:** For all outcomes except mortality, the quality is downgraded to moderate as several of the studies included in Collins’ meta-analysis were not blinded and there was an inadequate description of the allocation procedures. A certain degree of heterogeneity was observed across studies for the effect on non-fatal pulmonary emboli. The included studies were on patients undergoing general surgery, but adding Collins’ studies on orthopedic surgeries did not significantly change the relative effect estimate.

**PICO (2.2)**

**Population:** Thromboprophylaxis in patients at high risk of VTE

**Intervention:** Heparin

**Comparator:** No prophylaxis

**Outcomes:** DVT, non-fatal pulmonary embolism
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>138 per 1000</td>
<td>61 per 1000</td>
<td>77 fewer (CI 95 fewer - 51 fewer)</td>
<td>12.698 (22)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance.</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>69 per 1000</td>
<td>30 per 1000</td>
<td>39 fewer (CI 48 fewer - 28 fewer)</td>
<td>12.698 (22)</td>
</tr>
<tr>
<td>Major bleed (5 weeks)</td>
<td>Moderate Risk of bias and indirectness of borderline importance</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>4 per 1000</td>
<td>6 per 1000</td>
<td>2 more (CI 1 more - 3 more)</td>
<td>12.929 (44)</td>
</tr>
</tbody>
</table>

**PICO References**


**PICO Summary**


**Baseline risk:** The risk of VTE without prophylaxis is based on partially indirect data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rate is adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. The baseline risks for high-risk patients are then calculated by using the adjusted NPR data and applying relative estimates from Pedersen et al, who found a relative risk increase of VTE of 5.3 (95 % CI 3.99 to 7.05) in patients with previous venous thrombosis. For other patient categories they found a relative risk increase of 1.58 (1.01 to 2.47) in patients > 80 years and RR 1.73 (1.24 to 2.41) in patients with three or more points on the Charlson comorbidity index.
The baseline risk of major bleeding is based on indirect data from a population undergoing total hip or knee arthroplasty: Neumann et al. Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 ( 10):710 -9. It is thus possible that the real absolute incidence of major bleeding is somewhat higher than what we use here.

**Quality of the documentation:** For all outcomes except mortality, the quality is downgraded to moderate as several of the studies included in Collins' meta-analysis were not blinded and there was an inadequate description of the allocation procedures. A certain degree of heterogeneity was observed across studies for the effect on non-fatal pulmonary emboli. The included studies were on patients undergoing general surgery, but adding Collins' studies on orthopedic surgeries did not significantly change the relative effect estimate.
3 - Major orthopedic surgery: patients at low risk of thrombosis

Total Hip and Knee Arthroplasty

**Weak Recommendation**

We suggest thromboprophylaxis with low molecular weight heparin, low-dose direct factor Xa inhibitor (apixaban, rivaroxaban) or dabigatran for the first 10 postoperative days.

We suggest against extending thromboprophylaxis beyond 10 days.

**Practical Advice**

For patients with liver or kidney disease, low body weight, age over 75 years or patients on drugs with the possibility of interactions with the new oral anticoagulants, we recommend to adjust the dose according to the drug information or to choose an alternative drug.

**Risk factors for thromboembolic events (VTE)**

In the absence of validated risk scores we have identified the following risk factors:

- Previous VTE (relative risk increase of 5.3)
- Age 80 years or older (relative risk increase of 1.58)
- High degree of comorbidities (at least 3 points on the Charlson Comorbidity index. Relative risk increase of 1.73)

**Suggested dosage** (patients with a hip fracture should only use LMWH)

- **Sc LMWH:** either dalteparin 5000 IU, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 12 hours before or after surgery
- Apixaban 2.5 mg x 2 started 12 hours after surgery
- Dabigatran 110 mg for the first dose, followed by 220 mg x 1 started 1-4 hours after surgery
- Rivaroxaban 10 mg x 1 started 6-10 hours after surgery

**Key Info**

**Benefits and harms**

**Risk of thrombosis without thromboprophylaxis per 1.000 patients for the first 5 postoperative weeks:**

- 13 symptomatic DVTs + 6 pulmonary emboli (LE).

With thromboprophylaxis this is reduced to 6 symptomatic DVTs and 3 pulmonary emboli.

- Approximately 2/3 of VTEs occur during the first two postoperative weeks.

- Using prophylaxis for 30 days increases the number of major bleeds with 2 per 1.000 patients (from 4 to 6/1000), but does not affect the number of reoperations due to bleeding.

**Quality of evidence**
Overall moderate quality of the evidence. The baseline risk of VTE is derived from compiled data from the control arms of the recent randomized trials on the new oral anticoagulants versus LMWH. The relative effect of thromboprophylaxis is derived from three meta-analysis and one cohort study with possible risk of bias. The quality of the evidence is further downgraded because of use of indirect data as the included studies were on a patients undergoing general surgery.

Preference and values
We believe that most patients will choose short-term prophylaxis although the absolute reduction of VTE is moderate, given that the risks of prophylaxis is considered to be relatively small. We believe, however, that most patients will choose to refrain from extended thromboprophylaxis as this provides only a marginal additional benefit closely balanced with an increased risk of major bleeds.

Resources and other considerations
The cost-effectiveness of thromboprophylaxis in these patients is questionable. A cost-benefit analysis is currently being conducted and may influence the final recommendation.

Rationale
Historical data show a substantially higher baseline risk of postoperative thromboembolic events than registry (NPR) data provides evidence for. Updated surgical techniques and active rehabilitation with early mobilization has led to declining incidence rates of VTE. Furthermore, studies on thromboprophylaxis have often included screening of DVT, and have thus reported both asymptomatic and symptomatic cases. Asymptomatic DVT is unlikely to have clinical significance, i.e. they are not considered to require treatment.

We have derived the baseline risk of VTE from the control arm in a recent meta-analysis of up to 21 studies on LMWH versus NOAC. In the calculation we have assumed that all patients received extended thromboprophylaxis for 5 weeks, this not being the actual case as some patients received thromboprophylaxis for a substantial shorter time period. We have in parallel collected data from the National Patient Registry (NPR) for the period from 2008 to 2011; finding that these data correspond well with incidence rates reported in recent randomized trials. We have applied a conservative calculation that rather over- than underestimates the risk of not using thromboprophylaxis.

We believe that it is important that patients are mobilized as soon as possible after surgery, but the evidence of the benefits of this approach is currently limited.

There have been arguments against the new oral anticoagulants as their lack of an antidote may increase the risk of having to postpone any urgent reoperation, increasing the risk of infection. This is however not a frequent problem, as we are expecting less than one reoperation due to bleeding per 1000 patients receiving thromboprophylaxis. Lack of long-term data is another argument against NOACs, but it is unlikely that time will uncover any serious issues, as thromboprophylaxis is administered for such a short time period.

The guideline panel considered a baseline incidence of up to 10 symptomatic DVTs and 10 pulmonary emboli per 1.000 patients operated insufficient to warrant a recommendation in favor of thromboprophylaxis to all patients undergoing arthroplasty due to small absolute benefits. We have
therefore opted for a weak recommendation in favor of limited thromboprophylaxis as we believe that the decision should be made as part of a shared decision making between the orthopedic surgeon and the individual patient. We suggest against extended thromboprophylaxis due to a minimal additional risk reduction. Orthopedic surgeons may consider extending thromboprophylaxis in selected patients at increased risk of VTE, with an expected greater benefit of treatment.

References


Gomez-Outes et al. Dabigatran, rivaroxaban, or apixaban versus enoxaparin for thromboprophylaxis. BMJ 2012;344:e3675 22700784 10.1136/bmj.e3675


PICO (3.1)

Population: Thromboprophylaxis in total hip or knee arthroplasty

Intervention: Heparin

Comparator: No prophylaxis

Outcomes: Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds, bleeds that require reoperation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Imprecise estimates and use of indirect data</td>
<td>RR: 1.01 (CI 0.68 - 1.48)</td>
<td>1 per 1000</td>
<td>0 per 1000</td>
<td>0 more (CI 0 fewer - 0 more)</td>
<td>9252 (10 studies)</td>
</tr>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>13 per 1000</td>
<td>6 per 1000</td>
<td>7 fewer (CI 9 fewer - 5 fewer)</td>
<td>12.698 (22 studies)</td>
</tr>
</tbody>
</table>
### Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>6 per 1000</td>
<td>3 per 1000</td>
<td>3 fewer (CI 4 fewer - 2 fewer)</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td>Major bleeds (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>4 per 1000</td>
<td>6 per 1000</td>
<td>2 more (CI 1 more - 3 more)</td>
<td>12.929 (44 studies)</td>
</tr>
<tr>
<td>Bleeds requiring reoperation (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>0 per 1000</td>
<td>0 per 1000</td>
<td>0 more (CI 0 more - 0 more)</td>
<td>12.929 (44 studies)</td>
</tr>
</tbody>
</table>

### PICO References


### PICO Summary


**Baseline risk**: The baseline risk of mortality is derived from: Poultsides et al. Meta-analysis of cause of death following total joint replacement using different thromboprophylaxis regimens. J Bone Joint Surg Br. 2012, 94-B:113 -21. In the included studies there were only two deaths 0-42 days postoperatively, both of unknown cause. The study showed no effect of thromboprophylaxis on either all cause mortality or fatal pulmonary embolism.

The baseline risk of VTE and major bleeding are derived from: Neumann et al. Oral direct Factor Xa
inhibitors versus low-molecular-weight heparin to preventable venous thromboembolism in Patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med. 2012 May 15; 156 (10):710-9. We have applied the incidence rates in the LMWH arm of the included studies and adjusted for the effects of LMWH.

Quality of the evidence: Of the studies included in the systematic review by Collins et al there were several studies that were not blinded and allocation procedure were not sufficiently described. There was a certain degree of heterogeneity across studies on the effect on non-fatal pulmonary embolism, but this is not significant. The included population underwent general surgery. We however believe that the relative effect is similar for orthopedic patients, which is supported by other findings in Collins extended meta-analysis. The relative effect on symptomatic DVTs is believed to be the same as for non-fatal pulmonary embolism.

Mortality: As the meta-analysis by Poultsides et al did not include enough patients to demonstrate any effect of thromboprophylaxis on mortality, we derived the relative effect estimates of thromboprophylaxis on mortality using indirect data from a recent large meta-analysis on internal medicine patients (Lederle et al).

Wound complications, including infection: Jameson et al found that of a total of 85,642 patients with hip arthroplasty recorded in the National Joint Registry for England and Wales, 312 (0.36%) were re-operated due to wound complications.

Fast-track general joint replacement surgery

**Weak Recommendation**

We suggest thromboprophylaxis with low-molecular-weight heparin until discharge (1-4 days). We suggest against extending thromboprophylaxis beyond discharge.

**Practical Advice**

If increased risk of bleeding, including recent use of antiplatelet agents (e.g. aspirin) and low platelet count, we suggest not to use thromboprophylaxis.

Suggested dosage of s.c. low-molecular-weight heparin: dalteparin 5000 IU x 1, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 6-8 hours after surgery.

This recommendation is based on the fast track protocol as described by Husted et al. 2010 with a modification of the startup time.

**Key Info**

**Benefits and harms**

- 1-4 days of thromboprophylaxis with low-molecular-weight heparin reduces the number of DVTs from 10 to 5/1000 patients and reduces the rate of pulmonary emboli from 9 to 3/1000
during the first 30 postoperative days. During the following 60 postoperative days we expect only 1 additional symptomatic DVT.

There are no data on the risk of major bleeds.

**Quality of evidence**
Moderate quality evidence, with relative effect estimates derived from a meta-analysis of randomized trials on patients undergoing general surgery, with potential risk of bias. Baseline risk estimates are derived from a large cohort study of high quality considered applicable to Norway.

**Preference and values**
We believe that most patients will choose thromboprophylaxis although the absolute reduction of thromboembolic events is moderate, given the modest burden of short term self-injections.

**Resources and other considerations**
No increased resource requirements.

**Rationale**
We believe most patients will value the absolute reduction in venous thromboembolic events enough to accept self-injections with LMWH over a few days. Using short-term drug treatment with a delayed start-up will also likely reduce the risk of seepage from the wound, bleeding and deep wound infections. We have not included low-dose direct factor Xa inhibitor (apixaban, rivaroxaban) or dabigatran as they have not yet been studied in this population.

**References**

**PICO (3.3)**
**Population:** Thromboprophylaxis in fast-track surgery
**Intervention:** Heparin
**Comparator:** No prophylaxis
**Outcomes:** DVT, fatal and non-fatal pulmonary emboli, major bleeding
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal pulmonary embolism</td>
<td>Moderate Imprecise estimates</td>
<td>RR: 1.01 (CI 0.68 - 1.48)</td>
<td>1 per 1000</td>
<td>0 per 1000</td>
<td>0 more (CI 0 fewer - 0 more )</td>
<td>13.452 (30 studies)</td>
</tr>
<tr>
<td>DVT</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>10 per 1000</td>
<td>4 per 1000</td>
<td>6 fewer (CI 7 fewer - 4 fewer )</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>7 per 1000</td>
<td>3 per 1000</td>
<td>4 fewer (CI 5 fewer - 3 fewer )</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td>Major bleeds</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>5 per 1000</td>
<td>8 per 1000</td>
<td>3 more (CI 2 more - 4 more )</td>
<td>12.929 (44 studies)</td>
</tr>
</tbody>
</table>

**PICO References**


**PICO Summary**


**Quality of the evidence**: For all outcomes except for mortality we rated down the quality of the evidence to moderate as several studies included in the Collins' meta-analysis were not blinded, did not clearly describe randomization procedures and there was a certain degree of heterogeneity across studies on relative effect of non-fatal pulmonary embolism.
Fractures of the proximal femur: surgery with prosthesis or osteosynthesis

Strong Recommendation

We recommend thromboprophylaxis with low-molecular-weight heparin (LMWH) for the first 10 postoperative days.

Practical Advice

Risk factors for thromboembolic events (VTE):
In the absence of validated risk scores we have identified the following risk factors:
- Previous VTE (relative risk increase of 5.3)
- Age 80 years or older (relative risk increase of 1.58)
- High degree of comorbidities (at least 3 points on the Charlson Comorbidity index. Relative risk increase of 1.73)

If the patient has an increased risk of bleeding, including recent use of antiplatelet agent (eg. aspirin) and a low platelet count, we suggest to not use thromboprophylaxis.

Suggested dosage:
- Sc LMWH: either dalteparin 5000 IU, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 12 hours before or after surgery

Key Info

Benefits and harms
Risk of VTE without thromboprophylaxis per 1000 patients during the first 5 postoperative weeks:
26 symptomatic DVTs and 13 pulmonary emboli.
With thromboprophylaxis the incidence of VTE is reduced to 11 DVTs and 6 pulmonary emboli per 1000 treated patients.

Approximately 2/3 of VTE events occur during the first two postoperative weeks.

Thromboprophylaxis does not reduce the rate of fatal pulmonary emboli. The rate of all cause mortality is however reduced from 34 to 28/1000 patients during hospitalization with an additional 11 fewer deaths during the next 30 days.

With thromboprophylaxis the rate of bleeding requiring transfusions increases from 24 to 38/1000 patients over the course of 35 days.

Quality of evidence
Moderate quality of the evidence. The recommendation is based on data from the National Patient Registry for the period 2008-11, a meta-analysis and a cohort study.

Preference and values
We believe that virtually all patients will choose thromboprophylaxis despite the moderate absolute reduction of VTE events, given a likely positive effect on mortality and a relatively modest risk profile.
Resources and other considerations
No increased resource demands.

Rationale
We believe it to be important that patients are mobilized as soon as possible after surgery, but the evidence on the positive effect of this is lacking.

When calculating the baseline risk of VTE, based on data from the National Patient Registry, we have assumed that all patients received extended thromboprophylaxis. We know that this is incorrect, but we do not know which patients received thromboprophylaxis, over what period of time, or which of them experienced any complications. We have therefore opted for a conservative approach, rather over- than underestimating the risk of not using thromboprophylaxis.

Studies on arthroplastic surgery have not shown an effect of thromboprophylaxis on the incidence of fatal pulmonary emboli. There has however been shown a positive effect on all-cause mortality in patients with hip fractures, but keeping in mind that a cohort study showed that deep wound infections resulted in a threefold increase in 30-day mortality.

We are uncertain whether the mortality reducing effect of thromboprophylaxis is due to the orthopedic condition itself or the patient's age and comorbidities. The apparent effect on mortality is nevertheless why we give a weak recommendation in favor of extended thromboprophylaxis. The decision regarding extended thromboprophylaxis should be made together with the individual patient.

References

PICO (3.4)
Population: Thromboprophylaxis in patients with a hip fracture
Intervention: Heparin
Comparator: No prophylaxis
Outcomes: Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds, bleeds that require reoperation
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality (5 weeks)</td>
<td>Moderate Imprecise estimates</td>
<td>RR: 0.82</td>
<td>94 per 1000</td>
<td>77 per 1000</td>
<td>17 fewer</td>
<td>13,452 (30 studies)</td>
</tr>
<tr>
<td>DVT (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>26 per 1000</td>
<td>11 per 1000</td>
<td>15 fewer (CI 18 fewer - 10 fewer)</td>
<td>12,698 (22 studies)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>13 per 1000</td>
<td>6 per 1000</td>
<td>7 fewer (CI 9 fewer - 5 fewer)</td>
<td>12,698 (22 studies)</td>
</tr>
<tr>
<td>Bleeding requiring transfusion (5 weeks)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>24 per 1000</td>
<td>38 per 1000</td>
<td>14 more (CI 8 more - 21 more)</td>
<td>12,929 (44 studies)</td>
</tr>
</tbody>
</table>

**PICO References**

**PICO Summary**

**Baseline risk:** The risk of VTE and all cause mortality without prophylaxis is based on data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rates are adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. This probably overestimates the baseline risk. We believe that the reported incidence rates of pulmonary emboli to be credible, but that the rates of DVT have been underreported to the registry. We have therefore, based on incidence rates in randomized trials, applied a ratio of 2:1 between DVT and pulmonary emboli and calculated the baseline estimates of DVT based on the reported incidence of pulmonary emboli to the registry.
For bleeds the baseline risk is based on data from the placebo arm of the PEP trial: (Pulmonary Embolism Prevention (PEP) Trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet. 2000;355(9212):1295-1302. This study only reported rates of bleeding requiring transfusions, which is a broader term than major bleeds.


**Mortality:** According to a meta-analysis by Poultsides et al. (2012) all-cause mortality is divided accordingly: 25% due to fatal pulmonary embolism, 9% due to fatal bleeds and 48% due to other cardiopulmonary causes.

---

**Weak Recommendation**

We suggest extending thromboprophylaxis for up to 35 days following surgery.

**Practical Advice**

**Risk factors for thromboembolic events (VTE):**

In the absence of validated risk scores we have identified the following risk factors:

- Previous VTE (relative risk increase of 5.3)
- Age 80 years or older (relative risk increase of 1.58)
- High degree of comorbidities (at least 3 points on the Charlson Comorbidity index. Relative risk increase of 1.73)

If the patient has an increased risk of bleeding, including recent use of antiplatelet agent (eg. aspirin) and a low platelet count, we suggest to not use thromboprophylaxis.

**Suggested dosage:**

Sc LMWH: either dalteparin 5000 IU, enoxaparin 40 mg x 1 or tinzaparin 4500 IU x 1 started 12 hours before or after surgery

**Key Info**

**Benefits and harms**

Risk of VTE without thromboprophylaxis per 1000 patients during the first 5 postoperative weeks:

- 26 symptomatic DVTs and 13 pulmonary emboli.

With thromboprophylaxis the incidence of VTE is reduced to 11 DVTs and 6 pulmonary emboli per 1000 treated patients.

Approximately 2/3 of VTE events occur during the first two postoperative weeks.

Thromboprophylaxis does not reduce the rate of fatal pulmonary emboli. The rate of all cause mortality is however reduced from 34 to 28/1000 patients during hospitalization and there are an additional 11 fewer deaths during the next 30 days.
With thromboprophylaxis the rate of bleeding requiring transfusions increases from 24 to 38/1000 patients over the course of 35 days.

**Quality of evidence**
Moderate quality of the evidence. The recommendation is based on data from the National Patient Registry for the period 2008-11, a meta-analysis and a cohort study.

**Preference and values**
We believe that virtually all patients will choose thromboprophylaxis despite the moderate absolute reduction of VTE events, given a likely positive effect on mortality and a relatively modest risk profile.

**Resources and other considerations**
No increased resource demands.

**Rationale**
We believe it to be important that patients are mobilized as soon as possible after surgery, but the evidence on the positive effect of this is lacking.

When calculating the baseline risk of VTE, based on data from the National Patient Registry, we have assumed that all patients received extended thromboprophylaxis. We know that this is incorrect, but we do not know which patients received thromboprophylaxis, over what period of time, or which of them experienced any complications. We have therefore opted for a conservative approach, rather than over- than underestimating the risk of not using thromboprophylaxis.

Studies on arthroplastic surgery have not shown an effect of thromboprophylaxis on the incidence of fatal pulmonary emboli. There has however been shown a positive effect on all-cause mortality in patients with hip fractures, but keeping in mind that a cohort study showed that deep wound infections resulted in a threefold increase in 30-day mortality.

We are uncertain whether the mortality reducing effect of thromboprophylaxis is due to the orthopedic condition itself or the patient's age and comorbidities. The apparent effect on mortality is nevertheless why we give a weak recommendation in favor of extended thromboprophylaxis. The decision regarding extended thromboprophylaxis should be made together with the individual patient.

**References**
## PICO (3.4)

**Population:** Thromboprophylaxis in patients with a hip fracture  
**Intervention:** Heparin  
**Comparator:** No prophylaxis  
**Outcomes:** Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds, bleeds that require reoperation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
</table>
| All cause mortality (5 weeks)   | Moderate imprecise estimates   | RR: 0.82  
(CI 0.69 - 0.99) | 94             per 1000 | 77            per 1000 | 17 fewer  
(CI 29 fewer - 1 fewer) | 13.452 (30 studies) |
| DVT (5 weeks)                   | Moderate Risk of bias and partly indirect data | RR: 0.44  
(CI 0.31 - 0.63) | 26             per 1000 | 11            per 1000 | 15 fewer  
(CI 18 fewer - 10 fewer) | 12.698 (22 studies) |
| Non-fatal pulmonary embolism (5 weeks) | Moderate Risk of bias and partly indirect data | RR: 0.44  
(CI 0.31 - 0.63) | 13             per 1000 | 6             per 1000 | 7 fewer  
(CI 9 fewer - 5 fewer) | 12.698 (22 studies) |
| Bleeding requiring transfusion (5 weeks) | Moderate Risk of bias and partly indirect data | RR: 1.57  
(CI 1.32 - 1.87) | 24             per 1000 | 38             per 1000 | 14 more  
(CI 8 more - 21 more) | 12.929 (44 studies) |

### PICO References


### PICO Summary

**Baseline risk:** The risk of VTE and all cause mortality without prophylaxis is based on data from the National Patient Registry (NPR) on all patients with hip fractures in the period 2008-2011 with a total of 27,805 patients. The reported incidence rates are adjusted for the effect of LMWH. We calculated a conservative baseline estimate as we assumed all patients received thromboprophylaxis for 30 days after discharge. This probably overestimates the baseline risk. We believe that the reported incidence rates of pulmonary emboli to be credible, but that the rates of DVT have been underreported to the registry. We have therefore, based on incidence rates in randomized trials, applied a ratio of 2:1 between DVT and pulmonary emboli and calculated the baseline estimates of DVT based on the reported incidence of pulmonary emboli to the registry.

For bleeds the baseline risk is based on data from the placebo arm of the PEP trial: (Pulmonary Embolism Prevention (PEP) Trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet. 2000;355(9212):1295-1302. This study only reported rates of bleeding requiring transfusions, which is a broader term than major bleeds.


**Mortality:** According to a meta-analysis by Poultsides et al. (2012) all-cause mortality is divided accordingly: 25% due to fatal pulmonary embolism, 9% due to fatal bleeds and 48% due to other cardiopulmonary causes.
4 - Other interventions and screening

Extremity injuries distal to the knee, including those that require immobilization

**Strong Recommendation**

We recommend against thromboprophylaxis.

**Practical Advice**

**Key Info**

**Benefits and harms**

Per 1000 patients not on thromboprophylaxis we expect 2 symptomatic DVTs and 2 pulmonary emboli during the first 90 days following surgery. With thromboprophylaxis this is reduced to 1 DVT and 1 pulmonary embolism.

There is no effect on number of fatal pulmonary emboli. The number of major bleeds increases from 5 to 8/1000 patients on thromboprophylaxis.

**Quality of evidence**

Moderate quality evidence. The absolute effect estimates (baseline data) are based on indirect documentation from a large registry study of high quality, considered applicable to Norway.

**Preference and values**

We believe that all or nearly all patients will choose not to take thromboprophylaxis given the marginal benefits on thromboembolic events finely balanced with increased bleeds and the burden of treatment.

**Resources and other considerations**

No increased resource requirements.

**Rationale**

We believe few patients will want thromboprophylaxis given the minimal absolute reduction in venous thromboembolic events, and the risks associated with treatment. We believe it is important that patients are mobilized as soon as possible after surgery, even if the evidence supporting the positive effects is lacking.

Individual patients with additional pathology or injuries giving an increased baseline risk of VTE will fall under the recommendation on patients at moderate to high risk.
References


PICO (4.1)

Population: Thromboprophylaxis in patients with lower leg injuries

Intervention: Heparin

Comparator: No prophylaxis

Outcomes: Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds,

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal pulmonary embolism (during 90 days)</td>
<td>Moderate Large confidence intervals</td>
<td>RR: 1.01 (CI 0.68 - 1.48)</td>
<td>0 per 1000</td>
<td>0 per 1000</td>
<td>0 fewer (CI 0 fewer - 0 fewer)</td>
<td>9252 (10 studies)</td>
</tr>
<tr>
<td>DVT (during 90 days)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>2 per 1000</td>
<td>1 per 1000</td>
<td>1 fewer (CI 1 fewer - 1 fewer)</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (during 90 days)</td>
<td>Moderate Risk of bias and partly indirect data</td>
<td>RR: 0.44 (CI 0.31 - 0.63)</td>
<td>2 per 1000</td>
<td>1 per 1000</td>
<td>1 fewer (CI 1 fewer - 1 fewer)</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td>Major bleeding (up to 30 days after discharge)</td>
<td>Moderate Risk of bias and partially indirect data</td>
<td>RR: 1.57 (CI 1.32 - 1.87)</td>
<td>5 per 1000</td>
<td>8 per 1000</td>
<td>3 more (CI 2 more - 4 more)</td>
<td>12.929 (44)</td>
</tr>
</tbody>
</table>

PICO References


PICO Summary


Quality of the evidence: For all outcomes except for mortality we rated down the quality of the evidence to moderate as several studies included in the Collins’ meta-analysis were not blinded, did not clearly describe allocation procedures and there was a certain degree of heterogeneity across studies on relative effect of non-fatal pulmonary embolism.

Arthroscopic surgery of the knee and ankle

Strong Recommendation
We recommend against thromboprophylaxis.

Practical Advice

Key Info

Benefits and harms
Per 1000 patients not on thromboprophylaxis we expect 2 symptomatic DVTs and 2 pulmonary emboli during the first 90 days following surgery. With thromboprophylaxis this is reduced to 1 DVT and 1 pulmonary embolism.

There is no effect on number of fatal pulmonary emboli. The number of major bleeds increases from 5 to 8/1000 patients on thromboprophylaxis.

Quality of evidence
Moderate quality of the evidence, downgraded due to uncertain applicability of the relative
effect estimates derived from a meta-analysis of randomized trials of different surgical
populations. With regards to the baseline estimates of VTE and major bleeds we have high
confidence in the effect estimates, based on a large registry study of high quality with full
applicability to a Norwegian setting.

Preference and values
We believe that all or nearly all patients will choose not to take thromboprophylaxis given the
marginal benefits on thromboembolic events finely balanced with increased bleeds and the
burden of treatment.

Resources and other considerations
No increased resource requirements.

Rationale
We believe few patients will appreciate the minimal absolute reduction in venous thromboembolic
events sufficiently to accept the risks of thromboprophylaxis. We believe it is important to
mobilize patients as soon as possible after surgery, but the evidence of the positive effects of this is
lacking.

References
Collins et al. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative
NEJM198805053181805
22315265 10.1378/chest.11-2404
Neumann et al. Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to prevent venous
thromboembolism in patients undergoing total hip or knee replacement: a systematic review and
0003-4819-156-10-201205150-00421
Maletis et al. Incidence of symptomatic venous thromboembolism after elective knee arthroscopy. J

PICO (4.2)
Population: Thromboprophylaxis in arthroscopy in knee or ankle
Intervention: Heparin
Comparator: No prophylaxis
Outcomes: Fatal pulmonary embolism, DVT, non-fatal pulmonary embolism, major bleeds,
<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No prophylaxis</th>
<th>Heparin</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal pulmonary embolism (during 90 days)</td>
<td>Moderate</td>
<td>RR: 1.01</td>
<td>0 per 1000</td>
<td>0 per 1000</td>
<td>0 fewer</td>
<td>9252 (10 studies)</td>
</tr>
<tr>
<td></td>
<td><em>Large confidence intervals</em></td>
<td>(CI 0.68 - 1.48)</td>
<td></td>
<td></td>
<td>(CI 0 fewer - 0 fewer)</td>
<td></td>
</tr>
<tr>
<td>DVT (during 90 days)</td>
<td>Moderate</td>
<td>RR: 0.44</td>
<td>2 per 1000</td>
<td>1 per 1000</td>
<td>1 fewer</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td></td>
<td><em>Risk of bias and partly indirect data</em></td>
<td>(CI 0.31 - 0.63)</td>
<td></td>
<td></td>
<td>(CI 1 fewer - 1 fewer)</td>
<td></td>
</tr>
<tr>
<td>Non-fatal pulmonary embolism (during 90 days)</td>
<td>Moderate</td>
<td>RR: 0.44</td>
<td>2 per 1000</td>
<td>1 per 1000</td>
<td>1 fewer</td>
<td>12.698 (22 studies)</td>
</tr>
<tr>
<td></td>
<td><em>Risk of bias and partly indirect data</em></td>
<td>(CI 0.31 - 0.63)</td>
<td></td>
<td></td>
<td>(CI 1 fewer - 1 fewer)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding (up to 30 days after discharge)</td>
<td>Moderate</td>
<td>RR: 1.57</td>
<td>5 per 1000</td>
<td>8 per 1000</td>
<td>3 more</td>
<td>12.929 (44)</td>
</tr>
<tr>
<td></td>
<td><em>Risk of bias and partially indirect data</em></td>
<td>(CI 1.32 - 1.87)</td>
<td></td>
<td></td>
<td>(CI 2 more - 4 more)</td>
<td></td>
</tr>
</tbody>
</table>

**PICO References**


**PICO Summary**


**Quality of the evidence**: For all outcomes except for mortality we rated down the quality of the evidence to moderate as several studies included in the Collins’ meta-analysis were not blinded, did...
not clearly describe allocation procedures and there was a certain degree of heterogeneity across studies on relative effect of non-fatal pulmonary embolism.

DVT screening

**Strong Recommendation**

In asymptomatic patients, we recommend against DVT screening with ultrasound or venography.

**Practical Advice**

**Key Info**

<table>
<thead>
<tr>
<th>Benefits and harms</th>
<th>There is no proven benefit of treating asymptomatic cases of deep venous thrombosis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of evidence</td>
<td>Moderate quality evidence. The recommendation is based on two randomized trials.</td>
</tr>
<tr>
<td>Preference and values</td>
<td>This is a professional decision that should be made at the departmental level without the influence of patient preferences.</td>
</tr>
<tr>
<td>Resources and other considerations</td>
<td>No increased resource requirements.</td>
</tr>
</tbody>
</table>

**Rationale**

There is no evidence showing benefit of treating asymptomatic cases of deep venous thrombosis, while at the same time there is an increased risk of complications due to excessive anticoagulation due to an increased risk of bleeding.

**References**


**PICO (4.3)**

**Population:** Major orthopedic surgery

**Intervention:** Screening of DVT using ultrasound
**Comparator:** No screening

**Outcomes:** Mortality, pulmonary embolism, DVT, Major bleeding

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Confidence in effect estimates</th>
<th>Relative effect</th>
<th>No screening</th>
<th>Screening of DVT using ultrasound</th>
<th>Difference with</th>
<th>Participants (studies), Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT + Pulmonary embolism</td>
<td>Moderate Wide confidence intervals</td>
<td>RR: 0.78</td>
<td>28 per 1000</td>
<td>22 per 1000</td>
<td>6 fewer</td>
<td>1024 (1 study)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(CI 0.21 - 2.9)</td>
<td></td>
<td></td>
<td>(CI 22 fewer - 53 more)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>Moderate Wide confidence intervals</td>
<td>RR: 2.93</td>
<td>0 per 1000</td>
<td>2 per 1000</td>
<td>2 more</td>
<td>1024 (1 study)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(CI 0.12 - )</td>
<td></td>
<td></td>
<td>(CI 2 fewer - 6 more)</td>
<td></td>
</tr>
</tbody>
</table>

**PICO References**


**PICO Summary**


**Venous thromboembolism:** Robison et al. found fewer than 10 VTE events in the study population of 1024 patients. In the control group, they found two cases of non-fatal pulmonary embolism and 3 symptomatic DVTs during 90 days postoperatively. In the intervention group there were no pulmonary emboli and 4 symptomatic DVTs during 90 days postoperatively. Before discharge they discovered a total of 13 asymptomatic DVTs at screening, all of which were treated with warfarin (INR 2-3). This resulted in one major bleeding in the surgical wound.

**Mortality** rates could not be calculated.
References


