International Consensus Statement 2013
Guidelines According to Scientific Evidence

Developed under the auspices of the:

Cardiovascular Disease Educational and Research Trust (UK)
European Venous Forum
North American Thrombosis Forum
International Union of Angiology and Angiology
Union Internationale du Phlebologie
The Risk of VTE in General and Vascular Surgical Patients

- Patients who undergo general and vascular surgical procedures are at risk of developing VTE.\textsuperscript{1-6}

- In the absence of prophylaxis, the risk of silent DVT:
  - 25\% (95\% CI 24\% to 26\%) in general surgery
  - 19\% (95\% CI 15\% to 25\%) in abdominal vascular surgery
  - 15\% (95\% CI 9\% to 23\%) in peripheral vascular reconstruction

## Frequency of DVT in General and Vascular Surgery in Absence of Prophylaxis

<table>
<thead>
<tr>
<th>Patient Groups</th>
<th>Number of Studies</th>
<th>Patients (N)</th>
<th>DVT Incidence (weighted mean)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clagett &amp; Reisch, 1988&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>4310</td>
<td>1084 (255)</td>
<td>24% to 26%</td>
</tr>
<tr>
<td><strong>General Surgery (Asian studies with FUT)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cunningham et al, 1974&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td>68</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Nandi et al, 1980&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
<td>150</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Shead et al, 1980&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td>50</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Inada et al, 1983&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
<td>256</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Phornphibulaya et al, 1984&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
<td>74</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4</td>
<td>598</td>
<td>74 (12.4%)</td>
<td>10% to 15%</td>
</tr>
</tbody>
</table>

* Diagnosed by surveillance with objective methods: Phlebography, FUT or DUS

# Frequency of DVT in General and Vascular Surgery in Absence of Prophylaxis

<table>
<thead>
<tr>
<th>Patient Groups</th>
<th>Number of Studies</th>
<th>Patients (N)</th>
<th>DVT Incidence (weighted mean)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdominal Vascular Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hartsuck &amp; Greenfield, 1973</td>
<td>1</td>
<td>26</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Angelides et al, 1977</td>
<td>2</td>
<td>88</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Belch et al, 1980</td>
<td>3</td>
<td>25</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Olin et al, 1993</td>
<td>4</td>
<td>50</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Killewich et al, 1997</td>
<td>5</td>
<td>48</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hollyoak et al, 2001</td>
<td>6</td>
<td>21</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6</strong></td>
<td><strong>258</strong></td>
<td><strong>50 (19%)</strong></td>
<td><strong>15% to 25%</strong></td>
</tr>
</tbody>
</table>

* Diagnosed by surveillance with objective methods: Phlebography, FUT or DUS

## Frequency of DVT in General and Vascular Surgery in Absence of Prophylaxis

<table>
<thead>
<tr>
<th>Patient Groups</th>
<th>Number of Studies</th>
<th>Patients (N)</th>
<th>DVT Incidence (weighted mean)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral Vascular Reconstruction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamer et al, 1972&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td>21</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Passman et al, 2000&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td>53</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hollyoak et al, 2001&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
<td>28</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3</strong></td>
<td><strong>102</strong></td>
<td><strong>15 (15%)</strong></td>
<td><strong>9% to 23%</strong></td>
</tr>
</tbody>
</table>

* Diagnosed by surveillance with objective methods: Phlebography, FUT or DUS

Risk of DVT in General and Vascular Surgery in Absence of Prophylaxis

- Meta-analysis of 32 studies involving 5,091 general surgical patients without prophylaxis, the frequency of clinical PE was 1.6% (95% CI 1.3% to 2.0%) and fatal PE 0.8% (95% CI 0.62% to 1.1%)\(^1\)

- Contrary to the belief that postoperative DVT is rare in Asians, recent studies have demonstrated risk
  - DVT incidence was 12.4% (95% CI 10% to 15%) in Asians using the fibrinogen uptake test in five studies\(^2-6\)
  - Meta-analysis (4 studies) showed the adjusted incidence of PE and fatal PE was 1.0% (95% CI 0.0 to 2.0) and 0.4% (95% CI 0.0% to 1.0%) respectively\(^7\)
  - Multi-centre study in Japan using venography demonstrated without prophylaxis, the incidence of postoperative DVT was similar to Caucasians (24%)\(^8\)

Risk of DVT in General and Vascular Surgery Patients\textsuperscript{1-5}

- Risk of DVT is increased by age, obesity, malignancy, history of VTE, and hereditary or acquired thrombophilia
- Affected by the nature and duration of the operation, type of anaesthesia, immobility, dehydration, sepsis, varicose veins, hormone therapy and pregnancy

## Risk Stratification of Patients

Known clinical risk factors allow for classification of patients into high, moderate and low risk of developing VTE.

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency of Calf Vein Thrombosis</th>
<th>Frequency of Proximal Vein Thrombosis</th>
<th>Frequency of Fatal PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk</td>
<td>40-80%</td>
<td>10-30%</td>
<td>&gt;1%</td>
</tr>
<tr>
<td>Moderate-risk</td>
<td>10-40%</td>
<td>1-10%</td>
<td>0.1-1%</td>
</tr>
<tr>
<td>Low-risk</td>
<td>&lt;10%</td>
<td>&lt;1%</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

The definition of risk categories in general surgical patients using FUT and in hospital pulmonary embolism (modified from Salzman EW, Hirsh J. Prevention of venous thromboembolism. In: Colman RW, Hirsh J, Marder VJ, et al., eds. *Hemostasis and thrombosis, basic principles and clinical practice.* New York: Lippincott; 1982:986). Although based on old studies the percentages shown in this table are still used to define the category of risk.
Risk Categories According to Clinical Risk Factors in General Surgical Patients

- **High Risk**
  - Major General Surgery, age >60
  - Major General Surgery, age 40-60 & cancer or history of DVT/PE or other risk factors including thrombophilia

- **Moderate Risk**
  - Major General Surgery, age 40-60 without other risk factors*
  - Minor surgery, age > 60
  - Minor surgery, age 40-60 with history of DVT/PE or other risk factors

- **Low Risk**
  - Major General Surgery, age <40; No other risk factors*
  - Minor surgery, age 40-60; No other risk factors*

* The risk is increased by infectious disease, presence of varicose veins, general immobility.
  Minor surgery: Operations other than abdominal lasting less than 45 minutes
  Major surgery: Any intra-abdominal operation and all other operations lasting more than 45 minutes.
Alternative Method of DVT Risk Stratification of Patients

- Another approach is to use a scoring system based on weighting risk factors according to their tendency to be associated with a thrombotic event

  - Studies in nearly 10,000 patients demonstrate a linear association between the risk score and development of symptomatic thrombosis up to 60 days after operation
  - Scores > 8 were associated with 6.5% incidence of clinical events at 30 days and 11.3% incidence at 60 days

Risk of DVT Continues Post-Discharge

- Studies in abdominal or pelvic surgery patients demonstrate the DVT risk continues after discharge from hospital\textsuperscript{1-3}
- Has implications for duration of thromboprophylaxis
  - Patients having operations for cancer have been shown to benefit from 30 days of LMWH (for evidence, see section on cancer).

Risk of DVT following laparoscopic surgery is low.

Two small prospective studies with no prophylaxis demonstrated an incidence of DVT detected by duplex ultrasound or venography of ~0-2%.\(^1,^2\)

Large series from surveys,\(^3^-^5\) registries,\(^6^-^9\) literature review,\(^10\) and a population study\(^11\) indicate that the risk for clinical post-operative VTE after laparoscopic procedures is less than 1%.

Prospective studies with some form of prophylaxis was used confirmed the low incidence\(^12^-^16\)

- There was one exception in which 11/20 patients developed DVT\(^17\)

Risk of VTE Following Bariatric Surgery

- Obesity is an independent risk factor for sudden post-operative fatal PE\(^1,2\)
- Bariatric surgery is associated with clinical DVT in 1.2% to 1.6% of cases and with PE in 0.8% to 3.2% depending on the objective method used for the diagnosis\(^3-9\)
- Risk factors in patients having bariatric surgery include:
  - \(\text{BMI} > 55\), venous stasis syndrome, past history of VTE, obesity hypoventilation syndrome, pulmonary hypertension, cardiomyopathy and obstructive sleep apnea\(^10\)

Risk of VTE Following Plastic Surgery

- Reported incidence of VTE in patients undergoing plastic surgery\(^1\)
  - 0.3% for abdominoplasty
  - 0.8% for abdominoplasty and concomitant plastic surgery
  - 2.2% for abdominoplasty combined with intra-abdominal surgery
  - 3.4% for circumferential abdominoplasty

- In a survey involving 10,000 abdominoplasties without prophylaxis, the incidence of symptomatic PE was 1%\(^2\)

- In a large plastic surgery cohort, the 60 day clinically relevant VTE incidence was related to the Caprini score
  - patients with a score of 5-6 had a 1.3% rate, a score of 7-8 had a 2.7% rate and a score of > 8 had an 11.3% rate by 60 days

General Considerations of Therapy
Low Dose Unfractionated Heparin

- In the 1970s, LDUH (5,000 IU every 8 or 12 h subcutaneously) reduced the incidence of both DVT and fatal PE\(^1\)-\(^3\)
  - The International Multi-centre Trial that included 4,121 patients randomised to LDUH or no prophylaxis, reported a reduction in fibrinogen uptake test detected DVT, clinical DVT, clinical PE, and fatal PE.\(^2\),\(^3\)

- Two meta-analyses comparing LDUH with no prophylaxis showed the incidence of asymptomatic DVT was reduced from 22% to 9% (RR 0.41; 95% CI 0.35 to 0.47) and fatal PE from 0.8% to 0.3% (RR 0.39; 95% CI 0.17 to 0.87)\(^4\),\(^5\)
  - The price was a small increase in bleeding complications from 3.8% to 5.9% (RR 1.56; 95% CI 1.21 to 1.99)

General Considerations of Therapy
Low-Molecular-Weight Heparin (LMWH)

- A multi-center study found that LMWH reduced the incidence of fatal PE and the overall surgical mortality as compared with controls without prophylaxis\(^1\)

- Two smaller randomized placebo-controlled trials in patients having major oncological abdominal surgery\(^2\) and emergency abdominal surgery\(^3\) demonstrated LMWH reduced the rate of asymptomatic DVT

General Considerations of Therapy
Low-Molecular-Weight Heparin (LMWH)

- 16 studies\(^1\)-\(^{16}\) and 9 meta-analyses\(^{17\text{--}25}\) compared LMWH with LDUH
  - Six studies compared different doses of LDUH or LMWH\(^7,26\text{--}30\)
  - Four of the meta-analyses reported that there was no difference in total mortality comparing LMWH with LDUH\(^{18,20\text{--}22}\)
  - Two meta-analyses reported a reduced incidence of symptomatic PE with LMWH from 0.70% to 0.31% (RR 0.43; 95% CI 0.33 to 0.54)\(^{18,20}\) and one showed a decrease in symptomatic VTE\(^{22}\)
- The overall conclusion was LMWH was more effective than LDUH in reducing PE and could be administered once daily versus the 2-3 times daily for LDUH

General Considerations of Therapy
Low-Molecular-Weight Heparin (LMWH)

- Additional considerations
  - LMWHs have a lower risk of heparin-induced thrombocytopenia (HIT) than LDUH\textsuperscript{1,2}
  - High dose LMWH is more effective but is associated with a higher incidence of hemorrhagic complications than LDUH, whereas a low dose of LMWH has a similar efficacy with less bleeding\textsuperscript{3}
  - Regulatory bodies in Europe and North America now consider the various LMWHs to be distinct drug products. They require clinical validation for specific indications for each drug. Therapeutic interchange among these products is not appropriate\textsuperscript{4}

In a double-blind double-dummy randomized study (2,927 patients) in high risk major abdominal surgery, fondaparinux 2.5 mg once daily was found to be at least as effective as peri-operative dalteparin 5000U daily in preventing venographically detected DVT.  

- Incidence of DVT was 6.1% in the dalteparin group and 4.6% in the fondaparinux group (P=0.14).
- In the subgroup of 1,941 patients with cancer, the incidence of DVT was reduced from 7.7% in the dalteparin group to 4.7% in the fondaparinux group (RR 0.74; 95% CI 0.40 to 0.93) (P = 0.02).
- No difference in major bleeding (2.4% vs 2.8%) provided fondaparinux was administered at least six hours after operation.

Antiplatelet agents including high-dose aspirin (500-1500 mg/day) reduce DVT by 30% and PE by 50%

- In a meta-analysis of 22 RCTs\(^1\) of 1,459 general surgical patients where DVT was diagnosed by surveillance with FUT, the incidence of DVT was reduced from 27% in the control group to 19% in the antiplatelet therapy group (RR 0.71; 95% CI 0.62 to 0.82).

- In the same meta-analysis data on PE were available in 26 RCTs of 3,419 patients. The incidence of PE was reduced from 1.7% in the control group to 0.5% in the antiplatelet group (RR 0.28; 95% CI 0.16 to 0.48).

- In view of the availability of more effective methods of prophylaxis and the hazards of high-dose aspirin, aspirin is not considered as an alternative prophylaxis.

Graduated elastic compression (GEC) stockings reduce the incidence of asymptomatic DVT by approximately 50-60%\(^1-8\) and three systematic reviews\(^9-11\)

- However, the number of patients studied has been too small to be able to assess the effects on the development of PE

- A Cochrane systematic review demonstrated that in four studies with 530 patients, the incidence of DVT was reduced from 35.6% in the control group to 15.9% in the compression group\(^12\)

- In another five studies involving 848 patients, elastic compression added to a background of additional antithrombotics reduced the incidence of DVT from 10.5% in the control group to 1.9% in the compression group

- Effect of graduated elastic compression stockings in the prevention of DVT diagnosed by objective methods (FUT or phlebography) in non-orthopedic surgical RCTs

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>GECS Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% Cl</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsapogas, general surgery</td>
<td>2</td>
<td>54</td>
<td>6</td>
<td>44</td>
<td>4.1%</td>
<td>0.27 [0.06, 1.28]</td>
<td>1971</td>
</tr>
<tr>
<td>Holford, major surgery</td>
<td>11</td>
<td>47</td>
<td>23</td>
<td>48</td>
<td>14.2%</td>
<td>0.49 [0.27, 0.89]</td>
<td>1976</td>
</tr>
<tr>
<td>Scurr, general surgery</td>
<td>8</td>
<td>70</td>
<td>26</td>
<td>70</td>
<td>16.2%</td>
<td>0.31 [0.15, 0.63]</td>
<td>1977</td>
</tr>
<tr>
<td>Borow, various surgical</td>
<td>14</td>
<td>91</td>
<td>32</td>
<td>89</td>
<td>20.2%</td>
<td>0.43 [0.25, 0.75]</td>
<td>1981</td>
</tr>
<tr>
<td>Inada, abdominal surgery</td>
<td>4</td>
<td>110</td>
<td>16</td>
<td>110</td>
<td>10.0%</td>
<td>0.25 [0.09, 0.72]</td>
<td>1983</td>
</tr>
<tr>
<td>Allan, general surgery</td>
<td>15</td>
<td>97</td>
<td>37</td>
<td>103</td>
<td>22.4%</td>
<td>0.43 [0.25, 0.73]</td>
<td>1983</td>
</tr>
<tr>
<td>Turner, gynaecol surgery</td>
<td>0</td>
<td>104</td>
<td>4</td>
<td>92</td>
<td>3.0%</td>
<td>0.10 [0.01, 1.80]</td>
<td>1984</td>
</tr>
<tr>
<td>Turpie, neurosurgery</td>
<td>7</td>
<td>80</td>
<td>16</td>
<td>81</td>
<td>9.9%</td>
<td>0.44 [0.19, 1.02]</td>
<td>1989</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>653</td>
<td></td>
<td>637</td>
<td></td>
<td>100.0%</td>
<td>0.39 [0.30, 0.50]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>160</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 3.08, df = 7 (P = 0.88); I² = 0%</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 7.08 (P &lt; 0.000001)</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

General Considerations of Therapy
Intermittent Pneumatic Compression (IPC)

- IPC tested in 11 RCTs (1,318 patients)\textsuperscript{1-11} was found to reduce the incidence of asymptomatic DVT from 25\% in the control group to 7.9\% in the IPC group (RR 0.32; 95\% CI 0.24 to 0.42)

General Considerations of Therapy

Intermittent Pneumatic Compression

- Effect of IPC in prevention of DVT diagnosed by objective methods (FUT or phlebography) in non-orthopaedic surgical RCTs\textsuperscript{1-10}

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IPC Events</th>
<th>IPC Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Risk Ratio (M-H, Fixed, 95% CI) Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabri*</td>
<td>2</td>
<td>39</td>
<td>12</td>
<td>39</td>
<td>7.3%</td>
<td>0.17 [0.04, 0.70] 1971</td>
</tr>
<tr>
<td>Hills</td>
<td>6</td>
<td>50</td>
<td>15</td>
<td>50</td>
<td>9.2%</td>
<td>0.40 [0.17, 0.95] 1972</td>
</tr>
<tr>
<td>Robert</td>
<td>6</td>
<td>94</td>
<td>27</td>
<td>104</td>
<td>15.6%</td>
<td>0.25 [0.11, 0.57] 1974</td>
</tr>
<tr>
<td>Clark*</td>
<td>1</td>
<td>37</td>
<td>7</td>
<td>36</td>
<td>4.3%</td>
<td>0.14 [0.02, 1.07] 1974</td>
</tr>
<tr>
<td>Turpie, a</td>
<td>8</td>
<td>103</td>
<td>20</td>
<td>96</td>
<td>12.6%</td>
<td>0.37 [0.17, 0.81] 1977</td>
</tr>
<tr>
<td>Coe</td>
<td>2</td>
<td>29</td>
<td>6</td>
<td>24</td>
<td>4.0%</td>
<td>0.28 [0.06, 1.24] 1978</td>
</tr>
<tr>
<td>Skillman</td>
<td>4</td>
<td>47</td>
<td>12</td>
<td>48</td>
<td>7.2%</td>
<td>0.34 [0.12, 0.98] 1978</td>
</tr>
<tr>
<td>Turpie, b</td>
<td>1</td>
<td>65</td>
<td>12</td>
<td>63</td>
<td>7.4%</td>
<td>0.08 [0.01, 0.60] 1979</td>
</tr>
<tr>
<td>Borow &amp; Goldson</td>
<td>9</td>
<td>79</td>
<td>32</td>
<td>89</td>
<td>18.4%</td>
<td>0.32 [0.16, 0.62] 1981</td>
</tr>
<tr>
<td>Butson</td>
<td>6</td>
<td>62</td>
<td>4</td>
<td>57</td>
<td>2.5%</td>
<td>1.38 [0.41, 4.64] 1981</td>
</tr>
<tr>
<td>Clarke-Pearson</td>
<td>7</td>
<td>55</td>
<td>18</td>
<td>52</td>
<td>11.3%</td>
<td>0.37 [0.17, 0.81] 1984</td>
</tr>
</tbody>
</table>

| Total (95% CI)         | 660        | 658       | 100.0%         | 0.32 [0.24, 0.42] |

Heterogeneity: Chi\textsuperscript{2} = 9.81, df = 10 (P = 0.46); I\textsuperscript{2} = 0%

Test for overall effect: Z = 7.70 (P < 0.00001)

General Considerations of Therapy
Mechanical Compression versus LDUH or LMWH

- A systematic review of 16 RCT of mechanical compression (MC) versus LDUH or LMWH demonstrated the pooled risk reduction for MC versus LDUH or LMWH was 1.07 (95% CI 0.72 to 1.61 for DVT and 1.03 (95% CI 0.48 to 2.22) for PE.
  - MC was associated with significant reduced risk of postoperative bleeding compared with LDUH or LMWH (RR 0.47; 95% CI 0.31 to 0.70).
  - Among the studies that used LDUH, there was a non-significant trend towards a lower risk of DVT with heparin compared with MC (RR 0.71; 95% CI 0.42 to 1.19).
  - Among the studies that used LMWH, there was a significant higher risk of DVT with MC (RR 1.80; 95% CI 1.16 to 2.79) compared with heparin, but LMWH was still associated with an increased risk of bleeding.

General Considerations of Therapy
Combined Modalities: GEC versus GEC plus LDUH

Effect of graduated elastic compression (GEC) stockings versus low dose unfractionated heparin (LDUH) plus GEC in the prevention of DVT diagnosed by objective methods (FUT or phlebography)\(^1-4\)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LDUH &amp; GEC</th>
<th>GEC</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Nicolaides, prostatectomy</td>
<td>1</td>
<td>122</td>
<td>29</td>
<td>122</td>
</tr>
<tr>
<td>Moser, general surgery</td>
<td>2</td>
<td>20</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Borow, gen surg &amp; orthop</td>
<td>2</td>
<td>63</td>
<td>15</td>
<td>106</td>
</tr>
<tr>
<td>Rasmussen general surgery</td>
<td>23</td>
<td>89</td>
<td>22</td>
<td>74</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>294</strong></td>
<td><strong>322</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td><strong>28</strong></td>
<td><strong>71</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: (\tau^2 = 1.81); (\chi^2 = 16.77), df = 3 ((P = 0.0008)); (I^2 = 82%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: (Z = 1.74) ((P = 0.08))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

General Considerations of Therapy
Combined Modalities: DUH versus LDUH plus GEC

- Effect of low dose unfractionated heparin (LDUH) versus LDUH plus graduated elastic compression (GEC) in the prevention of DVT in non-orthopedic surgical patients diagnosed by objective methods (FUT or phlebography)\textsuperscript{1-6}

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LDH &amp; GEC Events</th>
<th>Total</th>
<th>LDH Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moser &amp; Froidevaux</td>
<td>2</td>
<td>20</td>
<td>0</td>
<td>15</td>
<td>7.1%</td>
<td>3.81 [0.20, 73.95]</td>
<td>1976</td>
</tr>
<tr>
<td>Torngren</td>
<td>4</td>
<td>98</td>
<td>12</td>
<td>98</td>
<td>19.5%</td>
<td>0.33 [0.11, 1.00]</td>
<td>1980</td>
</tr>
<tr>
<td>Borow &amp; Goldson</td>
<td>2</td>
<td>63</td>
<td>23</td>
<td>86</td>
<td>16.5%</td>
<td>0.12 [0.03, 0.49]</td>
<td>1983</td>
</tr>
<tr>
<td>Wille-Jorgensen, a</td>
<td>2</td>
<td>90</td>
<td>11</td>
<td>86</td>
<td>15.9%</td>
<td>0.17 [0.04, 0.76]</td>
<td>1985</td>
</tr>
<tr>
<td>Rasmussen</td>
<td>23</td>
<td>89</td>
<td>25</td>
<td>85</td>
<td>24.9%</td>
<td>0.88 [0.54, 1.42]</td>
<td>1988</td>
</tr>
<tr>
<td>Wille-Jorgensen, b</td>
<td>2</td>
<td>79</td>
<td>12</td>
<td>81</td>
<td>16.0%</td>
<td>0.17 [0.04, 0.74]</td>
<td>1991</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>439</td>
<td>451</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.34 [0.14, 0.87]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>35</td>
<td>83</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau\textsuperscript{2} = 0.83; Chi\textsuperscript{2} = 16.83, df = 5 (P = 0.005); I\textsuperscript{2} = 70%

Test for overall effect: Z = 2.25 (P = 0.02)

General Considerations of Therapy

Electrical Stimulation

- In a study of the efficacy of electrical calf stimulation during surgery using one leg as control in general surgical patients (110 patients), the incidence of asymptomatic DVT was 21% in the unstimulated leg and 8.2% in the stimulated leg (OR 0.33; 95% CI 0.15 to 0.77)\(^1\)

- Another study of 60 patients reported the incidence of asymptomatic DVT was 15% in the unstimulated leg and 1.6% in the stimulated leg (OR 0.11; 95% CI 0.01 to 0.90)\(^2\)

- In a RCT, electrical calf stimulation was applied to both legs of 37 patients compared to 40 controls. The incidence of asymptomatic DVT was 30% in the unstimulated group and 14% in the stimulated group (OR 0.35; 95% CI 0.90 to 1.16)\(^3\)

  - In this RCT, perfusion lung scanning and chest x-rays were performed the day before operation and 4-6 days after operation. The incidence of silent PE was 35% in the control group and 10% in the stimulated group (OR 0.33; 95% CI 0.11 to 0.97)

General Considerations of Therapy

Electrical Stimulation

- Most studies of electrical stimulation were performed prior to 1990 and the equipment used produced painful stimuli so that electrical calf muscle stimulation could be used only during general anesthesia.

- Modern equipment now commercially available produces muscle contractions as a result of electrical impulses that are painless and can be tolerated by patients throughout the day.

- The efficacy of such modern equipment should be determined in adequately powered RCT before any recommendations can be made.
Duration of Prophylaxis

- Duration of prophylaxis in most studies is 5-7 days
- Studies suggested that the risk continues after discharge from hospital\(^1-8\)
  - RCT have demonstrated that extending prophylaxis from one week to one month reduces asymptomatic DVT by 50-70\%\(^9-13\)
  - 3 meta-analyses suggest the relative risk reduction for preventing VTE following extended prophylaxis is 60-70\%\(^{14-16}\)
- Extended prophylaxis with bemiparin was associated with an 88\% reduction in proximal DVT and a 24\% reduction in the composite endpoint of DVT, nonfatal PE and death from any cause\(^17\)

Duration of Prophylaxis

- Further studies are needed to determine the optimal duration of extended prophylaxis and whether or not mortality is influenced
  - There are no studies on extended prophylaxis after vascular surgery
- Extended duration of pharmacological prophylaxis (>7 days) should be considered if patients develop complications such as infection during the post-operative hospitalization period\(^1\-^2\)
- Obese patients undergoing bariatric surgery should be evaluated for post-discharge VTE risk and considered for extended pharmacological prophylaxis\(^3\)

VTE Prophylaxis Recommendations
Low-Risk General, Vascular, Bariatric and Plastic Surgical Patients

- *Low-risk patients* are those without risk factors undergoing minor surgery
- The data are insufficient to make any recommendations
- On the basis of risk/benefit ratio and extrapolation from studies in moderate-risk patients, it is common practice in some countries to use GEC stockings in addition to early ambulation and adequate hydration
  - Level of evidence: Low
VTE Prophylaxis Recommendations
Moderate-Risk General, Vascular, Bariatric and Plastic Surgical Patients

- **Moderate-risk patients** are over 40 years of age and undergoing major surgery for benign disease in the absence of additional risk factors
- **LMWH** (initiated and dosed according to labelling) or **LDUH** is recommended
  - Level of evidence: High
  - LMWH is the preferred option because it is administered as one injection daily and is associated with a lower incidence of HIT
- An alternative method, especially in patients at risk for or with active bleeding, is **GEC** with **IPC** used continuously until the patient is fully ambulant
  - Level of evidence: High
- **LMWH** may be added if risk of bleeding is minimized
VTE Prophylaxis Recommendations
High-Risk General, Vascular, Bariatric and Plastic Surgical Patients

- **High-risk patients** are over 60 years of age and undergoing major surgery for benign disease or any patient with additional risk factors
- LMWH or fondaparinux initiated and dosed according to labelling is recommended
  - Level of evidence: High
- In the absence of LMWH or fondaparinux, LDUH 5000 IU commenced pre-operatively and continued twice or 3 times daily can be used
  - Level of evidence: High
- Any of the above therapies may be combined with mechanical methods (GEC and/or IPC), particularly in the presence of multiple risk factors
  - Level of evidence: High
VTE Prophylaxis Recommendations
Laparoscopic Surgery

- Patients undergoing laparoscopic surgery who do not have any additional risk factors should receive GEC
  - Level of evidence: Low
- LDUH, LMWH, fondaparinux or IPC with GEC should be used in the presence of additional risk factors
  - Level of evidence: Low
VTE Prophylaxis Recommendations
Abdominal or Pelvic Surgery

- Patients undergoing abdominal or pelvic major surgery for cancer and do not present contraindications to extended prophylaxis should receive LMWH up to one month after operation
  - Level of evidence: High
Patients undergoing bariatric surgical procedures should receive LMWH (higher dosage) alone or in combination with GEC and IPC

- Level of evidence: Moderate
VTE Prophylaxis Recommendations
Major Vascular Surgery

- Patients undergoing major vascular procedures should receive LMWH or fondaparinux
  - Level of evidence: Low
- In the absence of LMWH or fondaparinux, LDUH 5000 IU commenced pre-operatively and continued twice or 3 times daily can be used
  - Level of evidence: Low
VTE Prophylaxis Recommendations
Plastic Surgery

- High-risk patients having plastic surgery should receive LMWH, fondaparinux starting 24 hours after surgery or a combination of LMWH with IPC and GES
  - Level of evidence: Low

- In the absence of LMWH or fondaparinux, LDUH 5000 IU commenced pre-operatively and continued twice or 3 times daily can be used
  - Level of evidence: Low

- GEC is contraindicated in patients with peripheral arterial disease because of anecdotal reports of gangrene