Thromboprophylaxis in medical & surgical patients – for how long?
or... NICE HAT – but should we buy it?
Correctly targeted thromboprophylaxis matters

Nick was 57 years old & cared for his elderly mother
He had cerebral palsy and epilepsy
He died of a pulmonary embolism in hospital
Nick’s family want us to learn from his story
Informing patients of their risks matters
If you deliver near complete compliance with VTE risk assessment / prophylaxis, will you prevent all VTE?
10 years of HAT data at Salisbury
(as a % of all admissions: 1=6 weeks, 2=12 weeks)

NB: HAT now 0.19% hospital admissions and 17.4% of VTE is HAT with 43% = distal DVT
### Hampshire HAT rates (approx 20% all VTE)

#### Graph
- **National HAT rate (%):** Blue line
- **HHFT HAT rate (%):** Red line

#### Table: Specialty-wise VTE Occurrence

<table>
<thead>
<tr>
<th>Specialty</th>
<th>DVT</th>
<th>PE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopaedics</td>
<td>7</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Surgery</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Medicine (includes elderly care and stroke)</td>
<td>6</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Obstetrics &amp; Gynaecology</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Clinical Haematology</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>18</td>
<td>11</td>
<td>29</td>
</tr>
</tbody>
</table>

#### No. of VTEs

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of VTEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidable</td>
<td>0</td>
</tr>
<tr>
<td>Possibly avoidable</td>
<td>1</td>
</tr>
<tr>
<td>Unavoidable</td>
<td>28</td>
</tr>
</tbody>
</table>
Relative risk of VTE by time since surgery

Relative risk for time without surgery = 1

Siân Sweetland et al. BMJ 2009;339:bmj.b4583
Assess all medical patients to identify the risk of VTE and bleeding:
• as soon as possible after admission to hospital or by the time of the first consultant review
• using a tool published by a national UK body, professional network or peer-reviewed journal. The most commonly used risk assessment tool for medical patients is the Department of Health VTE risk assessment tool.

DoH tool: Never scientifically tested, may overestimate risk costing NHS £22 million per year!
Other options: Caprini Score (surgical) – IMPROVE, Padua or Caprini (non-surgical)
Currently 8% VTE exemplar centres are considering using an alternative tool, larger scale trials badly needed!

<table>
<thead>
<tr>
<th>Thrombosis risk factors - Patient related</th>
<th>Thrombosis risk factors - Admission related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer or cancer treatment</td>
<td>Significantly reduced mobility for &gt;3 days</td>
</tr>
<tr>
<td>Age&gt;60</td>
<td>Hip or knee replacement</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Hip fracture</td>
</tr>
<tr>
<td>Known thrombophilies</td>
<td>Total anaesthetic + surgical time &gt; 90 minutes</td>
</tr>
<tr>
<td>Obesity (BMI&gt;30kg/m2)</td>
<td>Surgery involving pelvis or lower limb with total anaesthetic + surgical time &gt; 60 minutes</td>
</tr>
<tr>
<td>One or more significant medical comorbidities (eg. heart disease, metabolic, endocrine or respiratory pathologies, acute infectious disease, inflammatory conditions)</td>
<td>Acute surgical admission with inflammatory or intra-abdominal condition</td>
</tr>
<tr>
<td>Personal history or first-degree relative with a history of VTE</td>
<td>Critical care admission</td>
</tr>
<tr>
<td>Use of hormone replacement therapy</td>
<td>Surgery with significant reduction in mobility</td>
</tr>
<tr>
<td>Use of estruspor-containing contraception</td>
<td></td>
</tr>
<tr>
<td>Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR&gt;2)</td>
<td>Lumbar puncture / spinal or epidural anaesthesia expected in the next 12 hours</td>
</tr>
<tr>
<td>Acute stroke</td>
<td>Lumbar puncture / spinal or epidural anaesthesia within the previous 4 hours</td>
</tr>
<tr>
<td>Thrombocytopenia (with platelets &lt;75x109/l)</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled systolic hypertension (BP &gt;230/120mmHg or higher)</td>
<td></td>
</tr>
<tr>
<td>Untreated bleeding disorders (such as haemophilia or von Willebrand’s disease)</td>
<td></td>
</tr>
</tbody>
</table>
Padua Prediction score

Barbar et al JTH 2010, 8(11): 2450-2457
Acutely ill medical patients

Offer pharmacological VTE prophylaxis for a minimum of 7 days to acutely ill medical patients whose risk of VTE outweighs their risk of bleeding:

- Use LMWH as first-line treatment.
- If LMWH is contraindicated, use fondaparinux sodium.

SDH admitted 42,508 patients in 2017
Median LOS for medicine = 3.4 days (Surgery = 1.0 days)
78.8% received chemical thromboprophylaxis
(7 days would have cost >£180,000 & might have prevented 13 VTE events in 2016/17)

Dubious value – not supported by 96% exemplar centres on survey in Oct 2018
# Landmark trials for LMWH prophylaxis in medical inpatients

<table>
<thead>
<tr>
<th>Study</th>
<th>RRR</th>
<th>Thromboprophylaxis</th>
<th>Patients with VTE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDENOX¹</td>
<td>63%</td>
<td>Placebo</td>
<td>14.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enoxaparin 40 mg</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PREVENT²</td>
<td>49%</td>
<td>Placebo</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dalteparin 5000IU</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>P=0.0015</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**RRR** = relative risk reduction
Medical population in landmark clinical trials

• MEDENOX: 6-14 days, inpatient only, **median LOS 7d**
• PREVENT: 14 days, **median LOS 13d**

- Projected stay at least 4 - 6 days
- > 40 years
- Congestive heart failure, acute respiratory failure
- *Or* significant other medical conditions other medical conditions (eg acute infection) PLUS
  - age > 75 yrs
  - cancer
  - previous VTE
  - obesity
# Abdominal surgery

Add pharmacological VTE prophylaxis for a minimum of 7 days for people undergoing abdominal surgery whose risk of VTE outweighs their risk of bleeding, taking into account individual patient factors and according to clinical judgement. Choose either:

- LMWH or
- fondaparinux sodium

Consider extending pharmacological VTE prophylaxis to 28 days postoperatively for people who have had major cancer surgery in the abdomen.

**Dubious value – not supported by 95% exemplar centres on survey in Oct 2018**
Surgical trials

- Majority of trials in general surgical patients < 7 days (Collins et al 1988)

- In the largest trial, requirement for admission > 7 days was an inclusion criteria (Kakkar et al 1975)
People with cancer

**Do not** offer VTE prophylaxis to people with cancer who are receiving treatments and who are mobile unless they are also at risk of VTE because of something other than the cancer.

Consider pharmacological VTE prophylaxis for people with **myeloma** who are receiving chemotherapy with thalidomide, pomalidomide or lenalidomide **with steroids**.

**Sensible – but in practice many clots occur on prophylaxis in myeloma**

Consider VTE for people with **pancreatic cancer** who are receiving chemotherapy.

If giving VTE prophylaxis to people with cancer, continue for as long as they are receiving chemotherapy.
Palliative care

Consider pharmacological VTE prophylaxis for people who are having palliative care. Take into account temporary increases in thrombotic risk factors, risk of bleeding, likely life expectancy and the views of the person and their family members or carers (as appropriate):

- Use LMWH as first-line treatment.
- If LMWH is contraindicated, use fondaparinux sodium.

Do not offer VTE prophylaxis to people in the last days of life.

Tip: “if you wouldn’t treat a clot, don’t scan and don’t give prophylaxis”
Fragility fractures of the pelvis, hip and proximal femur

Offer VTE prophylaxis for a month to people with fragility fractures of the pelvis, hip or proximal femur if the risk of VTE outweighs the risk of bleeding. Choose either:

- **LMWH**, starting 6–12 hours after surgery or
- **fondaparinux sodium**, starting 6 hours after surgery, providing there is low risk of bleeding.

**OK – but frail people bleed +++ too**

Issue of frailty / falls and anticoagulation – 54 CT heads, only 4 ICH – all on warfarin. We do **LOTS** of CT heads.
Elective hip replacement

Offer VTE prophylaxis to people undergoing elective hip replacement surgery whose risk of VTE outweighs their risk of bleeding. Choose any one of:

- LMWH for 10 days followed by aspirin (75 or 150 mg) for a further 28 days.
- LMWH for 28 days combined with anti-embolism stockings (until discharge).
- Rivaroxaban
Elective knee replacement

Offer VTE prophylaxis to people undergoing elective knee replacement surgery whose VTE risk outweighs their risk of bleeding. Choose any one of:

- **Aspirin** (75 or 150 mg) for 14 days
- **LMWH** for 14 days combined with anti-embolism stockings until discharge.
- **Rivaroxaban**
“The inclusion of aspirin … was primarily based on the results from the economic model”
There may be more evidence out there we are ignoring...

13472 primary THR and TKRs in a joint registry
Only deemed high risk if higher risk factors (exclude age alone & BMI 30-35) – this led to 86% being lower risk

23% aspirin / clopidogrel
77% mechanical prophylaxis only
0.48/0.42 % PE/DVT

No statistical difference in HAT between those given chemical prophylaxis and those not

***Unpublished (as yet) retrospective data – but low HAT matches RCA findings...***
Pregnant women and women who gave birth or had a miscarriage or termination of pregnancy in the past 6 weeks

Consider LMWH for all women who are admitted to hospital or a midwife-led unit if they are pregnant or gave birth, had a miscarriage or had a termination of pregnancy in the past 6 weeks, and whose risk of VTE outweighs their risk of bleeding.

SDH had 216 admissions in this group (miscarriage / TOP) in 2016/17. No thromboprophylaxis was given. No patients developed thrombosis.
Vegetarians / Vegans

Be aware that heparins are of animal origin and this may be of concern to some people. Discuss the alternatives with people who have concerns about using animal products, after discussing their suitability, advantages and disadvantages with the person.

Bigger picture?

- 5% population are vegan / vegetarian
- In 2013, of the 100 most commonly prescribed drugs by GPs, 74 contained lactose, gelatine or magnesium stearate potentially animal derived (21% didn’t state animal products, 47% definitely had them)

Tatham & Patel BMJ Feb 2014
Jumping on the bandwagon...more guidance reiterating NICE89

http://m.clinmed.rcpjournals.org/content/19/2/100
### Main Changes

- The guideline now incorporates patients over 16 years of age.
- Risk assessment can be with ‘tool published by a national UK body, professional network or peer-reviewed journal’.
- All medical patients & most surgical patients requiring pharmacological thromboprophylaxis should have it for a minimum of 7 days.
- Pharmacological prophylaxis should be started within 14 hours of admission.
- Risk assessment should occur as soon as possible or by the first consultant review.
- Reassessment should take place at consultant review or if clinical condition changes.
- All acute psychiatric patients to be risk assessed and considered for LMWH.
- Elective THR & TKR can have aspirin as an alternative to LMWH/DOAC.
- UFH or LMWH can be used in renal impairment, using a reduced dose.

“All medical patients & most surgical patients requiring pharmacological thromboprophylaxis should have it for a minimum of 7 days”
Our NHS patients

• Threshold
  – Lower threshold for considering patients ‘at risk’ of VTE than clinical trials

• LOS
  – Median LOS following emergency admission is 3 days (after exclusion of admissions <24hours) *(NHS Digital 2018)*
  – 80% of elective surgery performed as day surgery in 2013 *(Appleby 2015)*
Annual additional cost to NHS

- >100,000 consecutive admissions
- % of patients with LOS <7 days recommended LMWH
  - medical 61%, surgical 57% (day case surgery excluded)
- Drug cost > £35 million
- District nurse (30% patients) > £185 million

- Diversion of scare resources
  - Nursing time to train patients
  - District nurses
  - Dispensing time

Lester et al, accepted for publication BJHaem
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Limited evidence that longer is better & it’s expensive! Probably not…. (but do lose the stockings!)
Acknowledgements

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VTE Exemplars
Thrombosis UK