VTE: the current situation

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Disclosure of interests

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Honoraria: Sanofi, Bayer, Boehringer-Ingelheim, Pfizer
VTE: the current situation

- Current VTE prevention structures
- Have we made a difference?
- What is new in VTE prevention?
- What next for VTE prevention in the NHS?
Where we started

• Limited awareness of burden of hospital-associated thrombosis
• Inconsistent approach to VTE prevention
• No risk assessment for VTE risk
• Prophylaxis use in mainly surgical patients
• No knowledge of VTE outcomes
The National VTE Prevention Programme in England

• **Systematic approach:**
  Uniform VTE risk assessment tool → NICE guidance VTE prevention

• **VTE at heart of Quality Framework:** CQUIN, CQC, NHSLA

• **Increasing awareness of outcomes:** NOF VTE indicator

• **Leadership:**
  ‘Four Professions’ leadership
  National VTE Exemplar Centres Network

Roberts, Durkin & Arya, Br J Haem 2017; 178:162-170
VTE prevention care pathways for all adult hospitalised patients

**Care pathway**

1. **Patient admitted to hospital**
   - Assess VTE risk.
   - Assess bleeding risk.

2. **Balance risks of VTE and bleeding**
   - Offer VTE prophylaxis if appropriate. Do not offer pharmacological VTE prophylaxis if patient has any risk factor for bleeding and risk of bleeding outweighs risk of VTE.

3. **Reassess risks of VTE and bleeding within 24 hours of admission and whenever clinical situation changes**

**Assessing risks of VTE and bleeding**

**Patients who are at risk of VTE**

- **Medical patients**
  - Active cancer or cancer treatment
  - Active bleeding
  - Age > 65 years
  - Clinical condition
  - Dehydration
  - Known thrombophilia
  - Obesity (BMI > 30 kg/m²)
  - One or more significant medical comorbidities (for example: heart disease, metabolic, endocrine or respiratory pathology; acute infectious diseases; inflammatory conditions)
  - Personal history or first-degree relative with a history of VTE
  - Use of HRT
  - Use of oestrogen-containing contraceptive therapy
  - Varicose veins with phlebitis

- **Surgical patients and patients with trauma**
  - Total anaesthetic + surgical time > 90 minutes
  - Total anaesthetic + surgical time > 60 minutes
  - If surgery involves pelvis or lower limb and total anaesthetic + surgical time > 60 minutes
  - Acute surgical admission with inflammatory or intra-abdominal condition
  - Expected to have significant reduction in mobility or
  - If any VTE risk factor present

**VTE risk factors**

- Host factors
  - Active cancer or cancer treatment
  - Age > 65 years
  - Clinical condition
  - Dehydration
  - Known thrombophilia
  - Obesity (BMI > 30 kg/m²)
  - One or more significant medical comorbidities (for example: heart disease, metabolic, endocrine or respiratory pathology; acute infectious diseases; inflammatory conditions)
  - Personal history or first-degree relative with a history of VTE
  - Use of HRT
  - Use of oestrogen-containing contraceptive therapy
  - Varicose veins with phlebitis

- For women who are pregnant or have given birth within the previous 6 weeks (see page 23).

**Patients who are at risk of bleeding**

- Active bleeding
- Acquired bleeding disorders (such as active liver failure)
- Concomitant use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR > 2)
- Lumbar puncture/an epidural/spinal anaesthesia within the previous 4 hours or expected within the next 12 hours
- Acute stroke
- Thrombocytopenia (platelets < 50 x 10⁹/L)
- Uncontrolled systolic hypertension (≥ 140 mmHg)
- Untreated inherited bleeding disorders (such as haemophilia or von Willebrand's disease)

**Medical patients**

- **General medical patients**
  - Does risk of VTE outweigh risk of bleeding?
    - Yes
    - Is pharmacological VTE prophylaxis contraindicated?
      - Yes
      - Has patient been admitted for stroke?
        - Yes
        - Consider offering mechanical VTE prophylaxis with any one of:
          - Anti-embolism stockings (thigh or knee length)
          - Foot impulse devices
          - Intermittent pneumatic compression devices (thigh or knee length)
        - Reassess risks of bleeding and VTE within 24 hours of admission and whenever clinical situation changes
      - No
      - Continue until patient no longer at increased risk of VTE
    - No
  - offer pharmacological VTE prophylaxis with any one of:
    - Fondaparinux
    - LMWH
    - UFH

- **See page 13**
Mandatory risk assessment of all adult hospitalised patients
Commissioning for Quality and Innovation (CQUIN) 2010–2014

• **National CQUIN goal:** reduce avoidable death, disability and chronic ill health from VTE

• **Quality indicator:** >95% of all adult inpatients risk assessed for VTE on admission to hospital, using the national tool
VTE PREVENTION PATHWAY

1. Identify at-risk patient
2. Counsel at-risk patient
3. Prescribe thromboprophylaxis
4. Administer thromboprophylaxis

NICE Quality Standard 3
Identifying potentially preventable cases of HAT

Thrombosis Team
- Data collection
- Notification
- Learning

Trust Quality Framework

Admitting consultant
VTE Education

- 4 e-training modules created by King’s Thrombosis Centre in partnership with HEE
- Part of mandatory training at every Trust in England
- Currently being updated
Uptake of VTE prevention training
>60,000 completions
Preventing VTE

- Link Nurse/Midwives
- Patient information
- Electronic VTEp systems
- RCA of HAT cases
- Audit programme
- Supportive managers
- Staff education
- Thrombosis team

VTE Prevention

Thrombosis Centre

- Preventing Venous Thromboembolism (VTE)
- A guide for patients at King's College Hospital

VTE Assessments
- MRSA Swabs
- MRSA Results
- eDrug Charts
The VTE Exemplar Centres Network

Instituted by DH in 2007 to develop and disseminate best practice in VTE prevention and care; currently 32 centres of excellence
A global VTE network: Australia
A global VTE network: India
Global Leaders

- Comprehensive, systematic approach to VTE prevention
- First national initiative of its kind anywhere in the world
- Key patient safety initiative:
  - Delivering high quality care
  - Reducing avoidable harm
  - Safer hospitals
- Delivered change, enabled by levers provided by NHS
- Consistent >95% VTE risk assessment within acute care in England
Has the National VTE Prevention Programme made a difference?
VTE prevention in the NHS

• VTE is high on Trust Quality and Patient Safety agendas.

• There is local and national oversight of VTE risk assessment rates.

• Local audit of VTE prevention and monitoring of HAT

• Impact on outcomes?
VTE risk assessment rates

Note: 'NHS acute providers' & 'All providers of NHS funded acute care' overlap.
Usage of prophylactic LMWH

Heparin Volume to the NHS Secondary Care by Year

LMWH shortages
### Reducing Risks

#### Question 7
Did Patient receive any of the following - please select all that apply

<table>
<thead>
<tr>
<th>Option</th>
<th>Enoxaparin</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>AES (Anti embolism Stockings / TED stockings)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>IPC (intermittent pneumatic compression)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Already on warfarin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None prescribed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Question 8
If Enoxaparin was prescribed what was the dose?

<table>
<thead>
<tr>
<th>Dose</th>
<th>20mg od</th>
<th>40mg od</th>
<th>40mg bd</th>
<th>60mg bd</th>
<th>Other, please specify</th>
<th>Enoxaparin not prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Question 9
Is the patient wearing AES?

<table>
<thead>
<tr>
<th>Answer</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Audit findings: Standard 4

Was pharmacological or mechanical TP correct?

King’s College Hospital data
Local audit of LMWH omissions

<table>
<thead>
<tr>
<th></th>
<th>Oct-Dec 16</th>
<th>Jan - Mar 18</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of doses prescribed</strong></td>
<td>41508</td>
<td>34342</td>
</tr>
<tr>
<td><strong>No. of omissions</strong></td>
<td>5334</td>
<td>2829</td>
</tr>
<tr>
<td><strong>Percentage of doses omitted</strong></td>
<td>13%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Absolute reduction in total omissions of 5%, relative reduction of 46%

King’s College Hospital data
Reasons for LMWH omissions

- Refused by patient
- Clinical reasons for omission e.g. low BP, allergy
- Omitted on instruction of prescriber
- Patient away from ward
- Drug not available
- Prescription illegible/incomplete
- Other [please specify]

King’s College Hospital data
• At John Hopkins: 12% prescribed doses LMWH not administered, 40% missed >1 dose 60% due to patient or family member refusal

• Quality improvement programmes have targeted prescription of prophylaxis alone Missed doses constitute the next target for quality improvement

• Two approaches:
  1. Web-based education module for nurses
  2. Patient education bundle
Effect of Real-time Patient-Centered Education Bundle on Administration of Venous Thromboembolism Prevention in Hospitalized Patients

A Surgical units

B Medicine units

Impact of national VTE prevention programme in England on real world outcomes:
Understanding VTE outcomes

- Limitations of thromboprophylaxis
- Limitations of coding
- Limitations of death reporting
- Limitations of the outcome indicator as marker for quality of VTE prevention process
Surveillance Bias and the Validity of the VTE Quality Measure

Hospital VTE Prophylaxis Adherence Rates & Risk-Adjusted VTE Event Rates

Impact of national VTE prevention programme in England

Impact of the national venous thromboembolism risk assessment tool in secondary care in England: retrospective population-based database study

David Catterick\textsuperscript{a,b} and Beverly J. Hunt\textsuperscript{c}

2. Heart 2013; 0:1–6.
Deaths from VTE related events within 90 days post discharge from hospital rate per 100,000 adult admissions, 2007/08 to 2017/2018

VTE death rates per 100,000 admissions

What we have learnt from RCA of hospital-associated thrombosis

- **Multidisciplinary approach** in prophylaxis implementation help reduce preventable HATs.
- **Multifaceted interventions** including education and electronic prompts improve prophylaxis prescription and administration.
- **Rapid communication** of learning from incidents via regular teaching sessions reduce repetitive errors.
HAT root cause analysis:
Majority of cases received appropriate thromboprophylaxis

King’s College Hospital data
Limitations of the current approach to VTE prevention

- Paucity of real world outcome data
- Outdated risk estimates
- Outdated prophylaxis studies
- Absence of standardised approach to audit and RCA
Limitations of the current approach to VTE prevention

- Modern studies particularly in medical patients show low event rates and limited benefit of extended thromboprophylaxis
- Are we overusing prophylaxis in certain indications?
- No knowledge of bleeding rates
- Many grey areas:
  - LL immobilisation
  - Mental health
  - Rehab / nursing homes
What’s new in VTE prevention?
APEX: extended thromboprophylaxis with betrixaban in acutely ill medical patients

- 7513 acutely ill medical patients with reduced mobility & specific risk factors for VTE: extended duration betrixaban vs standard duration enoxaparin

- Sequential analyses in 3 prespecified, progressively inclusive cohorts, based on elevated D-dimer and age $\geq$75 years.

- Conclusion: Among acutely ill medical patients with elevated D-dimer no significant difference in primary efficacy outcome

- APEX landmark analysis: d6 to d35 prophylaxis with betrixaban reduces symptomatic VTE 1.33% to 0.88% (NNT 233) “50-60% medical inpatients eligible”  Bleeding 0.7% vs 0.6%

Betrixaban licensed by FDA but not by EMA

Cohen et al, Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients. NEJM 2016; 375:534-44
MARINER Study: rivaroxaban for thromboprophylaxis after hospitalization for medical illness

Patients identified on basis of IMPROVE score ≥4 or IMPROVE of 2/3 + high D-dimer; Received 45 days Riva 10 mg od vs placebo after discharge

Primary efficacy outcome: 0.83% riva vs 1.1% placebo

Secondary outcome, symptomatic nonfatal PE: 0.18% riva vs 0.43% placebo

Major bleeding: 0.28% riva vs 0.15% placebo

Conclusion: Rivaroxaban given to medical patients for 45 days after hospital discharge did not significantly lower risk of symptomatic VTE / VTE death. Incidence of major bleeding was low.

Spyropoulos et al Rivaroxaban for Thromboprophylaxis after Hospitalization for Medical Illness. NEJM 2018; 379:1118-1127
DOACs for thromboprophylaxis in ambulatory patients with cancer

<table>
<thead>
<tr>
<th>Cumulative Analysis of the AVERT and CASSINI Trials.‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td><strong>CASSINI Trial</strong></td>
</tr>
<tr>
<td>Rivaroxaban</td>
</tr>
<tr>
<td>number/total number (percent)</td>
</tr>
<tr>
<td>PRIMARY EFFICACY OUTCOME</td>
</tr>
<tr>
<td>ITT analysis</td>
</tr>
<tr>
<td>Analysis during treatment period</td>
</tr>
<tr>
<td>Symptomatic VTE: ITT analysis</td>
</tr>
<tr>
<td>Major bleeding</td>
</tr>
<tr>
<td>Death from any cause</td>
</tr>
</tbody>
</table>

- **AVERT study**: apixaban was associated with lower incidence of VTE than placebo but with a higher incidence of major bleeding; 37% discontinued treatment.

- **CASSINI study**: incidence of VTE lower with rivaroxaban in the per-protocol analysis but not in the primary ITT analysis; no difference in major bleeding; 47% discontinued treatment.

Among critically ill patients receiving pharmacologic thromboprophylaxis, adjunctive IPC did not lower incidence of proximal DVT vs pharmacologic thromboprophylaxis alone.

NICE recommends risk assessment using a tool published by a national UK body, professional network or peer-reviewed journal

- Are you planning to change the VTE risk assessment tool used?
  - YES: 2
  - NO: 23

Acutely ill medical patients and majority of surgical patients offer pharmacological prophylaxis for a minimum of 7 days

- Do you routinely give 7 days pharmacological prophylaxis as indicated in NG89?
  - YES: 1
  - NO: 17

For selected patients: 7

National VTE Exemplar Centres Network survey 2018, BJH (in press)
2018 American Society of Hematology Guidelines on VTE

Prophylaxis for Medical Patients

• Strong recommendations included
  – pharmacological VTE prophylaxis in acutely or critically ill inpatients at acceptable bleeding risk
  – use of mechanical prophylaxis when bleeding risk is unacceptable
  – against the use of DOACs during hospitalization
  – against extending pharmacological prophylaxis after hospital discharge.

• Conditional recommendations included
  – not to use VTE prophylaxis routinely in long-term care patients or outpatients with minor VTE risk factors.
  – use of graduated compression stockings or LMWH in long-distance travelers only if they are at high risk for VTE

VTE prevention in England: where we are now

- VTE prevention is ‘business as usual’ in the NHS in England and remains a priority within hospitals
- VTE risk assessment remains ~95%
- Linked to NICE NG89
- Audit and RCA of HAT cases are not universally performed
- Post-discharge VTE deaths continue to fall
- National VTE Exemplar Centres Network continues to grow
What we could have done differently...

- Design risk assessment tool to enable subsequent validation
- Better understand outcomes at outset
- National standardised audit process
- National registry for hospital-associated thrombosis
Feasibility study for a NCA for VTE prevention

The Healthcare Quality Improvement Partnership (HQIP) commissioned the Health Innovation Network (HIN) to complete a one year feasibility study for a National Clinical Audit for Venous Thromboembolism (VTE) Prevention in adult hospital inpatients.
More research required!

- Risk assessment models
- Thromboprophylaxis choice and duration
- Real world outcomes
- Patient-centred approaches
- Focus on special patient populations: pregnancy, obesity, cancer, trauma
Preventing HAT

• National VTE prevention programme has developed a comprehensive systems-based approach to VTE prevention
• There have been demonstrable improvements in process measures and VTE outcomes
• Substantial burden of HAT remains
• Sustaining and improving best practice in VTE prevention is a continuing challenge
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