Reducing Hospital-associated Thrombosis

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Disclosure of interests

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Honoraria: Sanofi, Bayer, Boehringer-Ingelheim, Pfizer
Reducing hospital-associated thrombosis

• 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.
   - 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
  - Age > 65 years
  - Clinical care admission
  - Dehydration
  - Known thrombophilia
  - Obesity (BMI > 30 kg/m²)
  - One or more significant medical comorbidities (for example: heart disease, metabolic, endocrine or respiratory pathologies, acute infectious diseases, inflammatory conditions)
  - Personal history or first-degree relative with a history of VTE
  - Use of HRT
  - Use of oestrogen-containing contraceptives therapy
  - Varicose veins with phlebitis

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

**Patients who are at risk of bleeding**

- Active bleeding
- Acquired bleeding disorders (such as acute liver failure)
- Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR > 2)
- Lumbar puncture/lumbar epidural anaesthesia within the previous 4 hours or expected within the next 12 hours
- Acute stroke
- Thrombocytopenia (platelets < 75 x 10⁹)
- Uncontrolled systemic hypertension (≥ 230/120 mmHg)
- Uncontrolled systemic bleeding disorders (such as haemophilia or von Willebrand’s disease)

**Medical patients**

1. **Does risk of VTE outweigh risk of bleeding?**
   - **Yes**
   - **No**

2. **Is pharmacological VTE prophylaxis contraindicated?**
   - **Yes**
   - **No**

3. **Has patient been admitted for stroke?**
   - **Yes**
   - **No**

4. **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)

5. **Offer pharmacological VTE prophylaxis with any one of:**
   - Fondaparinux
   - LMWH
   - UFH

6. **Continue until patient no longer at increased risk of VTE**

7. **Reassess risks of bleeding and VTE within 24 hours of admission and whenever clinical situation changes.**
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
Root cause analysis of cases of HAT

HAT

- Coding
- Diagnostics
- Autopsies
- Bereavement
- Other hospitals
- DVT/AC clinic

Thrombosis Team
- Data collection
- Notification
- Learning

Admitting consultant

Trust Quality Framework
Patient empowerment
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

Preventing Venous Thromboembolism (VTE)
A guide for patients at King's College Hospital
The VTE Exemplar Centres Network

Instituted by DH in 2007 to develop and disseminate best practice in VTE prevention and care; currently 33 centres of excellence
The National VTE Exemplar Centres Network
A global VTE network: Wales

Princess of Wales & Neath Port Talbot hospital

Glan Clwyd, Betsi Cadwaladr Health Board
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

<table>
<thead>
<tr>
<th></th>
<th>Did Patient receive any of the following - please select all that apply</th>
</tr>
</thead>
</table>
| 7 | Enoxaparin
|   | AES (Anti embolism Stockings / TED stockings)
|   | IPC (intermittent pneumatic compression)
|   | Already on warfarin
|   | None prescribed
|   | Rivaroxaban
|   | UFH (un-fractionated Heparin)
|   | Other (please specify)

<table>
<thead>
<tr>
<th></th>
<th>If Enoxaparin was prescribed what was the dose?</th>
</tr>
</thead>
</table>
| 8 | 20mg od
|   | 40mg od
|   | 40mg bd
|   | 60mg bd
|   | Other, please specify
|   | Enoxaparin not prescribed

<table>
<thead>
<tr>
<th></th>
<th>Is the patient wearing AES?</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</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>
<tr>
<td><strong>over doses prescribed</strong></td>
<td></td>
<td></td>
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</tbody>
</table>

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

King’s College Hospital data
Reasons for LMWH omissions

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

Jan - Mar 18
Oct - Dec 16

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

Quality improvement programmes have targeted prescription of prophylaxis alone. Missed doses constitute the next horizon 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

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\(^{a,b}\) and Beverly J. Hunt\(^c\)

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

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.
Local CIRs for HAT 2010-2016

**HAT Crude Incidence Rates per 1000 Patient Admissions 2010 to 2016**

- **CIR per 1000 PA**
- **Power (CIR per 1000 PA)**

Rowswell HR and Nokes TJC, Open Heart 2017
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 and 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 ≥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%

Cohen et al, Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients. NEJM 2016; 375:534-44

Betrixaban licensed by FDA but not by EMEA
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>
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<tr>
<td><strong>Outcome</strong></td>
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<tr>
<td></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.

PREVENT study: Adjunctive intermittent pneumatic compression for thromboprophylaxis

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

Changes in VTE prevention guidance: NG89

- Change of age limit from 18 years to 16 years
- Any VTE risk assessment tool
- Minimum of 7 days LMWH for medical patients and majority of surgical patients
- Aspirin for prophylaxis after TKR
- Complex recommendations regarding use of mechanical thromboprophylaxis
- Risk assess acute psychiatric patients and consider pharmacological VTE prophylaxis
NICE GC92 → NG89

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)
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) have 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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