

# **VTE: the current situation**

## Roopen Arya King's College Hospital



# **Disclosure of interests**

Research funding: Bayer, Covidien

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  $\Rightarrow$  NICE guidance VTE prevention

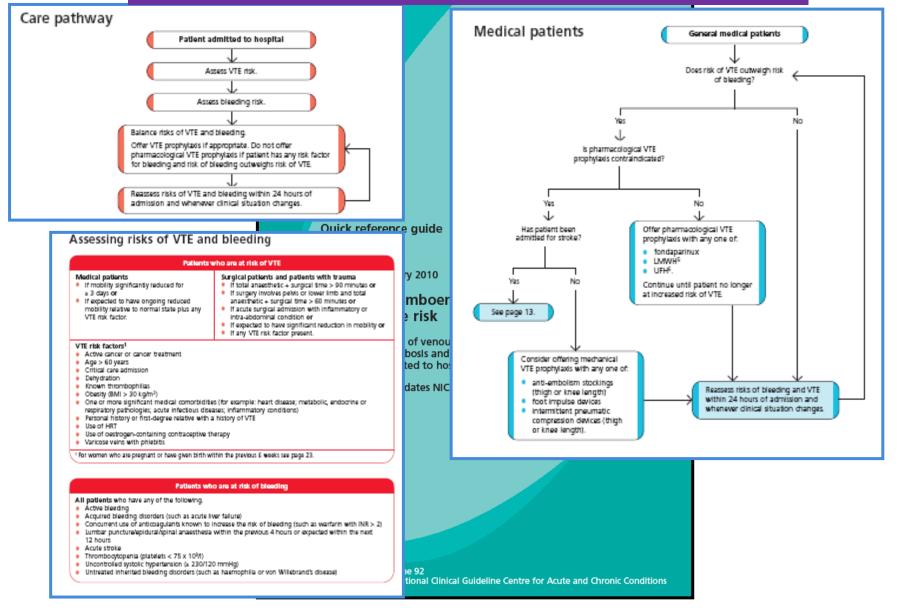
- VTE at heart of Quality Framework: CQUIN, CQC, NHSLA
- Increasing awareness of outcomes: NOF VTE indicator
- Leadership:

'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

England



### RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

All patients should be risk assessed on admission to hospital. Patients should be reassessed within 24 hours of admission and whenever the clinical situation changes.

#### STEP ONE

Assess all patients admitted to hospital for level of mobility (tick one box). All surgical patients, and all medical patients with significantly reduced mobility, should be considered for further risk assessment.

#### STEP TWO

Review the patient-related factors shown on the assessment sheet against thrombosis risk,

## Mandatory risk assessment of all adult hospitalised patients

Mobility - all patients

(fick one box)

Surgical patient

Thrombosis risk

Patient related

The risk factors identified are not exhaustive. Clinicians may consider additional risks in individual patients and offer thromboprophylaxis as appropriate.

#### STEP THREE

Review the patient-related factors shown against bleeding risk and tick each box that applies (more than one box can be ticked).

Any tick should prompt clinical staff to consider if bleeding risk is sufficient to preclude pharmacological intervention.

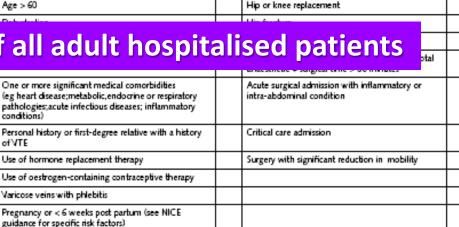
#### Guidance on thromboprophylaxis is available at:

National Institute for Health and Clinical Excellence (2010) Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. NICE clinical guideline 92. London: National Institute for Health and Clinical Excellence.

http://www.nice.org.uk/guidance/CG92

This document has been authorised by the Department of Health Gateway reference no: 10278





Tick

Tick

Admission related

Bleeding risk						
Patient related	Tick	Admission related	Tick			
Active bleeding		Neurosurgery, spinal surgery or eye surgery				
Acquired bleeding disorders (such as acute liver failure)		Other procedure with high bleeding risk				
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR >2)		Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours				
Acute stroke		Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours				
Thrombocytopaenia (platelets< 75x10%)						
Uncontrolled systolic hypertension Q30/120 mmHg or higher)						
Untreated inherited bleeding disorders (such as haemophilia and von Willebrand's disease)						

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Medical patient NOT expected to

Risk assessment now complete

Significantly reduced mobility for 3 days or more

have significantly reduced mobility relative to normal state Tick

Tick

### RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

to normal state

Medical patient expected to have

ongoing reduced mobility relative

Tick

Assess for thrombosis and bleeding risk below

Active cancer or cancer treatment

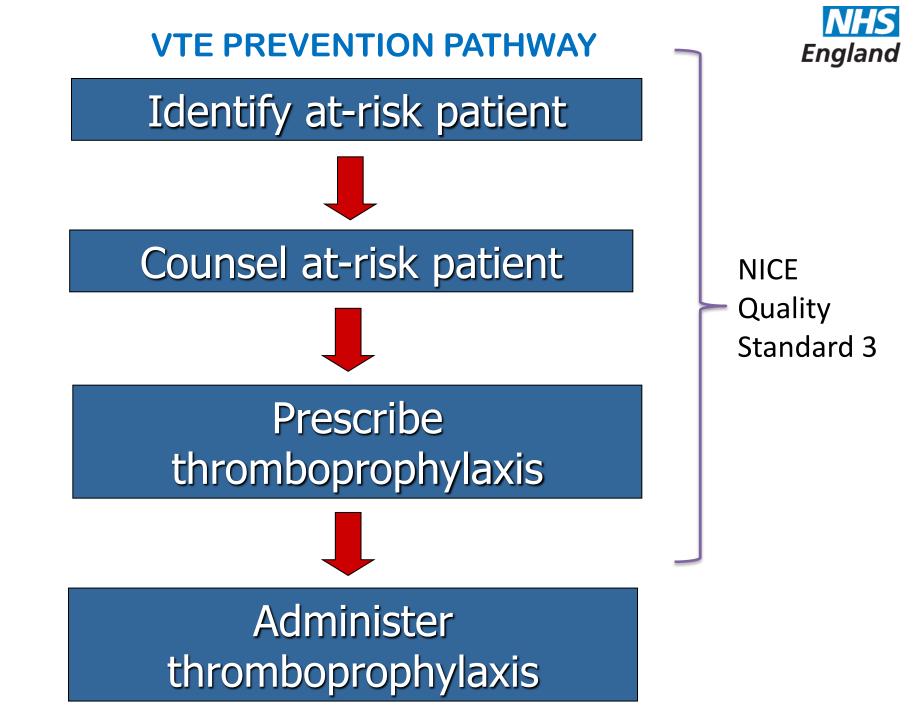


# Commissioning for Quality and Innovation (CQUIN) 2010–2014

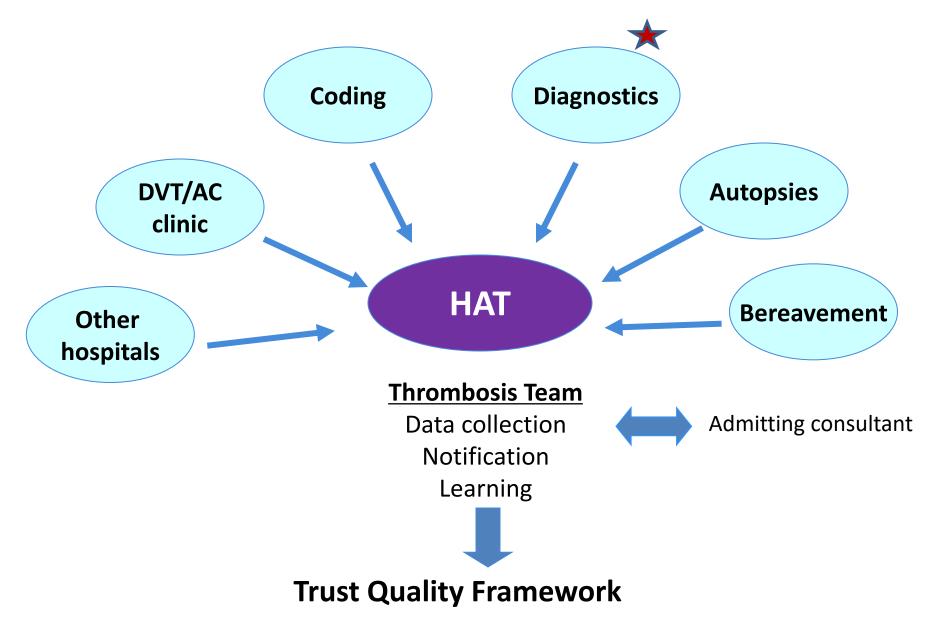
- National CQUIN goal: reduce avoidable death, disability and chronic ill health from VTE
- Quality indicator:

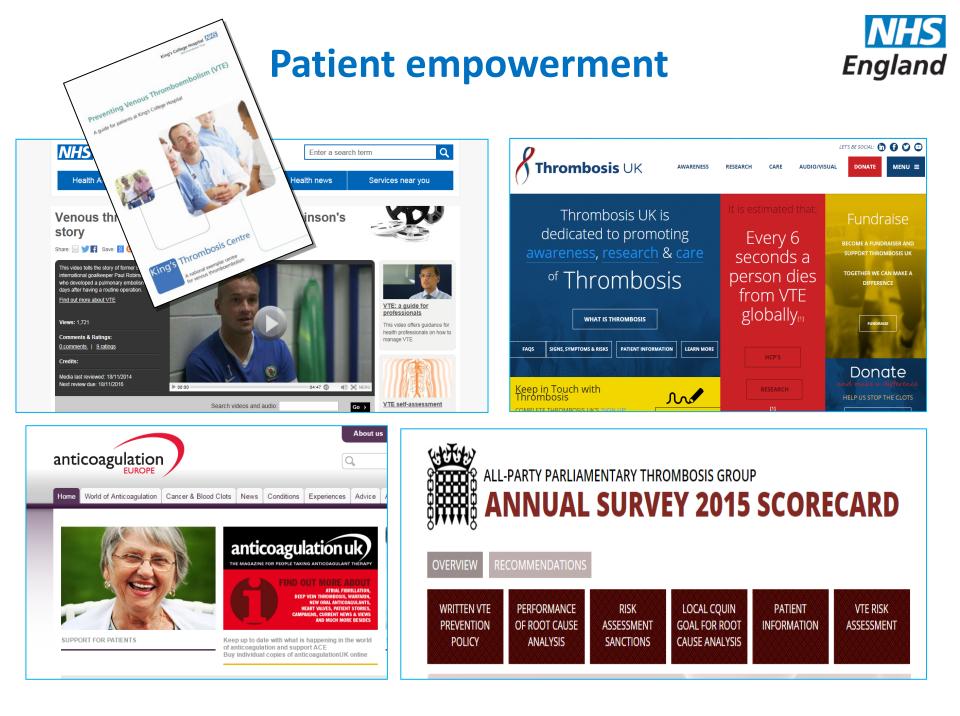
   >95% of all adult
   inpatients risk assessed
   for VTE on admission to
   hospital, using the
   national tool





# Identifying potentially preventable cases of HAT









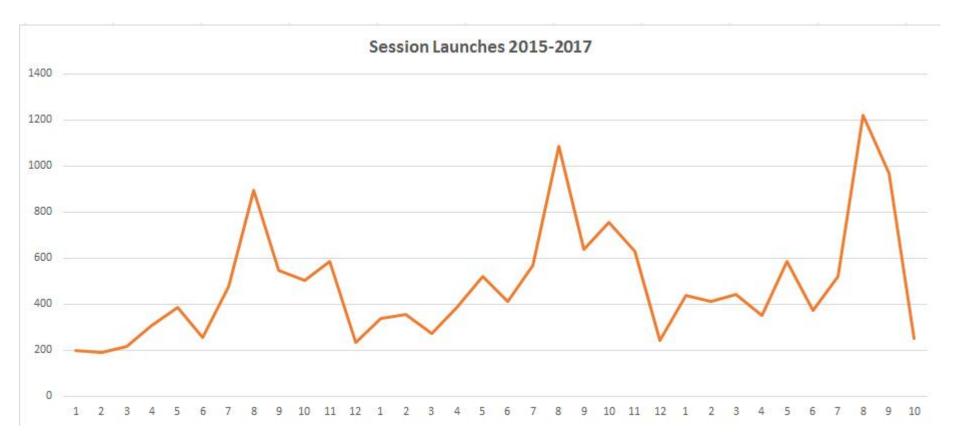
## **VTE Education**

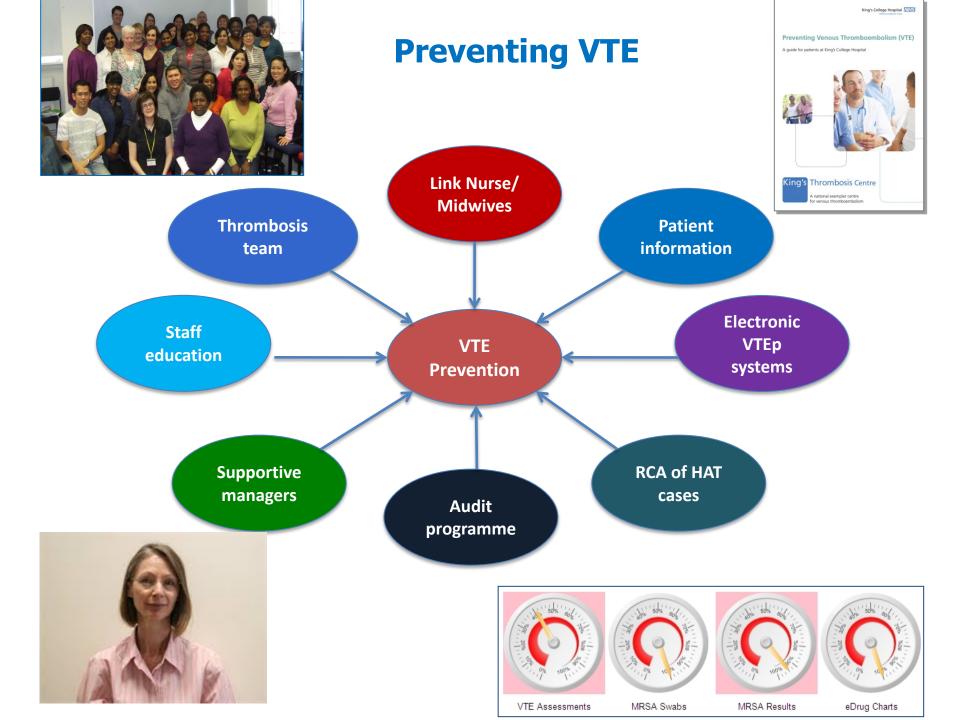
- 4 e-training modules created by King's Thrombosis Centre in partnership with HEE
- Part of mandatory training at every Trust in England
- Currently being updated

e-Learning for Healthcare	An extraordinary project in terms of breadth and skill of content e-Learning Age - Judges citation Health Education England			
Home Programm	es About Latest News Support Demo Contact Us search Q			
A web ba	VTE ased education resource designed to help raise awareness ove understanding of Venous Thromboembolism			
Menu	More information			
Programme home	VTE prevention e-learning course			
More information	These resources have been developed in partnership with the NHS England National VTE Prevention Programme. The e-learning session for healthcare professionals in			
Meet the team	Secondary Care first published in 2010 and updated in 2013 is aimed at nurses, pharmacists and junior doctors to help them understand the concept of hospital-			
Access the e-learning	associated thrombosis and how to prevent it. Three new sessions have been developed in 2014. The first is aimed at Primary Care to increase the awareness of healthcare-related VTE and enhance the quality of palient care with respect to VTE prevention prior to hospital admission and after discharge. It is designed for all healthcare professionals including GPs, nurses, health visitors, midwives and community pharmacists. The second session has been developed for commissioners. This e-tearing session provides a brief overview of venous thromboembolism as a condition and outlines the key role that commissioners in the delivery of acute care services across a range of medical & surgical specialities is undergrindued by a high quality approach to VTE prevention in order to improve outcomes for patients. The third e-tearing session is simed at undergraduates and is focused on the pathophysiology of VTE and pre-disposing risk factors, as well as outlining why prevention is so important in the context of the national programme.			
e-LfH is a Health Education England Programme in partnership with the NHS and Professional Bodies				
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# Uptake of VTE prevention training >60,000 completions







### 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





### **The National VTE Exemplar Centres Network**







## 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?

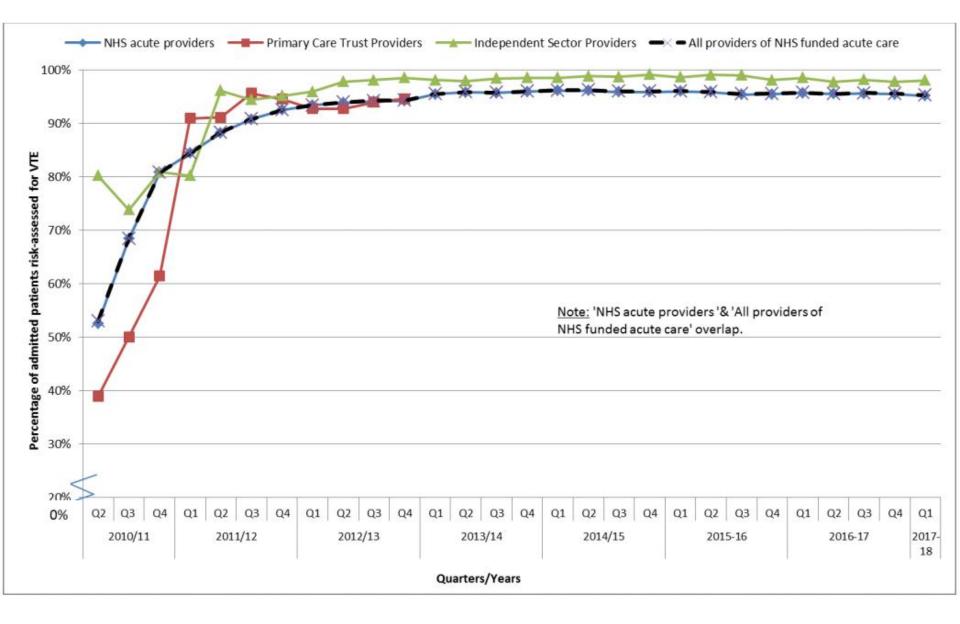


# VTE prevention in the NHS

- 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?

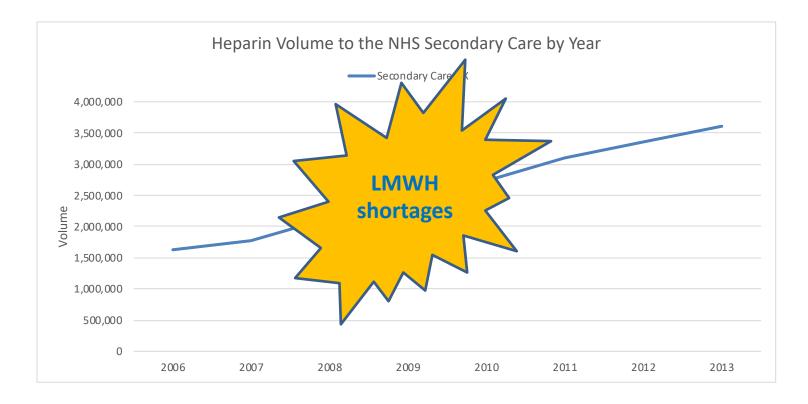
# **VTE risk assessment rates**







# Usage of prophylactic LMWH





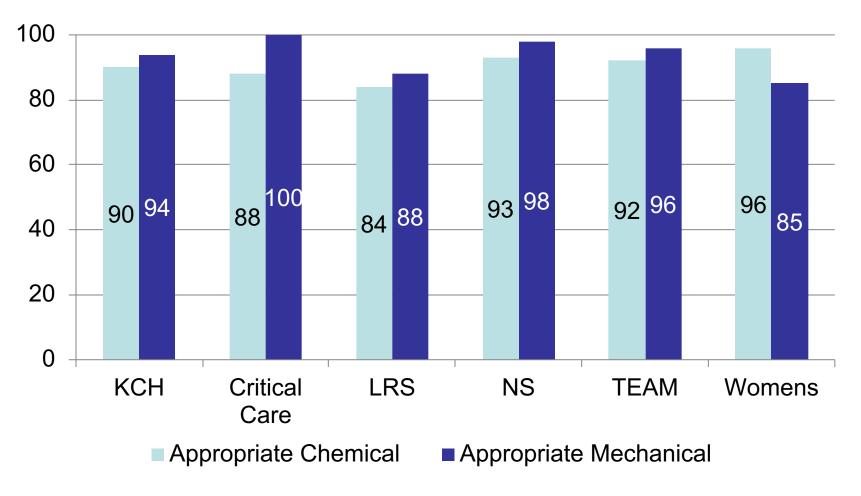
### Welcome to the Survey Centre



	Proce	Ű							
Reducing Risks									
		Enoxaparin		Rivaroxaban					
	Did Patient receive any of the following - please select all that apply	AES (Anti embolism Stockings / TED stockings)	V	UFH (un-fraction Heparin)	ated				
		IPC (intermittent pneumatic compression)		Other (please sp	ecify)				
		Already on warfarin		None prescribed					
	If Enoxaparin was prescribed what was the dose?	20mg od 40mg od 40	mg bd 60mg bd	Other, please specify	Enoxaparin not prescribed				
		<u> </u>	0 0	O	0				
		Ye	25		No				
9	Is the patient wearing AES?	(	)		$\odot$				

## Audit findings: Standard 4

### Was pharmacological or mechanical TP correct?

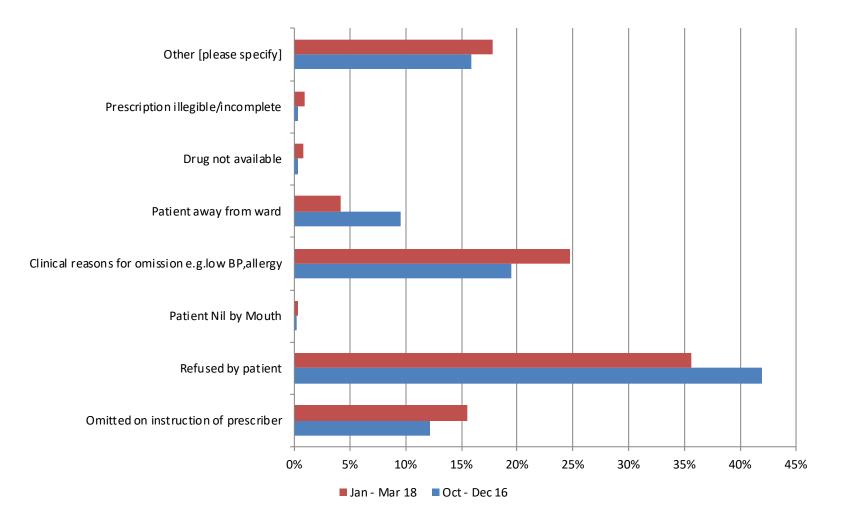


# Local audit of LMWH omissions

	Oct-Dec 16	Jan - Mar 18
No. of doses prescribed	41508	34342
No. of omissions	5334	2829
Percentage of doses omitted over doses prescribed	13%	8%

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

# **Reasons for LMWH omissions**



The Joint Commission Journal on Quality and Patient Safety 2019; 45:145–147

### Please stop using venous thromboembolism (VTE) outcomes for Pay-for-Performance and Public reporting

Elliott R. Haut, MD, PhD, FACS

COMMENTARY

Solo advances

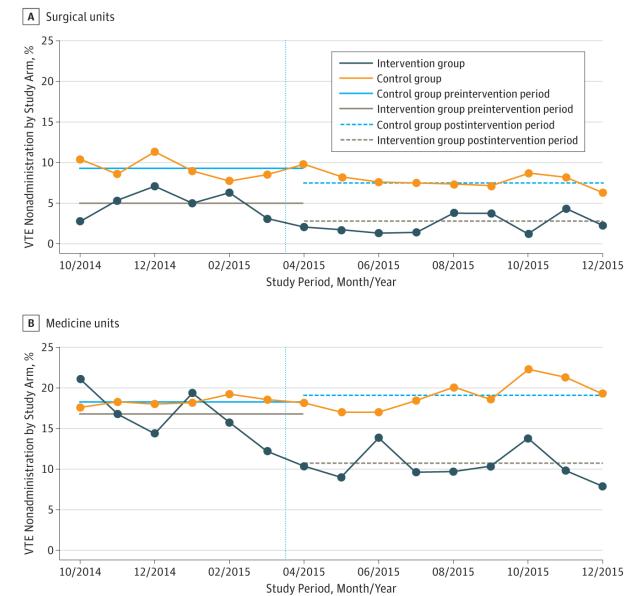
#### TO THE EDITOR:

What the 2018 ASH venous thromboembolism guidelines omitted: nonadministration of pharmacologic prophylaxis in hospitalized patients

Oluwafemi P. Owodunni,<sup>1</sup> Brandyn D. Lau,<sup>2-5</sup> Michael B. Streiff,<sup>4,6</sup> Peggy S. Kraus,<sup>7</sup> Deborah B. Hobson,<sup>1,8</sup> Dauryne L. Shaffer,<sup>1,8</sup> Kristen L. W. Webster,<sup>1,4</sup> Mujan Varasteh Kia,<sup>1</sup> Christine G. Holzmueller,<sup>1,4</sup> and Elliott R. Haut<sup>1,4,5,9,10</sup>

- 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



JAMA Netw Open. 2018;1(7):e184741. doi:10.1001/jamanetworkopen.2018.4741



# Impact of national VTE prevention programme in England on <u>real world outcomes</u>:



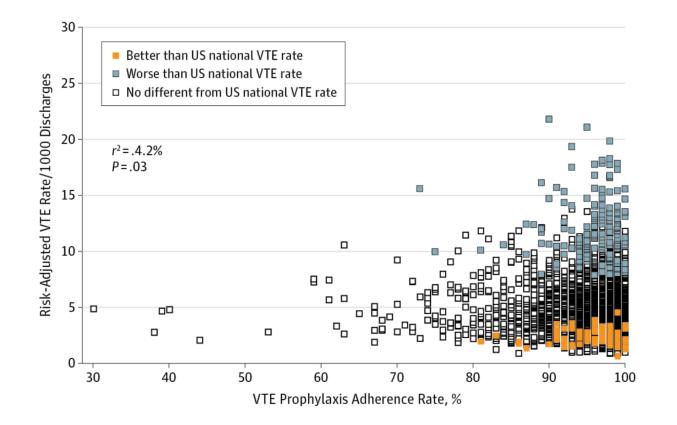
# **Understanding VTE outcomes**

- 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



Bilimoria et al, JAMA. 2013;310(14):1482-1489.



# Impact of national VTE prevention programme in England

Global burden of cardiovascular disease

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

David Catterick<sup>a,b</sup> and Beverly J. Hunt<sup>c</sup>

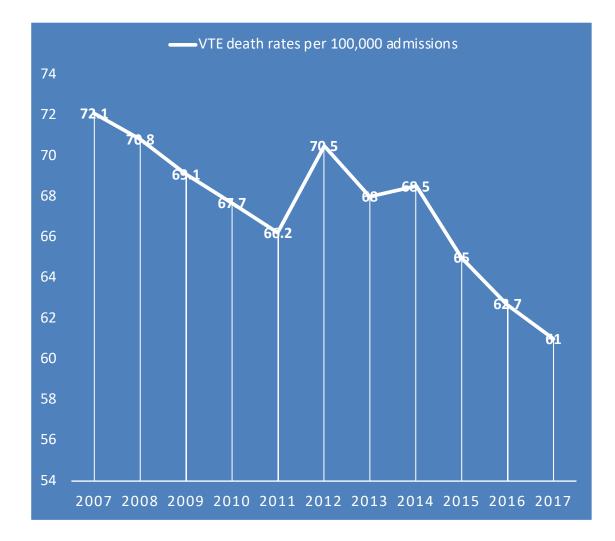
Domenico Pagano<sup>1,2</sup>

- 1. Blood Coagul Fibrinolysis 2014; 25(6):571-62.
- 2. Heart 2013; 0:1–6.
- 3. Chest. 2013 ; 144(4):1276-81.



Deaths from VTE related events within 90 days post discharge from hospital rate per 100,000 adult admissions, 2007/08 to 2017/2018





Roberts et al. Developing a national programme for VTE prevention. Br J Haematol. 2017;178(1):162-170

# What we have learnt from RCA of hospital-associated thrombosis

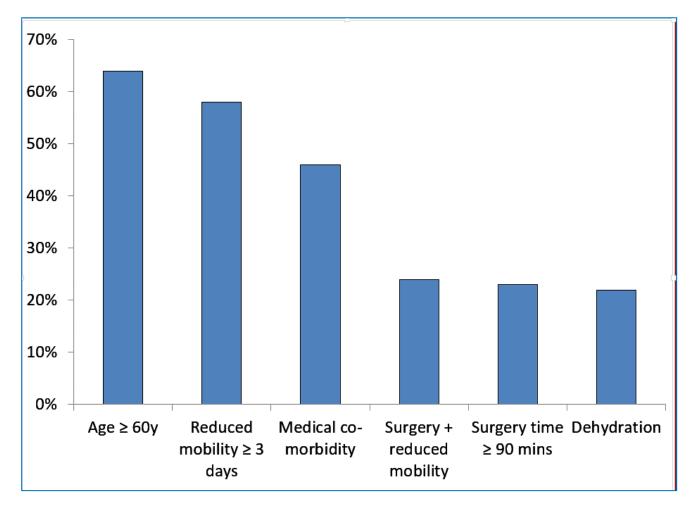
- **Multidisciplinary approach** in prophylaxis implementation help reduce preventable HATs.
- **Multifaceted interventions** including education and electronic prompts improve prophylaxis prescription and administration.
- **Rapid communication** of learning from incidents via regular teaching sessions reduce repetitive errors.



King's Thrombosis Centre

## HAT root cause analysis:

### Majority of cases received appropriate thromboprophylaxis





# 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?

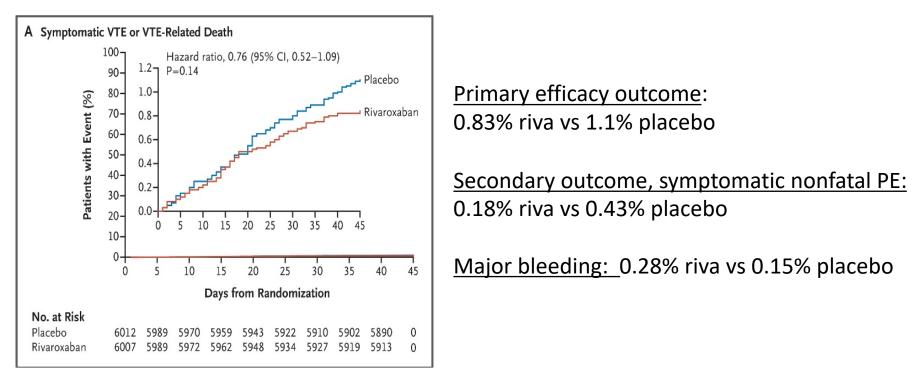
## APEX: extended thromboprophylaxis with betrixaban in acutely ill medical patients

- 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 <a>75 years.</a>
- 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

## 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** 



<u>Conclusion</u>: 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

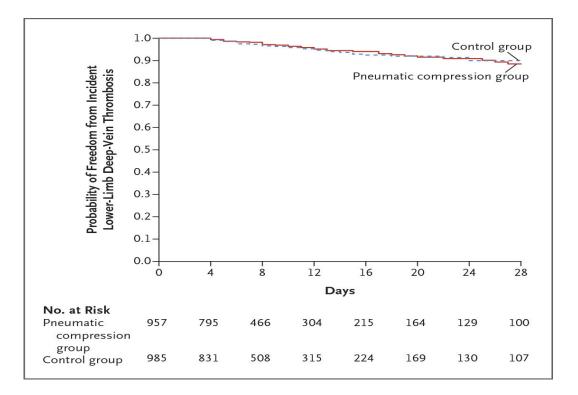
#### DOACs for thromboprophylaxis in ambulatory patients with cancer

Cumulative Analysis of the AVERT and CASSINI Trials.*									
Outcome	CASSINI Trial		AVERT Trial		Cumulative Values				
	Rivaroxaban	Placebo	Apixaban	Placebo	DOACs	Placebo	Relative Risk (95% CI)	Absolute Difference percentage	No. Needed to Treat or Harm†
			number/total	number (percent)	)			points	
Primary efficacy outcome									
ITT analysis	25/420 (6.0)	37/421 (8.8)	12/288 (4.2)	28/275 (10.2)	37/708 (5.2)	65/696 (9.3)	0.56 (0.38–0.83)	-4.1	24
Analysis during treatment period	11/420 (2.6)	27/421 (6.4)	3/288 (1.0)	20/275 (7.3)	14/708 (2.0)	47/696 (6.8)	0.29 (0.16–0.53)	-4.8	21
Symptomatic VTE: ITT analysis	15/420 (3.6)	19/421 (4.5)	9/288 (3.1)	22/275 (8.0)	24/708 (3.4)	41/696 (5.9)	0.58 (0.35–0.94)	-2.5	40
Major bleeding	8/405 (2.0)	4/404 (1.0)	10/288 (3.5)	5/275 (1.8)	18/693 (2.6)	9/679 (1.3)	1.96 (0.88–4.33)	1.3	77
Death from any cause	84/420 (20.0)	100/421 (23.8)	35/288 (12.2)	27/275 (9.8)	119/708 (16.8)	127/696 (18.2)	0.92 (0.73–1.16)	-1.4	71

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

G Agnelli et al. Direct Oral Anticoagulants for Thromboprophylaxis in Ambulatory Patients with Cancer. NEJM. 2019 Feb 21;380(8):781-783.

## PREVENT study: Adjunctive intermittent pneumatic compression for thromboprophylaxis



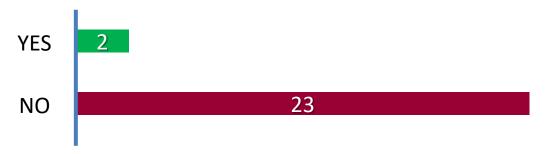
Among critically ill patients receiving pharmacologic thromboprophylaxis, adjunctive IPC did not lower incidence of proximal DVT vs pharmacologic thromboprophylaxis alone.

YM Arabi et al. Adjunctive Intermittent Pneumatic Compression for Venous Thromboprophylaxis. NEJM 2019 Feb. DOI: 10.1056/NEJMoa1816150

### NICE GC92 - NG89

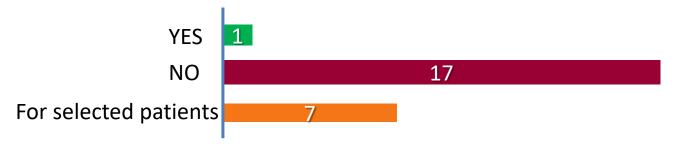
NICE recommends risk assessment using a tool published by a national UK body, professional network or peer-reviewed journal

• Are you planning to change the VTE risk assessment tool used?



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?



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

Tseng E and Cushman M for American Society of Hematology Prophylaxis for Hospitalized and Non-Hospitalized Medical Patients. Available athttps://www.hematology.org/Clinicians/Guidelines-Quality/VTE/9179.aspx. Accessed on April 2, 2019.



## 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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