Learning from venous thromboembolism claims in primary care

Dr Matthew Fay

GPWER Cardiovascular Medicine Bradford, UK

Trustee Atrial Fibrillation Association

Trustee Thrombosis UK

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Declaration of interests

- The Westcliffe Health Innovations has received support from: AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol Myers Squibb, Medtronic, Novartis, Pfizer, Roche.

- An advisor to: Arrhythmia Alliance, Heart Valve Voice, National Stroke Association, Pumping Marvellous, Syncope Trust

- A trustee of Thrombosis UK and AF Association

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The size of the problem

"The challenge is that the "classic" presentation with abrupt onset of pleuritic chest pain, shortness of breath, and hypoxia is rarely the case. Studies of patients who die unexpectedly of pulmonary embolism reveal that they complained of nagging symptoms often for weeks before death related to pulmonary embolism. **Forty percent of these patients had been seen by a physician in the weeks prior to their death**[2]"

Unusual Presentation of A Massive Pulmonary Embolism

Safi M et al[1]

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1. Safi M, Rostami RT, Taherkhani M. Unusual presentation of a massive pulmonary embolism. J Tehran Heart Cent. 2011 Winter;6(1):41-4. Epub 2011 Feb 28. PMID: 23074604; PMCID: PMC3466862.
2. Kline JA, Runyon MS. Pulmonary embolism and deep venous thrombosis. In: Marx JA, Hockenberger RS, Walls RM, editors. *Rosen's Emergency Medicine Concepts and Clinical Practice.* 6th ed. London: mosby; 2006. pp. 1368–1382

How do identify some with VTE?

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PLOS ONE

"I Can't Find Anything Wrong: It Must Be a Pulmonary Embolism": Diagnosing Suspected Pulmonary Embolism in Primary Care, a Qualitative Study

Marie Barais[1]*, Nathalie Morio[1], Amélie Cuzon Breton[1], Pierre Barraine[1], Amélie Calvez[1], Erik Stolper[2,3], Paul Van Royen[3], Claire Liétard[4]

1 Université de Bretagne Occidentale, Faculté de Médecine et des Sciences de la Santé de Brest, Département Universitaire de Médecine Générale, Brest, France, **2** Faculty of Health, Medicine and Life Sciences, Caphri School for Public Health and Primary Care, Department of Family Medicine, Maastricht University, Maastricht, The Netherlands, **3** Department of Primary and Interdisciplinary Care, University of Antwerp, Antwerp, Belgium, **4** Université Européenne de Bretagne, Faculté de Médecine et des Sciences de la Santé de Brest -Laboratoire de Santé Publique, Epidémiologie, Brest, France

Barais M, Morio N, Cuzon Breton A, Barraine P, Calvez A, et al. (2014) "I Can't Find Anything Wrong: It Must Be a Pulmonary Embolism": Diagnosing Suspected Pulmonary Embolism in Primary Care, a Qualitative Study. PLoS ONE 9(5): e98112. doi:10.1371/journal.pone.0098112

Abstract

Background: Before using any prediction rule oriented towards pulmonary embolism (PE), family physicians (FPs) should have some suspicion of this diagnosis. The diagnostic reasoning process leading to the suspicion of PE is not well described in primary care.

Objective: to explore the diagnostic reasoning of FPs when pulmonary embolism is suspected.

Method: Semi-structured qualitative interviews with 28 FPs. The regional hospital supplied data of all their cases of pulmonary embolism from June to November 2011. The patient's FP was identified where he/she had been the physician who had sent the patient to the emergency unit. The first consecutive 14 FPs who agreed to participate made up the first group. A second group was chosen using a purposeful sampling method. The topic guide focused on the circumstances leading to the suspicion of PE. A thematic analysis was performed, by three researchers, using a grounded theory coding paradigm.

Results: In the FPs' experience, the suspicion of pulmonary embolism arose out of four considerations: the absence of indicative clinical signs for diagnoses other than PE, a sudden change in the condition of the patient, a gut feeling that something was seriously wrong and an earlier failure to diagnose PE. The FPs interviewed did not use rules in their diagnostic process.

Conclusion: This study illustrated the diagnostic role of gut feelings in the specific context of suspected pulmonary embolism in primary care. The FPs used the sense of alarm as a tool to prevent the diagnostic error of missing a PE. The diagnostic accuracy of gut feelings has yet to be evaluated.

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Barais M, Morio N, Cuzon Breton A, Barraine P, Calvez A, et al. (2014) ''I Can't Find Anything Wrong: It Must Be a Pulmonary Embolism'': Diagnosing Suspected Pulmonary Embolism in Primary Care, a Qualitative Study. PLoS ONE 9(5): e98112. doi:10.1371/journal.pone.0098112

British Journal of General Practice
bringing research to clinical practice

Research

Diagnostic delay of pulmonary embolism in primary and secondary care: a retrospective cohort study

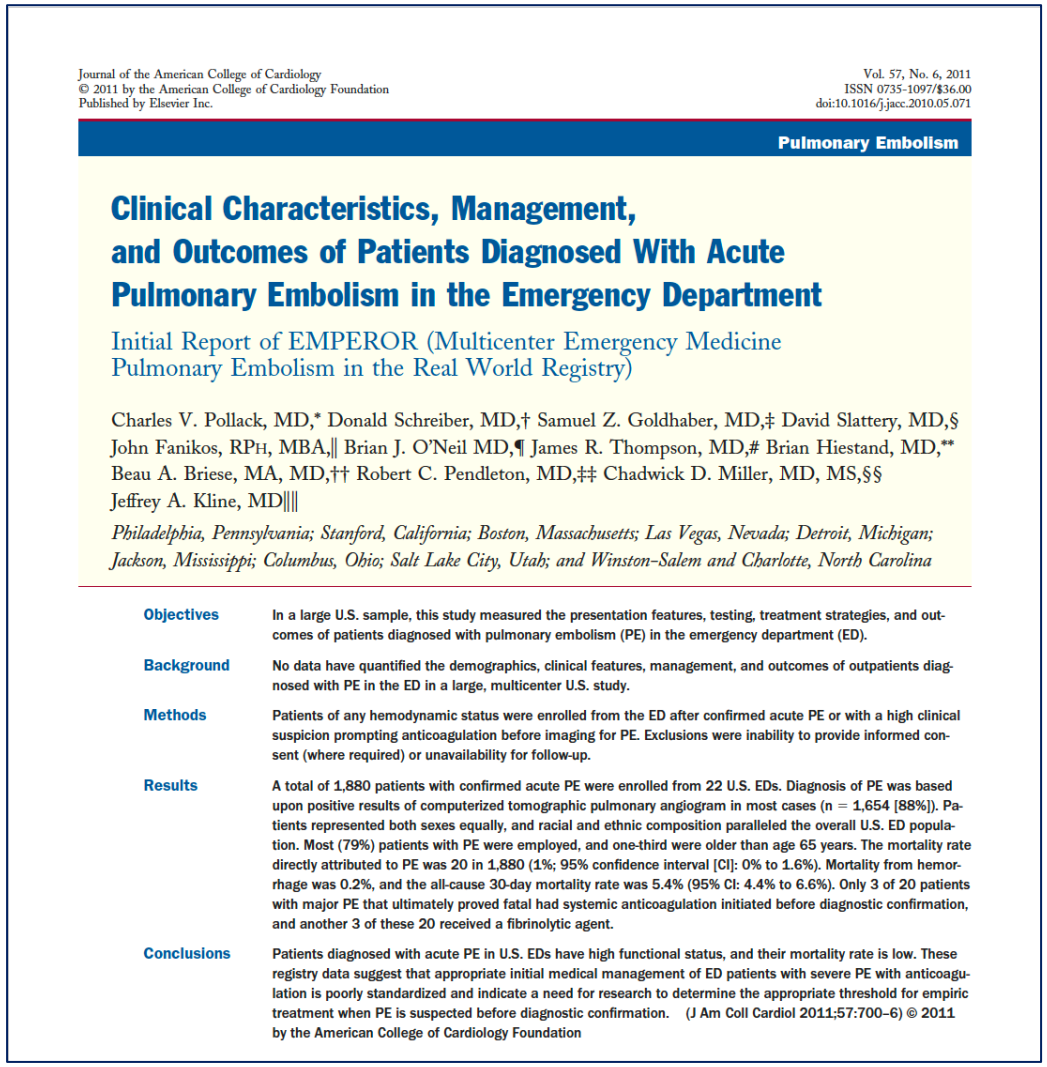
Stefan Walen, Roger AMJ Damoiseaux, Steven M Uil and Jan WK van den Berg

British Journal of General Practice 2016; 66 (647): e444-e450. **DOI:** https://doi.org/10.3399/bjgp16X685201

Total diagnostic delay

On average, patients were diagnosed 8.6 +/– 25.5 days after symptom onset (median 3 days, range 0–346). In total, 59 patients (22.6%) were diagnosed with PE within a day of the onset of symptoms. Sixty-two patients (23.8%) had a diagnostic delay of longer than a week and 16 (6.1%) had a diagnostic delay of longer than a month. Multivariate analysis of clinical variables (Table 4) showed that calf pain (odds ratio [OR] 0.49, 95% confidence interval [CI] = 0.24 to 0.98, $P = 0.05$) and chest pain (OR 0.51, 95% CI = 0.28 to 0.92, $P = 0.03$) were associated with an early diagnosis. Sex, age, and the presence of risk factors for PE were not significantly associated with a delay in diagnosis.

What does EMPEROR tell us?



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Pulmonary Embolism

Clinical Characteristics, Management, and Outcomes of Patients Diagnosed With Acute Pulmonary Embolism in the Emergency Department

Initial Report of EMPEROR (Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry)

Charles V. Pollack, MD,* Donald Schreiber, MD,† Samuel Z. Goldhaber, MD,‡ David Slattery, MD,§ John Fanikos, RPH, MBA,‖ Brian J. O'Neil MD,¶ James R. Thompson, MD,# Brian Hiestand, MD,** Beau A. Briese, MA, MD,†† Robert C. Pendleton, MD,‡‡ Chadwick D. Miller, MD, MS,§§ Jeffrey A. Kline, MD‖‖

Philadelphia, Pennsylvania; Stanford, California; Boston, Massachusetts; Las Vegas, Nevada; Detroit, Michigan; Jackson, Mississippi; Columbus, Ohio; Salt Lake City, Utah; and Winston-Salem and Charlotte, North Carolina

Objectives In a large U.S. sample, this study measured the presentation features, testing, treatment strategies, and outcomes of patients diagnosed with pulmonary embolism (PE) in the emergency department (ED).

Background No data have quantified the demographics, clinical features, management, and outcomes of outpatients diagnosed with PE in the ED in a large, multicenter U.S. study.

Methods Patients of any hemodynamic status were enrolled from the ED after confirmed acute PE or with a high clinical suspicion prompting anticoagulation before imaging for PE. Exclusions were inability to provide informed consent (where required) or unavailability for follow-up.

Results A total of 1,880 patients with confirmed acute PE were enrolled from 22 U.S. EDs. Diagnosis of PE was based upon positive results of computerized tomographic pulmonary angiogram in most cases (n = 1,654 [88%]). Patients represented both sexes equally, and racial and ethnic composition paralleled the overall U.S. ED population. Most (79%) patients with PE were employed, and one-third were older than age 65 years. The mortality rate directly attributed to PE was 20 in 1,880 (1%; 95% confidence interval [CI]: 0% to 1.6%). Mortality from hemorrhage was 0.2%, and the all-cause 30-day mortality rate was 5.4% (95% CI: 4.4% to 6.6%). Only 3 of 20 patients with major PE that ultimately proved fatal had systemic anticoagulation initiated before diagnostic confirmation, and another 3 of these 20 received a fibrinolytic agent.

Conclusions Patients diagnosed with acute PE in U.S. EDs have high functional status, and their mortality rate is low. These registry data suggest that appropriate initial medical management of ED patients with severe PE with anticoagulation is poorly standardized and indicate a need for research to determine the appropriate threshold for empiric treatment when PE is suspected before diagnostic confirmation. (J Am Coll Cardiol 2011;57:700–6) © 2011 by the American College of Cardiology Foundation

These registry data suggest that appropriate initial medical management of ED patients with severe PE with anticoagulation is poorly standardized and indicate a need for research to determine the appropriate threshold for empiric treatment when PE is suspected before diagnostic confirmation.[1]

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1. Pollack CV, Schreiber D, Goldhaber SZ, Slattery D, Fanikos J, O'Neil BJ, Thompson JR, Hiestand B, Briese BA, Pendleton RC, Miller CD, Kline JA. Clinical characteristics, management, and outcomes of patients diagnosed with acute pulmonary embolism in the emergency department: initial report of EMPEROR (Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry). J Am Coll Cardiol. 2011 Feb 8;57(6):700-6. doi: 10.1016/j.jacc.2010.05.071. PMID: 21292129.

Pathways in Venous Thromboembolic Disease

- Compare with Cardiac Chest Pain Pathways

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SUSPECTED ACUTE CORONARY SYNDROME GUIDELINE

NORTH BRISTOL NHS TRUST (June 2018)

HISTORY AND EXAMINATION

Use this protocol for patients with cardiac-sounding chest pain lasting longer than 15 mins

12-LEAD ELECTROCARDIOGRAM at regular intervals (eg within 30 minutes) with ongoing chest pain; ECG when pain-free

STEMI PATHWAY

ST ELEVATION
Two leads: >2 mm in V1-6
or >1 mm in other leads

LEFT BUNDLE BRANCH BLOCK
New or with a good history

MIDDLE PATHWAY

ST DEPRESSION
>0.5 mm
OR DEEP T WAVE INVERSION
>2 mm deep

LOW RISK PATHWAY

Chest Pain resolved
AND
NORMAL or Non-Diagnostic ECG

For pregnancy-related chest pain D/W obstetric registrar before discharge

OXYGEN if indicated, sublingual **GTN, MORPHINE** 5mg IV, **ASPIRIN** 300mg PO, **ONDANSETRON** 4mg IV

PRIMARY ANGIOPLASTY

0117 3425999 for PPCI at BHI
OR
Bleep 9227 (Mon-Fri 9am-4pm)

Administer
TICAGRELOR 180mg STAT

In exceptional circumstances (eg. if PPCI not available within 90 minutes):

TENECTEPLASE (as per protocol)

Following thrombolysis give a bolus of **FONDAPARINUX** 2.5mg IV stat followed (24 hours later) by 2.5mg S/C once daily
(Use **UFH** if eGFR < 20ml/min)
BISOPROLOL 2.5mg PO stat, unless contraindicated
CLOPIDOGREL 600 mg PO stat followed by 75mg PO for 1 month
ISOSORBIDE DINITRATE 2-10mg/hour IV infusion if pain

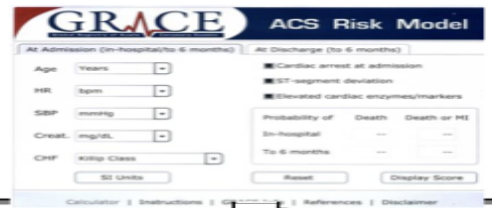
If failed reperfusion at 90 mins (< than 50% ST-segment resolution) refer for **RESCUE PCI by calling BHI on**

STEMI

ACS Pathway

Troponin at presentation and at 3 hours post presentation

Risk stratify patients using GRACE



UA or NSTEMI

SEE OVER FOR MIDDLE PATHWAY

TnT and TIMI Score at presentation

>30ng/L

TnT <14ng/L AND TIMI 0/1

TnT 14-30ng/L OR TIMI >1

Repeat TnT at 2 hours post presentation

>30ng/L

<14ng/L

14-30ng/L

Repeat TnT at 3 hours post presentation

>30ng/L

14-30ng/L *and* delta < +/-7ng/L

<14ng/L

LOW RISK

DISCHARGE FROM ED or SAU
Consider other diagnoses

If angina still possible, perform CAD risk estimation and refer to **Chest Pain Clinic** as appropriate according to CAD protocol

Aspirin 75mg od, **Bisoprolol** 2.5-5mg od, **Atorvastatin** 80mg od, **Ramipril**

Coronary angiography within 72 hrs at discretion of the responsible physician.
If angiography not possible consider functional testing.

Enter Cardiac Rehab programme, then follow-up in **Post-MI clinic** after 4 weeks

However!

- Assessment of anginal chest pain, NICE CG 95* states:

Anginal Pain is:

- Constricting discomfort in the front of the chest, or in the neck, shoulders, jaw or arms
- Precipitated by physical exertion
- Relieved by rest or GTN within about 5 minutes.

- All 3 of the features above is defined as typical angina.
- 2 of 3 of the features above is defined as atypical angina.
- 1 of 3 of the features above is defined as non-anginal chest pain.

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* https://www.nice.org.uk/guidance/CG95

Pathways in Venous Thromboembolic Disease

- Compare this with issues around PE and DVT

Symptoms & Signs of PE

Feature	PE confirmed	PE not confirmed
Dyspnoea	50%	51%
Pleuritic Chest Pain	39%	28%
Cough	23%	23%
Substernal Chest Pain	15%	17%
Fever	10%	10%
Haemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Signs of a DVT (unilateral extremity swelling)	24%	18%

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Clinical characteristics of patients with suspected PE in the emergency department (adapted from Pollack *et al.* (2011)).

Back to Basics

- **Risk factors include:-Enduring**

  - Previous venous thromboembolism
  - Cancer (known or undiagnosed)
  - Increasing age
  - Being overweight or obese
  - Male sex
  - Heart failure
  - Acquired or familial thrombophilia
  - Chronic low-grade injury to the vascular wall (for example vasculitis, hypoxia from venous stasis, or chemotherapy).

Back to Basics

- **Risk factors include:-Transient**
  - Immobility, significant trauma, or direct trauma to a vein.
  - Hormone treatment (for example oestrogen-containing contraception or hormone replacement therapy).
  - Pregnancy and the postpartum period.
  - Dehydration.

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Tests:-Risk Scores

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Tests:-Risk Scores

Two level DVT Wells score

Criteria	Score
Active cancer (treatment ongoing, within the last 6 months, or palliative).	1
Paralysis, paresis, or recent plaster immobilization of the legs	1
Recently bedridden for 3 days or more, or major surgery within the last 12 weeks requiring general or local anaesthetics	1
Localized tenderness along the distribution of the deep venous system (such as the back of the calf)	1
Entire leg is swollen.	1
Calf swelling by more than 3 cm compared with the asymptomatic leg (measured 10 cm below the tibial tuberosity).	1
Pitting oedema (greater than on the asymptomatic leg)	1
Collateral superficial veins (non-varicose).	1
Previously documented DVT	1
If an alternative cause is considered more likely than DVT.	-2

DVT low risk ≤1

Two level PE Wells score

Criteria	Score
Active cancer (treatment on-going, within the last 6 months, or palliative).	1
Heamoptysis	1
Recently bedridden for 3 days or more	1.5
Surgery within the previous 4 weeks	1.5
Heart Rate of greater than 100bpm	1.5
Previous DVT or PE.	1.5
There are clinical features of a DVT	3
If an alternative diagnosis is considered less likely than PE.	3

PE low risk ≤3

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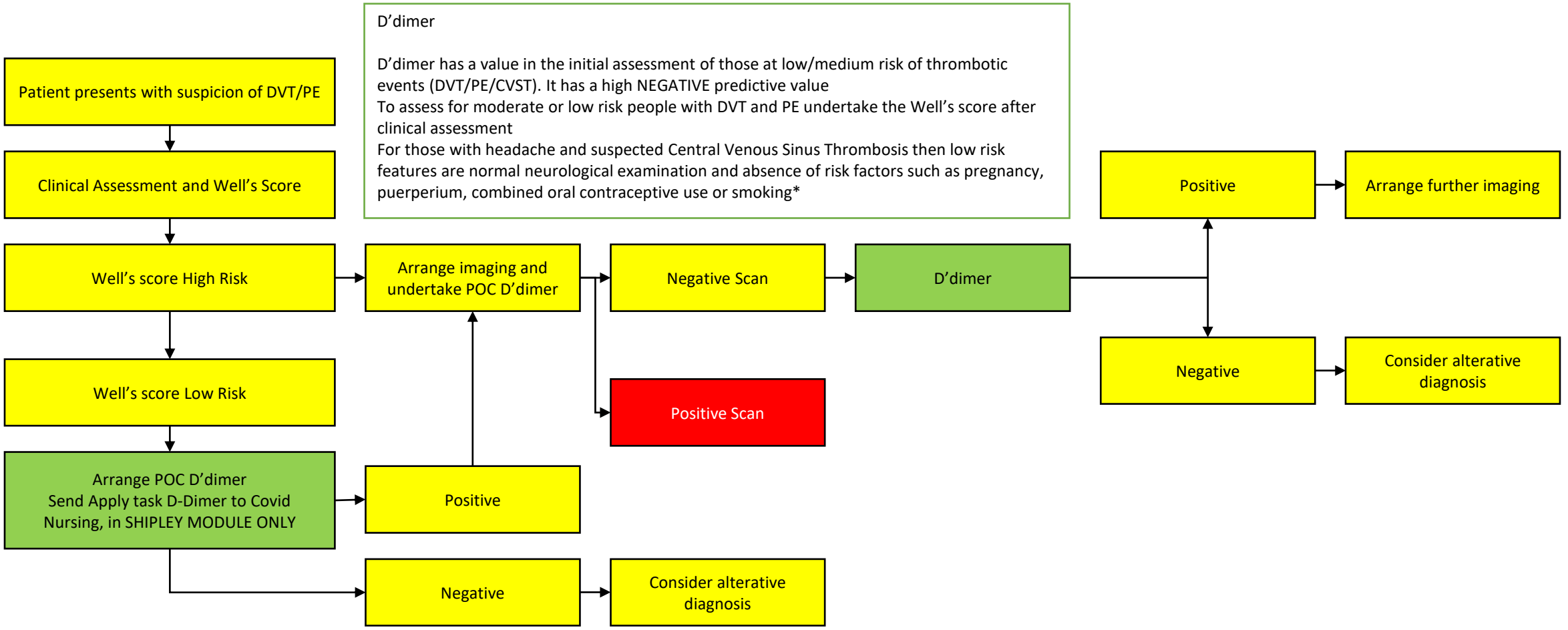
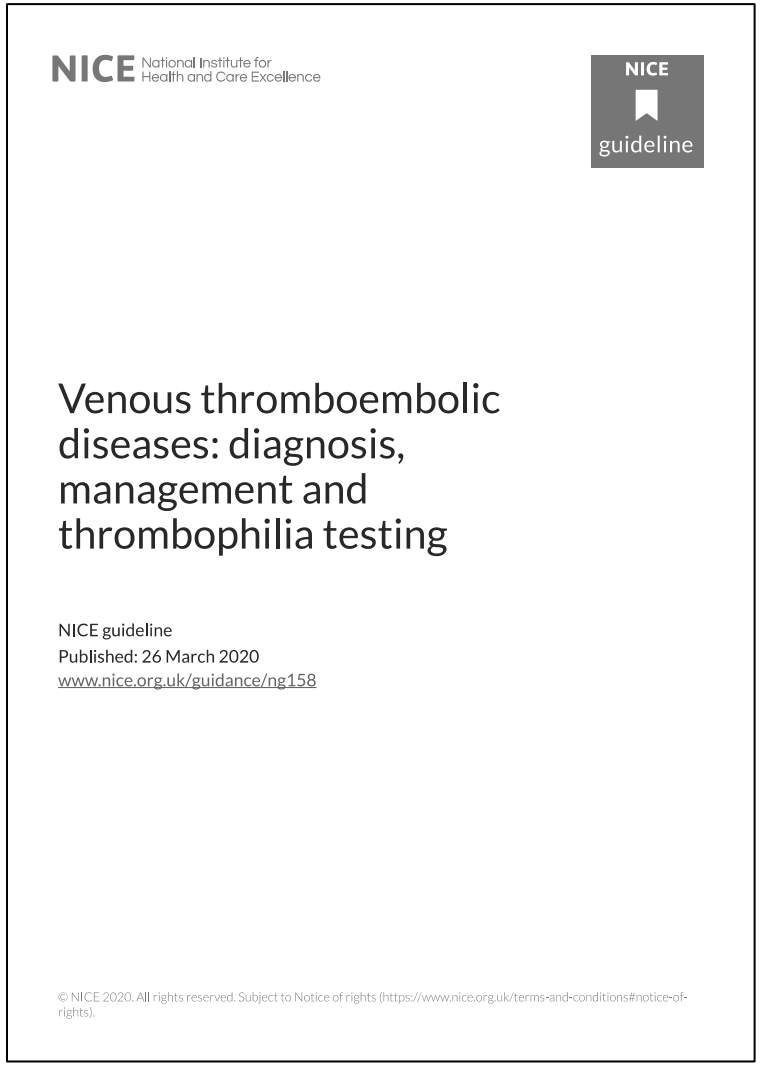
Would easy access to D-Dimer help?



What does NICE say?


NICE National Institute for Health and Care Excellence

NICE guideline

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

NICE guideline
Published: 26 March 2020
www.nice.org.uk/guidance/ng158

DVT unlikely (Wells score 1 point or less)

1.1.8 Offer people with an **unlikely** DVT Wells score (1 point or less):

- a D-dimer test with the result available within 4 hours (see the section on D-dimer testing) **or**
- if the D-dimer test result cannot be obtained within 4 hours, offer interim therapeutic anticoagulation while awaiting the result (see the section on interim therapeutic anticoagulation for suspected DVT or PE). **[2012, amended 2020]**

1.1.9 If the D-dimer test result is negative, follow the actions in recommendation 1.1.7. **[2012]**

1.1.10 If the D-dimer test result is positive, offer:

- a proximal leg vein ultrasound scan, with the result available within 4 hours if possible **or**
- interim therapeutic anticoagulation (see the section on interim therapeutic anticoagulation for suspected DVT or PE) and a proximal leg vein ultrasound scan with the result available within 24 hours. **[2012, amended 2020]**

1.1.11 If the proximal leg vein ultrasound scan is:

- positive, follow the actions in recommendation 1.1.5
- negative, follow the actions in recommendation 1.1.7. **[2012]**

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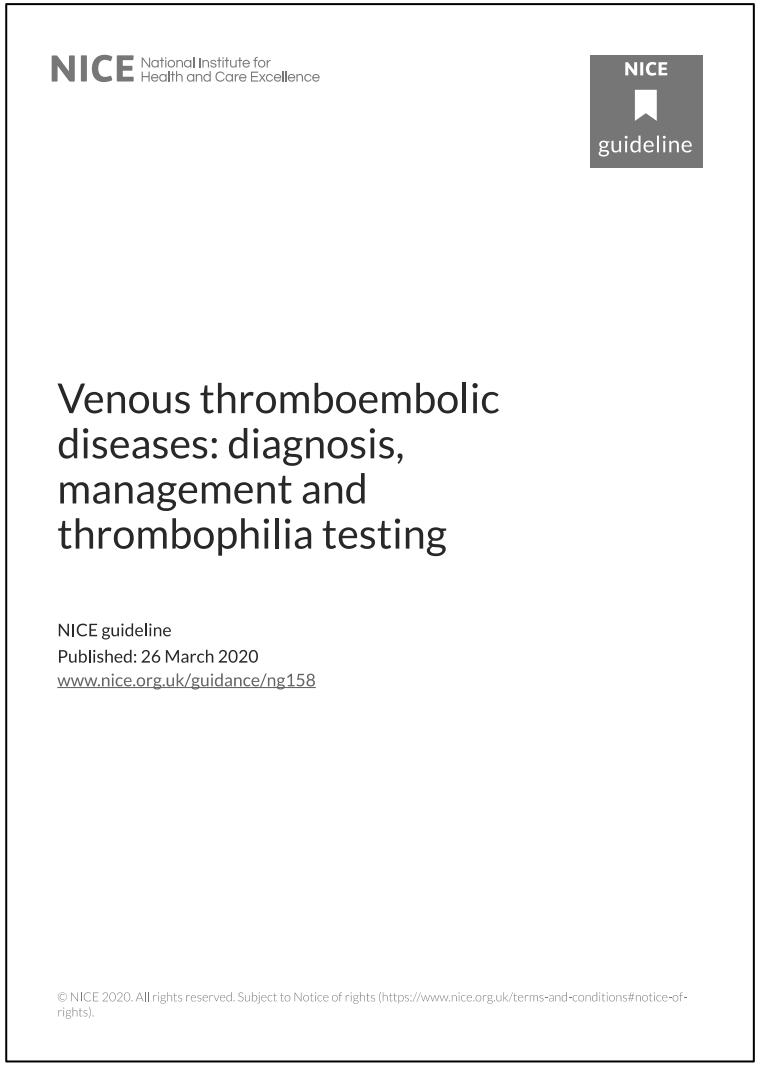
https://www.nice.org.uk/guidance/ng158
Accessed 23rd August 2022

What does NICE say?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PE unlikely (Wells score 4 points or less)

1.1.21 Offer people with an **unlikely** PE Wells score (4 points or less):

- a D-dimer test with the result available within 4 hours if possible (see the section on D-dimer testing) **or**
- if the D-dimer test result cannot be obtained within 4 hours, offer interim therapeutic anticoagulation while awaiting the result (see the section on interim therapeutic anticoagulation for suspected DVT or PE).

If the D-dimer test result is:

- positive, follow the actions in recommendations 1.1.18 and 1.1.19
- negative:
  - stop interim therapeutic anticoagulation (but do not stop long-term anticoagulation if being used for secondary prevention)
  - think about alternative diagnoses
- tell the person that it is not likely they have PE. Discuss with them the signs and symptoms of PE and when and where to seek further medical help. **[2012, amended 2020]**

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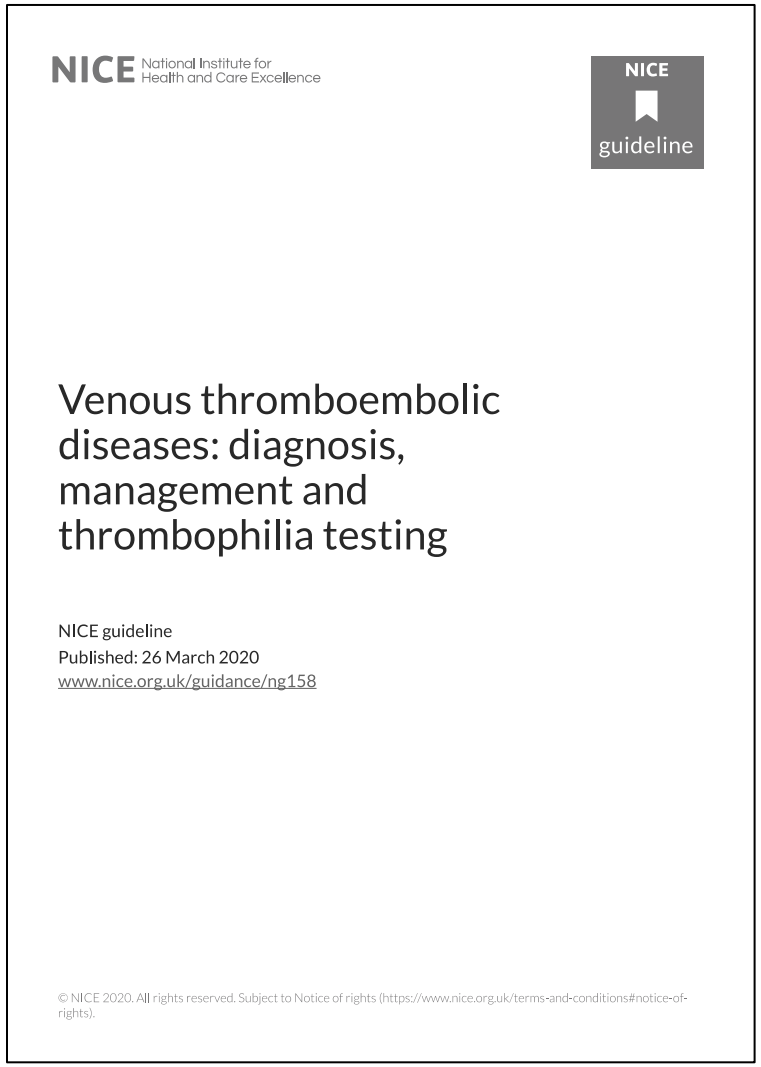
What does NICE say?



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D-dimer testing

1.1.12 When offering D-dimer testing for suspected DVT or PE, consider a point-of-care test if laboratory facilities are not immediately available. **[2020]**

1.1.13 If using a point-of-care D-dimer test, choose a fully quantitative test. **[2020]**

1.1.14 When using a point-of-care or laboratory D-dimer test, consider an age-adjusted D-dimer test threshold for people aged over 50. **[2020]**

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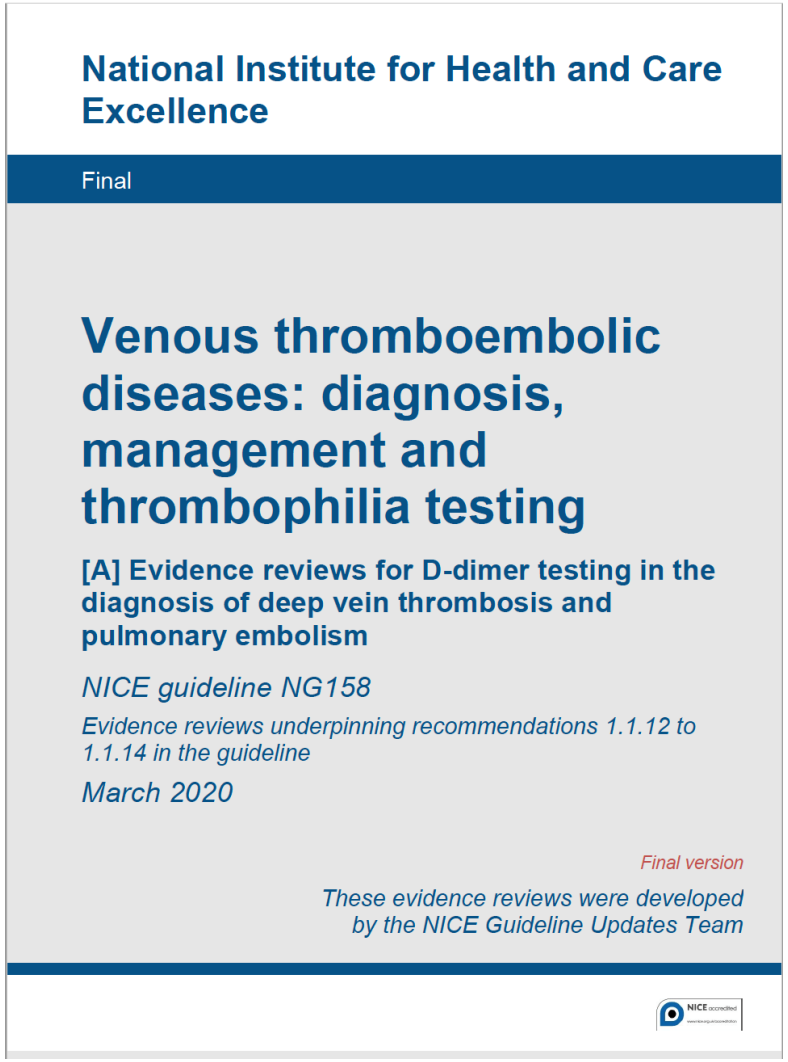
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Final

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

[A] Evidence reviews for D-dimer testing in the diagnosis of deep vein thrombosis and pulmonary embolism

NICE guideline NG158

Evidence reviews underpinning recommendations 1.1.12 to 1.1.14 in the guideline

March 2020

Final version

These evidence reviews were developed by the NICE Guideline Updates Team

In patients with suspected DVT, evidence from the de novo cost-consequences model developed for this guideline suggests that compared to laboratory testing:

Excluding primary care costs, the overall point-of-care testing strategy is less costly than laboratory testing (-£1,331 [-£10,777 to £8,721)]). When primary costs are included, the overall point-of care testing strategy becomes significantly less costly (-£20,166 [-£30,296 to -£9,527])

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https://www.nice.org.uk/guidance/ng158/evidence/a-ddimer-testing-in-the-diagnosis-of-deep-vein-thrombosis-and-pulmonary-embolism-pdf-8710588334
Accessed 23rd August 2022

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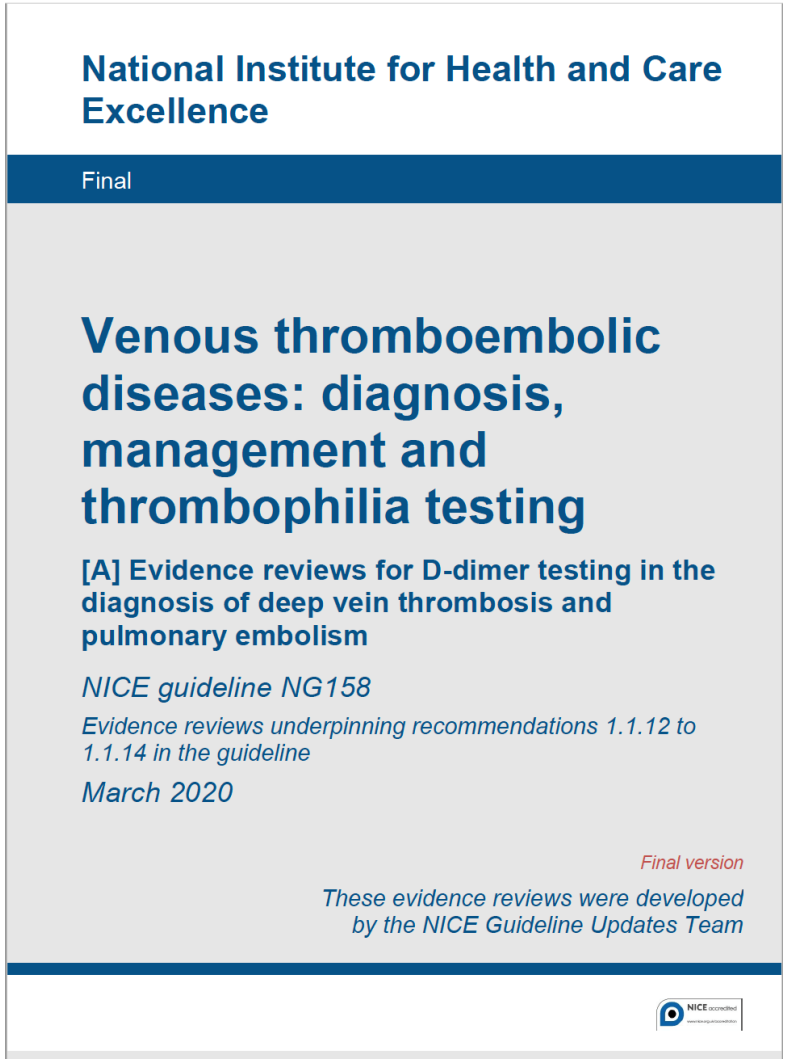
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Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

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March 2020

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In patients with suspected PE, evidence from the de novo cost-consequences model developed for this guideline suggests that compared to laboratory testing:

Overall, point-of-care D-dimer testing results in a small increase (2 per 1,000 people) in the number of false negative results and a large decrease (151 per 1,000) in the number of false positive results, although neither of these findings is statistically significant at the 5% level. Excluding primary care costs, the overall point-of-care testing strategy is less costly than laboratory testing (-£14,374 [-£37,279 to £10,115]). When primary costs are included, the overall point-of care testing strategy becomes significantly less costly (-£33,725 [-£59,124 to -£6,331]).

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https://www.nice.org.uk/guidance/ng158/evidence/a-ddimer-testing-in-the-diagnosis-of-deep-vein-thrombosis-and-pulmonary-embolism-pdf-8710588334
Accessed 23rd August 2022

Safety Netting

- **With some many variables…**
  - **What to watch out for:**
    - Progressive symptoms
    - Heamoptysis
    - Stepwise changes
    - Palpitations
    - Episode of collapse/syncope (A&E)
  - **What to watch for that may suggest not VTE:**
    - Purulent sputum production
    - Fever/flu like symptoms
    - Change in stool suggesting GI bleeding
  - **Patient focus:**
    - Increasing anxiety about the situation

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WINNER of the WTD 2021 Activity of the Year

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Thrombosis is the formation of blood clots, also known as deep vein thrombosis (DVT) or pulmonary embolism (PE).

Blood clots can be fatal and need urgent medical investigation for diagnosis and treatment.

If you develop:

- **unexplained ongoing pain in the leg muscles**
- **unexplained light headedness, a blackout or**
- **unexplained breathlessness or cough**

Seek medical advice and ask – **"Could this be a clot?"**

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What actions can you take as a clinician?

1. Detailed clinical history, insightful questioning to draw out patient information, using key questions rather than relying upon the patient to provide and deliver that information.[19]

2. Pre-test probability of VTE to be recorded in detailed consultation notes.

3. Use of VTE risk assessment tools and reassessment to be recorded in hospital and where appropriate, post operatively in detailed consultation notes.

4. Consider use of digital text or app facility providing patients with advice and safety netting, and clinicians with assurance that patients and their families have access to recall safety netting information if they require clarification.

5. Encourage the patient to vocalise their concerns, creating a more collaborative clinician–patient relationship, leading to a patient co-creation approach to treatment options.

6. Clinicians to attend multidisciplinary training programmes supported by Royal Colleges and Health Education England programmes, with a focus on reducing diagnostic error and implementing existing national guidelines and recommendations.

Summary

- There is a great deal of poor education regarding thrombosis in GP training
- Need to maintain the discussion
- Think about the diagnosis and risk score
- Point of Care D-dimer may assist
- Keep the pathway simple
- Keep the intervention simple
- Ensure the patient knows what is happening to them and why

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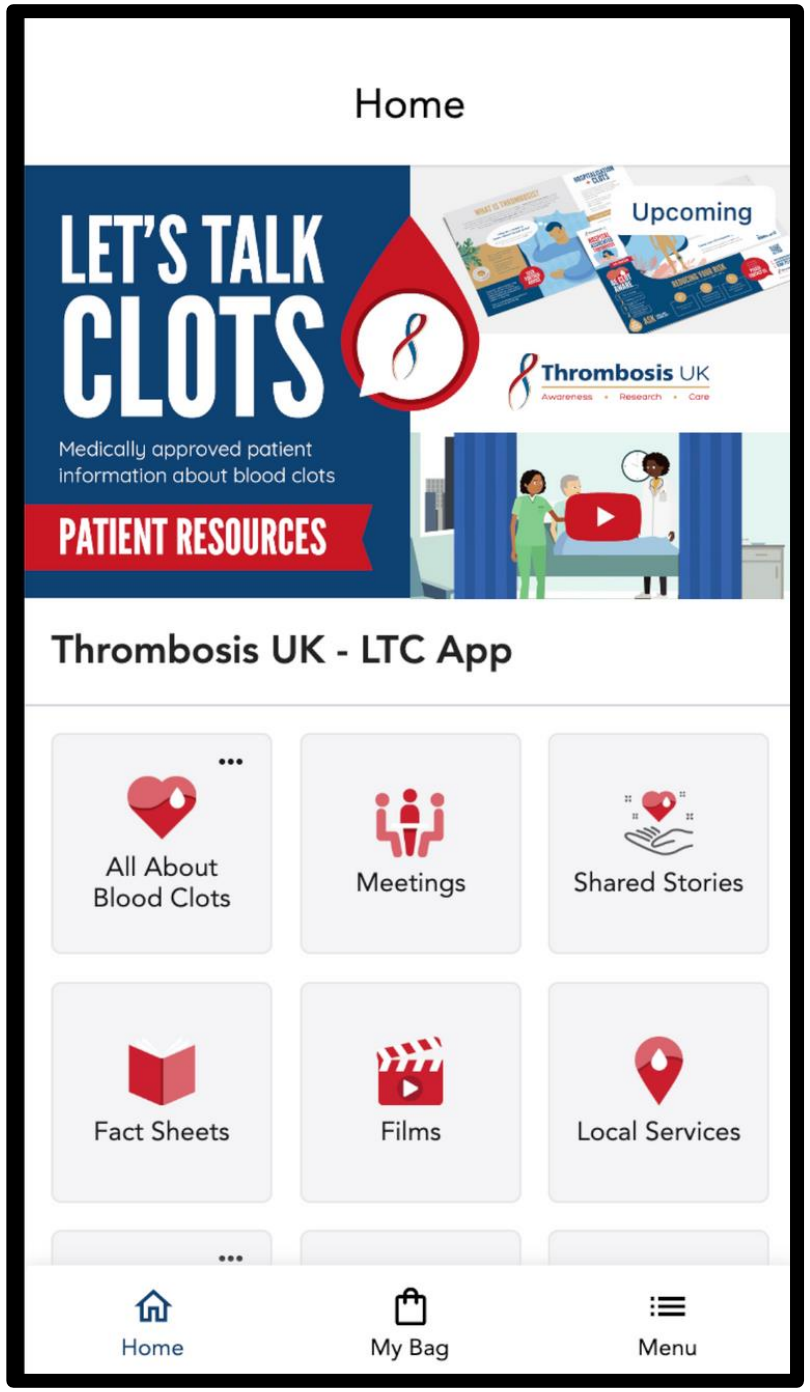
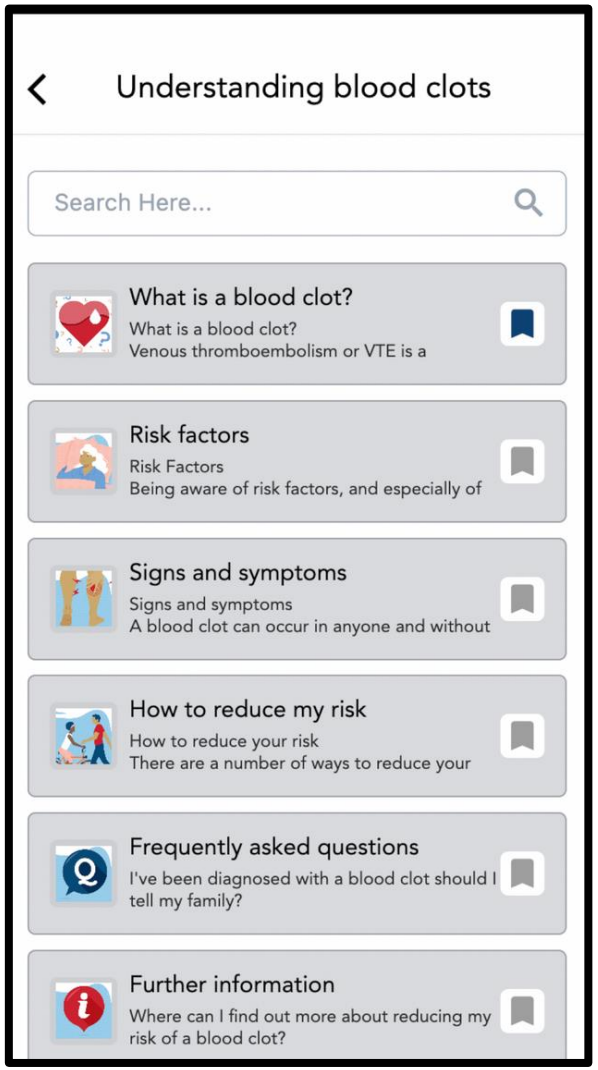
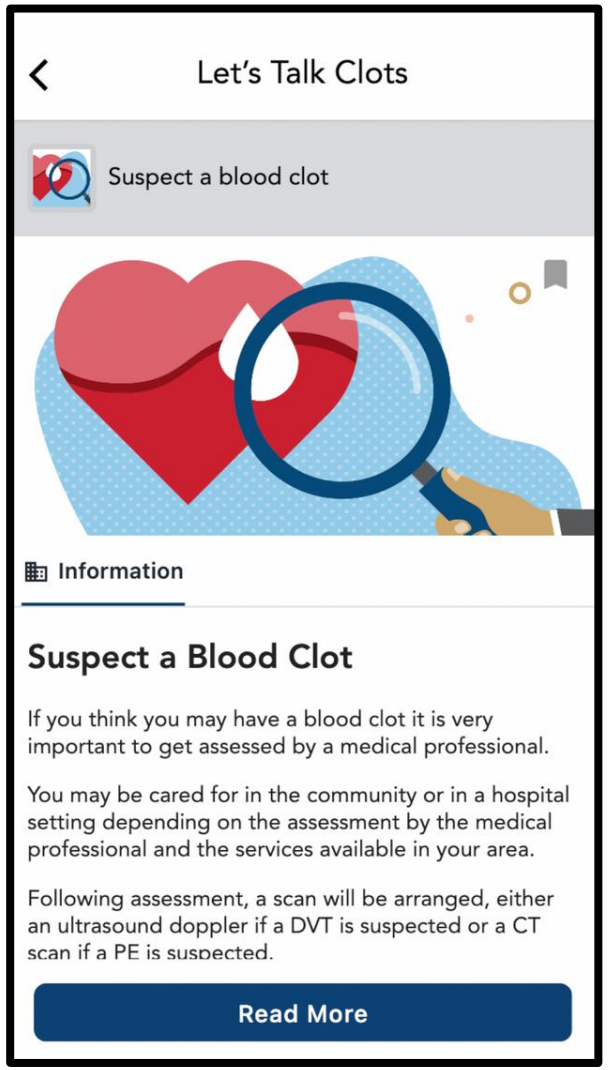
Let’s Talk Clots patient information app







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