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2 NATIONAL INSTITUTE FOR HEALTH AND CARE 3 EXCELLENCE

Guideline

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (update)

Draft for consultation, June 2023

This is an update to NICE guideline NG158 (published March 2020). We have:

- reviewed the evidence on the use of Wells score and D-dimer in the diagnostic pathways for pulmonary embolism (PE) and deep vein thrombosis (DVT) in people with COVID-19, and updated recommendations
- refreshed the wording in recommendation 1.1.16 on the use of the pulmonary embolism rule-out criteria (PERC).

Who is it for?

- Commissioners and providers of venous thromboembolism services
- Healthcare professionals in primary, secondary and tertiary care
- Adults (18 and over) with COVID-19 and suspected or confirmed DVT or PE,
 their families and carers

What does it include?

- the updated recommendations
- rationale and impact sections that explain why the committee made the updated recommendations and how they might affect practice.

Information about how the guideline was developed is on the <u>guideline's</u> <u>webpage</u>. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

Commenting on this update

We have reviewed the evidence on the diagnosis of VTE in people with COVID-19. Recommendations 1.1.6, 1.1.7, 1.1.11, 1.1.20 and 1.1.21 have been updated. You are invited to comment on the parts of these recommendations marked [2023]. We have also made minor wording changes to recommendation 1.1.16 for clarification, and you are invited to comment on these. See tables 3 and 4 for details of the changes.

We have not reviewed the evidence for the recommendations (or parts of recommendations) shaded in grey, and cannot accept comments on them.

Sections of the guideline that have had no changes at all have been temporarily removed for this consultation and will be re-instated when the final guideline is published. See the current version of the guideline.

See <u>update information</u> for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2023 recommendations are in the evidence review and supporting document. Evidence for the 2020 and 2012 recommendations is in the <u>supporting evidence for the 2020 guideline</u>.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2 1.1 Diagnosis and initial management

Signs or symptoms of DVT

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- 1.1.1 For people who present with signs or symptoms of DVT, such as a
 swollen or painful leg, assess their general medical history and do a
- 6 physical examination to exclude other causes. [2012]
- 7 1.1.2 If DVT is suspected, use the 2-level DVT Wells score (table 1) to estimate the clinical probability of DVT. [2012]

9 Table 1 Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1

⁴ Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

Clinical feature	Points	
Previously documented DVT	1	
An alternative diagnosis is at least as likely as DVT	-2	
Clinical probability simplified score	Points	
DVT likely	2 points or more	
DVT unlikely	1 point or less	
Adapted with permission from Wells et al. (2003) Evaluation of D-dimer in the diagnosis of		

1 2 suspected deep-vein thrombosis.

DVT likely (Wells score 2 points or more)

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- 3 4 1.1.3 Offer people with a **likely** DVT Wells score (2 points or more): 5 • a proximal leg vein ultrasound scan, with the result available within 6 4 hours if possible (if the scan result cannot be obtained within 4 hours 7 follow recommendation 1.1.4) 8 a D-dimer test if the scan result is negative. [2012] 9 1.1.4 If a proximal leg vein ultrasound scan result cannot be obtained within 10 4 hours, offer people with a DVT Wells score of 2 points or more: 11 • a D-dimer test. then • interim therapeutic anticoagulation (see the section on interim 12 13 therapeutic anticoagulation for suspected DVT or PE) and 14 • a proximal leg vein ultrasound scan with the result available within 24 hours. [2012, amended 2020] 15 16 1.1.5 For people with a positive proximal leg vein ultrasound scan:
 - offer or continue anticoagulation treatment (see the section on anticoagulation treatment for confirmed DVT or PE) or
 - if anticoagulation treatment is contraindicated, offer a mechanical intervention (see the section on mechanical interventions).

For people with symptomatic iliofemoral DVT see the section on thrombolytic therapy. [2012]

1	1.1.6	For people with a negative proximal leg vein ultrasound scan and a
2		positive D-dimer test result:
3		• stop interim therapeutic anticoagulation, but do not stop:
4		 long-term anticoagulation when used for secondary prevention
5		[2012, amended 2020], or
6		 short-term anticoagulation when used for primary VTE prevention in
7		people with COVID-19 (see the recommendations on VTE
8		prophylaxis in the NICE guideline on managing COVID-19) [2023]
9		• offer a repeat proximal leg vein ultrasound scan 6 to 8 days later and
10		 if the repeat scan result is positive, follow the actions in
11		recommendation 1.1.5 [2012, amended 2020]
12		 if the repeat scan result is negative, follow the actions in
13		recommendation 1.1.7. [2012, amended 2020]
14	1.1.7	For people with a negative proximal leg vein ultrasound scan and a
15		negative D-dimer test result:
16		• stop interim therapeutic anticoagulation, but do not stop:
17		 long-term anticoagulation when used for secondary prevention
18		[2012, amended 2020], or
19		 short-term anticoagulation when used for primary VTE prevention in
20		people with COVID-19 (see the recommendations on VTE
21		prophylaxis in the NICE guideline on managing COVID-19) [2023]
22		think about alternative diagnoses [2012, amended 2020]
23		• tell the person that it is not likely they have DVT. Discuss with them the
24		signs and symptoms of DVT and when and where to seek further
25		medical help. [2012, amended 2020]
26	DVT unlik	cely (Wells score 1 point or less)
27	1.1.8	Offer people with an unlikely DVT Wells score (1 point or less):

4		a D dimer test with the result available within 4 hours (see the section
1		 a D-dimer test with the result available within 4 hours (see the section
2		on <u>D-dimer testing</u>) or
3		• if the D-dimer test result cannot be obtained within 4 hours, offer interim
4		therapeutic anticoagulation while awaiting the result (see the section on
5		interim therapeutic anticoagulation for suspected DVT or PE). [2012,
6		amended 2020]
7	1.1.9	If the D-dimer test result is negative, follow the actions in
8		recommendation 1.1.7. [2012]
9	1.1.10	If the D-dimer test result is positive, offer:
10		a proximal leg vein ultrasound scan, with the result available within
11		4 hours if possible or
12		 interim therapeutic anticoagulation (see the section on interim
13		therapeutic anticoagulation for suspected DVT or PE) and a proximal
14		leg vein ultrasound scan with the result available within 24 hours.
15		[2012, amended 2020]
10		[2012, amended 2020]
16	1.1.11	If the proximal leg vein ultrasound scan is:
17		• positive, follow the actions in recommendation 1.1.5 [2012]
18		 negative, follow the actions in recommendation 1.1.7, that is:
19		 stop interim therapeutic anticoagulation, but do not stop:
20		♦ long-term anticoagulation when used for secondary prevention
21		[2012], or
22		♦ short-term anticoagulation when used for primary VTE prevention
23		in people with COVID-19 (see the recommendations on VTE
24		prophylaxis in the NICE guideline on managing COVID-19) [2023]
25		 think about alternative diagnoses [2012]

tell the person that it is not likely they have DVT. Discuss with them
 the signs and symptoms of DVT and when and where to seek further
 medical help. [2012]

For a short explanation of why the committee made the 2023 recommendations and how they might affect practice, see the <u>rationale and impact section on the</u> <u>diagnosis and initial management in people with COVID-19</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review I: diagnosing VTE in people with COVID-19.

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D-dimer testing

6	1.1.12	When offering D-dimer testing for suspected DVT or PE, consider a
7		point-of-care test if laboratory facilities are not immediately available.
8		[2020]
9	1.1.13	If using a point-of-care D-dimer test, choose a fully quantitative test.
10		[2020]
11	1.1.14	When using a point-of-care or laboratory D-dimer test, consider an
12		age-adjusted D-dimer test threshold for people aged over 50. [2020]

For a short explanation of why the committee made these 2020 recommendations and how they might affect practice, see the <u>rationale and impact section on D-dimer testing</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review A: D-dimer testing in the diagnosis of deep vein thrombosis and <u>pulmonary embolism</u>.

⁸ Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

Signs or symptoms of PE

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1.1.15 For people who present with signs or symptoms of PE, such as chest pain, shortness of breath or coughing up blood, assess their general medical history, do a physical examination and offer a chest X-ray to exclude other causes. [2012]

6 Pulmonary embolism rule-out criteria (the PERC rule)

- 1.1.16 If clinical suspicion of PE is low based on the overall clinical impression (from general medical history, physical examination and any initial investigations such as electrocardiography or chest X-ray), and other diagnoses are feasible, consider using the <u>pulmonary embolism rule-out criteria</u> (PERC) to help determine whether any further investigations for PE are needed.
- Be aware that the PERC rule has not been validated in people with COVID-19. **[2020, amended 2023]**

For a short explanation of why the committee made the 2020 recommendation and refreshed the recommendation in 2023 and how it might affect practice, see the <u>rationale and impact section on the pulmonary embolism rule-out criteria (the PERC rule)</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review B: the use of the pulmonary embolism rule-out criteria for diagnosis of pulmonary embolism and <u>supporting document: refresh of</u> recommendation 1.1.16 on the PERC rule.

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- 1.1.17 If PE is suspected, use the 2-level PE Wells score (table 2) to estimate the clinical probability of PE. **[2012]**
- 9 Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

Table 2 Two-level PE Wells score

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate more than 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1
Clinical probability simplified score	Points
PE likely	More than 4 points
PE unlikely	4 points or less

Adapted with permission from Wells et al. (2000) <u>Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer.</u>

PE likely (Wells score more than 4 points)

- 1.1.18 For people with a **likely** PE Wells score (more than 4 points):
 - offer a computed tomography pulmonary angiogram (CTPA)
 immediately if possible or
 - for people with an allergy to contrast media, severe renal impairment
 (<u>estimated creatinine clearance</u> less than 30 ml/min) or a high risk from
 irradiation, assess the suitability of a ventilation/perfusion single photon
 emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT
 scan is not available, a V/Q planar scan, as an alternative to CTPA.

If a CTPA, V/Q SPECT or V/Q planar scan cannot be done immediately, offer interim therapeutic anticoagulation (see the section on interim therapeutic anticoagulation for suspected DVT or PE). [2012, amended 2020]

1	1.1.19	If PE is identified by CTPA, V/Q SPECT or V/Q planar scan:
2 3 4 5 6 7 8		 offer or continue anticoagulation treatment (see the section on anticoagulation treatment for confirmed DVT or PE) or if anticoagulation treatment is contraindicated, consider a mechanical intervention (see the section on mechanical interventions). For people with PE and haemodynamic instability see the section on thrombolytic therapy. [2012, amended 2020]
9	1.1.20	If PE is not identified by CTPA, V/Q SPECT or V/Q planar scan:
10 11		 consider a proximal leg vein ultrasound scan if DVT is suspected [2012, amended 2020]
12		if DVT is not suspected:
13		 stop interim therapeutic anticoagulation, but do not stop:
14		♦ long-term anticoagulation when used for secondary prevention
15		[2012, amended 2020], or
16		♦ short-term anticoagulation when used for primary VTE prevention
17		in people with COVID-19 (see the recommendations on VTE
18		prophylaxis in the NICE guideline on managing COVID-19) [2023]
19		 think about alternative diagnoses [2012, amended 2020]
20		 tell the person that it is not likely they have PE. Discuss with them
21		the signs and symptoms of PE and when and where to seek further
22		medical help. [2012, amended 2020]
23	PE unlike	ly (Wells score 4 points or less)
24	1.1.21	Offer people with an unlikely PE Wells score (4 points or less):
25		a D-dimer test with the result available within 4 hours if possible (see
26		the section on D-dimer testing) [2012, amended 2020], or

¹¹ Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

1	 if the D-dimer test result cannot be obtained within 4 hours (in any
2	setting), offer interim therapeutic anticoagulation while awaiting the
3	result (see the section on interim therapeutic anticoagulation for
4	suspected DVT or PE). [2012, amended 2020]
5	
6	If the D-dimer test result is:
7	 positive, follow the actions in recommendations 1.1.18 and 1.1.19
8	[2012, amended 2020]
9	negative:
10	 stop interim therapeutic anticoagulation, but do not stop:
11	♦ long-term anticoagulation when used for secondary prevention
12	[2012, amended 2020], or
13	♦ short-term anticoagulation when used for primary VTE prevention
14	in people with COVID-19 (see the recommendations on VTE
15	prophylaxis in the NICE guideline on managing COVID-19) [2023]
16	 think about alternative diagnoses [2012, amended 2020]
17	• tell the person that it is not likely they have PE. Discuss with them the
18	signs and symptoms of PE and when and where to seek further
19	medical help. [2012, amended 2020]

For a short explanation of why the committee made the 2023 recommendation and how they might affect practice, see the <u>rationale and impact section on the</u>

<u>diagnosis and initial management in people with COVID-19</u>.

Full details of the evidence and the committee's discussion are in <u>evidence</u> review I: diagnosing VTE in people with COVID-19.

Signs or symptoms of both DVT and PE

1.1.22 For people who present with signs or symptoms of both DVT and PE,
carry out initial diagnostic investigations for either DVT or PE, basing the
choice of diagnostic investigations on clinical judgement. [2012]

5 Rationale and impact

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- 6 These sections briefly explain why the committee made the recommendations and
- 7 how they might affect practice. They link to details of the evidence and a full
- 8 description of the committee's discussion.

9 Diagnosis and initial management in people with COVID-19

- 10 Recommendations 1.1.1 to 1.1.22
- 11 Why the committee made the recommendations
- 12 The following text covers the 2023 changes to the recommendations.
- 13 The committee were aware of the increased risk of VTE in people with COVID-19
- and that diagnosis of VTE in this population can be complicated. They may present
- with symptoms similar to PE, and with elevated D-dimer levels even in the absence
- of VTE. However, limited evidence suggested that raising the D-dimer threshold for
- 17 recommending imaging in people with COVID-19 would probably increase the
- 18 number of missed VTE diagnoses.
- 19 The committee agreed that there are now fewer cases of COVID-19-related VTE due
- 20 to changes over time in people's response to COVID-19 that have made it less
- 21 severe. For example, much of the population has now had COVID-19 or has been
- vaccinated. In addition, evolution of the SARS-CoV-2 variants has led to a milder
- 23 disease. Therefore, the committee decided that the current pathway for diagnosing
- 24 PE or DVT, including the use of D-dimer testing, is still appropriate for people with
- 25 COVID-19. This is because healthcare professionals would still have a high
- 26 suspicion of PE for people who rapidly deteriorate with symptoms indicative of PE.
 - 13 Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

- 1 The committee noted that people with COVID-19 who need supplemental oxygen or
- 2 other respiratory support will be receiving prophylactic or therapeutic doses of
- 3 anticoagulation depending on the severity of illness. They agreed that it may not be
- 4 appropriate to stop this management even when the results of the imaging
- 5 investigations are negative because immunothrombosis occurring at the capillary
- 6 level associated with COVID-19 is beyond the sensitivity of standard CT pulmonary
- 7 angiogram. NICE's guideline on managing COVID-19 has advice on when to stop
- 8 anticoagulation for primary prevention in this population.

9 How the recommendations might affect practice

- 10 The following text covers the 2023 changes to the recommendations.
- 11 Imaging investigations are indicated in people with a low-risk Wells score but positive
- 12 D-dimer test. People with COVID-19, a low-risk Wells score and elevated D-dimers
- are likely to have imaging based on the current diagnostic pathway. As there may be
- other reasons for elevated D-dimer levels in the COVID-19 population and because
- the evidence suggests an increase in false-positive D-dimer results, these
- 16 recommendations may lead to an increase in the number of people who have
- 17 imaging but turn out not to have VTE. However, the incidence rate for COVID-19
- related hospital admissions is currently much lower compared with that during the
- 19 early pandemic, so imaging rates may not increase substantially in practice.
- 20 VTE prevention with anticoagulation for people with COVID-19 who need
- 21 supplemental oxygen or other respiratory support is standard practice. Therefore, the
- 22 recommendations for continuing this management following a negative imaging
- result is unlikely to result in a change in practice or an increase in resources.
- 24 Return to recommendations
- 25 Pulmonary embolism rule-out criteria (the PERC rule)
- 26 Recommendation 1.1.16

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	Why the	committee	made the	recomme	ndation
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- 2 In people with signs or symptoms of PE, but in whom clinical suspicion of PE is low
- 3 (based on the overall clinical impression and that other diagnoses are feasible),
- 4 there was some evidence showing that applying the PERC rule can safely identify
- 5 people who are unlikely to benefit from any further investigations for PE. The
- 6 committee agreed that using the PERC rule can reduce anxiety and avoid
- 7 unnecessary D-dimer testing, imaging and interim anticoagulation treatment for
- 8 people with a low probability of PE and none of the PERC criteria. However, the
- 9 evidence was limited so the committee agreed to recommend that the PERC rule be
- 10 considered as part of initial assessment for PE.
- 11 The committee noted that the largest randomised trial evaluating the implementation
- of the PERC rule used a percentage to quantify low risk (less than 15% risk of PE).
- However, the committee agreed with the recent report by the Healthcare safety
- 14 investigation branch (HSIB) on diagnosing PE in emergency departments, that this
- 15 judgement is difficult to quantify in practice. They therefore decided that using
- wording such as 'low risk' would be less confusing. The committee described that
- 17 identification of low risk is based on clinical gestalt informed by general medical
- history, physical examination and initial investigations. For example, a healthcare
- 19 professional may consider using the PERC to rule out PE from the differential
- 20 diagnosis if the presenting patient was young with new onset atraumatic chest pain
- 21 or shortness of breath, but who had no concerning historical or clinical features for
- 22 PE and a feasible alternative diagnosis (such as lower respiratory tract infection).
- 23 The committee noted that the studies evaluating PERC all took place in emergency
- 24 departments. But they could see no reason why its use should be limited to this
- 25 setting or why the diagnostic accuracy of PERC would differ in other settings such as
- outside of the hospital. They reiterated that it was the experience of diagnosing PE
- that was important for applying the rule as opposed to the setting.
- 28 People with COVID-19 are considered to have a higher risk of VTE than the general
- 29 population, and risk increases with severity of disease. The committee discussed

- 1 that the PERC rule may not be suitable to rule out PE in people with COVID-19
- 2 because of the increased risk of VTE in this population. However, they also
- 3 acknowledged that the tool has not been validated in this population. Taken together,
- 4 the committee wanted to raise awareness around the use of PERC in the COVID-19
- 5 population.

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How the recommendation might affect practice

- 7 The PERC rule is not widely used in current practice. This recommendation is
- 8 expected to increase its use in a subgroup of people in whom clinical suspicion of PE
- 9 is low and for whom discharge is being considered. Increased use of PERC can be
- 10 expected to reduce the need for D-dimer testing and imaging for people with none of
- the PERC criteria for PE, leading to some reductions in waiting times in primary care
- 12 and emergency departments. It will also help to avoid unnecessary anticoagulation
- treatment. However, the overall impact of this recommendation is not expected to be
- substantial because of the limited population it affects.
- 15 Return to recommendation

Context

- 17 In venous thromboembolism (VTE), a blood clot forms in a vein, usually in the deep
- 18 veins of the legs or pelvis. This is known as deep vein thrombosis (DVT). The blood
- 19 clot can dislodge and travel in the blood, particularly to the pulmonary arteries. This
- 20 is known as pulmonary embolism (PE). The term 'VTE' includes both DVT and PE.
- 21 Failure to diagnose and treat VTE correctly can result in fatal PE, in which the blood
- 22 clot blocks the blood supply to the lungs. However, diagnosis of VTE is not always
- 23 straightforward. This guideline includes advice on the Wells score, D-dimer
- 24 measurement, ultrasound and radiological imaging. It also offers guidance on
- 25 treating VTE, investigations for cancer in people with VTE and thrombophilia testing.
- 26 The guideline covers adults with suspected or confirmed DVT or PE. It does not
- cover children or young people aged under 18, or women who are pregnant.

- 1 Since the publication of the updated guideline in 2020, new evidence has emerged
- 2 that indicates higher risk of VTE and elevated D-dimer levels in people with COVID-
- 3 19. In addition, a Healthcare safety investigation branch (HSIB) report published
- 4 March 2022 reported difficulties in using the PERC for ruling out pulmonary
- 5 embolism. This 2023 update includes updated recommendations in these areas.

6 Finding more information and committee details

- 7 To find our guidance on related topics, including guidance in development, see
- 8 NICE's topic page on embolism and thrombosis.
- 9 For full details of the evidence and the guideline committee's discussions, see the
- 10 <u>evidence reviews</u>. You can also find information about <u>how the guideline was</u>
- 11 <u>developed</u>, including <u>details of the committee</u>.
- 12 NICE has produced tools and resources to help you put this guideline into practice.
- 13 For general help and advice on putting our guidelines into practice, see resources to
- 14 help you put NICE guidance into practice.

15 Update information

- 16 **June 2023**
- 17 This is an update of NICE guideline NG158 (published March 2020). We have
- reviewed the evidence for the diagnosis of VTE in people with COVID-19.
- 19 We refreshed the wording for recommendation 1.1.16 from the 2020 guideline for
- 20 clarity.
- 21 Recommendations (or parts of recommendations) are marked [2023] if the evidence
- has been reviewed. The recommendation marked [2020, amended 2023] has been
- 23 refreshed without an evidence review.
- 24 For recommendations (or parts of recommendations) ending [2012], [2012,
- amended 2020] or [2020], we have not reviewed the evidence.
 - 17 Venous thromboembolic diseases: diagnosis, management, and thrombophilia testing (update): DRAFT FOR CONSULTATION (June 2023)

1 See also the <u>previous NICE guideline and supporting documents</u>

2 Table 3 Recommendations that have been updated

Recommendation in 2020 guideline	Replaced with	Reason for change
1.1.6 For people with a negative proximal leg vein ultrasound scan and a positive D-dimer test result:	1.1.6 For people with a negative proximal leg vein ultrasound scan and a positive D-dimer test result:	We have reviewed the evidence on the diagnosis of VTE in people with COVID-19 and added
 stop interim therapeutic anticoagulation (but do not stop long-term anticoagulation if being used for secondary prevention) offer a repeat proximal leg vein ultrasound scan 6 to 8 days later and if the repeat scan result is positive, follow the actions in recommendation 1.1.5 if the repeat scan result is negative, follow the actions in recommendation 1.1.7. 	 stop interim therapeutic anticoagulation, but do not stop: long-term anticoagulation when used for secondary prevention, or short-term anticoagulation when used for primary VTE prevention in people with COVID-19 (see the recommendations on VTE prophylaxis in the NICE guideline on managing COVID-19) offer a repeat proximal leg vein ultrasound scan 6 to 8 days later and if the repeat scan result is positive, follow the actions in recommendation 1.1.5 if the repeat scan result is negative, follow the actions in recommendation 1.1.7. 	advice to continue anticoagulation if being used for VTE prevention in people with COVID-19 (including a cross-referral to NICE guideline NG191 on managing COVID-19.
1.1.7 For people with a negative proximal leg vein ultrasound scan and a negative D-dimer test result:	1.1.7 For people with a negative proximal leg vein ultrasound scan and a negative D-dimer test result:	We have reviewed the evidence on the diagnosis of VTE in people with COVID-19 and added
stop interim therapeutic anticoagulation (but do not stop long-term anticoagulation if being	 stop interim therapeutic anticoagulation, but do not stop: long-term anticoagulation when 	advice to continue anticoagulation if being used for VTE prevention in people with COVID-19 (including a cross-referral

Recommendation in 2020 guideline	Replaced with	Reason for change
used for secondary prevention) think about alternative diagnoses tell the person that it is not likely they have DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help.	used for secondary prevention, or - short-term anticoagulation when used for primary VTE prevention in people with COVID-19 (see the recommendations on VTE prophylaxis in the NICE guideline on managing COVID-19) think about alternative diagnoses tell the person that it is not likely they have DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help.	to NICE guideline NG191 on managing COVID-19.
 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, that is: 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 DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help. 	 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, that is: stop interim therapeutic anticoagulation, but do not stop: long-term anticoagulation when used for secondary prevention, or short-term anticoagulation when used for primary VTE prevention in people with COVID-19 (see the recommendations on VTE prophylaxis in the NICE guideline 	We have reviewed the evidence on the diagnosis of VTE in people with COVID-19 and added advice to continue anticoagulation if being used for VTE prevention in people with COVID-19 (including a cross-referral to NICE guideline NG191 on managing COVID-19.

Recommendation in 2020 guideline	Replaced with	Reason for change
1.1.20 If PE is not identified by CTPA, V/Q SPECT or V/Q planar scan: • consider a proximal leg vein ultrasound scan if DVT is suspected	on managing COVID- 19) - think about alternative diagnoses - tell the person that it is not likely they have DVT. Discuss with them the signs and symptoms of DVT and when and where to seek further medical help. 1.1.20 If PE is not identified by CTPA, V/Q SPECT or V/Q planar scan: • consider a proximal leg vein ultrasound scan if DVT is suspected	We have reviewed the evidence on the diagnosis of VTE in people with COVID-19 and added advice to continue anticoagulation if being used for VTE prevention in
 if DVT is not suspected: 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. 	if DVT is not suspected: - stop interim therapeutic anticoagulation, but do not stop: o long-term anticoagulation when used for secondary prevention) or o short-term anticoagulation when used for primary VTE prevention in people with COVID-19 (see the recommendations on VTE prophylaxis in the NICE guideline on managing COVID-19) - 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	people with COVID-19 (including a cross-referral to NICE guideline NG191 on managing COVID-19.

testing) or if the D-dimer test result cannot be obtained within 4 hours (in any setting), 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) - think about alternative diagnoses if the D-dimer test result cannot be obtained within 4 hours (in any setting), 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: o long-term anticoagulation when used for	Recommendation in 2020 guideline	Replaced with	Reason for change
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 (in any setting), 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) - think about alternative diagnoses 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 (in any setting), offer interim therapeutic anticoagulation within 4 hours (in any setting), offer interim therapeutic anticoagulation for suspected DVT or PE). If the D-dimer test 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			
not likely they have PE. Discuss with them the signs and symptoms of PE and when and where to seek further medical help. prevention or short-term anticoagulation when used for primary VTE prevention in people with COVID-19 (see	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 (in any setting), 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	seek further medical help. 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 (in any setting), 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: o long-term anticoagulation when used for secondary prevention or o short-term anticoagulation when used for primary VTE prevention in people	We have reviewed the evidence on the diagnosis of VTE in people with COVID-19 and added advice to continue anticoagulation if being used for VTE prevention in people with COVID-19 (including a cross-referral to NICE guideline NG191

Recommendation in 2020 guideline	Replaced with	Reason for change
	in the NICE guideline on managing COVID- 19)	
	- 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.	

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2 Table 4 Amended recommendation wording (with no change to intent) without

3 an evidence review

Recommendation in current guideline	Recommendation in updated guideline	Reason for change
1.1.16 If clinical suspicion of PE is low (the clinician estimates the likelihood of PE to be less than 15% based on the overall clinical impression, and other diagnoses are feasible), consider using the pulmonary embolism rule-out criteria (PERC) to help determine whether any further investigations for PE are needed. [2020]	1.1.16 If clinical suspicion of PE is low based on the overall clinical impression (from general medical history, physical examination and any initial investigations such as electrocardiography or chest X-ray), and other diagnoses are feasible, consider using the pulmonary embolism rule-out criteria (PERC) to help determine whether any further investigations for PE are needed. Be aware that the PERC rule has not been validated in people with COVID-19. [2020, amended 2023]	Minor wording change for clarification. We removed reference to the less than 15% risk of PE from the recommendation as this was a barrier to implementation. We also added a statement to highlight that the PERC rule has not been validated in people with COVID-19.

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5 Minor changes since publication

- 1 **September 2022:** In recommendation 1.1.21 we clarified that the 4-hour time
- window for the D-dimer test result applies to any setting. See the <u>surveillance</u>
- 3 decision for more information.
- 4 August 2022: We amended and clarified recommendation 1.1.11, and corrected an
- 5 error in the visual summary.
- 6 July 2022: We clarified the information in recommendations 1.1.6, 1.1.7, 1.1.20 and
- 7 1.1.21 about stopping interim therapeutic anticoagulation. We also corrected a cross-
- 8 reference in recommendation 1.1.11.

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