

Pulmonary embolism



Pulmonary embolus

Overview

PE is a relatively common and potentially life-threatening cardiopulmonary illness that can be difficult to diagnose ¹. The most recent population-based study of incidence and mortality in a defined population showed once again that the 30-day case-fatality rate was relatively high in patients with PE compared to those with DVT (9.7% versus 4.6%, risk ratio 2.1) ². The key to effective management of PE is appropriate clinical suspicion, the application of validated exclusion algorithms, followed by definitive diagnostic imaging. The data presented in the last VERITY report appeared to show good practice patterns with respect to PTP and D-dimer, but significant weaknesses in the proper undertaking of V/Q scanning and very limited uptake of CTPA. This year, we have looked closely at the definitive diagnostic imaging with a particular hope that CTPA uptake has increased, which will transform PE diagnosis and bring it up the standard of North America.

With respect to location of treatment, analyses presented in the last VERITY report showed limited outpatient treatment of patients with PE, despite the fact that VERITY hospitals are using outpatient care for patients with DVT. In this year's report, we once again present the Aujesky score ³ as a potential risk scoring system to support safe outpatient treatment, but data are limited and a definitive answer will not be forthcoming until an additional VERITY study specifically to validate the Aujesky score is complete.

Primary and final diagnosis

There are now 1,028 patients with confirmed PE in the database. When VERITY was moved on-line, the data requested on the primary suspected diagnosis was simplified. Since then, 773 patients have been recorded with a primary suspected diagnosis of PE, which was confirmed as PE in 474 cases (61%).

		Final diagnosis			
		Non-PE	PE	Unspecified	All
Primary diagnosis	Non-PE	41,006	121	4,359	45,486
	PE	762	870	218	1,850
	Unspecified	4,576	37	4,047	8,660
	All	46,344	1,028	8,624	55,996

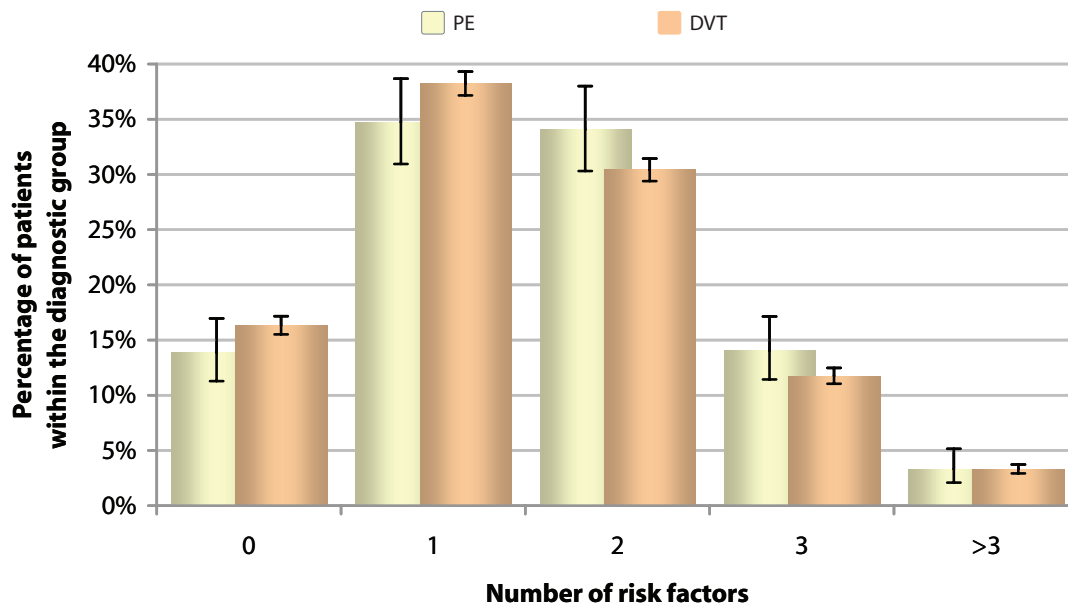
Risk factors in PE

Number of risk factors

These data are identical to previous VERITY findings, suggesting that there is no difference in the number of risk factors described in patients with PE or DVT, with most patients found to have one or two VTE risk factors.

		Final diagnosis				
		Non-VTE	DVT	PE	Unspecified	All
Number of risk factors	0	7,606	1,285	84	1,131	10,106
	1	10,235	3,010	210	1,923	15,378
	2	5,436	2,394	206	1,260	9,296
	3	1,635	924	85	420	3,064
	>3	361	260	20	112	753
	Unspecified	9,615	3,583	423	3,778	17,399
	All	34,888	11,456	1,028	8,624	55,996

Number of risk factors according to final diagnosis (n=8,478)



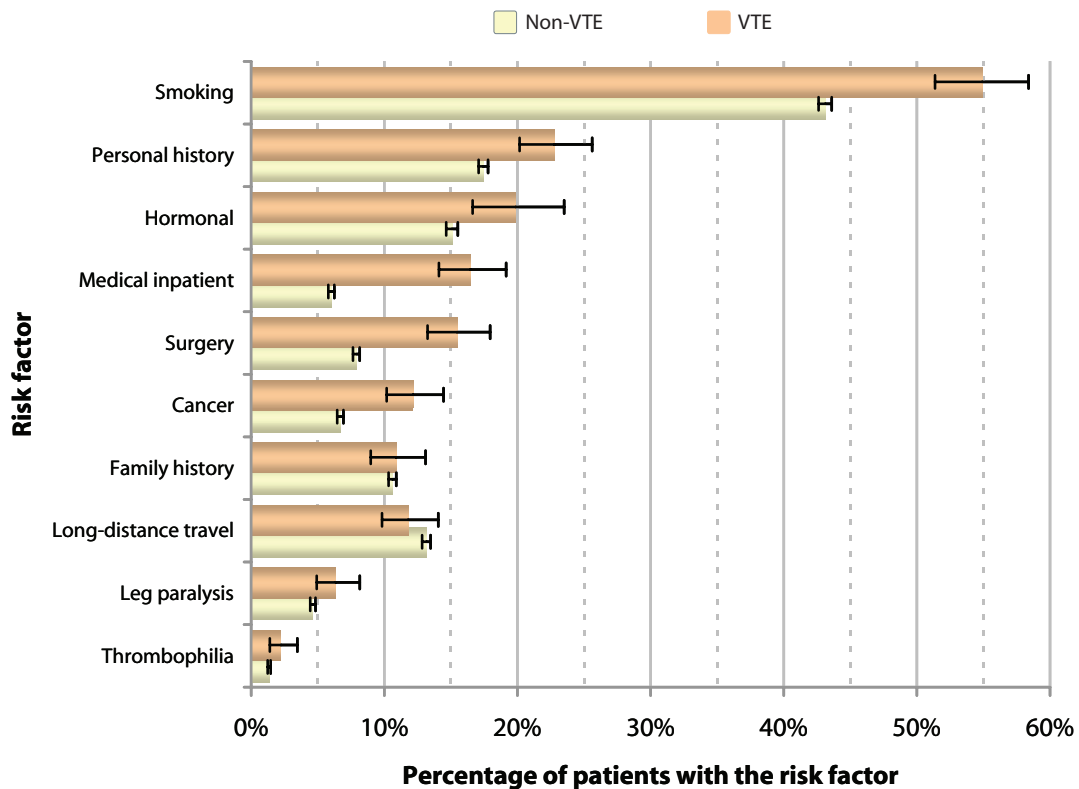
Risk factors in PE

These findings remain consistent year-on-year and, as patient numbers increase and the confidence intervals narrow, clear risk factors for PE can be identified. PE patients are more likely to have smoked, to have experienced previous thrombosis, to have a hormonal risk factor, to have been a medical or surgical inpatient or to have a recent history of cancer. This profile is similar to that described for DVT.

Because we have recorded more detailed reasons for hospitalisation, we had hoped to identify more closely the relationship between hospitalisation and its interaction with other risk factors such as smoking. However, the numbers are still quite small and no firm conclusions can be drawn yet, but it is interesting to note that of 54 cases of suspected PE with lung disease (such as pneumonia and COPD) and smoking as a risk factor, 10 cases were confirmed with PE (19%).

		Final diagnosis			
		Absent	Present	Unspecified	All
Risk factors	Smoking history	359	437	232	1,028
	Personal history of VTE	729	215	84	1,028
	Hormonal	436	108	33	577
	Medical inpatient	725	143	160	1,028
	Surgical inpatient	804	147	77	1,028
	Cancer	831	115	82	1,028
	Family history of VTE	828	101	99	1,028
	History of long-distance travel	831	111	86	1,028
	Leg paralysis / fracture	884	60	84	1,028
	History of thrombophilia	881	20	127	1,028

Presence of selected risk factors for both PE and non-PE patients

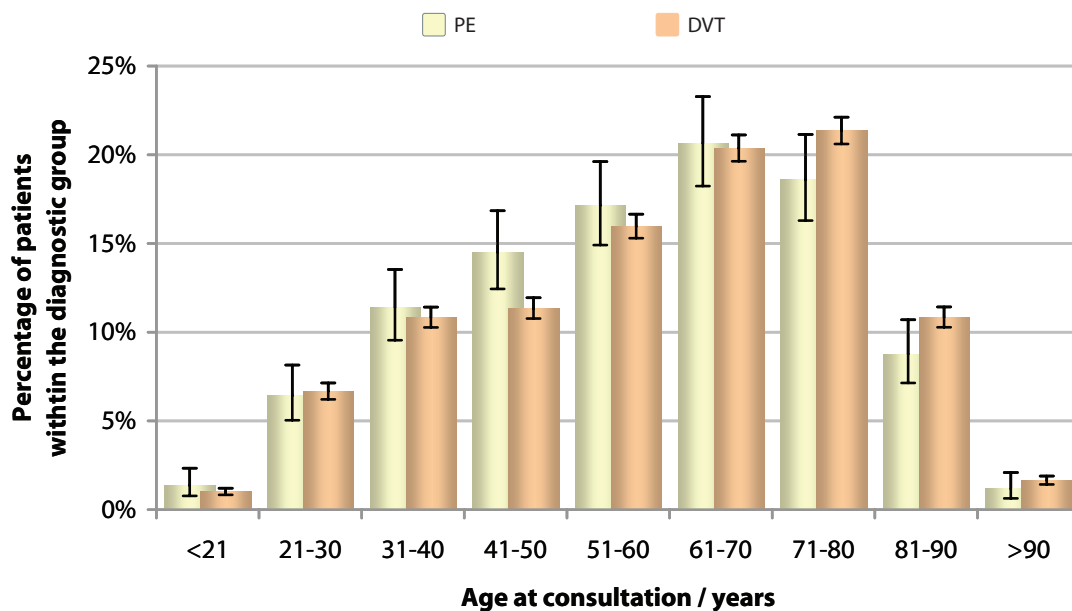


Age and disease

These data are almost identical year-on-year, and show as expected that the age profile of patients with DVT or PE is similar, with the age distributions skewed towards the older age brackets. One significant difference that has appeared with the large number of patients in this year's analysis is the higher proportion of patients with PE than DVT in the 5th decade.

		Final diagnosis				
		Non-VTE	DVT	PE	Unspecified	All
Age at consultation / years	<21	535	115	14	133	797
	21-30	2,046	763	66	531	3,406
	31-40	3,524	1,240	117	874	5,755
	41-50	46,00	1,299	149	1,119	7,167
	51-60	5,939	1,828	176	1,335	9,278
	61-70	6,340	2,332	212	1,670	10,554
	71-80	7,204	2,445	191	1,795	11,635
	81-90	4,053	1,241	90	1,020	6,404
	>90	615	188	12	137	952
	Unspecified	32	5	1	10	48
	All	34,888	11,456	1,028	8,624	55,996

Age distributions according to final diagnosis (n=12,478)



The diagnosis of PE

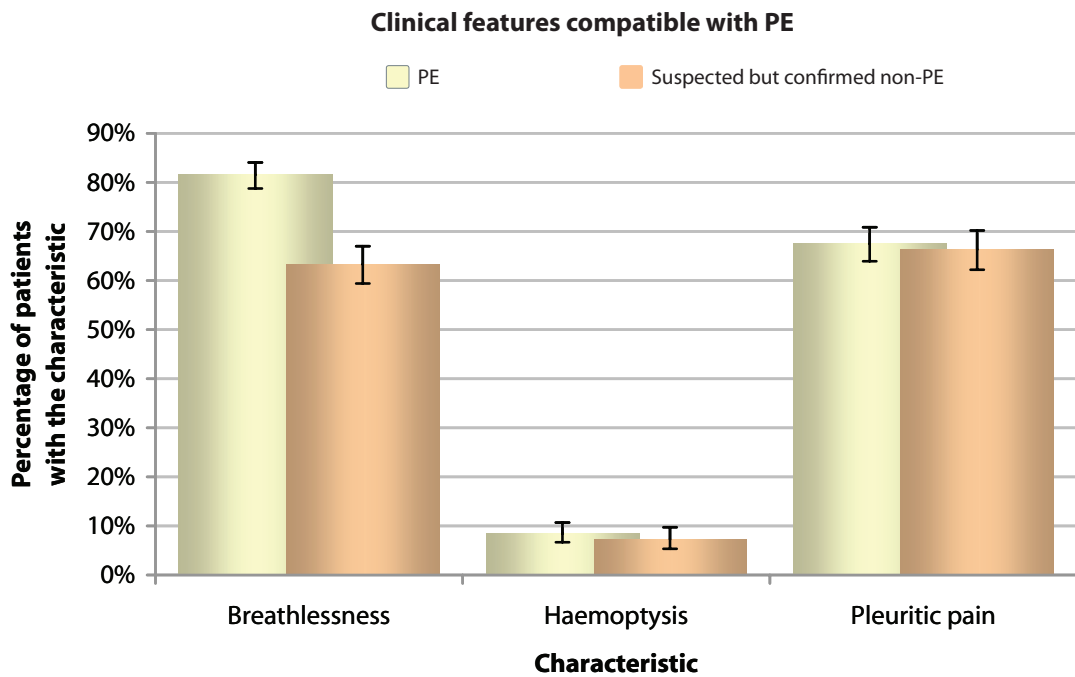
Although using the Wells algorithm for pretest probability of PE requires that a patient has clinical features compatible with PE (namely, breathlessness, pleuritic chest pain and / or haemoptysis), these features alone are unreliable and show poor sensitivity for PE. Reviewing the 773 patients with suspected PE confirms this, with only breathlessness significantly over-represented in the PE patients. This is interesting and goes along with the British Thoracic Society (BTS) Guidelines⁴, which state:

It requires that the patient has clinical features compatible with PE - namely, breathlessness and / or tachypnoea, with or without pleuritic chest pain and / or haemoptysis. Two other factors are sought:

- a. *the absence of another reasonable clinical explanation, and*
- b. *the presence of a major risk factor.*

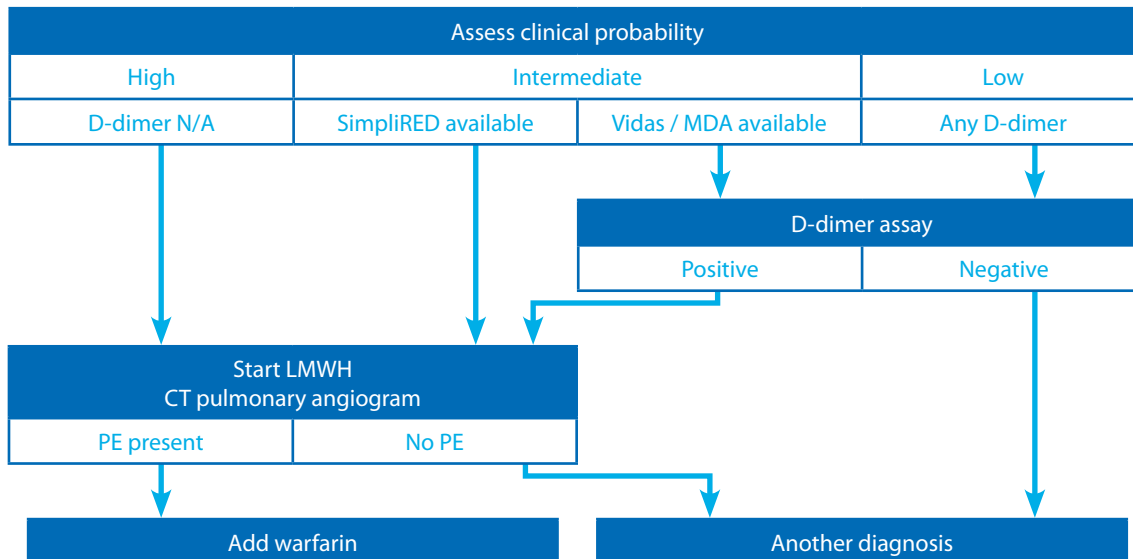
Where (a) and (b) are both true the probability is high; if only one is true the probability is intermediate; and if neither is true the probability is low. Some hospitals prefer a scoring system that places patients into one of only two categories - PE likely and PE unlikely.

The use of a formal estimate of the probability of PE using a PTP score is the validated assessment before requesting special investigations.

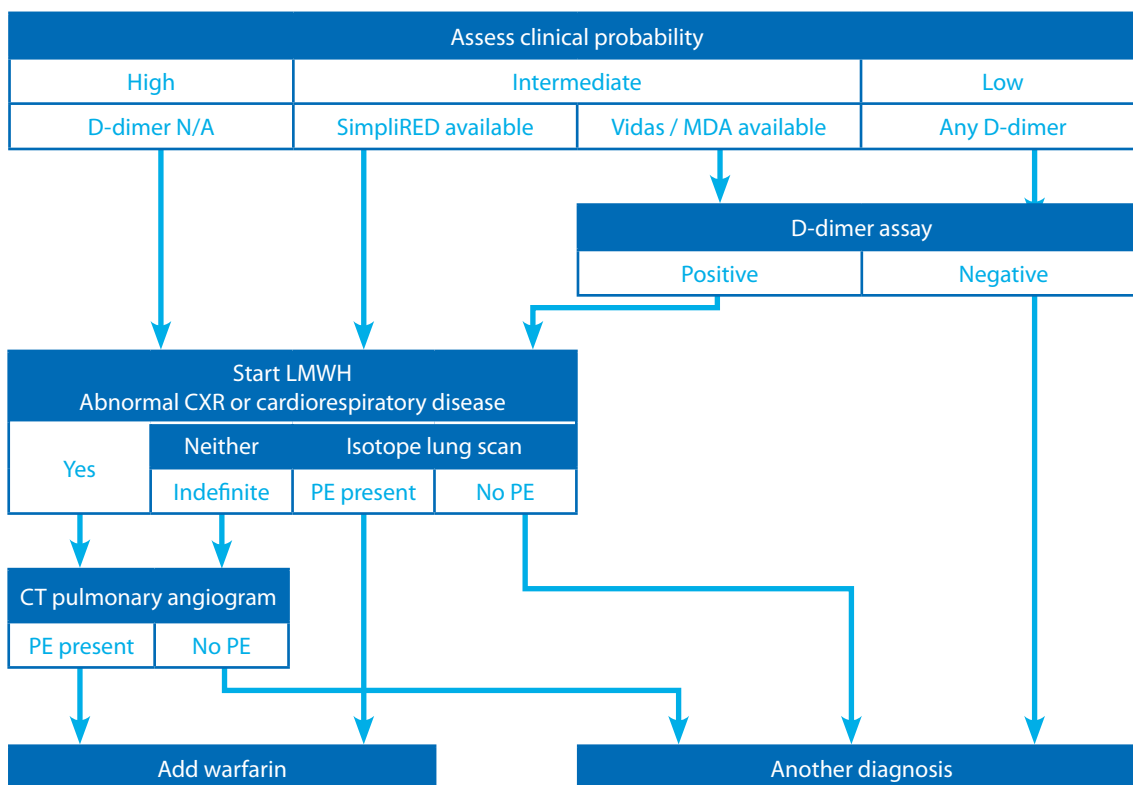


British Thoracic Society Guidelines for the management of suspected acute pulmonary embolism

A Management of suspected non-massive pulmonary embolism with isotope lung scanning off site only



B Management of suspected non-massive pulmonary embolism with isotope lung scanning available on site



Pulmonary embolism

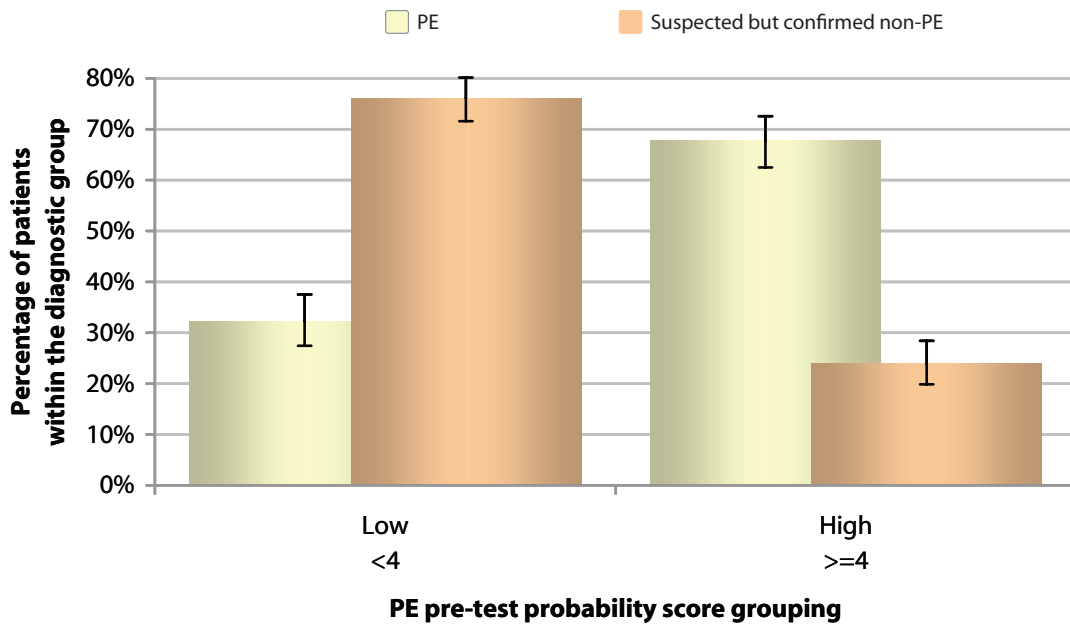
PTP score and final diagnosis

As we have seen in the previous pages, the limitations of clinical examination in establishing a diagnosis of PE, as well as the perils of anticoagulating unnecessarily or not treating clots at all, mandate use of judicious objective diagnostic testing in the evaluation of PE. The BTS guidelines suggest PTP, when used in conjunction with D-dimer, can substantially reduce the imaging requirement.

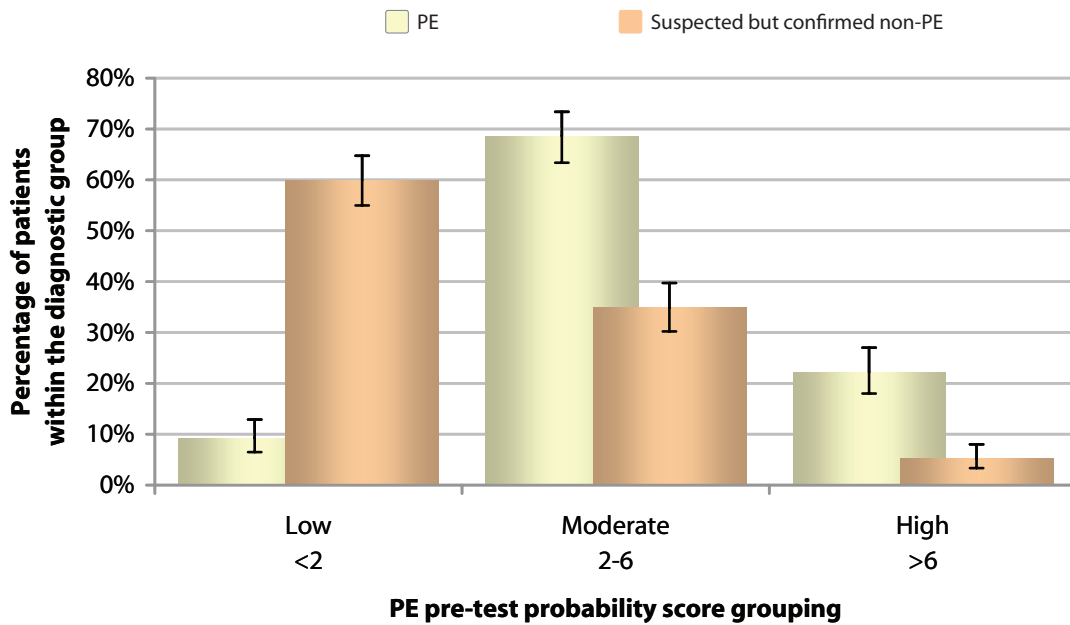
A number of ways of interpreting the Wells PTP are employed by VERITY hospitals. Calderdale uses the definition of low (<4) and high (\geq 4) PTP, which is widely used in European and Canadian algorithms, whereas at Southampton, Derriford and King's Lynn, the scoring of low (<2), moderate (2-6) and high risk (>6) is employed, as described in the BTS guidelines. These different PTP thresholds are compared in the graphs on the next page.

			Diagnostic group	
			PE	Suspected but confirmed non-PE
Risk factors	Low	<4	112	306
	High	\geq 4	235	96
	Low	<2	32	241
	Moderate	2-6	238	140
	High	>6	77	21
	Unspecified		681	360
	All		1,028	762

PTP score distributions for patients with confirmed PE versus patients with suspected but confirmed non-PE (n=347 and n=402 respectively)



PTP score distributions for patients with confirmed PE versus patients with suspected but confirmed non-PE (n=347 and n=402 respectively)



Investigations in patients with a primary diagnosis of PE

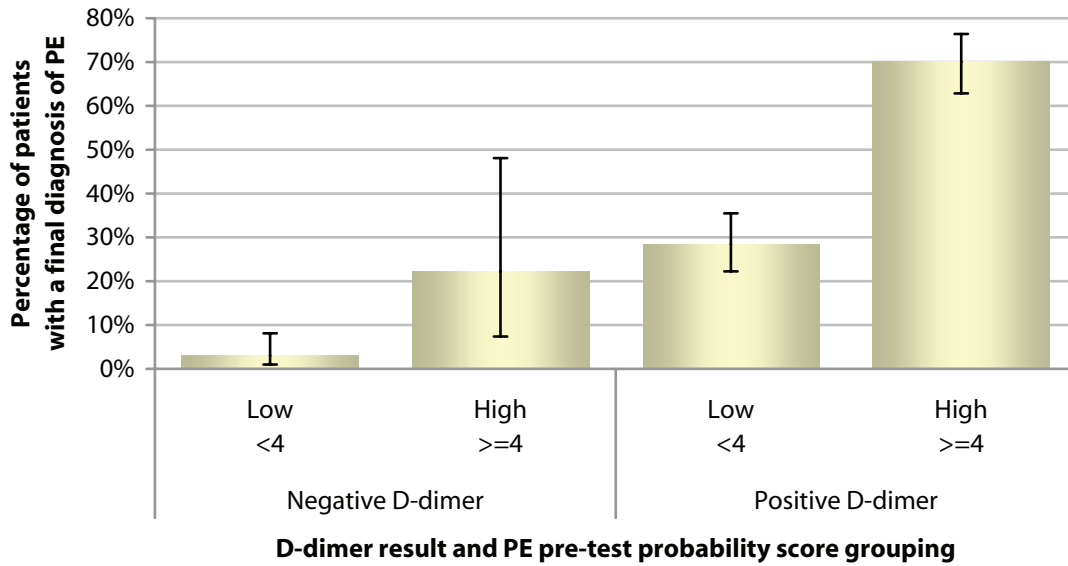
PTP score, D-dimer and final diagnosis

As previously, the data validate the strategy of excluding PE on the basis of a low PTP in combination with a negative D-dimer. Of the 4 patients with a low PTP and negative D-dimer found to have PE, 1 case reported in the last report was subsequently excluded as a PE after several radiology opinions. We will initiate contact with the centres to determine the diagnostic profile of the 3 other patients. We again note the lack of methodical follow-up for these patients, which means that we do not know if any of the excluded diagnoses of PE later re-presented with PE.

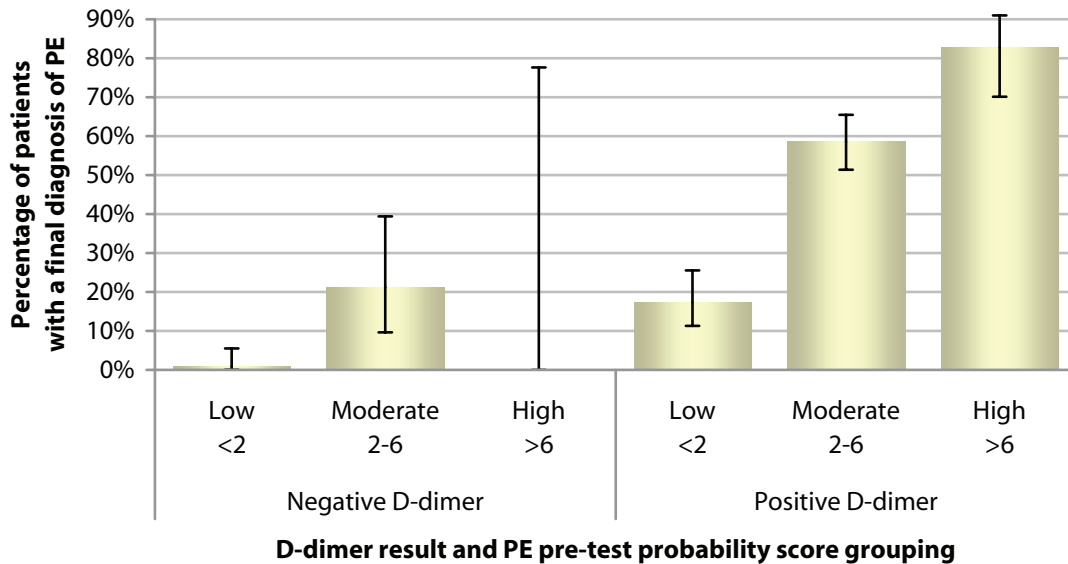
Pulmonary embolism

				Final diagnosis			
				Not PE	PE	Unspecified	All
D-dimer test results and PE PTP	Negative D-dimer	Low	<4	127	4	4	135
		High	≥4	14	4	5	23
		Low	<2	113	1	3	1,395
		Moderate	2-6	26	7	5	1,791
		High	>6	2	0	1	41
		Unspecified		70	8	19	97
	Positive D-dimer	Low	<4	136	54	11	201
		High	≥4	56	131	25	212
		Low	<2	100	21	5	126
		Moderate	2-6	82	116	25	223
		High	>6	10	48	6	64
		Unspecified		182	201	54	437
	D-dimer not specified	Low	<4	43	33	6	82
		High	≥4	26	80	13	119
		Low	<2	28	4	4	36
		Moderate	2-6	32	85	10	127
		High	>6	9	24	5	38
		Unspecified		108	355	81	544

Final diagnosis, D-dimer results and PE pre-test probability for patients with a suspected PE using groupings of <4 and ≥4 for the PE PTP (n=526)



Final diagnosis, D-dimer results and PE pre-test probability for patients with a suspected PE using groupings of <2, 2-6 and >6 for the PE PTP (n=526)



Definitive diagnostic imaging for PE

The ability to rapidly and accurately diagnose PE is critical to improving survival and quality of life because fast, appropriate treatment decreases mortality and the likelihood of morbidity from thromboembolic pulmonary hypertension or post-thrombotic syndrome. Although the initial challenge is to consider PE as a possible diagnosis, and then perform appropriate exclusion tests such as PTP and D-dimer shown in the previous pages, the main challenge in the UK remains obtaining the necessary definitive diagnostic test results for PE.

Computed tomographic (CT) scanning of the chest has revolutionized the diagnostic approach to suspected PE. Ventilation/perfusion lung scanning used to be the pivotal imaging test, but the lung scan is problematic because it rarely provides a definitive *high probability* or *normal* result. Furthermore, recent studies have validated a strategy of using a clinical probability assessment, D-dimer screening, and multi-slice chest CT scanning, without the need for venous ultrasonography in patients whose CT scans are negative, to rule out the diagnosis of PE. In this next section, we review the different screening tools for PE.

Ventilation/perfusion scan (V/Q scan)

This test, also called a nuclear isotope lung scan, uses small amounts of radioactive tracers (radioisotopes) to study airflow (ventilation) and blood flow (perfusion) in the lungs. The radioisotopes are attached to radiopharmaceuticals. In the first part of the test a small amount of radiopharmaceutical is inhaled while a camera that is able to detect radioactive substances takes pictures of the movement of air in the patient's lungs. A small amount of a different radiopharmaceutical is then injected into an arm vein and pictures are taken of blood flow in the blood vessels of the lungs. Comparing the results of the two studies helps provide a more accurate diagnosis of pulmonary embolism than does either study alone. The entire procedure usually takes less than an hour. The patient is exposed to a small amount of radioactivity, but the test can still be performed on pregnant women.

The V/Q scan is hindered because it rarely provides a definitive *high probability* or *normal* result, but frequently an ambiguous result, requiring other tests to confirm a diagnosis of VTE. Furthermore, even when the scan is reported as *normal*, there is still a 4% chance of PE. Just as troubling, high probability scans are associated with a 12% false positive rate. The BTS guidelines give a level B recommendation that V/Q can be the initial investigation only if the chest X-ray is normal and there is no concurrent cardiopulmonary disease. Non-diagnostic scans should be followed up with a further investigation. For these reasons, lung scans are being replaced by more sensitive and rapid tests, such as spiral computerized tomography (CT) scans, which VERITY has been encouraging.

Computed Tomography (CT)

Computed tomographic (CT) scanning of the chest has revolutionized the diagnosis of PE. A CT scan allows the doctor to see patients' organs in two-dimensional *slices*. Split-second computer processing creates these images as a series of very thin x-ray beams pass through the body. CT combines the use of x-rays with computerised analysis of the images. Beams of x-rays are passed from a rotating device through the area of interest in the patient's body from several different angles to create cross-sectional images, which then are assembled by computer into a three-dimensional picture of the area being studied.

CT pulmonary angiography (CTPA) is an examination that uses x-rays to visualise blood flow in arterial and venous vessels throughout the body, from arteries serving the brain to those bringing blood to the lungs, kidneys, and arms and legs. Compared to angiography, which involves placing a sizable catheter and injecting contrast material into a large artery or vein, CTPA is a much less invasive and more patient-friendly procedure, requiring contrast material injection into a small peripheral vein using a small needle or catheter and rarely requiring hospital admission.

Now, a newer type of CT scan, called a spiral or helical CT, is fast becoming the first-line test for diagnosing suspected PE. A spiral CT differs from conventional CT in several ways: the scanner rotates continuously around the patients body, following a spiral path to create three-dimensional images; it can detect abnormalities with a greater degree of accuracy, and is faster, scanning the pulmonary arteries in less than 20 seconds as opposed to 20 minutes or more for a standard CT. Speed is important because it allows the dye to be *captured* while still in the arteries. Spiral CT is nearly as sensitive in detecting most cases of PE as a conventional pulmonary angiogram and much more sensitive than a V/Q scan. However, a spiral CT exposes the patient to more radiation than a standard X-ray does, as well as to the risk of an allergic reaction to the contrast medium.

Magnetic resonance imaging (MRI)

MRI does not use X-rays, but is based on radio signal detection. The MRI scanner is like a short tunnel surrounded by a giant circular magnet. The patient lies on a couch and a *receiving device* (another smaller magnet) is placed behind, or around, the part of the body being examined. This detects the tiny radio signals emitted from the patient's body. The couch then slides into the scanner. When each *picture* is being taken the patient needs to keep still for a few minutes otherwise the scan pictures may be blurred. The couch is then slid a little further in as several scans are done to obtain pictures of *slices* of the area of the body being examined. The scan itself is painless. The whole procedure can take 30-60 minutes, depending on the size of the area being examined and how many *pictures* are taken. In some cases an injection of a special contrast dye is given into the bloodstream *via* a vein on the arm. This helps to give clearer pictures of certain tissues or organs being examined. A computer creates tissue *slices* from data generated by the powerful magnetic field and radio waves; because MRI is expensive (*equipment and running costs*), it is usually reserved for pregnant women and people whose kidneys may be harmed by dyes used in other tests.

Why we have been encouraging CTPA through VERITY

The Department of Health spent £90 million in 2003 on replacing CT and MRI scanners installed before 1997. Additionally, in October 2005, funding was given for more PET scans to be used in cancer care. Prior to this many of the CT scanners were in constant usage for cancer patients (*approximately 35-40% for diagnosis and staging of cancer*), but with the increased funding for PET scanners, it is expected that CT scanners should be more available for non-cancer diagnoses and treatment.

Prior to 1997, the traditional single-slice-per-rotation CT scanner cost around £400,000, and produced one image per one-second rotation of the x-ray tube in the gantry. A traditional CT study would be scheduled every 30 minutes with a typical day producing 16 patient studies of 60 to 80 images each. The traditional CT scanner is rapidly being replaced by the multi-slice CT scanner which fits into the same procedure room with little modification.

The multi-slice CT scanner is the new standard in healthcare and will produce 4 to 16 imaging slices per rotation and operate at two rotations per second or 8 to 36 images per second, at a cost of £0.6 – 0.8 million per machine. When a multi-slice scanner simply replaces a single-slice scanner, facilities seldom see the expected increase in use. A multi-slice CT study would require only 6 minutes per procedure, but patients are often scheduled every 18 to 20 minutes due to facility and staffing issues. However, Patricia Hewitt launched the *NHS Modernisation Plan* giving high priority to recruiting and retaining radiographers. Hence, there should be sufficient staff to support rapid CT scanning. A staff of three often can cut turnover time from 10 minutes to 3 minutes. With the much shorter examination and turnover times, patient waiting areas often become the limiting factor in department efficiency. However, the government is committed to reducing waiting times for NHS patients, and have committed to speedier access to diagnostic tests such as scanners, as part of this commitment, so facility changes should support this. By providing adequate area design and technical support, a multi-slice CT scanner can schedule patients every 9 minutes for general procedures, enabling more than 54 patient studies per day - a 400% increase in total procedures performed.

VERITY data on CTPA

Verity has been encouraging the use of CTPA and we are aware of a major change in practice in a number of hospitals, for example Calderdale, where CTPA is now used exclusively for the imaging of suspected PE. The question asked in the database is somewhat ambiguous, because CT and PA can be recorded independently but not together. Combining the findings, CTPA use has increased from 13.5% in the old database to 30.2% and to 36.3% in the cases recorded in the last 12 months. In Calderdale, CTPA was employed in 100% of PE cases in the last 12 months. In Portsmouth, the numbers have grown from 5.3% to 19.1% to 25.6% in the last 12 months.

Patients with a primary suspected diagnosis of PE or DVT & PE

		Database		
		Old database	New database	Last 12-month period analysed
CTPA usage	Neither	822	573	281
	CT alone	87	163	103
	PA alone	38	64	46
	CT and PA	3	21	11
	CT or PA	128	248	160
	Unspecified	29	50	35
	All	979	871	476

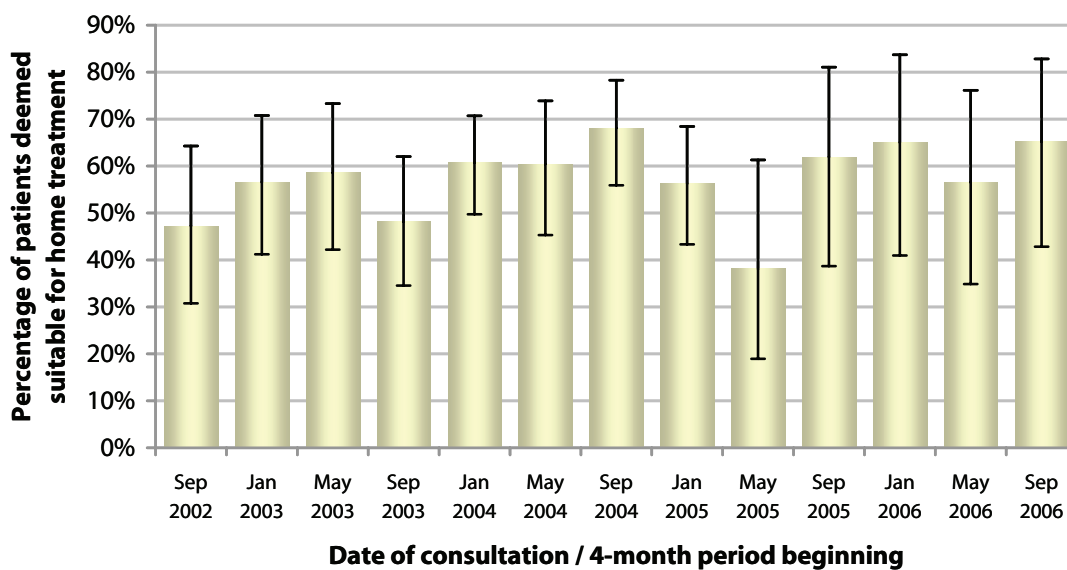
Treatment of patients with PE

Location of treatment

The findings show there has been little change in PE treatment into outpatient clinics over the period that the VERITY registry has been operational. There is an ongoing study in four VERITY hospitals to attempt to validate the Aujesky score (described on page 55), which will hopefully offer hospitals a validated risk score to assess individuals suitability to outpatient care.

		Suitable for home treatment			
		No	Yes	Unspecified	All
Date of consultation four-month period beginning	Sep 2002	19	17	4	40
	Jan 2003	20	26	6	52
	May 2003	17	24	6	47
	Sep 2003	28	26	6	60
	Jan 2004	35	54	12	101
	May 2004	19	29	4	52
	Sep 2004	23	49	6	78
	Jan 2005	28	36	28	92
	May 2005	13	8	57	78
	Sep 2005	8	13	70	91
	Jan 2006	7	13	76	96
	May 2006	10	13	91	114
	Sep 2006	8	15	84	107
	All	235	323	450	1,008

Suitability of PE patients for home treatment (n=558)



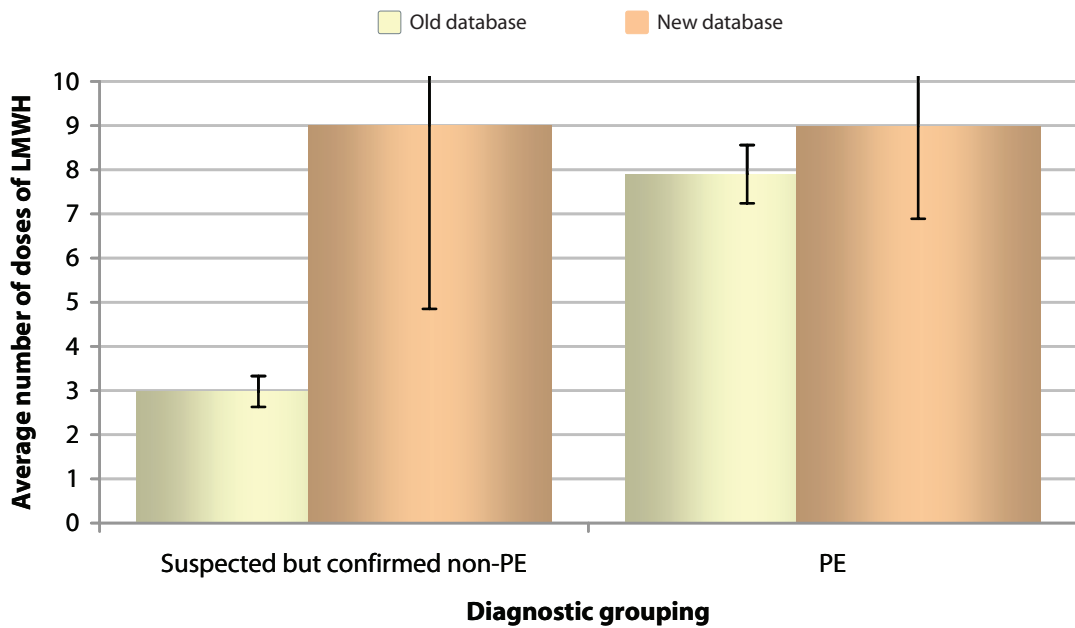
Doses of LMWH

When comparing the old and new databases, there has been a marked increase in the number of doses of LMWH received by patients with suspected but unconfirmed PE (n=9), which matches the average number of doses in patients with confirmed PE. This is unexpected and further data analysis will be undertaken to explain this unusual finding.

			Average number of doses of LMWH
Diagnostic grouping	Old data	Suspected but confirmed non-PE	2.98 (n=484; SE=0.35)
		PE	7.90 (n=513; SE=0.66)
	New data	Suspected but confirmed non-PE	9.00 (n=57; SE=4.15)
		PE	8.98 (n=113; SE=2.09)

Pulmonary embolism

Average number of doses of LMWH for suspected but confirmed non-PE patients and PE patients; bars denote standard errors



A new risk prediction for PE patients

The Aujesky score was published as a clinical prediction model to classify patients with PE into categories of increasing risk of adverse medical outcomes and mortality, with a validation process that demonstrated that the model was highly reliable ³.

The prediction rule is based on 11 characteristics and stratifies patients into 5 classes of severity; classes I and II have 30-day mortality of 0.0-1.9% and 1.7-3.5% respectively. The researchers concluded that patients estimated to be at very low (class I) or low (class II) risk could be discharged early or managed entirely as outpatients using LMWH. There is an ongoing study in four VERITY hospitals to attempt to validate the Aujesky score, but no data are available yet to present. It is anticipated that the PE screen on VERITY will be changed in the near future to allow an ongoing assessment of this score in an attempt to validate outpatient treatment of PE in UK hospitals through VERITY.

Prediction of the risk of adverse events in PE patients

Predictors	Points
Demographic characteristics	
Age	Age ⁱ
Male gender	10
Comorbid illnesses	
Cancer	30
Heart failure	10
Chronic lung disease	10
Clinical findings	
Pulse $\geq 110 \text{ min}^{-1}$	20
Systolic blood pressure $< 100 \text{ mmHg}$	30
Respiratory rate $\geq 30 \text{ min}^{-1}$	20
Altered mental status ⁱⁱ	60
Arterial oxygen saturation $< 90\%$ ⁱⁱⁱ	20
Temperature $< 36 \text{ }^\circ\text{C}$	20

A total point score for a given patient is obtained by summing the patient's age in years and the points for each applicable characteristic. Points assignments correspond with the following risk classes:

Class I	≤ 65	very low risk
Class II	66-85	low risk
Class III	86-105	intermediate risk
Class IV	106-125	high risk
Class V	> 125	very high risk

- i. Patient's age in years.
- ii. With and without the administration of supplemental oxygen.
- iii. Defined as disorientation, lethargy, stupor or coma.

Conclusions

Diagnosing PE will always remain an interesting clinical challenge because classical symptoms and signs are not present in many cases. VERITY has confirmed this again, with only breathlessness, but not pleuritic chest pain or haemoptysis over-represented in the PE population. As noted in a recent review ¹:

PE can present with subtle findings in young, previously healthy patients who have excellent cardiac reserve; with increasing age, PE can masquerade as other illnesses such as acute coronary syndrome or exacerbation of COPD. Accurate diagnosis of PE is particularly difficult when patients present with two concurrent illnesses, such as obvious pneumonia plus occult PE or obvious congestive heart failure plus occult PE.

Diagnostic techniques and treatments for PE continue to evolve. In the last VERITY publication we reported good practice in the initial part of the diagnostic algorithm, namely clinical PTP and D-Dimer testing. However, the main challenge in the UK was obtaining the necessary definitive diagnostic test results for PE testing. CTPA was limited to 21.2% of all suspected cases, V/Q scanning being the diagnostic test chosen despite its limitations. This year, the picture has changed, with the overall proportion of patients diagnosed with CTPA increasing from 13.5% to 30.2%, and to 36.3% in the last 12 months, with certain centres such as Calderdale now using CTPA in all cases of suspected PE. VERITY has been encouraging the use of CTPA and these changes may reflect the Department of Health-funded initiatives to ensure better patient access to this particular test.

Most hospitals seem wary of treating PE in the community, so four Verity hospitals are involved in an ongoing study to validate the Aujesky Score, which assesses PE severity. We are hopeful that patients who are identified as low risk by the score can be discharged early or have their treatment entirely in the outpatient setting and findings will be reported on the VERITY website shortly. However, we wish to highlight again the importance of knowing patient outcome to validate a new treatment approach such as outpatient PE treatment. Therefore, we ask again if VERITY hospitals would consider following up their patients at 3 months and record three simple adverse events: death, recurrence or major bleed.

As described in the Overview and Cancer chapters, we are particularly interested in collecting quantitative D-dimer findings on patients with suspected and confirmed VTE (including PE patients) as a research project to assess the impact of elevated levels on patient outcome. We ask that you record the quantitative D-dimer value (if available) for all PE cases entered into VERITY.

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