

# Overview

**Database overview**

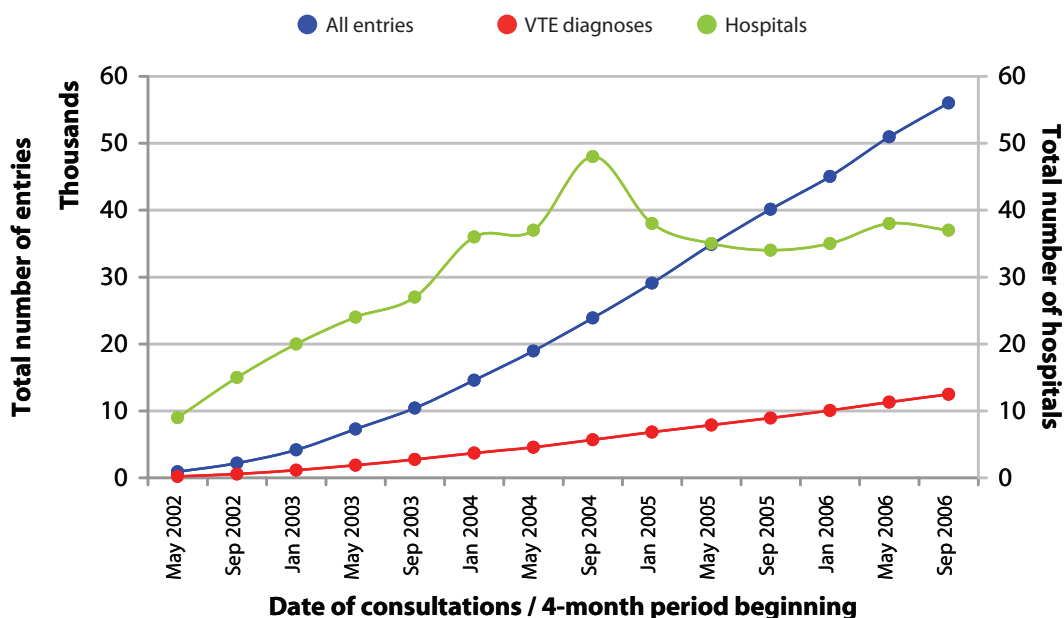
**Entries in the database**

Since the last data analysis in early 2005, the database has doubled in size, with just under 56,000 patient entries and around 12,500 cases of confirmed VTE. The graph below also shows the number of hospitals actively submitting patients to the registry, which fell from a high of around 50 at the end of 2004, to around 40 in early 2005; this is around the time that the database was changed and web-based data entry introduced.

Patients with a recent history of surgery, medical illness or immobilization make up around a fifth of the VTE cases; more than 12% of VTE cases have a history of cancer, and the number of pregnant or *post partum* women in the database has increased to more than 1,000 patients.

		Final diagnosis					All
		Non-VTE	DVT	PE	PE + DVT	Unspecified	
Patient groups	Cancer <sup>i</sup>	1,484	1,457	79	36	493	3,549
	Pregnant and <i>post partum</i> <sup>ii</sup>	113	740	56	20	127	1,056
	Medical history / immobilised <sup>iii</sup>	1,515	1,078	114	29	491	3,227
	Surgical history <sup>iv</sup>	2,360	1,140	124	23	645	4,292
	All entries	34,888	11,456	768	260	8,624	55,996

**The growth of the database (n=55,996 entries)**



- i. Cancer: any patient identified as currently having cancer or having had treatment for cancer within the last 6 months.
- ii. Patients recorded as pregnant or *post partum* in the new database question.
- iii. Medical history / immobilised: any patient positively identified as having been either a medical inpatient / immobilised for more than three days in the last four weeks.
- iv. Surgical history: any patient positively identified as having had major surgery in the last four weeks.

### Data submitted by each centre

More than 20 NHS centres undertaking the management of VTE in an outpatient setting have contributed >1,000 cases each to VERITY, more than 32,000 cases in total, which is very pleasing. However, as in previous years, the number of unspecified cases remains troubling. As a VTE registry, we hoped that centres would enter the correct diagnosis (VTE or not), but this is not always the case and the number of indeterminate cases remains too high. In previous years, this large number of unspecified final diagnoses reflected, at least in part, difficulties in interpreting the question asked for patients who do not have DVT. The movement to the web-based data entry, which asks fewer and more tailored questions, has helped, as can be seen with the data from Derriford Hospital, where the number of unspecified cases has actually fallen compared to the data presented in the last report.

Centre	Final diagnosis			
	Non-VTE	VTE	Unspecified	All
Derriford Hospital, Plymouth	2,944	1,425	1,899	6,268
Southend Hospital NHS Trust	3,604	664	526	4,794
Queen Alexandra Hospital, Portsmouth	3,042	998	289	4,329
Gwent Healthcare NHS Trust	2,600	665	424	3,689
Northampton General Hospital	1,352	353	638	2,343
Glan Clwyd Hospital, Rhyl	1,799	411	114	2,324
King's Mill Hospital, Sutton-in-Ashfield	1,396	403	487	2,286
Belfast City Hospital HSS Trust	1,841	341	85	2,267
Bangor Hospital	1,502	312	252	2,066
Hinchingbrooke Hospital, Huntingdon	1,371	339	140	1,850
Queen's Medical Centre, Nottingham	1,225	425	185	1,835
Southern Derbyshire Acute Hospitals NHS Trust	1,004	493	258	1,755
Craigavon Area Hospital, Portadown	1,145	166	83	1,394
Inverclyde General Hospital	944	193	207	1,344
Neville Hall Hospital, Abergavenny	601	158	515	1,274
Addenbrooke's NHS Trust, Cambridge	751	222	269	1,242
King's College Hospital, London	796	341	95	1,232
City Hospital, Birmingham	998	149	75	1,222
Southampton University Hospitals NHS Trust	372	523	287	1,182
Barnsley District General Hospital NHS Trust	730	248	127	1,105
Poole Hospital	444	135	273	852
Caerphilly District Miners' Hospital	575	130	103	808
The Royal Surrey County Hospital NHS Trust	369	158	173	700
Broomfield Hospital, Chelmsford	575	112	11	698
Bristol Royal Infirmary	431	157	70	658
Walsgrave Hospital, Coventry	100	480	62	642
Mater Hospital Trust, Belfast	482	76	82	640
Calderdale Hospitals NHS Trust, Halifax	403	208	6	617
Sandwell District General Hospital, W. Bromwich	1	408	143	552
Queen Elizabeth II Hospital, Welwyn Garden City	4	416	132	552
Others	1,487	1,375	614	3,476
<b>All</b>	<b>34,888</b>	<b>12,484</b>	<b>8,624</b>	<b>55,996</b>

### Risk factors for VTE

VTE remains a public health issue. The estimated annual incidence in the general population is about 1 per 1,000<sup>1</sup> and thrombosis causes mortality and morbidity, which is particularly associated with hospitalised patients<sup>1,2,3,4</sup>.

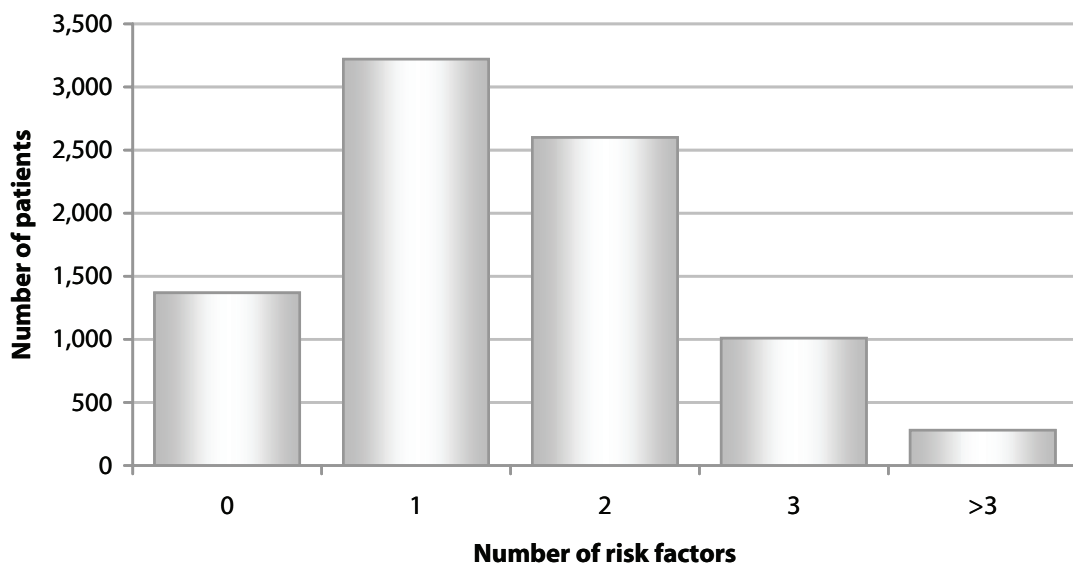
Common risk factors associated with increased risk of VTE such as age, surgery, cancer, immobilisation, pregnancy, fractures, oral contraceptives and medical illness are recorded in VERITY. The precise definitions of some of the risk factors were changed when the data collection forms were updated and moved to an on-line data-entry system. In particular, any ambiguity regarding immobilisation in the context of acute medical illness was removed, with the diagnoses of heart failure and respiratory failure now recorded in the database.

### Number of risk factors and diagnosis

This table and the following three charts show the relationship between the number of risk factors at presentation and the likelihood of a final diagnosis of VTE. Year-on-year, these findings are almost identical, confirming that as the number of risk factors increases, so the proportion of patients with a positive diagnosis of VTE increases. One consistent finding worthy of mention and further analysis is the group of patients with idiopathic VTE *i.e.* patients with confirmed VTE who presented with no known risk factors. Of the 8,975 patients in the registry with no recorded risk factors, more than 15% (n=1,369) were diagnosed with VTE. Looking at patients with multiple risk factors, it is interesting to note that very few DVT patients present with more than 3 risk factors (n=280).

		Final diagnosis			
		Non-VTE	DVT	Unspecified	All
Number of risk factors	0	7,606	1,369	1,131	<b>10,106</b>
	1	10,235	3,220	1,923	<b>15,378</b>
	2	5,436	2,600	1,260	<b>9,296</b>
	3	1,635	1,009	420	<b>3,064</b>
	>3	361	280	112	<b>753</b>
	Unspecified	9,615	4,006	3,778	<b>17,399</b>
	<b>All</b>	<b>34,888</b>	<b>12,484</b>	<b>8,624</b>	<b>55,996</b>

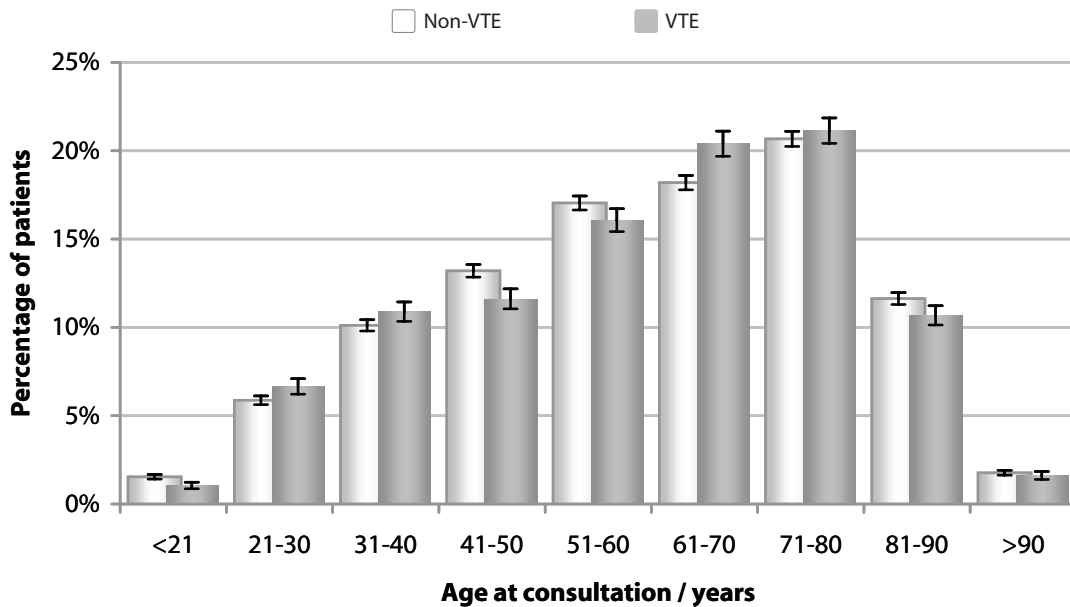
**Number of risk factors for patients with VTE (n=8,478)**



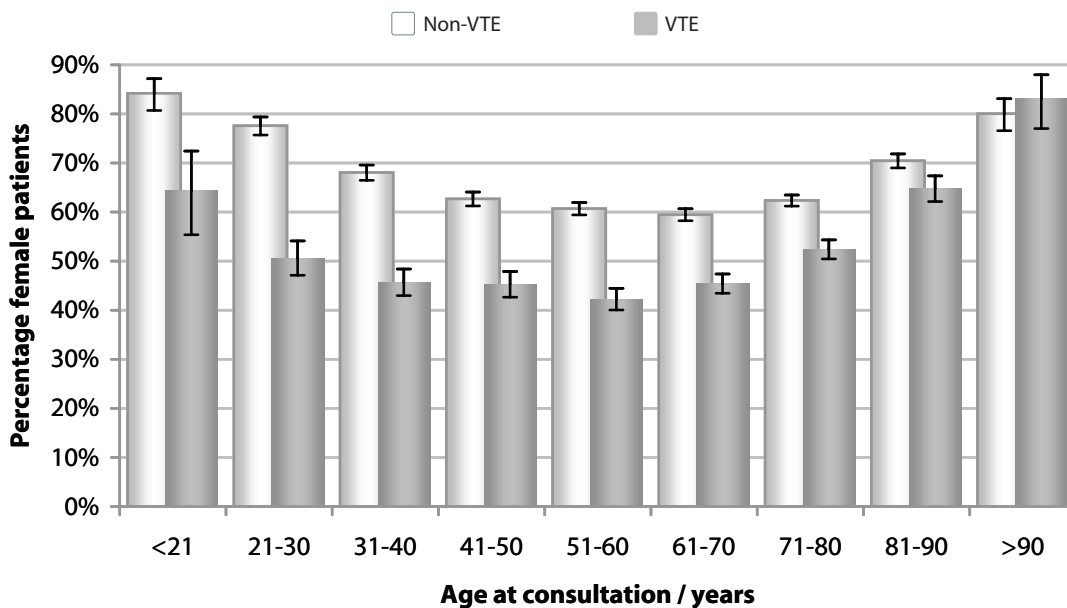
**Age and gender for patients with VTE**

The findings are similar to previous years, with increasing age closely associated with VTE. A finding we had regarded as unexpected in the past - that in the patient-population with confirmed VTE, males outnumber females in the middle decades (41-50, 51-60 and 61-70) - has been confirmed again in this year's analysis. As we noted before, this finding was contrary to a previous report<sup>5</sup>, which showed a marked over-representation of females with recent VTE compared with males in the 46-74 age groups. However, further review shows the association between gender and VTE is not clear cut. Different studies have described different results. Two retrospective cohort studies<sup>6,7</sup>, one case-control study<sup>8</sup> and the LITE study<sup>9</sup> all identified a higher risk of symptomatic VTE in males. In keeping with our findings for females, a French study identified a higher incidence of VTE in females, but confined to the age groups 20-39 years and above 75 years<sup>10</sup>.

**Age distributions and final diagnosis (n=47,334)**



**Age and gender distributions (n=46,522)**

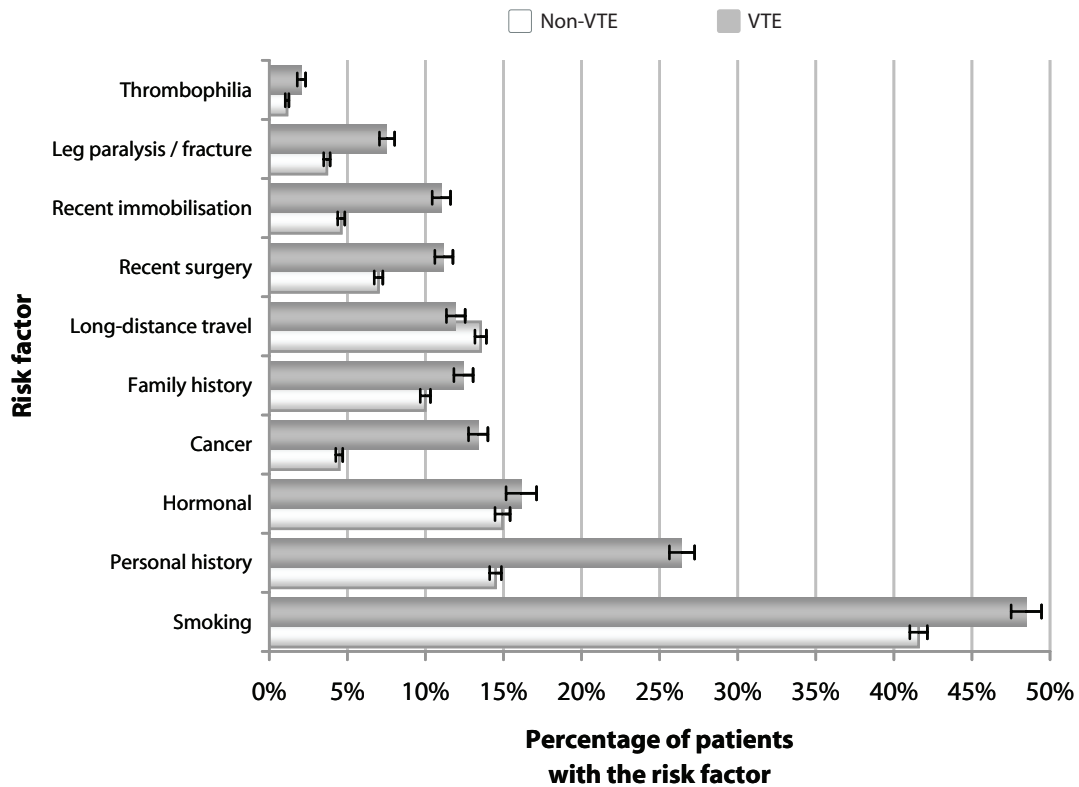


**Rates of different risk factors in patients who have VTE**

Several patient characteristics are over-represented in the VTE population compared with non-VTE patients, confirming these factors as risk factors for VTE. Risk factors most strongly associated with VTE are: personal history of VTE, cancer, medical illness, surgery, and paralysis. These factors are the same as described in previous reports and confirm what is commonly known. Certain risk factors, such as a previous history of VTE, are described commonly in non-VTE cases. This would be expected, because nurses or physicians referring patients for suspected VTE would have undertaken a pre-test probability, and the presence of a risk factor such as previous VTE would increase the score, increasing the chance of been referred for further review.

		Presence of risk factor			
		Absent	Present	Unspecified	All
Risk factor	Smoking	5,256	4,946	2,282	12,484
	Personal history of VTE	8,504	3,054	926	12,484
	Hormonal <sup>v</sup>	4,652	894	541	6,087
	Cancer	10,187	1,572	725	12,484
	Family history of VTE	9,895	1,404	1,185	12,484
	History of long-distance travel	10,031	1,359	1,094	12,484
	Recent surgery	10,237	1,287	960	12,484
	Recent immobilisation	9,872	1,221	1,391	12,484
	Leg paralysis / fracture	10,550	859	1,075	12,484
	Thrombophilia	10,968	229	1,287	12,484

**Presence of various risk factors and final diagnosis**



v. Data recorded for female patients only.

### The process of VTE diagnosis

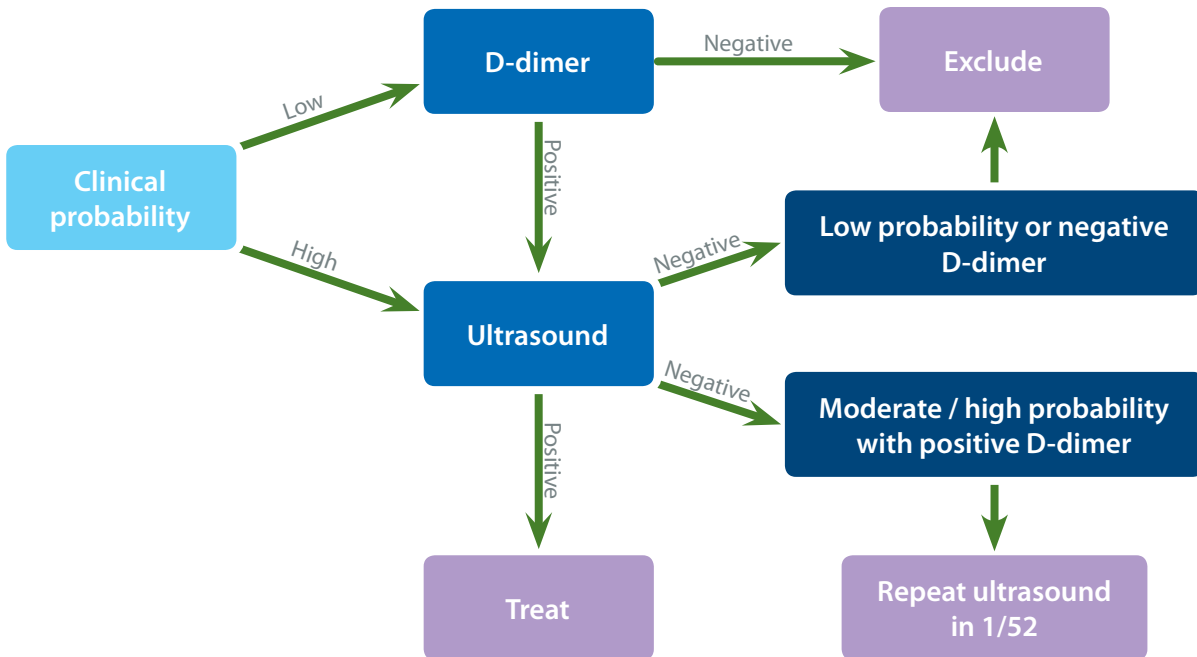
Extensive efforts have been devoted to developing non-invasive diagnostic strategies for the safe exclusion of a diagnosis of VTE, which reduce the use of imaging techniques and speed up the diagnostic process. It is now accepted that standardised clinical assessment to derive a pre-test probability (PTP) based on a clinical score is the preferred method. With its high negative predictive value, the D-dimer test represents an excellent non-invasive triage test in patients with suspected VTE and when combined with a low PTP, a negative D-dimer can safely exclude VTE and limit the number of patients requiring further evaluation with imaging techniques.

### Diagnosis of DVT

The British Committee for Standards in Haematology guideline reviewed the various approaches to the diagnosis of DVT in symptomatic outpatients and the potential for clinical assessment and D-dimer assays to reduce the need for diagnostic imaging<sup>11</sup>. The guideline describes the use of these methods alone and in combination with each other. Based on the evidence, one possible algorithm is offered (shown below).

### Task Force of the British Committee for Standards in Haematology

Patients with a moderate PTP could follow the path of the low probability patients if a sensitive D-dimer test is used and local assessment shows this to be safe, otherwise they should have an initial ultrasound as for the high-probability patients.



### Recommendations of the Task Force of the British Committee for Standards in Haematology

- In non-pregnant patients suspected of having a first DVT, PTP and D-dimers can be used to reduce the need for diagnostic imaging (III B).
- A low PTP and negative D-dimers excludes the diagnosis without need for diagnostic imaging (III B).
- The reliability of negative D-dimer results to exclude the diagnosis in patients with moderate PTP is critically dependant on the sensitivity of the test used. This requires local assessment and audit (IV C).
- D-dimers should not be used alone to exclude the diagnosis in patients with a high PTP (III B).
- A low PTP and negative initial ultrasound excludes the diagnosis without need for serial ultrasound or venography (III B).
- Negative D-dimers and a negative initial ultrasound excludes the diagnosis without need for serial ultrasound or venography (III B).

The BCSH guideline notes that many algorithms can be designed according to the principles outlined and suggests that one way hospitals can vary the algorithm is by altering the order in which tests are done in the different clinical groups. The guideline recommends that each institution design their own algorithm according to their resources and patient population. Given this recommendation, narratives describing the algorithm used at four VERITY centres are provided below.

#### Royal Gwent Hospital

Patients with suspected DVT are clinically assessed and scored using the Wells PTP and D-dimer (lab method). If the D-dimer is low (<300), the patient is discharged back to the GP. If the D-dimer value is intermediate (300–500), the patient is assessed by photoplethysmography – a negative result results in discharge; if positive, an ultrasound is requested and usually performed within 24 hours. If negative, the patient is discharged; if positive, the patient is reviewed by the Medical Assessment Unit, where enoxaparin and warfarin are initiated. If the D-dimer is high (>500), an ultrasound is requested and the same process followed. Virtually all patients are treated on a daily basis by an anticoagulant nurse until the INR is therapeutic. Their care is then passed to the INR Clinic, where a postal system of INR monitoring is used.

#### Portsmouth

Patients with suspected DVT are clinically assessed and scored using the Wells PTP. If the PTP is low, a D-dimer is performed. If the D-dimer is positive or if the PTP is high, an ultrasound is performed. If negative, but the PTP is high, patients are treated with enoxaparin and ultrasound is repeated 7-10 days later, or occasionally a venogram is performed if there are poor views on ultrasound. Patients are treated with enoxaparin and warfarin, or enoxaparin only in patients with active cancer / receiving chemotherapy.

#### Southend

Patients with suspected DVT are clinically assessed and no further tests are conducted if the clinical suspicion is low. If the suspicion is high, a D-dimer is performed. A level <190 is considered negative (viapool auto D-dimer test). If the D-dimer is >190, ultrasound is performed. If negative, ultrasound may be repeated in 5-7 days if suspicion remains high. Patients with a positive ultrasound are treated with enoxaparin and warfarin. Ultrasound is repeated after 3-6 months if there is suspicion that a DVT is still present.

#### Derriford

Patients are assessed using a modified Wells score and D-dimer. If the PTP is low, the patient is referred back to their GP irrespective of the D-dimer finding. If the PTP is high / intermediate and D-dimer is positive, patients are initiated on LMWH and booked for an ultrasound scan. If positive, the patient is initiated on warfarin. If negative, LMWH is stopped and ultrasound is repeated in 7 days. Patients are discharged after a negative test, or restarted on LMWH and initiated on warfarin if positive. If the PTP is high / intermediate and the D-dimer negative, the D-dimer is repeated 3 days later. If negative, the patient is discharged; if the repeat D-dimer is positive, LMWH is initiated and an ultrasound is performed. If this is negative, LMWH is stopped and ultrasound is repeated in 7 days. If positive, LMWH is restarted and warfarin is initiated. iv-drug users, cancer patients and

pregnant women are given enoxaparin exclusively. Proximal DVT is treated for 6 months, distal DVT for 6 weeks, but if spontaneous, for 3 months. If there is a previous history of VTE, the patient is referred to a consultant to decide warfarin duration.

### Moving towards quantitative D-dimer as a VERITY research tool

Given this acceptance of the optimal approach to excluding DVT, the findings presented in the next few pages on D-dimer and PTP findings will be the last that focus solely on VTE exclusion alone. From now on, our interest in D-dimer will move to focusing on D-dimer values, and the role of quantitative D-dimer as a potential marker for poor outcome in those with VTE, including those patients with cancer (see page 92) and even in patients who do not have VTE. The abstract shown below from Dr Peter Rose's group at Warwick (was presented as an oral presentation at this year's BSH conference), shows the potential importance of quantitative D-dimer as an important clinical measure. From now on, we ask that the actual D-dimer value is recorded in VERITY. Watch the VERITY website to find out more about this development.

### What do elevated D-dimer levels mean in patients without VTE?

Use of D-dimer levels along with clinical probability scores in the diagnosis of venous thrombosis is well established. High quantitative D-dimer levels at presentation have recently been shown to be a predictor for poor survival and underlying malignancy in patients with VTE. Do quantitative D-dimer levels in patients without VTE have a similar predictive value?

This study included 2,263 (1,518 female patients; 745 male patients) consecutive patient episodes from the prospectively maintained database of patients without venous thrombosis at a university teaching hospital, between February 2001 and December 2005. All patients with suspected venous thrombosis underwent a Doppler ultrasound examination to rule out venous thrombosis. D-dimer assays were done using Bio-Merieux kit containing mouse monoclonal antibody. The database was regularly updated (6-monthly) using hospital information systems, questionnaires and clinical review. Statistical analysis was carried out using SPSS 13.0 for Windows and GraphPad InStat® Version 3.06 for Windows software's. Overall survival (OS) was estimated by the Kaplan-Meier method. Cox regression analysis by forward likelihood ratio was subsequently used to explore the independent effect of variables that showed a significant influence on OS.

Median age at presentation was 69 years (range: 18-105 years). Median D-dimer level was 1,000 µg FEU ml<sup>-1</sup> (range: 300-35,500 µg FEU ml<sup>-1</sup>). 1,165 patients (51.7%) had a D-dimer level of >1,000 µg FEU ml<sup>-1</sup> and 40 (2%) had a D-dimer level of >8,000 µg FEU ml<sup>-1</sup> at presentation. 1,472 patients (65.4%) were aged above 60 years. Median follow up was 22 months (range: 0-65 months).

D-dimer level >1,000 µg FEU ml<sup>-1</sup>, >4,000 µg FEU ml<sup>-1</sup> and >8,000 µg FEU ml<sup>-1</sup> were associated with decreased overall survival (log rank test: p value: 0.002, < 0.001 and <0.001 respectively). Age >60 years was also associated with decreased overall survival (log rank test: p value: <0.001). D-dimer >8,000 µg FEU ml<sup>-1</sup> and age >60 years were an independent prognostic factor for poor overall survival on Cox regression analysis (p value: <0.001). 27.5% of patients with a D-dimer level >8,000 µg FEU ml<sup>-1</sup> had cancer (Fisher's exact test; p value: 0.003). 17% of patients with a D-dimer level >4,000 µg FEU ml<sup>-1</sup> had cancer (Fisher's exact test; p value: 0.04). 12.4% of patients with a D-dimer level >1,000 µg FEU ml<sup>-1</sup> had cancer (Fisher's exact test; p value: 0.02).

This study shows that elevated D-dimer levels at presentation even in patients without venous thrombosis is a marker for poor survival and a predictor for underlying malignancy. We have previously shown that D-dimer >8,000 µg FEU ml<sup>-1</sup> is a predictor for poor survival and underlying malignancy in patients with proven venous thrombosis. This suggests heightened fibrinolytic activity in the absence or presence of established venous thrombosis may be a marker for underlying malignancy and is associated with poor prognosis. Further studies are warranted to establish in different medical conditions the presence or absence of increased fibrinolysis and impact on clinical outcome.

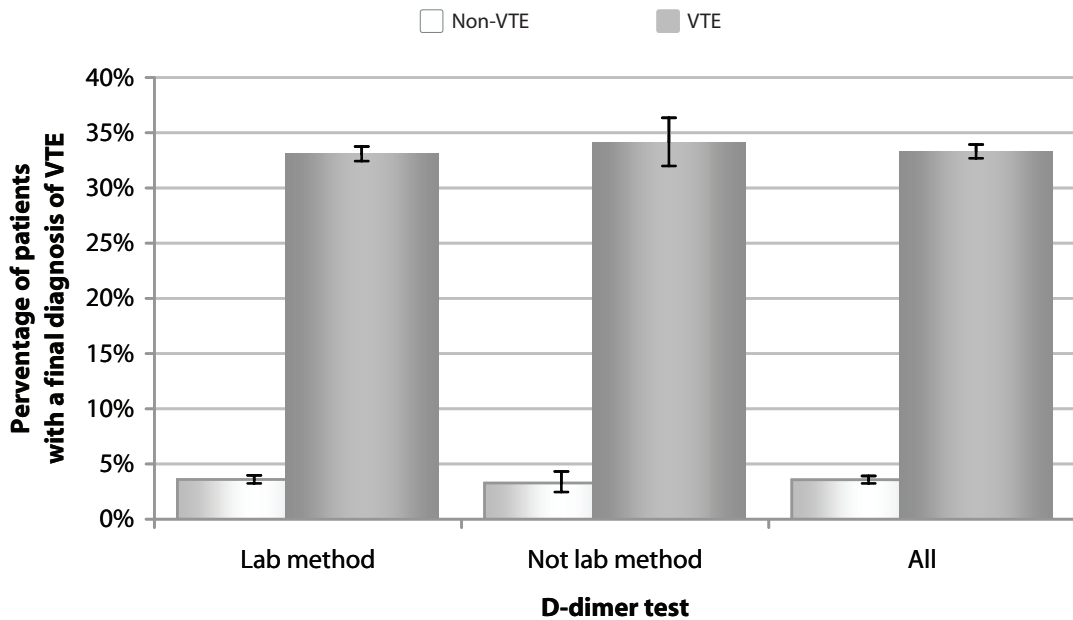
**D-dimer result and final diagnosis**

Diagnostic tests require a trade-off between sensitivity and specificity. A test that is highly sensitive limits false-negative results, with the benefit of a patient being able to begin appropriate treatment. A test that is highly specific is valuable as it limits unnecessary confirmatory tests, as well as incorrect treatment. Diagnosing VTE requires high sensitivity, as a missed DVT is terrible for the patient, and ideally high specificity, as a false-positive means inappropriate anticoagulation with all its associated risks.

Defining the sensitivity and the specificity of D-dimer allows an informed and accurate interpretation of the findings. This year, the sensitivity of D-dimer testing was 94.4%. These findings are remarkably consistent with those presented in the last report which are, in turn, in keeping with the findings in the literature. A recent large review of the evidence for D-dimer and pre-test probability found a similar result<sup>12</sup>. The evidence in 5 systematic reviews regarding the use of D-dimer, in isolation, was strong, with the sensitivities of the enzyme-linked immunosorbent assay (ELISA) and quantitative rapid ELISA, pooled across studies, of approximately 95%. Pooled specificities were in the 40% to 50% range for these assays, compared with specificity this year in VERITY of 44.3%.

		Final diagnosis			
		Non-VTE	VTE	Unspecified	All
D-dimer result	Negative	11,720	433	1,433	<b>13,586</b>
	Positive	14,746	7,364	2,908	<b>25,018</b>
	Unspecified / Not done	8,422	4,687	4,283	<b>17,392</b>
	All	<b>34,888</b>	<b>12,484</b>	<b>8,624</b>	<b>55,996</b>

**Final diagnosis and D-dimer test (n=34,263)**

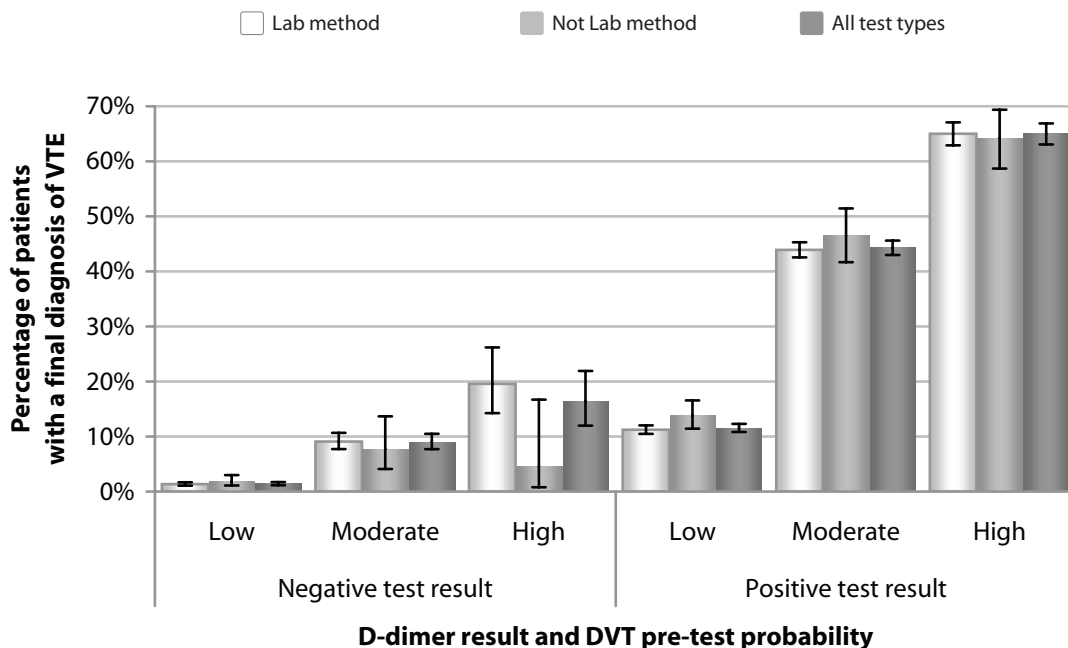


**D-dimer result, DVT pre-test probability and final diagnosis**

The negative predictive value (NPV) of low PTP and negative D-dimer remain essentially unchanged from levels presented in previous VERITY reports (98.5%). In total, 95 patients with a low PTP and negative D-dimer were shown to have VTE. This year 38 DVT patients had a PTP >2 who had a negative D-dimer result, again suggesting that if PTP>2, patients should progress to definitive diagnostic testing without D-dimer, particularly if the patients are elderly. We wish to emphasise again that without patient follow-up at 3 months, these data are not fully validated and do not allow a direct comparison between the VERITY data and published findings.

			Final diagnosis					
			Non-VTE	DVT	PE	PE & DVT	Unspecified	All
D-dimer test results and DVT PTP	Negative D-dimer	Low <=0	6,565	80	13	1	377	7,036
		Moderate 1-2	1,546	150	0	3	155	1,854
		High >2	194	38	0	0	16	248
		Unspecified	3,415	135	11	2	885	4,448
	Positive D-dimer	Low <=0	6,555	722	120	14	590	8,001
		Moderate 1-2	3,119	2,384	27	69	448	6,047
		High >2	854	1,549	7	30	213	2,653
		Unspecified	4,218	2,243	144	55	1,657	8,317
	D-dimer not specified	Low <=0	3,616	259	108	5	643	4,631
		Moderate 1-2	1,803	1,382	22	26	518	3,751
		High >2	506	911	7	8	229	1,661
		Unspecified	2,497	1,603	309	47	2,893	7,349

**Final diagnosis, D-dimer result, D-dimer test and DVT pre-test probability (n=24,040)**

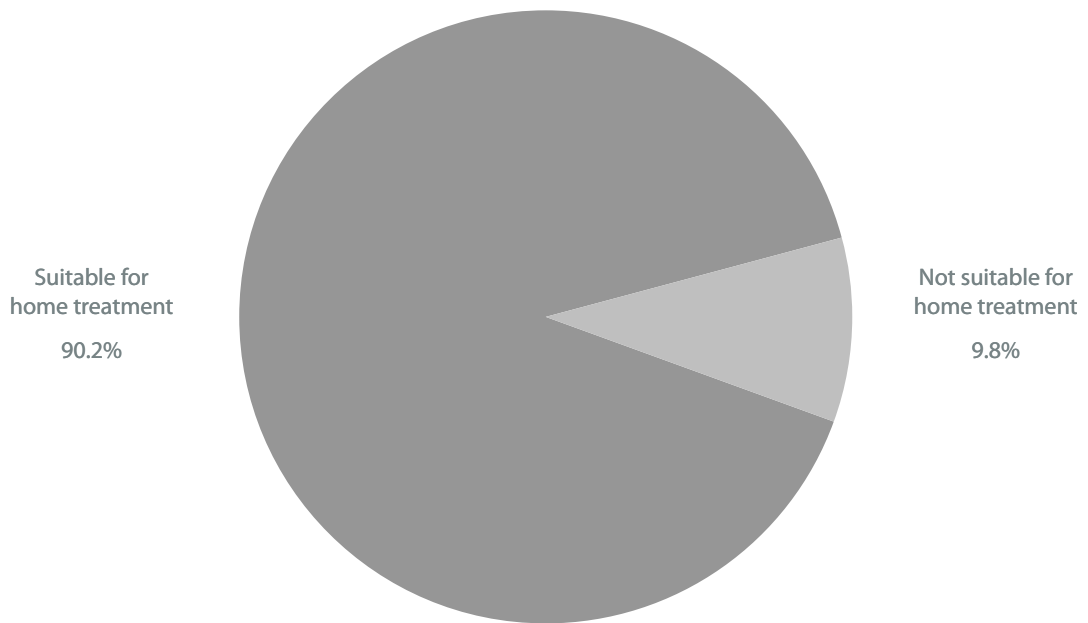


**Treatment of DVT**

The findings this year show that the number of patients treated as outpatients is around the same level as previously reported at about 90%. There had been a year-on-year increase, starting out at a rate of 86.1% in 2003, which now appears to have levelled out at around 90%.

		Suitable for home treatment			
		No	Yes	Unspecified	All
Database version	Old	554	5,124	288	<b>5,966</b>
	New	164	1,460	3,866	<b>5,490</b>
	<b>Both</b>	<b>718</b>	<b>6,584</b>	<b>4,154</b>	<b>11,456</b>

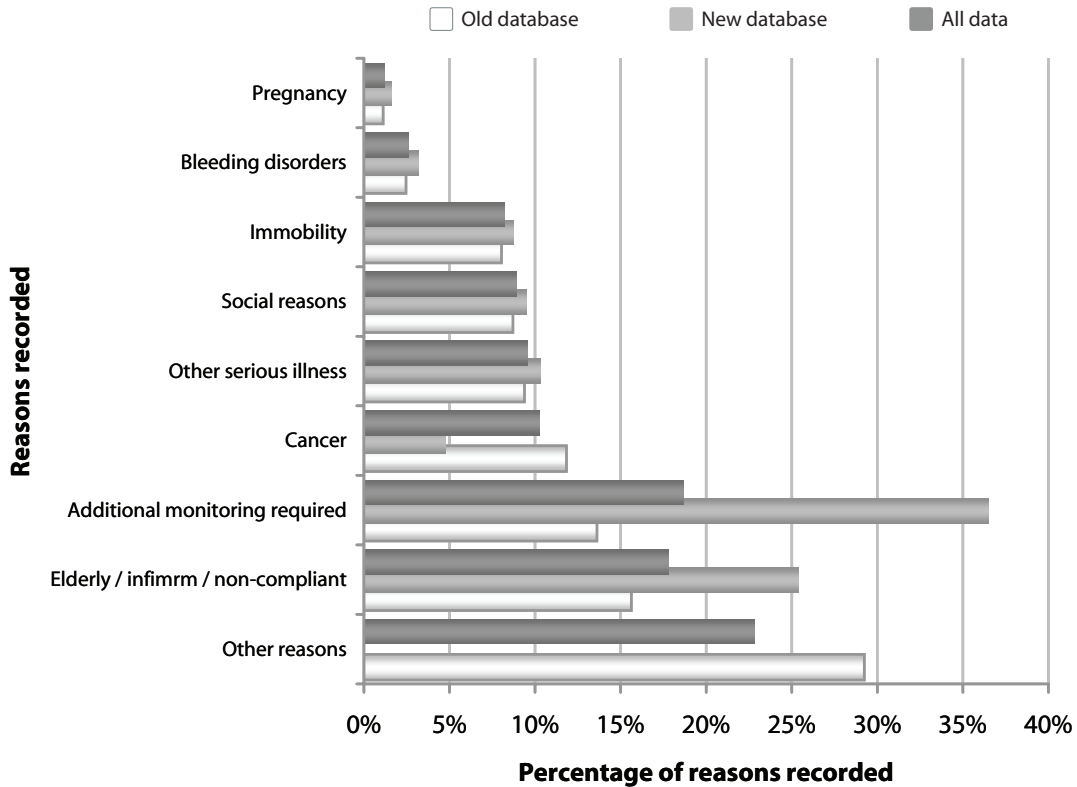
**Suitability for home treatment amongst patients with confirmed DVT (n=7,302)**



**Reasons for not treating DVT as an outpatient**

The reasons for not treating as an outpatient have changed somewhat from the last report. In particular, if we compare the old database to the new database, we can see that cancer as a reason for not treating out of hospital has fallen markedly, from 12% of patients to <5%. This may reflect the findings presented in the last report that suggested that outpatient treatment for acute DVT in cancer patients is both feasible and safe.

**Reasons that patients with DVT were deemed unsuitable for home treatment;  
(patients unsuitable for home treatment with a reason recorded n=574)**

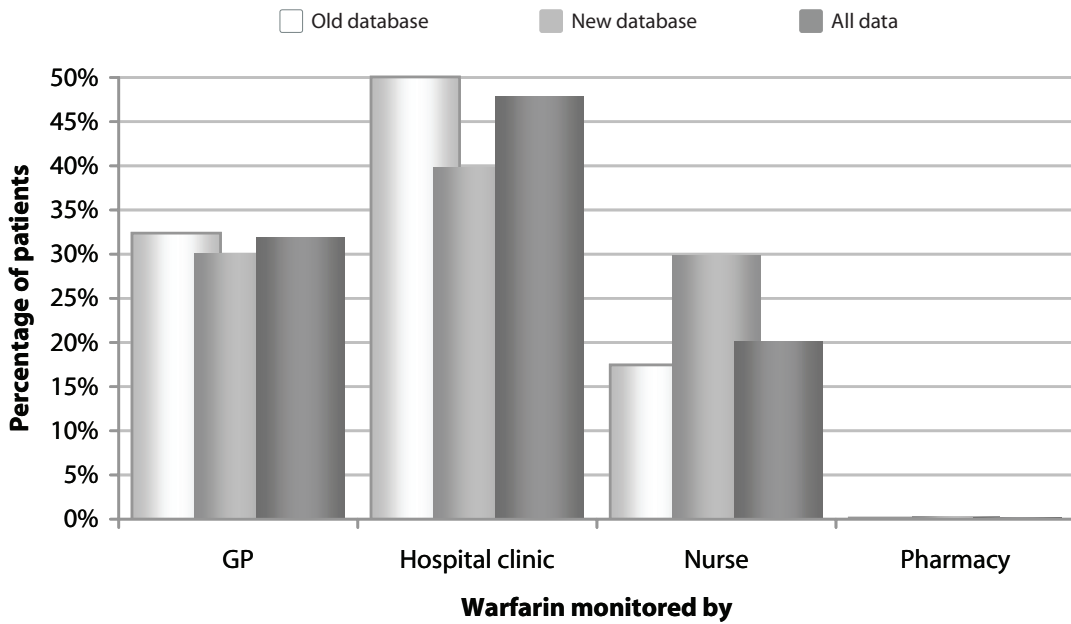


Overview

**Warfarin monitoring**

Warfarin is a difficult drug to use, with a narrow therapeutic index, but it remains the mainstay of oral anticoagulant treatment. Patients who take warfarin have to closely monitor their anticoagulation because of the careful balance required between too much and too little, which can cause bleeding or re-thrombosis respectively. These data are interesting and show that the majority of patients are managed by anticoagulation clinics. This is good practice and given the evidence that patients managed by anticoagulation clinics have fewer bleeding and thromboembolic events than those who receive usual medical care. Around 30% of patients have their warfarin managed by their GP; very few patients are managed by a pharmacy.

**Warfarin monitoring in patients with confirmed VTE  
(n=5,232 & n=1,452 respectively)**



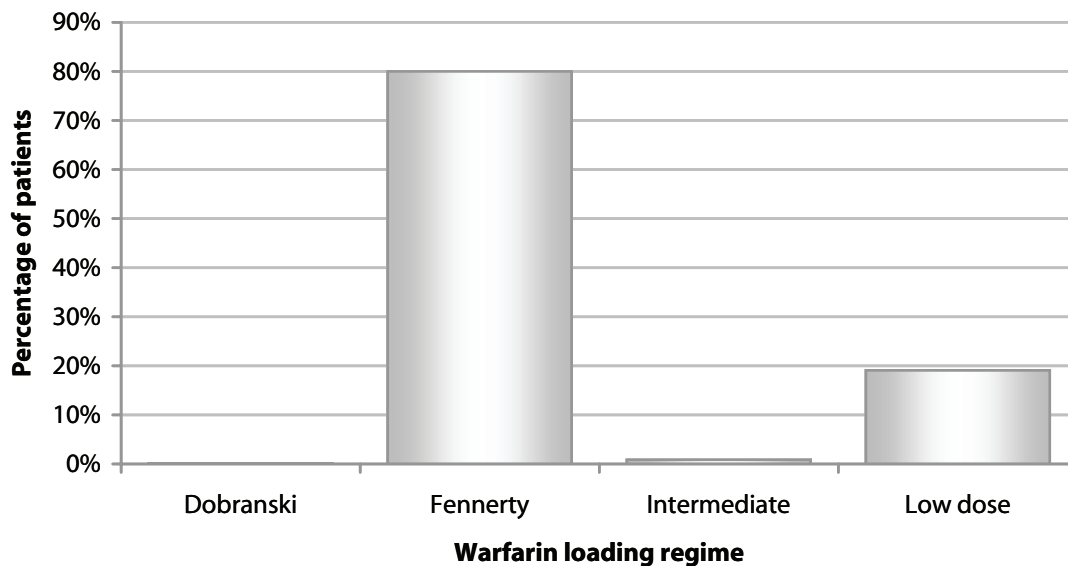
### Warfarin loading regime

The induction phase of any warfarin treatment is difficult because of the complex pharmacokinetics and pharmacodynamics of oral anticoagulants. We know that excessive anticoagulation during this phase may predispose to bleeding, whereas prolonged sub-therapeutic anticoagulation predisposes to re-thrombosis. Indeed, the risk of haemorrhage during oral anticoagulant therapy appears to be highest during the first days of treatment. In an attempt to minimize the risks during initiation, there have been many studies designed to define the best approach. It is clear is that with the larger proportion of patients having their warfarin initiated entirely as outpatients, daily laboratory monitoring is not always feasible and hence the use of established algorithms should be encouraged. In VERITY, the Fennerty regime is the most widely used.

The British Society of Haematology makes firm recommendations on warfarin initiation <sup>13</sup>:

- For outpatients who do not require rapid anticoagulation a slow-loading regimen is safe and achieves therapeutic anticoagulation in the majority of patients within 3-4 weeks (grade B, level IIb). This appears to avoid over-anticoagulation and bleeding associated with rapid loading.
- For patients requiring rapid initiation of oral anticoagulation regimens that start with 5 mg doses or a single 10 mg dose followed by 5 mg doses may be preferable to regimens that start with repeated 10 mg doses in certain patient groups, e.g. the elderly (>60 years of age), those with liver disease or cardiac failure and those at high risk of bleeding (grade B, level IIb).

Warfarin loading regimes for patients with VTE (n=1,170)



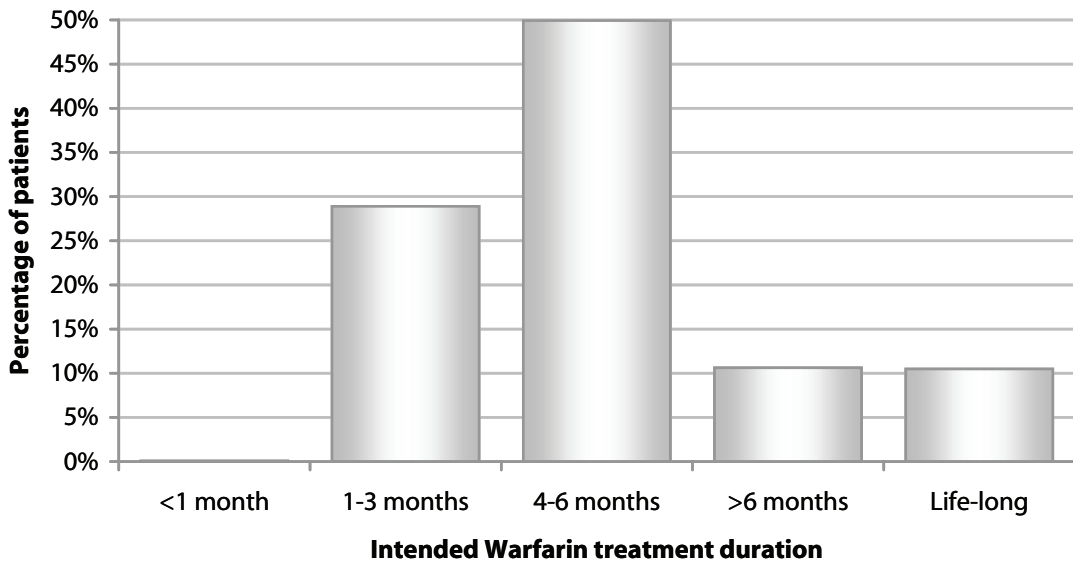
**Planned duration of warfarin treatment**

The duration of warfarin therapy creates a lot of debate and many well-designed studies have been conducted to define what constitutes best practice. In general, at least 6 weeks anticoagulation is recommended after calf vein thrombosis and at least 3 months after proximal DVT or PE. For patients with temporary risk factors and a low risk of recurrence 3 months of treatment may be sufficient. For patients with idiopathic VTE or permanent risk factors at least 6 months anticoagulation is recommended.

The findings below are interesting, showing that at least 20% of patients are intended to receive warfarin for longer than 6 months, with half recommend to receive warfarin for 4-6 months. These durations are generally in keeping with recommendations <sup>13</sup>.

Overview

**Intended duration of warfarin treatment for patients with VTE (n=1,450)**

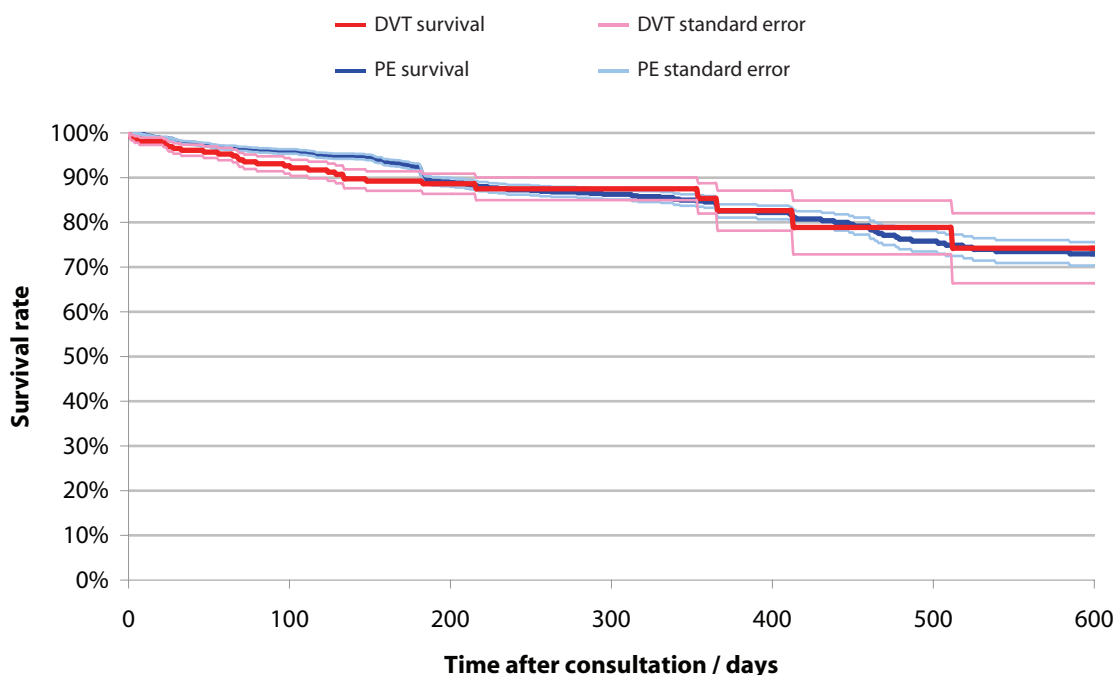


## Outcomes

These data (only 2,890 follow up records received from 55,996 entries) confirm previous findings that routine follow-up to assess outcome after diagnosis of symptomatic VTE does not happen in the UK. This reflects the literature, in which there are few descriptions of the outcome of patients with primary VTE treated in the usual, local hospital setting. This aspect of data collection in VERITY has been the most disappointing, because without outcome data, it is difficult to fully assess the data that has been collected. The parameters used to assess treatment success are the rates of recurrence and major bleeding events; death is normally a secondary endpoint. Without these data, the ability of the registry to act as a benchmark for the other centres, particularly in the context of clinical governance, is limited.

Of the limited follow up data in the registry, mortality is presented here as a Kaplan-Meier survival curve. The graph shows similar survival between DVT and PE patients. This is unexpected and differs from previous VERITY reports and literature findings, which show poorer survival for PE patients. There are few PE follow-ups, with relatively more follow-up in the surviving PE patients, which suggests that this finding could possibly be a data artefact. Again, it is difficult to comment further on the impact of clinical practice on outcomes without more detailed assessment and follow-up data that includes recurrence rates.

**Kaplan-Meier survival curves for patients with confirmed diagnoses of VTE (n=2,890)**



## Conclusions

The database has doubled in size since the last analysis in 2005, with around 56,000 patient entries and around 12,500 cases of confirmed VTE. The number of hospitals actively submitting patients to the registry is about 40. Patients with a recent history of surgery, medical illness or immobilization make up around a fifth of the VTE cases; more than 12% of VTE cases have a history of cancer, and the number of pregnant or post partum women in the database has increased to more than 1,000 patients.

The data remain remarkably consistent year-on-year, providing an internal validation of the data. The risk factor profiles again confirm the importance of increasing age, a personal history of VTE, cancer, recent admission to hospital (surgical and medical patients) in patients presenting with VTE, and these risk factors are confirmed by the recent NICE guidelines as key measures of thrombotic risk.

Assessing D-dimer and PTP has continued to offer important insights into the reliability of these exclusion tests. VERITY findings have previously confirmed the value of these methods, and this year, we report that the sensitivity of D-dimer testing was 94.4%, and when combined with PTP, the negative predictive value to exclude deep vein thrombosis (DVT) was 98.5%. There was no apparent difference between D-dimer testing performed in the laboratory compared with near-patient testing. The BCSH guidelines recommend that all patients are screened with an initial PTP, followed by a D-dimer for those with a low PTP, before any definitive diagnostic tests are conducted. This validated algorithm is backed by the VERITY data, and this year, the algorithms used to assess VTE in four VERITY centres are presented.

Given the acceptance of diagnostic exclusion algorithms for VTE, the focus of the VERITY registry will now change and the interest in D-dimer will move to focusing on D-dimer values, and the role of quantitative D-dimer as a potential marker of outcome, including those with VTE, patients with cancer and in patients who do not have VTE. Recent research carried out by Dr Peter Rose's group at Warwick shows the potential importance of quantitative D-dimer as an important clinical measure.

There had been a year-on-year increase in the proportion of patients treated as outpatients (86.1% in 2003, 88.9% in 2004, 89.6% in 2005 and 90.2% this year), which appears to have levelled at around 90%. This year, markedly fewer patients were excluded from out of hospital treatment because of cancer (12% falling to <5%). The principal warfarin initiation algorithm is Fennerty, and the monitoring of warfarin treatment is predominantly undertaken by a hospital clinic or GP.

The follow-up data available this year are very disappointing, with few data describing the main end-points for assessing treatment efficacy - namely recurrent VTE events or bleeding. The limited mortality data are presented in the report as Kaplan-Meier survival curves, and show, unexpectedly, similar survival in patients with PE.

As the registry enters its fifth year, and as more and more data are collected on risk and patterns of care in this outpatient treatment setting, it is vital that follow-up data and outcome events (such as bleeding and recurrence) are collected diligently so that the power of this database can be increased. Without a concerted effort to assess outcome, the strength of conclusions that can be drawn from a clinical governance viewpoint are severely limited.

## References

1. White RH. The epidemiology of venous thromboembolism. *Circulation*. 2003; **107 (Suppl 1)**: I4–8.
2. Lensing AWA, *et al*. Deep-vein thrombosis. *Lancet*. 1999; **353**: 479–856.
3. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation*. 2003; **107 (Suppl 1)**: I9–16.
4. House of Commons Health Committee. The prevention of venous thromboembolism in hospitalised patients. HC 99. The Stationary Office, London.
5. Di Minno G, *et al*. The first ambulatory screening on thromboembolism: a multicentre, cross-sectional, observational study on risk factors for venous thromboembolism. *J Thromb Haemost*. 2005; **3**: 1459-1466.
6. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and PE: a 25-year population-based study. *Arch Intern Med*. 1998; **158**: 585-593.
7. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Patwardhan NA, Jovanovic B, *et al*. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and PE. The Worcester DVT Study. *Arch Intern Med*. 1991; **151**: 933-938.
8. Cogo A, Bernardi E, Prandoni P, Girolami B, Noventa F, Simioni P, *et al*. Acquired risk factors for DVT in symptomatic outpatients. *Arch Intern Med*. 1994; **154**: 164-168.
9. Tsai AW, Cushman M, Rosamond WD, Heckbert SR, Polak JF, Folsom AR. Cardiovascular risk factors and venous thromboembolism incidence. The Longitudinal Investigation of Thromboembolism Etiology. *Arch Intern Med*. 2001; **162**: 1182-1189.
10. Oger E. Incidence of venous thromboembolism: a community-based study in Western France. *EPI-GETBP Study Group*. *Thromb Haemost*. 2000; **83**: 657-660.
11. Keeling D, *et al*. The Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology. The diagnosis of deep vein thrombosis in symptomatic outpatients and the potential for clinical assessment and D-dimer assays to reduce the need for diagnostic imaging. *Br J Haematol*. 2004; **124**: 15-25.
12. Di Nisio M, *et al*. Diagnostic accuracy of D-dimer test for exclusion of venous thromboembolism: a systematic review. *J Thromb Haemost*. 2007; **5**: 296-304.
13. Baglin T, *et al* (for the British Committee for Standards in Haematology). Guidelines on oral anticoagulation (warfarin): third edition - 2005 update. *British Journal of Haematology*. 2006; **132**: 277–285.