

# The VERITY Steering Committee



## Fourth Venous Thromboembolism Registry Report

**2007**

*Compiled by*

**Denise O'Shaughnessy** DPhil FRCP FRCPath MBA

**Peter Rose** FRCP FRCPath

**Nicholas Scriven** FRCP

**Roopen Arya** PhD FRCP MRCPath

**Tim Nokes** FRCP FRCPath

**Tim Farren** BSc (Hons), AIBMS

**Peter Walton** MA MB BChir MBA

**Aidan McManus** BSc PhD

**MMRx Communications**

**Robin Kinsman** BSc PhD

*the VERITY Steering Committee*

*Dendrite Clinical Systems*



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59A Bell Street, Henley-on-Thames, Oxfordshire RG9 2BA, United Kingdom

Phone: +44 1491 411 288

Fax: +44 1491 411 377

E-mail: [publishing@e-dendrite.com](mailto:publishing@e-dendrite.com)

**Printed &  
bound by**



## **Foreword**

Denise O'Shaughnessy, the VERITY Steering Committee and Dendrite are to be congratulated on the publication of this fourth VERITY report, which comes some two years after the last report. Since 2005 the database has doubled in size and now includes around 56,000 patients of whom 12,000 have a confirmed diagnosis of venous thromboembolism (VTE). Uniquely the registry continues to record findings on all patients with suspected as well as confirmed VTE.

The risk factor findings confirm the previously described factors that place patients at risk of VTE. Patient profiles show that patients with a recent history of surgery, medical illness or immobilisation make up around a fifth of the VTE cases; more than 12% of VTE cases have a history of cancer, and entries for pregnant or *post partum* women with suspected VTE have increased to more than 1,000 patients.

The report provides important insights into the association of cancer and thrombosis. In particular, with over 3,000 patients with cancer recorded, there is an increasing number of the more uncommon cancers registered in the database. According to the data in VERITY, compared with patients with the most common forms of cancer, patients with these more uncommon cancers are much more likely to have a confirmed positive diagnosis of VTE.

There are certain areas where clinical practice appears to have improved, in particular the increased uptake of CTPA in the diagnosis of pulmonary embolism. However, although the outpatient treatment of deep vein thrombosis (DVT) continues to rise, year-on-year, this has not transferred, as yet, to the pulmonary embolism population. This remains an important development area for VERITY, with a new focus on validating a risk score to give confidence to centres to manage low-risk patients presenting with pulmonary embolism in the outpatient setting.

Although this enormous data resource is undoubtedly of immense value to the participating centres, the number of hospitals actively recruiting into the registry remains modest at 38. This is despite the fact that the registry is open and free to all centres, thanks to an unrestricted educational grant from sanofi-aventis, who are to be commended for continuing to embrace an open registry for all patients with suspected thrombosis. I suggest that all hospitals, but particularly those with specialist thrombosis services, consider joining the registry. VERITY makes an important contribution to our understanding of VTE in the United Kingdom and it has an important role to play beyond the assessment of treatment of DVT. There is now the opportunity to extend the reach beyond the core hospitals to create a truly national VTE registry.

Measuring patient outcomes against a risk-stratified expectation is a key step in improving performance. One of the hopes of the Steering Committee remains that patient outcomes will be recorded after a venous thrombosis episode. Only by doing so can we begin properly to assess and monitor practice and improve care. The previous VERITY report highlighted the findings of both the Health Select Committee, which noted the problem of VTE in hospitalised patients, and the Department of Health's response, which recognised that there was no systematic approach to identifying and managing hospital patients at risk of VTE. Since publication of that report, both the Chief Medical Officer and NICE have published recommendations. The NHS now has a clear strategy for the prevention of VTE in hospital patients. Over the next two years we will see this strategy implemented as reduction of the incidence of VTE in hospital patients becomes a systems responsibility and physicians have to work with the system to ensure patients are assessed for their thrombosis risk and that prevention measures are put in place.

This fourth VERITY report is an excellent resource for further research. VERITY continues to make an important contribution to our understanding of VTE. I am sure that VERITY will have a central role to play in the continuing development of thrombosis care in the UK.

**Professor Isobel Walker**

**Past President of the British Society for Haematology  
Consultant Haematologist, Glasgow Royal Infirmary**

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## Executive summary

### Introducing VERITY – a national venous thromboembolism registry

VERITY is a UK, prospective, observational registry with the goal of developing and improving the management of patients with venous thromboembolism (VTE) through increasing knowledge and sharing best practice. The registry records patient demographics, the diagnostic strategies and treatment approaches taken within the overall management of patients who present with a suspected VTE to hospitals which have an outpatient treatment facility.

The approach of managing patients with suspected VTE in the outpatient setting was a major development when the registry was set up in 2001. Now, the ultimate aim is to facilitate benchmarking (*i.e.* the continuous systematic search for and implementation of best practice) in the area of VTE, with the hope that this will lead to uniform improvements in patient care.

### VERITY findings in 2007

The VERITY findings have been published regularly and this latest report shows the database has doubled in size since the last analysis, with just under 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. VERITY is one of the largest VTE registries in the world and these data open the door to a better understanding of VTE in the UK.

### Clinical diagnostic algorithms, D-dimer blood tests and diagnosis

In recent years, extensive efforts have been devoted to developing non-invasive and more cost-effective diagnostic strategies for VTE. The main emphasis of these methods is the safe exclusion of a diagnosis of VTE and so reducing the need for costly imaging techniques and improving the diagnostic time-frame.

The Health Technology Assessment completed in 2006 by Dr Steve Goodacre in Sheffield on the measurement of the clinical and cost-effectiveness of non invasive diagnostic testing strategies for DVT, concluded that, generally, the most cost-effective care for patients suspected of VTE was to follow a clinical algorithm using a clinical pre-test probability (PTP), such as the Wells score and employing D-dimer testing before sending patients for definitive tests such as Doppler ultrasound, although this may not be the case for certain populations such as the elderly and those with cancer.

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 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. The guideline describes the use of these methods alone and in combination with each other. Based on the evidence, one possible algorithm is shown, and the diagnostic approach used at four VERITY hospitals is also provided.

VERITY offers important insights into the practice of pulmonary embolism (PE) diagnosis, once PTP and D-dimer have suggested the value of a diagnostic test. Although diagnostic algorithms have been validated for the diagnosis of PE, previous VERITY findings showed that they are not always followed. However, this year's findings now show a movement away from V/Q scanning and an increased uptake of CT pulmonary angiography (from 13.5% to 36.3% in the last 12 months), which should be regarded as the diagnostic test of choice. It is hoped that the VERITY findings will continue to influence this aspect of care in the diagnosis and treatment of PE.

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

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. In the near future, the actual D-dimer value will be requested in VERITY. Watch the VERITY website to find out more about this development.

### Outpatient treatment of venous thromboembolism

Outpatient treatment of uncomplicated DVT is now commonplace, but remains less common for patients with PE. In VERITY, around 10% of DVT patients were deemed unsuitable for home treatment, which has remained unchanged over the last 2 years. The proportion of patients deemed unsuitable for home treatment because of cancer has fallen since the last report (12% to <5%), which had suggested that cancer patients should not necessarily be automatically excluded from home treatment.

The case for home treatment for PE has not made an impact yet on the proportion of patients treated out of hospital, with little change in the number of patients treated in the community in the last 3 years and most hospitals seem wary of considering this treatment option. The proportion remains at around two thirds of patients in the limited number of hospitals that treat any patients in the outpatient setting. An ongoing study at four VERITY centres is attempting to validate the Aujesky risk score to facilitate greater uptake of out-of-hospital treatment.

### Outcomes after treatment for venous thromboembolism

VERITY has confirmed that few hospitals routinely record outcomes after the diagnosis of symptomatic VTE. This year, there was again a poor record of follow-up. It had been hoped that more diligent follow up would occur because it is this outcome data that provides the key to understanding how practice can be improved, but a change in how this part of the registry data is collected is now warranted. More details will be provided on the website.

### Cancer and venous thromboembolism

There are considerable numbers of cancer patients in the registry (n=3,056). In terms of absolute numbers of cancer patients, the most common forms of cancer in the general population (breast, prostate, colorectal and lung) again match the most common cancers with VTE found in the registry. However, comparing the incidence of each cancer type in the VTE patients to the non-VTE patients by calculating a ratio shows certain cancers are particularly prevalent in the VTE population and therefore particularly associated with VTE (endocrine, pancreatic and CNS cancers). Ongoing analysis of the cancer data in VERITY will be completed shortly and will be published in thrombosis journals.

### Government reports on the prevention of venous thromboembolism

Last year the House of Commons Health Select Committee produced a report which recommended that surgeons, physicians and other health personnel, as well as the public, are made more aware of VTE, including the incidence, the causes, as well as prevention methods. The Committee estimated that 25,000 deaths occurred each year due to VTE in hospitalised patients. In response to this, the Department of Health set up a VTE Expert Working Group to assess practice and develop a strategy for change in the prevention of VTE in Britain. The Expert Working Group report was published by the Chief Medical Officer in April 2007 with formal recommendations, positioning the prevention of VTE as a patient safety issue, and recommending mandatory risk assessment for all inpatients. The long-awaited NICE guideline identifies the best approaches to preventing VTE in surgical patients at risk of VTE and also recommends risk assessment for all patients admitted to hospital. An implementation working group has been formed to define a national risk assessment model and take forward the process of implementing these guidelines, a process that will substantially alter how thrombosis prevention is managed within the NHS.

We hope that VERITY will continue to play an important part in highlighting how practice can be changed to improve the care of patients with thrombosis.

## Data management of the 2007 report

This report is prepared from data that were collected using three data-capture systems. The data have been integrated into a single, unified Dendrite registry for the purposes of this report (see figure opposite).

Data from the original VERITY database, the software for which resided on the user's local computer, and data from the first incarnation of the web-based database were exported to a single flat file format (*Import file 1*) and then imported into the Dendrite system using the dedicated Import Manager Module<sup>®</sup>. These data are referred to using the shorthand *old data* in the text.

An export from the newer on-line database was also prepared (*Import file 2*) and the data from this file were then imported into a separate, parallel Dendrite registry, again using the Import Manager Module<sup>®</sup>, to sit alongside the registry holding the data from *Import file 1*. The data from this second import file are sometimes referred to as *new data* in order to differentiate them from the data originating from *Import file 1*. This bifurcation between old and new is useful because it highlights the fact that the two source files represent time-periods before and after a major revision of the VERITY dataset.

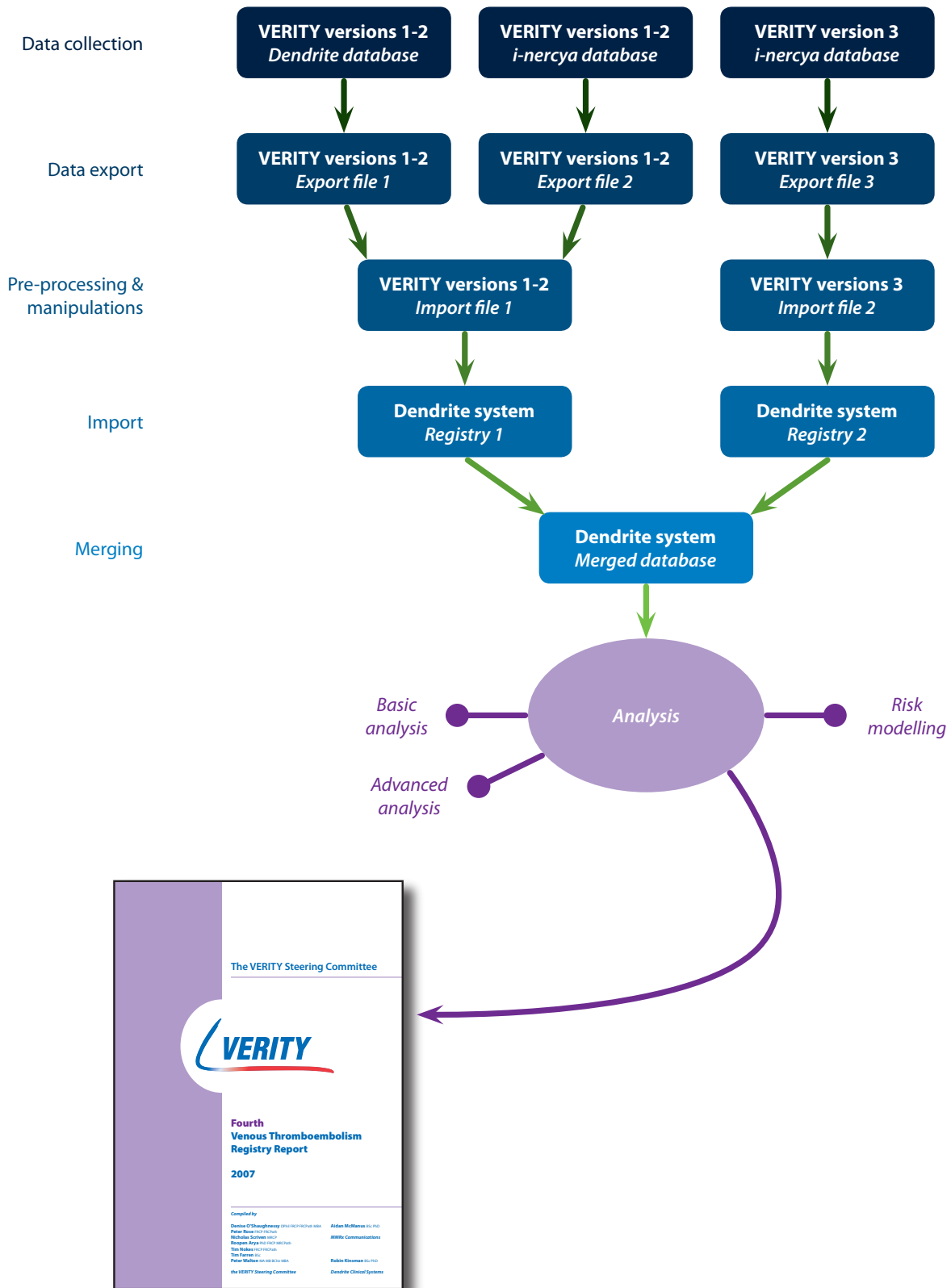
Each move from one data-capture system to another coincided with changes to some of the questions in the VERITY dataset: principally employing the processes of simplification and expansion. Simplification involved the removal of extraneous questions and / or response options, and expansion the addition of some questions so as to increase the detail collected on some aspects of the patient's history such as the medical and surgical inpatient stay. Consequently, some questions exist only in the earliest version of VERITY whilst others exist only in the latest version of VERITY; some questions that exist in all incarnations of the database have undergone minor changes, removing or amalgamating some of the response-options that were deemed unnecessary, redundant or too detailed. This explains why some of the analyses are restricted to certain time-frames, whilst other analyses may cover the entire life-span of VERITY.

The contents of the two import registries were then merged into a single, unified database using standard correspondence functions in the Dendrite software.

Preliminary analyses were performed in the Dendrite software and then post-import data manipulations were effected using Business Object's Crystal Reports<sup>™</sup>, with links to the data using Dendrite's object architecture-based software.

Charts were prepared for presentation using Microsoft Excel<sup>™</sup>, and finally the report was assembled using Adobe's InDesign CS2<sup>™</sup> software.

**Schematic of the data management of the 2007 report**



Introduction

**List of active contributors in 2006**

**Contributors**

<b>Centre</b>	<b>Clinician</b> Name title and specialty	<b>Nurse</b> Name, title and specialty
Bangor Hospital	<b>Dr Hassan Mohammed</b> <i>Consultant Physician</i>	<b>Sian Hughes</b> <b>Rhianwen Griffiths</b> <i>Thrombosis Nurse Specialists</i>
Barnsley District General Hospital NHS Trust	<b>Dr Dominic Chan Lam</b> <i>Consultant Haematologist</i>	<b>Denise Brown</b> <i>Clinical Nurse Specialist</i>
Belfast City Hospital HSS Trust	<b>Dr Elizabeth Dowe</b> <b>Dr Ruth Spedding</b> <b>Mr Brendan Sinnott</b> <i>Consultant Emergency Medicine</i>	<b>Dervilla Mackle</b> <i>DVT Sister</i> <b>Rosemary Lavery</b> <i>Nurse</i>
Bristol Royal Infirmary	<b>Dr Andrew Mumford</b> <i>Consultant Haematologist</i>	<b>Pat Coggins</b> <b>Rachel Heneker</b> <b>Emma Kinnaid</b> <i>DVT Nurses</i>
Calderdale Hospitals NHS Trust, Halifax	<b>Dr Nick Scriven</b> <i>Consultant Physician</i>	<b>Jane Peacock</b> <i>Parenteral Therapy Manager</i>
City Hospital, Birmingham	<b>Dr Nigel Langford</b> <i>Consultant Physician</i>	<b>Manjit Singh</b> <b>Karl Tonks</b> <i>Anticoagulation Nurses</i>
City Hospitals Sunderland NHS Foundation Trust	<b>Dr Mansy</b> <i>Consultant Physician</i>	<b>Karen Pike</b> <b>Caroline Snaith</b> <i>DVT Nurse Specialists</i>
Craigavon Area Hospital, Portadown	<b>Mr Seamus O'Reilly</b> <i>Consultant Emergency Medicine</i>	<b>Dawn Richardson</b> <i>DVT Nurse</i>
Derriford Hospital, Plymouth	<b>Dr Jamie Fulton</b> <i>Consultant Physician</i> <b>Dr Tim Nokes</b> <i>Consultant Haematologist</i>	<b>Zara Lester</b> <i>Senior Staff Nurse</i> <b>Cathy Nurrish</b> <b>Mary Graham</b> <i>Staff Nurses</i>
Eastbourne District General Hospital	<b>Dr Pamela Gover</b> <i>Physician</i>	<b>Chris Truluck</b> <i>Nurse Specialist</i>
Frimley Park Hospital NHS Trust	<b>Dr Peter Alton</b> <i>Haematologist</i>	<b>Jayne Hughes</b> <b>Mary Weatherley</b> <b>Carol Coole</b> <i>DVT Nurses</i>
Glan Clwyd Hospital, Rhyl	<b>Dr David Gozzard</b> <i>Consultant Haematologist</i>	<b>Judith Colclough</b> <i>DVT Nurse</i>
Gwent Healthcare NHS Trust	<b>Dr Sarah Lewis</b> <i>Clinical Director</i>	<b>Fran Pressley</b> Royal Gwent Hospital <b>Cheryl Rogers</b> Neville Hall Hospital, Abergavenny <b>Karen Davies</b> Caerphilly District Miners <i>Clinical Lead Nurses</i>

<b>Centre</b>	<b>Clinician</b> Name title and specialty	<b>Nurse</b> Name, title and specialty
Hinchingbrooke Hospital, Huntingdon	<b>Dr Kathy Hoggarth</b> <i>Consultant Haematologist</i> <b>Dr Kanchan Rege</b> <i>Consultant Haematologist</i>	<b>Jane Day</b> <b>Sue Jones</b> <i>Anticoagulation Nurse Specialists</i>
Inverclyde General Hospital	<b>Dr David Marshall</b> <i>Consultant Physician</i>	<b>Susan McGeachie</b> <i>DVT Nurse Specialist</i>
King's College Hospital, London	<b>Dr Roopen Arya</b> <i>Consultant Haematologist</i>	<b>James Lambie</b> <i>DVT Nurse</i>
King's Mill Hospital, Sutton-in-Ashfield	<b>Dr Tim Moorby</b> <i>Consultant Haematologist</i>	<b>Pam Draycott</b> <b>Beverly Marshall</b> <i>DVT Nurse Specialists</i>
Mater Hospital Trust, Belfast	<b>Dr Paul Curran</b> <i>A &amp; E Consultant</i>	<b>Rea Conlan</b> <b>Nona Conaghan</b> <i>DVT Nurses</i>
Musgrove Park Hospital, Taunton	<b>Dr AP Lambert</b> <i>Consultant Physician</i>	<b>Megan Stephens</b> <b>Judy Read</b> <i>Nurses, Medical Day Centre</i>
Northampton General Hospital	<b>Dr Sonia Swart</b> <i>Consultant Haematologist</i>	<b>Gill Askens</b> <i>Anticoagulation Nurse Specialist</i>
Queen Alexandra Hospital, Portsmouth	<b>Dr Lorraine Albon</b> <i>Consultant Physician</i>	<b>Kim Carter</b> <i>MAU DVT Nurse Specialist</i>
Queen Elizabeth II Hospital, Welwyn Garden City	<b>Dr Christopher Tew</b> <i>Consultant Haematologist</i>	<b>Mary Pearce</b> <i>Anticoagulation nurse specialist</i>
Queen's Medical Centre, Nottingham	<b>Dr Jerry Dolan</b> <b>Dr Bethan Myers</b> <i>Consultant Haematologist</i>	<b>Thelma Bell</b> <i>Anticoagulation Nurse Specialist</i> <b>Julie Davies</b> <i>Thromboprophylaxis Nurse Specialist</i> <b>Janet Thompson</b> <i>Thrombosis Nurse Specialist</i>
Royal Hallamshire Hospital, Sheffield	<b>Dr Rhona MacLean</b> <i>Consultant Haematologist</i>	<b>Emma Jewiss</b> <i>Sister, Emergency Admissions Unit</i>
Royal Surrey Hospital County Hospital NHS Trust	<b>Dr Janet Shirley</b> <i>Consultant Haematologist</i>	<b>Karen Bulley</b> <i>Matron Medical Assessment Unit</i>
Sandwell District General Hospital, West Bromwich	<b>Dr Farooq Wandroo</b> <i>Consultant Haematologist</i>	<b>Sam Plaha</b> <b>Jackie Martin</b> <i>Community DVT Project Managers</i>
Scarborough General Hospital	<b>Dr Ed Smith</b> <i>Consultant in A&amp;E</i> <b>Dr Ranjit Perera</b> <i>Consultant Geriatrician</i>	<b>Sue Bacon</b> <i>Clinical Nurse Specialist in DVT</i>

**Contributors**

<b>Centre</b>	<b>Clinician</b> Name title and specialty	<b>Nurse</b> Name, title and specialty
Selly Oak Hospital, Birmingham	<b>Dr Lynn Lambert</b> <i>Consultant Emergency Physician</i> <b>Dr Nandan Gautam</b> <i>Consultant in Medicine &amp; Critical Care</i>	<b>Heather Dudley</b> <i>DVT nurse</i>
Southern Derbyshire NHS Trust	<b>Dr A McKernan</b> <i>Consultant Haematologist</i>	<b>Diane Usher</b> <b>Julie Ann Johnson</b> <i>DVT Specialist Nurses</i>
Southend Hospital	<b>Dr John Whitear</b> <i>Associate Specialist</i>	<b>Jackie Horgan</b> <i>Clinical Nurse Specialist</i> <b>Julie Morgan</b> <b>Kerstin Streeton</b> <i>DVT Clinical Nurse Specialists</i>
Walsall Hospitals NHS Trust	<b>Dr G Galvin</b> <i>Consultant Haematologist</i>	<b>Kim Perrins</b> <i>DVT Nurse</i> <b>Sukhbinder Boparai</b> <i>Clinical Nurse Specialist</i>
Walsgrave Hospital, Coventry	<b>Dr Peter Rose</b> <i>Consultant Haematologist</i>	<b>Eileen Cheyne</b> <b>Sharon Holden</b> <i>Clinical Nurse Specialists</i> <b>Karen French</b> <b>Rita James</b> <i>DVT Nurses</i>

## Report terminology

### Diagnosis terminology

The term **venous thromboembolism** (VTE), includes **deep venous thrombosis** (DVT) and **pulmonary embolism** (PE), with **DVT+PE** used to indicate patients in whom a diagnosis of both forms of VTE has been made. Patients with a primary suspected diagnosis of PE are described as **suspected PE**; those with confirmed PE are described as **PE** and those shown not to have PE are referred to as **non-PE**. In cases where a diagnosis other than VTE is recorded, the term **other** is used. In a proportion of cases in the database, the final diagnosis has not been indicated, either because the final diagnosis remains unconfirmed, or because the data have not been entered. In these cases, the patients are termed **unspecified**.

### Definitions

<b>Computed Tomography scan (CT):</b>	a diagnostic test for pulmonary embolism in which multiple X-ray images are integrated to produce a composite image of the pulmonary circulation.
<b>D-dimer</b>	a by-product of the degradation of fibrin composed of two cross-linked fibrin subunits. The presence of elevated levels of D-dimer in plasma may indicate underlying VTE.
<b>Doppler ultrasound</b>	this is a diagnostic test for deep vein thrombosis in which venous blood flow is visualised using ultrasound.
<b>INR (International Normalised Ratio)</b>	this term refers to a system of standardising blood coagulation results using an international sensitivity index for thromboplastin reagents and coagulation instruments.
<b>Negative predictive value (NPV)</b>	the probability that a patient will test negative, when restricted to all patients who test negative: $TN / (TN + FN) \times 100\%$ .
<b>Pre-test probability (PTP)</b>	a method of assessing the likelihood of venous thromboembolism in a patient using a scoring system based on clinical signs, symptoms and risk factors.
<b>Pulmonary angiography</b>	a diagnostic test for pulmonary embolism in which the pulmonary blood vessels are visualised on X-ray following injection of a contrast medium.
<b>Sensitivity</b>	the number of true positives detected as a proportion of all positives; all positives are (detected) true positives (TP) plus the (undetected) false negatives (FN) = $TP / (TP + FN) \times 100\%$ .
<b>Specificity</b>	the number of true negatives as a proportion of all the negatives; all negatives are (detected) true negatives (TN) plus the (misdiagnosed) false positives (FP) = $TN / (TN + FP) \times 100\%$ .
<b>Ventilation-perfusion scan (V/Q scan):</b>	a diagnostic test for pulmonary embolism examining airflow and blood flow in the lungs. Airflow is visualised following inhalation of radioactive Xenon gas. Blood flow is visualised following intravenous administration of radioactive Technetium.

### Conventions used in the report

There are a number of conventions used in the report in an attempt to ensure that the data are presented in a simple and consistent way. These conventions relate largely to the tables and graphs, and some of these conventions are outlined below.

### Conventions used in tables

On the whole, unless otherwise stated, the tables in this report record numbers of patient-entries (see the example below reproduced from page 22).

Terminology

		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>
	All	<b>34,888</b>	<b>12,484</b>	<b>8,624</b>	<b>55,996</b>

The numbers in each table are colour-coded so that patient-entries with complete data for all of the components under consideration (in this example **both** the number of risk factors **and** a final diagnosis) are shown in regular black text. If one or more of the database questions under analysis is blank, the data are reported as *unspecified* in purple text. The totals for both rows and columns are highlighted as bold text.

Some tables record percentage values; in such cases this is made clear by the use of an appropriate title within the table and a % symbol after the numeric value. Yet other tables report average numbers (doses of LMWH for example) and, again, this is made clear by the use of an appropriate title within the table.

Rows and columns within tables have been ordered so that they are either in ascending order (number of risk factors: 0, 1, 2, 3, >3; DVT pre-test probability score: Low, Medium, High) or with negative response options first (No, Non-VTE, No cancer) followed by positive response options (Yes, VTE, types of cancer).

Row and column titles are as detailed as possible within the confines of the space available on the page. Where a title in either a row or a column is not as detailed as the authors would have liked, then footnotes have been added to provide clarification.

There are some charts in the report that are not accompanied by data in a tabular format. In such cases the tables are omitted for one of a number of reasons:

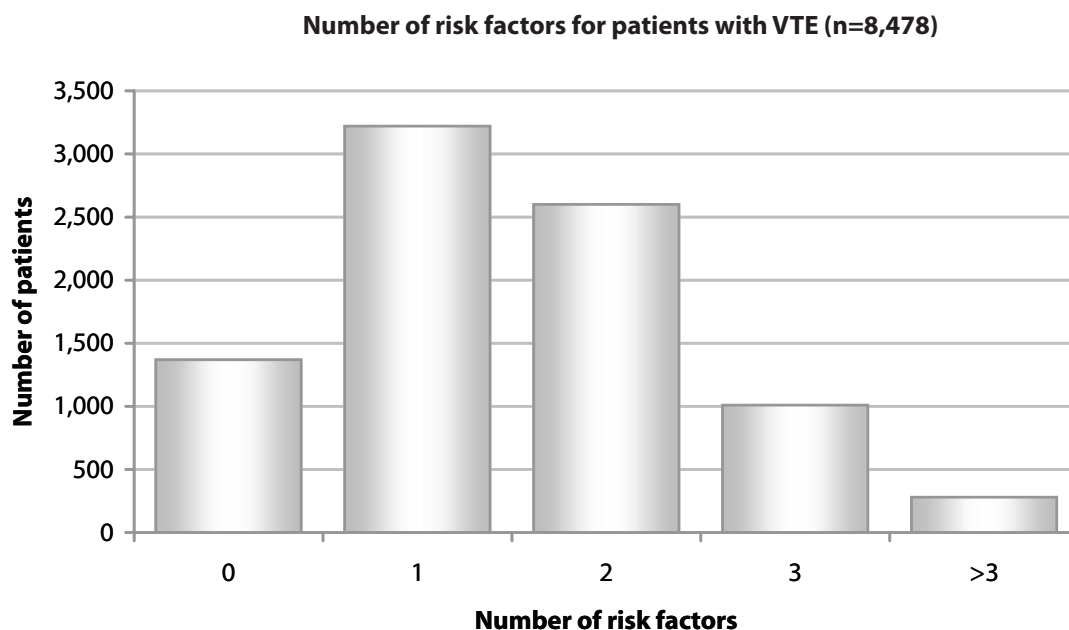
- insufficient space on the page to accommodate both the table and graph.
- there would be more rows / columns of data than could reasonably be accommodated on the page (Kaplan-Meier survival curves).
- the tabular data had already been presented elsewhere in the report.

### Conventions used in graphs

The basic principles applied when preparing graphs for the VERITY report were based, as far as possible, upon William S. Cleveland's book *The elements of graphing data*<sup>i</sup>. This book details both best practice and the theoretical bases that underlie these practices, demonstrating that there are sound, scientific reasons for plotting charts in particular ways.

**Counts:** The counts (shown as n= in each graph's title) associated with graphs are affected by a number of independent factors and will therefore vary from chapter to chapter and from page to page. Most obviously, many of the charts in the VERITY report are graphic representations of results for a particular group (or sub-set) extracted from the database, such as patients with cancer, pregnant patients, and so on. This clearly restricts the total number of database-entries available for any such analysis. In addition to this, some entries within the group under consideration have data missing in one or more of the database questions being examined (reported as unspecified in tables); entries with missing data are excluded from the analysis used to generate the graph because they do not add any useful information.

For example, in the uppermost graph on page 22 (reproduced below), only the patient-entries with VTE **and** with a known number of risk factors are included in the analysis; this comes to 4,603 patient-entries (673 + 1,678 + 1,440 + 630 + 182 from examining the table; the 1,521 VTE patient-entries with an unspecified number of risk factors are excluded from the chart).



**Confidence interval:** In the charts prepared for this report, most of the bars plotted around rates (percentage values) represent 95% confidence intervals. The width of the confidence interval gives some idea of how certain we can be about the calculated rate of an event or occurrence. If the confidence intervals around two rates do not overlap, then we can say, with a specified level of confidence, that the rates in these two populations are different; if the bars do overlap, we cannot make such an assertion.

i. Cleveland WS. *The elements of graphing data*. 1985, 1994. Hobart Press, New Jersey, USA.



### Phlegmasia cerulea dolens

An 85-year-old woman with newly diagnosed metastatic non-small-cell lung cancer was admitted for pain control. Two days after admission, bluish discoloration of the left great toe was noted. Doppler ultrasonography revealed a left femoropopliteal DVT. Anticoagulation with heparin was initiated, but there was progressive swelling and cyanosis of the leg (Panels A and B). The patient was referred for prophylactic placement of an inferior vena cava filter. Fluoroscopy revealed that the clot had extended into the left iliac vein and lower inferior vena cava. Filter placement was successful. However, despite continued intravenous anticoagulation and attempts at mechanical thrombectomy, the clinical findings progressed to venous gangrene. Phlegmasia cerulea dolens (blue, painful leg) is an uncommon manifestation of DVT and results from massive thrombosis compromising venous outflow, which causes ischaemia.

Barham K and Shah T. *N Engl J Med.* 2007; **356**: e3. Copyright © 2007 Massachusetts Medical Society. All rights reserved.

# Overview

**Database overview**

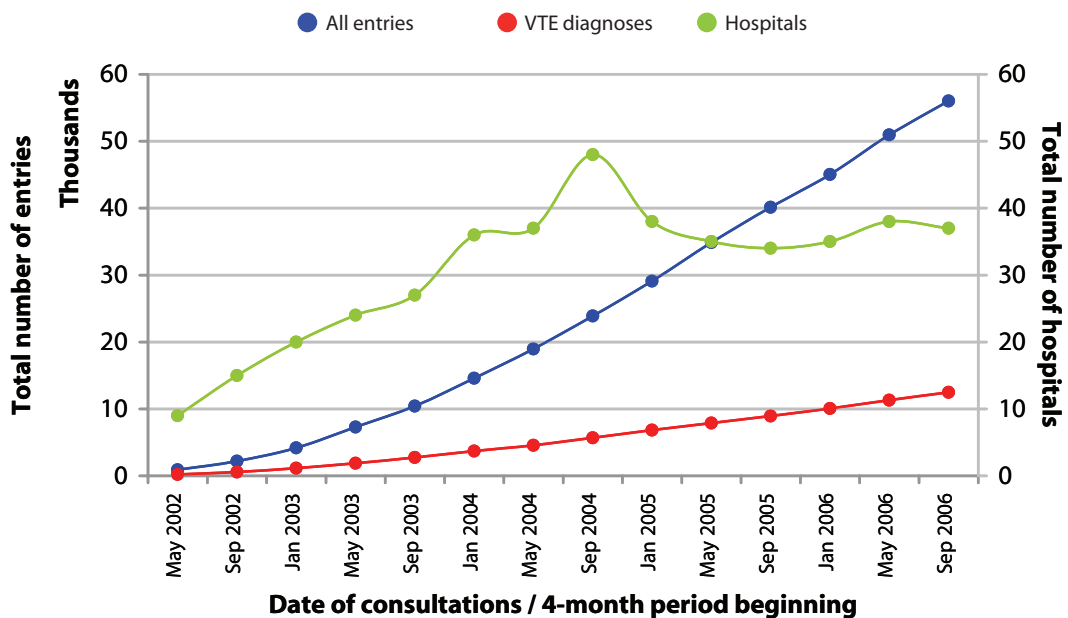
**Entries in the database**

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>.

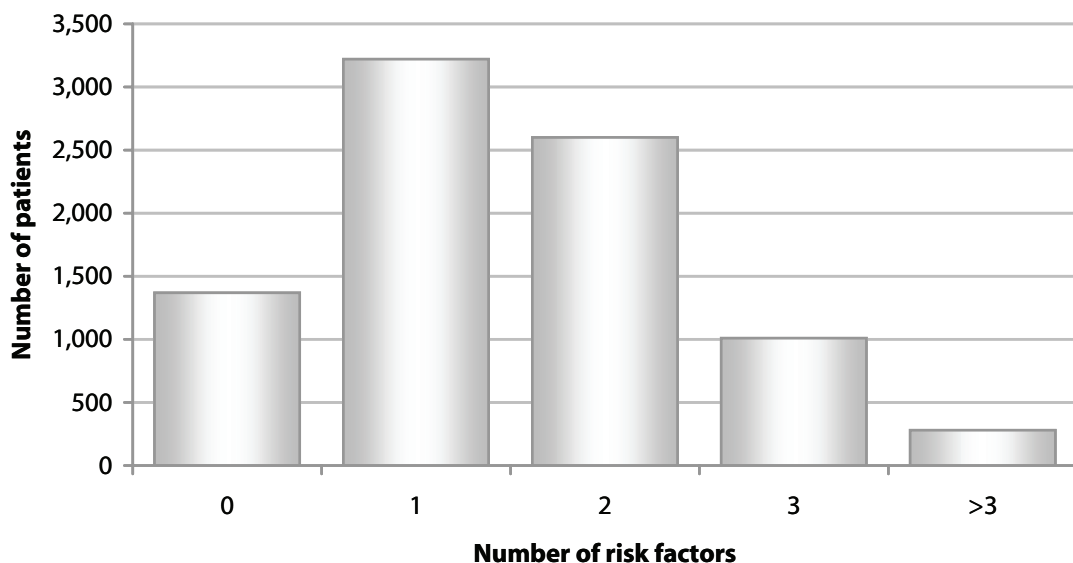
Common risk factors associated with increased risk of VTE such as age, surgery, cancer, immobilisation, pregnancy, fractures, oral contraceptives and medical illness are recorded in VERITY. The precise definitions of some of the risk factors were changed when the data collection forms were updated and 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>

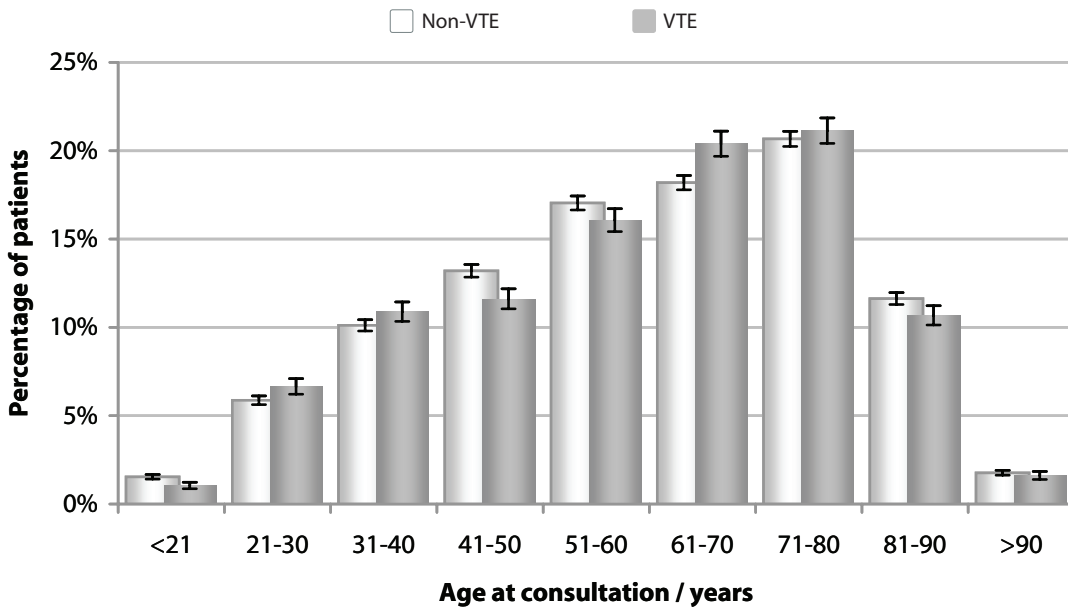
**Number of risk factors for patients with VTE (n=8,478)**



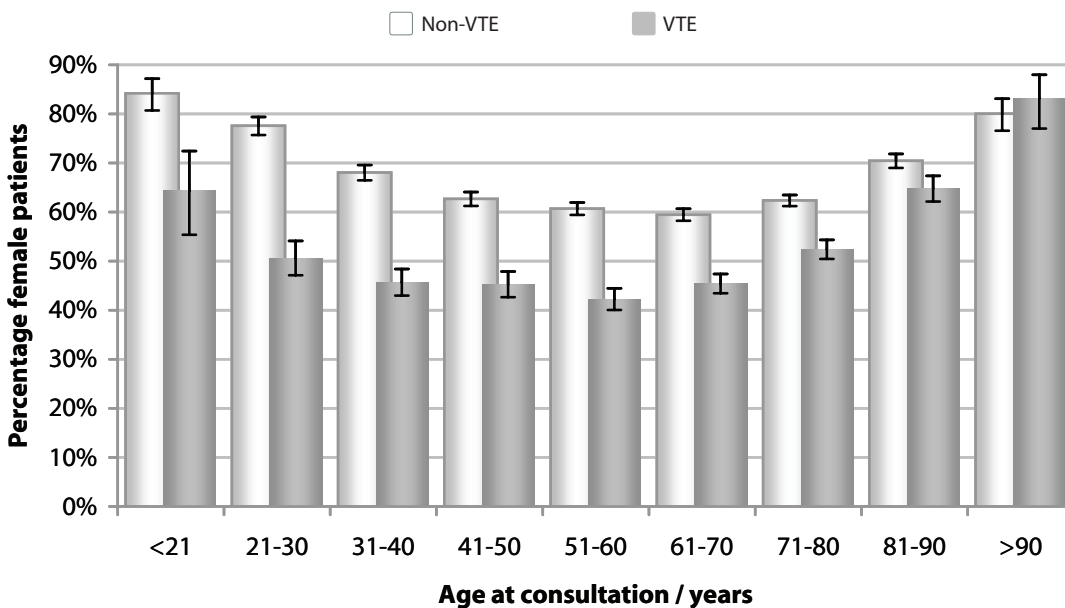
**Age and gender for patients with VTE**

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)**

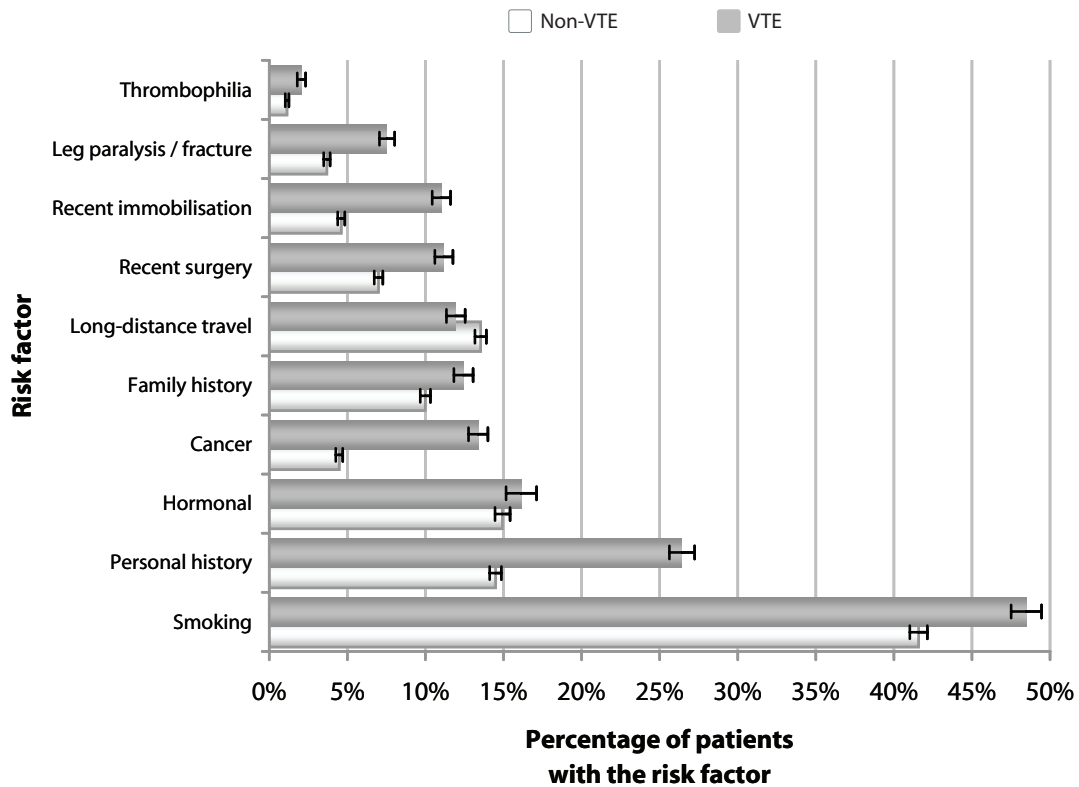


**Rates of different risk factors in patients who have VTE**

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

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



v. Data recorded for female patients only.

### The process of VTE diagnosis

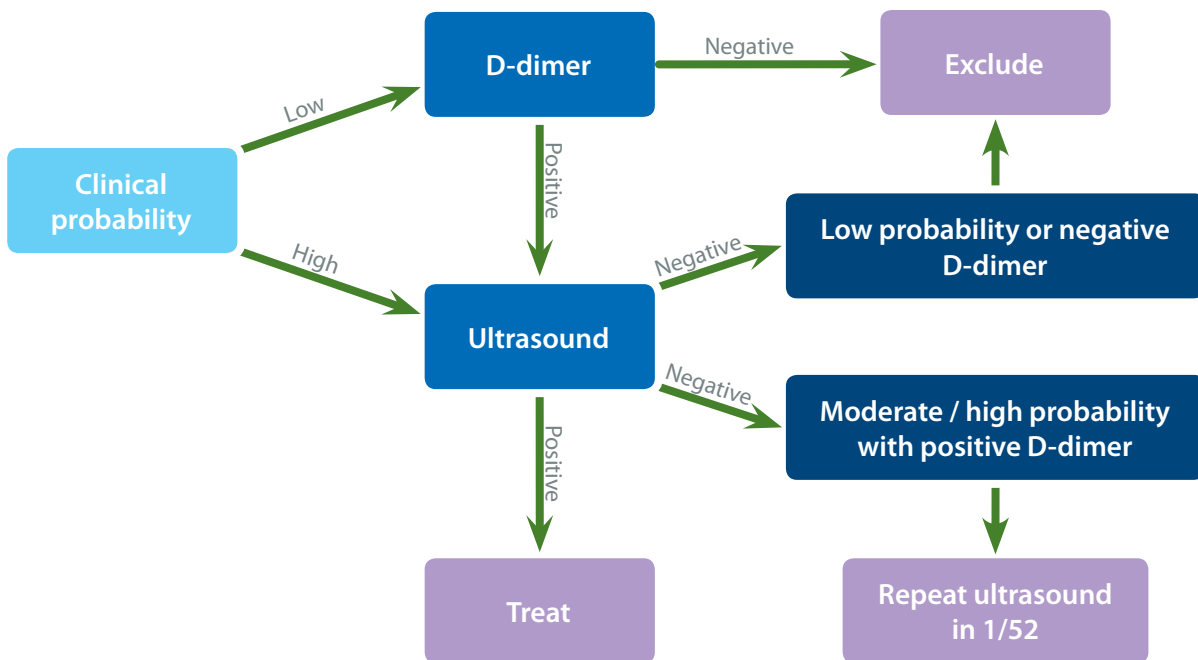
Extensive efforts have been devoted to developing non-invasive diagnostic strategies for the safe exclusion of a diagnosis of VTE, which reduce the use of imaging techniques and speed up the diagnostic process. It is now accepted that standardised clinical assessment to derive a pre-test probability (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.

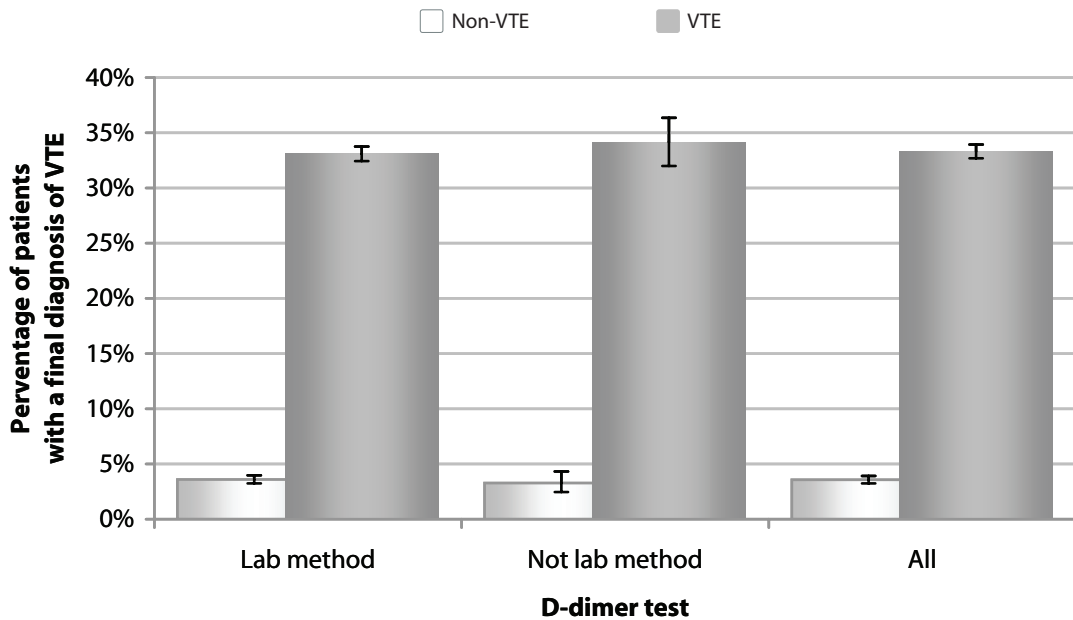
**D-dimer result and final diagnosis**

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	13,586
	Positive	14,746	7,364	2,908	25,018
	Unspecified / Not done	8,422	4,687	4,283	17,392
	<b>All</b>	<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)**

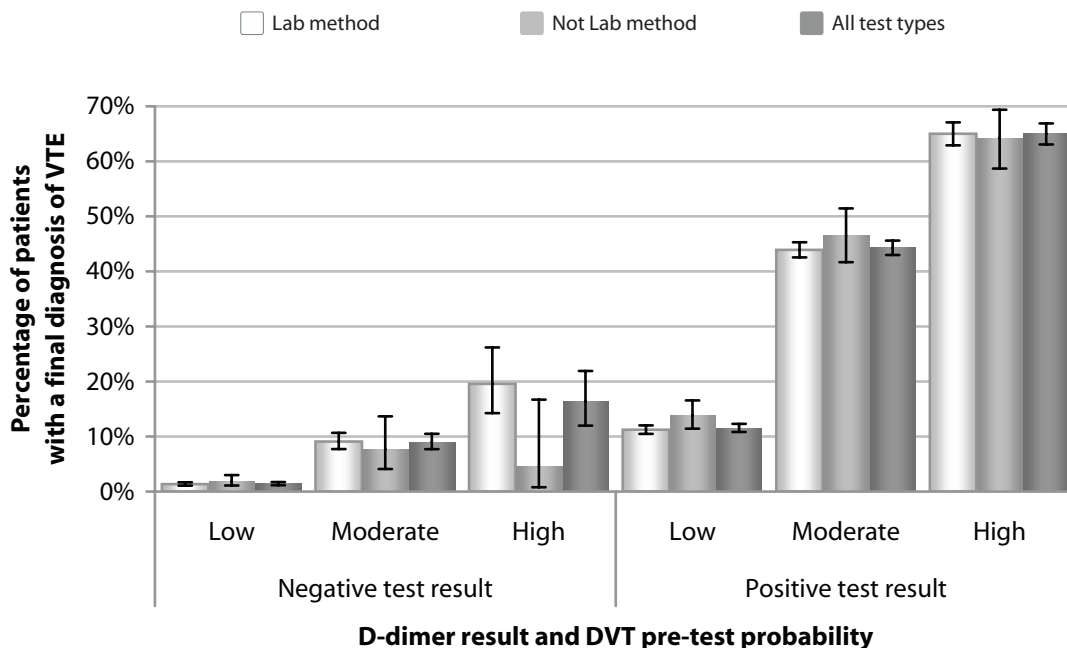


**D-dimer result, DVT pre-test probability and final diagnosis**

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					All
			Non-VTE	DVT	PE	PE & DVT	Unspecified	
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>

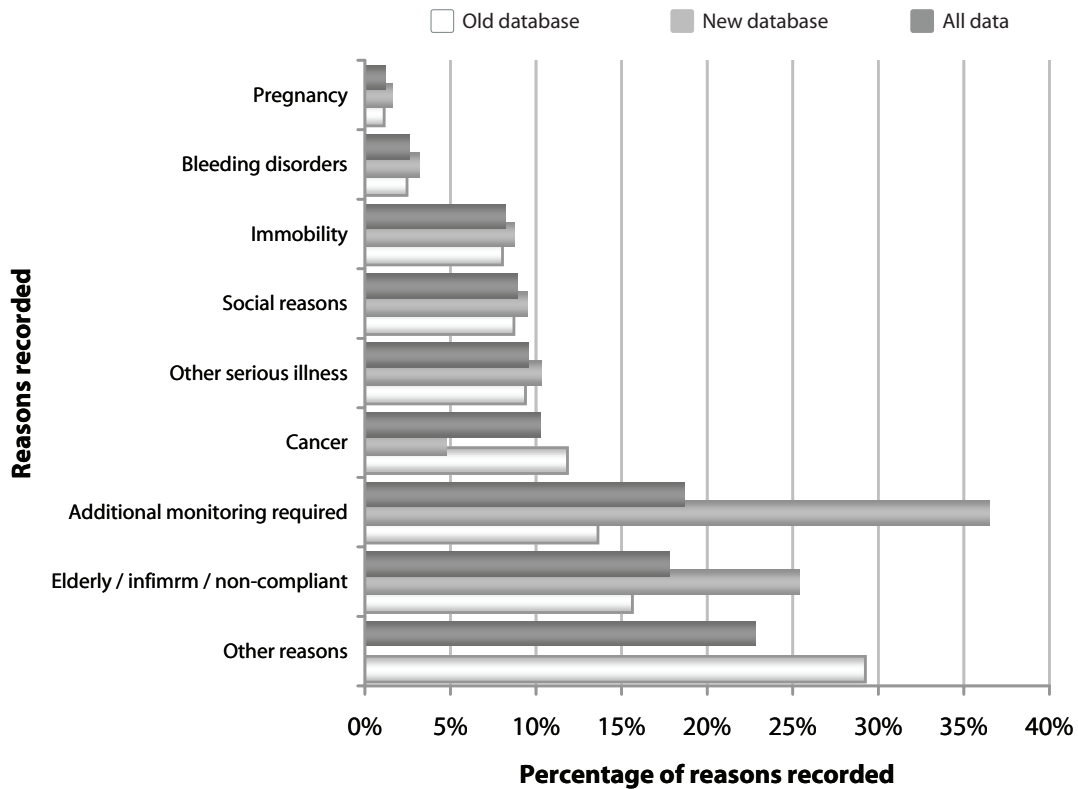
**Suitability for home treatment amongst patients with confirmed DVT (n=7,302)**



**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)**

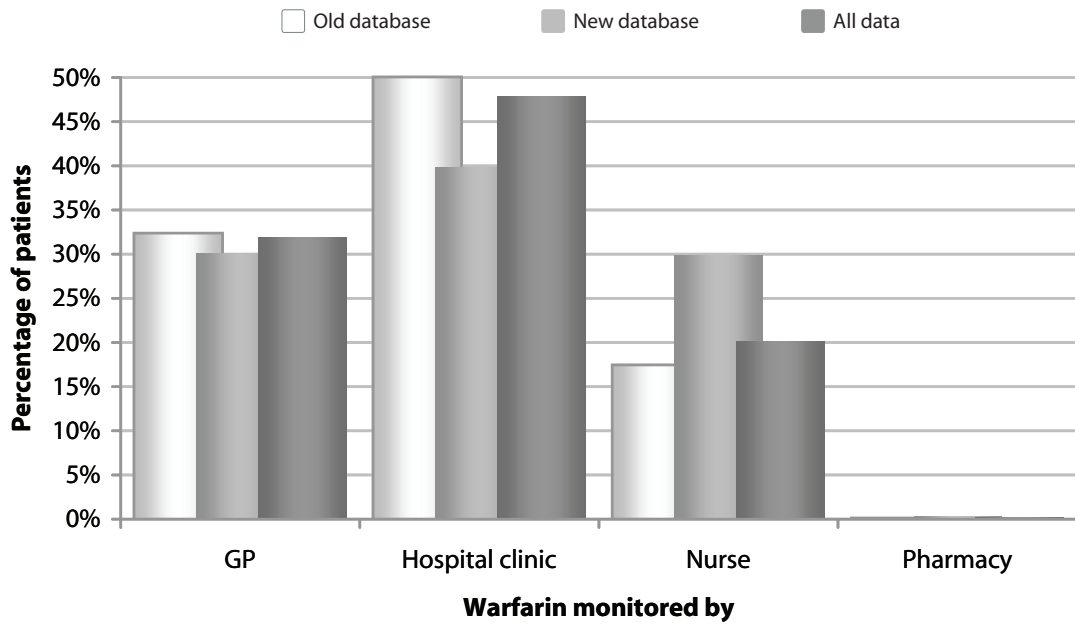


Overview

**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)**



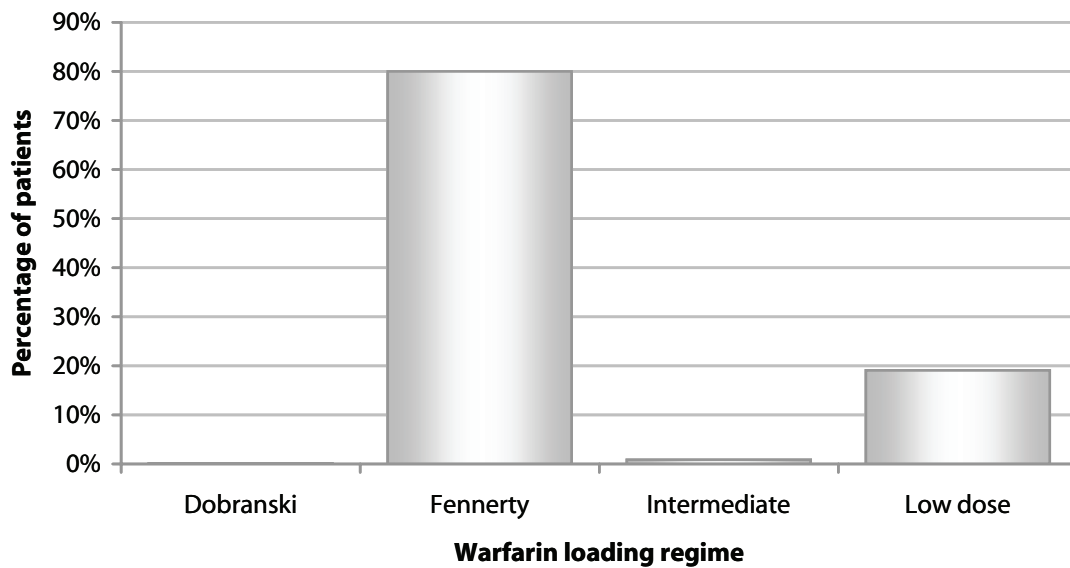
### Warfarin loading regime

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)

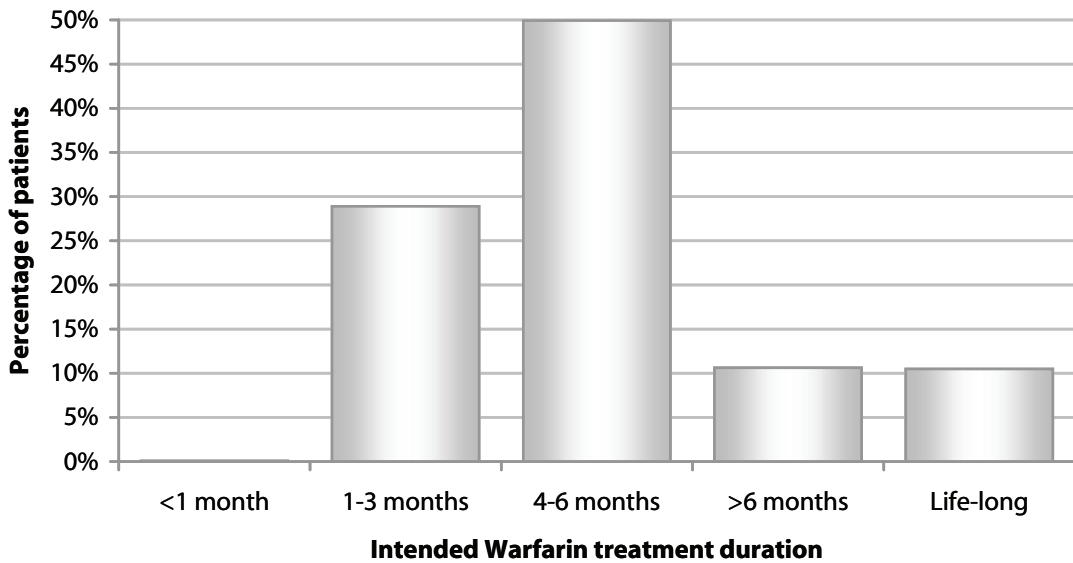


**Planned duration of warfarin treatment**

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>.

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

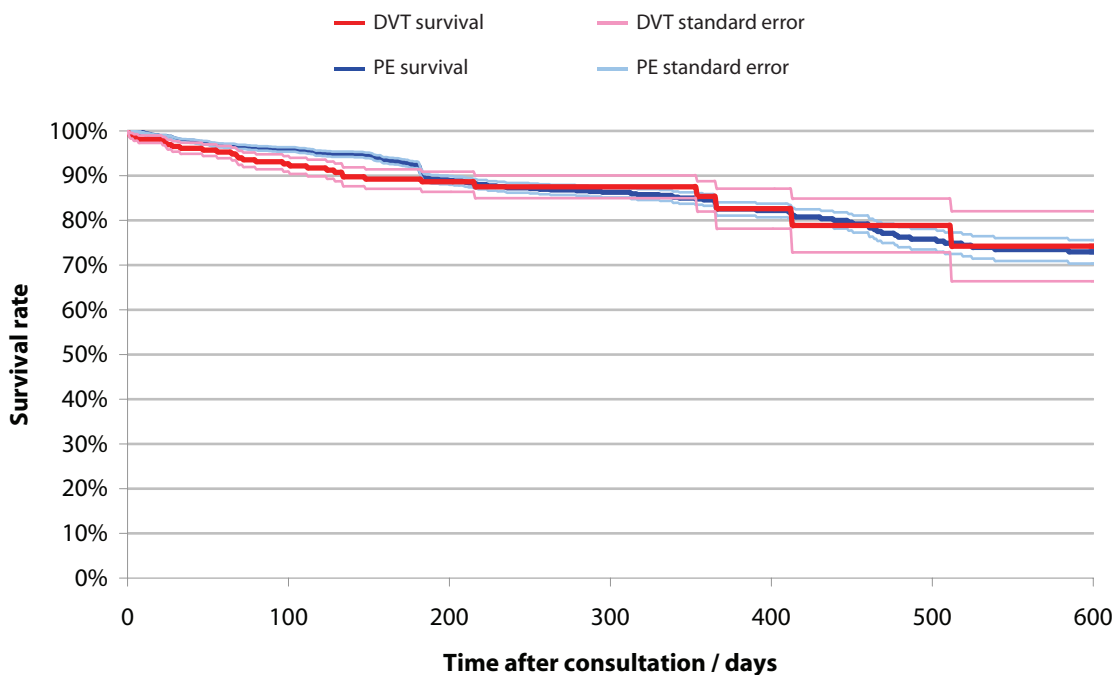


## Outcomes

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.

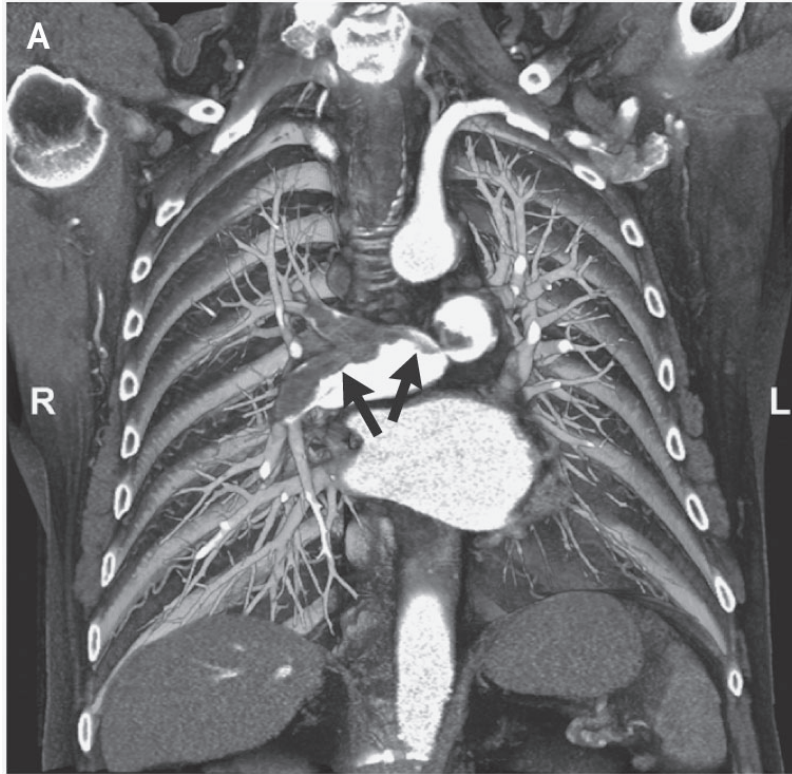
There had been a year-on-year increase in the proportion of patients treated as outpatients (86.1% in 2003, 88.9% in 2004, 89.6% in 2005 and 90.2% this year), which appears to have levelled at around 90%. This year, markedly fewer patients were excluded from out of hospital treatment because of cancer (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.

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**A case of pulmonary embolism as shown on contrast-enhanced 16-slice multidetector-row computed tomography**

An anterior view of the chest of a 72-year-old man, showing extensive, acute central pulmonary embolism with a *saddle embolus* (arrows) extending into the left and right central pulmonary arteries.

From Goldhaber SZ. Multislice Computed Tomography for Pulmonary Embolism - A Technological Marvel. *N Engl J Med.* 2005; **352**: 1812-1814. Copyright© 2003 Massachusetts Medical Society. All rights reserved.

# **Pulmonary embolism**



## Pulmonary embolus

### Overview

PE is a relatively common and potentially life-threatening cardiopulmonary illness that can be difficult to diagnose <sup>1</sup>. 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) <sup>2</sup>. 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 <sup>3</sup> 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%).

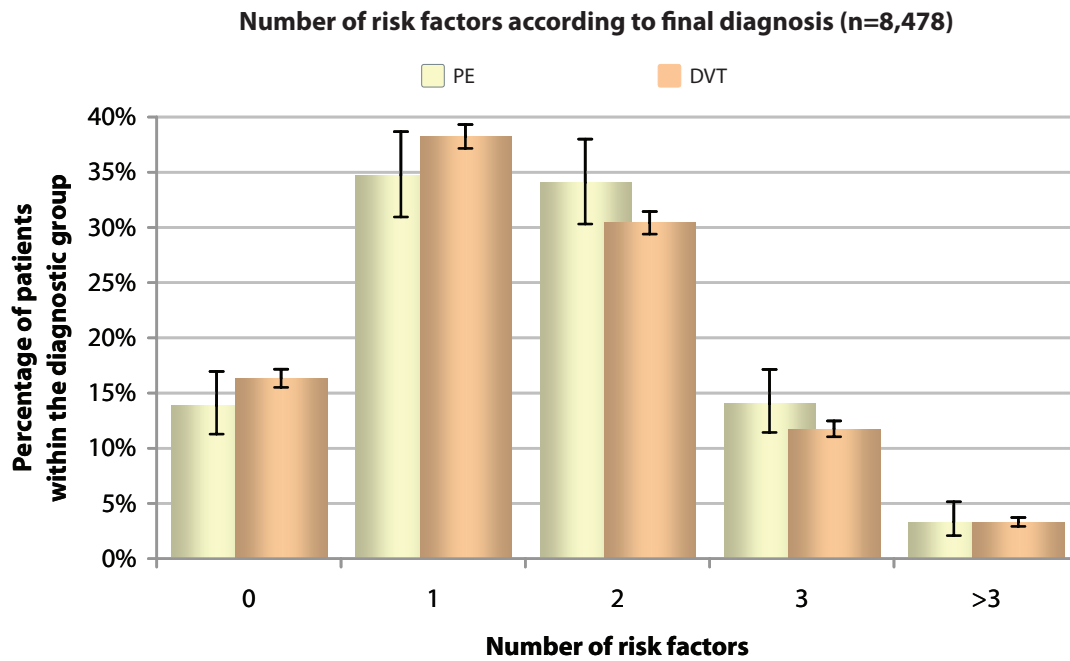
		Final diagnosis			
		Non-PE	PE	Unspecified	All
Primary diagnosis	Non-PE	41,006	121	4,359	<b>45,486</b>
	PE	762	870	218	<b>1,850</b>
	Unspecified	4,576	37	4,047	<b>8,660</b>
	All	<b>46,344</b>	<b>1,028</b>	<b>8,624</b>	<b>55,996</b>

### 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



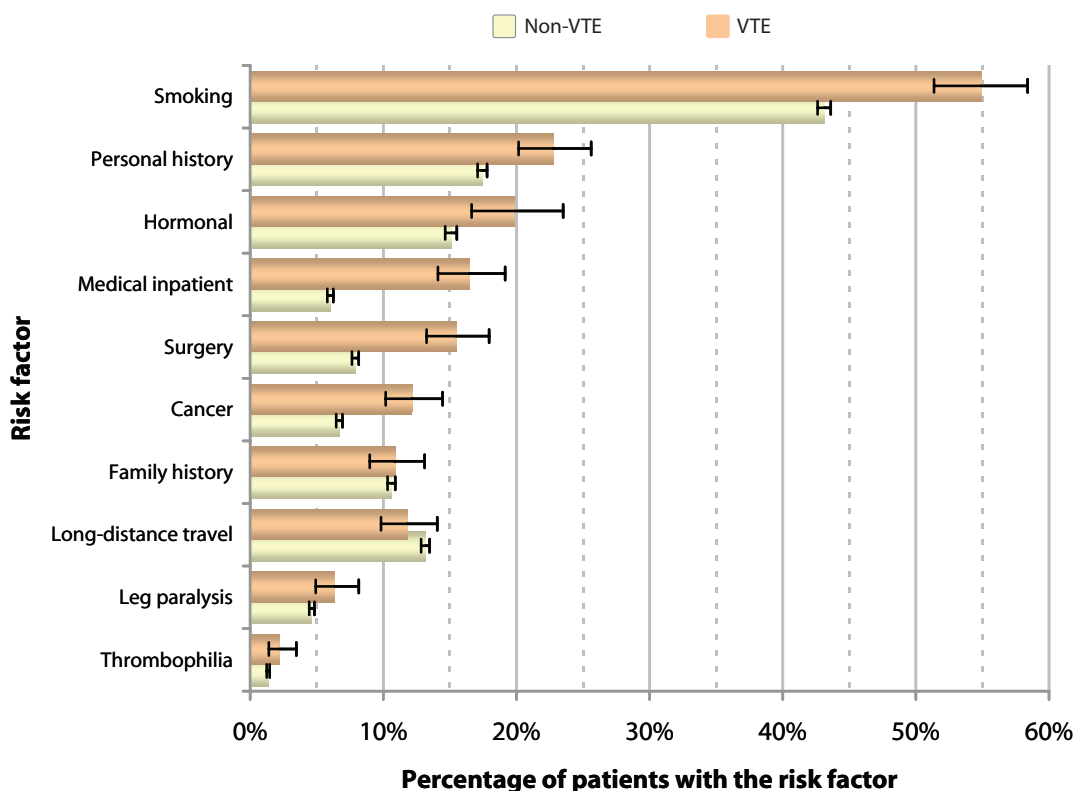
**Risk factors in PE**

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**

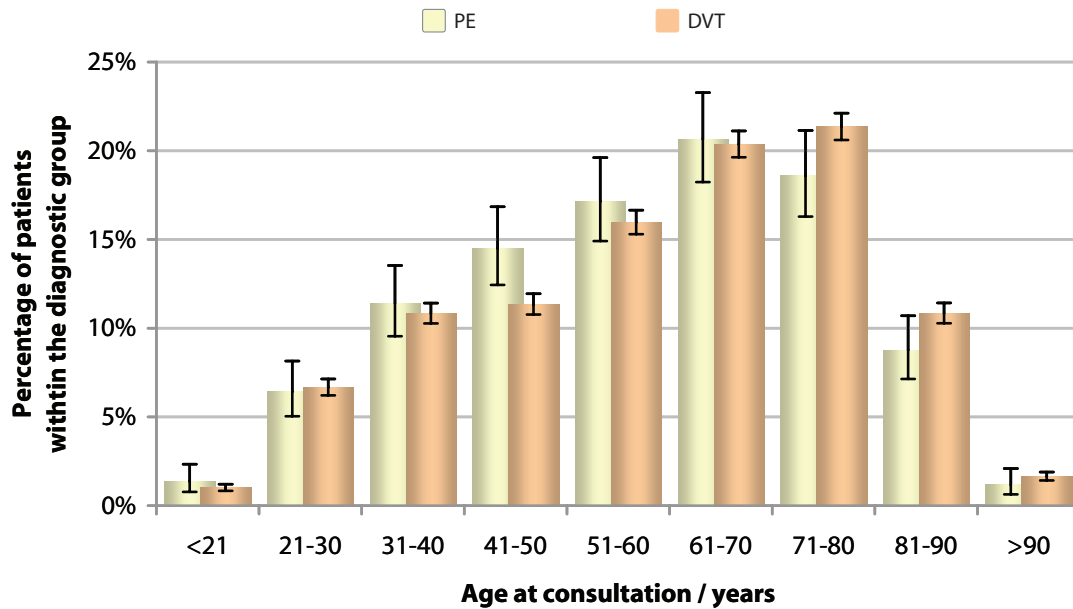


Age and disease

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 5<sup>th</sup> 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**

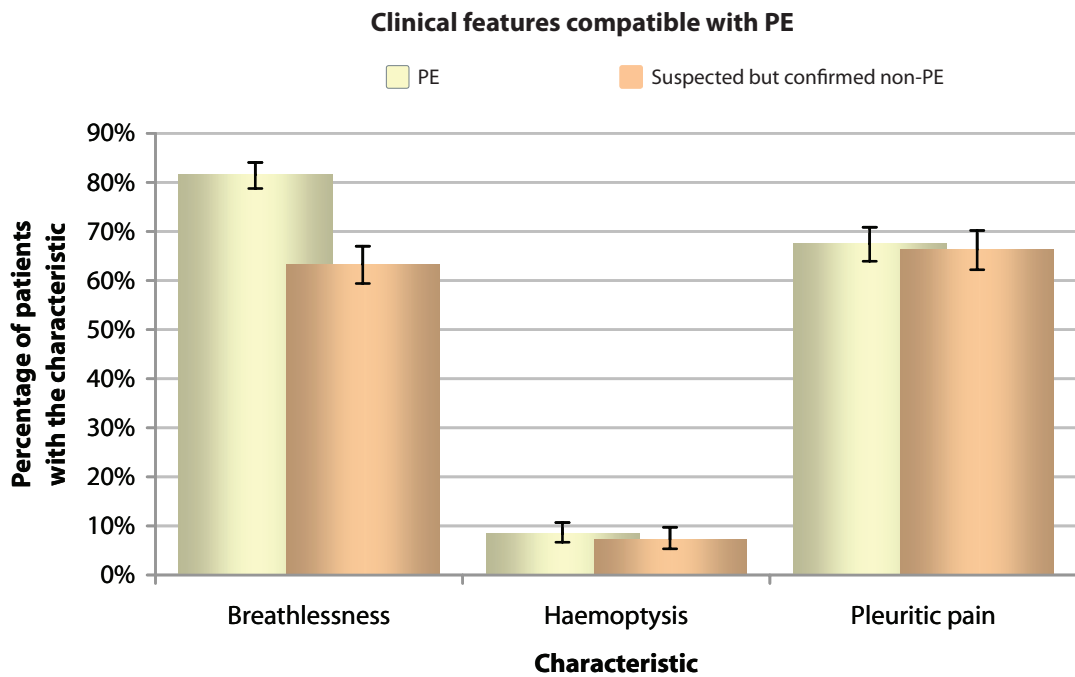
Although using the Wells algorithm for pretest probability of PE requires that a patient has clinical features compatible with PE (namely, breathlessness, pleuritic chest pain and / or haemoptysis), these features alone are unreliable and show poor sensitivity for PE. Reviewing the 773 patients with 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) Guidelines<sup>4</sup>, 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.*

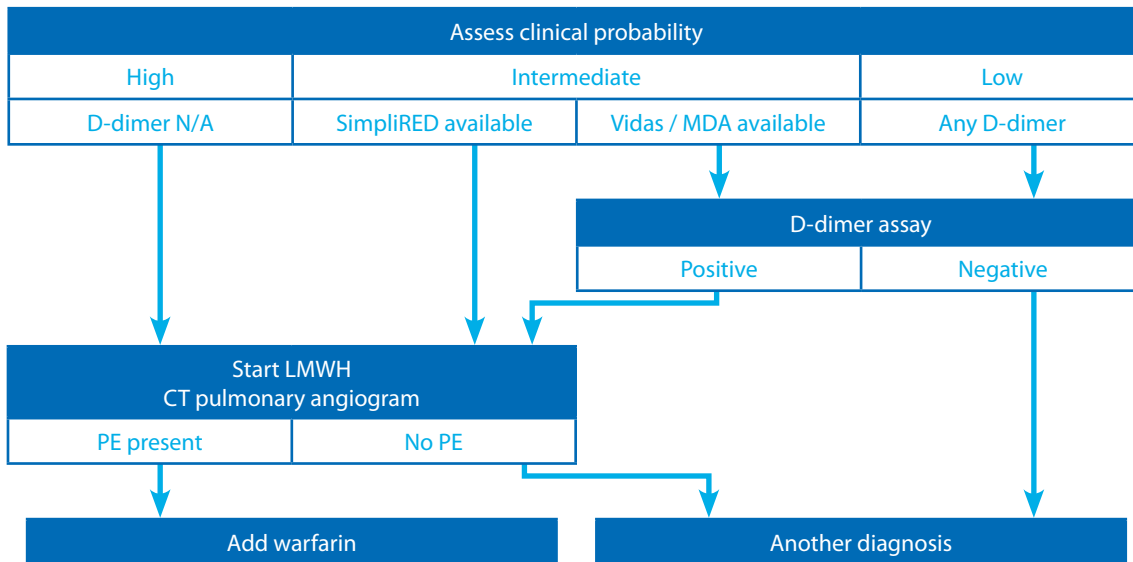
*Where (a) and (b) are both true the probability is high; if only one is true the probability is intermediate; and if neither is true the probability is low. Some hospitals prefer a scoring system that places patients into one of only two categories - PE likely and PE unlikely.*

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

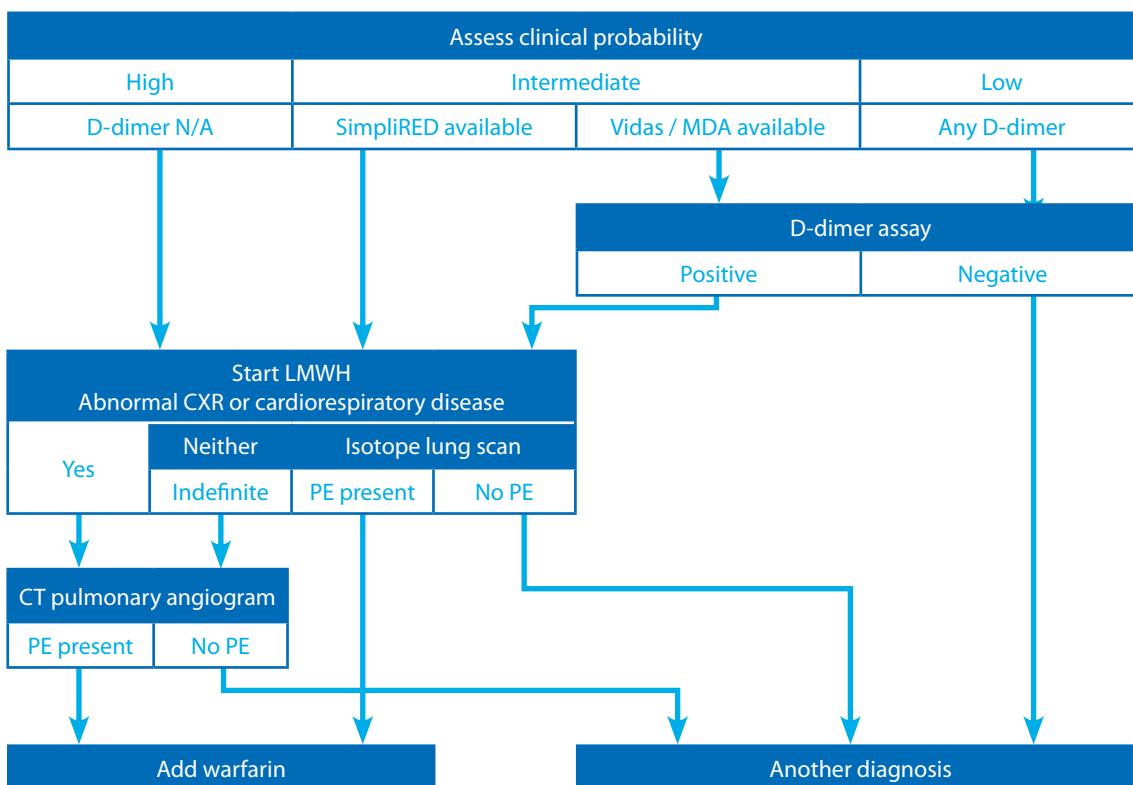


British Thoracic Society Guidelines for the management of suspected acute pulmonary embolism

**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

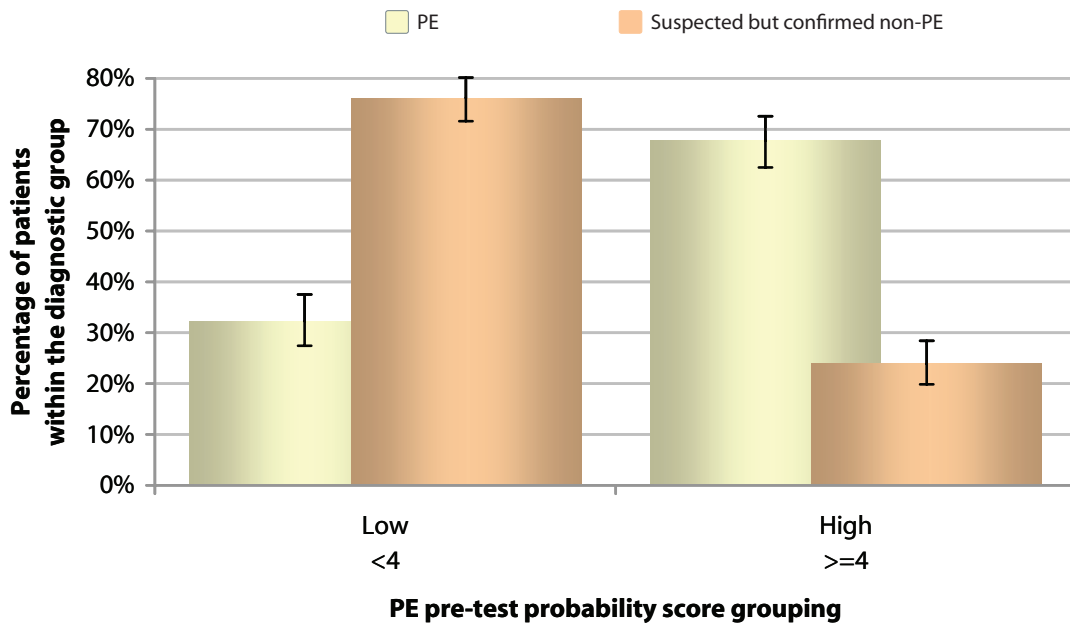
### PTP score and final diagnosis

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.

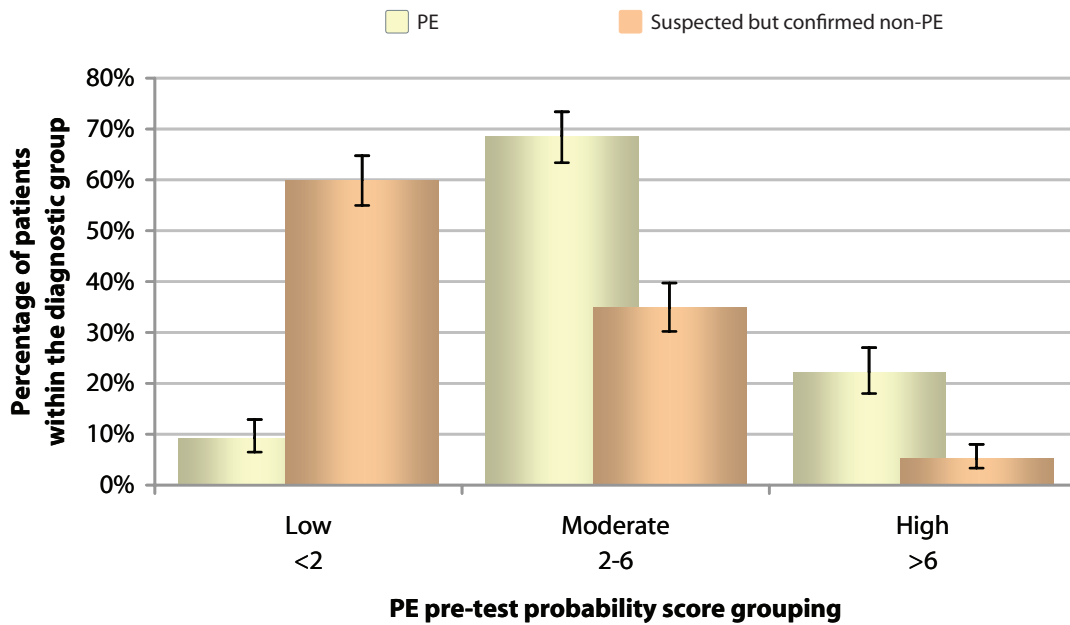
A number of ways of interpreting the Wells PTP are employed by VERITY hospitals. Calderdale uses the definition of low (<4) and high ( $\geq$ 4) PTP, which is widely used in European and Canadian algorithms, whereas at Southampton, Derriford and King's Lynn, the scoring of low (<2), moderate (2-6) and 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)



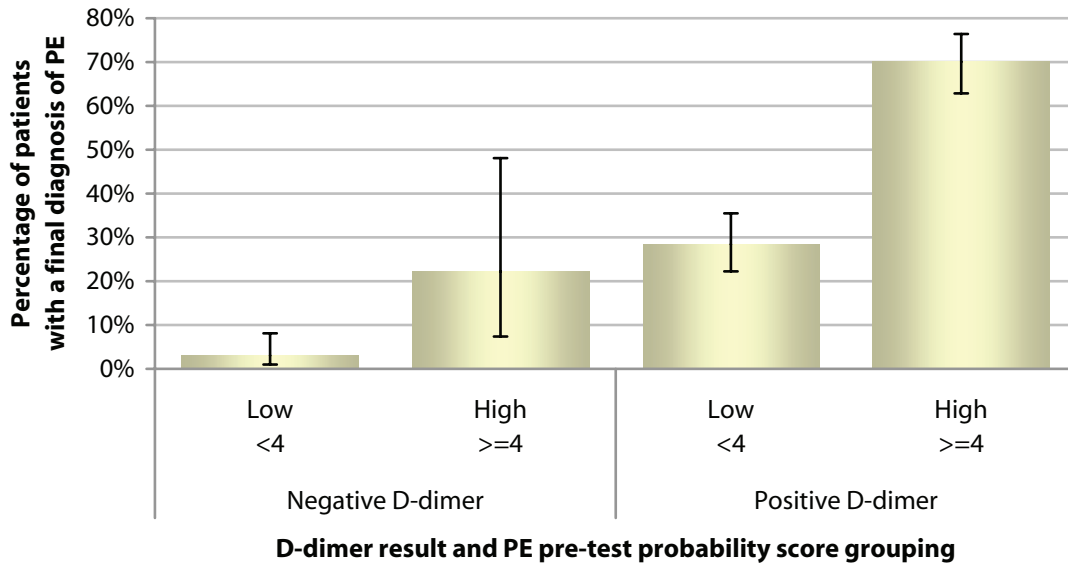
## Investigations in patients with a primary diagnosis of PE

### PTP score, D-dimer and final diagnosis

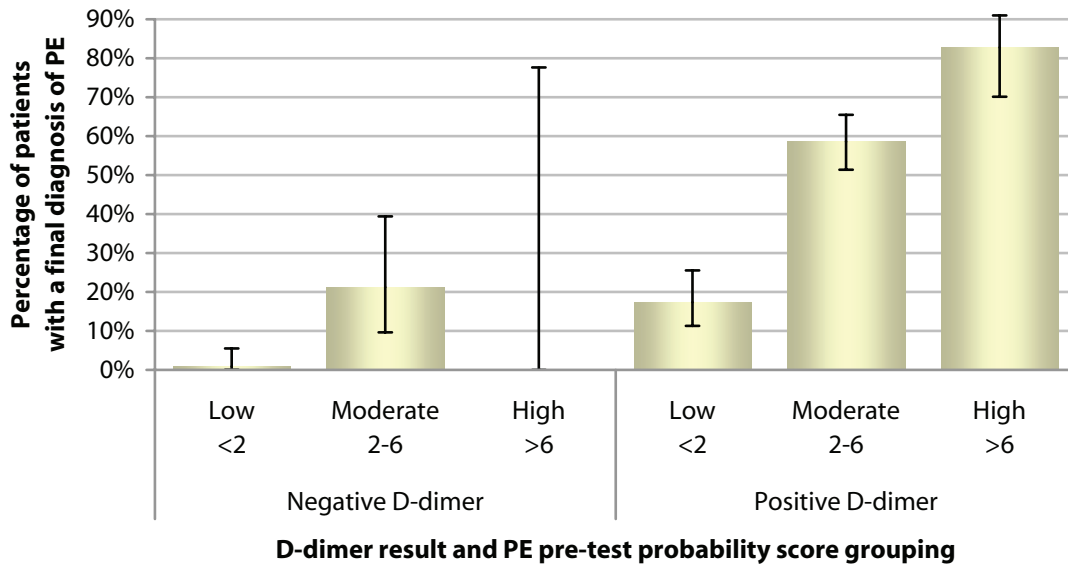
As previously, the data validate the strategy of excluding PE on the basis of a low PTP in combination with a negative D-dimer. Of the 4 patients with a low PTP and negative D-dimer found to have PE, 1 case reported in the last report was subsequently excluded as a PE after several radiology opinions. 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.

				Final diagnosis			
				Not PE	PE	Unspecified	All
Pulmonary embolism	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
	<b>All</b>	<b>979</b>	<b>871</b>	<b>476</b>

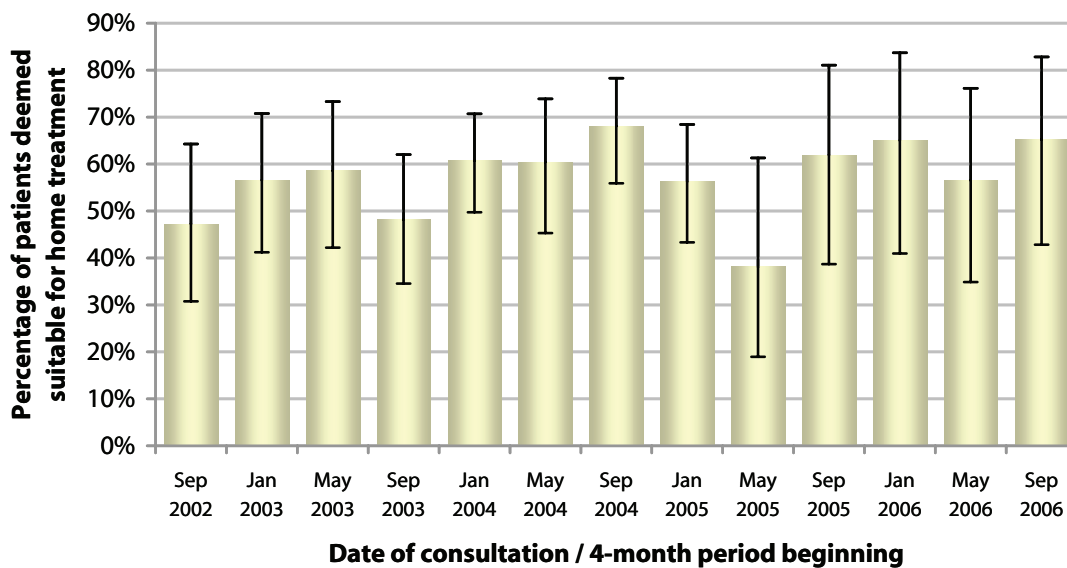
## Treatment of patients with PE

### 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)



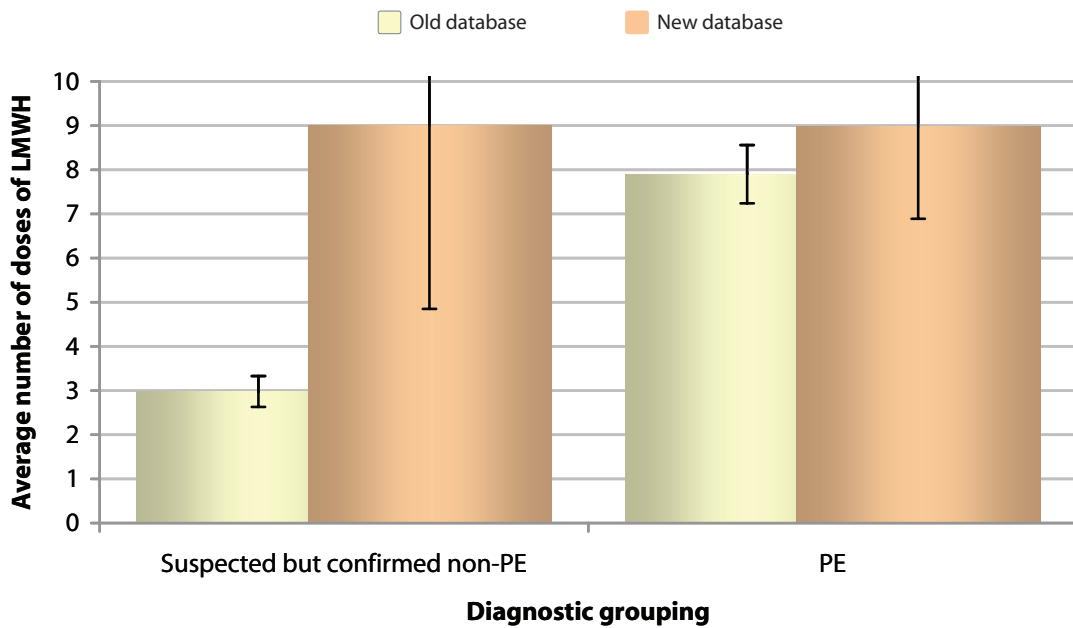
**Doses of LMWH**

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 <sup>3</sup>.

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
<b>Demographic characteristics</b>	
Age	Age <sup>i</sup>
Male gender	10
<b>Comorbid illnesses</b>	
Cancer	30
Heart failure	10
Chronic lung disease	10
<b>Clinical findings</b>	
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 <sup>ii</sup>	60
Arterial oxygen saturation $< 90\%$ <sup>iii</sup>	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	$\leq 65$	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 <sup>1</sup>:

*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.*

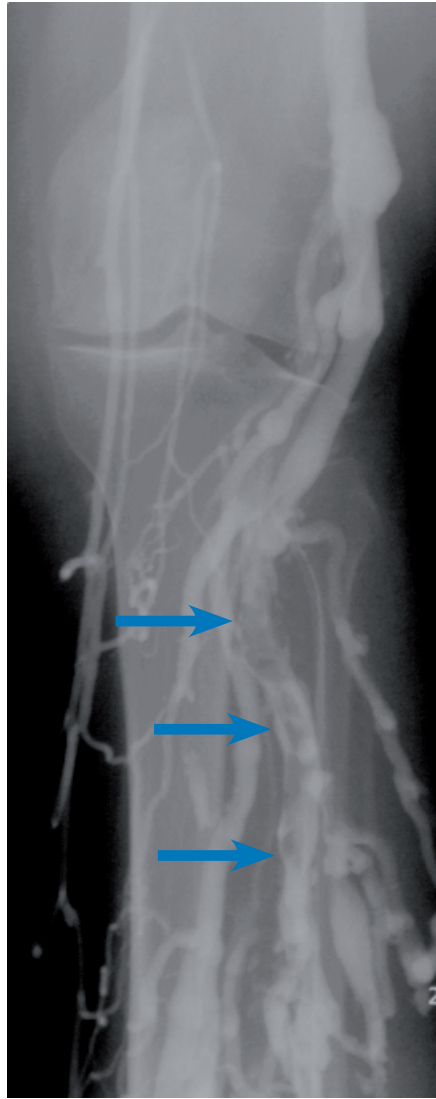
Diagnostic techniques and treatments for PE continue to evolve. In the last VERITY publication we reported good practice in the initial part of the diagnostic algorithm, namely clinical PTP and D-Dimer testing. However, the main challenge in the UK was obtaining the necessary definitive diagnostic test 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.

## References

1. Goldhaber SZ. Pulmonary embolism. *Lancet*. 2004; **363**: 1295–1305.
2. Naess IA, *et al*. Incidence and mortality of venous thrombosis: a population-based study. *J Thromb Haemost*. 2007; **5**: 692-699.
3. Aujesky D, *et al*. Derivation and validation of a prognostic model for pulmonary embolism. *Am J Respir Crit Care Med*. 2005; **172**: 1041-1046.
4. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax*. 2003; **58**: 470-483.



#### Contrast venogram of the calf

This venogram shows a single DVT, 5-10 cm long, in a patient immobilised because of an acute medical illness.

# **Thromboprophylaxis**



## Thromboprophylaxis

Preventing thrombosis with prophylaxis is a topical issue in modern medicine. As we described in the last VERITY report, the publication of the House of Commons Health Committee Enquiry on *The Prevention of Venous Thromboembolism in Hospitalised Patients* <sup>1</sup> in 2005 precipitated the Department of Health to form an independent expert working group to look at raising awareness of the incidence of VTE, to review what guidance is available and how best practice and awareness of VTE should be communicated widely within the NHS (see page 120). The report of the independent expert working group on the prevention of venous thromboembolism in hospitalised patients was recently published in full by the Chief Medical Officer, Sir Liam Donaldson <sup>2</sup>. In addition, the long-awaited NICE guideline on reducing the risk of VTE in inpatients undergoing surgery was also published in late April <sup>3</sup>.

The independent expert working group report highlights the fact that, although the risk factors associated with the development of VTE such as surgery, acute medical illness and certain predisposing risk factors are well characterised, risk assessment and the provision of appropriate preventative measures are not applied in routine clinical medicine. The report identifies VTE as a patient safety issue and the expert group recommends that the Healthcare Commission looks to seek conformity with this good practice guidance and signal that it intends to include VTE as part of its annual inspection guidance. This shift in emphasis to regarding VTE as a patient safety issue will have a profound effect on the way VTE prevention is perceived within the healthcare sector.

### VERITY and thromboprophylaxis

The VERITY registry offers us an unique opportunity to characterise the histories of patients presenting with symptomatic VTE. In the last report we saw that patients with VTE also often had a history of recent surgery, especially orthopaedic surgery; the VERITY data also indicated that these patients also reported a recent history of acute medical illness relatively frequently.

After the last report, we attempted to improve and simplify the whole VERITY experience for the front-line user by simplifying the case-report form. At the same time, we used that opportunity to refine the questions asked, particularly in relation to medical and surgical illness and the provision of thromboprophylaxis, to improve the quality and relevance of the data collected. The results from some of the new questions are presented in this chapter. We have attempted to characterise in more detail the medical and surgical histories of patients with VTE and the relationship with thromboprophylaxis provision, reflecting the different questions that are now asked on the VERITY case report form.

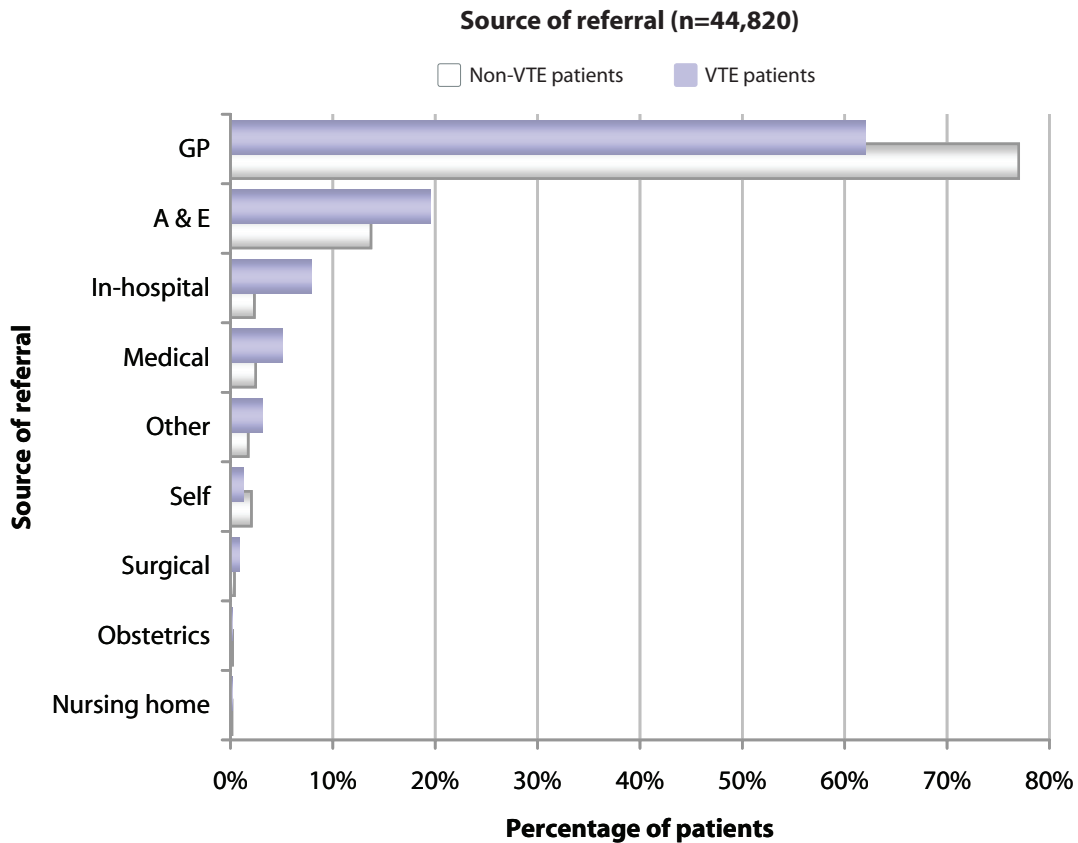
As an aide to your practice, we also include the guidance provided by the expert working group and NICE linked to the VERITY findings.

### Practice point

The VTE expert group recommends improvement of public and professional understanding of VTE at a national level, through improved communication of information to patients and the public, accompanied by improved and coordinated programmes of professional education <sup>2</sup>.

### Source of referral

The vast majority of patients are referred with suspected VTE from their GP. More than 60% of those with a confirmed VTE come *via* GP referral, as opposed to almost 80% of those patients who are eventually shown not to have VTE. For in-hospital referrals, including referral from A&E, medical and surgical units, the proportion of patients confirmed with VTE is higher. These findings are as expected, with GPs clearly more likely to refer patients with a view to excluding VTE. There are few referrals for VTE from medical and surgical wards, and virtually none from obstetric wards or nursing homes.



### Practice point

The VTE expert group recommends a documented **mandatory VTE risk assessment** of every hospitalised patient on admission <sup>2</sup>.

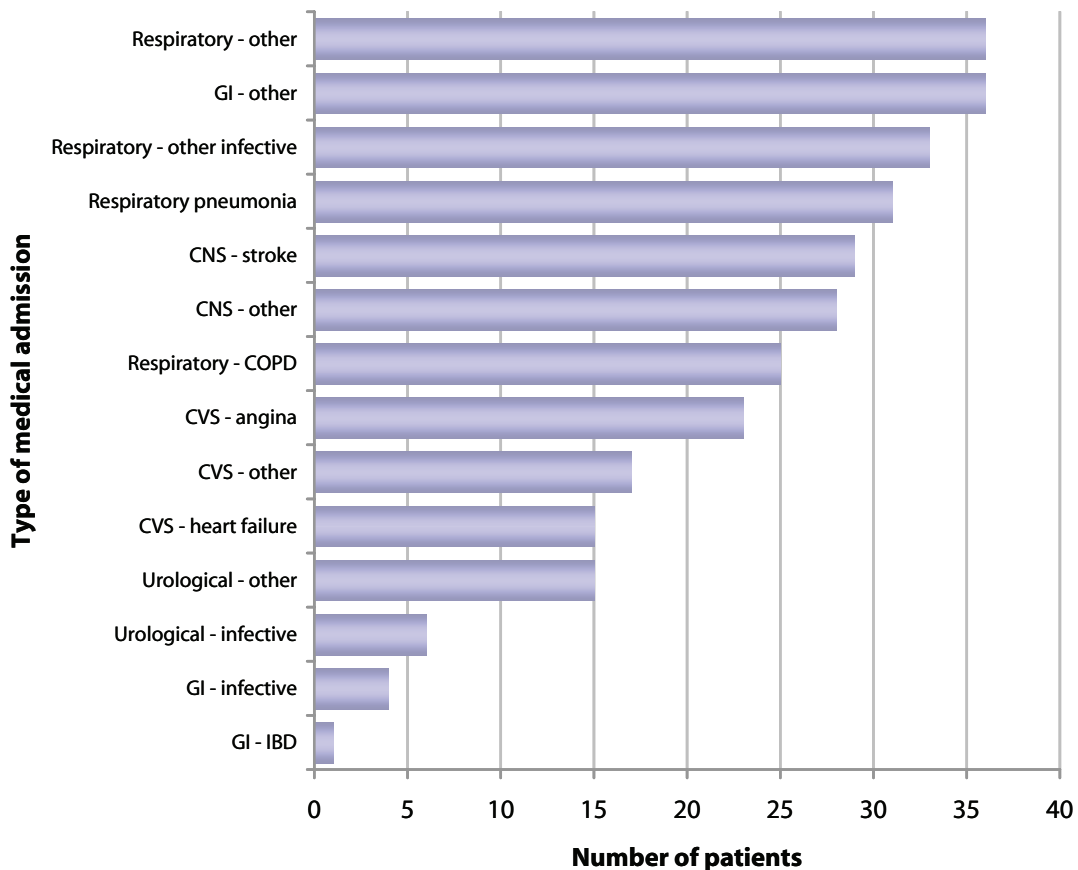
**Focus on patients with a medical inpatient history**

Fatal venous thromboembolic events occur more frequently in medical than surgical patients. In a 25-year analysis of fatal PE conducted at King’s College, London, the majority of PE-related deaths occurred in the non-surgical population and the level of venographically-detected DVT remained unchanged over 15 years in non-surgical patients, despite a significant fall seen in surgical patients<sup>4</sup>. We know that the risk of VTE in acute medical inpatients is a clinical concern and equally as important as in surgical inpatients. Acutely ill medical inpatients that have been enrolled in large, randomized, placebo-controlled studies had rates of distal DVT of about 10% and of proximal DVT of about 5%, placing them at moderate to high risk of VTE according to accepted levels of risk<sup>5,6,7</sup>. At-risk medical patients should be identified and appropriately targeted for thromboprophylaxis implementation.

Of the 639 patients with a medical inpatient history, the reason for hospital admission was reported in around half the cases (n=338). One of the reasons recorded for admission – musculoskeletal – is a general term that does not identify a medical illness and has not been presented (n=39). As we can see in the graph, there are a wide variety of reasons for admission, the most common overall being respiratory problems, in particular infection and pneumonia.

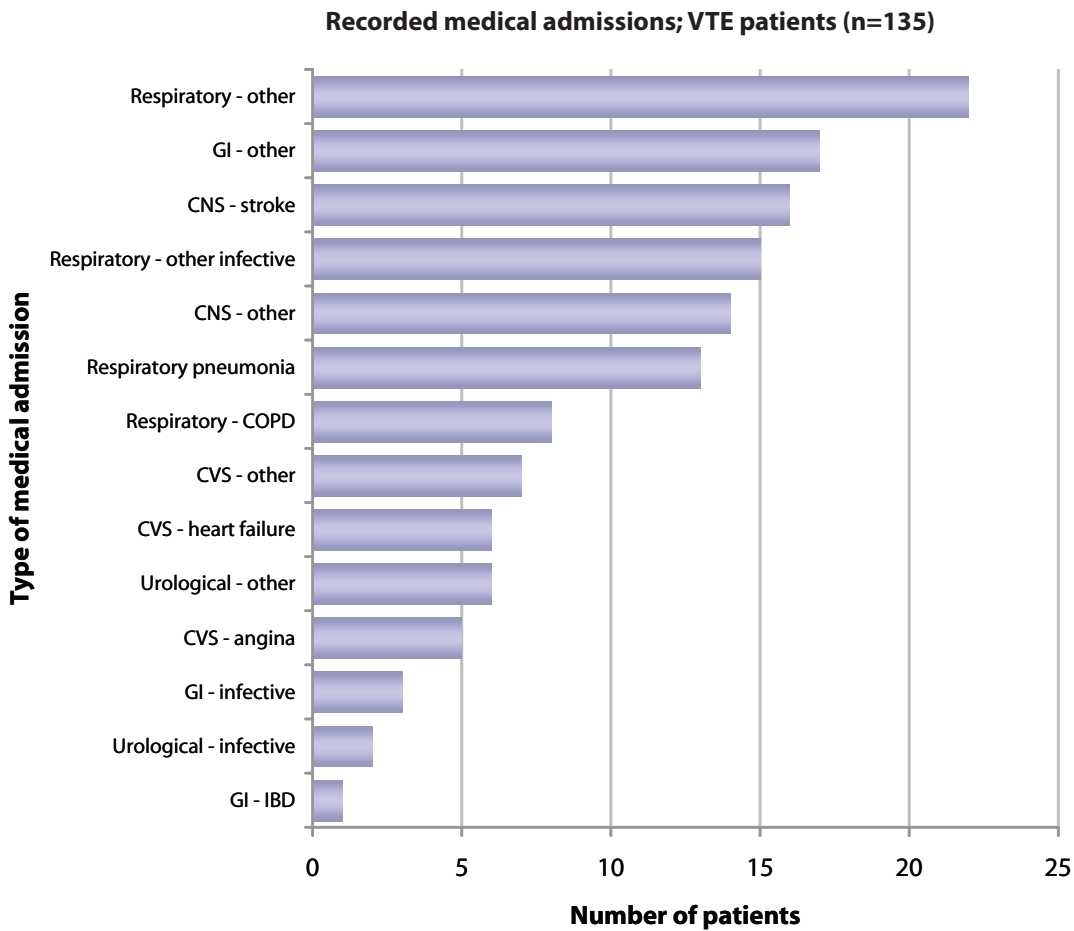
**Recorded medical admissions; all patients (n=299)**

**Thromboprophylaxis**



**Medical inpatient history for VTE patients**

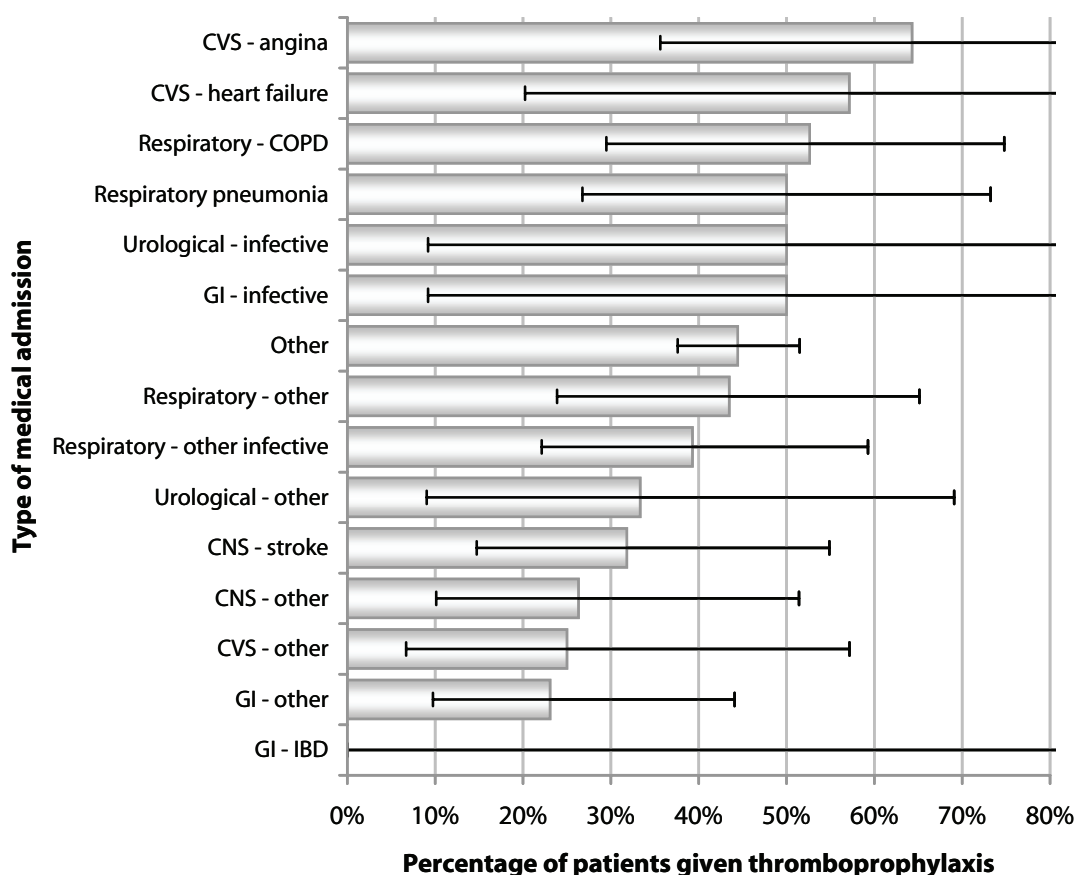
Of the 639 patients with a medical inpatient history, 43% were confirmed with VTE. Admissions for respiratory problems, GI-related illnesses and CNS events such as stroke were associated with relatively high numbers of cases with symptomatic VTE.



**Thromboprophylaxis in patients with a medical inpatient history**

Of the 639 patients with a medical inpatient history, we know if the patient received, or did not receive, thromboprophylaxis in 69% of cases (n=439). The highest levels of thromboprophylaxis provision were reported in cardiac patients, including those with heart failure. A relatively high proportion of patients with respiratory problems, such as COPD and pneumonia, received thromboprophylaxis. Levels were relatively low in stroke patients and patients with other CNS problems. This is understandable and reflects the fact that although stroke patients are at risk of VTE, there are different opinions and policies across hospitals on preventing DVT in stroke patients.

**The use of thromboprophylaxis in medical inpatients (n=413)**



**Thromboprophylaxis**

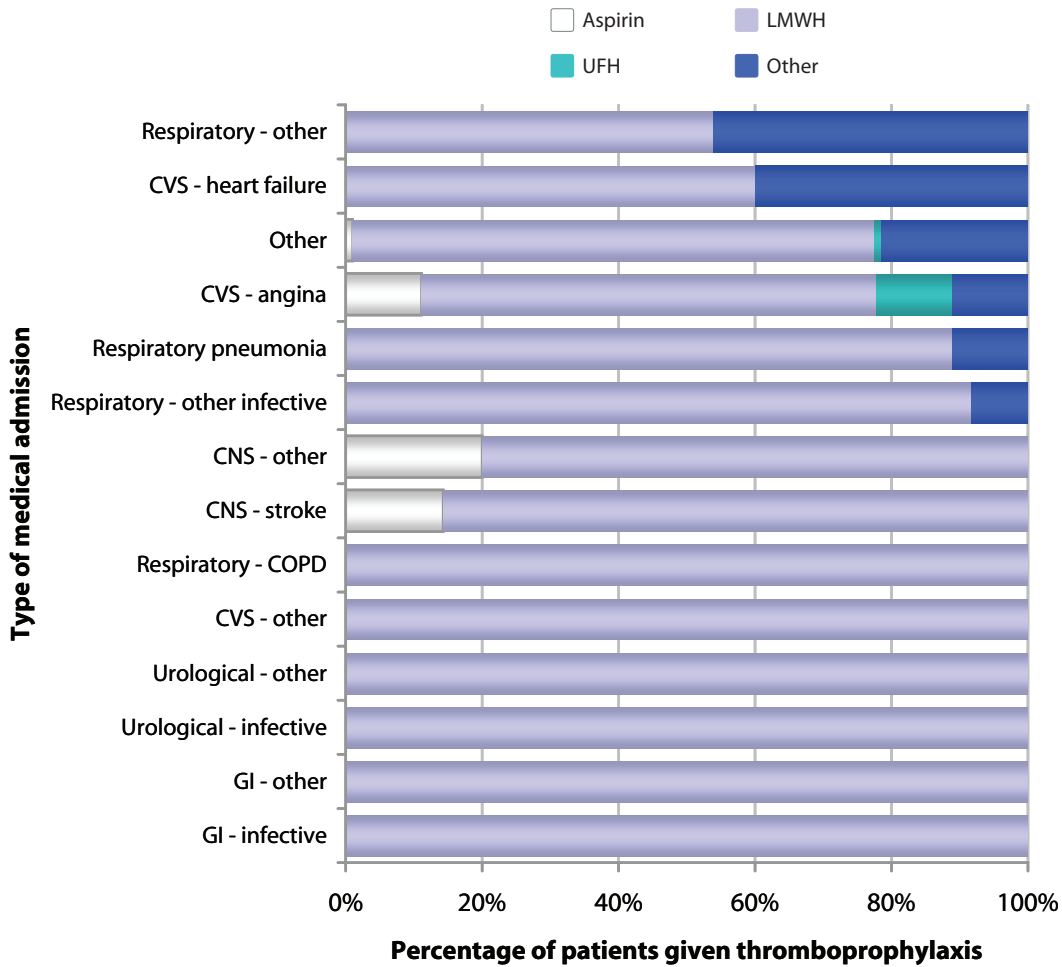
**Practice point**

Thromboprophylaxis strategy: the VTE expert group recommends that all medical patients should, as part of a mandatory risk assessment, be considered for thromboprophylaxis measures; in particular, patients likely to be in hospital for longer than four days and with reduced mobility, with either severe heart failure, respiratory failure (due either to exacerbation of chronic lung disease or pneumonia), acute infection, inflammatory illness or cancer (with additional risk factors for VTE) should be considered for the following regime: heparins (both unfractionated and low molecular-weight forms) are effective preventive treatments. Low-molecular-weight heparins are the preferred prophylactic method; aspirin is not recommended for thromboprophylaxis in medical patients; mechanical methods of prophylaxis have not to date been appropriately evaluated in acutely ill medical patients, and thus are not recommended at present <sup>2</sup>.

**Pharmacological thromboprophylaxis in patients with a medical inpatient history**

Of 439 patients with a medical inpatient history for whom thromboprophylaxis was recorded, 194 cases (44%) received thromboprophylaxis. The breakdown of the type of thromboprophylaxis is shown below. The majority of thromboprophylaxis given is LMWH; there is only very low-level use of aspirin or UFH. In respiratory and heart failure patients, another form of thromboprophylaxis was used.

**The type of thromboprophylaxis given to medical inpatients (n=182)**

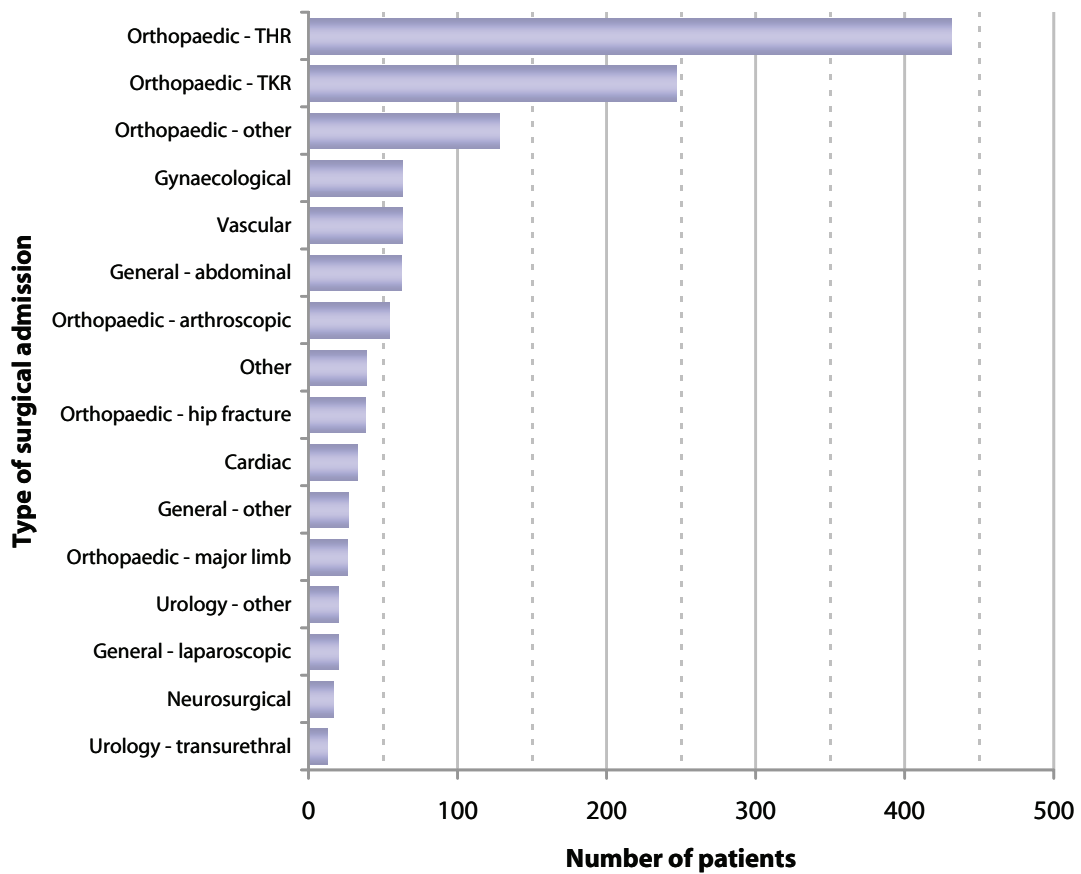


Thromboprophylaxis

**Focus on patients with a surgical inpatient history**

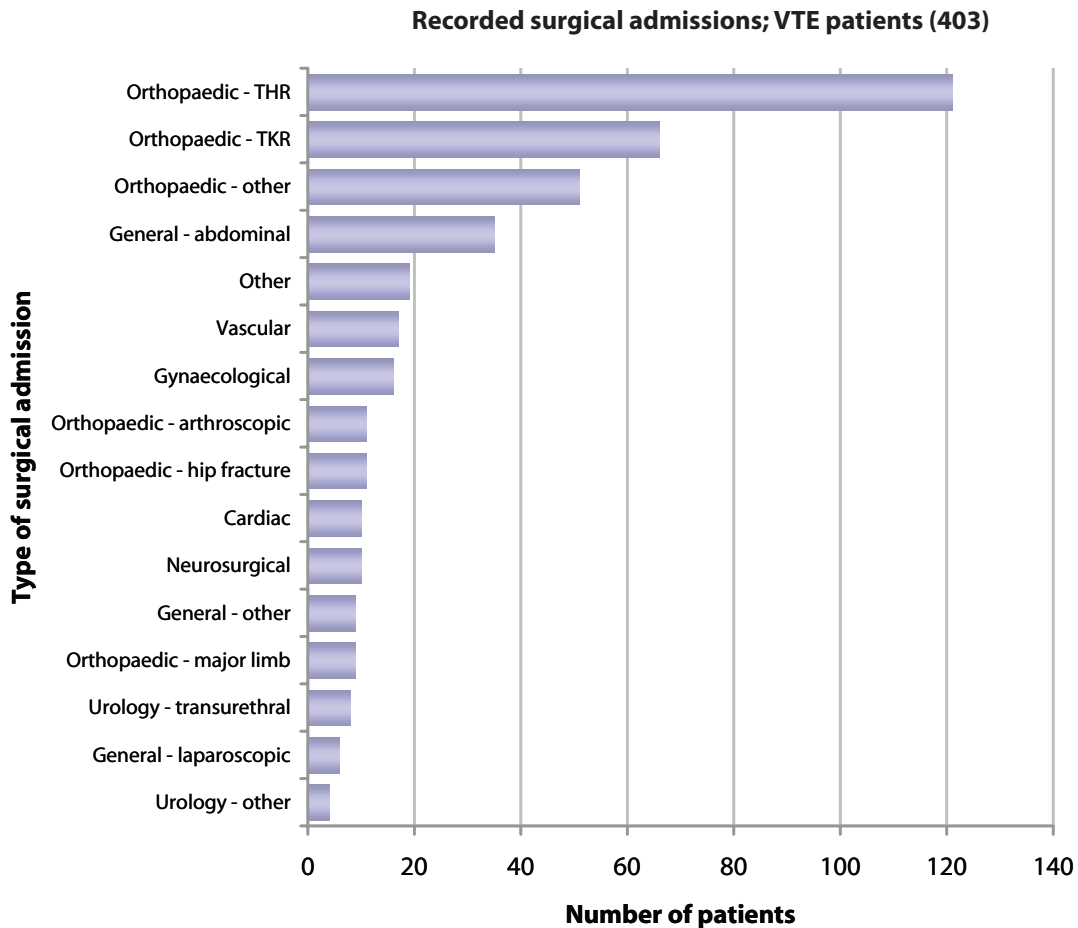
Of the 1,281 patients with a surgical inpatient history, the reason for hospital admission was reported in more than 96% of cases. As we can see in the graph, the vast majority of patients with suspected VTE and a history of recent stay in hospital for surgery have been admitted under the orthopaedic specialty. Abdominal, gynaecological and vascular surgical admission make up the second largest group of patients.

**Recorded surgical admissions; all patients (1,281)**



**Surgical inpatient history for VTE patients**

Of the 1,281 surgery patients, 31% had confirmed VTE (n=403). In this graph, it is clear that patients with a recent history of orthopaedic surgery make up by far the largest group of VTE patients with a recent history of admission for surgery: around 60% of all cases of confirmed VTE. Hospital admissions for abdominal, gynaecological and vascular surgery were also well represented in this group.



Thromboprophylaxis

**Practice point**

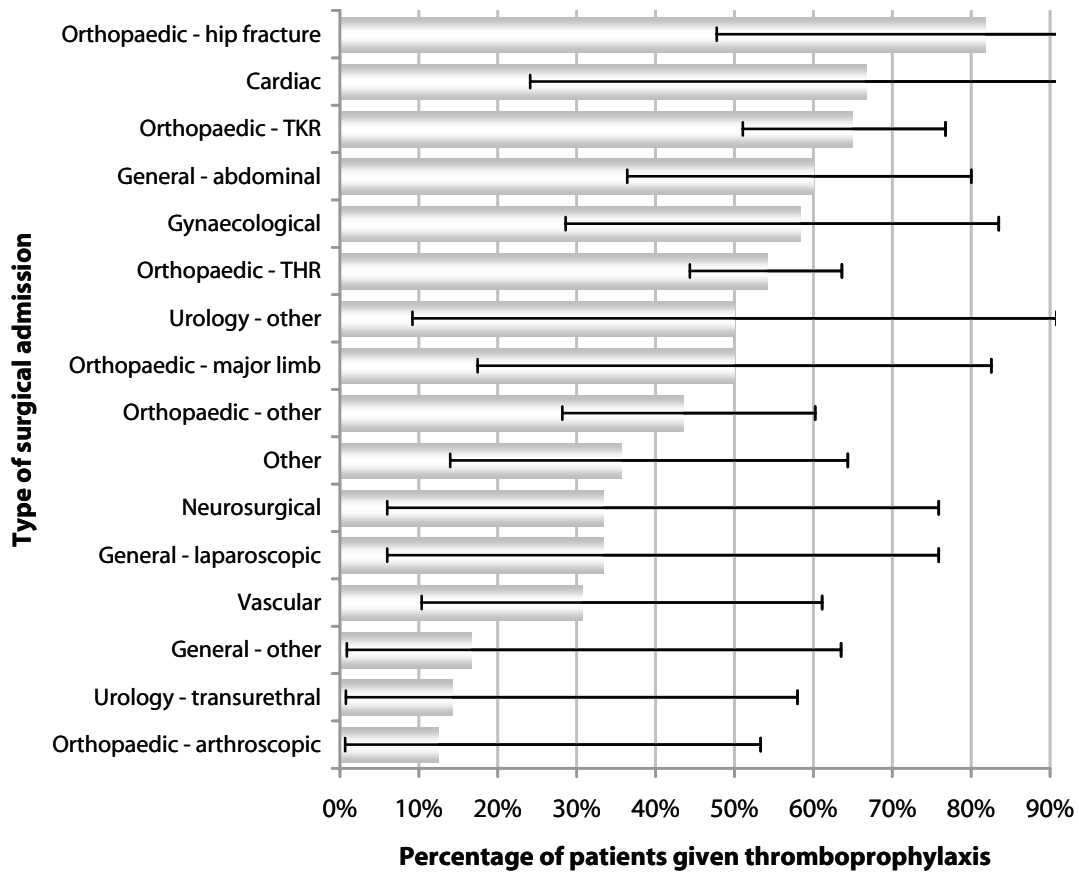
To reduce the risk of VTE for all inpatient surgical procedures, the NICE clinical guideline suggests:

- Assess patients for individual risk factors for VTE; advise patients to consider stopping combined oral contraceptives 4 weeks before elective surgery; inform patients that immobility associated with continuous travel of more than 3 hours in the 4 weeks before or after surgery may increase the risk of VTE.
- Before surgery, give verbal and written information on the risks of VTE and effectiveness of prophylaxis (mechanical and pharmacological).
- As part of each patient’s discharge plan, give verbal and written information on the signs and symptoms of DVT and PE, correct use of prophylaxis at home, and implications of not using prophylaxis correctly.

**Thromboprophylaxis in patients with a surgical inpatient history**

Of the 1,281 surgery patients, we know if the patient received, or did not receive, thromboprophylaxis in a quarter of cases (n=326). Overall, levels of thromboprophylaxis were quite high, with abdominal, gynaecological and orthopaedic surgery all around the 60% level. The highest levels of thromboprophylaxis provision were described in hip fracture patients (>80% of cases). Levels were low in general surgery described as *other* and arthroscopic and transurethral surgery.

**The use of thromboprophylaxis in surgical inpatients with VTE (n=326)**



**Thromboprophylaxis**

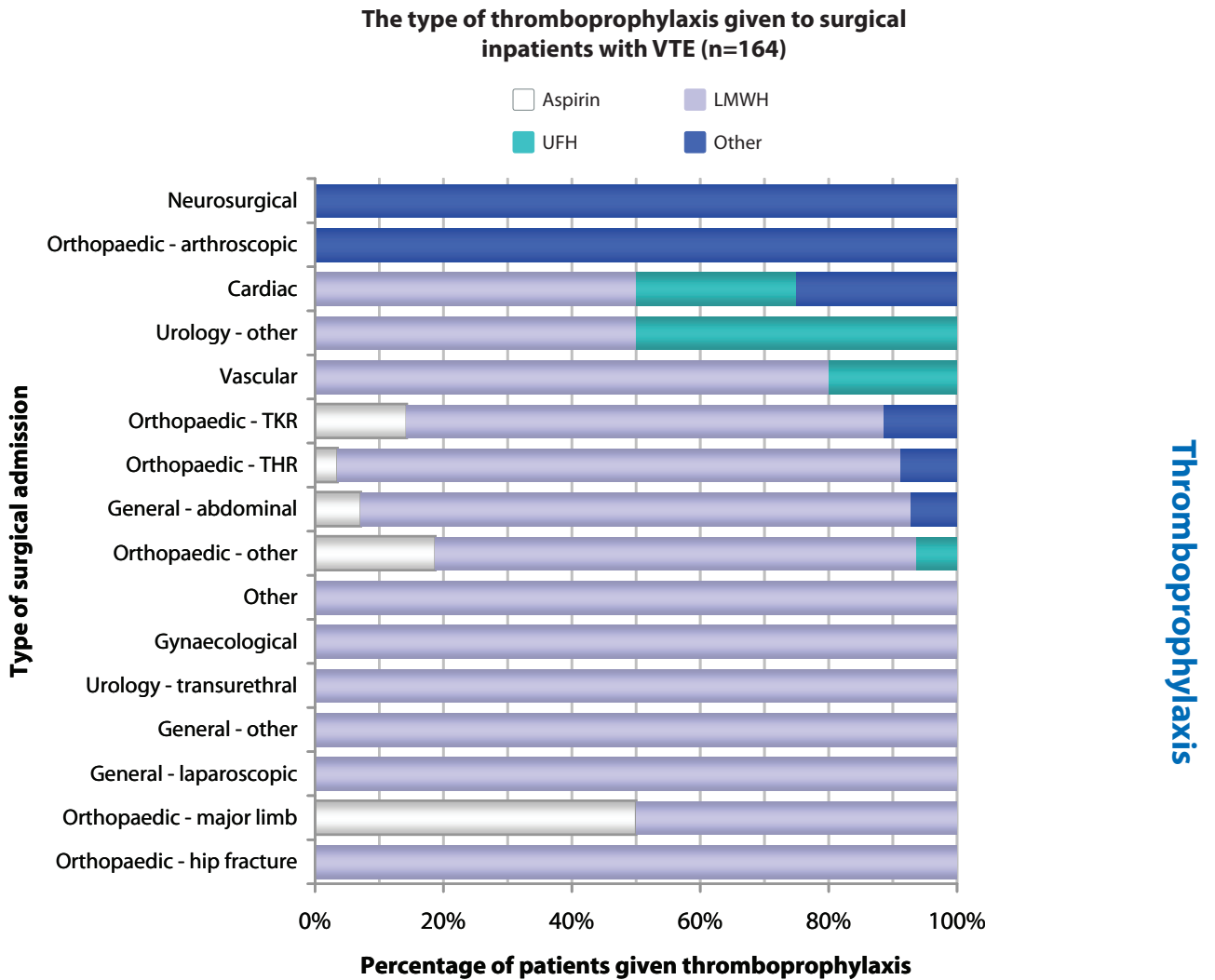
**Practice point**

The NICE clinical guideline recommends, in addition to mechanical prophylaxis, patients at increased risk of VTE because they have additional factors and patients having orthopaedic surgery should be offered low molecular weight heparin (LMWH). Fondaparinux, within its licensed indications, may be used as an alternative to LMWH. Patients having hip replacement surgery with one or more risk factors for VTE should have their LMWH or fondaparinux therapy continued for 4 weeks after surgery.

The VTE expert group recommends that intermediate-risk surgical patients or those with concomitant medical conditions should, as part of a mandatory risk assessment, be considered for the following thromboprophylaxis measures: graduated compression stockings combined with heparins (both unfractionated and low molecular weight forms); aspirin is not recommended for thromboprophylaxis in intermediate-risk surgical patients.

**Pharmacological thromboprophylaxis in patients with a surgical inpatient history**

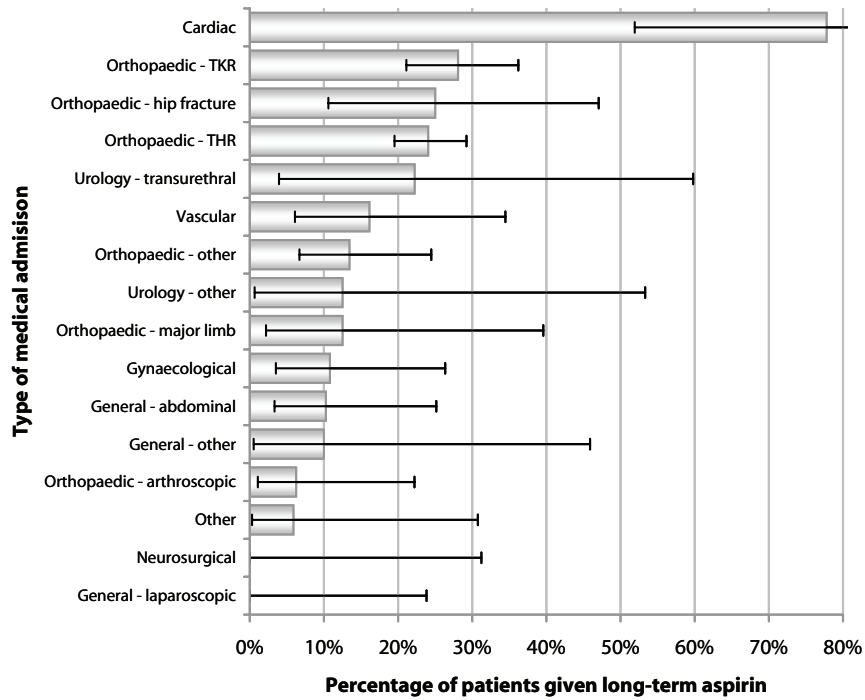
For the 326 patients with a surgical inpatient history for whom thromboprophylaxis status is known, about half (164 cases) received pharmacological thromboprophylaxis. The breakdown of the type of thromboprophylaxis is shown below; the majority of thromboprophylaxis given is LMWH. Notable exceptions are the use of aspirin in orthopaedic patients, the exclusive use of other forms of thromboprophylaxis in neurosurgery and arthroscopy and the use of UFH in urology and cardiac cases.



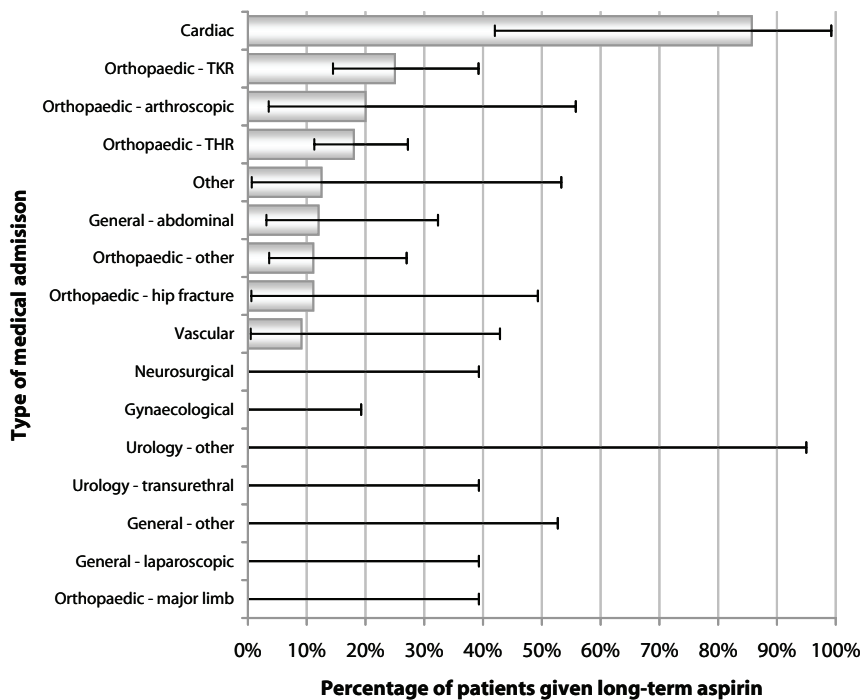
**Long-term aspirin use in patients with a surgical inpatient history**

Aspirin usage is marked in cardiac surgery patients; this is expected and follows cardiology guidelines that show the benefit of aspirin in preventing adverse outcomes in patients under cardiac care. There is long-term aspirin use in orthopaedic patients, both in all patients (upper graph) and those with VTE (lower graph), most likely reflecting, at least partially, long-term treatment for atherosclerotic disease in the elderly orthopaedic population.

**The long-term use of aspirin in surgical inpatients (n=789)**



**The long-term use of aspirin in surgical inpatients with VTE (n=301)**

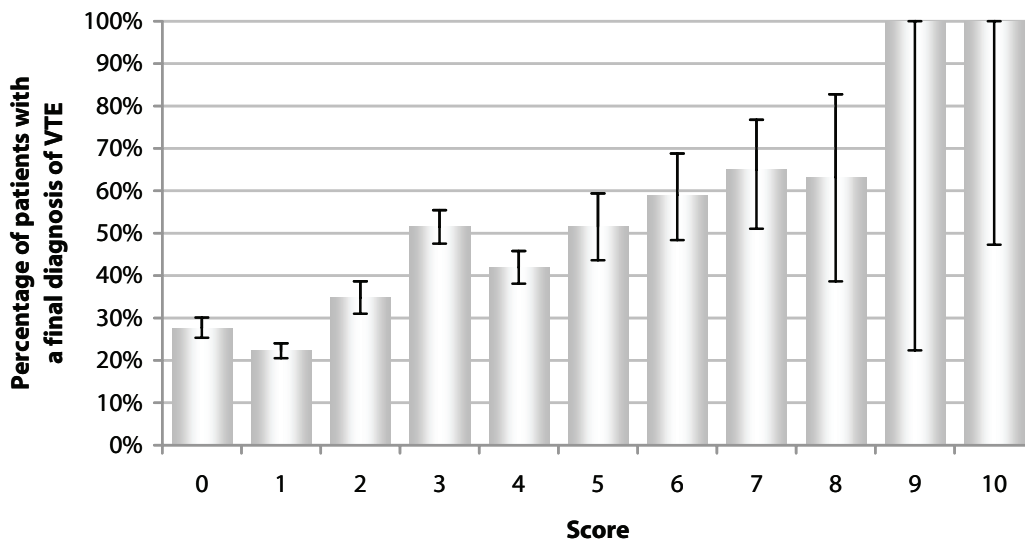


### Risk assessment for VTE

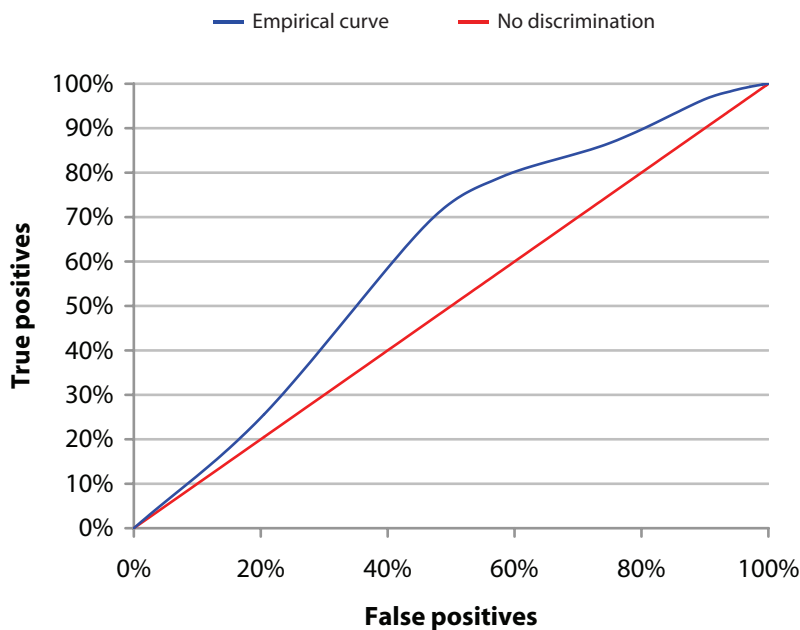
In the last report, we described the application of a VTE risk score to VERITY data based on eight principal risk factors, previously validated and shown to improve patient outcome<sup>8</sup>. Each risk factor was weighted according to a point scale. An increased risk of VTE was defined as a cumulative risk score of at least 4. In a previous randomised study, a computer alert using the risk score reduced the risk of VTE at 90 days by >40%.

For this report the data below have been updated, and we have performed a Receiver Operating Characteristic curve analysis (ROC) to determine how good the score is at discriminating between patients who do and do not have a final diagnosis of VTE. The ROC curve analysis suggests that the score is not a very good discriminator, and therefore more analysis has been initiated in an attempt to develop a valid risk assessment score for VTE.

**Final diagnosis and weighted risk score (n=5,841)**



**Receiver Operating Characteristic curve for the weighted risk score predicting a diagnosis of VTE (n=5,841; ROC area =0.611)**



### Independent expert working group on the prevention of venous thromboembolism

The VTE expert group report was published in late April and for the first time provides a framework for the management of VTE in the UK.

The framework was based on a review of the existing guidelines on the treatment and prevention of VTE that are considered to represent best practice and on a review of a huge volume of evidence relating to the natural history, pathophysiology, diagnosis, screening, and appropriateness of surrogate end points and prevention of VTE. The advice is structured in two sections:

- **Thromboprophylaxis strategy**, outlined as **Practice points** in this chapter
- **Systems, processes and knowledge base**, provided in full below:

The VTE expert group recommends:

1. A documented mandatory VTE risk assessment of every hospitalised patient on admission.
2. This VTE risk assessment be embedded within the Clinical Negligence Scheme for Trusts (CNST).
3. Improvement of public & professional understanding of VTE at a national level, through improved communication of information to patients and the public, accompanied by improved & coordinated programmes of professional education.
4. Establishment of VTE demonstration centres with an expanded role addressing demonstration of best practice, in order to inform development of comparable local systems in care networks and institutions. Such VTE demonstration centres would work together to develop a national risk assessment strategy, local quality control measures, audit of local practice, and would provide centralised educational material to support local educational programmes (*e.g. working with the National Centre for Anticoagulation Training*).
5. Core standards be set by the Department of Health for the NHS and independent sector in order to ensure that there is ultimately 100% compliance with the requirement for risk assessment of each and every adult admitted to hospital in England. These should be articulated in Standards for Better Health for the NHS and in Independent health care: national minimum standards.
  - a. Compliance with such standards be monitored by the Healthcare Commission through its assessment and inspection procedures. This would form part of an institution's self-assessment, with a separate analysis by the Healthcare Commission to test the validity of these responses.
  - b. The Department of Health refers responsible healthcare institutions that have no protocols for mandatory assessment and documentation, or have incomplete implementation of risk assessment, to the new expanded local thrombosis demonstration centres for further discussion and advice regarding best practice.
6. Evaluation of the impact on patients and the public of any future VTE strategy and associated implementation, including:
  - a. The development of a systematic approach to ensuring compliance with national quality assurance standards.
  - b. A communication strategy to promote better understanding.
  - c. A refinement of VTE-related health outcome measures (*better VTE metrics*).
  - d. Improvement in public and patient awareness and provision of guidelines about VTE risk (to include development of the existing VTE web pages on the Department's website at [www.dh.gov.uk/vte](http://www.dh.gov.uk/vte)).

### NICE clinical guideline on reducing the risk of VTE in inpatients undergoing surgery

The NICE clinical guideline was published in late April and provides thromboprophylaxis advice for inpatients undergoing surgery. To reduce the risk of VTE in all surgical specialities, the main recommendations of the guideline are:

- Patients should be assessed to identify their risk factors for developing VTE.
- Healthcare professionals should give patients verbal and written information, before surgery, about the risks of VTE and the effectiveness of prophylaxis.
- Inpatients having surgery should be offered thigh-length graduated compression / anti-embolism stockings from the time of admission to hospital unless contraindicated (for example, in patients with established peripheral arterial disease or diabetic neuropathy). If thigh-length stockings are inappropriate for a particular patient for reasons of compliance or fit, knee-length stockings may be used as a suitable alternative.
- The stocking compression profile should be equivalent to the Sigel profile, and approximately 18 mmHg at the ankle, 14 mmHg at the mid-calf and 8 mmHg at the upper thigh.
- Patients using graduated compression / anti-embolism stockings should be shown how to wear them correctly by healthcare professionals trained in the use of that product. Stocking use should be monitored and assistance provided if they are not being worn correctly.
- Intermittent pneumatic compression or foot impulse devices may be used as alternatives or in addition to graduated compression / anti-embolism stockings while surgical patients are in hospital.
- In addition to mechanical prophylaxis, patients at increased risk of VTE because they have individual risk factors and patients having orthopaedic surgery should be offered LMWH. Fondaparinux, within its licensed indications, may be used as an alternative to LMWH.
- LMWH or fondaparinux therapy should be continued for four weeks after hip fracture surgery.
- Regional anaesthesia reduces the risk of VTE compared with general anaesthesia. Its suitability for an individual patient and procedure should be considered, along with the patient's preferences, in addition to any other planned method of thromboprophylaxis.
- Healthcare professionals should encourage patients to mobilise as soon as possible after surgery.

The risk factors for VTE identified by NICE are:

- Active cancer or cancer treatment
- Active heart or respiratory failure
- Acute medical illness
- Age over 60 years
- Antiphospholipid syndrome
- Behcet's disease
- Central venous catheter *in situ*
- Continuous travel of more than three hours approximately four weeks before or after surgery
- Immobility *e.g.*, paralysis or leg in plaster
- Inflammatory bowel disease *e.g.*, Crohn's disease or ulcerative colitis
- Myeloproliferative disease
- Nephrotic syndrome
- Obesity (body mass index  $\geq 30$  kg m<sup>-2</sup>)
- Paraproteinaemia
- Paroxysmal nocturnal haemoglobinuria
- Personal or family history of VTE
- Pregnancy or *puerperium*
- Recent myocardial infarction or stroke
- Severe infection
- Use of oral contraceptives or hormonal replacement therapy
- Inherited thrombophilias *e.g.*
  - high levels of coagulation factors (*e.g.*, Factor VIII)
  - hyperhomocysteinaemia
  - Low activated protein C resistance (*e.g.*, Factor V Leiden)
  - Protein C, S and antithrombin deficiencies
  - Prothrombin 2021A gene mutation

## **Conclusions**

The change in the data fields that was introduced in 2005 has impacted positively on the thromboprophylaxis data now available. The question previously recorded on medical in-patient / immobility was too general and no detailed thromboprophylaxis provision was recorded. Now a broader range of information is recorded in the CRF about patients' recent medical history, in particular recent hospitalisation, specific medical illnesses and details of thromboprophylaxis are recorded. Reviewing the VERITY thromboprophylaxis findings this year gives an important insight into current practice.

Specific medical illnesses and surgical procedures, such as infectious respiratory disorders, stroke and orthopaedic procedures, accounted for the largest numbers of patients with confirmed VTE. Orthopaedic hip and knee surgery had the highest absolute numbers of patients with VTE; VTE was found in few patients with hip fracture, which may partially reflect the finding that these patients were associated with the highest level of thromboprophylaxis usage. Reviewing the thromboprophylaxis provision in medical patients with major illnesses, rates were highest in patients with heart failure and lowest in patients with stroke.

## **Identifying patients at risk of VTE**

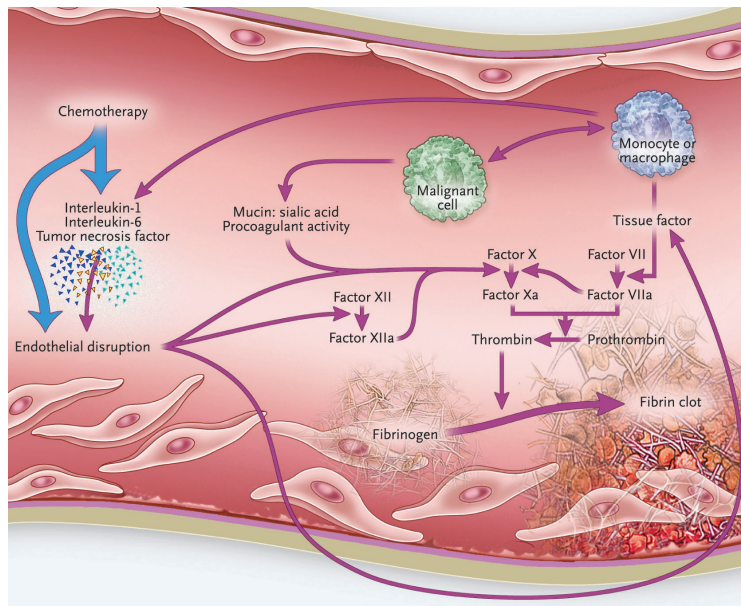
It is clear from the VTE expert working group's report and from the NICE guidelines that introducing a compulsory VTE risk assessment programme for all patients on admission to hospital is a key advance, but what is currently missing is a firm recommendation and agreed approach on how to formally assess risk. The CMO has therefore established a national VTE implementation working group to develop a national risk assessment tool and provide leadership both within the NHS and the wider healthcare sector in order to assess what needs to be done to ensure that a VTE risk assessment of every patient on admission to hospital becomes a reality.

## **Future developments**

The move to compulsory VTE risk assessment by next year will place hospitals under the spotlight and appropriate thromboprophylaxis provision will become a key parameter to assess for audit and clinical governance reasons. VERITY will remain an important resource for you, and the national risk assessment tool will be built into the VERITY CRF and outcomes reported, positioning VERITY as the national venous thromboembolism registry.

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8. Kucher N, *et al.* Electronic alerts to prevent venous thromboembolism among hospitalized patients. *N Engl J Med*. 2005; **352**: 969–977.



### Mechanisms of thrombosis and cancer

There are many causes of thrombosis in a cancer patient, many of which are associated with the tumour itself. For example, monocyte or macrophage lineage cells can interact with malignant cells and release cytokines, which can damage endothelium and change the vascular lining to a thrombogenic surface, and macrophages also activate platelets, factor XII, and factor X, which leads to the generation of thrombin. Tumour cells can release procoagulant substances such as cysteine proteases and tissue factor, which directly activate factor X or factor VII. Mucin secreted from adenocarcinomas can cause a non-enzymatic activation of factor X.

From Bick RL. Cancer-associated thrombosis. *N Eng J Med*. 2003;349:109-110. Copyright © 2003 Massachusetts Medical Society. All rights reserved.

# **VTE and cancer**

## VTE and cancer

### Overview

The association between cancer and thrombosis has been recognised for many years. VTE is a relatively common complication in patients with cancer, and is associated with both significant mortality and reduced survival<sup>1,2,3</sup>. Epidemiological studies have identified cancer as an important VTE risk factor and show that cancer patients are at substantially increased risk of both initial and recurrent VTE events<sup>1,2,4,5</sup>. The increase in risk is due to a number of factors, including chemotherapy, hormonal therapy and indwelling central venous catheters<sup>4</sup>; a persistent hypercoagulable state mediated by tumour activity is also considered a key feature in the pathogenesis of VTE<sup>6</sup>. The risk is higher for cancer surgery than in non-cancer patients undergoing surgery for benign disease. Overall, cancer increases the risk of thrombosis quite significantly by four- to six-fold<sup>4</sup>.

Many clinical questions regarding the care of cancer patients with VTE remain unanswered, but we are beginning to learn more about cancer and the risk of thrombosis *e.g.*, the IBIS 1 long-term follow-up study shows that the benefits of tamoxifen last 10 years, but the side effects, including the risk of VTE, fall away once treatment stops. Now, the VERITY database is large enough with sufficient cancer data to begin to make a difference in our understanding of which cancers are particularly associated with VTE, what cancers are associated with particularly poor survival if the patient has concomitant VTE and the role of D-dimer in identifying those VTE patients who may require cancer screening and further follow-up.

### Final diagnosis and cancer

This year, we have data on 3,056 patients with cancer. More patients with a confirmed diagnosis of VTE had a diagnosis of cancer than VTE-negative patients: 13.4% (1,572 / 11,759) *versus* 4.5% (1,484 / 33,146), respectively. VTE occurred twice as frequently in patients with cancer than in the non-cancer patients (51.4% [1,572 / 3,056] *versus* 24.3% [10,187 / 41,849], respectively). These findings are as expected and similar to previous results.

		Cancer status			
		No cancer	Cancer	Unspecified	All
Final diagnosis	DVT	9,356	1,457	643	<b>11,456</b>
	PE	627	79	62	<b>768</b>
	PE + DVT	204	36	20	<b>260</b>
	Non-VTE	31,662	1,484	1,742	<b>34,888</b>
	Unspecified	5,964	493	2,167	<b>8,624</b>
	<b>All</b>	<b>47,813</b>	<b>3,549</b>	<b>4,634</b>	<b>55,996</b>

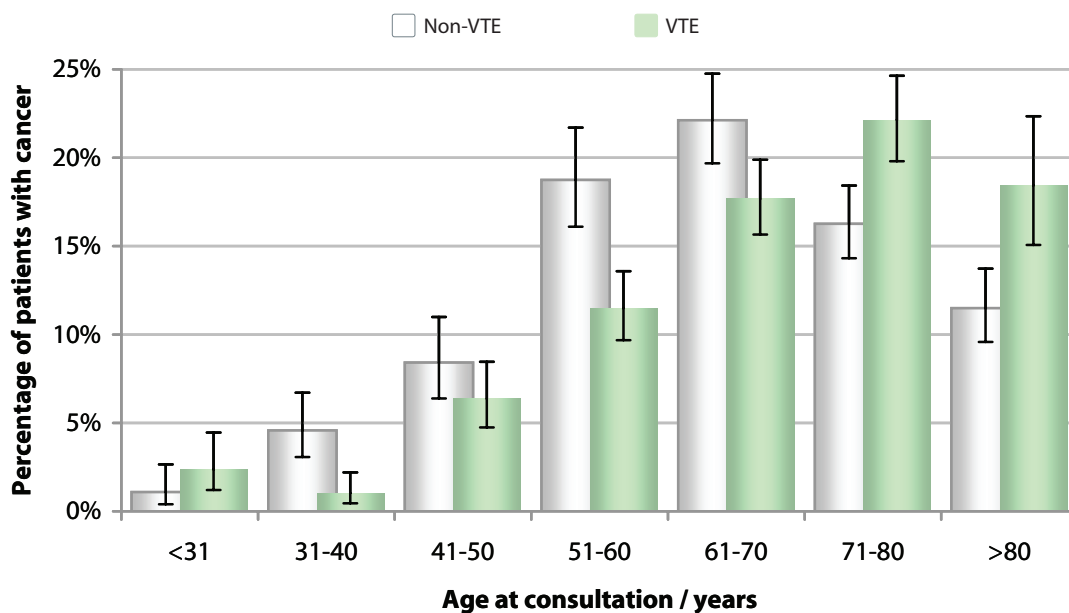
**Cancer, age and gender in patients with VTE**

The distributions of age, gender and cancer type are virtually identical to those presented in the last report and confirm that, overall, the rates of cancer and VTE increase with age as might be expected. The peak in the relative incidence of cancer in the female population occurs earlier (7<sup>th</sup> decade) than the peak in incidence for the male population (8<sup>th</sup> decade). As we noted in the last report, young patients with idiopathic VTE are highly unlikely to have an underlying malignancy.

		Gender and cancer status for patients with VTE								
		Female			Male			All		
		No cancer	Cancer	Unspecified	No cancer	Cancer	Unspecified	No cancer	Cancer	Unspecified
Age at consultation / years	<31	457	5	31	412	10	24	887	15	56
	31-40	543	26	43	675	7	46	1,232	34	91
	41-50	555	51	37	677	46	55	1,256	97	95
	51-60	633	146	50	955	124	55	1,618	277	109
	61-70	831	236	70	1,062	228	77	1,924	470	150
	71-80	1,076	209	73	915	260	59	2,020	480	136
	>80	847	110	53	376	85	32	1,244	199	88
	Unspecified	5	0	0	1	0	0	6	0	0
	All	4,947	783	357	5,073	760	348	10,187	1,572	725

Cancer

**Cancer rates broken down by age and gender for patients with VTE (n=11,557)**



### Specific types of cancer and age for patients with VTE

The most common forms of cancer are breast, prostate, colorectal and lung. The age-specific findings for patients with VTE indicate that these common cancers make up around half of all cancer patients with VTE, and that the proportion increases as the population ages. In the 31-40 age-group, 41.2% of cancer patients with VTE had one of these four common cancers, rising with age by decade to 55.3% in those patients >80 years. Therefore, although these cancer types may not have especially high rates of VTE, they make up the large proportion of cancer patients presenting with VTE.

Prostate cancer is 100% gender specific to males and breast cancer is predominantly gender specific to females (only 1% of all breast cancers are in men); in the graph below we can see clear age-related differences in the peak incidence of VTE, with marked peaks in breast cancer-associated VTE in the 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup> decades, but a marked peak for prostate cancer only in the 8<sup>th</sup> and 9<sup>th</sup> decades, and reflecting the peak incidence of these cancers.

		Type of cancer for patients with VTE									
		Any cancer			Breast			Prostate			
		No	Yes	Unspecified	No	Yes	Unspecified	No	Yes	Unspecified	
Cancer	Age at consultation / years	<31	887	15	56	899	0	59	899	0	59
	31-40	1,232	34	91	1,255	7	95	1,262	0	95	
	41-50	1,256	97	95	1,320	21	107	1,340	1	107	
	51-60	1,618	277	109	1,823	41	140	1,848	16	140	
	61-70	1,924	470	150	2,258	87	199	2,297	48	199	
	71-80	2,020	480	136	2,394	62	180	2,363	93	180	
	>80	1,244	199	88	1,378	43	110	1,377	44	110	
	Unspecified	6	0	0	6	0	0	6	0	0	
	<b>All</b>	<b>10,187</b>	<b>1,572</b>	<b>725</b>	<b>11,333</b>	<b>261</b>	<b>890</b>	<b>11,392</b>	<b>202</b>	<b>890</b>	

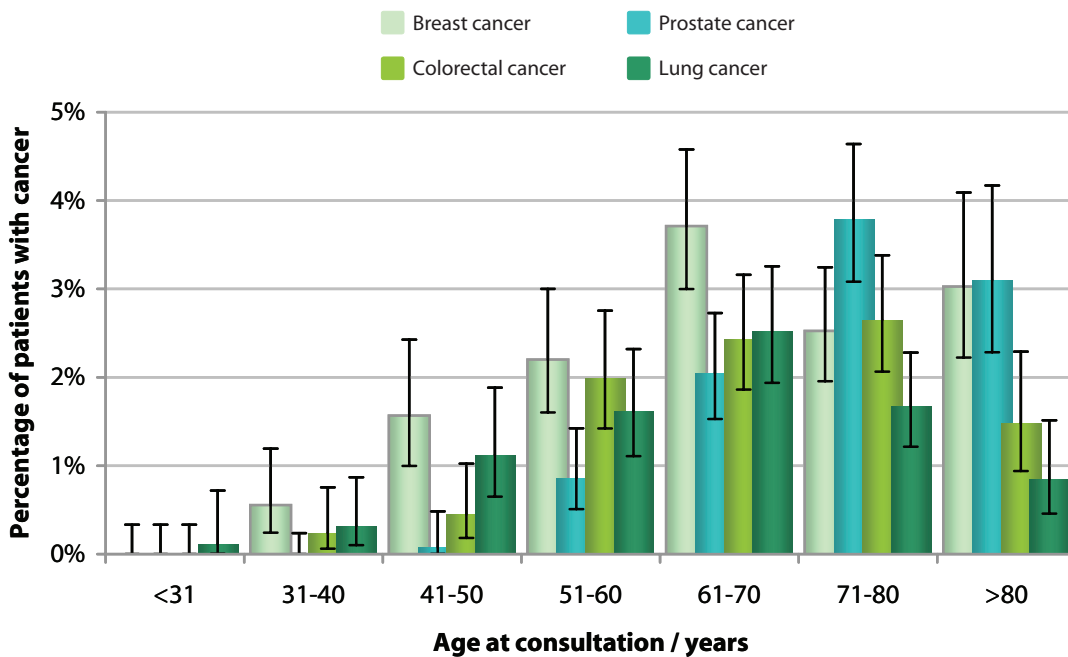
The age distribution of colorectal and lung cancer patients with VTE is shown in the table below. The highest rate of VTE occurs in the 8<sup>th</sup> decade in patients with colorectal cancer, and in the 7<sup>th</sup> decade in those with lung cancer.

Looking at the early age group, cancer is very uncommon in patients with VTE below the age of 40.

		Type of cancer for patients with VTE								
		Any cancer			Colorectal			Lung		
							Unspecified	No	Yes	Unspecified
Age at consultation / years	<31	887	15	56	899	0	59	898	1	59
	31-40	1,232	34	91	1,259	3	95	1,258	4	95
	41-50	1,256	97	95	1,335	6	107	1,326	15	107
	51-60	1,618	277	109	1,827	37	140	1,834	30	140
	61-70	1,924	470	150	2,288	57	199	2,286	59	199
	71-80	2,020	480	136	2,391	65	180	2,415	41	180
	>80	1,244	199	88	1,400	21	110	1,409	12	110
	Unspecified	6	0	0	6	0	0	6	0	0
	All	10,187	1,572	725	11,405	189	890	11,432	162	890

Cancer

Cancer rates broken down by age for the most frequently-occurring cancers in VERITY for patients with VTE (n=11,588)



## Different cancers

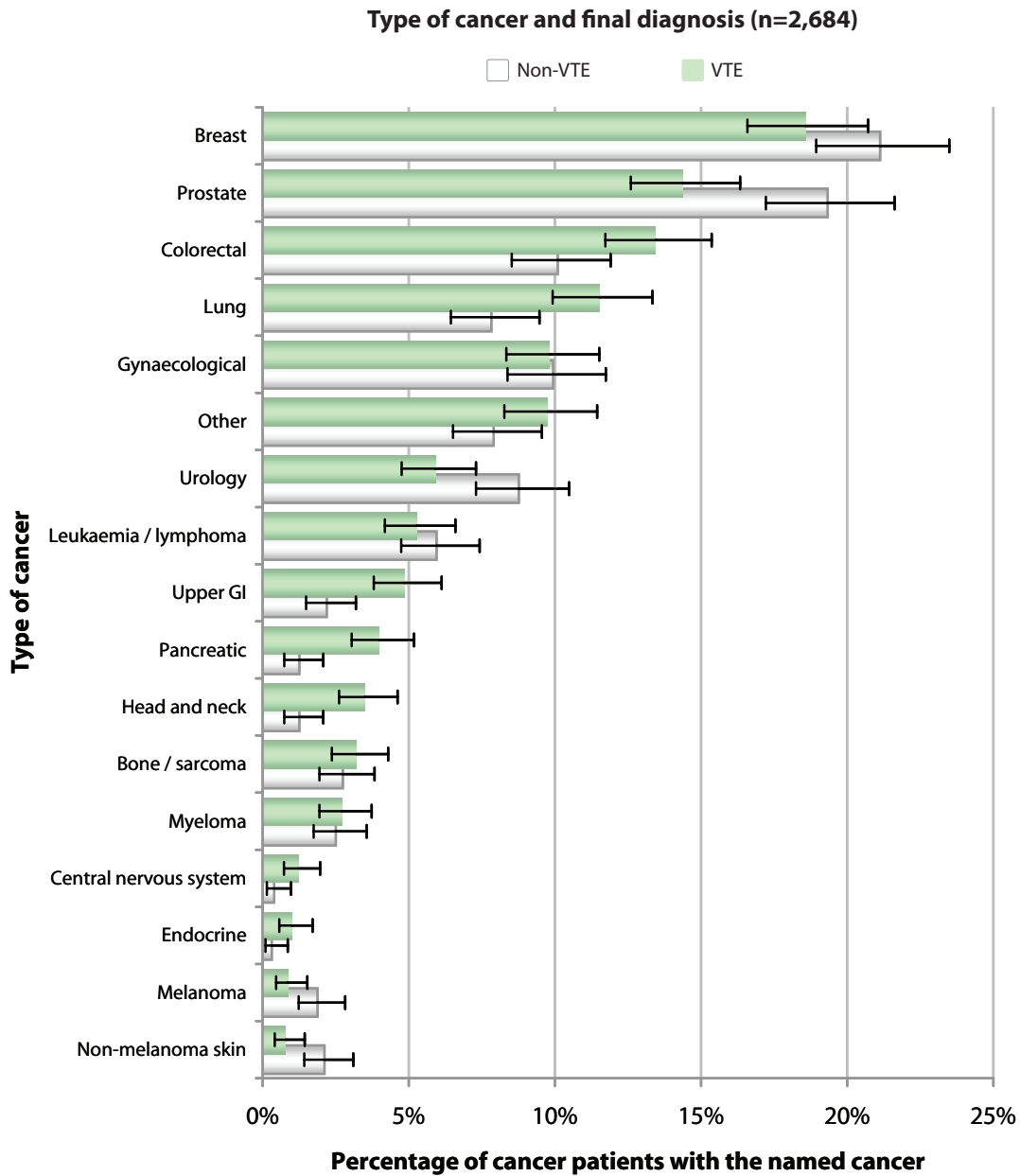
### Specific types of cancer and final diagnosis

Compared with the last report, there are considerably more cancer data in the registry. In terms of absolute numbers of cancer patients, the most common forms of cancer in the general population (breast, prostate, colorectal and lung) again match the most common cancers with VTE found in the registry. In cases for which we know the cancer status and VTE diagnosis, these four cancers were associated with the highest overall number of patients with VTE. This can be seen clearly in the next figure showing the type of cancer and final diagnosis.

## Cancer

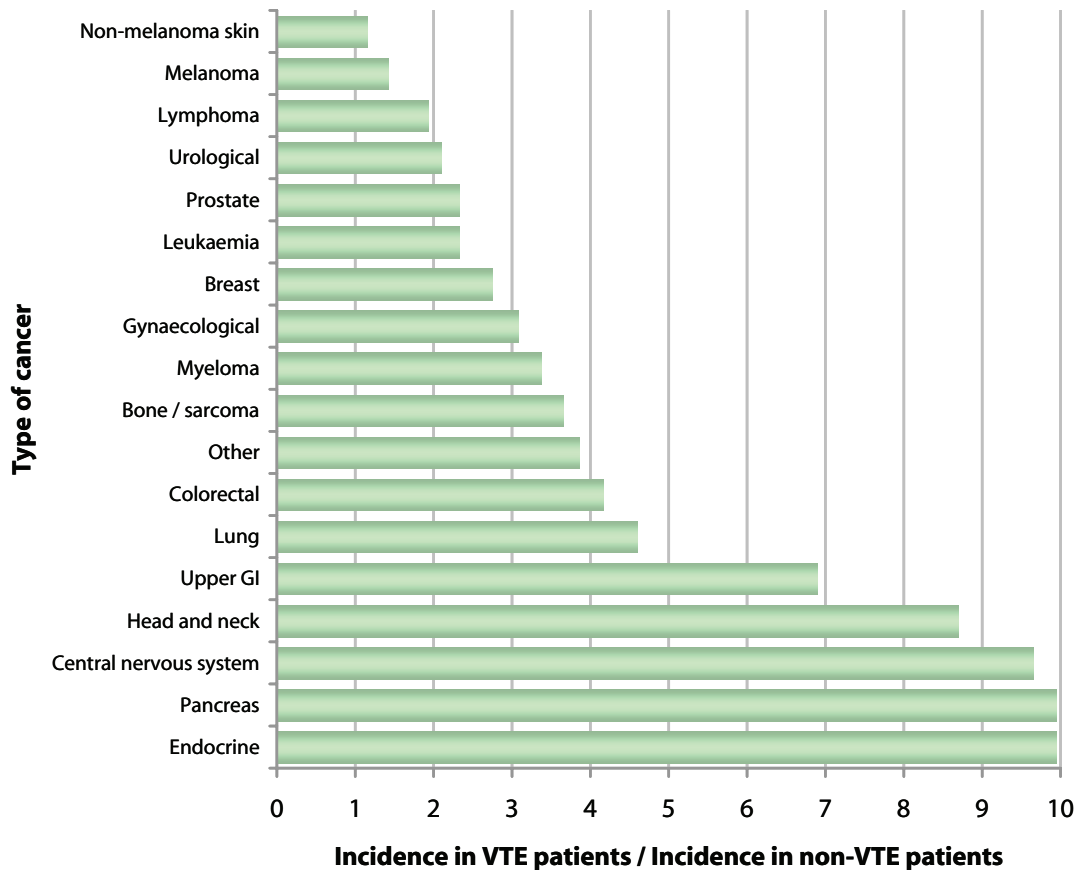
		Final diagnosis			
		Non-VTE	VTE	Unspecified	All
Type of cancer	No cancer	31,662	10,187	5,964	<b>47,813</b>
	Breast	270	261	74	<b>605</b>
	Prostate	247	202	67	<b>516</b>
	Colorectal	129	189	32	<b>350</b>
	Lung	100	162	42	<b>304</b>
	Other	101	137	33	<b>271</b>
	Gynaecological	127	138	52	<b>317</b>
	Urology	112	83	31	<b>226</b>
	Upper GI	28	68	11	<b>107</b>
	Bone / sarcoma	35	45	16	<b>96</b>
	Pancreatic	16	56	4	<b>76</b>
	Leukaemia / lymphoma	76	74	23	<b>173</b>
	Head and neck	16	49	7	<b>72</b>
	Myeloma	32	38	14	<b>84</b>
	Endocrine	4	14	3	<b>21</b>
	Central nervous system	5	17	1	<b>23</b>
	Melanoma	24	12	6	<b>42</b>
	Non-melanoma skin	27	11	10	<b>48</b>
	Unspecified cancer	206	166	112	<b>484</b>
	Unspecified	1,742	725	2,167	<b>4,634</b>
<b>All</b>	<b>34,888</b>	<b>12,484</b>	<b>8,624</b>	<b>55,996</b>	

This graph shows the percentages of each named cancer for the non-VTE and VTE patient-populations. There are now 2,446 patients with cancer type specified. These large numbers have resulted in tighter confidence intervals and allow us to identify three cancer types – upper GI tract cancer (as published in the previous VERITY report), pancreatic cancer and head and neck cancer – which are significantly more prevalent in the VTE patients than the non-VTE patients.



Comparing the incidence of each cancer type in the VTE patients to the non-VTE patients by calculating a ratio offers further insight into which cancers are particularly prevalent in the VTE population and therefore particularly associated with VTE. These findings presented below are very interesting and identify endocrine, pancreatic and CNS cancers as most strongly associated with VTE.

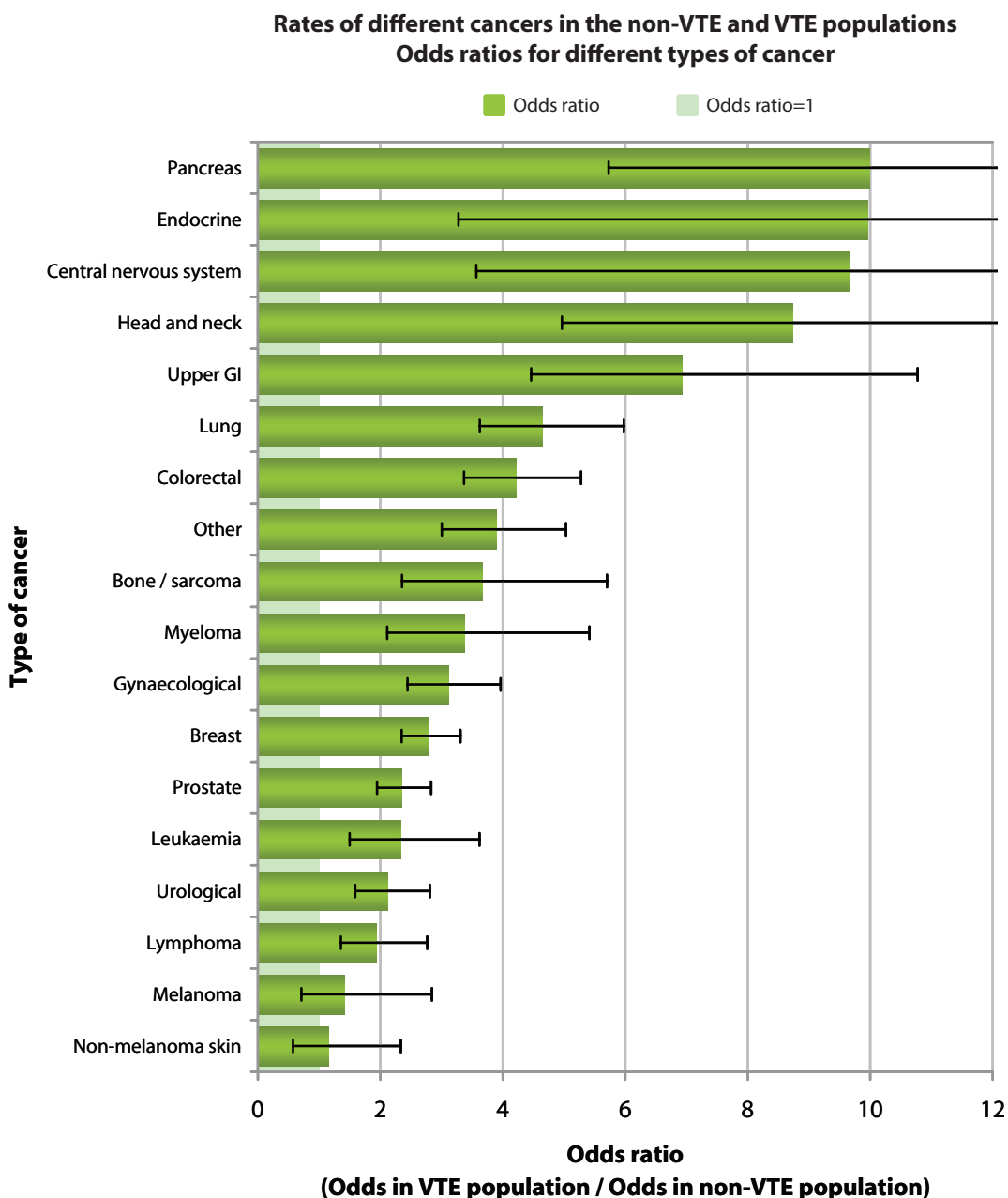
**The ratio of the incidence of each type of cancer in the VTE patient population to the to the incidence in the non-VTE patient population**



**Cancer**

Another way to present these data is to calculate odds ratios (OR) to compare the rates of different cancers in the non-VTE and VTE populations. OR is defined as the ratio of the odds of an event occurring in one group to the odds of it occurring in another group. An OR=1 indicates that a particular cancer is equally likely to be found in both groups. An OR>1 indicates that the cancer is more likely in the VTE group than the non-VTE group, if the 95% confidence intervals do not cross OR=1. This graph confirms that certain cancers are much more likely to be found in the VTE group, with pancreatic, endocrine and CNS tumours having an OR of around 10.

These findings are similar to those reported from the Californian Cancer Registry<sup>7</sup>. When linked to patient discharge data, it was shown that metastatic disease at the time of diagnosis was the strongest predictor of VTE and that the highest incidence of VTE (expressed as events / 100 patient-years) occurred during the first year of follow-up among cases with metastatic-stage pancreatic (20.0), stomach (10.7), bladder (7.9), uterine (6.4), renal (6.0), and lung (5.0) cancer.



Cancer

### D-dimer and cancer

D-dimer testing in patients with cancer is particularly interesting from both a diagnostic and research viewpoint. D-dimer in conjunction with PTP remains a valid exclusion approach for VTE, even in a population of patients with cancer. But as we noted earlier (see page 27), we wish to move towards a quantitative D-dimer assessment in VERITY. Quantitative D-dimer is of particular interest in cancer patients both for identifying patients at potential risk of an occult cancer, and because of the recently established relationship between elevated D-dimer levels and poor outcome in cancer patients with VTE (see page 92).

### D-dimer and pre-test probability

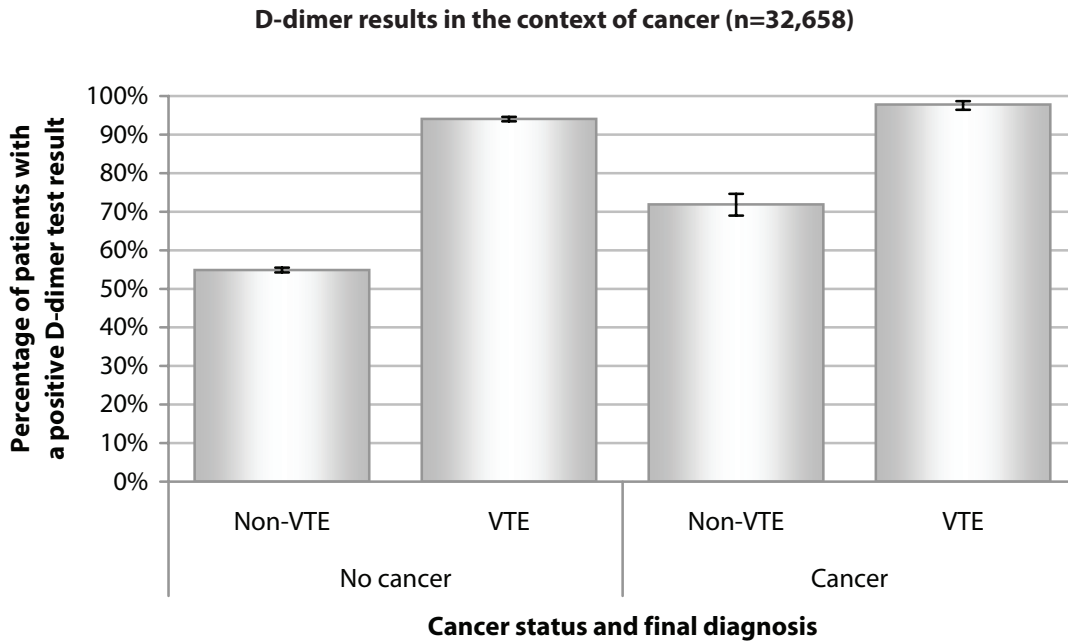
The assessment of PTP and D-dimer remains a valid investigation to exclude the diagnosis of DVT. In this table comparing cancer patients with non-cancer patients, the combination of negative D-dimer and low PTP had a negative predictive value of 100% - no cancer patients with negative tests were found to have VTE.

**Cancer**

				Final diagnosis					
				Non-VTE	DVT	PE	PE & DVT	Unspecified	All
Cancer status, D-dimer test results and DVT pre-test probability	No cancer	Negative D-dimer	Low <=0	6,449	80	13	1	375	6,918
			Moderate 1-2	1,494	143	0	2	153	1,792
			High >2	166	30	0	0	11	207
			Unspecified	2,827	117	7	1	771	3,723
		Positive D-dimer	Low <=0	6,348	706	112	14	565	7,745
			Moderate 1-2	2,955	2,211	26	68	423	5,683
			High >2	727	1,242	7	20	177	2,173
			Unspecified	3,275	1,674	120	39	1,342	6,450
		D-dimer not specified	Low <=0	3,497	241	93	4	620	4,455
			Moderate 1-2	1,685	1,243	14	18	470	3,430
			High >2	410	650	7	7	170	1,244
			Unspecified	1,829	1,019	228	30	887	3,993
	Cancer	Negative D-dimer	Low <=0	116	0	0	0	2	118
			Moderate 1-2	52	7	0	1	2	62
			High >2	28	8	0	0	5	41
			Unspecified	87	1	0	0	29	117
Positive D-dimer		Low <=0	207	16	8	0	25	256	
		Moderate 1-2	164	173	1	1	25	364	
		High >2	127	307	0	10	36	480	
		Unspecified	226	233	6	5	115	585	
D-dimer not specified	Low <=0	119	18	15	1	23	176		
	Moderate 1-2	118	139	8	8	48	321		
	High >2	96	261	0	1	59	417		
	Unspecified	144	294	41	9	124	612		

**Comparison of D-dimer findings in cancer and non-cancer patients**

This graph is very similar to the previous VERITY analysis and confirms that in patients who are excluded from the diagnosis of VTE, a significantly higher proportion of patients with cancer have a positive D-dimer than non-cancer patients. This is expected and confirms that D-dimer is often increased in cancer patients and more than in non-cancer patients.



Cancer

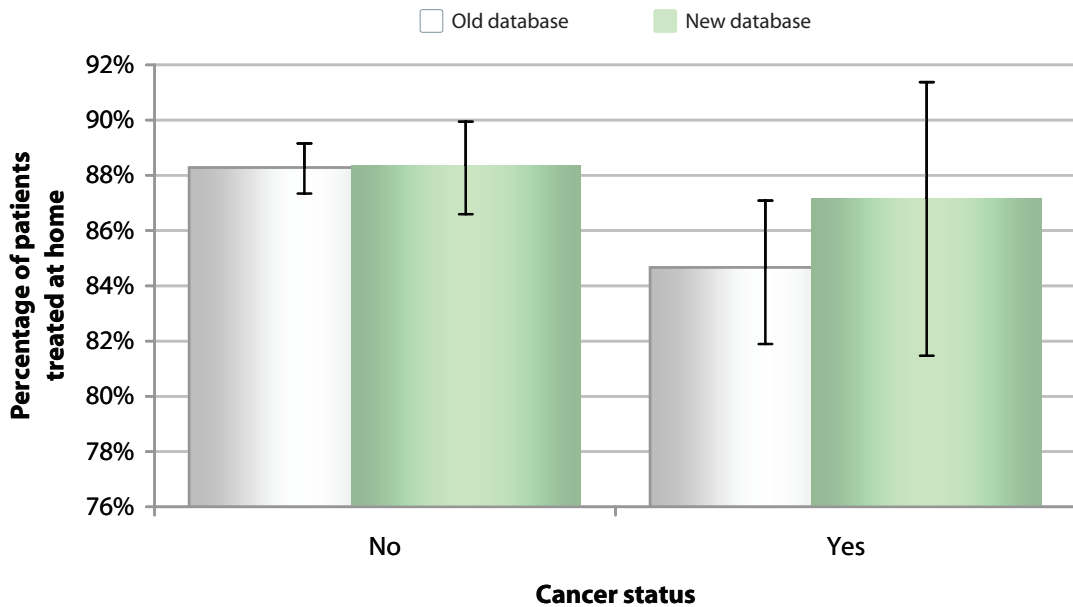
**Treatment**

**Location of treatment**

Despite the marked reduction in cancer given as a reason for not treating DVT out of hospital described on page 31, this has not yet manifested itself as an increase in the number of cancer patients treated out of hospital, with a slight decrease apparent in the graph below. Nonetheless, the proportion of cancer patients with DVT treated out of hospital remains quite high at 87%.

			Treated at home			
			No	Yes	Unspecified	All
Cancer status and database version	Old db	No cancer	581	4,376	237	<b>5,194</b>
		Cancer	119	657	40	<b>816</b>
		Unspecified	54	356	36	<b>446</b>
		All	<b>754</b>	<b>5,389</b>	<b>313</b>	<b>6,456</b>
	New db	No cancer	170	1,292	3,531	<b>4,993</b>
		Cancer	25	170	561	<b>756</b>
		Unspecified	21	57	201	<b>279</b>
		All	<b>216</b>	<b>1,519</b>	<b>4,293</b>	<b>6,028</b>

**Location of treatment and cancer status for VTE patients (n=7,390)**

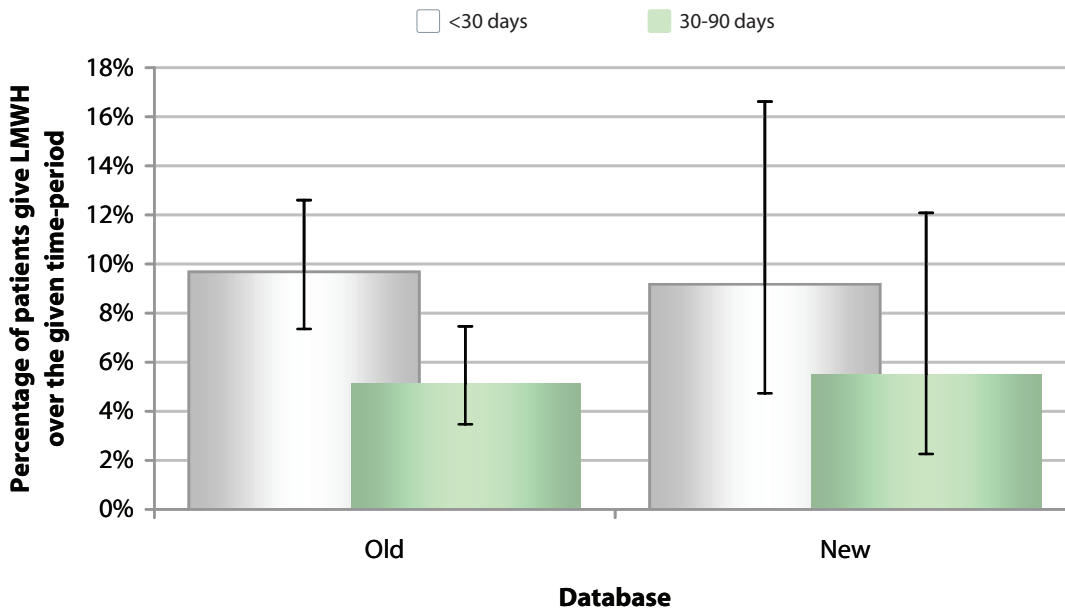


**Cancer**

**Duration of LMWH therapy and cancer**

In patients with cancer who develop VTE, clinical guidelines recommend that secondary prevention should be with LMWH for 3 to 6 months<sup>8</sup>. However, reviewing the data shown below shows that only a small proportion of cancer patients receive extended treatment with LMWH. About 9% received treatment for longer than 30 days and only about 5% for longer than 90 days. Comparing the old and new databases shows little change over time. This suggests a slow uptake of the recommendation for LMWH to replace warfarin in the treatment of VTE in cancer patients. However, we are aware that two hospitals (Portsmouth and Derriford) have switched completely to LMWH for the treatment of DVT of cancer patients, and it is somewhat surprising that these changes have not yet manifested themselves in the overall database analysis.

**Duration of LMWH therapy in patients with VTE in the context of cancer  
(Old n=527 and New n=109)**

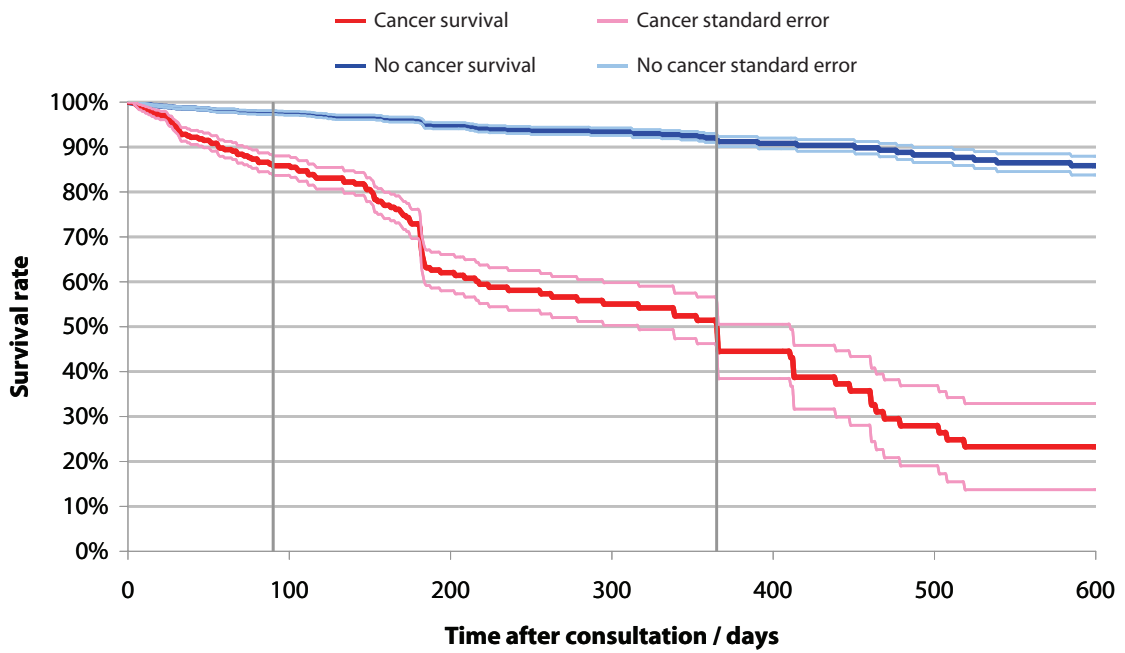


Cancer

**Outcomes**

The Kaplan-Meier survival curve below compares cancer patients with non-cancer patients in 2,772 patients with VTE. As shown in the last report, and as expected, VTE patients with cancer have a markedly poorer survival than cancer-free patients. This year, with more data available, the survival curve can be plotted to 600 days and shows that survival continues to fall to around 520 days, flattening out to day 600, with only 22% of patients alive at that time point.

**Kaplan-Meier survival curves for patients with confirmed diagnoses of VTE according to the presence or absence of cancer (n=2,772)**



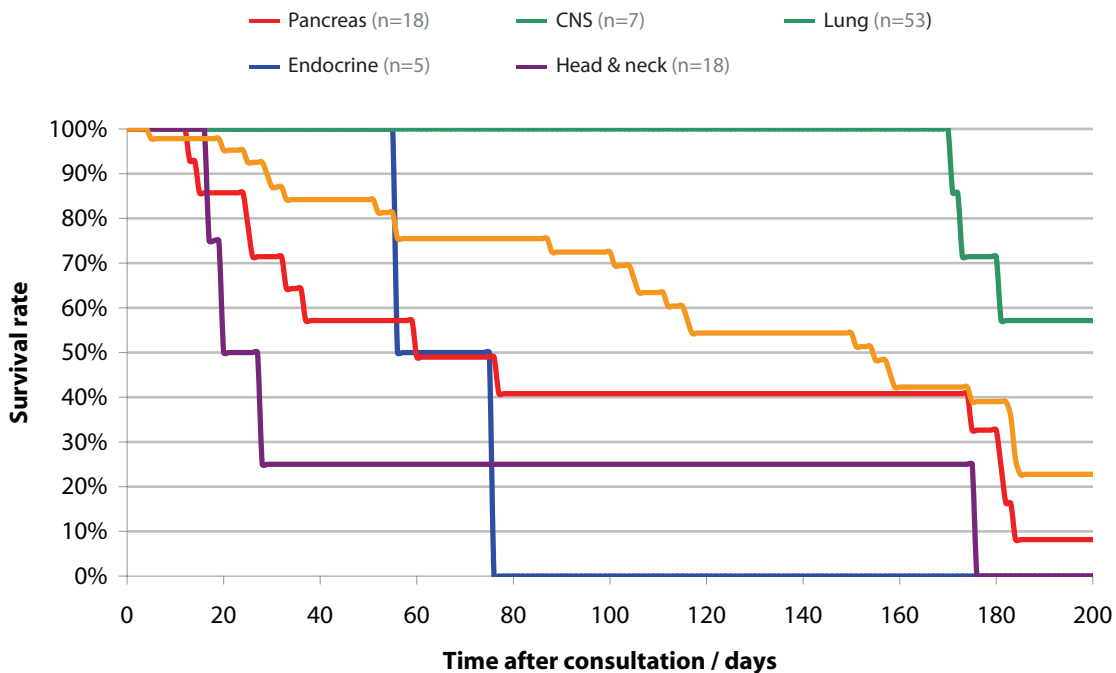
Cancer

**Outcomes in VTE patients with different types of cancer**

As described previously (see pages 83-85), certain cancer types are strongly associated with VTE. A key question we wish to answer is: what is the impact of VTE on survival in those particular cancer types? In this Kaplan-Meier survival curve, the numbers of cancers with follow up are quite small (endocrine n=5; pancreas n=18; CNS n=7; head and neck n=10; lung n=53) and we do not have comparisons of cancer patients' survival in the non-VTE population. However, we can begin to see a pattern, with particularly short survival associated with endocrine tumours, whereas with lung, the survival does not appear to be different from the overall cancer survival curve on the previous page. Clearly, these data are interesting and a VERITY project has been initiated to investigate further the association between cancer and VTE, with a particular focus on the impact of VTE on cancer survival.

The Californian Cancer Registry <sup>7</sup> again provides interesting data for current and future comparison. The Registry showed several interesting findings: that diagnosis of VTE was a significant predictor of decreased survival during the first year for all cancer types, and that metastatic disease at the time of diagnosis was the strongest predictor of VTE. With regard to staging, it is interesting to note that VTE was not a significant predictor of death for metastatic colorectal or breast cancer. VTE was a significant predictor of death among patients with local or regional-stage disease but not among patients with metastatic disease <sup>9,10</sup>.

**Kaplan-Meier survival curves for patients with confirmed cancer according to the patients final diagnosis (n=597)**



Cancer

### Outcomes in VTE patients with elevated D-dimer

As noted earlier (see page 27), we wish to move towards a quantitative D-dimer assessment in VERITY. Quantitative D-dimer is of particular interest in cancer patients because of the recently established relationship between elevated D-dimer levels and poor outcome in cancer patients with VTE. The case report from The Walsgrave, presented in the last VERITY report, has now been published <sup>11</sup> and confirms that high D-dimer is a marker of poor survival; the summary is presented below.

#### High D-dimer levels at presentation in patients with VTE is a marker of adverse clinical outcomes

S. Paneesha <sup>1</sup>, E. Cheyne <sup>2</sup>, K. French <sup>2</sup>, S. Bacchu <sup>2</sup>, A. Borg <sup>1</sup> and P. Rose <sup>1,2</sup>

<sup>1</sup> Department of Haematology, Warwick Hospital, Warwick, and

<sup>2</sup> Department of Haematology, University Hospital Coventry and Warwickshire NHS Trust, Coventry, UK

Qualitative D-dimer results, together with clinical probability scores, are well established in the diagnosis of VTE. The predictive value of quantitative D-dimer levels for various clinical outcomes in VTE patients is not fully understood. D-dimer levels obtained at presentation were analysed in 699 (360 men; 339 women) VTE patients for survival and occurrence of malignancy. Patients were followed for a median of 23 months. 17.2% patients had a D-dimer level >8,000 ng FEU / ml at presentation, which was associated with decreased overall survival (OS;  $p < 0.001$ ) and event-free survival (EFS;  $p < 0.001$ ). 25.4% patients had malignancy and 4% subsequently developed malignancy following VTE. 29.9% of patients with VTE and malignancy had a D-dimer level >8 mg l<sup>-1</sup> when compared with 13.4% of patients with VTE without malignancy ( $P < 0.001$ ). 50% of patients who developed subsequent malignancy following VTE had a presentation D-dimer >8,000 ng FEU / ml as compared with 13.3% of patients with VTE with out malignancy ( $p = 0.009$ ).

In conclusion, D-dimer >8,000 ng FEU ml<sup>-1</sup> at presentation in patients with VTE is a marker of poor OS, EFS and underlying malignancy. Consideration of screening for malignancy is recommended in patients with VTE with a presentation D-dimer >8,000 ng FEU ml<sup>-1</sup> and age >60 years.

## Outcomes in cancer patients with or without VTE

Cancer is known to be an adverse risk factor in patients with VTE but data on the potential adverse impact of VTE on survival in patients with malignancy is conflicting. In the previous report, we described an analysis of data from Walsgrave Hospital, that showed the impact of cancer on survival. This year, further analysis has been conducted using VERITY data and a summary of the data are presented below. These data were presented at the British Society of Haematology meeting in May 2007.

### **Venous thrombosis (VTE) has an adverse impact on the survival in patients with malignancy**

This study included 902 (463 males; 439 females) patients from the prospectively maintained database of patients from UK venous thromboembolism registry (VERITY) between February 2001 and December 2006. Counterpart group included 2,263 (745 males; 1,518 female) consecutive patients without venous thrombosis from one site, between February 2001 and December 2005. All patients underwent a Doppler ultrasound examination to confirm the diagnosis and determine the extent of venous thrombosis. At presentation, 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. Thrombosis recurrence was always confirmed by Doppler ultrasound examination. All Patients with thrombosis received standard treatment with low molecular weight heparin and warfarin. Statistical analysis was carried out using SPSS 13.0 for Windows software.

Median age at presentation was 66 years (range: 16-96 years). Median D-dimer level was 2,500  $\mu\text{g FEU ml}^{-1}$  (range: 100-40,000  $\mu\text{g FEU ml}^{-1}$ ). 17.3 % had D-dimer > 8,000  $\mu\text{g FEU ml}^{-1}$ . 61% had above knee & 34% had below knee VTE. 522 patients had no malignancy, 89 had bowel, 61 prostate, 56 breast, 41 gynaecological, 29 lung and 102 had miscellaneous carcinoma. Median follow-up was 21 months (range: 0-74 years). Mean overall survival (OS) in non-VTE patients without malignancy was 56 months as compared to 54 months in VTE patients with malignancy. Mean OS in VTE patients with carcinoma breast was 34 months (counterpart group: 47 months). Median OS in VTE patients with carcinoma bowel was 9 months (counterpart group: 36 months). Median OS in VTE patients with carcinoma prostate was 31 months (counterpart group: 33 months). Median OS in VTE patients with gynaecological carcinoma was 17 months (counterpart group: 50 months). Median OS in VTE patients with miscellaneous carcinoma was 9 months (counterpart group: 30 months). Median OS in VTE patients with carcinoma lung was 5 months (counterpart group: 4 months). Median D-dimer levels in VTE patients without malignancy, Ca Breast, Ca bowel, Ca Prostate, Gynaecological Ca, Miscellaneous Ca and Ca Lung respectively were 2,200, 3,650, 4,100, 2,850, 3,140, 3,230 & 3,400  $\mu\text{g FEU ml}^{-1}$ . D-dimer > 8,000  $\mu\text{g FEU ml}^{-1}$  was associated with shorter survival (Log rank test; p value < 0.001).

Our study shows occurrence of VTE shortens the survival in patients with malignancies. Our study also shows D-dimer > 8,000  $\mu\text{g FEU ml}^{-1}$  is associated with significant shorter survival. More studies are warranted to determine whether this adverse impact correlates with the thrombogenesis of underlying malignancy rather than recurrence and also can it be negated by optimum anticoagulant therapy.

## Conclusions

Epidemiological studies have identified cancer as an important risk factor for VTE but many clinical questions remain unanswered. This year, we have data on 3,056 patients with cancer, 1,572 patients with VTE and 1,484 patients without VTE.

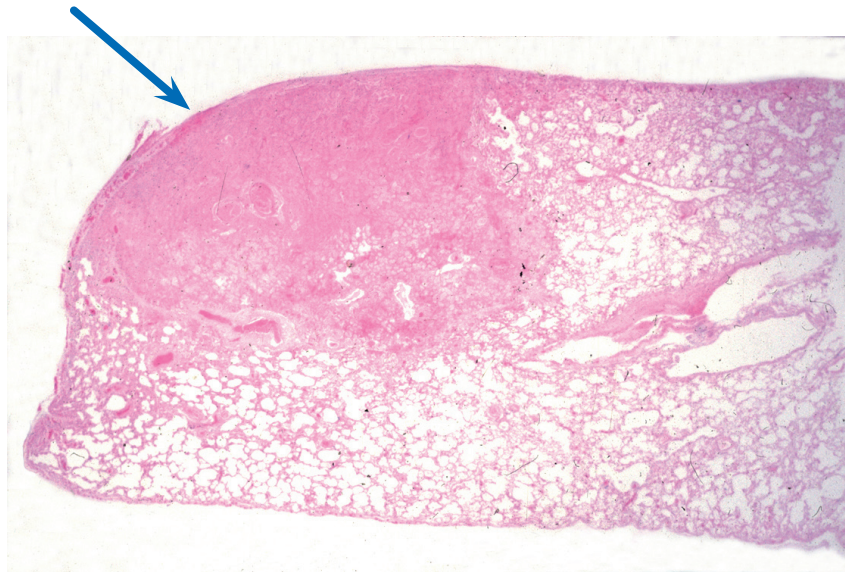
As previously, patients with VTE and the most common forms of cancer (breast, prostate, colorectal and lung) show interesting differences in age distribution, with breast cancer patients showing peaks in the middle age groups (4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> decades). In calculating the ratio of the incidence of each cancer in the VTE population to the incidence in non-VTE patients, we can see that the particular cancers are particularly associated with VTE. The odds ratio is low for breast and prostate; for lung and colorectal cancers, the odds ratio is intermediate; but for endocrine, CNS and head and neck cancers, very high odds ratios are apparent. This is very interesting data and we will now attempt to correlate these findings with patient outcome.

With limited outcome data, it remains difficult to draw firm conclusions on the relationship between VTE and cancer. Nevertheless, VTE patients with cancer have a poorer outcome than patients without cancer. We would particularly like to assess the impact that VTE has on cancer survival, but the data are not extensive enough as yet. We hope that the VERITY cancer project that has been initiated will give sufficient data to begin to answer this important question.

Regarding the diagnosis and treatment of VTE in cancer patients, the findings validate combined PTP and D-dimer in this mixed population of cancer and non-cancer patients. Quantitative D-dimer now appears to be a valuable measure in cancer patients, with the publication by Walsgrave of a correlation between elevated D-dimer and survival. The proportion of cancer patients with VTE who were treated as outpatients was slightly less than VTE patients who did not have cancer, in keeping with the previous findings. As we suggested in the last report, the use of LMWH for secondary prophylaxis of VTE needs to be addressed. The use of guideline-recommended extended LMWH therapy in cancer patients remains limited, although we are aware that this practice has been adopted at two VERITY hospitals (Portsmouth and Derriford).

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### **Pulmonary infarction and death as a result of pulmonary embolism**

This histological section of lung tissue was prepared from *post mortem* material. The infarction occurred in an obese lady, who became suddenly short of breath while walking to the hospital entrance for a cigarette, 8 days after surgery for appendicitis. Within minutes, she had collapsed and could not be resuscitated.

The main histological feature (arrowed) is due to severe haemorrhage into the alveoli. Inflammatory cells, particularly neutrophils are beginning to invade the infarcted tissue and there is evidence of necrotic cell death. Pleurisy (inflammation of the overlying pleura) is also visible on some sections. Several of the large pulmonary arterial vessels adjacent to the red area are blocked by thrombo-embolus. Necrosis and inflammation could not occur within a few minutes of the embolic event, suggesting this infarction reflected a pulmonary embolism that occurred about 24-48 hours prior to death.

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# **VTE and pregnancy**

## VTE and pregnancy

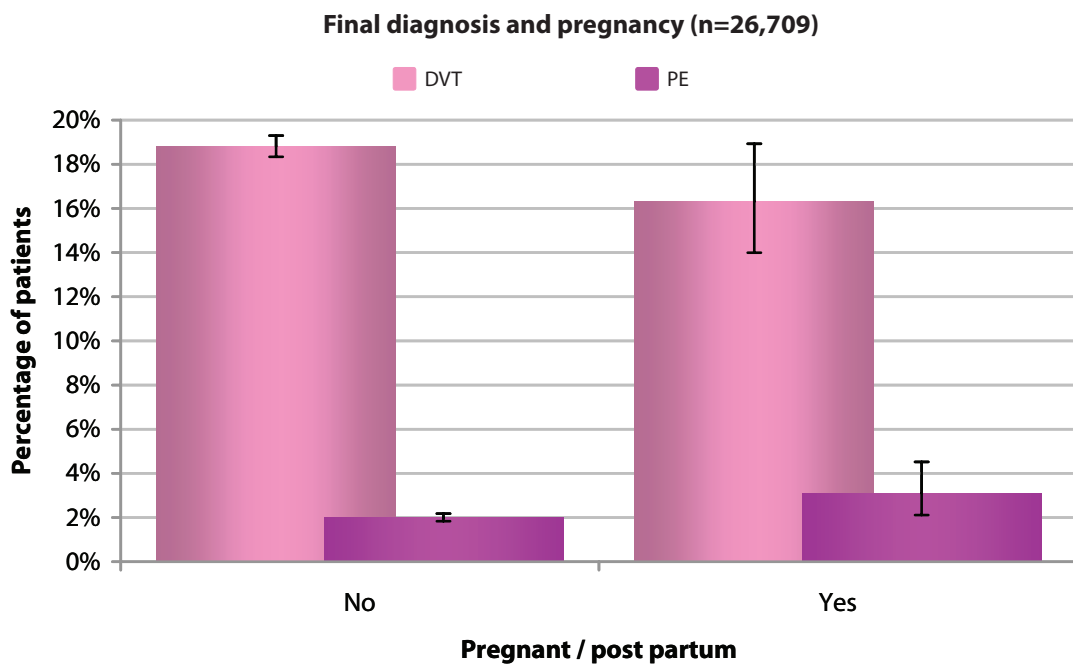
### Overview

VTE is a rare but serious complication of pregnancy. The Confidential Enquiry into Maternal and Child Health (CEMACH; [www.cemach.org.uk](http://www.cemach.org.uk))<sup>1</sup> provides important figures for deaths caused by PE, but there remains a paucity of knowledge about the overall rate of VTE, risk factors for VTE and the extent of long-term morbidity from VTE in pregnant women. In addition, it is not completely clear to what extent risk factors for VTE among men and non-pregnant women can be generalized to pregnant and *puerperal* women as pregnancy and *puerperium* themselves are associated with an increased thrombotic risk. Recent data suggest that smoking and obesity are risk factors for VTE in pregnancy and the *puerperium* compared with non-pregnant age and sex-matched controls<sup>2</sup>.

In this chapter, we review the risk factor profile of pregnant women with VTE and attempt to offer useful information based on the simple questions asked in VERITY about pregnant women. We attempt to establish more firmly the risk factors for pregnant women by comparing with the clinical characteristics of all non-pregnant women in the same age range in VERITY. In addition, we present the current guidelines on thromboprophylaxis for women at risk of VTE during pregnancy issued by the RCOG in 2004<sup>3</sup>.

		Final diagnosis					
		Non-VTE	DVT	PE	PE + DVT	Unspecified	All
Pregnancy status	Not pregnant / <i>post partum</i>	20,437	4,855	417	99	3,874	29,682
	Pregnant / <i>post partum</i>	726	147	23	5	139	1,040
	Unspecified	1,004	508	23	10	1,272	2,817
	<b>All</b>	<b>22,167</b>	<b>5,510</b>	<b>463</b>	<b>114</b>	<b>5,285</b>	<b>33,539</b>

Pregnancy



**Diagnosis of VTE in pregnancy and *post partum***

Overall, there are 1,040 women in the combined database recorded as pregnant or *post partum*. In the old database (n=633), there are 90 cases of VTE associated with pregnancy / *post partum*. In the new, on-line database (n=407), a distinction is made between pregnancy and *post partum*, with 30 pregnancy-associated VTE and 55 *post partum* VTE.

		Final diagnosis					All
		Non-VTE	DVT	PE	PE + DVT	Unspecified	
Pregnancy status	Pregnant	175	28	1	1	18	226
	<i>Post partum</i>	118	48	6	1	21	181

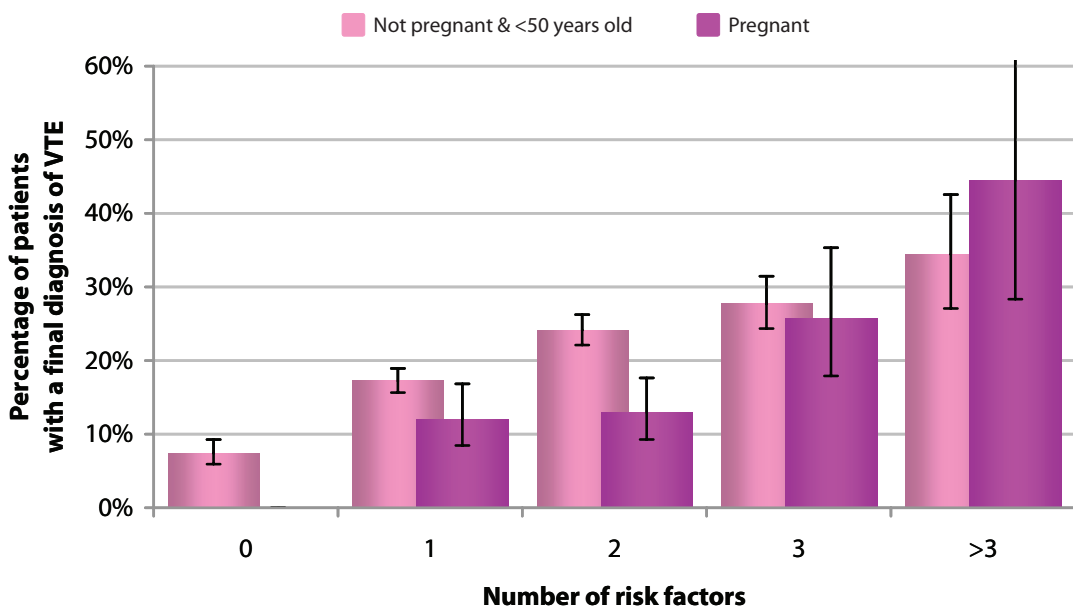
**Risk factors and pregnancy**

This comparison of number of risk figures for pregnant and non-pregnant women is interesting, suggesting that there is little difference between the two groups. Although the proportion of women with two risk factors is higher in the non-pregnant control population, this simply reflects the fact that pregnancy itself is included as a risk factor. The graph below shows that all pregnant women with VTE have at least one risk factor, again reflecting the pregnancy risk factor. It is notable that 31 women diagnosed with VTE had no risk factors other than their pregnancy. In the previous VERITY report, we reviewed the women with two risk factors (pregnancy plus one other) and found the most common second risk factor by far was a history of smoking (54% of this group) followed by family history, which was reported for 10% of the group. In the next graph on page 101 we review these and other risk factors for VTE in more detail.

			Final diagnosis			
			Non-VTE	VTE	Unspecified	All
Pregnancy status and number of risk factors	Not pregnant and <50 years	0	935	75	129	1,139
		1	1,730	360	316	2,406
		2	1,284	408	252	1,944
		3	458	176	102	736
		>3	101	53	27	181
		Unspecified	1,367	304	271	1,942
	Pregnant	0	0	0	0	0
		1	226	31	21	278
		2	236	35	38	309
		3	78	27	20	125
		>3	20	16	7	43
		Unspecified	166	66	53	285

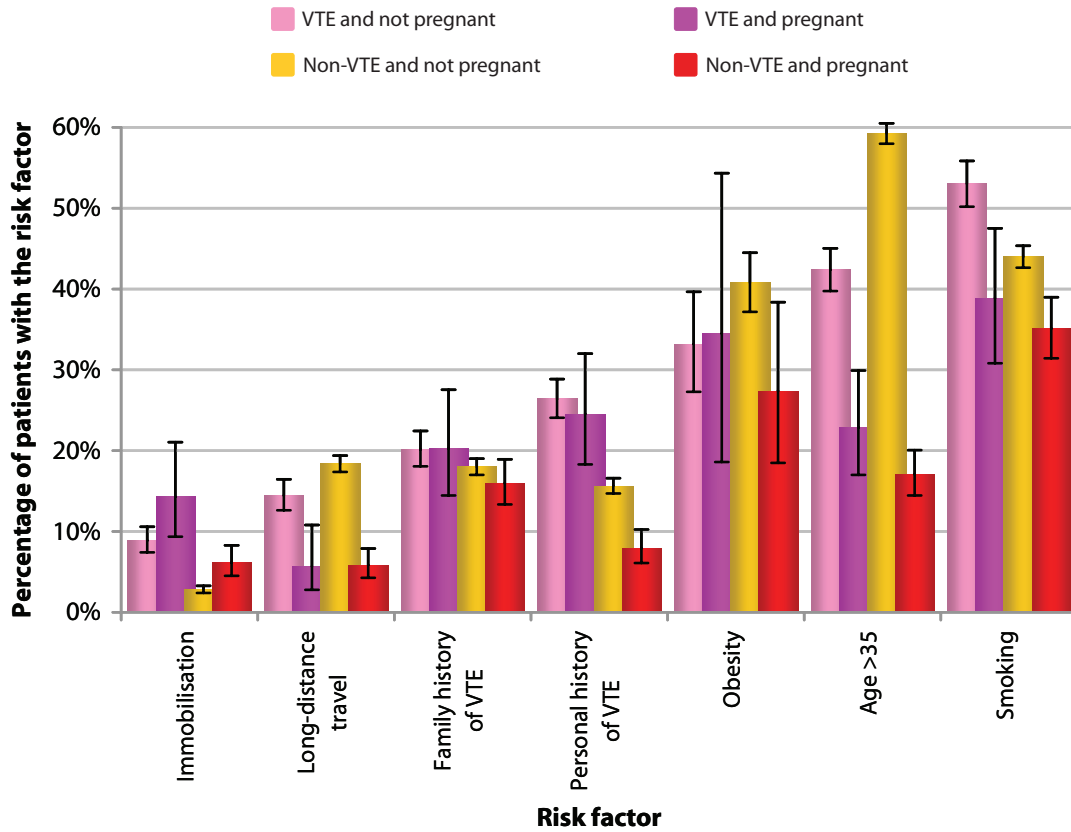
Pregnancy

**Final diagnosis and pregnancy (n=6,249)**



The graph below compares 4 different populations of women to investigate further the risk factors for VTE in pregnancy. The graph compares pregnant and non-pregnant women with and without a diagnosis of VTE. Comparing smoking rates in women with VTE, we can see that smoking is significantly under-represented as a positive risk factor for VTE in pregnant women. However, in women with VTE, there is no difference in a personal history of VTE or obesity in pregnant and non-pregnant women.

**Risk factor presence according to the patient's final diagnosis and recorded pregnancy status; female patients only**

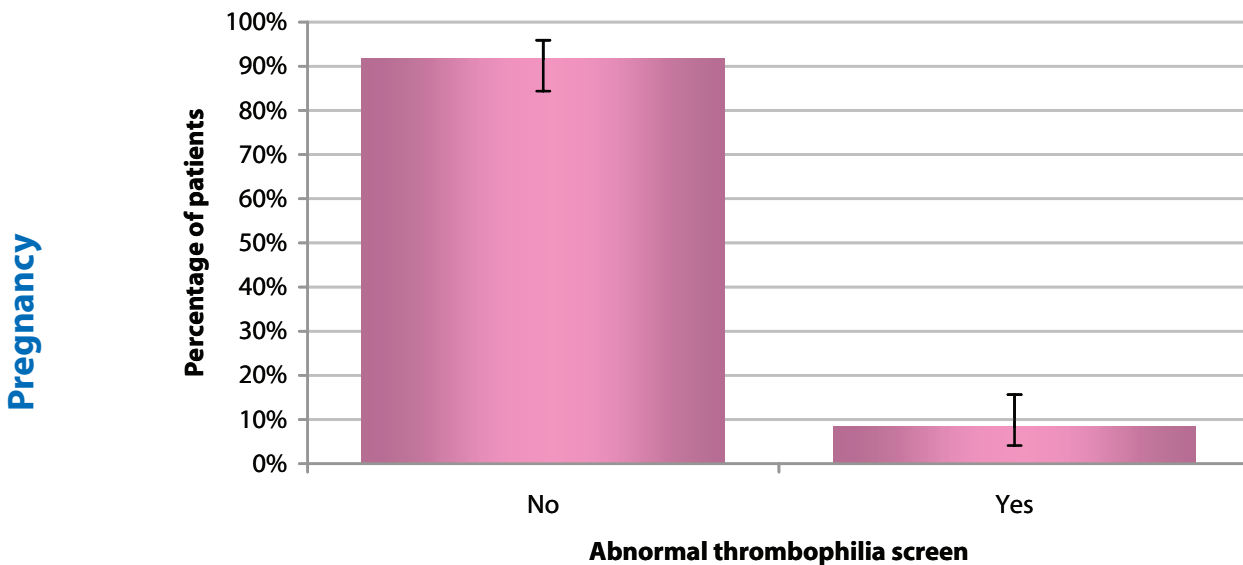


Pregnancy

Recurrence risk is increased in pregnant women who have already suffered from VTE<sup>4,5</sup>, and is higher in women with thrombophilia or following idiopathic events<sup>5,6,7,8</sup>. A higher prevalence of combined and homozygous thrombophilic defects has been found in women with VTE during pregnancy compared with age-matched women without previous VTE<sup>9</sup>. Very recently, the TREATS study found the highest risk in pregnancy was found for factor V Leiden (FVL) and VTE; in particular, homozygous carriers of this mutation are approximately 34 times more likely to develop VTE in pregnancy than non-carriers. Significant risks for individual thrombophilic defects were also established for early, recurrent and late pregnancy loss; pre-eclampsia; placental abruption; and intrauterine growth restriction<sup>10</sup>.

In the new database, of those pregnant women for whom we know their previous VTE status (n=170), 10 women have had a prior thromboembolic event in a previous pregnancy and of these women, 5 women have suffered a further VTE event in this pregnancy. Although these numbers are small, it helps us begin to form a picture of prior VTE in pregnancy as a risk factor. This graph shows that about 9% of pregnant women in VERITY for whom we know if the thrombophilia screen was completed have an abnormal finding. Reviewing these numbers in more detail, the pregnancy thrombophilia screen question was completed in 53 cases; 4 pregnant women had an abnormal screen and 3 were confirmed with VTE. It is difficult to interpret the meaning of these results further, but they do confirm that of those found to have thrombophilia, a high percentage were confirmed to have VTE.

**Thrombophilia screen results for pregnant / post partum patients (n=108)**



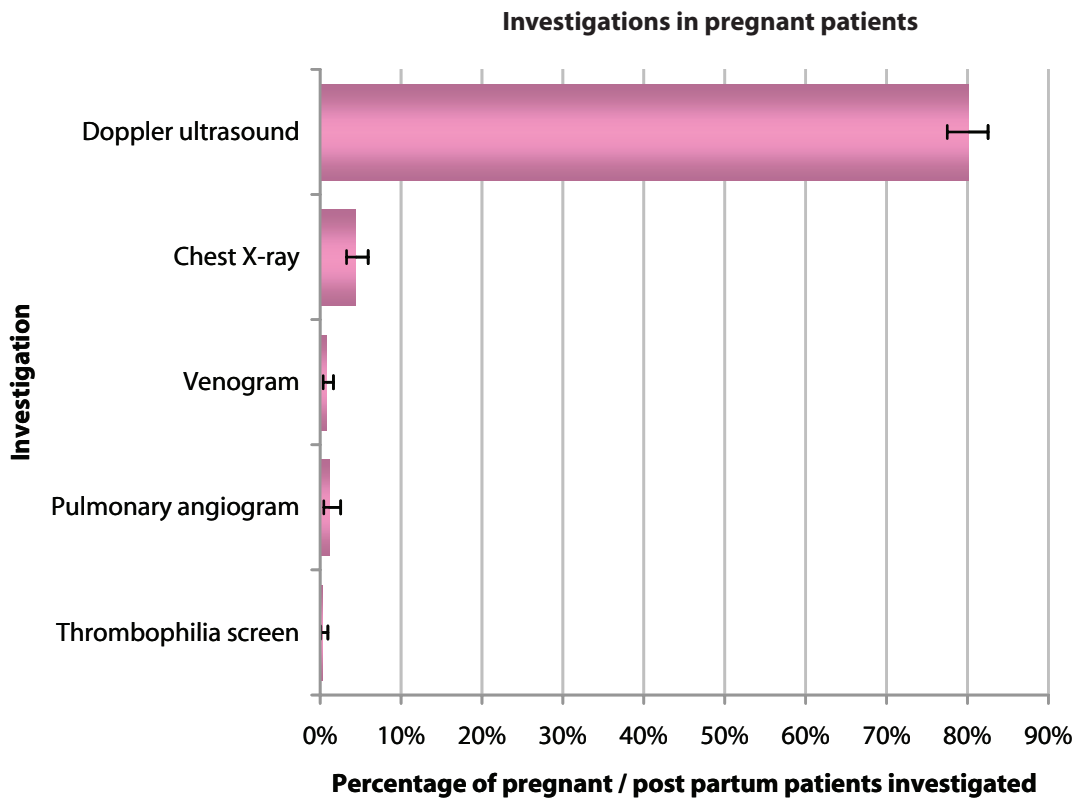
### Diagnosis and pregnancy

As previously described and as expected, duplex ultrasound is the main diagnostic tool for VTE in pregnancy, and was performed in a very high proportion (80%) of pregnant women in the database.

### Investigations and pregnancy

A key finding is the lack of additional diagnostic tests, particularly those used in the diagnosis of PE. These data show that only 6 pulmonary angiograms were performed, despite the fact that there are 28 cases of PE in pregnant women. Again we emphasise that it is important to fully investigate PE in pregnancy and not base the diagnosis on signs and symptoms and inference. PE diagnostic tests such as CTPA present a low risk of radiation exposure to the abdomen and therefore should not pose a significant threat to the foetus, and should not be avoided.

		Investigation performed			
		No	Yes	Unspecified	All
Investigation	Doppler ultrasound	198	799	43	1,040
	Chest X-ray	953	44	43	1,040
	Pulmonary angiogram	531	6	503	1,040
	Venogram	988	8	44	1,040
	Thrombophilia screen	993	3	44	1,040



Pregnancy

**Use and doses of LMWH**

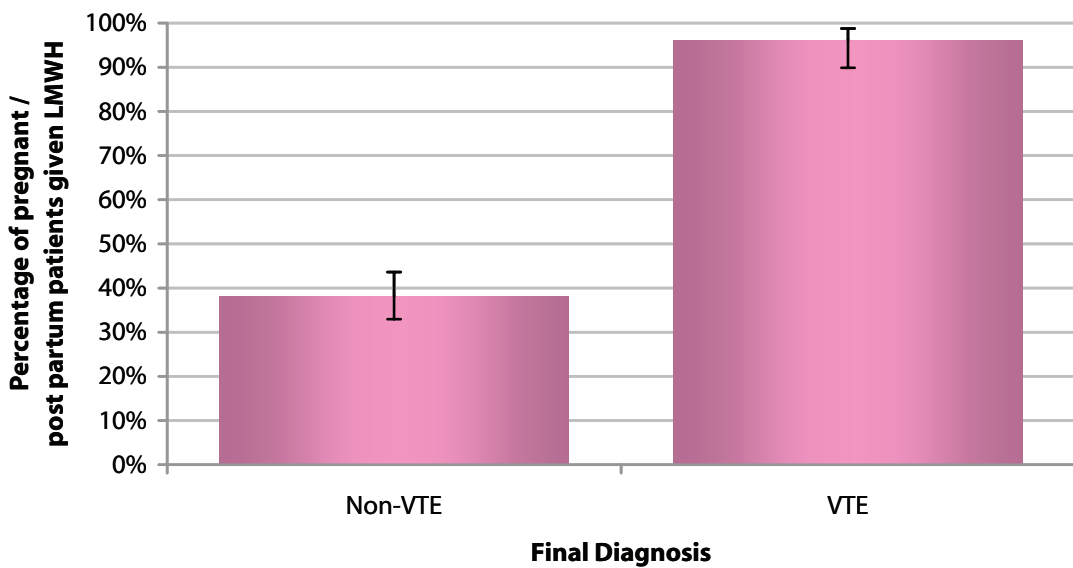
These data below confirm the previous VERITY finding that LMWH is being commenced in pregnant patients with suspected VTE while awaiting confirmation of diagnosis, with almost 40% of patients with suspected but unconfirmed VTE receiving treatment. In at least a proportion of patients, this heparin treatment will reflect heparin thromboprophylaxis because of the woman’s risk profile. LMWH was given to more than 95% of pregnant women with VTE.

**Doses of LMWH**

An interesting finding from the new database is that there has been a large increase in the proportion of patients receiving LMWH for longer duration compared with the findings presented in the last report. The average number of doses of LMWH was almost 50 in the new database. The patient numbers are small, but this change in practice will be investigated further and reported on the VERITY website.

		Final diagnosis			
		Non-VTE	VTE	Unspecified	All
LMWH used	No	206	4	30	<b>240</b>
	Yes	127	100	33	<b>260</b>
	Unspecified	393	71	76	<b>540</b>
	All	726	175	139	<b>1,040</b>

**LMWH use and final diagnosis for pregnant patients (n=437)**



Pregnancy

**RCOG guideline 37 Thromboprophylaxis during pregnancy, labour and after vaginal delivery**

All women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital or develops other intercurrent problems. C

Women with previous VTE should be screened for inherited and acquired thrombophilia, ideally before pregnancy. B

Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided. ✓

Women with previous VTE should be offered *post partum* thromboprophylaxis with LMWH. It may be reasonable not to use antenatal thromboprophylaxis with heparin in women with a single previous VTE associated with a temporary risk factor that has now resolved. C

Women with previous recurrent VTE or a previous VTE and a family history of VTE in a first-degree relative should be offered thromboprophylaxis with LMWH antenatally, and for at least six weeks *post partum*. B

Women with asymptomatic inherited or acquired thrombophilia may qualify for antenatal or postnatal thromboprophylaxis, depending on the specific thrombophilia and the presence of other risk factors. C

Women with three or more persisting risk factors should be considered for thromboprophylaxis with LMWH antenatally and for three to five days *post partum*. ✓

Women should be reassessed before or during labour for risk factors for VTE. Age over 35 years and BMI greater than 30 or body weight greater than 90 kg are important independent risk factors for *post partum* VTE even after vaginal delivery. The combination of either of these risk factors with any other risk factor for VTE (such as pre-eclampsia or immobility) or the presence of two other persisting risk factors should lead the clinician to consider the use of LMWH for three to five days *post partum*. ✓

Antenatal thromboprophylaxis should begin as early in pregnancy as practical. *Post partum* prophylaxis should begin as soon as possible after delivery (but see precautions after use of regional anaesthesia). B

LMWHs are the agents of choice for antenatal thromboprophylaxis. They are as effective as and safer than unfractionated heparin in pregnancy. B

Warfarin should usually be avoided during pregnancy. It is safe after delivery and during breast-feeding. B

Once the woman is in labour or thinks she is in labour, she should be advised not to inject any further heparin. She should be reassessed on admission to hospital and further doses should be prescribed by medical staff. ✓

## **Conclusions**

Pregnancy-related VTE remains an emotive topic, with the feeling that any VTE event, but particularly death from VTE, could have been prevented with effective risk assessment and appropriate thromboprophylaxis. However, it is important to realise that the risk factor profile of pregnant patients with VTE is not fully characterised, the interaction between VTE risk factors not fully understood, and the optimal thromboprophylaxis strategy is not fully investigated and defined.

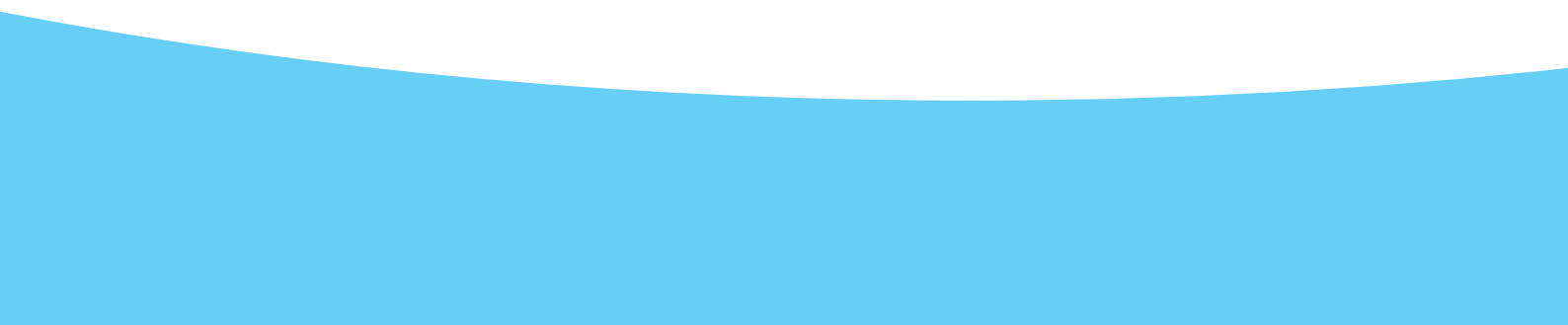
The VERITY data show that fewer pregnant patients with VTE smoke than non-pregnant patients with VTE, which suggests that smoking is not particularly associated with VTE in pregnant women. This contrasts with recent findings that smoking appeared to be an independent risk factor for VTE during pregnancy and the *puerperium*, and other studies, such as a large Swedish register study, found a tobacco consumption-dependent increase in the risk of VTE among pregnant smokers <sup>11</sup>, and a population based case-control study from North America among women with a first lifetime VTE during pregnancy or *post partum* found that smoking was an independent risk factor for VTE <sup>12</sup>.

There is controversy in the literature over the adequacy of testing for thrombophilia in pregnant patients with VTE. The number of cases with this risk factor recorded are quite low in VERITY and because of this, we were not able to confirm either an increased frequency of thrombophilia in VTE cases compared to non-pregnant patients in the same age range, or an increase in the frequency of VTE in cases of confirmed thrombophilia; nonetheless, of the 4 pregnant women with an abnormal thrombophilia screen, 3 were confirmed with VTE, in keeping with the view that thrombophilia is an important risk factor in pregnant women.

For the prevention of VTE in pregnant women, a management strategy of risk assessment, followed by heparin prophylaxis at an intensity and duration defined by the level of perceived venous thromboembolic risk, is the suggested approach.

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# Appendices

### **VERITY database form**

The remit of the VERITY database has expanded beyond its original intent to facilitate the collection of data on patients presenting with suspected venous thromboembolism to specialist VTE assessment clinics in the UK. In response to users' requests, the database fields record more detail, in particular, on steps taken to prevent thrombosis, and additional data are recorded on warfarin anticoagulation.

The following form documents all the database fields in the VERITY database at the time the data were harvested for this report. This current version of the database reflects major changes that were introduced at the end of 2005. The changes were made in an attempt to improve and simplify the whole VERITY experience for the front-line user; readers are referred to the VERITY Report 2004 for a record of the database fields employed in the collection of the majority of the data used in this VERITY Report 2005.

These forms offer an insight into the scope and depth of the database and demonstrate that the analyses presented in this report are just a sample of the analyses that are be possible.

**VERITY**  
**Database form**  
**Version 3.1; page 1**

Hospital number	<input type="text"/>	Date of birth	<input type="text" value="dd / mm / yyyy"/>
Given name	<input type="text"/>	Family name	<input type="text"/>
Gender	<input type="radio"/> Male <input type="radio"/> Female <input type="radio"/> Unknown		

**Referral and risk factors**

Date of referral	<input type="text"/>		
Source of referral	<input type="radio"/> GP <input type="radio"/> Medical <input type="radio"/> Nursing home <input type="radio"/> A & E <input type="radio"/> In-hospital <input type="radio"/> Self <input type="radio"/> Surgical <input type="radio"/> Obstetrics <input type="radio"/> Other		
Out-of-hours consultation	<input type="radio"/> No <input type="radio"/> Yes		
Consultant responsible	<input type="text"/>		
Recent immobilisation <sup>1</sup>	<input type="radio"/> No <input type="radio"/> COPD / Resp failure <input type="radio"/> MI <input type="radio"/> IHD <input type="radio"/> Ischaemic stroke <input type="radio"/> Other <input type="radio"/> Heart failure <input type="radio"/> Severe infection <input type="radio"/> Unspecified		
Major surgery within the last 4 weeks	<input type="radio"/> No <input type="radio"/> Vascular <input type="radio"/> Urology <input type="radio"/> Orthopaedic <input type="radio"/> Cardiac <input type="radio"/> Other <input type="radio"/> General <input type="radio"/> Gynae		
Smoking history	<input type="radio"/> Never <input type="radio"/> Ex-smoker <input type="radio"/> Current smoker		
Hormonal risk factor	<input type="radio"/> No <input type="radio"/> Post partum <input type="radio"/> OCP <input type="radio"/> Pregnant <input type="radio"/> HRT <input type="radio"/> Other		
History of thrombophilia	<input type="radio"/> No <input type="radio"/> Yes		
Family history of VTE	<input type="radio"/> No <input type="radio"/> Yes		
Personal history of VTE	<input type="radio"/> No <input type="radio"/> Yes		
History of long-distance travel	<input type="radio"/> No <input type="radio"/> Flight <input type="radio"/> Car <input type="radio"/> Other		
Duration of long-distance travel	<input type="radio"/> Not applicable <input type="radio"/> 1-4 <input type="radio"/> 6-8 <input type="radio"/> 5-6 <input type="radio"/> >8		
Leg paralysis <sup>2</sup>	<input type="radio"/> No <input type="radio"/> Yes		
Cancer <sup>3</sup>	<input type="radio"/> No <input type="radio"/> Yes		
IV drug user	<input type="radio"/> No <input type="radio"/> Yes		

<sup>1</sup> Medical inpatient / immobilisation >3 days within the last 4 weeks

<sup>2</sup> Leg paralysis / fracture / plaster

<sup>3</sup> Cancer - currently or treatment in the last 6 months

This form is laid out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.



Hospital number  Date of consultation

**Diagnosis and treatment**

1° suspected diagnosis  DVT  PE  DVT & PE

Alternate diagnosis to DVT  More likely  Less likely

DVT PTP score  PE PTP score

Signs / symptoms of DVT

<input type="radio"/> None	<input type="checkbox"/> Unilateral pitting oedema
<input type="checkbox"/> Entire leg swollen	<input type="checkbox"/> Tenderness over deep veins
<input type="checkbox"/> Calf swelling >3 cm	<input type="checkbox"/> Dilated superficial veins

Initial investigations

<input type="radio"/> None	<input type="checkbox"/> Venogram
<input type="checkbox"/> D-dimer	<input type="checkbox"/> Plethysmyography / LRR
<input type="checkbox"/> Doppler ultrasound	<input type="checkbox"/> Abdominal ultrasound
<input type="checkbox"/> Chest X-ray	<input type="checkbox"/> Thrombophilia screening

Date of chest X-ray

Results of chest X-ray  Normal  Abnormal - consistent with PE  
 Abnormal - unrelated to PE

Date of doppler

Results of doppler  Normal  Positive  
 Indeterminate  Other

Date of repeat doppler

Results of repeat doppler  Normal  Positive  
 Indeterminate  Other

Date of D-dimer assay

D-dimer assay test  Lab method  Simplify  
 SimpliRed  Unspecified

Results of D-dimer assay  Negative  Positive

Date of venogram

Results of venogram  Negative  Positive

Date of plethysmyography

Results of plethysmyography / LRR  Normal  Positive  
 Indeterminate  Other

This form is layed out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.

**VERITY**  
**Database form**  
**Version 3.1; page 3**

Hospital number  Date of consultation

**Diagnosis and treatment / cont...**

Date of abdominal u'sound

Results of abdominal ultrasound  
 Normal  
 Indeterminate  Positive  Other

Thrombophilia screen date

Results of screen  
 Normal  Genetic thrombo'

Final diagnosis  
 DVT  DVT & PE  PE  
 DVT excluded  Musculoskeletal  Infection  
 Other

**Pulmonary embolus data**

Breathlessness  No  Yes

Haemoptysis  No  Yes

Pleuritic pain  No  Yes

Pulse rate  Oxygen saturation

Breathing rate

Alternate diagnosis to PE  More likely  Less likely

PE investigations  
 None  CT scan  VQ scan  
 Pulmonary angio  CXR

Date of CT scan

Results of CT scan  Negative  Positive

Date of VQ scan

Results of VQ scan  
 Normal  Indeterminate  
 Low  Medium  High

Date of pulmonary angio

Results of pulmonary angio  Negative  Positive  Indeterminate

Location where patient managed  
 A & E  Outpatient clinic  
 GP  MAU

This form is layed out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.



VERITY  
Database form  
Version 3.1; page 4

Hospital number  Date of consultation

**Cancer**

Type of cancer

<input type="radio"/> Not applicable	<input type="checkbox"/> Lung	<input type="checkbox"/> Colorectal
<input type="checkbox"/> Breast	<input type="checkbox"/> Leukaemia	<input type="checkbox"/> Lymphoma
<input type="checkbox"/> Prostate	<input type="checkbox"/> Pancreas	<input type="checkbox"/> Head & neck
<input type="checkbox"/> Melanoma	<input type="checkbox"/> CNS	<input type="checkbox"/> Non-melanoma skin
<input type="checkbox"/> Myeloma	<input type="checkbox"/> Urological	<input type="checkbox"/> Bone / sarcoma
<input type="checkbox"/> Gynaecological	<input type="checkbox"/> Upper GI	<input type="checkbox"/> Other
<input type="checkbox"/> Endocrine		

Date of cancer diagnosis

Active treatment  No  Yes

Type of treatment  Radiotherapy  Chemotherapy  Surgery  
 Other drug

Type of drug treatment  Planned duration of anticoagulation

Type of anticoagulation<sup>1</sup>  Warfarin  LMWH HD / RT-LT  LMWH HD-LT  LMWH RD-LT

**Pregnant patients**

Is the patient  Pregnant  Post partum

History of VTE in pregnancy  No  Yes  
Abnormal thrombophilia screen  No  Yes

Gestation at diagnosis  Intended duration of anticoagulant treatment

Type of anticoagulant treatment  Warfarin only  LMWH only  Warfarin + LMWH  UFH

<sup>1</sup> LMWH = Low Molecular Weight Heparin; HD = High dose; RD = Reduced dose; LT = long term

This form is laid out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.

**VERITY**  
**Database form**  
**Version 3.1; page 5**

Hospital number  Date of consultation

**Medical or surgical risk**

Inpatient medical admission  No  Yes

Type of medical admission

<input type="checkbox"/> CVS - angina / MI	<input type="checkbox"/> CNS - other
<input type="checkbox"/> CVS - heart failure	<input type="checkbox"/> Musculoskeletal
<input type="checkbox"/> CVS - other	<input type="checkbox"/> GI - IBD
<input type="checkbox"/> Respiratory - COAD	<input type="checkbox"/> GI - infective
<input type="checkbox"/> Respiratory - pneumonia	<input type="checkbox"/> GI Other
<input type="checkbox"/> Respiratory - other infective	<input type="checkbox"/> Urological - infective
<input type="checkbox"/> Respiratory - other	<input type="checkbox"/> Urological - other
<input type="checkbox"/> CNS - stroke	<input type="checkbox"/> Other

Inpatient surgical admission  No  Yes

Type of surgical admission

<input type="checkbox"/> Orthopaedic - THR	<input type="checkbox"/> General - other
<input type="checkbox"/> Orthopaedic - TKR	<input type="checkbox"/> Urology - transurethral
<input type="checkbox"/> Orthopaedic - hip failure	<input type="checkbox"/> Urology - other
<input type="checkbox"/> Orthopaedic - major limb	<input type="checkbox"/> Vascular
<input type="checkbox"/> Orthopaedic	<input type="checkbox"/> Gynaecological
<input type="checkbox"/> Orthopaedic - other	<input type="checkbox"/> Neurosurgical
<input type="checkbox"/> General - abdominal	<input type="checkbox"/> Cardiac
<input type="checkbox"/> General - laparoscopic	<input type="checkbox"/> Other

Length of admission

Patient given thromboprophylaxis  No  Yes Patient on long term aspirin  No  Yes

Type of pharmacological thromboprophylaxis given

<input type="radio"/> LMWH - 20 mg / 2,000-3,000 iu	<input type="radio"/> UFH
<input type="radio"/> LMWH - 40 mg / 3,000-5,000 iu	<input type="radio"/> Aspirin only
<input type="radio"/> LMWH - other	<input type="radio"/> Other

LMWH other details  Other details

Type of mechanical thromboprophylaxis given

<input type="radio"/> None	<input type="radio"/> Stockings
<input type="radio"/> Compression device	<input type="radio"/> Other

This form is layed out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.



Hospital number  Date of consultation

**Acute follow up**

Clexane treatment  No  Yes

Clexane prescribed by  GP  Pharmacy  Not known  
 Hospital doctor  Nurse

Date Clexane started  Date Clexane stopped

Number of Clexane doses

Date Warfarin started  Date INR therapeutic

Daily INR 'til therapeutic

<input type="text" value="day 1"/>	<input type="text" value="day 4"/>	<input type="text" value="day 7"/>
<input type="text" value="day 2"/>	<input type="text" value="day 5"/>	<input type="text" value="day 8"/>
<input type="text" value="day 3"/>	<input type="text" value="day 6"/>	<input type="text" value="day 9"/>

Warfarin monitoring  GP  Pharmacy  Not known  
 Hospital clinic  Nurse

Warfarin loading regime used  Fennerty<sup>i</sup>  Low dose - Glasgow<sup>iii</sup>  Intermediate dose<sup>v</sup>  
 Dobranski<sup>ii</sup>  Low dose - St Peters<sup>iv</sup>

Intended duration of warfarin treatment  <1 month  4-6 months  Life-long  
 1-3 months  >6 months

If patient not started on warfarin reason why

This VTE whilst on warfarin  No  Yes

Patient treated at home  No  Yes

Why was patient not treated at home

<input type="radio"/> Elderly / infirm	<input type="radio"/> Non-compliant
<input type="radio"/> Additional monitoring required	<input type="radio"/> Other serious illness
<input type="radio"/> Bleeding disorders	<input type="radio"/> GI bleed
<input type="radio"/> Cancer	<input type="radio"/> Pregnancy
<input type="radio"/> Immobility	<input type="radio"/> Social reasons
<input type="radio"/> Other serious illness	

Date of initiation of outpatient treatment  Date discharged from DVT service

- i. Fennerty: 10 mg loading two doses
- ii. Dobranski
- iii. Low dose Glasgow: 5 mg loading for 3 days
- iv. Low dose - St Peters: Male patients: 6 mg daily for 5 days; Female patients: 4-5 mg daily for 5 days
- v. Intermediate dose: 7 mg daily for 3 days used post partum

This form is layed out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.

**VERITY**  
**Database form**  
**Version 3.1; page 7**

Hospital number  Date of follow up event

**Long term follow up**

VTE complication

<input type="radio"/> None	<input type="radio"/> Re-thrombosis
<input type="radio"/> Contralateral DVT	<input type="radio"/> Extension of thrombosis
<input type="radio"/> Secondary PE after DVT	<input type="radio"/> Other

Bleeding complications

<input type="radio"/> None	<input type="radio"/> Major
<input type="radio"/> Minor	

Heparin induced thrombocytopenia

<input type="radio"/> No	Patient admitted as a result of this complication	<input type="radio"/> No
<input type="radio"/> Yes		<input type="radio"/> Yes

New diagnosis of cancer following VTE

<input type="radio"/> None	<input type="checkbox"/> Lung	<input type="checkbox"/> Colorectal
<input type="checkbox"/> Breast	<input type="checkbox"/> Leukaemia	<input type="checkbox"/> Lymphoma
<input type="checkbox"/> Prostate	<input type="checkbox"/> Pancreas	<input type="checkbox"/> Head & neck
<input type="checkbox"/> Melanoma	<input type="checkbox"/> CNS	<input type="checkbox"/> Non-melanoma skin
<input type="checkbox"/> Myeloma	<input type="checkbox"/> Urological	<input type="checkbox"/> Bone / sarcoma
<input type="checkbox"/> Gynaecological	<input type="checkbox"/> Upper GI	<input type="checkbox"/> Other
<input type="checkbox"/> Endocrine		

Patient still anticoagulated

<input type="radio"/> No	<input type="radio"/> Yes
--------------------------	---------------------------

Post anticoagulation D-dimer performed

<input type="radio"/> No
<input type="radio"/> Yes

Patient status

<input type="radio"/> Alive	Cause of death	<input type="text"/>
<input type="radio"/> Dead		

This form is laid out so that questions requiring a single response are identified by round radio buttons next to the options, whereas questions where more than one response may be selected are identified by square tick-boxes next to the options.

## Appendices

### Pre-test probability

#### Deep vein thrombosis pre-test probability

A clinical model for predicting pre-test probability for deep vein thrombosis <sup>i</sup>

Clinical feature	Score
Active cancer (treatment ongoing or within 6 months or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for more than 3 days or major surgery within 4 weeks	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling >3cm asymptomatic leg (10 cm below tibial tuberosity)	1
Pitting oedema (greater in symptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Alternative diagnosis as likely or greater than that of deep vein thrombosis	-2

Low probability	≤0
Moderate probability	1-2
High probability	≥2

In patients with symptoms in both legs the more symptomatic leg is assessed.

#### Pulmonary embolus pre-test probability

Variables used to determine pre-test probability score in patients with suspected pulmonary embolism <sup>ii</sup>

Clinical feature	Score
Clinical signs / symptoms of DVT (leg swelling / pain with palpation of deep veins)	3
An alternative diagnosis is less likely	3
Heart rate >100 bpm	1.5
Immobilisation or surgery in the previous 4 weeks	1.5
Previous deep-vein thrombosis / pulmonary embolism	1.5
Haemoptysis	1
Malignancy (at treatment, treated in the last 6 months or palliative)	1

Low probability	<2
Moderate probability	2-6
High probability	>6

- i. Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, *et al.* Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet* 1997; **350** (9094): 1795-1798.
- ii. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, *et al.* Derivation of a simple clinical model to categorise patients probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer. *Thromb Haemostat* 2000; **83** (3): 416-420.

### A new weighted risk score

A clinical model for predicting pre-test probability for deep vein thrombosis<sup>1</sup>

Clinical feature	Score
Active cancer (treatment ongoing or within 6 months or palliative)	3
Personal history of venous thromboembolism	3
Thrombophilia	3
Recent major surgery	2
Advanced age (>74 years)	1
Obesity ( $\geq 30$ )	1
Medical inpatient / immobilisation >3 days within the last 4 weeks / leg paralysis	1
Hormonal therapy (oral therapy or hormone replacement therapy)	1

An increased risk of venous thromboembolism was defined as a score of 5 or more.

**Dear Colleague letter from the Chief Medical Officer**

The following text is reproduced from a *Dear Colleague* letter issued by Sir Liam Donaldson, the Chief Medical Officer, on the 19<sup>th</sup> April 2007.

Dear Colleague

**Recommendations of the expert working group on the prevention of venous thromboembolism (VTE) in hospitalised patients**

I wrote to you in July 2005 about the key findings of the Health Committee report on the Prevention of Venous Thromboembolism in Hospitalised Patients and the Government's response. The Government agreed that more needed to be done to prevent the estimated 25,000 deaths a year from this condition.

I also took the opportunity in that earlier letter to draw to your attention to a selection of the key existing guidelines that aid the prevention of venous thromboembolism in hospitalised patients (see [www.dh.gov.uk/vte](http://www.dh.gov.uk/vte) for further information).

In order to help inform the development of a comprehensive strategy, that includes both treatment and prevention of venous thromboembolism, an independent expert group was established and asked to report to me by July 2006.

I have now received the report, and the group has produced a number of recommendations on the systems and processes needed to develop a systematic approach for the prevention of VTE.

In addition, the group has made recommendations on the use of thromboprophylaxis following their assessment of existing clinical guidance and evidence on the prevention VTE, and specifically the use of mechanical devices (foot-pumps), aspirin and other pharmacological preparations (heparin or other anti-Xa agent).

As the group's terms of reference make clear, its purpose is to recommend action for implementation pending publication of National Institute for Health and Clinical Excellence (NICE) VTE clinical guidelines. The group was also asked to limit its recommendations to implementation of existing VTE guidance and good practice. It is the role of NICE to develop and publish new guidance and NICE is expected to issue its guidance on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high risk surgical procedures in April 2007. Every attempt has been made to ensure complementarity between the group's report and the forthcoming NICE guideline on this sub-group of patients.

As the expert group's recommendations are based on existing guidance and evidence, and have the potential to prevent avoidable deaths from VTE, I am taking this opportunity to bring these to your attention immediately. The VTE expert group has recommended that:

- All medical patients should, as part of a mandatory risk assessment, be considered for thromboprophylaxis measures; in particular, patients likely to be in hospital for longer than four days and with reduced mobility, with either severe heart failure, respiratory failure (due either to exacerbation of chronic lung disease or pneumonia), acute infection, inflammatory illness or cancer (with additional risk factors for VTE) should be considered for the following regime:
  - heparins (both unfractionated and low-molecular-weight forms) are effective preventive treatments. Low-molecular-weight heparins are the preferred prophylactic method;
  - aspirin is not recommended for thromboprophylaxis in medical patients;
  - mechanical methods of prophylaxis have not to date been appropriately evaluated in acutely ill medical patients, and thus are not recommended at present.

- All high risk surgical / orthopaedic patients should be managed according to the available evidence. The NICE clinical guideline on the prevention of venous thromboembolism in patients undergoing orthopaedic surgery and other high risk procedures is scheduled to be published in April 2007.
- Intermediate risk surgical patients or those with concomitant medical conditions should, as part of a mandatory risk assessment, be considered for the following thromboprophylaxis measures:
  - graduated compression stockings combined with heparins (both unfractionated or low-molecular-weight forms)
  - aspirin is not recommended for thromboprophylaxis in intermediate risk surgical patients.
- Low risk surgical patients do not require specific prophylaxis other than early mobilisation because of duration or nature of surgical procedure unless other factors are present which increase overall risk and thus place them in intermediate or high risk categories.
  - aspirin is not recommended for thromboprophylaxis in low risk surgical patients.

An electronic copy of the report and separate annexes is available to view and download at [www.dh.gov.uk/vte](http://www.dh.gov.uk/vte)

Copies of *Report of the independent expert working group on the prevention of venous thromboembolism in hospitalised patients* (product code 278830) can be ordered from DH Publications, tel: 08701 555 455, email [dh@prolog.uk.com](mailto:dh@prolog.uk.com)

Yours sincerely

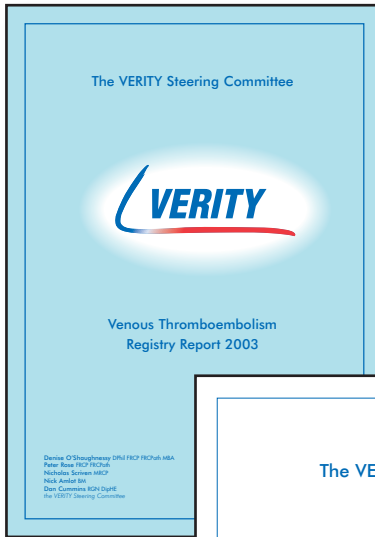
Sir Liam Donaldson  
Chief Medical Officer

### Publications from VERITY

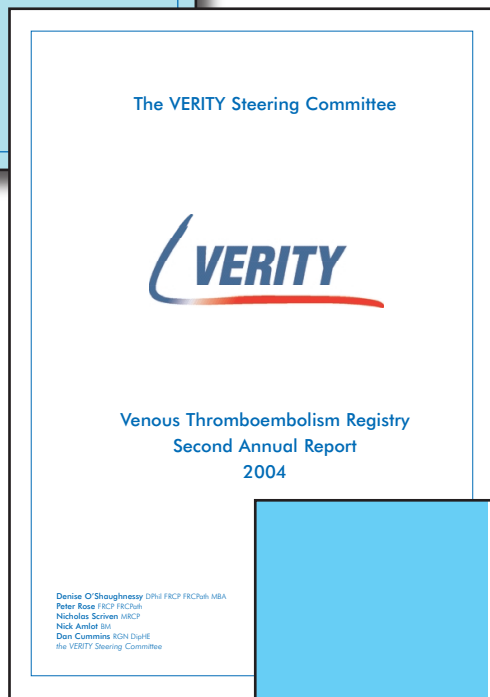
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2. O'Shaughnessy D, Rose P, Scriven N, Amlot N, Cummins D, Kinsman R. Venous thromboembolism Registry Report 2003. Henley-on-Thames: Dendrite Clinical Systems.
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5. O'Shaughnessy D, Rose P, Cummins D, Scriven N, Kinsman R, Walton P, Amlot N. Risk factor profile and outcomes of patients treated for venous thromboembolism with low molecular weight heparin (enoxaparin): Findings from the Venous thromboembolism RegIsTrY (VERITY). *Blood*. 2003; **102 (11)**: Abs 4219.
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13. O'Shaughnessy D, Rose P, Pressley F, Scriven N, Arya R, Amlot N on behalf of the VERITY investigators . Venous thromboembolism occurs commonly out-of-hospital in patients recently immobilised through surgery or illness: findings from the VERITY outpatient treatment registry. *J Thromb Haemost*. 2005; **3 (Suppl. 1)**: Abs P0471.
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Previous reports



**2003 Report**  
ISBN 1-903968-05-4



**2004 Report**  
ISBN 1-903968-08-9



**2005 Report**  
ISBN 1-903968-14-3

Appendices

**Notes**

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**Notes**

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**Notes**

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**Notes**

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