Annals of Internal Medicine | ARTICLE

# Safely Ruling Out Deep Venous Thrombosis in Primary Care

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**Background:** Up to 90% of patients referred for ultrasonography with suspected deep venous thrombosis (DVT) of the leg do not have the disease.

**Objective:** To evaluate the safety and efficiency of using a clinical decision rule that includes a point-of-care D-dimer assay at initial presentation in primary care to exclude DVT.

**Design:** A prospective management study.

**Setting:** Approximately 300 primary care practices in 3 regions of the Netherlands (Amsterdam, Maastricht, and Utrecht).

**Patients:** 1028 consecutive patients with clinically suspected DVT.

**Intervention:** Patients were managed on the basis of the result of the clinical decision rule, which included a D-dimer result. Patients with a score of 3 or less were not referred for ultrasonography and received no anticoagulant treatment; patients with a score of 4 or more were referred for ultrasonography.

**Measurements:** The primary outcome was symptomatic, objectively confirmed, venous thromboembolism during 3-month follow-up.

**Results:** The mean age of the 1028 study patients was 58 years, and 37% of patients were men. A valid score was obtained in 1002 patients (98%). In 500 patients (49%), with a score of 3 or less, 7 developed venous thromboembolism within 3 months (incidence, 1.4% [95% CI, 0.6% to 2.9%]). A total of 502 patients (49%) had a score of 4 or more; 3 did not have ultrasonography. Ultrasonography showed DVT in 125 patients (25%), for an overall prevalence in evaluable patients of 13% (125 of 1002). Of the 374 patients who had normal ultrasonography results, 4 developed venous thromboembolism within 3 months (1.1% [CI, 0.3% to 2.7%]).

**Limitation:** The study lacked a randomized design and relied on clinical follow-up to detect missed thrombotic disease.

**Conclusion:** A diagnostic management strategy in primary care by using a simple clinical decision rule and a point-of-care D-dimer assay reduces the need for referral to secondary care of patients with clinically suspected DVT by almost 50% and is associated with a low risk for subsequent venous thromboembolic events.

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Each year, more than 140 000 persons in the United Kingdom present to their primary care physician with signs and symptoms suggestive of deep venous thrombosis (DVT) of the leg (1, 2). Because DVT is a potentially life-threatening disorder, current practice is to refer all patients for diagnostic testing services. These services are readily available, use noninvasive tests (such as, ultrasonography and D-dimer testing), and provide the referring physician with the assurance that DVT is not missed (3, 4). However, many studies have revealed that 80% to 90% of these referred patients do not have DVT (4–6). Therefore, it would be ideal to safely exclude DVT at initial presentation in a large proportion of these patients and thereby avoid referral.

The recent introduction of rapid point-of-care D-dimer assays that can be included in a specific clinical decision rule makes it possible to do a diagnostic work-up in a primary care setting (7–9). We recently found that the use of a decision rule—initially developed and validated in secondary care—was not accurate enough for primary care patients suspected of having DVT because the prevalence of thrombosis was still 2.9% among patients with a low probability (based on the Wells score and a normal quantitative D-dimer) compared with 0.9% reported in the original publication by Wells and colleagues (10, 11). Therefore, we developed and validated such a decision rule specifically for the primary care setting (10, 12) that included clinical items and the D-dimer assay result. A major difference between the rules, taking into account the additional use of D-dimer for low-probability patients in the Wells rule, is the replacement of the subjective phrase "alternative diagnosis more likely" with the more objective phrase "absence of leg trauma." In primary care, the category of low probability based on the new rule had a 0.7% prevalence for thrombosis (13). However, as Reilly and Evans (14) recently outlined, development and validation studies should be followed by a prospective impact or management study demonstrating that the rule could be used

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***Context***

Primary care physicians need office-based methods to rule out suspected deep venous thrombosis (DVT).

***Contribution***

The authors conducted a management trial of a prediction rule that uses clinical findings and a point-of-care D-dimer test to identify patients at very low risk for suspected DVT. They managed 1028 patients from approximately 300 primary care practices according to the rule, which identified nearly half (49%) to be at low enough risk to withhold imaging tests and anticoagulation treatment. In 3 months, 1.4% (95% CI, 0.6% to 2.9%) of low-risk patients had venous thromboembolism.

***Caution***

There was no control group. Authors relied on symptoms to detect subsequent venous thromboembolism.

***Implication***

Office-based methods can safely rule out DVT.

*—The Editors*

by physicians to direct care before the rule is implemented in daily practice.

Therefore, we conducted this study in a large series of consecutive patients in a primary care setting to evaluate the safety and efficiency of excluding DVT by using a clinical decision rule and a point-of-care D-dimer assay. In addition, we measured the yield of ultrasonography in the referred patients.

## METHODS

### Study Overview

In this prospective study in primary care, we managed patients suspected of having DVT by using a clinical decision rule that included a point-of-care D-dimer test. We did not refer patients with a low probability of DVT for further testing or administer treatment; we followed them for 3 months to record the incidence of venous thromboembolism (10, 12).

### Setting and Patients

We invited the affiliated general practices of the 3 academic centers (who organized the study) to participate. Approximately 300 general practitioners agreed to participate. From March 2005 to January 2007, consecutive patients who presented with clinically suspected DVT were eligible for the study on the basis of the presence of at least 1 of 3 lower extremity symptoms: swelling, redness, or pain. We excluded patients if they were younger than 18 years, received anticoagulant treatment (that is, vitamin K antagonists or low-molecular-weight heparin) at presentation, or declined to participate. We obtained written informed consent, and the local institutional review boards approved the study.

### Diagnostic Strategy

General practitioners applied a clinical decision rule, provided on a worksheet, to all study patients. This clinical decision rule was developed to safely exclude clinically suspected DVT in primary care patients. It included clinical items and a D-dimer assay result (**Table 1**) (10, 12).

Because we aimed to improve the management of patients suspected of having DVT in a primary care setting, we explicitly selected a rapid point-of-care D-dimer assay (Clearview Simplify D-dimer assay, Inverness Medical, Bedford, United Kingdom) (8, 15, 16). This allowed the general practitioner to use the decision rule outside of office hours and during house calls. We drew a capillary blood sample by using the finger-prick method (15). The test result was considered abnormal if, next to the control band, a second band appeared within 10 minutes (15). Participating physicians and their assistants received a single, brief instruction on how to use the D-dimer assay and the clinical rule.

Physicians calculated the score for each patient by using the clinical decision rule (**Table 1**) (10, 12) and managed patients accordingly. Those with a score of 3 or less did not receive anticoagulant treatment or a referral for ultrasonography, but they were instructed to contact their general practitioner if symptoms became worse. Patients with a score of 4 or greater received a referral for ultrasonography. Deep venous thrombosis was considered present when 1 of the proximal veins of the lower extremities was noncompressible on ultrasonography (4).

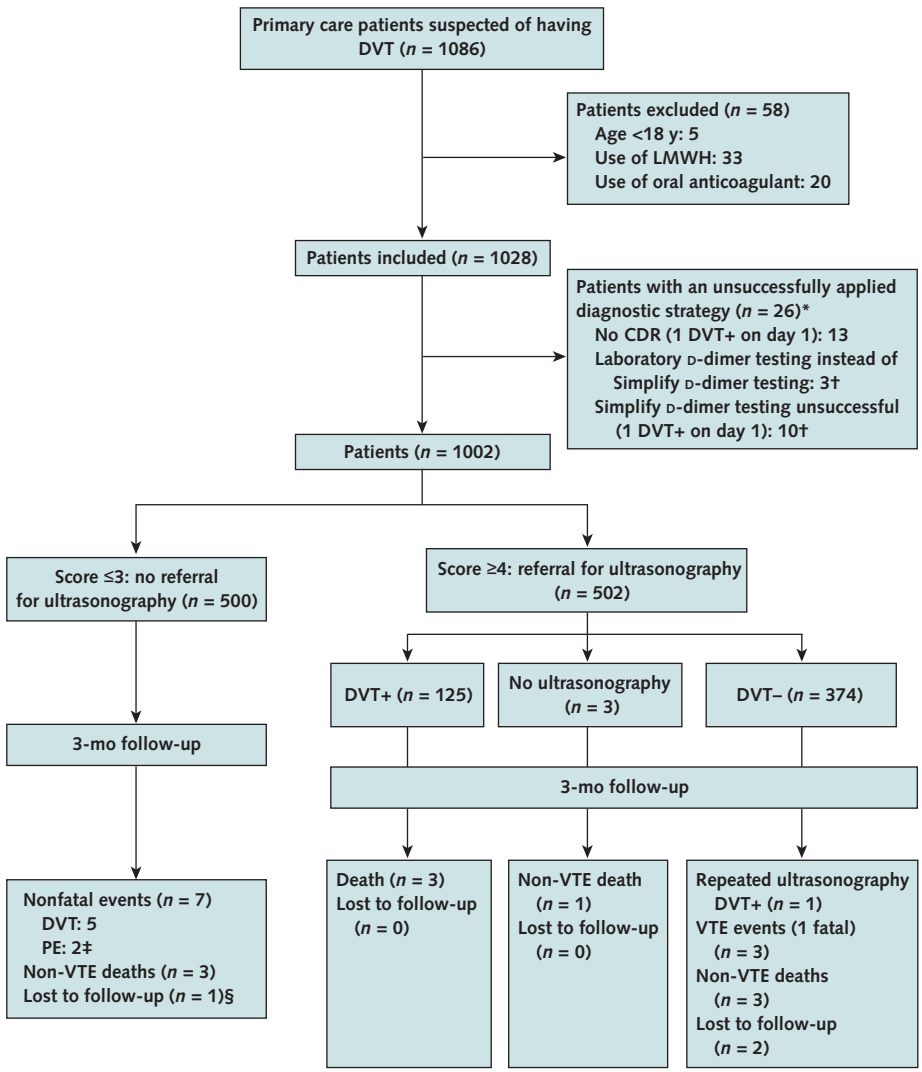
All patients visited their general practitioner between days 5 and 9 for reevaluation. Three months after entering the study, all patients received a questionnaire addressing signs and symptoms of (recurrent) venous thromboembolism. We contacted patients who did not respond (30%) through their general practitioners. If we had any suspicion of a (recurrent) venous thromboembolic event during the 3-month follow-up, based on the information presented in the questionnaire, we retrieved additional medical informa-

***Table 1.*** **Clinical Decision Rule***

| Variable | Points |
|---|---|
| Male | 1 |
| Use of hormonal contraceptives | 1 |
| Active cancer in past 6 mo | 1 |
| Surgery in previous month | 1 |
| Absence of leg trauma | 1 |
| Distention of collateral leg veins | 1 |
| Difference in calf circumference ≥3 cm† | 2 |
| Abnormal D-dimer assay (Clearview Simplify‡) result | 6 |

* Patients with a score ≤3 did not receive a referral for ultrasonography; patients with a score ≥4 did.
† Calf circumference was measured 10 cm below the tibial tubercle.
‡ Inverness Medical, Bedford, United Kingdom.

*Figure.* **Study flow diagram.**




CDR = clinical decision rule; DVT = deep venous thrombosis; DVT+ = deep venous thrombosis confirmed by ultrasonography; DVT− = deep venous thrombosis excluded by ultrasonography; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; VTE = venous thromboembolism.

* All patients were referred for ultrasonography on the day of presentation. No clinical events occurred in this group.

† Clearview Simplify D-dimer assay, Inverness Medical, Bedford, United Kingdom.

‡ Incidence of VTE, 1.4% (95% CI, 0.6% to 2.9%).

§ If the 1 patient lost to follow-up had developed VTE, the percentage missed by the procedure would have been 1.6% instead of 1.4%.

tion of patients from their general practitioners, including letters from hospital specialists.

### Outcome Measure

We defined the primary outcome as the incidence of symptomatic venous thromboembolism during 3-month follow-up. This included fatal pulmonary embolism, nonfatal pulmonary embolism, and DVT. An independent adjudication committee, unaware of the patient's result of the clinical decision rule, evaluated all suspected venous thromboembolic events and deaths. A diagnosis of pulmonary embolism or DVT was based on a priori–defined and generally accepted criteria (**Appendix Table**, available at www.annals.org) (17). Deaths were classified as "caused by pulmonary embolism" when autopsy was done if an objective test result was positive for pulmonary embolism before death or if pulmonary embolism could not be confidently excluded as the cause of death (17).

### Statistical Analysis

On the basis of an expected incidence of venous thromboembolism in 1% of patients (those with a score ≤3) during 3-month follow-up and the exclusion of a predetermined incidence of 4% or more, we calculated that 488 patients needed to be included in this low-risk group (type I error, 0.05; type II error, 0.2). The primary analysis

*Table 2.* **Demographic and Clinical Characteristics of the Study Sample (*n* = 1028)**

| Characteristic | Value |
|---|---|
| Mean age (SD), *y* | 57.7 (17.1) |
| Men, *n (%)** | 375 (37) |
| Leg symptoms, *n (%)* | |
| Pain | 874 (87) |
| Swelling | 784 (78) |
| Redness | 371 (37) |
| Absence of leg trauma, *n (%)** | 737 (73) |
| Varicose veins or venous insufficiency, *n (%)* | 337 (33) |
| Distention of collateral leg veins, *n (%)** | 151 (15) |
| Difference in calf circumference ≥3 cm, *n (%)** | 304 (30) |
| Median duration of symptoms (IQR), *d* | 5 (3–10) |
| Previous DVT, *n (%)* | 159 (15) |
| Previous PE, *n (%)* | 51 (5) |
| Paresis, *n (%)* | 13 (1) |
| Surgery in previous month, *n (%)** | 81 (8) |
| Recent immobilization, *n (%)* | 75 (7) |
| Bed rest >3 d, *n (%)* | 72 (7) |
| Active cancer in past 6 mo, *n (%)** | 54 (5) |
| Cancer not treated in the past 6 mo, *n (%)* | 64 (6) |
| Use of hormonal contraceptives, *n (%)** | 107 (10) |
| Travel (car, bus, or airplane) >4 h, *n (%)* | 90 (9) |

DVT = deep venous thrombosis; IQR = interquartile range; PE = pulmonary embolism.
* This characteristic is also part of the clinical decision rule.

was about the incidence (with exact 95% CI) of symptomatic venous thromboembolism during 3-month follow-up in the group of patients with a score of 3 or less who were not referred for further testing or treatment. In addition, we calculated the percentage of patients with a score of 3 or less. Furthermore, we calculated the probability of venous thromboembolism on leg ultrasonography at baseline or during follow-up, according to the results of the clinical decision rule without the D-dimer assay result, as well as the D-dimer assay result alone. For this purpose, a cutoff of 3 or less was also used because on the basis of this cutoff, patients with a negative D-dimer result should still receive a referral for ultrasonography.

### Role of the Funding Source

The study was funded by the Netherlands Organization for Scientific Research. The funding source had no role in the design, conduct, or reporting of the study or in the decision to submit the manuscript for publication.

## RESULTS

### Patients

We assessed 1086 consecutive patients with clinically suspected DVT. We excluded 58 patients (5.3%) because of predefined exclusion criteria (**Figure**). **Table 2** shows characteristics of the 1028 study patients, including the items of the clinical decision rule. The mean age was 58 years, and 37% were men. Suspicion of DVT that led to study inclusion was based most commonly on leg pain (87%) and leg swelling (78%).

### Results of the Clinical Decision Rule

In 500 of 1028 patients (49%), the score was 3 or less and DVT was ruled out (**Figure**). These patients did not receive referral for further testing or anticoagulant treatment. During the 3-month follow-up, 7 of 500 patients developed venous thromboembolism (incidence, 1.4% [95% CI, 0.6% to 2.9%]). **Table 3** shows details of these 7 nonfatal events.

In 502 of 1028 patients (49%), the score was 4 or greater (**Figure**). Ultrasonography was done for 499 patients and showed that 125 patients (25%) had DVT. Of the 374 patients who had a normal ultrasonogram, 4 developed venous thromboembolism during the 3-month follow-up (1.1% [CI, 0.3% to 2.7%]).

In 26 patients (2%), the rule was not completed according to protocol (**Figure**) because the physician did not complete the rule, used a laboratory D-dimer rather than a

*Table 3.* **Clinical Details of 7 Patients With CDR Scores ≤3 and a Venous Thromboembolic Event During Follow-up***

| Sex | Age, *y* | CDR Score | Positive Rule Items | Medical History | Time to Event, *d* | Event Type |
|---|---|---|---|---|---|---|
| Male | 79 | 2 | Male, absence of leg trauma | Previous TIA, use of antiplatelet drugs | 2 | DVT, popliteal vein |
| Female | 71 | 3 | Vein distention, difference in calf circumference ≥3 cm | Previous MI, use of antiplatelet drugs | 1 | DVT, popliteal vein |
| Female | 54 | 2 | Absence of leg trauma, vein distention | None | 45 | PE |
| Male | 71 | 2 | Male, absence of leg trauma | None | 7 | DVT, popliteal vein |
| Male | 52 | 2 | Male, absence of leg trauma | Previous recurrent VTE | 8 | DVT, popliteal vein |
| Female | 44 | 2 | Use of oral hormonal contraceptives, absence of leg trauma | None | 13 | DVT, popliteal vein |
| Female | 52 | 1 | Use of oral hormonal contraceptives | None | 3 | PE |

CDR = clinical decision rule; DVT = deep venous thrombosis; MI = myocardial infarction; PE = pulmonary embolism; TIA = transient ischemic attack, VTE = venous thromboembolism.
* All patients had a negative D-dimer test result.

point-of-care D-dimer, or the point-of-care D-dimer procedure was not successful. These patients received a referral for ultrasonography; 2 patients (8%) had DVT.

### Scenario Analysis

If a physician would use only the clinical characteristics of the decision rule and not refer patients with a score of 3 or less, DVT would be missed in 9.6% of patients (**Table 4**). If a physician would use only the D-dimer assay and not refer patients with a normal result, DVT would be missed in 3.4% of patients. The combination of findings thus reduced this percentage to 1.4%. Patients with a score of 4 or greater, based on clinical items, have a 35.9% probability of having DVT. Among these patients, those with a normal D-dimer result still have a 23.5% probability of having DVT, whereas probability increases to 42.6% among those with an abnormal D-dimer result.

*Table 4.* **Scenario Analysis**

| Variable | Patients, *n** | Patients With VTE, *n* | Proportion of Patients (95% CI) |
|---|---|---|---|
| **D-Dimer assay only** | | | |
| Normal | 551 | 19 | 3.4 (2–5) |
| Abnormal | 446 | 115 | 25.8 (22–30) |
| **Clinical items only, score ≤3** | 852 | 82 | 9.6 (7–12) |
| D-Dimer assay | | | |
| Normal | 500 | 7 | 1.4 (1–3) |
| Abnormal | 352 | 75 | 21.3 (19–28) |
| **Clinical items only, score ≥4** | 145 | 52 | 35.9 (28–44) |
| D-Dimer assay | | | |
| Normal | 51 | 12 | 23.5 (13–37) |
| Abnormal | 94 | 40 | 42.6 (32–53) |

VTE = venous thromboembolism.
* In 2 of 999 complete patients (those having both a D-dimer test result and clinical score) patients, it was unknown whether the score was ≥4 because of the D-dimer assay or clinical decision rule items.

## DISCUSSION

To our knowledge, our management study, in which physicians actually use the rule to direct their care, is the first to show that primary care physicians can safely rule out DVT in approximately half of their patients by using a simple clinical decision rule that includes a point-of-care D-dimer test. The observed incidence of venous thromboembolism during 3-month follow-up (1.4% [CI, 0.6% to 2.9%]) compares favorably with earlier studies that used this strategy in secondary care (**Table 5**) (8, 9, 11, 18–30). Also, in a worst-case scenario, if we considered the 1 patient (of 500) with a score of 3 or less who had no referral for ultrasonography and was lost to follow-up to have had a VTE event, the resulting hypothetical estimate of 1.6% (CI, 0.6% to 3.5%) (calculated as: [7 + 1]/500) of missed VTEs differs very little from the original estimate of 1.4% (CI, 0.6% to 2.9%). Furthermore, our findings indicate that ultrasonography in the referred patients is efficient, with confirmed thrombosis in 1 of 4 patients. The additional benefits are that the burden on diagnostic resources will diminish and that this strategy is more convenient for patients.

Limitations of our study include the lack of a randomized design and the reliance on clinical follow-up to detect missed thrombotic disease. Some other methodological aspects of our study require comment. First, in total, approximately 300 primary care physicians participated. They included a wide spectrum of consecutive patients, both during and outside office hours. The clinical characteristics of the study patients are similar to those of patients in other recent studies conducted in referral centers. Therefore, we believe that our findings can be generalized to most patients suspected of having DVT. Moreover, our strategy proved to be feasible in 97.5% of eligible patients (1002 of 1028 patients) (**Figure**). We obtained the results in the setting of a true management study, and participating health professionals received a single, concise instruction at the start of the study only, which suggests a good prospect for implementation in daily practice. The high feasibility with minimal training suggests transferability to other care settings, including nighttime care.

Second, both the clinical items and the point-of-care D-dimer test included in the tested strategy are important to rule out DVT because the number of patients with DVT missed by either component alone is unacceptably high (**Table 4**). In the presence of a high clinical score (≥4), a normal D-dimer result is unreliable, because 24% of these patients will have DVT. This observation, which is in agreement with others, emphasizes that a physician should refrain from D-dimer testing when the clinical score is high (6, 31).

Third, we needed a D-dimer assay that uses capillary whole blood, can be done in the general practitioner's office or at a patient's home, and provides an instant and easy-to-interpret outcome. As a result, we used a qualitative D-dimer assay (8, 32). The small proportion of patients (1.4% [CI, 0.6% to 2.9%]) with a low clinical score (≤3) who had VTEs (during 3-month follow-up) suggests that a safe exclusion of DVT can be reached in patients with a low clinical score (≤3) and a negative qualitative D-dimer assay result. Moreover, we obtained a low clinical score in approximately 50% of patients (502 of 1002), which suggests that a large proportion of patients can be safely spared referral for ultrasonography. Thus, the test is clinically efficient.

Fourth, the clinical decision rule that we evaluated was specifically designed for and derived in the primary care setting (10, 12). Our findings underscore the feasibility and safety of this rule.

Finally, 1 potential concern of the introduction of an easily accessible diagnostic test for outpatient use with relatively poor test characteristics is its indiscriminate use as a

*Table 5.* **Thromboembolic Outcomes During 3-Month Follow-up in Patients Suspected of Having VTE and Managed Without Anticoagulants***

| Author, Year (Reference) | Total Patients, *n* | VTE Type | Patients Who Avoided Additional Testing, *n (%)* | Clinical Probability | Total Thromboembolic Events [95% CI], *n/n (%)* | D-Dimer Test† | Prevalence of VTE in Sample, *n (%)* | Setting |
|---|---|---|---|---|---|---|---|---|
| Bates et al., 2003 (18) | 556 | DVT | 283 (51) | Low and moderate | 1/283 (0.4 [0–2.0]) | MDA | 56 (10) | Canada, tertiary care |
| Anderson et al., 2003 (19) | 1075 | DVT | 316 (29) | Low | 3/316 (1.0 [0.2–2.8]) | SimpliRED or IL Test | 195 (18) | Canada, tertiary care |
| Perrier et al., 2004 (20) | 965 | PE | 280 (29) | All | 0/280 (0.0 [0–1.1]) | VIDAS | 222 (23) | Switzerland, hospitals |
| Leclercq et al., 2003 (21) | 202 | Both | 64 (32) | Low and moderate | 0/64 (0.0 [0.0–4.6]) | TINAQUANT | 59 (29) | The Netherlands, hospital |
| Wells et al., 2001 (11) | 930 | PE | 437 (47) | Low | 2/218 (0.9 [0.1–3.3]) | SimpliRED | 86 (10) | Canada, tertiary care |
| Schutgens et al., 2003 (22) | 812 | DVT | 176 (22) | Not high | 1/176 (0.6 [0.1–3.1]) | TINAQUANT | 317 (39) | The Netherlands, hospital |
| Kearon et al., 2001 (23) | 445 | DVT | 177 (40) | Low | 1/177 (0.6 [0–3.1]) | SimpliRED | 64 (14) | Canada, tertiary care |
| Kruip et al., 2002 (24) | 234 | PE | 60 (26) | Low | 0/60 (0.0 [0–5.0]) | VIDAS | 52 (22) | The Netherlands, hospital |
| Janes and Ashford, 2001 (25) | 431 | DVT | 98 (23) | Low | 1/98 (1.0 [0.3–5.6]) | SimpliRED | 93 (22) | United Kingdom, hospital |
| Ten Wolde et al., 2004 (26) | 631 | PE | 95 (15) | Low | 0/95 (0.0 [0–3.1]) | TINAQUANT | 123 (20) | The Netherlands, hospital |
| Wells et al., 2003 (9) | 556 | DVT | 218 (39) | Unlikely | 2/218 (0.9 [0.1–3.3]) | SimpliRED or IL Test | 87 (16) | Canada, tertiary care |
| Goekoop et al., 2007 (27) | 941 | PE | 450 (51) | Low | 2/450 (0.4 [0–1.1]) | VIDAS | 106 (12.3) | The Netherlands, hospital |
| Elf et al., 2008 (28) | 357 | DVT | 110 (31) | Low | 1/110 (0.9 [0.02–4.96]) | Auto Dimer (92%), NycoCard (6%), STA-LIA (2%) | 84 (23.5) | Sweden, hospital |
| Ljungqvist et al., 2008 (29) | 328 | Both | 151 (46) | Low | 0/151 (0 [0.0–2.0]) | TINAQUANT | 45 (25) | Sweden, hospital |
| van Belle et al., 2006 (30) | 3306 | PE | 1058 (32) | Unlikely | 5/1028 (0.5 [0.2–1.0]) | VIDAS or TINAQUANT | 674 (20.4) | The Netherlands, hospital |
| Büller et al., 2009 (current study) | 1028 | DVT | 500 (49) | Low | 7/500 (1.4 [0.6–2.9]) | Simplify (POC) | 125 (13) | The Netherlands, primary care |
| Total‡ | 12 797 | – | 4473 (35) | – | 26/4224 (0.6 [0.4–0.9]) | – | 2388 (18.7) | – |

DVT = deep venous thrombosis; PE = pulmonary embolism; POC = point of care; VTE = venous thromboembolism.
* Based on normal D-dimer test results and clinical probability. Data from ten Cate-Hoek and Prins (5).
† MDA and VIDAS, bioMérieux, Marcy l'Étoile, France; SimpliRED and IL Test, Agen Biomedical, Brisbane, Australia; TINAQUANT, Roche Diagnostica, Mannheim, Germany; Auto Dimer, Biopool International, Umeå, Sweden; NycoCard, Axis-Shield, Oslo, Norway; STA-LIA, Diagnostica Stago, Asnières, France; Simplify, Clearview Simplify D-dimer assay, Inverness Medical, Bedford, United Kingdom.
‡ A weighted average was calculated.

first test in a testing cascade. However, if such a test is embedded in a strategy that effectively incorporates pretest probability, it can be safely used.

Our study and its outcomes confirm the usefulness of this approach. Our findings indicate that primary care physicians now have a simple tool available to safely refute the diagnosis of DVT in a large proportion of their patients.

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*Appendix Table.* **Adjudication Criteria Used for the AMUSE Study**

| Variable | Criteria |
|---|---|
| DVT | A noncompressible proximal vein detected on CUS or an intraluminal filling defect detected on venography. |
| PE | A perfusion defect ≥75% of a segment with a local normal ventilation result (high probability); an intraluminal filling defect or a sudden cutoff of vessels >2.5 mm in diameter on pulmonary angiography; an intraluminal filling defect in segmental or more proximal branches on spiral CT; or a non–high-probability ventilation–perfusion scan in combination with any of the criteria for symptoms of occurrence or recurrence of DVT in the leg (as specified in the DVT criteria). |
| Assigned to cause of death | |
| VTE | DVT or PE documented in relation to death; PE documented by autopsy (thrombus in a pulmonary artery considered to have substantially contributed to death); death that cannot be attributed to a documented cause for which PE or DVT cannot be ruled out; if an autopsy has not been done, PE was considered likely if the clinical presentation was compatible with PE (e.g., severe hypotension and sudden dyspnea); or if death is unexplained (i.e., a patient has died unwitnessed and autopsy has not been done). |
| Bleeding | Bleeding |
| Cancer | Active cancer and clinical course compatible with cancer and without signs or symptoms indicative of PE or bleeding responsible for death. |
| Other | Signs, symptoms, and investigations strongly suggest a cause other than PE, bleeding, or cancer. |

AMUSE = Amsterdam Maastricht Utrecht Study on thromboEmbolism; CT = computed tomography; CUS = compression ultrasonography; DVT = deep venous thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.