

Prediction of Pulmonary Embolism in the Emergency Department: The Revised Geneva Score

Grégoire Le Gal, MD; Marc Righini, MD; Pierre-Marie Roy, MD; Olivier Sanchez, MD; Drahomir Aujesky, MD, MSc; Henri Bounameaux, MD; and Arnaud Perrier, MD

Background: Diagnosis of pulmonary embolism requires clinical probability assessment. Implicit assessment is accurate but is not standardized, and current prediction rules have shortcomings.

Objective: To construct a simple score based entirely on clinical variables and independent from physicians' implicit judgment.

Design: Derivation and external validation of the score in 2 independent management studies on pulmonary embolism diagnosis.

Setting: Emergency departments of 3 university hospitals in Europe.

Patients: Consecutive patients admitted for clinically suspected pulmonary embolism.

Measurements: Collected data included demographic characteristics, risk factors, and clinical signs and symptoms suggestive of venous thromboembolism. The variables statistically significantly associated with pulmonary embolism in univariate analysis were included in a multivariate logistic regression model. Points were assigned according to the regression coefficients. The score was then externally validated in an independent cohort.

Results: The score comprised 8 variables (points): age older than 65 years (1 point), previous deep venous thrombosis or pulmonary embolism (3 points), surgery or fracture within 1 month (2 points), active malignant condition (2 points), unilateral lower limb pain (3 points), hemoptysis (2 points), heart rate of 75 to 94 beats/min (3 points) or 95 beats/min or more (5 points), and pain on lower-limb deep venous palpation and unilateral edema (4 points). In the validation set, the prevalence of pulmonary embolism was 8% in the low-probability category (0 to 3 points), 28% in the intermediate-probability category (4 to 10 points), and 74% in the high-probability category (≥ 11 points).

Limitations: Interobserver agreement for the score items was not studied.

Conclusions: The proposed score is entirely standardized and is based on clinical variables. It has sustained internal and external validation and should now be tested for clinical usefulness in an outcome study.

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For author affiliations, see end of text.

In recent years, clinical probability assessment into 3 categories has become an important component of strategies for optimal diagnosis of pulmonary embolism (1–7) using noninvasive tests (3, 6). For instance, highly sensitive D-dimer assays safely rule out pulmonary embolism in patients with a low or intermediate clinical probability (7, 8), while less sensitive assays have been validated only in low-probability patients in outcome studies (1, 9). Clinical assessment has been shown to be useful for reducing the requirement for invasive tests in outcome studies (1, 2, 7, 8) and to be cost-effective (10).

The landmark Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study (11) determined the clinical probability of pulmonary embolism by clinicians' implicit global judgment on the basis of history, risk factors, physical examination, and results of simple tests. Although proven valid in subsequent management studies (2, 8, 12), that evaluation has an important limitation in its implicitness, particularly in environments where patients are managed by less experienced physicians. Therefore, investigators developed prediction rules, the most widely validated of which are the Wells score (13) and the Geneva score (14). Both rules were compared with implicit judgment and demonstrated similar accuracy (15). However, those rules also have limitations. Computation of the Geneva score (14) requires arterial blood gas values while breathing room air, a variable that was not available in 15% of the patients in the external validation sample (15). The Wells score includes the clinician's judgment of

whether an alternative diagnosis is more likely than a pulmonary embolism diagnosis (13). That criterion carries a major weight in this score and can obviously not be standardized.

Therefore, we derived a new prediction rule that is entirely based on clinical variables and is independent of physicians' implicit judgment by using a large multicenter cohort of patients admitted to the emergency department for clinically suspected pulmonary embolism (7). We also performed an external retrospective validation of this new rule in a distinct cohort of patients in the emergency department with suspected pulmonary embolism (16).

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Appendix Figures
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Context

Using clinical findings to estimate the probability of disease can help guide management decisions.

Contribution

These investigators used data from 2 independent studies to derive and validate an 8-item score for predicting pulmonary embolism in patients seen in the emergency department for suspected embolism. Items addressed age, previous thrombosis, recent surgery or fracture, malignant condition, unilateral leg pain, unilateral leg edema, hemoptysis, and heart rate. The prevalence of pulmonary embolism in patients with low, intermediate, and high scores was 8%, 28%, and 74%, respectively.

Implications

We should now assess whether using this prediction rule affects patient outcomes.

—The Editors

METHODS**Derivation Step****Patients and Study Design**

The prediction rule was derived from a multicenter prospective outcome study that was designed to evaluate a diagnostic strategy for pulmonary embolism combining clinical probability assessment, plasma D-dimer measurement, lower-limb venous ultrasonography, and helical computed tomography (CT) in the emergency department (7). Briefly, all consecutive patients admitted to the emergency departments of 3 general and teaching hospitals (Geneva University Hospital, Switzerland; University Hospital, Lausanne, Switzerland; and Angers University Hospital, Angers, France) were eligible for the study if they had suspected pulmonary embolism, defined as acute onset of new or worsening shortness of breath or chest pain without any other obvious cause. Exclusion criteria were 1) ongoing anticoagulant treatment, 2) contraindication to CT (known allergy to contrast iodine agents or risk for allergic reaction, creatinine clearance <0.50 mL/s [<30 mL/min] calculated by the Cockcroft–Gault formula [17], or pregnancy), 3) suspected massive pulmonary embolism with shock, or 4) estimated life expectancy less than 3 months. We obtained written informed consent from all patients. The ethics committee at each study site approved the study. Between October 2000 and June 2002, we screened 1280 patients with suspected pulmonary embolism. We excluded patients because of CT ($n = 258$) or protocol violations ($n = 67$). The total study sample consisted of 965 patients.

All patients underwent a standardized sequential diagnostic work-up. At admission, the physician in charge of the patient in the emergency department performed a clinical evaluation of the patient and filled out a standardized

data form. The form recorded demographic characteristics; risk factors; clinical signs and symptoms of venous thromboembolism; results of arterial blood gas analysis, electrocardiography, and chest radiography; and the likelihood of an alternative diagnosis compared with that of pulmonary embolism. It contained definitions or explanations only for potentially equivocal items. On the basis of that information, the physician assigned each patient into a clinical probability category by using the Geneva prediction rule (14) with possible override by implicit assessment (15). The physician then performed sequential tests (Appendix Figure 1, available at www.annals.org). We ruled out pulmonary embolism by 1) a D-dimer level (by enzyme-linked immunosorbent assay [Vidas DD New Assay, bioMérieux, Marcy l'Etoile, France]) less than the cutoff value of 500 $\mu\text{g/L}$; 2) negative results on lower-limb venous compression ultrasonography and helical CT in patients without high clinical probability and with a positive D-dimer test result; and 3) a negative result on pulmonary angiography in patients with high clinical probability. Finally, we ruled out pulmonary embolism in patients with inconclusive results on CT, either by a normal pulmonary angiogram; a normal ventilation–perfusion lung scan; or the combination of a low-probability ventilation–perfusion scan, a low clinical probability, and negative results on venous ultrasonography. We diagnosed pulmonary embolism by 1) a proximal deep venous thrombosis found on lower-limb ultrasonography, 2) a positive helical CT scan, 3) a positive pulmonary angiogram in patients with high clinical probability, and 4) a high-probability ventilation–perfusion lung scan in patients with inconclusive results on CT. We followed all patients for 3 months. The risk for thromboembolic events during follow-up in patients who met the criteria for absence of pulmonary embolism and who were not receiving anticoagulant therapy was 1.0% (95% CI, 0.5% to 2.1%).

Score Derivation

We evaluated all of the clinical variables in our database that are known to be potentially associated with pulmonary embolism except dyspnea and chest pain, which were the inclusion criteria in the study. We excluded hormone replacement therapy because of the recent dramatic reduction in its prescription (18). To obtain a rule entirely based on clinical variables, we did not use the results of blood gas analysis, electrocardiography, and chest radiography. We also left out the likelihood of an alternative diagnosis compared with that of pulmonary embolism to achieve an entirely standardized score. Finally, we did not evaluate variables for which more than 2% of data were missing, namely body weight, temperature, and respiratory rate.

We performed univariate analyses to select predictor variables for the multivariate model and to determine the significance and strength of the association between each

candidate predictor and pulmonary embolism. We assessed significance by using the chi-square test for nominal categorical variables and the Mann–Whitney U test for continuous variables. A 2-tailed *P* value less than 0.05 indicated statistical significance. We then categorized the continuous variables that were statistically significantly associated with pulmonary embolism, choosing the most discriminative cutoff point or points.

We included variables that were statistically significantly associated with pulmonary embolism in univariate analysis in a multivariate logistic regression model. We then removed non–statistically significant variables and calculated a regression coefficient for each statistically significant variable in the final model. We assigned points for the score according to the regression coefficients, with 1 point corresponding to a value close to the smallest regression coefficient and serving as the least common denominator for assigning point values for the score items. We then computed the score for each patient, performed a receiver-

operating characteristic (ROC) curve analysis (19), and computed the area under the ROC curve and its corresponding 95% CI. Finally, we chose the cutoff value that discriminated among the low-, intermediate-, and high-probability groups to identify 1) a low-probability group with a prevalence of pulmonary embolism of approximately 10% and 2) a high-probability group with a prevalence of pulmonary embolism more than 60%. We assessed the predictive accuracy of the final score categories by the proportion of patients with pulmonary embolism in each group.

Validation Step

Internal Validation

We performed a cross-validation procedure by splitting the sample randomly into 10 equal groups. We performed the logistic regression model on 9 groups, and we applied the resulting prediction equation to the 10th group. We repeated this procedure 10 times, rotating the

Table 1. Characteristics of the Study Sample (Derivation Sample)*

Characteristic	Missing Values, <i>n</i> (%)	Value
Patients with confirmed PE	0	222 (23.0%)
General characteristics		
Mean age	0	60.6 y (SD, 19.4)
Mean weight	83 (8.6)	72.6 kg (SD, 16.1)
Men	0	403 (41.8%)
Risk factors		
Patients with family history of DVT or PE	6 (0.6)	102 (10.6%)
Patients with personal history of DVT or PE	2 (0.2)	166 (17.2%)
Patients with known congestive heart failure	0	95 (9.8%)
Patients with previous stroke	0	29 (3.0%)
Patients with COPD	0	99 (10.3%)
Patients who had surgery, fracture, or both within 1 mo	0	67 (6.9%)
Patients who were immobile within 1 mo	0	165 (17.1%)
Patients with active malignant condition	3 (0.3)	89 (9.2%)
Patients currently using oral contraceptive	1 (0.1)	69 (7.2%)
Pregnant or postpartum patients	0	10 (1.0%)
Symptoms		
Patients with syncope	2 (0.2)	68 (7.0%)
Patients with recent cough	0	197 (20.4%)
Patients with hemoptysis	0	43 (4.5%)
Patients with dyspnea	0	637 (66.0%)
Patients with chest pain	0	681 (70.6%)
Patients with unilateral lower-limb pain	0	138 (14.3%)
Clinical examination		
General signs		
Mean central temperature	37 (3.8)	36.9 °C (SD, 0.8)
Mean heart rate	4 (0.4)	86.3 beats/min (SD, 19.7)
Mean respiratory rate	59 (6.1)	20.2 cycles/min (SD, 7.0)
Mean systolic blood pressure	6 (0.6)	140 mm Hg (SD, 23)
Mean diastolic blood pressure	7 (0.7)	81 mm Hg (SD, 15)
Signs related to PE		
Patients with chronic venous insufficiency	3 (0.3)	199 (20.6%)
Patients with varicose veins	15 (1.6)	227 (23.5%)
Patients with unilateral edema and pain on deep venous palpation	0	51 (5.3%)
Patients with abnormal chest auscultation	2 (0.2)	158 (16.4%)
Patients with neck vein distention	2 (0.2)	108 (11.2%)

* COPD = chronic obstructive pulmonary disease; DVT = deep venous thrombosis; PE = pulmonary embolism.

Table 2. The Revised Geneva Score*

Variable	Regression Coefficients	Points
Risk factors		
Age > 65 y	0.39	1
Previous DVT or PE	1.05	3
Surgery (under general anesthesia) or fracture (of the lower limbs) within 1 mo	0.78	2
Active malignant condition (solid or hematologic malignant condition, currently active or considered cured < 1 y)	0.45	2
Symptoms		
Unilateral lower-limb pain	0.97	3
Hemoptysis	0.74	2
Clinical signs		
Heart rate		
75–94 beats/min	1.20	3
≥95 beats/min	0.67	5
Pain on lower-limb deep venous palpation and unilateral edema	1.34	4
Clinical probability		
Low		0–3 total
Intermediate		4–10 total
High		≥11 total

* DVT = deep venous thrombosis; PE = pulmonary embolism.

cross-validation subset each time. We also performed ROC curve analysis.

External Validation

We validated the score in an independent cohort of patients included in a prospective outcome study that assessed the performances of a diagnostic strategy based on clinical probability, plasma D-dimer measurement, lower-limb venous ultrasonography, and multidetector helical CT for pulmonary embolism (16). We included consecutive patients admitted to the emergency departments of 3 teaching hospitals (Geneva University Hospital; Angers University Hospital; and Hôpital Européen Georges-Pompidou, Paris, France) for suspected pulmonary embolism between September 2002 and October 2003. The diagnostic algorithm was similar to that of the derivation sample study, and the diagnostic criteria for the presence and absence of pulmonary embolism were identical to those of the derivation sample (7). **Appendix Figure 2** (available at www.annals.org) shows the flow of the study in the validation set. All patients were also followed for 3 months. The risk for thromboembolic events during follow-up in patients who met the criteria for absence of pulmonary embolism and who were not receiving anticoagulant therapy was 1.0% (CI, 0.4% to 2.2%). The data collection form was identical to that used in the derivation study, allowing retrospective calculation of the score for each patient.

We assessed the calibration of the score (that is, its ability to predict a probability of pulmonary embolism cor-

responding to the observed proportion of confirmed cases of pulmonary embolism) by using the Hosmer–Lemeshow goodness-of-fit statistic. Briefly, we sorted patients from the validation sample in increasing order of their estimated probability of pulmonary embolism and then divided them into 10 groups of approximately equal numbers of patients. We compared the numbers of observed and predicted confirmed cases of pulmonary embolism in the 10 groups by using a chi-square test. A *P* value more than 0.05 indicated a non–statistically significant discrepancy between observed and predicted events. We assessed the discrimination ability of the score in the external validation data set by an ROC curve analysis. We computed the area under the ROC curve and its 95% CI. We assessed the predictive accuracy of the score by calculating the prevalence of pulmonary embolism in the 3 clinical probability categories (low, intermediate, and high). We performed statistical analyses by using SPSS software, version 12.0 (SPSS Inc., Chicago, Illinois).

Role of the Funding Sources

The 2 studies that we used in our paper were supported by grants from the Hirsch Fund of the University of Geneva, the Swiss National Research Foundation (grant 32-61773.00), the Royal College of Physicians and Surgeons of Canada (grants 97/4-T10 and 00/4-T9), La Fondation Québécoise pour le Progrès de la Médecine Interne and Les Internistes et Rhumatologues Associés de l'Hôpital du Sacré-Cœur, and the Direction of Clinical Research of the Angers University Hospital (grant 2001/021). The funding sources had no role in the design, analysis, or reporting of the study or in the decision to submit the paper for publication.

RESULTS

Table 1 presents the general characteristics of the derivation sample and the collected clinical variables. The overall prevalence of pulmonary embolism was 23.0% (222 of 965 patients).

Table 3. Calibration Assessment: Observed and Predicted Patients with and without Pulmonary Embolism in 10 Groups of Patients with Increasing Score*

Group	Patients with PE, <i>n</i>		Patients without PE, <i>n</i>		Total
	Observed	Predicted	Observed	Predicted	
1	2	3.8	64	62.2	66
2	6	7.4	66	64.6	72
3	9	11.1	87	84.8	96
4	12	13.5	70	68.5	82
5	11	8.6	35	37.4	46
6	23	18.9	69	73.1	92
7	18	19.9	57	55.1	75
8	27	21.4	41	46.6	68
9	33	33.3	42	41.7	75
10	51	54.1	26	22.9	77

* PE = pulmonary embolism.

Score Derivation

We found a statistically significant association with the diagnosis of pulmonary embolism for 10 variables: age, previous venous thromboembolism, recent surgery, active malignant condition, hemoptysis, unilateral lower-limb pain, heart rate, chronic venous insufficiency, varicose veins, and unilateral edema associated with pain provoked by deep venous palpation. Among the numerical variables, age was categorized into 2 groups (<65 years and ≥ 65 years) and heart rate was categorized into 3 groups (<75 beats/min, 75 to 94 beats/min, and ≥ 95 beats/min). We included all 10 variables in a multivariate logistic regression model. In the multivariate analysis, varicose veins and chronic venous insufficiency were not independently associated with pulmonary embolism. We assigned points for the score according to the regression coefficients obtained from the final model, including the 8 variables that independently predicted pulmonary embolism in multivariate analysis (Table 2). A regression coefficient of 0.3 corresponded approximately to 1 point. Table 2 presents the final score (the revised Geneva score) and the optimal cut-off values to reach the predefined prevalence of pulmonary embolism in each clinical probability category (see Methods).

Score Accuracy

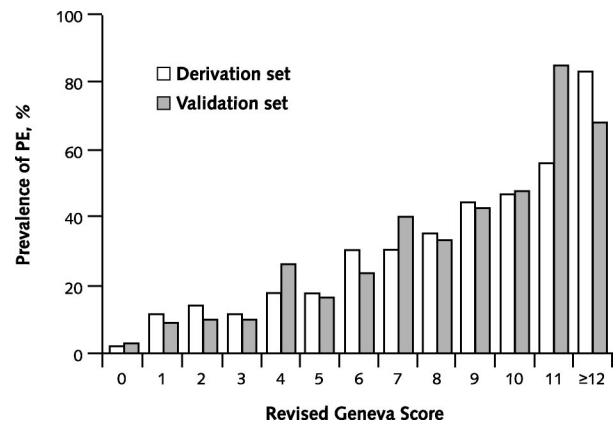
In the derivation sample, we retrospectively computed the revised Geneva score in 956 of the 965 patients (values were missing for 9 patients [0.9%]); the area under the ROC curve was 0.74 (CI, 0.70 to 0.78). In the internal cross-validation, the area under the ROC curve was 0.73 (CI, 0.69 to 0.77). In the external validation set, we could calculate the score for 749 of the 756 patients (values were missing for 7 patients [0.9%]); the area under the ROC curve was 0.74 (CI, 0.70 to 0.78).

The score also demonstrated good calibration. We split patients into 10 groups with increasing predicted probability of pulmonary embolism. The Hosmer–Lemeshow goodness-of-fit test result was nonsignificant ($P = 0.55$), indicating that the observed and predicted numbers of patients with and without pulmonary embolism did not statistically significantly differ (Table 3). The Figure shows the prevalence of pulmonary embolism according to the number of points in the derivation and validation sets. As shown in Table 4, the accuracy of the score and the proportion of patients classified into each clinical probability category were similar in the derivation and the validation samples.

DISCUSSION

In our analysis, we present a clinical prediction rule derived from a large cohort of consecutive emergency department outpatients with suspected pulmonary embolism. The score is standardized and relies exclusively on clinical information. It allows physicians to classify patients into 3 categories corresponding to an increasing prevalence of

Figure. Prevalence of pulmonary embolism (PE) according to the revised Geneva score in the derivation and validation sets.



Patients with scores ≥ 12 were pooled because of small numbers.

pulmonary embolism. In the validation sample, the prevalence of pulmonary embolism was 8%, 29%, and 74% in the low, intermediate, and high clinical probability categories, respectively (Table 3).

Is this score clinically credible? We considered all of the known main risk factors and clinical signs of venous thromboembolism for inclusion in the model. Some potentially relevant data, such as pregnancy or the postpartum period, were not statistically significantly associated with pulmonary embolism, probably because few patients in our sample had those characteristics. However, we believe that no obvious items are missing and that our score may apply to a large proportion of patients with suspected pulmonary embolism. Moreover, all the data required for the score are routinely collected in the context of suspected pulmonary embolism and are available from the patient's history and physical examination. Therefore, the score may be easy to compute. Of interest, the clinical characteristics entering in our score are very similar to those of the Canadian prediction rule for pulmonary embolism developed by Wells and colleagues (13), although we derived our score in an entirely distinct population from western Europe, hence adding content validity.

We derived our score by using a recommended method (20, 21). We clearly identified pulmonary embolism, the outcome of interest, and defined it by accepted diagnostic criteria verified by a formal 3-month follow-up. A commonly accepted rule requires that at least 10 outcome events per independent variable should be included in a prediction rule (22). In our derivation sample, 222 patients had confirmed pulmonary embolism and the final score comprised only 8 variables. Furthermore, because patients were consecutive outpatients admitted to emergency departments for suspected pulmonary embolism or were self-referred because of symptoms suggestive of pulmonary

Table 4. Proportion of Patients Classified by the Geneva Revised Score in Each Clinical Probability Category and Predictive Accuracy of the Revised Geneva Score*

Clinical Probability	Derivation Set			Validation Set		
	Patients, n (%)†	Patients with PE, n	Patients with Confirmed PE (95% CI), %	Patients, n (%)	Patients with PE, n	Patients with Confirmed PE (95% CI), %
Low	354 (37.0)	32	9.0 (6.6–12.5)	229 (30.6)	18	7.9 (5.0–12.1)
Intermediate	549 (57.4)	151	27.5 (23.9–31.4)	463 (61.8)	132	28.5 (24.6–32.8)
High	53 (5.5)	38	71.7 (58.4–82.0)	57 (7.6)	42	73.7 (61.0–83.4)
All	956	221	23.1 (20.6–25.9)	749	192	25.6 (22.6–28.9)

* PE = pulmonary embolism.

† The percentages do not add up to 100% because of rounding.

embolism, generalization of this score seems possible. We did not provide an explicit evaluation method for each collected item and we did not test interrater reproducibility of those items, which are limitations of our score. However, we precisely defined the predictors used to build the score, and they are reasonably straightforward. We used classical statistical methods: univariate analysis to screen for the association between candidate variables and pulmonary embolism, followed by a multivariate analysis that included all statistically significant predictors.

Is this score valid and accurate? Different clinicians, partially in different centers, performed external validation of the score in a cohort of patients that was entirely distinct from the derivation sample (16). As shown in **Table 3**, the score performs as well in the derivation and validation sets and allows physicians to stratify patients into 3 clinical probability groups with an increasing prevalence of pulmonary embolism. Generalizability of our score might be a concern. Indeed, data collection, diagnostic criteria, and the diagnostic algorithm in the validation data set were similar or identical to those in the derivation data set. Also, validation data came from 2 of the 3 hospitals involved in the derivation study. In fact, more than 200 residents rotating in the emergency department collected data, and the likelihood that the same physicians worked up patients in both the derivation and validation sets is extremely low. Standardization of the diagnostic algorithm and criteria minimizes misclassification bias. We applied the score to the subset of 234 patients who were recruited in the only center that was not involved in the derivation study, and we obtained nearly identical results (data not shown). The score's predictive accuracy is at least as good as that of implicit clinical judgment (2, 8, 11). It is also similar to the accuracy of the Wells rule (13), although the score does not incorporate any subjective judgment, such as the likelihood of an alternative diagnosis.

The patients from the derivation and the validation sets came from management rather than diagnostic studies. Therefore, not all patients received a diagnosis by a gold standard criterion, and our score could be considered accurate for predicting which patients can be safely left untreated rather than for predicting pulmonary embolism.

This is probably not a major issue. First, a diagnostic study in which pulmonary angiography would be performed in every patient is no longer feasible and would only result in major selection bias. Second, our diagnostic criteria are now widely accepted. Third, the advent of increasingly sensitive techniques, such as the 64-detector row CT, entails the risk for detecting very small peripheral clots of questionable clinical significance and, hence, overtreatment. Therefore, the relevant clinical question is not whether a patient has pulmonary embolism but whether anticoagulant treatment is required. In that sense, our score is appropriate. Finally, incorporation bias might be a concern because patients were worked up according to clinical assessment based on the original Geneva score, which included 4 items of the revised score. However, clinicians collected all of the relevant clinical variables in suspected pulmonary embolism and not only those necessary to compute the original Geneva score. Therefore, we tested all clinical variables for association with pulmonary embolism. Moreover, as shown in **Appendix Figure 1** and **Appendix Figure 2** (available at www.annals.org), clinical assessment changed the diagnostic approach only in patients with a high clinical probability and negative results on lower-limb ultrasonography and thoracic CT, which constitute less than 1% of patients.

The score should be clinically useful since it identifies a large group of low-risk patients in whom the prevalence of pulmonary embolism is less than 10% and who can usually be managed entirely by noninvasive tests. Conversely, in the high-probability group with a proportion of confirmed pulmonary embolism of more than 60%, our score justifies the use of invasive tests to rule out pulmonary embolism when less sensitive noninvasive test results are negative. The proportion of patients who were classified by the score as having a low clinical probability is lower than that in recent Canadian studies (1, 23), but this is probably due to the higher prevalence of pulmonary embolism (about 25%) in our sample. This does not have a major bearing on clinical decision making, however, since patients with a low or intermediate clinical probability are managed in the same way in recent algorithms including CT (2, 7), provided a highly sensitive D-dimer

assay is used. Such assays have a sensitivity of approximately 97% and a specificity of approximately 40% (24). Considering an average prevalence of pulmonary embolism of 21% in patients with a low to intermediate probability (Table 3), the post-test probability after a negative D-dimer result would be only about 2%.

Nevertheless, although we collected the clinical data in the validation sample prospectively, we calculated this new score retrospectively. Hence, to be considered fully validated, the revised Geneva score should now be used prospectively in a formal outcome study with patient follow-up. In addition to verifying the score's accuracy and clinical usefulness, the outcome study should evaluate clinicians' adherence to it. In studies that used the previous Geneva score (7), clinicians chose to override score assessment by implicit judgment in 20% of the patients (15). Whether this is inevitable when an entirely standardized score is proposed for clinical decision making or whether our revised score might be more acceptable to clinicians remains to be demonstrated.

In summary, we developed a new prediction score for emergency department outpatients with suspected pulmonary embolism that is entirely standardized and is based on simple clinical variables. This revised Geneva score is clinically relevant, is easy to compute, and has sustained internal and external validation. It should now be tested for clinical usefulness in a formal outcome study.

From Brest University Hospital, Brest, France; Geneva University Hospital, Geneva, Switzerland; Angers University Hospital, Angers, France; Hôpital Européen Georges-Pompidou, Paris, France; and Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.

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Requests for Single Reprints: Grégoire Le Gal, MD, EA 3878, Département de Médecine Interne et Pneumologie, CHU de la Cavale Blanche, 29609 Brest Cedex, France; e-mail, gregoire.legal@chu-brest.fr.

Current author addresses and author contributions are available at www.annals.org.

References

1. Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med.* 2001;135:98-107. [PMID: 11453709]
2. Musset D, Parent F, Meyer G, Maître S, Girard P, Leroyer C, et al. Diagnostic strategy for patients with suspected pulmonary embolism: a prospective

- multicentre outcome study. *Lancet.* 2002;360:1914-20. [PMID: 12493257]
3. Perrier A, Bounameaux H. Cost-effective diagnosis of deep vein thrombosis and pulmonary embolism. *Thromb Haemost.* 2001;86:475-87. [PMID: 11487038]
4. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax.* 2003;58:470-83. [PMID: 12775856]
5. Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. *Eur Heart J.* 2000;21:1301-36. [PMID: 10952823]
6. Kruij MJ, Leclercq MG, van der Heul C, Prins MH, Büller HR. Diagnostic strategies for excluding pulmonary embolism in clinical outcome studies. A systematic review. *Ann Intern Med.* 2003;138:941-51. [PMID: 12809450]
7. Perrier A, Roy PM, Aujesky D, Chagnon I, Howarth N, Gourdier AL, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. *Am J Med.* 2004;116:291-9. [PMID: 14984813]
8. Perrier A, Desmarais S, Miron MJ, de Moerloose P, Lepage R, Slosman D, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet.* 1999;353:190-5. [PMID: 9923874]
9. Kelly J, Hunt BJ. A clinical probability assessment and D-dimer measurement should be the initial step in the investigation of suspected venous thromboembolism. *Chest.* 2003;124:1116-9. [PMID: 12970044]
10. Perrier A, Nendaz MR, Sarasin FP, Howarth N, Bounameaux H. Cost-effectiveness analysis of diagnostic strategies for suspected pulmonary embolism including helical computed tomography. *Am J Respir Crit Care Med.* 2003;167:39-44. [PMID: 12502474]
11. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). The PIOPED Investigators. *JAMA.* 1990;263:2753-9. [PMID: 2332918]
12. Perrier A, Bounameaux H, Morabia A, de Moerloose P, Slosman D, Didier D, et al. Diagnosis of pulmonary embolism by a decision analysis-based strategy including clinical probability, D-dimer levels, and ultrasonography: a management study. *Arch Intern Med.* 1996;156:531-6. [PMID: 8604959]
13. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost.* 2000;83:416-20. [PMID: 10744147]
14. Wicki J, Perneger TV, Junod AF, Bounameaux H, Perrier A. Assessing clinical probability of pulmonary embolism in the emergency ward: a simple score. *Arch Intern Med.* 2001;161:92-7. [PMID: 11146703]
15. Chagnon I, Bounameaux H, Aujesky D, Roy PM, Gourdier AL, Cornuz J, et al. Comparison of two clinical prediction rules and implicit assessment among patients with suspected pulmonary embolism. *Am J Med.* 2002;113:269-75. [PMID: 12361811]
16. Perrier A, Roy PM, Sanchez O, Le Gal G, Meyer G, Gourdier AL, et al. Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med.* 2005;352:1760-8. [PMID: 15858185]
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976;16:31-41. [PMID: 1244564]
18. Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy: annual trends and response to recent evidence. *JAMA.* 2004;291:47-53. [PMID: 14709575]
19. McNeil BJ, Hanley JA, Funkenstien HH, Wallman J. Paired receiver operating characteristic curves and the effect of history on radiographic interpretation. CT of the head as a case study. *Radiology.* 1983;149:75-7. [PMID: 6611955]
20. Wasson JH, Sox HC. Clinical prediction rules. Have they come of age? [Editorial] *JAMA.* 1996;275:641-2. [PMID: 8594248]
21. Wyatt JC, Altman DG. Commentary: prognostic models: clinically useful or quickly forgotten? *BMJ.* 1995;311:1539-41.
22. Wasson JH, Sox HC, Neff RK, Goldman L. Clinical prediction rules. Applications and methodological standards. *N Engl J Med.* 1985;313:793-9. [PMID: 3897864]
23. Wells PS, Ginsberg JS, Anderson DR, Kearon C, Gent M, Turpie AG, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. *Ann Intern Med.* 1998;129:997-1005. [PMID: 9867786]
24. Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. *Ann Intern Med.* 2004;140:589-602. [PMID: 15096330]

Current Author Addresses: Dr. Le Gal: EA 3878, Département de Médecine Interne et Pneumologie, CHU de la Cavale Blanche, 29609 Brest Cedex, France.

Drs. Righini, Bounameaux, and Perrier: Geneva University Hospital, Rue Micheli du Crest 24, 1211 Geneva, Switzerland.

Dr. Roy: Emergency Service, CHU, 4 Rue Larrey, 49033 Angers, France.

Dr. Sanchez: Service of Pneumology, Hôpital Européen Georges-Pompidou, 20 Rue Leblanc, 75015 Paris, France.

Dr. Aujesky: Centre Hospitalier Universitaire Vaudois, Rue du Bugnon 46, 1011 Lausanne, Switzerland.

Author Contributions: Conception and design: G. Le Gal, M. Righini, H. Bounameaux, A. Perrier.

Analysis and interpretation of the data: G. Le Gal, M. Righini, A. Perrier.

Drafting of the article: G. Le Gal, A. Perrier.

Critical revision of the article for important intellectual content: M. Righini, D. Aujesky, H. Bounameaux.

Final approval of the article: G. Le Gal, M. Righini, P.-M. Roy, O. Sanchez, D. Aujesky, H. Bounameaux, A. Perrier.

Provision of study materials or patients: M. Righini, P.-M. Roy, O. Sanchez, D. Aujesky.

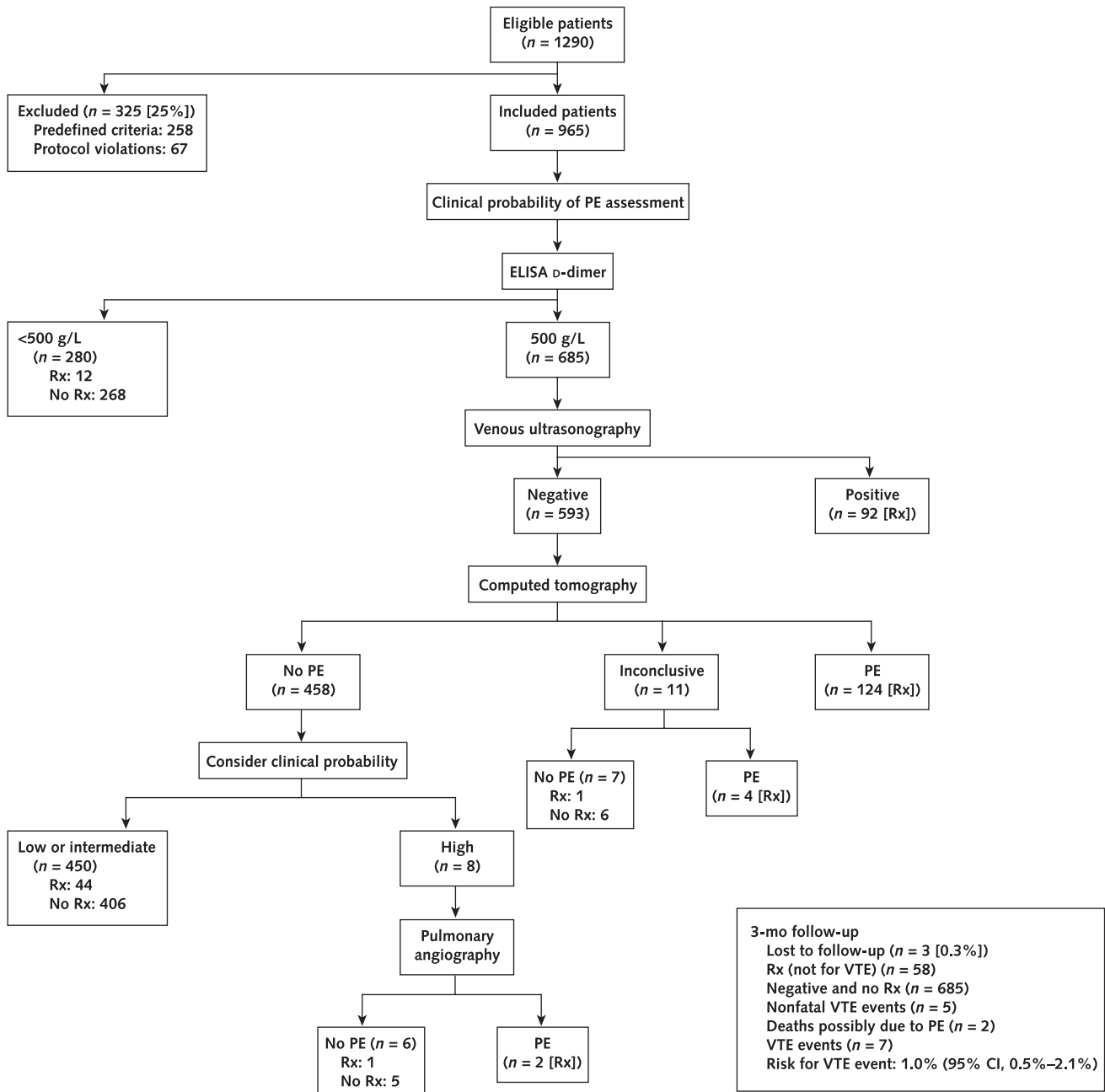
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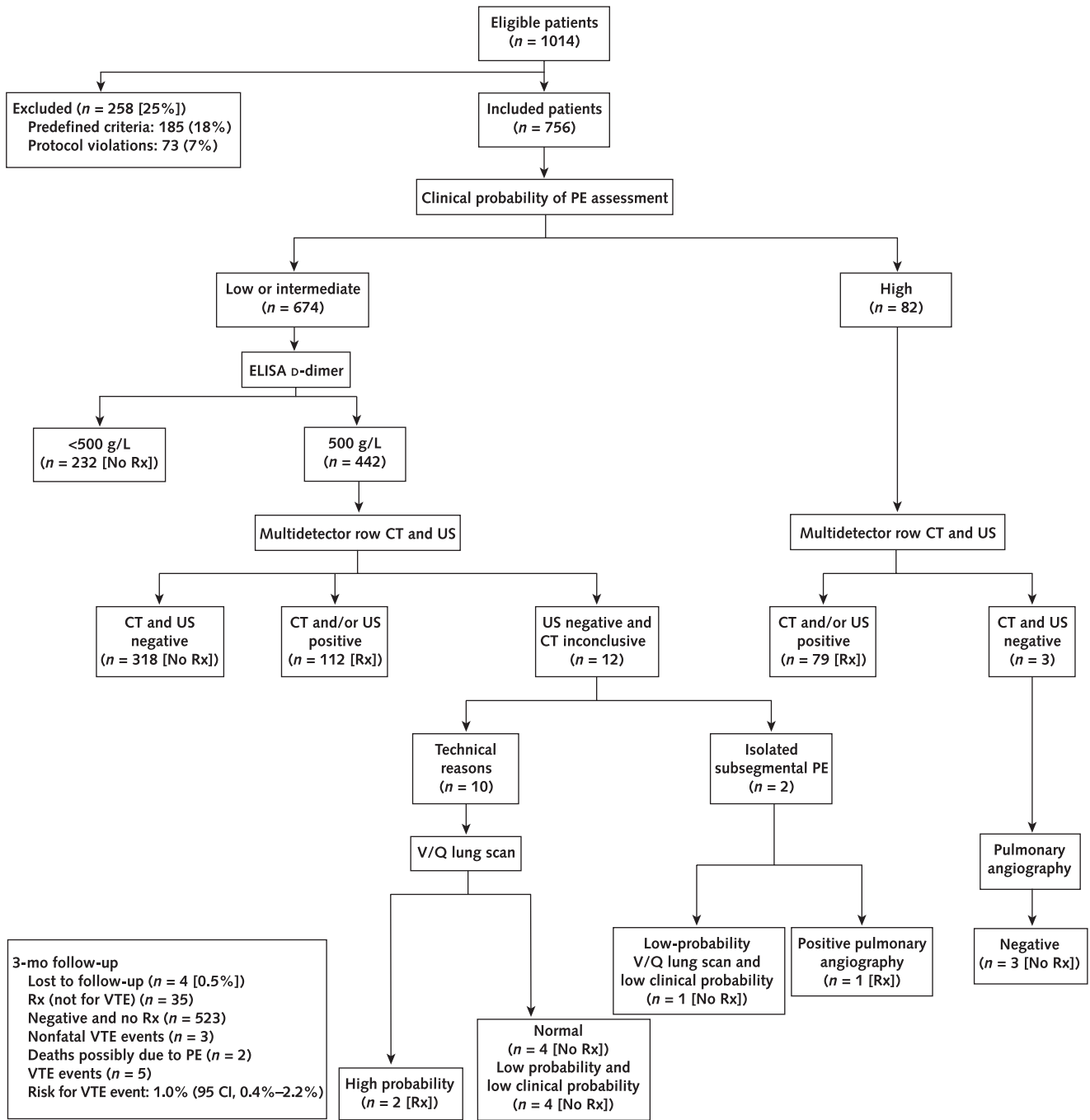
Collection and assembly of data: P.-M. Roy, O. Sanchez.

Appendix Figure 1. Diagnostic flow chart of the derivation set.



ELISA = enzyme-linked immunosorbent assay; PE = pulmonary embolism; Rx = anticoagulant therapy; VTE = venous thromboembolism. Adapted from Perrier et al. (7), © 2004, with permission of the Massachusetts Medical Society.

Appendix Figure 2. Diagnostic flow chart of the validation set.



CT = computed tomography; ELISA = enzyme-linked immunosorbent assay; PE = pulmonary embolism; Rx = anticoagulant therapy; US = ultrasonography; V/Q = ventilation-perfusion; VTE = venous thromboembolism. Adapted from Perrier et al. (16), © 2005, with permission of the Massachusetts Medical Society.