Appendix- Box A: Design of the systematic review on diagnostic prediction models for diagnosis of suspected pulmonary embolism, based on the CHARMS checklist (21)

Item	
1. Scope of the review	Review of all existing **prediction models** for diagnosis of pulmonary embolism (PE), and subsequent external validation of these models in an independent cohort of 598 primary care patients suspected of PE. The models are intended to inform physicians on referral to secondary care, or withholding from invasive diagnostic testing based on the model's estimated probability of having PE. In case of low probability: no referral to secondary care or no invasive diagnostic testing.
2. Type of primary studies	Diagnostic prediction model development studies with or without external validation in independent data.
3. Target population	Primary care patients in whom the diagnosis pulmonary embolism is considered: - Unexplained acute dyspnoea, and/ or - Unexplained cough, and/ or - Pain on inspiration
4. Outcome to be predicted	Pulmonary embolism present or absent as determined by an established reference standard, such as spiral CT scanning, pulmonary angiography, ventilation-perfusion scanning, clinical follow-up or a combination of these.

Appendix- Table A: Details of the retrieved derivation studies based on the CHARMS checklist (20)

	original Wells rule (20)	**simplified & modified Wells rule (33)**	**Geneva score (32)**	**revised Geneva score (34)**	**simplified revised Geneva score (35)**	**Charlotte rule (38)**	**PE rule-out criteria (PERC) (37)**	**Pisa rule (31)**	**revised Pisa rule (36)**
Objective	Derivation diagnostic prediction model	Simplification of Wells rule	Derivation diagnostic prediction model	Derivation diagnostic prediction model	Simplification of revised Geneva score	Derivation diagnostic prediction model	Derivation diagnostic prediction model	Derivation diagnostic prediction model	Simplification of Pisa Rule (no X-thorax)
Source of data	Prospective cohort	Prospective cohort	2 prospective cohorts	Prospective cohort	2 prospective cohorts	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort
Participants	- consecutive in- and outpatients with suspected PE. - inclusion period NR. - hospital setting: NR.	- see (42) - consecutive in- and outpatients with suspected PE. - inclusion Nov 2002- Aug 2004 - 12 Dutch hospitals (5 academic, 7 general urban)	- see (43,44) - consecutive patients presenting at ER with suspected PE. - inclusion Oct 1 1992- Oct 31 1997. - 1 academic hospital	- consecutive patients presenting at ER with suspected PE. - inclusion Oct 2000 – Jun 2002. - 3 hospitals in Switzerland and France.	Study A (39): consecutive patients presenting at ER with suspected PE. - inclusion Aug 2002- Nov 2003. - 3 hospitals (France& Swiss). Study B (42): consecutive in- outpatients with suspected PE. - inclusion Nov 2002- Aug 2004. - 1 Dutch tertiary centre.	- patients presenting at ER, (highly) suspected PE. PE work-up already planned. - inclusion 1996- 2000. - 7 ERs in United States.	- patients presenting at ER, evident clinical suspicion of PE. - inclusion period NR. - 10 ERs in United States.	- consecutive patients referred to hospital with suspected PE: - inclusion Nov 1 1991- Dec 31 1999 - 70% referred from medical/surgical departments & ER; 30% of 4 peripheral hospitals.	- consecutive patients referred to hospital with suspected PE: - inclusion Nov 1 1991- Dec 31 1999. - 70% referred from medical/surgical departments& ER; 30% of 4 peripheral hospitals.
Outcomes to be predicted	- PE present/ absent. - imaging in all patients. - 3 months follow-up. - outcome assessment blinded for other information.	- PE present/ absent. - DPM & D-dimer for exclusion, CT in high risk and/or positive D-dimer. - 3 months follow-up. - final diagnosis: trained radiologist. - blinding: NR.	- PE present/ absent. - sequence of non-invasive instruments (including clinical assessment, lung scan, ELISA D-dimer, lower limb CUS). - angiogram if inconclusive workup. - blinding: NR.	- PE present/ absent. - DPM & negative D-dimer (VIDAS) for exclusion, imaging if high risk. - 3 months follow-up. - blinding: NR.	- Study A: see (39) - Study B: see (42)	- PE present/ absent. - imaging in all patients (angiography, VQ scan, CT scanning) , or autopsy. - 6 months follow-up. - interpretation of imaging by assessors blinded for other information.	- PE present/ absent. - in 650 patients PE ruled out by structured protocol with D-dimer & alveolar dead space measurement - 90 days follow-up. - remaining patients diagnosis by imaging. - blinding: NR.	- PE present/ absent. - imaging (angiography, perfusion scan) or autopsy in all patients. - 6 months follow-up. - blinding: NR.	- PE present/ absent. - imaging (angiography, perfusion scan) or autopsy in all patients - 6 months follow-up. - outcome assessment blinded to clinical information.
Candidate predictors	- 40 candidate predictors. - patients history, physical examination, additional testing. - dichotomization of continuous variable. - predictor measurement at patient presentation, blinded for final diagnosis (outcome).	- predictors of original Wells rule. - predictor assessment blinded for outcome: NR.	- 30 candidate predictors. - patient characteristics, risk factors VTE, symptoms, signs, X-thorax, blood gas analysis. - blinded for final diagnosis - dichotomization and categorization of continuous variables.	- 26 candidate predictors. - patient history and physical examination predictors, no subjective items. - predictor categories: age, heart rate. - predictor measurement at patient presentation, blinded for final diagnosis (outcome).	- predictors of revised Geneva score. - predictor assessment blinded for outcome.	- 26 candidate predictors. - patients' history, physical examination, additional testing. - continuous variables dichotomized if included in model. - predictor assessment blinded for outcome: NR.	- 21 candidate predictors. - patient characteristics. - assessment at patient presentation, before diagnosis; 4 items retrospectively assessed. - dichotomization of significant continuous variables.	- 34 candidate predictors. - clinical history, physical examination, ECG/ X-thorax, PaO2, PaCO2. - standardized form before further objective testing. - split of continuous variables into tertiles.	- 16 candidate predictors. - see Pisa rule, without blood gas or X-thorax. - standardized form before further objective testing. - split of continuous variable age into quartiles.
Sample size	- 1,260 suspected patients included. - PE present in 222 patients (17.6%). - EPV <10 (222/40).	- 3,306 suspected patients included. - PE present in 674 patients (20%). - EPV n.a.	- 1,090 suspected patients included. - PE present in 296 patients (27%). - EPV ≈10	- 1,280 suspected patients screened, 965 patients included. - PE present in 222 patients (23.0%). - EPV <10 (222/26).	- 1,049 suspected patients included. - PE present in 241 patients (23.0%). - EPV n.a.	- 934 suspected patients included. - PE present in 181 patients (19.4%). - EPV <10.	- 3,148 suspected patients included. - PE present in 348 patients (11.0%). - EPV >10	- 1,100 suspected patients included. - PE present in 440 patients (40%). - EPV >10	- 1,100 suspected patients included - PE present in 440 patients (40%). - EPV >10
Missing data	- no D-dimer result in 49 patients. - no info on other missing data.	- D-dimer missing in 2% of all patients with low probability (≤ 4). - DPM score in 3,298 patients (99.8%).	- exclusion of 3 patients with missing data (details NR) - 104 patients with missing data.	- number of participants with missing data for each predictor reported. - predictor exclusion if	- study A& B: minimal loss-to–follow-up. - missing D-dimer data: 2.4% in low risk, 9.5% in intermediate	- no clear description of variables missing per participants. - exclusion if >5% missing (arterial blood	- missing data: none.	- missing data: NR	- missing data: NR

			- DPM developed in 986 patients	>2% missing data.	risk, 4.3% in PE-unlikely group.	gas analysis).			
Model development	- multivariable logistic regression. - predictor selection: univariable regression <0.15 - stepwise regression with p<0.05 during multivariable modelling. - no shrinkage of predictor weights.	- evaluation of simplified & modified Wells rules by assigning 1 or 2 point(s) per item if present.	- multivariable logistic regression. - predictor selection: univariable regression <0.05. - full model approach with p<0.05 multivariable modelling. - cross-validation procedure to examine degree overfitting: substantial overfitting was ruled out.	- multivariable logistic regression. - predictor selection: univariable regression <0.05. - removal of non-statistically significant variables from model. - no shrinkage of predictor weights.	- evaluation of revised Geneva score by assigning 1 point per item if present.	- multivariable logistic regression. - predictor selection: exclusion if underrepresentation, poor inter-observer reliability, missing data, or if ≥2 predictors can be collapsed into 1. - if significant in multivariable model (P<0.05) used in decision tree. - shrinkage: NR.	- multivariable logistic regression. - all candidate variables in model. - variable selection via modified backward stepwise process: exclusion of categorical & dichotomized variables with lower 95% CI bound for Cohen's K <0.40. - shrinkage: NR	- multivariable logistic regression. - predictor selection: backward selection P>0.20. Remaining variables kept in model if individually statistically significant. Forward selection of removed variables, kept in model if statistically significant or deemed to be confounder. - pairwise interactions tested.	- multivariable logistic regression. - predictor selection: backward selection. Remaining variables kept in model if individually statistical significant. If change coefficients >10% after removal, reintroduction variable. - age & sex kept in model regardless of statistical significance.
Model performance	- discrimination and calibration: NR. - comparison of predictive values using different cut-offs.	- discrimination: AUC ROC curve. - calibration: NR. - a priori cut-offs used.	- discrimination: comparison of AUCs for naïve & cross-validated scores. - calibration: NR. - comparison with empirical assessment by ED physician.	- discrimination: AUC ROC curve. - calibration: Hosmer-Lemeshow P=0.55. - predicted-observed table.	- discrimination AUC ROC curve. - calibration: NR.	- discrimination: NR. - calibration: goodness-of-fit by Hosmer-Lemeshow test.	- discrimination: NR - calibration: model fit: likelihood ratio chi-squared, Hosmer-Lemeshow. - diagnostic performance in 2 populations. - no reclassification or NRI.	- discrimination: AUC final model, with 95% CIs by 1000 bootstrap samples. - calibration: NR.	- discrimination: AUC final model, with 95% CIs by 1000 bootstrap samples. - calibration: NR.
Model evaluation	- internal validation: random split-sample; 80% derivation set, 20% validation set. - external validation: NR. - no further adjustment or update.	n.a.	- internal validation: cross-validation. - external validation: NR. - no further adjustment or update.	- internal validation: random split-sample 90% derivation, 10% validation set; procedure 10x repeated. - external validation: independent cohort (temporal). - no further adjustment or update.	n.a.	- internal validation by generating 95% CIs for the odds ratios using bootstrap. - external validation: NR.	- internal validation: NR. - external validation in 2 populations. - no further adjustment or update.	- internal validation: cross-validation 90% derivation set; 10% validation set, procedure 10x repeated. - external validation NR.	- internal validation: assessment overall accuracy (AUC ROC) estimated in 1000 bootstrap samples. - external validation: independent sample of 400 patients ('03-'05).
Results	- final model with original regression coefficients, odds ratios & rounded predictor weights. - intercept NR.	- original regression coefficients and odds ratios reported. - intercept NR. - no comparison of distribution predictors in derivation & validation set.	- final model with regression coefficients. - intercept: NR. - model with rounded predictor weights reported.	- final model with original regression coefficients and rounded predictor weights. - intercept NR. - comparison of distribution different predicted risk groups for derivation & validation set.	- new regression coefficients reported. - intercept: NR. - no comparison of distribution predictors in derivation & validation set.	- decision tree based on significant factors of multivariable model.	- final model with intercept & regression coefficients. - block rule presentation.	- final model with intercept & regression coefficients. - graph to estimate probability of PE. - comparison probability estimates and actual PE prevalence.	- final model with intercept & regression coefficients. - comparison probability estimates and actual PE prevalence.

NR= not reported; n.a.= not applicable; PE= pulmonary embolism; DPM= diagnostic prediction model; EPV = events per variable; AUC= area under the curve; ROC curve= receiver operating characteristics curve; 95% CI= 95% confidence interval

Extra references

42 Van Belle B, Büller H, Huisman M, Kaasjager K, Kamphuisen P. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 2006;295:172-9.

43 Perrier AM, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet* 1999;353:190-5.

44 Perrier A, Desmarais S, Goehring C, et al. D-dimer testing for suspected pulmonary embolism in outpatients. *Am J Respir Crit Care Med* 1997;156:492-6.

Appendix- Table B: Overview of all diagnostic prediction models to rule out PE identified by the systematic literature search.

Wells rule (20, 33)

		Original	**Modified**	**Simplified**
	Regression coefficients	Points		
Clinical signs & symptoms DVT	1.8	3.0	2	1
Alternative diagnosis less likely	1.5	3.0	2	1
Heart rate > 100 bpm	1.1	1.5	1	1
Immobilization	0.92	1.5	1	1
Previous VTE	0.87	1.5	1	1
Haemoptysis	0.87	1.0	1	1
Malignancy	0.81	1.0	1	1
Cut-off for PE unlikely		*≤4*	*≤2*	*≤1*

Geneva score (32)

		Original
	Regression coefficients	Points
Age 60-79 years	0.6	1
>= 80	1.0	2
Previous VTE	1.1	2
Surgery	1.5	3
Pulse rate >100 bpm	0.5	1
PaCO2, kPa		
<4.8	1.1	2
4.8-5.19	0.6	1
PaO2, kPa		
<6.5	2.0	4
6.5- 7.99	1.4	3
8- 9.49	1.0	2
9.5- 10.99	0.6	1
Chest X-ray		
Platelike atelectasis	0.7	1
Elevation of hemidiaphragm	0.5	1
Cut-offs clinical probability	*Low*	*<5*
	Intermediate	*5-8*
	High	*>8*

revised Geneva score (34, 35)

		Original	**Simplified**
	Regression coefficients	Points	
Age >65 years	0.39	1	1
Previous VTE	1.05	3	1
Surgery/ bone fracture	0.78	2	1
Malignancy	0.45	2	1
Unilateral lower limb pain	0.97	3	1
Haemoptysis	0.74	2	1
Heart rate			
75-94 bpm	1.20	3	1
≥ 95 bpm	0.67	5	1
Pain on deep venous palpation and unilateral oedema	1.34	4	1
Cut-off for PE unlikely		*≤5*	*≤2*

DVT= deep venous thrombosis; bpm = beats per minute; VTE= venous thromboembolic event.

Pisa rule (31)

	Regression coefficients
Male sex	0.81
Age	
63-72	0.59
≥73	0.92
Pre-existing	
CVD	-0.56
Pulmonary	-0.97
Thrombophlebitis	0.69
Symptoms	
Dyspnoea	1.29
Chest pain	0.64
Haemoptysis	0.89
Temp >38.0C	-1.17
ECT sings of acute right ventricular overload	1.53
Findings X-thorax	
Oligemia	3.86
Amputation of hilar artery	3.92
Consolidation (infarction)	3.55
Consolidation (non-infarction)	-1.23
Pulmonary Oedema	-2.83
Constant	-3.26
Clinical probability: Low	*0-10%*
Intermediate	*11-50%*
Moderately high	*51-90%*
High	*>90%*

revised Pisa rule (36)

	Regression coefficients
Age	
57-67	0.80
68-74	0.87
≥75	1.14
Male sex	0.60
Immobilization	0.42
Pre-existing	
CVD	-0.51
Pulmonary	-0.89
Thrombophlebitis	0.64
Symptoms	
Dyspnoea	2.00
Orthopnoea	-1.51
Chest pain	1.01
Fainting/ syncope	0.66
Haemoptysis	0.93
Leg Swelling	0.80
Temp >38.0C	-1.47
Wheezes	-1.20
Crackles	-0.61
Acute cor pulmonale on ECG	1.96
Constant	-3.43
Clinical probability: Low	*0-10%*
Intermediate	*11-50%*
Moderately high	*51-80%*
High	*81-100%*

PERC (37)

For a negative result, the clinician must answer "no" to the following 8 questions:

- Is the patient aged >49 y?
- Is the pulse >99 beats/min?
- Is the pulse oximetry reading <95% while the patient breathes room air?
- Is there a history of haemoptysis?
- Is the patient receiving exogenous oestrogen?
- Does the patient have a previous diagnosis of venous thromboembolism?
- Has the patient had recent surgery or trauma that required endotracheal intubation or hospitalization in the previous 4 weeks?
- Does the patient have unilateral leg swelling (on the basis of visual observation of asymmetry of the calves)?

Charlotte rule (38)

This rule classifies patients as either safe (eligible for D-dimer testing) or unsafe.

- If the patient is aged ≤50 y and his or her heart rate is less than or equal to their systolic blood pressure (shock index ≤1.0), the patient is safe.

- If the patient is aged >50 y or has a shock index >1.0, the clinician should ask 4 sequential questions:
  - Does the patient have unexplained hypoxemia?
  - Does the patient have unilateral leg swelling?
  - Has the patient had surgery that required general anaesthesia in the past 4 weeks?
  - Does the patient have haemoptysis?

If the answer to all 4 questions is "no," then the patient is safe.

Appendix- Table C: TRIPOD Checklist: Prediction Model Development and Validation

Section/ Topic			Checklist Item	Page of original manuscript
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	4
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	5
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	5-6
	5b	D;V	Describe eligibility criteria for participants.	5-6
	5c	D;V	Give details of treatments received, if relevant.	n.a.
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	6
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	6
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	6
Sample size	8	D;V	Explain how the study size was arrived at.	6
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	n.a.
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	n.a.
	10c	V	For validation, describe how the predictions were calculated.	7
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	7-8
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	n.a.
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	7
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	9, 20
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9-10, 20
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	20
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	20
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	n.a
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	n.a.
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	n.a.
	15b	D	Explain how to the use the prediction model.	n.a.
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	9-10, 21-24
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	n.a.
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11-14
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	11-14
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	11-14
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	11-14
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	S1-11
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	15

Appendix- Table C: TRIPOD Checklist: Prediction Model Development and Validation

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Appendix- Figure A: Systematic literature search in PubMed & Embase databases

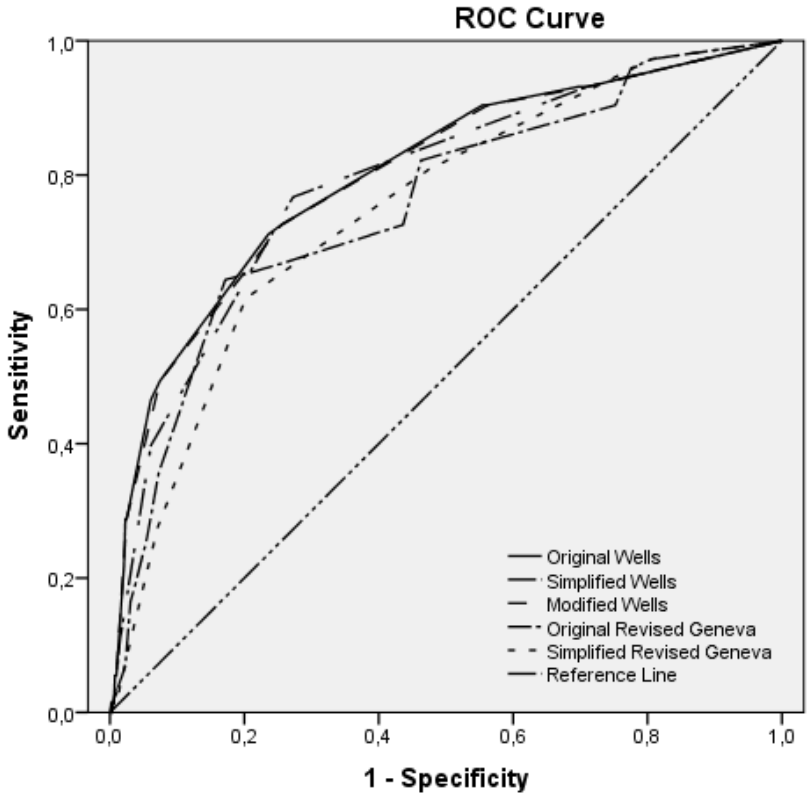
PubMed 13-10-2014

("Pulmonary Embolism"[Mesh:noexp] OR (lung embolism[tiab] OR lung embolisms[tiab]) OR (pulmonary embolism[tiab] OR pulmonary embolism/clinical[tiab] OR pulmonary embolism/infarction[tiab] OR pulmonary embolisms[tiab]) OR (pulmonary thromboembolism[tiab] OR pulmonary thromboembolisms[tiab])) AND ("Epidemiologic Research Design"[Mesh] OR "Epidemiologic Studies"[Mesh] OR "Probability"[Mesh] OR probability[tiab] OR probabilities[tiab] OR "Outcome Assessment (Health Care)"[Mesh] OR ((validitat[tiab] OR validitate[tiab] OR validitates[tiab] OR validitation[tiab] OR validite[tiab] OR validited[tiab] OR validities[tiab] OR validiting[tiab] OR validition[tiab] OR validitiy[tiab] OR validity[tiab] OR validity/accuracy[tiab] OR validity/applicability[tiab] OR validity/biomarker[tiab] OR validity/clinical[tiab] OR validity/credibility[tiab] OR validity/diagnostic[tiab] OR validity/effective[tiab] OR validity/expresses[tiab] OR validity/feasibility[tiab] OR validity/generalizability[tiab] OR validity/invalidity[tiab] OR validity/no[tiab] OR validity/predictive[tiab] OR validity/quality[tiab] OR validity/relationship[tiab] OR validity/reliability[tiab] OR validity/representativity[tiab] OR validity/reproducibility[tiab] OR validity/scientific[tiab] OR validity/screening[tiab] OR validity/test[tiab] OR validity/utility[tiab] OR validity/validation[tiab] OR validity/viability[tiab] OR validity'[tiab] OR validity's[tiab] OR validityof[tiab]) AND and reliability[tiab]) OR (clinical prediction rule[tiab] OR clinical prediction rules[tiab]) OR "Sensitivity and Specificity"[Mesh] OR (roc curve[tiab] OR roc curve/area[tiab] OR roc curve/sensitivity[tiab] OR roc curves[tiab]) OR (pretest[All Fields] AND clinical[All Fields] AND model[All Fields])) AND (("2010/01/01"[PDAT] : "2014/10/01"[PDAT]) AND "humans"[MeSH Terms] AND (Dutch[lang] OR English[lang] OR German[lang] OR French[lang] OR Italian[lang] OR Spanish[lang]) NOT ("child"[MeSH Terms:noexp] OR "infant"[MeSH Terms:noexp] OR "infant"[MeSH Terms] OR "child, preschool"[MeSH Terms] OR "infant, newborn"[MeSH Terms])) NOT (Editorial[ptyp] OR Letter[ptyp] OR Meta-Analysis[ptyp] OR Practice Guideline[ptyp] OR Review[ptyp])

Embase 13-10-2014

#18 #17 AND [abstracts]/lim	2,817
#17 #16 AND [embase]/lim AND [2010-2014]/py	3,124
#16 #15 AND #5	5,690
#15 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	594,515
#14 (pretest NEXT/1 clinical):ab,ti AND model*:ab,ti AND [embase]/lim	19
#13 (roc NEXT/1 curve*):ab,ti AND [embase]/lim	22,479
#12 'roc curve' AND [embase]/lim	17,076
#11 'sensitivity and specificity' AND [embase]/lim	160,017
#10 clinical:ab,ti AND prediction:ab,ti AND rule*:ab,ti AND [embase]/lim	1,707
#9 valid*:ab,ti AND reliab*:ab,ti AND [embase]/lim	60,561
#8 'outcome assessment' AND [embase]/lim	238,342
#7 probabilit*:ab,ti AND [embase]/lim	125,955
#6 'probability'/exp AND [embase]/lim	40,775
#5 #1 OR #2 OR #3 OR #4	55,578
#4 (pulmonary NEXT/1 thromboembolism*):ab,ti AND [embase]/lim	2,528
#3 (lung NEXT/1 embolism*):ab,ti	502
#2 (pulmonary NEXT/1 embolism*):ab,ti AND [embase]/lim	26,815
#1 'lung embolism' AND [embase]/lim	51,880

Appendix- Figure B: Receiver operating characteristics (ROC) curves with estimated c-statistics (95% confidence intervals) of the five prediction models (without D-dimer testing) in the AMUSE-2 cohort

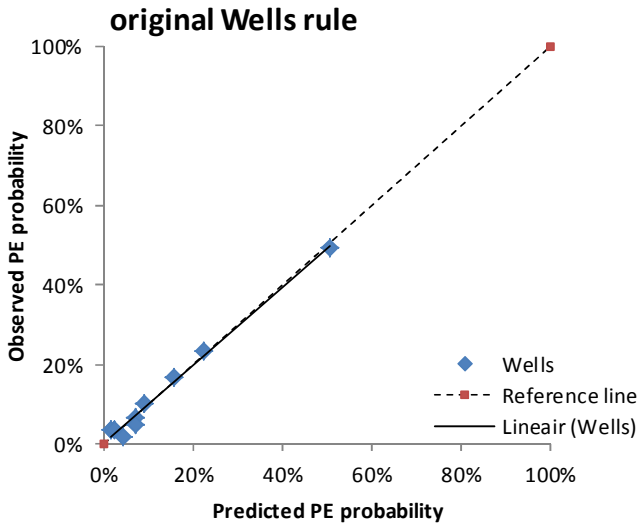


	c-statistic
Original Wells	0.80 (0.74 to 0.86)
Simplified Wells	0.79 (0.73 to 0.85)
Modified Wells	0.80 (0.74 to 0.86)
Original Revised Geneva	0.76 (0.69 to 0.82)
Simplified Revised Geneva	0.75 (0.69 to 0.81)

Appendix- Figure C Calibration plots of the original, modified and simplified Wells rules and the original and simplified revised Geneva scores in the AMUSE-2 cohort consisting of 598 patients suspected of pulmonary embolism in primary care, based on the predicted probability of pulmonary embolism present by calculating the linear predictor for each of the models.

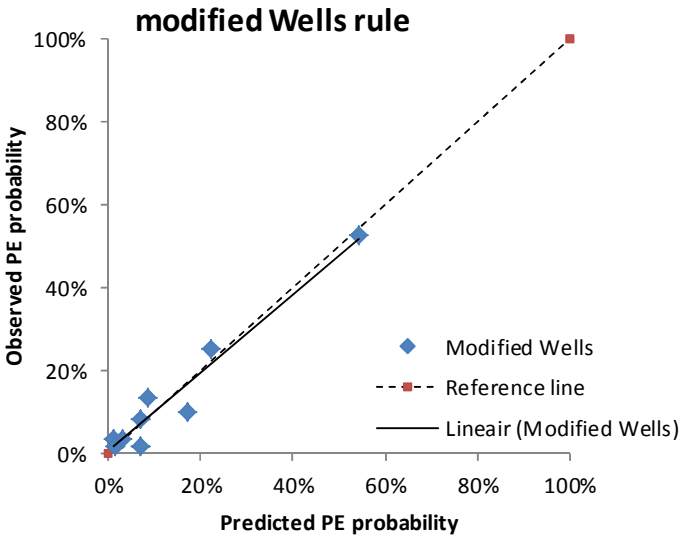
original Wells rule

predicted	observed	PE	n=
1,7%	3,4%	2	59
1,7%	3,3%	2	60
2,5%	3,3%	2	60
4,5%	1,7%	1	60
7,1%	6,7%	4	60
7,1%	5,0%	3	60
9,0%	10,0%	6	60
15,9%	16,7%	10	60
22,3%	23,3%	14	60
50,8%	49,2%	29	59



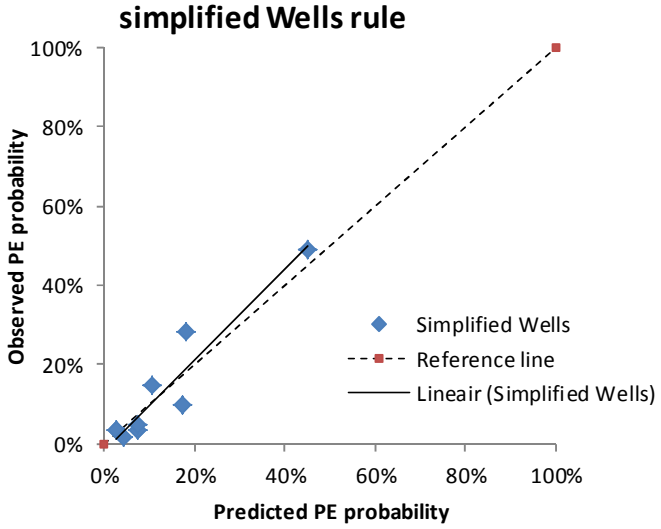
modified Wells

predicted	observed	PE	n=
1,0%	3,4%	2	59
1,0%	3,3%	2	60
1,6%	1,7%	1	60
2,9%	3,3%	2	60
7,1%	1,7%	1	60
7,1%	8,3%	5	60
8,4%	13,3%	8	60
17,1%	10,0%	6	60
22,2%	25,0%	15	60
54,2%	52,5%	31	59



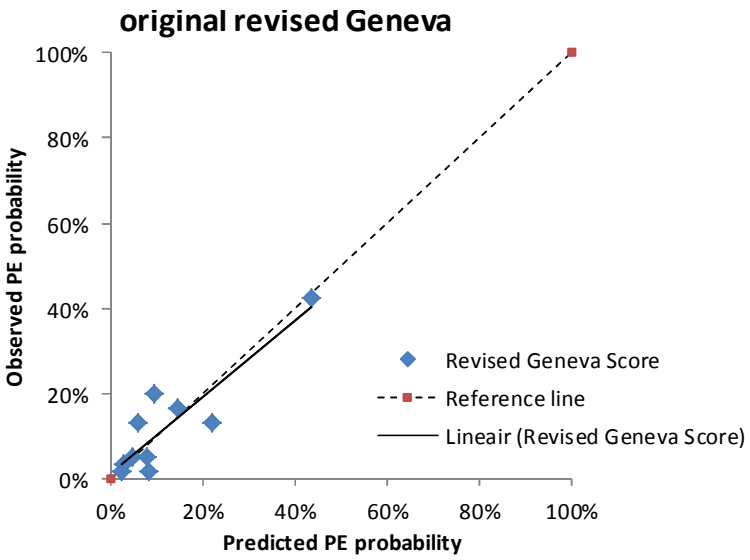
simplified Wells

predicted	observed	PE	n=
2,8%	3,4%	2	59
2,8%	3,3%	2	60
4,4%	1,7%	1	60
7,2%	3,3%	2	60
7,2%	3,3%	2	60
7,2%	5,0%	3	60
10,6%	15,0%	9	60
17,4%	10,0%	6	60
18,0%	28,3%	17	60
45,1%	49,2%	29	59



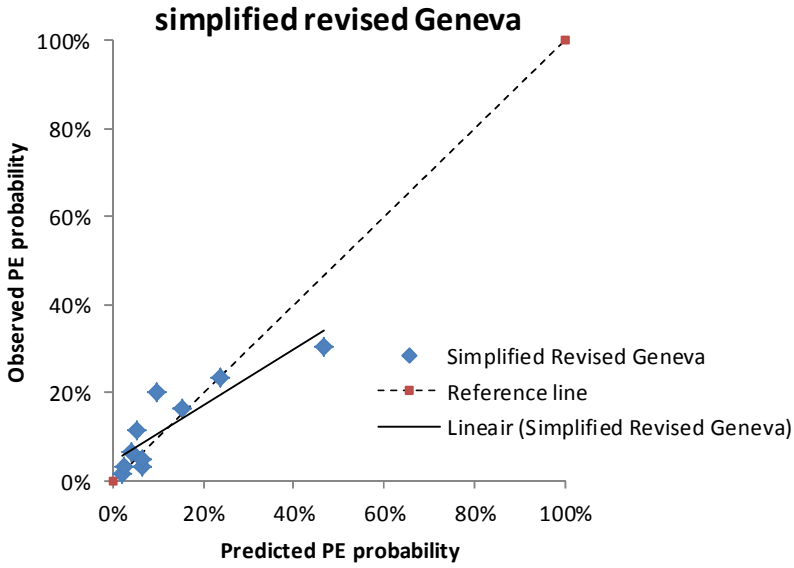
original revised Geneva

predicted	observed	PE	n=
2,7%	1,7%	1	59
2,9%	3,3%	2	60
5,0%	5,0%	3	60
6,0%	13,3%	8	60
8,1%	5,0%	3	60
8,3%	1,7%	1	60
9,6%	20,0%	12	60
14,5%	16,7%	10	60
21,9%	13,3%	8	60
43,5%	42,4%	25	59



simplified revised Geneva score

predicted	observed	PE	n=
2,1%	1,7%	1	59
2,5%	3,3%	2	60
4,0%	6,7%	4	60
5,5%	11,7%	7	60
6,5%	3,3%	2	60
6,5%	5,0%	3	60
9,7%	20,0%	12	60
15,3%	16,7%	10	60
23,8%	23,3%	14	60
46,6%	30,5%	18	59



PE= pulmonary embolism; n= number of patients per decile