Computerised clinical decision support for suspected PE

David Jiménez, Santiago Resano, Remedios Otero, Carolina Jurkoj, Ana Karina Portillo, Pedro Ruiz-Artacho, Jesús Corres, Agustina Vicente, Paul L den Exter, Menno V Huisman, Lisa Moores, Roger D Yusen, for the IRYCIS Pulmonary Embolism Study Group

ABSTRACT
This study aimed to determine the effect of an evidence-based clinical decision support (CDS) algorithm on the use and yield of CT pulmonary angiography (CTPA) and on outcomes of patients evaluated in the emergency department (ED) for suspected PE. The study included 1363 consecutive patients evaluated for suspected PE in an ED during 12 months before and 12 months after initiation of CDS use. Introduction of CDS was associated with decreased CTPA use (55% vs 49%; absolute difference (AD), 6.3%; 95% CI 1.0% to 11.6%; p=0.02). The use of CDS was associated with fewer symptomatic venous thromboembolic events during follow-up in patients with an initial negative diagnostic evaluation for PE (0.7% vs 3.2%; AD 2.5%; 95% CI 0.9% to 4.6%; p<0.01).

INTRODUCTION
Challenges continue to exist regarding the efficient, appropriate, and safe evaluation of patients with suspected acute PE. Although the use of multidetector CT pulmonary angiography (CTPA) has increased the ability to accurately diagnose PE in comparison with other modalities, its use may lead to overdiagnosis and subsequent iatrogenic harm due to anticoagulant-associated complications.

Evidence-based diagnostic strategies improve outcomes of patients with PE. The use of electronic clinical information holds promise for improving the quality and efficiency of medical care. Recently, a study of a computer-based diagnostic decision-support (CDS) system for patients suspected of having acute PE in the emergency department (ED) showed a significant decrease in the use of CTPA and a significant increase in its yield. However, this and other studies have not evaluated the impact of CDS on the clinical outcomes of patients with suspected PE.

As a quality improvement initiative, we conducted this study to test the hypothesis that implementation of a CDS system, intended to guide diagnostic testing for PE, could change clinician behaviour, affect test PE diagnostic testing use and subsequently improve patient outcomes.

METHODS
Study design
We conducted a preintervention and postintervention study that compared clinical outcomes of cohorts of consecutive adult patients that presented to an academic urban ED with clinical suspicion of PE during the 12 months before (preintervention period, from 1 January 2011 to 31 December 2011) and the 12 months after (postintervention period, from 1 January 2012 to 31 December 2012) the initiation of CDS use.

Patients
Study eligibility required patient presentation to the ED, and ED clinician suspicion of acute symptomatic PE. Exclusion criteria included treatment with therapeutic doses of anticoagulants for more than 24 h, life expectancy less than 3 months, documented pregnancy, geographical inaccessibility precluding follow-up, age younger than 18 years, allergy to intravenous contrast agents, renal insufficiency (creatinine clearance <30 mL/min), logistic problems (eg, unavailability of CTPA, patient too ill to undergo CTPA) and haemodynamic instability.

Diagnosis of PE
For study eligibility and for follow-up, the study established the diagnosis of PE in patients by (i) a positive multidetector CTPA, (ii) a high probability ventilation-perfusion (VQ) scintigraphy, (iii) a lower limb venous compression ultrasonography positive for proximal deep vein thrombosis in patients with (a) an inconclusive VQ scan or (b) a negative CT scan and high subjective clinical suspicion or (iv) an autopsy positive for PE (for follow-up only).

Outcomes
Outcomes included use (number of examinations per 1000 ED visits) and yield (percentage of examinations positive for PE) of CTPA before and after CDS implementation. For patients who had an initial negative diagnostic evaluation for suspected PE, outcomes included blinded adjudication of symptomatic (fatal and non-fatal) venous thromboembolic events that occurred during the 3-month follow-up period.

Statistical analysis
Logistic regression evaluated the association between use of CDS and an outcome measure. In the multivariable model, variables that showed evidence of confounding for the effect of CDS on the outcome undergoing analysis were not removed.
from the model. Linear trend analysis according to trimester within the preintervention and the postintervention periods was used to assess for variations in the use and yield of CTPA within each period. Statistical significance was defined as a two-tailed p value of <0.05 for all analyses. Analyses were performed using SPSS, V15.0 (SPSS, Chicago, Illinois, USA).

RESULTS
Study sample
Study staff screened 1530 consecutive patients with suspected acute PE for eligibility, of whom 93 were excluded. The study enrolled the remaining eligible 1437 patients (see online supplementary figure).

Of the 696 patients enrolled during the preintervention period, 652 had analysable data and the diagnosis of PE was confirmed at the end of the diagnostic work-up in 160 (23%) patients. Of the 741 patients enrolled during the postintervention period, 711 had analysable data and the diagnosis of PE was confirmed at the end of the diagnostic work-up in 138 (19%) patients (see online supplementary figure).

Regarding the patients’ clinical characteristics at the time of presentation to the ED, the patients who entered the study during the postintervention period had significantly younger age (67.9 years vs 69.8 years, p=0.04) and longer duration of symptoms (5.4 days vs 4.1 days, p=0.04) compared with the patients who entered the study during the preintervention period. The two cohorts had a similar prevalence of risk factors for venous thromboembolism and signs and symptoms of PE.

Primary outcomes
A greater proportion of patients received CTPA testing (55% vs 49%, p=0.02) in the preintervention period than in the postintervention period (table 1). During the preintervention period, quarterly use of CTPA increased 21.5% overall, from 2.60 to 3.16 examinations per 1000 patients (p=0.17). During the postintervention period, quarterly use decreased 25.4% overall, from 3.19 to 2.38 examinations per 1000 patients (p=0.09).

Of the 362 CTPA examinations performed during the preintervention period, 112 (31%) were positive for PE. Of the 350 CTPA examinations performed during the postintervention period, 116 (33%) were positive for PE (absolute difference (AD) 2.2%; 95% CI of the AD, –4.8% to 9.2%; p=0.53). During the preintervention period, the quarterly yield decreased from 37.7% to 27.1% (p=0.26). During the postintervention period, the quarterly yield increased from 26.0% to 46.5% (p<0.01).

Secondary outcomes
Overall, the frequency of possible and definite venous thromboembolic events in patients who were untreated because of a negative initial work-up was low (20 of 1065 patients; 1.9%; 95% CI, 1.1% to 2.7%) during the 3 months of follow-up. Only seven patients (7 of 1065 patients; 0.7%; 95% CI 0.2% to 1.1%) died from definite (n=1) or possible PE (n=6). Sixteen events (16 of 492 patients; 3.2%; 95% CI 1.7% to 4.8%) occurred during the preintervention period, whereas four events (four of 573 patients; 0.7%; 95% CI 0.0% to 1.4%) occurred during the postintervention period (AD 2.5%; 95% CI of the AD, 0.9% to 4.6%; p<0.01).

Univariate logistic regression of the entire cohort showed that only the use of CDS (OR 0.22; 95% CI 0.07 to 0.68; p<0.01), and chronic lung disease (OR 2.72; 95% CI 0.89 to 8.27; p=0.08) were significantly associated with symptomatic thromboembolic events during follow-up. In the multivariate analysis, no variable showed evidence of confounding for the association between the use of CDS (OR 0.22; 95% CI 0.07 to 0.68; p<0.01), and thromboembolic events during follow-up.

DISCUSSION
This study demonstrated a decrease in the use of CTPA for the evaluation of acute PE in the ED associated with evidence-based CDS. Despite this decrease in CTPA use, its diagnostic yield did not significantly change. However, in non-anticoagulated patients in whom the initial diagnosis of PE was excluded, use of CDS was associated with a significant decrease in the incidence of symptomatic thromboembolic events during follow-up.

Diagnostic algorithms that combine clinical decision rules with D-dimer testing have demonstrated their effectiveness and safety for excluding acute PE and avoiding unnecessary testing. Thus, such decision rules have consequently been widely advocated by international guidelines. Still, adherence to these guidelines in routine practice is far from optimal, and a significant proportion of patients do not receive the recommended diagnostic work-up. Studies have highlighted the importance of correct adherence to validated diagnostic strategies and that reduces the incidence of symptomatic venous thromboembolism when a diagnostic strategy is consistently followed as a consequence of implementation of CDS.

After the introduction of CTPA, PE incidence has risen, all-cause mortality has changed little and case-fatality has decreased. The increased incidence of PE might reflect an epidemic of diagnostic testing that has created overdiagnosis, likely induced by the widespread use of multidetector CTPA at a low threshold to exclude PE. A meta-analysis confirmed that many of the emboli identified by multidetector CTPA are subsegmental emboli that do not lead to adverse outcomes even if left untreated. Thus, the use of CDS that leads to a reduction in CTPA investigations, that does not affect the diagnostic yield and that reduces the incidence of symptomatic venous thromboembolism during follow-up has important clinical relevance.

Strengths of this study included the consecutive enrolment of a large sample of patients and blinded adjudication of adverse events. In a smaller study of 404 patients evaluated for suspected PE with a CDS, clinicians did not adhere to the computer program in 27% of cases. Our CDS was mandatory, and during the study period, emergency physicians used this tool in 93% of patients with clinical suspicion of acute symptomatic PE. Usability, simplicity and minimisation of information...
requested might account for the high acceptance by emergency physicians. This study’s primary limitation consists of the retrospective study design, which may have resulted in selection bias. Also, the conduct of the study in a single academic centre that had ED clinicians enthusiastic about using the CDS tool developed at the same centre affects the generalisability of the results.

We conclude that the use of this study’s CDS tool significantly reduced the frequency of CTPA in patients with clinically suspected PE in the ED. In addition, in non-anticoagulated patients in whom the initial diagnosis of PE was excluded, use of the CDS was associated with a significant decrease in the incidence of symptomatic thromboembolic events during follow-up.

Author affiliations
1Respiratory Department, Ramón y Cajal Hospital, Instituto Ramón y Cajal de Investigación Sanitaria IRYCIS, and Alcala de Henares University, Madrid, Spain
2Radiology Department, Ramón y Cajal Hospital and Instituto Ramón y Cajal de Investigación Sanitaria IRYCIS, Madrid, Spain
3Respiratory Department, Hospital Universitario Virgen del Rocío, Sevilla, Spain
4Department of Internal Medicine, Ramón y Cajal Hospital and Instituto Ramón y Cajal de Investigación Sanitaria IRYCIS, Madrid, Spain
5Emergency Department, Hospital Clínico, Madrid, Spain
6Emergency Department, Ramón y Cajal Hospital and Instituto Ramón y Cajal de Investigación Sanitaria IRYCIS, Madrid, Spain
7Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden, The Netherlands
8F. Edward Hebert School of Medicine, Uniformed Services University, Bethesda, USA
9Divisions of Pulmonary and Critical Care Medicine and General Medical Sciences, Washington University School of Medicine, St. Louis, Missouri, USA

Correction notice This article has been corrected since it was published Online First. The provenance and peer review statement has been corrected.


Contributors Study concept and design: DJ, RO, MVH, LM and RDY. Acquisition of data: DJ, SR, CJ, AKP, PR-A, JC and AV. Drafting of the manuscript: DJ, SR, RO, CJ, AKP, PR-A, JC, AV, PLdE, MVH, LM and RDY. Critical revision of the manuscript for important intellectual content: DJ, SR, RO, CJ, AKP, PR-A, JC, AV, PLdE, MVH, LM and RDY. Study supervision: DJ and RDY. The corresponding author, DJ, had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Funding Supported by a FIS (080200, 000246), a SEPAR (2008) and a NM (2010) grant. Supported with an unrestricted educational grant by SANOFI.

Competing interests None.

Patient consent Obtained.

Ethics approval Ramon y Cajal Hospital IRB.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES