

Correlating pulmonary embolism severity with short term mortality to risk stratify for outpatient management

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Abstract

Aims: We ascertain less than 7-day mortality data in suspected pulmonary embolism (PE) in order to risk stratify patients suitable for outpatient imaging.

Methods: Retrospective identification of patients presenting to two emergency departments over a two-year period, with a radiologically confirmed PE. PESI and sPESI scores correlated with death at 1, 3, 7, 30 and 90 days.

Results: There was significant correlation between all PESI risk classes and death at 3, 7, 30 and 90 days ($p < 0.01$), but not day 1. No deaths occurred within 1 and 3 days in low risk PESI groups or within 90 days in the low risk sPESI.

Conclusion: PESI/sPESI could be reliably utilized to risk stratify patients being considered for outpatient investigation of PE.

Keywords

Pulmonary Embolism, Prognosis, Outpatients, Emergency Service, Imaging

Keypoints

1. Why is this topic important?

A patient admitted to hospital for diagnosed or suspected PE allows for monitoring and detection of any adverse effects. This can however lead to an increased risk of iatrogenic effects and an additional cost burden.

2. What does this study attempt to show?

Clinical decision rules (e.g. PESI & sPESI) are used to identify low risk patients who can be safely treated PE's as an outpatient, after they have had a confirmed PE. These tools were developed by looking at 30-day mortality rates. By looking at very early mortality rates (<7 days) this pilot study attempts to show how outpatient imaging could be used in low risk groups.

3. What are the key findings?

This retrospective study provides previously not known mortality data at 1, 3 and 7 days for each PESI & sPESI class. It suggests that these clinical decision rules could allow a select group of patients to have outpatient imaging to confirm their PE, as well as further on-going outpatient treatment.

4. How is patient care impacted?

By further utilising the PESI tool with respect to imaging, it could help reduce ED waiting times due to reduced time within the department, and also unnecessary admissions into hospital.

Introduction

Background

Pulmonary embolism (PE) confirmed through imaging, and deemed low risk, can be managed safely in the outpatient setting.¹ However, diagnostic imaging is generally conducted as an inpatient. There is limited evidence available regarding the safety of imaging patients with a clinically suspected PE as an outpatient.^{2,3} Well-validated clinical decision rules already exist to risk stratify the suitability for outpatient treatment of patients with radiologically confirmed PEs, the Pulmonary Embolism Severity Index (PESI) being one of the most widely used. The PESI provided an estimate for the risk of 30-day mortality from PE (Table 1).⁴ Scores determined from PESI were divided into five different classes of

severity each with increasing mortality, with PESI classes I and II (score ≤ 85) identified as being low risk for mortality and potentially suitable for safe outpatient care.⁵ These low-risk patients had no difference in 90-day mortality when treated with low molecular weight heparin as an outpatient compared to inpatient treatment.⁶

Due to the scoring complexities, a simplified PESI (sPESI) with less criteria was created (Table 1).⁷ Compared to PESI, the sPESI has similar prognostic accuracy at 30 days.⁷ A patient at low risk for mortality has a score of zero using sPESI.

The expected scenario for investigating a patient on an outpatient basis who presented to ED and was suspected clinically to have a PE would be to commence therapeutic anti-coagulation in ED, with outpatient imaging to occur within 24 to 48 hours,

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Table 1. The PESI and sPESI parameters^{4, 7}

Predictors	Points Assigned PESI	Points Assigned sPESI
Demographic characteristics		
Age (years)	Age	>80yrs = 1
Male sex	+10	-
Co-Morbid illnesses		
Cancer (previous or active)	+30	1
Heart failure	+10	HF or CLD = 1
Chronic Lung disease	+10	HF or CLD = 1
Clinical findings		
Pulse ≥ 110 / min	+20	1
Systolic Blood Pressure < 100 mmHg	+30	1
Respiratory Rate ≥ 30 / min	+20	-
Temperature <36°C	+20	-
Altered mental status (disorientation, lethargy, stupor or coma)	+60	-
Arterial oxygen saturation <90% (with or without administration supplemental oxygen)	+20	1

HF – Heart Failure, CLD – Chronic Lung Disease, PESI – Pulmonary Embolism Severity Index, sPESI – Simplified Pulmonary Embolism Severity Index

although over a weekend this could be delayed up to 3 to 4 days. Practice is starting to embrace imaging as an outpatient, but even the latest British Thoracic Society (BTS) guidelines recognise that there is sparse evidence with managing only suspected PE's.³ The guidelines also encourage imaging all patients within 24 hours, even if deemed low risk as pre existing scoring tools.³ A first step in evaluating the safety of outpatient strategy for the investigation of suspected PE would be to determine the short-term mortality from PE of high and low risk categories. Studies to date have examined the predictive properties of the PESI and sPESI for 30 and 90-day mortality, but little data exists for mortality under 30 days.⁸

The aim of this study was to investigate the diagnostic accuracy of the PESI and sPESI for predicting very early mortality at 1, 3 and 7 days in patients with a confirmed PE.

Methods

Study design & Setting

This was an observational, retrospective cohort study across two district general hospitals conducted between the 1st January 2013 to 31st December 2015. Ethical approval was obtained from “blinded for peer review”

Participants

All patients with a confirmed PE on CT Pulmonary Angiogram were identified by a keyword search for “pulmonary embolism” of all radiology reports on

the Trust Picture Archiving and Communication System (PACS). All identified reports were then examined to confirm a diagnosis of PE. Due to limitations in the software, this only consisted of CT Pulmonary Angiogram (CTPA) and excluded V/Q scans. From these cases, we excluded those aged <18 years, cases where there was ambiguity in the diagnosis of PE on the report, chronic PE (even if an acute PE was also identified due to potential confounding factors including current anticoagulation), if the CT was not requested from ED or an acute ward, or if the CT was not arranged within 7 days of admission, as after this time period it would suggest the PE was not the reason for the acute admission. Patients were excluded if PESI or outcome data could not be obtained. We excluded patients with a confirmed PE who presented in cardiac arrest as such patients would never be considered for outpatient investigation and so would not constitute the cohort of interest.

Methods and Measurements

Electronic and paper medical records were reviewed. A data collection form was created and refined through several trials on a small sample of medical records. To maintain consistency of data extraction each data point was defined and the section of the medical record where it was to be obtained specified. All medical records were reviewed by one trained researcher who was not blinded to the study objective. Variables that comprised the PESI and sPESI were obtained. Co-morbidities of cancer, chronic lung disease and heart failure were recorded as present

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if they were listed in the admitting doctors 'past medical history' We viewed hospital clinic letters where available to confirm a diagnosis, otherwise we contacted their GPs, if neither information was available we assumed the patient correctly conveyed their comorbidities. We did not rely on objective measures such as echocardiographic evidence of left ventricular dysfunction or lung function tests. Not relying on objective measures was the methodology used in the original derivation and validation studies of the PESI and sPESI, and is the way these scores are used in clinical practice.^{4,7} Any past or current history of cancer with the exception of basal and squamous cell skin cancers were considered present for this variable. Chronic lung disease was considered present if there was a diagnosis listed of emphysema, chronic bronchitis, chronic obstructive pulmonary disease, asthma, or bronchiectasis. Vitals signs used were those observations taken at triage. Mental status was assumed normal unless the triage nurse notes, ED nursing or medical notes specified GCS <15, disorientation, lethargy or stupor.

Medical records were used to determine the outcome variable which was death at 1, 3, 7, 30 and 90 days from admission. If the patient hadn't re-presented to the hospital trust after 90 days, their GP practices were contacted with a formal request of their current status or date-of-death as the GP is notified if a patient is admitted or if they die. Although not all "blinded for peer review" hospital records are linked, the trust consisted of multiple hospitals in the region.

Results

Statistical data analysis

For continuous variables with a normal distribution (age, PESI score), means with standard deviations were used to describe the data. Categorical data (mortality, PESI class) was presented as frequency counts and percentages.

Mortality rates at 1, 3, 7, 30 and 90 days were presented descriptively across PESI classes I-V. The overall mortality was compared between low risk patients (PESI I-II) and high-risk patients (PESI III-V) using the Kaplan-Meier survival analysis and the log-rank test.

To evaluate the diagnostic utility of the PESI and sPESI, calculations were made for sensitivity, specificity, negative predictive value, positive predictive value and likelihood ratio for predicting mortality for low and high-risk patients.

The data analysis was repeated to assess the characteristics of sPESI score. All data analysis was performed using SPSS 22.0 (SPSS Inc, Chicago IL, USA).

The study was designed and reported using the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines

Results

There were 4129 patients with "pulmonary embolism" mentioned on an imaging report. After exclusion criteria were applied to the full radiology report the medical records of 555 participants were examined. A further 246 met exclusion criteria. Four patients were lost to follow up as they had not re-attended the hospital trust within 90 days nor subsequently been in contact with their GP. Seventeen patients were missing a variable for PESI/sPESI scoring. 288 participants were included in the final analysis (Figure 1).

Demographics, mortality and PESI/sPESI scores for the study cohort are shown in Table 2. The mean age was 63 (min 18, max 100) and 149 (51%) were male. Twenty-two patients (7.6%) died before the end of the 90-day period. Overall mortality rate was 0.3% on day 1, 1% on day 3, 3.5% on day 7 and 6.3% at 30 days. Forty-six per cent of patients who died had a diagnosis of malignancy.

Mortality rates at days 1, 3, 7, 30 and 90 days for PESI and sPESI classes are presented in Table 3. There were no fatalities in the sPESI low risk group after 90 days of follow up.

The Kaplan-Meier survival curves for PESI low-risk (class I, II) vs. high-risk (class III, IV, V) showed significantly different trends in mortality (log rank test $p < 0.001$), see Figure 2

Data on diagnostic accuracy of dichotomized PESI and sPESI scores are provided in Table 3. Sensitivity was high for both measures at all time points. Of particular note it was 100% at days 1, 3 and 7 with the exception of the PESI score at day 7 (90%). Specificity was low (<50%) at each time point. The negative predictive value (NPV) for overall mortality was persistently high for both PESI (98% - 100%) and sPESI (100%).

Discussion

In this retrospective cohort pilot study, we investigated the diagnostic utility for very early mortality (<7 days) of PESI and sPESI. This would suggest that both these scores may be useful to identify patients at very low risk of death from PE within 1 week. Patients in whom PE is suspected clinically and who are identified as low risk using these scores may be appropriate to have investigations performed on an outpatient basis, supporting the new BTS guidelines and building upon the currently limited pool of evidence.³ However, this is a small retrospective diagnostic accuracy study and should be replicated in a larger prospective evaluation before implementing

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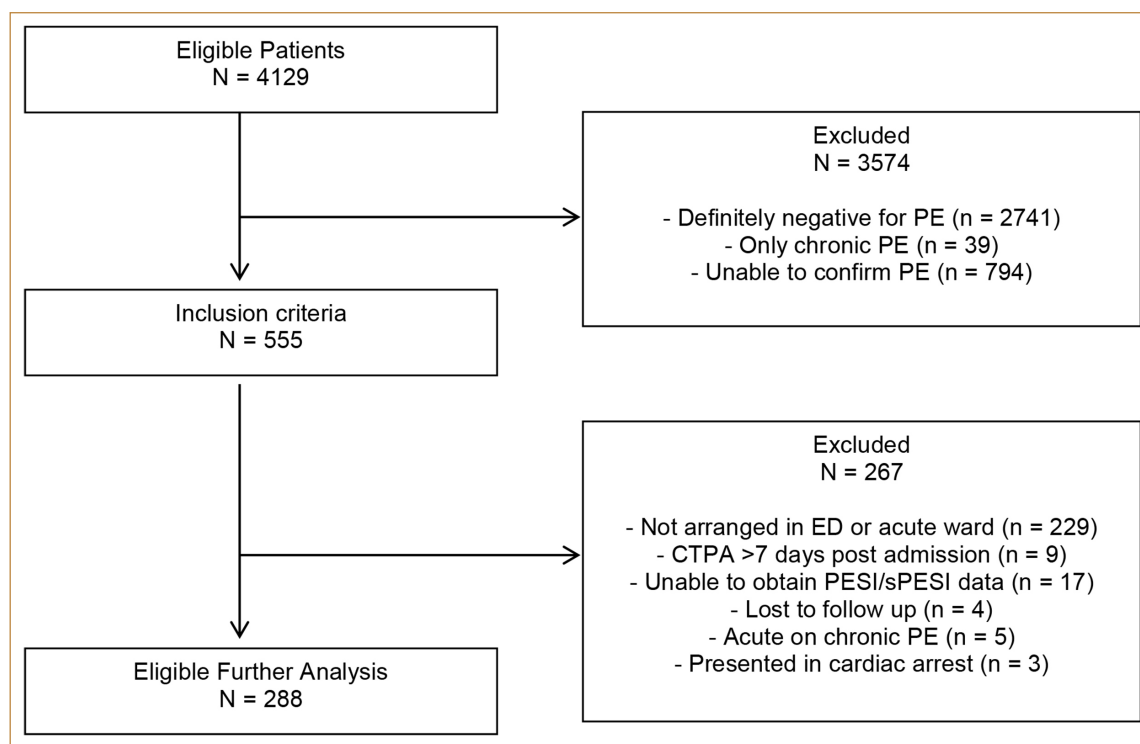


Figure 1. Flow diagram for inclusion and exclusion criteria in selection of participants

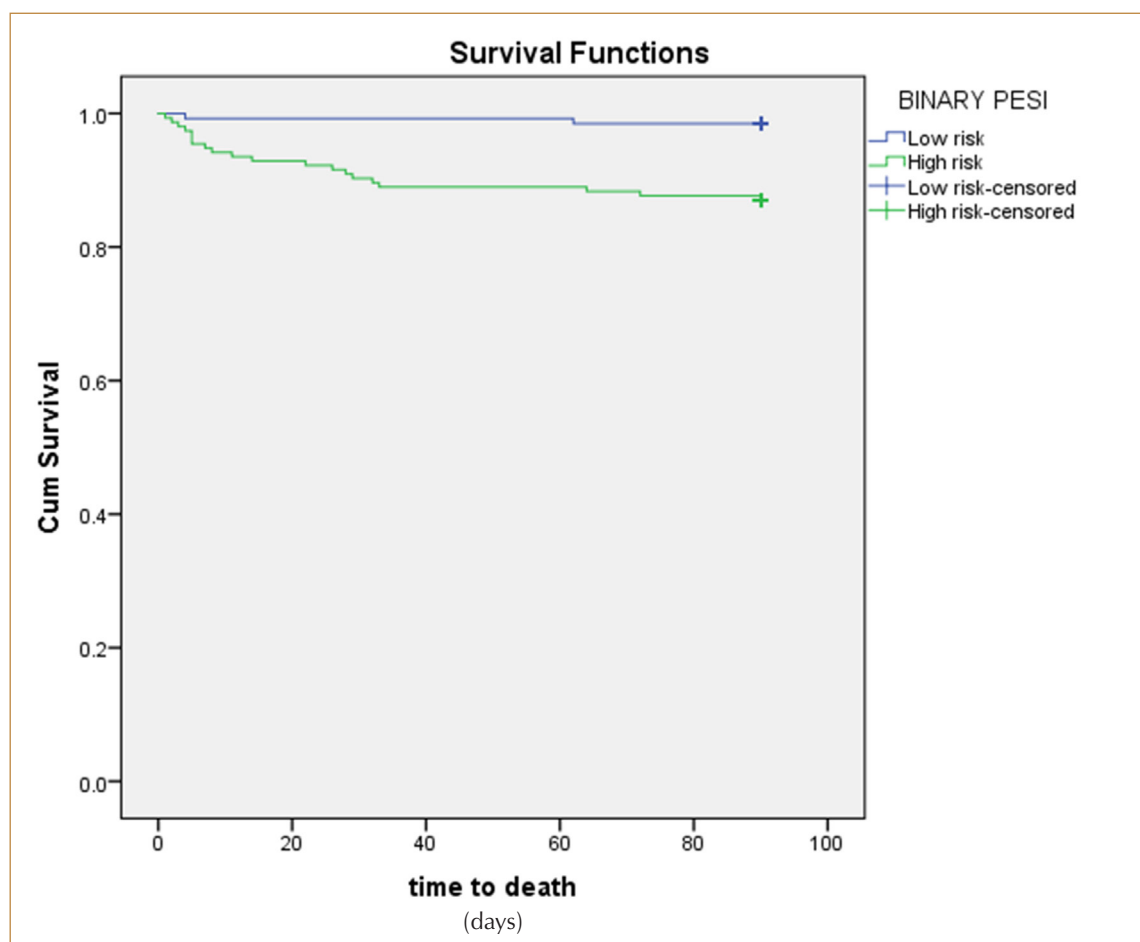


Figure 2. Kaplan-Meier curve for PESI low risk (class I & II) and high risk (class III, IV, & V)

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Table 2. Demographics overview

Sample size	288
Men (%)	149 (51)
Age (SD)	63 (18)
Mortality	
Day 1 (%)	1 (0.3%)
Day 3 (%)	3 (1.0%)
Day 7 (%)	10 (3.5%)
Day 30 (%)	18 (6.3%)
Day 90 (%)	22 (7.7%)
PESI score	
Mean (SD)	95 (2.3%)
Range	19-244
PESI Class	
Class I (%)	76 (26.4%)
Class II (%)	57 (19.8%)
Class III (%)	50 (17.4%)
Class IV (%)	47 (16.3%)
Class V (%)	58 (20.1%)
sPESI class	
Low risk	101 (35.1%)
High risk	187 (64.9%)

SD - Standard Deviation

this into clinical practice. This study also provides 90-day mortality data for sPESI, which was found to be limited from current available research.

Although the original PESI studies identify Class I & Class II as the lower risk categories with the potential of outpatient management, the results of this study suggests that patients in Class III could potentially be included for consideration of outpatient management as we saw no mortality in this group.⁴ This supports Rechen et al., with their retrospective observational study suggesting that a select group of intermediate and high risk patients can be managed safely as an outpatient.⁹ It is recognized however that this current studies results are based on a smaller sample size than was used in the development of PESI, and doesn't take into account non-fatal events.⁴ Further studies could investigate whether higher risk classes should be included in outpatient management based on an assessment of very early mortality.

Overall this supports the latest BTS guidelines, but challenges their assertion that imaging should occur within 24 hours.

The study found that the diagnostic utility of sPESI was similar to PESI, which is consistent with previous findings.¹⁰ The low risk sPESI group

however had smaller numbers than low-risk PESI (35% vs 46.2%). Therefore, although sPESI is simpler for physicians to use, and demonstrated no mortality up to 90 days in the low risk group, it identified fewer patients that would be suitable for consideration of outpatient management, limiting its usefulness in clinical practice.

Our study supports the view that low risk patients with clinical suspicion of acute PE, could potentially be managed as outpatients, with no significant mortality risk in the initial few days of presentation. It should be recognized, however, that PESI was intended to supplement, not replace, clinical judgment.⁴ Therefore, the physician's input is vital in assessing who can be managed at home regardless of scoring criteria, including co-morbidities as well as social factors such as access to care. To emphasize this point, within Class II there was one death within 7 days. This was a 53-year-old gentleman with a tachycardia of 120 beats per minute. His ECG implied significant right heart strain, and he was promptly admitted.

Limitations

There are several limitations that should be considered when interpreting the results of this study. The study is a two centre study, limiting the generalizability of the results. The study sample is small giving poor precision to our estimates as reflected by the wide confidence intervals. Data was obtained retrospectively through medical chart review. While all data was extracted by one researcher which may help to maintain consistency of data extraction, we did not perform a test of intra-rater reliability. The researcher was not blinded which may be a source of bias. The reliability of the data is dependent on the quality of recording in the medical charts. Documentation can be incomplete or misleading with variation in meaning and understanding between clinicians. In particular the absence of documentation of a variable in the medical record can be problematic, as it can be unclear if this means the variable was not present or just not recorded.

It is likely some patients who had a PE were missed. Where PE was diagnosed by V/Q scan these patients were not identified. Those with an unclear report for the diagnosis of PE were not included, but it is probable that some of these patients did indeed have a PE. This is shown by a large number (794 patients) in which a CTPA was unable to confirm a PE; of these, 19 stated a PE was possible but further imaging was required to confirm or to correlate clinically, 50 stated other differentials to explain a filling defect e.g. lymph node compression of an artery, and 725 in which the image quality couldn't

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Table 3. The mortality rate of each PESI & sPESI class, with the accompanying test characteristics, over a period of 1-90 days.

	Day 1	Day 3	Day 7	Day 30	Day 90
PESI	(%, 95% CI)	(%, 95% CI)	(%, 95% CI)	(%, 95% CI)	(%, 95% CI)
Class I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Class II	0 (0)	0 (0)	1 (1.8, 0-10.2)	1 (1.8, 0-10.2)	2 (3.5, 0-12.6)
Class III	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Class IV	0 (0)	0 (0)	2 (4.3, 0-15)	3 (6.4, 1.6-17.8)	5 (10.6, 4.2-23)
Class V	1 (1.8, 0-10)	3 (5.3, 0.12-14.7)	7 (12.3, 5-23.2)	14 (24.1, 14.9-36.7)	15 (25.8, 16.3-38.5)
sPESI					
Low risk	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
High risk	1 (0.5, 0-3.3)	3 (1.6, 0.3-4.8)	10 (5.4, 2.8-9.7)	18 (9.6, 6.1-14.8)	22 (11.8, 7.8-17.2)
PESI – dichotomised: Class I, II (low risk) or III, IV, V (high risk)					
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Sensitivity	100 (100)	100 (100)	90 (71.4-100)	94.4 (83.2-100)	90.9 (78.9-100)
Specificity	46.5 (41.1-52.2)	46.8 (41.7-52.1)	47.7 (41.8-53.6)	52.3 (46.8-58.3)	49.4 (43.5-55.4)
PPV	0.6 (0-3.9)	1.9 (0.4-5.8)	5.8 (2.9-10.8)	11 (6.9-17)	13 (8.4-19.6)
NPV	100 (100)	100 (100)	99 (98.8-100)	99 (98.7-100)	98 (96.5-100)
sPESI					
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Sensitivity	100 (100)	100 (100)	100	100 (100)	100 (100)
Specificity	35.3 (29.5-40.1)	35.6 (30-41.1)	36.5 (30.8-42.1)	37.5 (31.8-43.3)	38.1 (32.1-43.9)
PPV	0.5 (0-3.3)	1.6 (0.3-4.8)	5.34 (2.8-9.7)	9.6 (6.1-14.8)	11.8 (7.81-17.2)
NPV	100 (100)	100 (100)	100 (100)	100 (100)	100 (100)

% - Percentage of mortality within the PESI class. 95% CI – 95% Confidence intervals, PPV - positive predictive value, NPV - negative predictive value

exclude a PE; the latter was often due to motion artefact, and couldn't eliminate a small subsegmental PE. If the outcomes of those who were not included were different to the study cohort, this may have confounded our results.

The 4 patients not included due to loss to follow up should be considered. All 4 of them were high risk (86+ points), and therefore their inclusion would not have affected sensitivity.

The study didn't consider whether patients were admitted or discharged therefore the effects of inpatient management were not accounted for.

Conclusion

Patients with a PE who are identified as low risk using the sPESI and class I to III with PESI have a very low risk for mortality in the short term. Similar patients suspected clinically of having a PE may be appropriate to have investigations performed on an outpatient basis. However, this is a small retrospective

diagnostic accuracy pilot study and should be replicated in a larger prospective evaluation before implementing this into clinical practice.

Legend

PE – Pulmonary Embolism
PESI – Pulmonary Embolism Severity Index
sPESI – Simplified Pulmonary Embolism Severity Index
ED – Emergency Department
GP – General Practitioner
GCS – Glasgow Coma Scale
HF – Heart Failure
CLD – Chronic Lung Disease
CT – Computed Tomography
PPV – Positive Predictive Value
NPV – Negative Predictive Value

Competing interest

Nothing to declare.

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