i)Title

The effect of a clinical flowchart incorporating Wells score, PERC rule and age adjusted D-dimer on pulmonary embolism diagnosis, scan rates and diagnostic yield.

(ii) the full names, titles and degrees of the authors;

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(iii) each author's contribution

PB conceived the idea for the study, which was then designed with assistance from FT, JS, YW, MK, LB, MD and PC. PB supervised overall conduct of the study. Local sites were coordinated by PB, MK and LB. PB and JM were responsible for data collection from site A whilst JS was responsible for data collection from sites B and C. PB and JM performed all data entry. PB analysed the data, with statistical analysis performed by SG. All authors contributed to the final manuscript. PB takes overall responsibility for paper as a whole.

iv) Short running title

A flowchart consisting of Wells, PERC and age adjusted DD

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Objective

To assess the association between the use of a flowchart incorporating Wells score, PERC rule and age-adjusted Ddimer and subsequent imaging and yield rates of Computed Tomography Pulmonary Angiogram and Nuclear Medicine Ventilation Perfusion scans being ordered in the Emergency Department for the assessment of pulmonary embolism.

Methods

A flowchart governing Emergency Department pulmonary embolism investigation was introduced across three Emergency Departments in Melbourne, Australia for a twelve month period. Comparison of pulmonary embolism imaging rates and yield with the preceding twelve months was performed.

Results

1815 pre-implementation scans were performed compared with 1116 scans post implementation. Due to growth in patient attendances over this time, this equated to an imaging rate of 14.5 per 1000 presentations pre implementation and 8.6 per 1000 presentations post implementation (p<0.001).

Overall PE imaging yield rates rose from 9.9% to 16.5% (p<0.001).

A total of 179 pre-implementation pulmonary embolisms were identified, with an incidence of 1.4 per 1000 presentations. This compared to 185 pulmonary embolisms post implementation, with an incidence of 1.4 per 1000 presentations (p=0.994).

Conclusions

The introduction of a clinical flowchart incorporating Wells score, PERC rule and age-adjusted D-dimer was associated with an increase in Emergency Department Computed Tomography Pulmonary Angiogram and Nuclear Medicine Ventilation Perfusion yield rate from 9.9% to 16.5% across the three enrolment hospitals when investigating possible pulmonary embolism. This corresponded to a 40% relative reduction in pulmonary embolism imaging. Diagnosis rates remained unchanged and no cases of missed pulmonary embolism attributable to the flowchart were identified.

Key Words: pulmonary embolism, computed tomography pulmonary angiogram, ventilation perfusion scan, emergency department, d-dimer

Introduction

Over recent years, literature has amassed regarding Emergency Department (ED) investigation for pulmonary embolism (PE). In 1998, Wells devised a three point clinical scoring system classifying patients as low, intermediate

or high risk of having a PE¹. This was supplemented in the early 2000s by D-dimer measurement², with a negative result safely negating further investigation in most patients³. Over recent years it has been proposed that an age-adjusted cut-off for patients 50 years and older could increase yield even further^{4,5,6}. Parallel to these developments other clinical scoring systems emerged, such as the Pulmonary Embolism Rule-out Criteria (PERC) rule—a validated supplementary decision rule for low risk patients^{7,8}. There has been considerable discussion but little published literature around a strategy to specifically combine these three tools into a single flowchart.

This study aimed to assess whether the introduction of a clinical flowchart incorporating Wells score, PERC rule and age-adjusted D-dimer would be associated with a decrease overall imaging rates and increase the positive yield of Computed Tomography Pulmonary Angiogram (CTPA) and Nuclear Medicine Ventilation Perfusion (VQ) scans being ordered to asses for PE at one of the three EDs in Eastern Health (EH), Melbourne.

Methods

A three site before and after study was designed to compare ED CTPA and VQ ordering rates and yield before and after implementation of a flowchart governing PE investigation. To allow for possible seasonal variation we used 12 month data collection periods, with a pre implementation period from October 27 2014 to October 25 2015, and an implementation period from October 26 2015 to October 24 2016. Stakeholders from emergency medicine, radiology, respiratory medicine and haematology developed the flowchart and low risk ethics approval from EH ethics committee was obtained. **The enrolment sites were Box Hill hospital, Maroondah hospital and Angliss hospital with annual ED attendances for 2016 of approximately 64 000, 58 000 and 40 000 respectively . All three EDs are mixed adult/paediatric Level 3 Emergency Departments academically affiliated with the Eastern Health Clinical School, Monash University.** All CTPA and VQ scans on patients aged 16 and over who attended one of these three EH EDs based in Melbourne (Box Hill hospital, Maroondah hospital, Angliss hospital) during the study period were included in data analysis but it was left to the discretion of the senior treating ED doctor whether to ultimately

adhere to the flowchart. This was particularly emphasised in specific clinical situations where individual components of the flowchart lack validation (eg. patients aged under 18 years, pregnancy). Due to local differences in imaging test availabilities between the three enrolment hospitals two versions of the flowchart were introduced (figure 1), which differed only in their recommendation to proceed with CTPA vs VQ scan should imaging be required.

The implementation phase commenced upon integration of the flowchart into the ED Information System (EDIS) in use across all sites. This was configured to print out whenever a D-dimer, CTPA or VQ were requested. All medical imaging departments were instructed to proceed with imaging only after receiving the flowchart, unless specifically advised by a senior ED doctor to override it. Hard copies were also made available for cases where non-EDIS generated test requests were received. In the two weeks prior and immediately after implementation, staff were educated regarding these changes via one-on-one and group tutorials plus email communication.

For the duration of this study the D-dimer assay used at all three sites was D-Di Plus (Stago)⁹, reported as mg/L FEU. During the pre-implementation phase, results reported on our pathology system flagged an abnormal D-dimer greater than 0.3 mg/L by displaying this value in bold. Coinciding with the commencement of the implementation phase, this value was increased to 0.5 mg/L, however for patients with suspected PE clinicians were instructed to use 0.5 mg/L for patients aged less than 50 years, and an age adjusted D-dimer (age*0.01) if aged 50 years or greater.

All imaging data for the duration of the study period was obtained from the EH Radiology Information System database. To ensure familiarity with the project during the first 6 months of the implementation phase, regular audits were performed using both clinical notes from the EDIS and printed flowcharts. Individual clinicians were contacted by local site coordinators where there was a clear deviation from the flowchart.

All radiological results were reported by consultant radiologists. These were read by a research nurse, with any ambiguity flagged for further review by the lead researcher. A final diagnostic decision was then made after

consideration of all subsequent investigation and management decisions, either on discharge home from the ED or on discharge from the ward (for patients admitted from the ED). Only CTPA and VQ scans performed during an ED visit or Short Stay admission were included, with the exception of a small number of patients who had their imaging booked in ED and performed shortly after admission to a ward bed.

Results were entered into Microsoft Excel 2010, which was also used for descriptive analysis. Rates and their 95% confidence intervals (CI) were estimated using Stata Statistical Software version 14.2. Two-samples test of proportions were used to compare pre-implementation and implementation rates and yield.

Interrupted Time Series (ITS, also known as segmented regression) was used to analyse change in yield rates postintervention. This method uses time series methods, accounting for autocorrelation between variables and the preintervention period serves as a control period. Time lags were included in the ITS analysis to highlight possible differences in post implementation effect onset between the three sites. Newey-West standard errors for coefficients were estimated and the Cumby-Huizinga test for autocorrelation was conducted to determine optimum number of lags. This lead to inclusion of autocorrelation with a maximum of three lags in analysis of Sites A and B data while Site C and overall data were analysed without lags. The unit of analysis was month which ran from the 26th to the 25th of the following month.

Results

Basic demographic information and ED details are shown in Table 1. Comparisons of pre and post CTPA/VQ scan rates are shown in Table 2. In all tables and figures Site A refers to Box Hill hospital, site B refers to Maroondah hospital and site C refers to Angliss hospital.

Overall CTPA and VQ numbers at all 3 EDs

A total of 1815 scans (675 VQ scans and 1140 CTPAs) were performed during the pre-implementation period, compared with 1116 scans (446 VQ scans and 670 CTPAs) post implementation. Due to growth in patient attendances over this time, this equated to an imaging rate of 14.5 per 1000 presentations pre implementation and 8.6 per 1000 presentations post implementation. This difference was statistically significant (p<0.001) at all three sites. Confidence intervals and individual ED results are shown in Table 2.

CTPA and VQ yield rate at all 3 EDs

Combined PE yield rates for the three EDs rose from 9.9% to 16.5%. This result was also statistically significant (p<0.001) (Table 2).

Using ITS, there was no significant change in the imaging yields from pre- to post-intervention periods (Table 3) although a small change was observed for one site. The results presented in Table 3 and Figure 2 also suggest that there was a lag in uptake of the intervention. Two sites showed no significant changes in yield rates immediately following intervention, however significant increases were then observed in the second and/or third month.

Number of PEs identified

A total of 179 PEs were identified during the pre-implementation period, with an incidence of 1.4 per 1000 presentations. This compares to 184 PEs post implementation, with an incidence of 1.4 per 1000 presentations (p=0.994) (Table 2).

Inter-hospital comparison of results

Chi-squared analysis showed pre-implementation imaging rates and yield to differ significantly between sites (p<0.001, p=0.015), however this effect was no longer observed post implementation (p=0.780, p=0.762).

D-dimer sub analysis

A comparison of the subset of patients who proceeded to imaging after D-dimer is shown in Table 4. 233 fewer patients with a normal D-dimer received imaging post implementation. Of these, 126 had a D-dimer between 0.3-0.5 mg/L FEU and 91 had a D-dimer >0.5 mg/L FUE but less than the age adjusted cut off.

Analysis of possible missed PEs

Interrogation of the EDIS was performed for patients who presented post implementation and had a PE diagnosed within three months of a previous presentation to one of the three EH EDs. No instances were discovered where a PE had been considered but not imaged during the initial visit. Likewise, there were no coronial reports received by EH relating to a missed PE from ED post implementation. A search of the EH adverse events database showed one patient who represented to an EH ED with a PE two days after a previous presentation, however there was no clinical suspicion of PE during this earlier attendance and the flowchart was therefore not applied.

Effect on all of hospital ordering

Total CTPA and VQ ordering rates for EH during the study periods are shown in Figure 3.

Discussion

Like all diagnostic testing, the "ideal" yield for PE imaging in the ED is a balanced consideration¹⁰. A low yield increases risks such as radiation exposure^{11,12} and contrast nephropathy,¹³ whilst increasing the rate of false positive findings and incidental findings¹⁴, with an associated risk of treatment associated harm^{15,16}. A yield that is too high will have a statistically corresponding increase in false negatives, with associated harm from missed diagnosis of PE. There is considerable evidence that a structured approach to ED diagnosis of PE can increase yield rates. In 2013, Ong et al¹⁷ showed an increased yield in positive CTPA scans from 9% to 14% at Box Hill Hospital, Melbourne that corresponded with the introduction of a flowchart based on a combination of Wells score and D-dimer with a flat cut off of 0.3 mg. Similar recent work by Mills et al¹⁸ demonstrated an increase in CTPA from 8.1% to 10.6% with Wells

score based clinical decision support while Jimenez et al demonstrated a significant decrease in CTPA use via the introduction of computer based diagnostic decision support although they did not see a corresponding increase in imaging yield¹⁹. Internationally, adoption of an age adjusted D-dimer compared with a flat cut-off of 0.5 mg/L has been shown to safely increase the diagnostic yield of D-dimer testing and overall imaging yield^{4,5,6,20}, although Jones et al²¹ highlighted potential issues with the upfront use of D-dimer in undifferentiated ED patients. In 2017 the YEARS tool²² was demonstrated to achieve a 8.7% reduction in CTPA numbers over the use of Wells + age adjusted D-dimer by simply stratifying patients into two discrete D-dimer cut off groups depending on the presence or absence of three clinical features associated with PE.

Direct comparison of our findings with any of these studies is difficult, due to varying patient settings, differences in enrolment procedures and pathway elements, and large differences in baseline diagnostic yields. Nevertheless, multiple sources, such as the American College of Physicians²³, have recommended the adoption of a structured approach to PE diagnosis. The pathway examined in this paper draws heavily from many sources, all of which have demonstrated an improvement in PE imaging yield but there is little existing literature regarding the use of a single flowchart specifically combining Wells score, PERC rule, and age-adjusted D-dimer, nor the expected yield from such a strategy.

In the RESPECT-ED study²⁴, Mountain et al recently showed that diagnostic yield from CTPA in Australian EDs ranged from 9.3% - 17%, with a mean of 13.6%. The use of local guidelines was not explored in this paper; however this variation in yield suggests that current practice differs significantly between sites. Comparison with these results also shows that our mean combined implementation yield rate of 16.5% is higher than that which they experienced. Furthermore, our dataset also included VQ scans, for which all three of our sites experienced a lower implementation yield (12.9%) than for CTPA alone (19.1%). Of the 13 Australian sites included in RESPECT-ED, the highest CTPA yield was 17.0%.

Whilst the results showed an increase in yield of 6.6%, interrupted time series analysis suggests that there may already have been a small pre-existing trend towards increased yield at the three sites. Also, despite the described intervention occurring simultaneously across all three sites at the go live date, there was considerable variation in uptake tempo, with changes at sites B and C only becoming statistically significant when a two month delay is considered. This is not unexpected, given the lack of a run-in period and logistical complexity in changing practice amongst a large group of ED physicians across three different sites.

In addition to analysis of overall results, attempts have been made to quantify what effect on yield the various selection for D-dimer testing.

components had. Pre-post comparison of patients who had both a D-dimer test and imaging (Table 4) shows that 233 fewer patients with a normal D dimer received imaging post implementation. Of these, 126 could be attributed to the increase in D-dimer reference range from 0.3-0.5 mg/L FEU, and a further 91 to use of the age adjusted cut off. Somewhat surprisingly, a fall in associated PE diagnosis from 15% to 0% was also seen post implementation in patients with a normal D-dimer. In addition to the reduced imaging attributable to changes in D-dimer cut off parameters shown in Table 4, it can also be seen that 12 patients with a normal D-dimer were diagnosed with PE pre-implementation but none were identified post implementation. A possible explanation for this could be a greater proportion of pre-implementation patients with a high Wells score also having a D-dimer measured before imaging, and its inadequate sensitivity in this sub-group²⁵⁻²⁷. The post implementation increase in patients with an elevated D-dimer and PE diagnosis also suggests a more discriminatory approach to post-implementation patient

In the pre-implementation period Site A already had some basic PE decision support in place¹⁷, in contrast with Sites B and C, where no particular practice guidance existed. This contrast is highlighted by the significant difference in pre-implementation yield and imaging rates between site A compared with sites B and C. This difference disappeared during the implementation phase. With this in mind, EDs with existing PE decision support processes in place,

especially if already using a D-dimer cut off of 0.5 mg/L, are unlikely to see an increase in yield of the same magnitude as was experienced in this study. Nevertheless, we believe that our results demonstrate that a combined CTPA/VQ yield rate of over 15% is achievable in comparable Australian EDs performing a mix of CTPA and VQ scans, whilst for sites predominantly performing CTPA this is may be higher.

Accounting for the adjusted presentation numbers pre and post implementation, we estimate that use of the flowchart was associated with 772 fewer ED scans during the intervention period. As figure 3 illustrates, comparison of raw imaging numbers for the whole network between the two time periods shows a growth in non-ED scans by 189. Adjusting this for total organisational activity is problematic, especially as there was a 4.5% growth in occupied bed days recorded across the three campuses between the two periods. Nevertheless, even if a small portion of the imaging not performed in the ED was moved to an inpatient setting there is a potential for patient and organisational benefit, measured in terms of ED flow and NEAT-performance **against the National Emergency Access Target (NEAT)** of 90% of patients leaving the ED within 4 hours of arrival²⁸, although this must be weighed up against the potential for increased morbidity from delayed PE diagnosis²⁹⁻³¹.

Whilst it is possible that use of the flowchart resulted in an increase in missed PE diagnosis, investigation of hospital records, adverse event registers and coronial reports showed no evidence of this. There was also no statistical difference in the number of patients diagnosed with PE between the two periods and during the implementation phase no PEs were identified in the 86 patients who had a negative D-dimer but still proceeded to imaging.

A strength of this study is the way in which it was integrated into standard patient care across three discrete EDs. All patients scanned during the comparison periods were included, regardless of their treating physician or whether there was adherence to the flowchart. This is likely to enhance both reproducibility and sustainability. Our implementation also drew heavily from our experiences with existing evidence based change management strategies, which was an additional potential reason for the effect size that we saw³².

A limitation of this study was our inability to capture patients where PE was considered but neither D-dimer or imaging were performed, either due to a negative PERC score or failure to follow the flowchart. Whilst we encouraged clinicians to use the flowchart whenever PE was considered, differential diagnoses may have been considered and excluded without documentation. Similarly, although data were captured for all patients who had their D-dimer measured but did not proceed to imaging, they were excluded from final analysis due to the difficulty in determining whether D-dimer was being measured for PE as a differential diagnosis, or for alternative reasons (such as aortic dissection, DVT exclusion). Including these factors would have required a different study design.

Compliance with use of the flowchart was not formally assessed. The regular audits during the first 6 months of the implementation period were performed as part of the overall change management process rather than to measure this aspect of the study.

This was an uncontrolled before and after study, and it is possible that the observed effect was from factors other than the pathway introduction. Despite this, we feel that interrupted time series analysis shows a strong association between increased imaging yield and adoption of the pathway. The similarity in effect observed across the three sites and use of symmetrical twelve-month time periods also suggest that factors other than those described in this intervention were unlikely to have played a significant role.

Conclusions

The introduction of a clinical flowchart incorporating Wells score, PERC rule and age-adjusted D-dimer was associated with an increase in ED combined CTPA/VQ imaging yield rate from 9.9% to 16.5% across the three

enrolment hospitals when investigating possible PE. This corresponded to a 40% relative reduction in PE imaging. PE diagnosis rates remained unchanged and no cases of missed PEs attributable to the flowchart were identified. A larger, randomised, multi-centre study could identify whether such a strategy is transferable across all Australian EDs.

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Competing interests

None declared

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Table 1: Sex and mean age for patients having CTPA or VQ scanning

·	Pre-Imple	ementatio	n Phase	Implementation Phase						
<	Male	Female	Mean age [SD]	Male	Female	Mean age [SD]				
	n(%)	n(%)	(yrs)	n(%)	n(%)	(yrs)				
Site A	282	363	3 61.5		281	62.9				
	(44%)	(56%)	(18.0)	(37%)	(63%)	(19.5)				
Site B	304	458	58.1	167	241	59.2				
,	(40%)	(60%)	(18)	(41%)	(59%)	(18.4)				
Site C	146	262	53.3	84	180	54.8				
	(36%)	(64%)	(19)	(32%)	(68%)	(19.1)				
Combined	732	1083	58.2	415	701	59.6				
	(41%)	(59%)	(18.5)	(37%)	(63%)	(19.4)				

Abbreviations: SD = standard deviation

Table 2: Comparison of pre- and post- PE-related rates

-	Pre-implementation Phase				Post-Imp	Post-Implementation Phase				Comparison of pre- implementation and implementation phases		
,	Ν	n	Rate (per 1,000 presentations)	95% CI	Ν	n	Rate (per 1,000 presentations)	95% CI	Diff	95% CI	p-value	
Total numb	er of scans (n)											
Site A	49161	645	13.1	12.2, 14.2	52869	443	8.4	7.6, 9.2	-4.7	-6.0, -3.5	<0.001	
Site B	45909	762	16.6	15.5, 17.8	46292	408	8.8	8.0, 9.7	-7.8	-9.2, -6.3	<0.001	
Site C	30509	408	13.4	12.1, 14.7	30025	265	8.8	7.8, 10.0	-4.5	-6.2, -2.9	<0.001	
Combined	125579	1815	14.5	13.8, 15.1	129186	1116	8.6	8.1, 9.2	-5.8	-6.6, -5.0	<0.001	

Number of PE's identified (n)

Site A	49161	80	1.6	1.3, 2.0	52869	77	1.5	1.2, 1.8	-0.2	-0.6, 0.3	0.537
Site B	45909	68	1.5	1.2, 1.9	46292	68	1.5	1.2, 1.9	0.0	-0.5, 0.5	0.961
Site C	30509	31	1.0	0.7, 1.4	30025	39	1.3	0.9, 1.7	0.2	-0.3, 0.8	0.363
Combined	125579	179	1.4	1.2, 1.7	129186	184	1.4	1.2, 1.6	0.0	-0.3, 0.3	0.994
	N	n	%	95% CI	N	n	%	95% CI	Diff	95% CI	p-value
Yield rate											
Yield rate Site A	645	80	12.4	10.1, 15.2	446	77	17.4	14.1, 21.2	5.0	0.6, 9.3	0.022
Yield rate Site A Site B	645 762	80 68	12.4 8.9	10.1, 15.2 7.1, 11.1	446 408	77 68	17.4 16.7	14.1, 21.2 13.3, 20.6	5.0 7.7	0.6, 9.3 3.6, 11.9	0.022 <0.001
Yield rate Site A Site B Site C	645 762 408	80 68 31	12.4 8.9 7.6	10.1, 15.2 7.1, 11.1 5.4, 10.6	446 408 264	77 68 39	17.4 16.7 14.3	14.1, 21.2 13.3, 20.6 11.0, 19.1	5.0 7.7 6.7	0.6, 9.3 3.6, 11.9 1.8, 11.7	0.022 <0.001 0.005
Yield rate Site A Site B Site C Combined	645 762 408 1815	80 68 31 179	12.4 8.9 7.6 9.9	10.1, 15.2 7.1, 11.1 5.4, 10.6 8.6, 11.3	446 408 264 1118	77 68 39 184	17.4 16.7 14.3 16.5	14.1, 21.2 13.3, 20.6 11.0, 19.1 14.4, 18.8	5.0 7.7 6.7 6.6	0.6, 9.3 3.6, 11.9 1.8, 11.7 4.1, 9.2	0.022 <0.001 0.005 <0.001

N = ED presentations aged 16 years and over

n = number of scans

Table 3: Change in Yield rate after intervention (interrupted-time series)

Hospital Site	Change in	yield post-inter	vention	Change in slope			
	β	95% CI	p-value	β	95% CI	p-value	
Site A							
No delay	-0.01	-0.10, 0.07	0.749	0.01	-0.01, 0.01	0.382	
Delay = 1 month	0.03	-0.05, 0.12	0.419	0.01	-0.01, 0.02	0.427	
Delay = 2 month	0.08	0.03, 0.14	0.007	0.00	-0.01, 0.01	0.767	
Delay = 3 month	0.07	0.00, 0.14	0.038	0.00	-0.01, 0.01	0.725	
Site B							
No delay	0.10	-0.02, 0.22	0.090	-0.01	-0.02, 0.01	0.413	
Delay = 1 month	0.11	0.00, 0.22	0.047	-0.01	-0.03, 0.01	0.176	
Delay = 2 month	0.15	0.08, 0.23	<0.001	-0.02	-0.04, 0.00	0.021	
Delay = 3 month	0.11	-0.01, 0.22	0.064	-0.03	-0.05, 0.01	0.016	
Site C							
No delay	0.06	0.01, 0.11	0.025	-0.01	-0.02, 0.00	0.063	
Delay = 1 month	0.01	-0.04, 0.06	0.768	-0.01	-0.02, 0.00	0.063	
Delay = 2 month	0.00	-0.05, 0.05	0.990	-0.01	-0.02, 0.00	0.081	
Delay = 3 month	-0.01	-0.07, 0.05	0.761	-0.01	-0.02, 0.00	0.151	
All sites							
No delay	0.04	-0.02, 0.10	0.171	0.00	-0.01, 0.01	0.572	
Delay = 1 month	0.06	-0.01, 0.12	0.105	-0.01	-0.02, 0.01	0.388	
Delay = 2 month	0.09	0.05, 0.13	<0.001	-0.01	-0.02, 0.00	0.052	
Delay = 3 month	0.06	0.00, 0.13	0.045	-0.01	-0.03, 0.00	0.041	

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	Pre-implementation Phase		Implementation F	Comparison of yield rate pre-				
	No. of patients PEs identified		No. of patients	PEs identified	implementation and			
					impleme	implementation phases		
r	Ν	n(%)	Ν	n(%)	Diff	95% CI	p-value	
1								
d-dimer <0.3 mg/L FEU	39	3 (7.7)	23	0 (0.0)	-7.7	-16.1, 0.7	0.173	
d-dimer 0.3 – 0.49 mg/L FEU	162	4 (2.5)	36	0 (0.0)	-2.5	-4.9, 0.0	0.341	
d-dimer ≥0.5 mg/L but < age adjusted cut	141	5 (3.5)	50	0 (0.0)	-3.5	-6.6, 0.0	0.178	
off (for patients aged 50 or older)								

d-dimer ≥ age adjusted cut off and	269	49 (18.2)	419	88 (21.0)	2.8	-3.3, 8.8	0.372
patient aged >49yrs							
d-dimer ≥0.5 and patient aged <50 years	125	17 (13.6)	195	30 (15.4)	1.8	-6.1, 9.6	0.660
Total	736	78 (10.6)	723	118 (16.3)	5.7	2.3, 9.2	0.001

Figure Legends: Figure 1 Investigation pathway for pulmonary embolism – site a Alternative imaging recommendation - sites b and c Figure 2: Observed distribution of yield rate over time by hospital site Figure 3: Comparison of total organisational CTPA/VQ numbers 1. Chest X-Ray. Use to determine if another diagnosis is more likely than PE





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Figure 3. Comparison of total organisational CTPA/VQ numbers

Title Page

i)Title

The effect of a clinical flowchart incorporating Wells score, PERC rule and age adjusted D-dimer on pulmonary embolism diagnosis, scan rates and diagnostic yield.

(ii) the full names, titles and degrees of the authors;

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(iii) each author's contribution

PB conceived the idea for the study, which was then designed with assistance from FT, JS, YW, MK, LB, MD and PC. PB supervised overall conduct of the study. Local sites were coordinated by PB, MK and LB. PB and JM were responsible for data collection from site A whilst JS was responsible for data collection from sites B and C. PB and JM performed all data entry. PB analysed the data, with statistical analysis performed by SG. All authors contributed to the final manuscript. PB takes overall responsibility for paper as a whole.

iv) Short running title

A flowchart consisting of Wells, PERC and age adjusted DD

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