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How should we diagnose suspected deep-vein thrombosis?

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Summary

Background: Many different approaches are used to diagnose suspected deep-vein thrombosis (DVT), but there has been little formal comparison of strategies.
Aim: To identify the most cost-effective strategy for the UK National Health Service (NHS).
Design: Systematic review, meta-analysis and cost-effectiveness analysis.
Methods: We identified 18 strategies and estimated the diagnostic performance of constituent tests by systematic review and meta-analysis. Outcomes of testing and treatment were estimated from published data or by an expert panel. Costs were estimated from NHS reference costs and published data. We built a decision-analysis model to estimate, for each strategy, the overall accuracy, costs, and outcomes (valued as quality-adjusted life-years, QALYs), compared to a 'no testing, no treatment' alternative. Probabilistic analysis estimated the net benefit of each strategy at varying thresholds for willingness to pay for health gain.
Results: At the thresholds for willingness to pay recommended by the National Institute for Clinical Excellence (£20 000–£30 000 per QALY), the optimal strategy was to discharge patients with a low or intermediate Wells score and negative D-dimer, limiting ultrasound to those with a high score or positive D-dimer. Strategies using radiological testing for all patients were only cost-effective at £40 000 per QALY or more.
Discussion: The optimal strategy for DVT diagnosis is to use ultrasound selectively in patients with a high clinical risk or positive D-dimer. Radiological testing for all patients does not appear to be a cost-effective use of health service resources.

Introduction

Deep-vein thrombosis (DVT) is an important cause of morbidity and mortality, but most patients presenting with suggestive symptoms do not have DVT.[1] Investigations range from the accurate but expensive (contrast venography) to the cheap but unreliable (clinical assessment). Recent studies suggest that algorithms combining simple diagnostic tests may provide an acceptable way of reducing the need for expensive, definitive tests, but these studies have not explicitly weighed the costs and benefits of different diagnostic approaches.[2] Despite a wealth of published data, there is substantial variation between hospitals in their diagnostic approach to suspected DVT.[3]

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Choosing an appropriate diagnostic strategy requires explicit consideration of the benefits, harms and costs of diagnosis (or misdiagnosis). The benefit of using accurate but expensive tests (in terms of correctly identifying and treating those with DVT) needs to be weighed against their additional costs. We also need to consider whether health service resources used diagnosing DVT could be better spent elsewhere, and to decide how much we are willing to pay, as a society, to achieve health gains. Only then can we determine what is likely to be an appropriate diagnostic strategy for suspected DVT.

We aimed to estimate the accuracy and cost-effectiveness of available diagnostic strategies for suspected DVT and identify a practical, cost-effective strategy that could be implemented throughout the National Health Service (NHS).

Methods

We searched the literature to identify studies of diagnostic algorithms for suspected DVT that used widely available tests (i.e. Wells clinical score, D-dimer, ultrasound and venography)[3] and reported follow-up of patients with negative results. Four further algorithms, each based on a single test with high sensitivity for proximal DVT (contrast venography, above-knee ultrasound, full-leg ultrasound, and ultrasound with repeat if negative), and a zero-option alternative (no testing or treatment), were also included.

We developed a decision analysis model to compare algorithms in a hypothetical cohort of 1000 out-patients with suspected DVT. Estimates of the sensitivity and specificity for each algorithm were applied to the population to determine the proportions of patients with and without DVT who would receive treatment. This then determined which patients would suffer events relating to DVT or treatment over the minimum treatment period of 3 months. We then estimated subsequent lifetime health outcomes, valued as discounted quality-adjusted life years (QALYs), and costs accrued by testing and treatment.

Sensitivity and specificity

We undertook systematic literature review and meta-analysis of each diagnostic test used in the algorithms.[4–7] Estimates from meta-analysis were applied to each algorithm to estimate overall sensitivity and specificity. Sensitivities for proximal and distal DVT were estimated separately. In estimating overall sensitivity and specificity, we assumed, based upon empirical data,[5] that D-dimer specificity was dependent upon Wells score, while sensitivity was independent. In the absence of similar data for ultrasound, we assumed that the sensitivity and specificity of ultrasound were independent of both Wells score and D-dimer.

If the algorithm defined ultrasound as being above-knee only, we assumed that sensitivity for distal DVT was zero. Some algorithms recommend repeat ultrasound after 1 week if the initial scan is negative, based on the pathophysiological rationale that repeat scanning detects propagating distal DVT. On this basis, we assumed that repeat ultrasound results were entirely dependent upon initial ultrasound (i.e. that a false negative initial ultrasound for proximal DVT would remain false negative on repeat scanning) and that the results of repeat scanning only differed from initial scanning if the patient initially had a distal DVT that then propagated proximally. We assumed that contrast venography had perfect sensitivity and specificity, but would not be feasible in 10%, would cause DVT in 1%,[8,9] and carried a 1:55 000 risk of fatal analphylaxis.[10,11]

Population characteristics

We estimated the prevalence of proximal DVT from a recent study,[12] the additional proportion of distal DVT using data from our meta-analysis of ultrasound, and the mean age and sex distribution from the VERITY DVT registry.[1]

Probability of events

Anticoagulant treatment may lead to fatal haemorrhage, disabling intracranial haemorrhage, or other non-fatal haemorrhage. We estimated the probability of these events using a recent meta-analysis.[13] Proximal DVT may lead to fatal pulmonary embolus (PE), non-fatal PE, or post-thrombotic syndrome. We estimated the probability of these events in treated patients using a recent meta-analysis[14] and cohort study.[15] We assumed that a distal DVT carried a 21% probability of propagating proximally,[16] where it would then carry the same risks as proximal DVT.

Anticoagulant therapy has been the established treatment for DVT for over 40 years, so few data are available regarding the risks associated with untreated proximal DVT. To estimate the probability of fatal and non-fatal PE, we analysed studies that followed-up untreated patients after negative results from tests that do not have 100% sensitivity for DVT. We estimated the anticipated number of missed DVTs, given the estimated sensitivity of the tests used, and compared this to the actual occurrence of fatal or non-fatal PE to calculate the risks of these outcomes (full details available from the authors).[7] An expert panel estimated the probability of developing post-thrombotic syndrome to be ~33% in untreated patients.

Valuation of outcomes

Individuals who died from an initial event were assigned zero QALYs. We assumed that initial event-free survival was followed by normal quality-adjusted life expectancy of 11.58 QALYs for an individual aged 60 years, based on interim life tables[17] and estimates of age specific quality of life.[18] We estimated QALYs for individuals who suffered non-fatal events by adjusting normal expected quality-adjusted, life expectancy using decrements from published data[19] or expert panel estimates.

Valuation of costs

Clinical scoring was assumed to cost 5 min of consultant time. D-dimer assay costs were estimated using NHS Trust data.[20] NHS reference costs were used to estimate ultrasound and venography costs, with a higher estimate being used for full-leg scanning.[21] We used NHS reference costs for fatal and non-fatal PE. We valued post-thrombotic syndrome as a new vascular surgery out-patient visit plus two follow-up visits per annum[21] and two extra general practitioner (GP) consultations per annum.[22] We estimated treatment of proximal DVT using data from Boccalon *et al.*,[23] followed by 3 months of warfarin therapy. We took drug costs from the 2004 BNF,[24] and GP and nursing costs from Netten and Curtis.[22] The cost of non-fatal, non-intracranial bleeding was based on NHS reference cost data for gastrointestinal bleeding,[21] while fatal bleeding and non-fatal intracranial bleeding were based on data from Sandercock *et al.*[25]

Model analysis

The parameters used in the model are outlined in the Appendix (Tables 5–8). The time horizon was the lifetime of the patient. We assumed a health and social services perspective, and applied a discount rate of 3.5% to all future costs and benefits. Costs are expressed in 2003/4 UK sterling values.

A mathematical model was used to estimate the expected additional costs and QALYs accrued by each algorithm, compared to no testing. The model was analysed probabilistically. Probability distributions were assigned to parameters used in the model, and Monte Carlo simulation was used to sample randomly from those distributions, the model being recalculated for each simulation. A number of one-way sensitivity analyses were performed in addition to the probabilistic sensitivity analysis outlined above (full details available from the authors). The results were expressed as a net benefit (additional QALYs multiplied by λ, with the additional costs subtracted, where λ is the threshold willingness to pay per QALY). The optimal strategy is the one with the greatest mean net benefit. Thresholds for willingness to pay of £10 000, £20 000 and £30 000 per QALY were used, based on guidance from the National Institute for Clinical Excellence (NICE).[27]

Results

We identified 14 studies of algorithms combining Wells score, D-dimer, ultrasound or venography that followed-up patients with negative results

Table 1 Summary of studies of diagnostic algorithms for suspected DVT

Author	Total	Treated	Not treated	DVT/PE during follow-up	Duration of follow-up (months)	Treated (%)	Untreated suffering DVT or PE (%)
Anderson[28]	344	43	301	2	3	12	0.7
Wells[29]	150	40	110	2	3	27	1.8
Wells[30]	593	92	501	3	3	16	0.6
Kraajihagen[31]	1739	410	1329	15	3	24	1.1
Bernadi[32]	946	265	681	3	3	28	0.4
Walsh[33]	194	39	155	0	6	20	0
Bates[34]	556	51	505	5	3	9	1.0
Schutgens[35]	812	309	503	8	3	38	1.6
Anderson[36]	1075	193	882	4	3	18	0.5
Janes[37]	431	93	338	1	3	22	0.3
Perrier[38]	474	111	363	9	3	23	2.6
Tick[39]	811	343	462	7	3	43	1.5
Wells (intervention)[40]	566	85	481	2	3	15	0.4
Wells (control)[40]	530	77	453	6	3	15	1.4
Ruiz-Giminez[41]	569	150	419	3	3	26	0.7

Data are numbers, except where indicated

Table 2 Outline of the diagnostic algorithms

Algorithm number	Algorithm	Source
0	No testing or treatment.	
1	Venography for all patients.	
2	Above-knee ultrasound, repeat if negative.	
3	Full-leg ultrasound, repeat if distal found.	
4	Above-knee ultrasound, no repeat.	
5	Wells and above-knee US. If low, discharge if US negative, venogram if positive. If moderate, repeat US if negative, treat if positive. If high, venogram if US negative, treat if US positive.	Anderson,[28] Wells,[29] Wells[30]
6	SimpliRED DD and above-knee US. If US positive then treat. If both are negative then discharge. If DD positive and US negative, repeat US.	Kraaijenhagen,[31] Bernadi[32]
7	Wells. High or intermediate: above-knee US, treat if positive, venogram if negative. Low: above-knee US, treat if positive, discharge if negative.	Walsh[33]
8	Wells. High or intermediate: full-leg US, treat if positive, venogram if negative. Low: full-leg US, treat if positive, discharge if negative.	Walsh[33]
9	Latex DD: if positive above-knee US and repeat, if negative do Wells score. If high US and repeat. If intermediate or low discharge.	Bates[34]
10	Latex DD: if positive above-knee US and repeat, if negative do Wells score. If high US, if intermediate or low discharge.	Schutgens[35]
11	Wells. High: above-knee US, treat if positive, SimpliRED DD if negative. If DD positive venogram, if negative repeat US. Intermediate: US, treat if positive, DD if negative. If DD positive repeat US, if negative discharge. Low: DD, US if positive, discharge if negative.	Anderson[36]
12	Wells & SimpliRED DD. If Wells high or intermediate, or DD positive, do full-leg US. If Wells low and DD negative then discharge.	Janes[36]
13	ELISA DD. If negative discharge, if positive do above-knee US. Treat if US positive, do Wells if negative. High Wells: venogram. Intermediate or low Wells: discharge.	Perrier[38]
14	Wells. If high or intermediate: above-knee US. If positive treat, if negative SimpliRED DD. Repeat US if DD positive, discharge if DD negative. Low: US, discharge if negative, treat if positive.	Tick[39]
15	Wells. High or intermediate: above-knee US. If positive treat, if negative SimpliRED DD. Repeat US if DD positive discharge if DD negative. Low: DD, discharge if negative, US if positive.	Wells,[40] intervention (high/moderate combined)
16	Wells. High: above-knee US. If positive treat, if negative SimpliRED DD. Repeat US if DD positive, discharge if DD negative. Intermediate or low: DD, discharge if -negative, US if positive.	Wells,[40] intervention (moderate/low low combined)
17	Wells. High or intermediate: above-knee US. If positive treat, if negative repeat US. Low: US, treat if positive, discharge if negative.	Wells,[40] control (high/moderate combined), Ruiz-Giminez[41]
18	Wells. High: above-knee US. If positive treat, if negative repeat US. Intermediate and low: US, treat if positive, discharge if negative.	Wells,[40] control (moderate/low combined)

US, ultrasound; DD, D-dimer.

(Table 1). Rates of thromboembolism during follow-up of patients testing negative were low and are thus likely to be acceptable for clinical practice. One study evaluated two algorithms in a randomized trial,[40] three of the algorithms could be interpreted in two ways,[33,40] and several of the studies evaluated similar algorithms.[28–32,40,41] So although there were a total of 14 algorithms, these do not correspond exactly to the 14 studies. We labelled the 'no testing, no treatment' strategy as strategy 0, the four single-test strategies as 1 to 4, and the published algorithms as 5 to 18. All the strategies are described in Table 2.

Table 3 shows the proportion of patients who will receive treatment, according to whether they have proximal DVT, distal DVT that propagates proximally, distal DVT that does not propagate, or no DVT. A perfect strategy would treat all patients

Table 3 Diagnostic accuracy of the algorithms

Algorithm	Patients with proximal DVT treated (%)	Patients with propagating distal DVT treated (%)	Patients with non-propagating distal DVT treated (%)	Patients without DVT treated (%)
0	0.0	0.0	0.0	0.0
1	99.5	86.1	0.6	0.6
2	95.0	95.3	6.0	6.0
3	95.0	67.8	6.0	6.0
4	95.0	6.0	6.0	6.0
5	98.1	79.2	6.0	3.4
6	95.0	63.2	6.0	6.0
7	99.2	79.2	4.0	6.0
8	99.2	90.3	4.0	6.0
9	93.2	82.1	5.2	2.8
10	93.2	75.7	5.2	2.8
11	96.5	63.4	5.6	3.7
12	93.9	63.4	5.6	3.7
13	96.1	28.7	5.6	3.2
14	95.0	69.0	6.0	6.0
15	93.9	52.5	5.6	3.7
16	90.1	34.9	4.6	2.1
17	95.0	79.2	6.0	6.0
18	95.0	36.4	6.0	6.0

with proximal DVT or distal DVT that propagates proximally, but none of the other two groups. All the strategies appear to detect and treat >90% of patients with proximal DVT, thus explaining the low rates of thromboembolism reported in the studies in Table 1.

Table 4 shows the costs and QALYs accrued by each strategy, and the net benefit, assuming willingness to pay £10 000, £20 000 and £30 000 per QALY. If we are willing to pay £10 000 per QALY then strategy 16 will have the highest mean net benefit, whereas if we are willing to pay £20 000 or £30 000 per QALY, strategy 9 will have the highest mean net benefit.

Figure 1 shows the cost-effectiveness acceptability curves. These plot the probability that an algorithm will be the most cost-effective at each value for willingness to pay, from zero to £100 000 per QALY. Up to the £30 000 threshold, algorithms 16, 9 and 13 are most likely to be optimal; for thresholds of £40 000 to £70 000 per QALY, algorithm 5 is most likely to be optimal; and for thresholds of £80 000 to £100 000 per QALY, a strategy of venography for all is most likely to be optimal. The algorithms are shown in Figure 2.

Discussion

Guidance from the National Institute for Clinical Excellence (NICE)[27] suggests that the £20 000 per QALY threshold should be used to determine whether an intervention is cost-effective in the National Health Service (NHS). A higher threshold of £30 000 per QALY may be used if additional factors are considered in determining cost-effectiveness, while thresholds >£30 000 per QALY should only be used if there are strong additional factors. In our analysis, algorithm 16 was the most cost-effective strategy at the £10 000 per QALY threshold, while algorithm 9 was most cost-effective at the £20 000 and £30 000 per QALY thresholds. These algorithms are thus the most appropriate strategies for DVT diagnosis in the NHS.

Algorithms 9 and 16 both use a negative D-dimer to rule out DVT in low- and intermediate-risk patients, and use above-knee ultrasound in those with a positive D-dimer or high clinical score. They differ in the use of repeat ultrasound scanning. All patients receive a repeat scan in algorithm 9, whereas only those with a high Wells score and positive D-dimer receive repeat scanning in algorithm 16. Strategies that provide radiological testing (ultrasound or venography) for all patients are only likely to be cost-effective if we are willing to pay £40 000 per QALY or more. Algorithm 5, which uses ultrasound on all patients and venography selectively, is most likely to be optimal for thresholds from £40 000 to £70 000 per QALY, while algorithm 1 (venography for all patients) is most likely to be optimal if we are willing to pay

Table 4 Costs, QALYs and net benefit for each algorithm per 1000 patients

Algorithm	Costs associated with diagnostic testing (£)	Costs associated with treatment DVT or complications (£)	Total costs (£)	QALYS accrued	Net benefit (£10 000 per QALY)	Net benefit (£20 000 per QALY)	Net benefit (£30 000 per QALY)
0	£0	£144 040	£144 040	11 523			
1	£200 177	£158 688	£358 864	11 560	£158 222	£531 267	£904 313
2	£107 402	£197 075	£304 477	11 558	£186 762	£533 961	£881 159
3	£113 678	£196 909	£310 587	11 557	£174 425	£515 396	£856 367
4	£59 364	£196 536	£255 900	11 556	£215 154	£542 167	£869 180
5	£113 453	£179 394	£292 847	11 559	£215 082	£578 971	£942 859
6	£86 253	£196 881	£283 134	11 557	£200 838	£540 770	£880 702
7	£154 018	£196 819	£350 837	11 559	£151 806	£510 408	£869 011
8	£202 847	£196 886	£399 733	11 559	£101 365	£458 422	£815 480
9	£73 207	£174 521	£247 728	11 558	£246 994	£597 675*	£948 356*
10	£70 938	£174 483	£245 420	11 558	£247 860	£597 100	£946 341
11	£78 782	£181 190	£259 972	11 558	£238 392	£592 715	£947 039
12	£97 538	£180 936	£278 473	11 557	£211 000	£556 433	£901 866
13	£66 898	£177 069	£243 967	11 558	£241 956	£594 157	£941 200
14	£87 437	£196 916	£284 353	11 557	£196 964	£542 183	£883 431
15	£67 797	£180 870	£248 667	11 557	£234 113	£581 319	£924 291
16	£47 527	£168 556	£216 082	11 556	£255 673*	£591 904	£923 878
17	£92 058	£196 978	£289 036	11 557	£194 789	£542 135	£885 700
18	£72 268	£196 719	£268 987	11 556	£204 515	£542 806	£876 682

*The optimal strategy at each given threshold for willingness to pay.

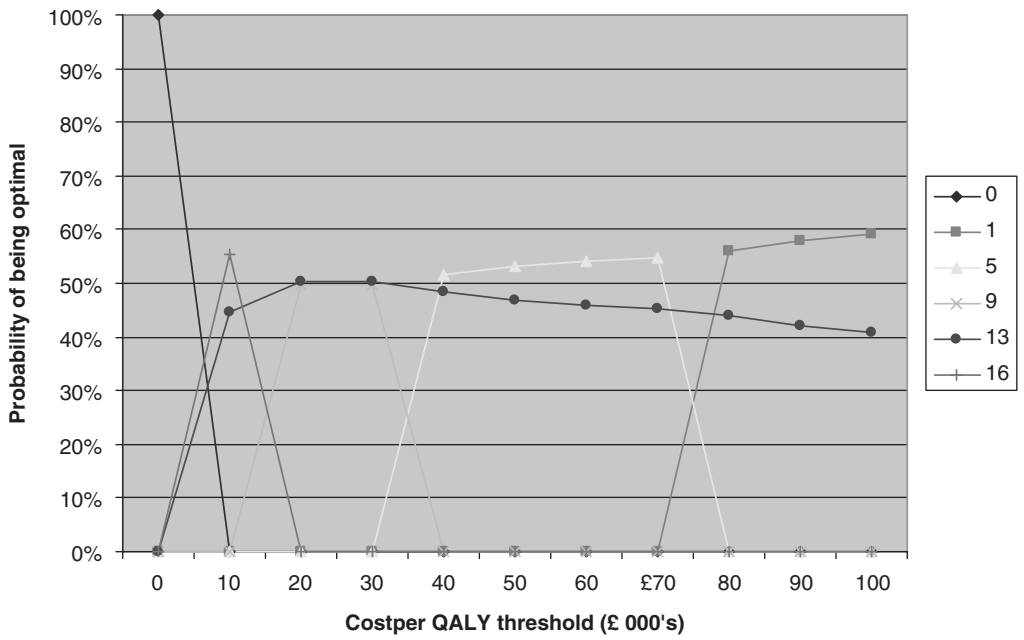

Figure 1. Cost-effectiveness acceptability curves showing the probability that each strategy is optimal at different threshold of cost per QALY thresholds.

£80 000 per QALY. However, these values all exceed the NICE recommended threshold, so it appears that diagnostic strategies based upon radiological testing for all patients are unlikely to represent a cost-effective use of resources.

A recent review of studies evaluating strategies that discharge patients with a low or intermediate Wells score and negative D-dimer concluded that this approach is 'safe'.[2] However, this conclusion is based upon a subjective judgement about whether

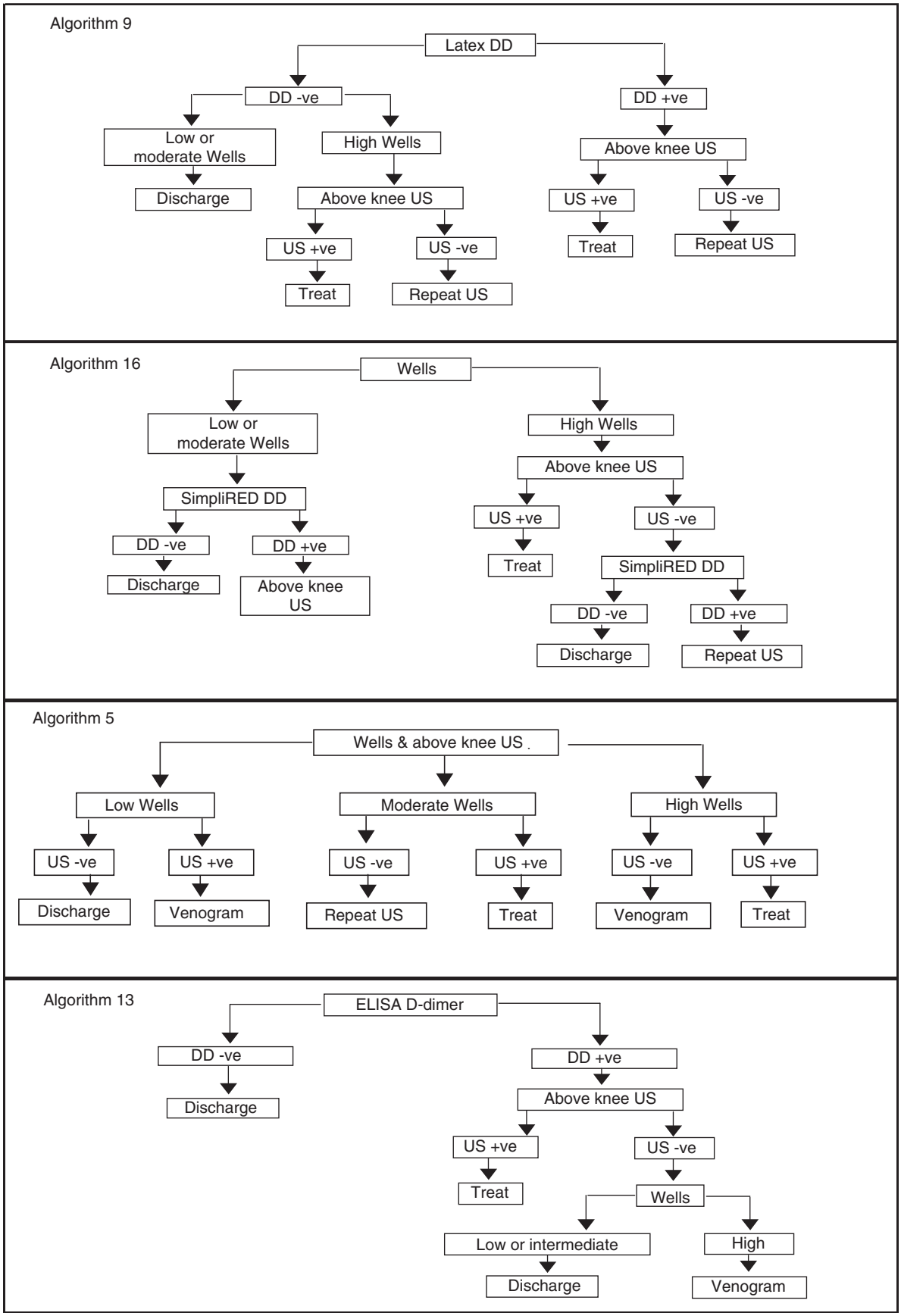

Figure 2. Algorithms 9, 16, 5 and 13.

a low probability of missed thromboembolism is acceptable, and thus considered 'safe'. Our analysis has explicitly weighed the costs and benefits of alternative strategies to show that this approach is cost-effective unless we are willing to pay £40 000 per QALY or more. One previous study used decision analysis to evaluate diagnostic testing for DVT,[42] comparing four strategies, incorporating combinations of clinical risk scoring, D-dimer and ultrasound, to a no treatment alternative. They estimated that the cheapest strategy (combining clinical risk scoring and D-dimer with a single ultrasound) was also the most cost-effective. This strategy was the same as algorithm 13 in our analysis and, consistent with the previous study, we found algorithm 13 to be highly cost-effective. However, this analysis only evaluated four strategies and did not make explicit the value judgement involved in deciding whether a strategy was cost-effective. By presenting our results as cost-effectiveness acceptability curves, we have shown how judgements regarding cost-effectiveness depend upon willingness to pay for health gain. Other cost-effectiveness analyses have focussed upon the cost-effectiveness of one particular technology and are less easily comparable.[43–45]

Our analysis has some limitations. Few data are available to determine how ultrasound results correlate with Wells score or D-dimer, so we had to assume that ultrasound was independent of these tests. One study has suggested that ultrasound performs better in those with a high Wells score.[46] If this is so, then our assumption will favour strategies that use ultrasound in patients with a low score. This means that we may have underestimated the cost-effectiveness of algorithms 9 and 16, but over-estimated the cost-effectiveness of algorithm 5. No data are available to determine whether D-dimer and ultrasound interact, but as these tests have a different pathophysiological basis, an assumption of independence is not unreasonable. Rates of thromboembolism among patients with negative tests reported in follow-up studies of algorithms combining Wells score, D-dimer and ultrasound (Table 1) are compatible with our estimates of overall sensitivity for the algorithms.

We only included algorithms that had been evaluated by management studies involving follow-up of patients with negative tests. There are numerous potential combinations of tests that could be used to diagnose DVT, but we felt that theoretical algorithms are unlikely to be widely adopted without empirical data showing how they work in practice. We also did not include algorithms that involved plethysmography in our analysis.[47,48] This test is not currently available in many hospitals,[3] does not appear to have adequate sensitivity or specificity to be used as a single test, and very little is known about how it interacts with other tests.[7] However, algorithms using plethysmography may offer a cost-effective alternative to the strategies examined here.[7]

Our model does not allow us to determine the potential impact of the strategy upon selection of patients for testing, and whether this influences cost-effectiveness. For example, a D-dimer based strategy (such as algorithm 9) may be used in a wider group of patients than a strategy requiring radiological testing for all. There is very little empirical data on whether patient selection is influenced by the diagnostic tests used. Future research is needed to evaluate this possibility and determine whether it has consequences for cost-effectiveness. Finally, this analysis applies principally to out-patients with a suspected first DVT. Our findings may not apply to certain patient groups, such as in-patients developing symptoms of DVT, patients with suspected recurrent DVT, pregnant patients, intravenous drug abusers or those with prolonged symptoms.

Conclusion

Diagnostic strategies for DVT that involve radiological testing for all patients are unlikely to be cost-effective at currently recommended thresholds of willingness to pay. We recommend widespread adoption throughout the NHS of a diagnostic strategy that uses Wells score and D-dimer to exclude DVT in low- and intermediate-risk patients.

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Appendix: Mean value, probability distribution and source of parameters used in the model (Tables 5–8)

Table 5 Probability of events

Variable description	Mean value	Probability distribution	Parameters	Source
Patient has proximal DVT	0.147	Beta	($\alpha = 41$, $\beta = 238$)	Kilroy[12]
Ratio of distal to proximal DVT	0.778	Beta	($\alpha = 14.5$, $\beta = 4.15$)	Goodacre[6]
Probability distal DVT propagates to proximal	0.214	Beta	($\alpha = 6$, $\beta = 22$)	Lagerstedt[16]
Outcomes of treated proximal DVT				
Probability of fatal PE	0.004	Beta	($\alpha = 17$, $\beta = 4204$)	Douketis[14]
Probability of non fatal PE	0.008	Beta	($\alpha = 33.4$, $\beta = 4070.6$)	Douketis[14]
Probability of PTS	0.053	Beta	($\alpha = 28$, $\beta = 500$)	Prandoni[15]
Outcomes of untreated proximal DVT				
Probability of fatal PE	0.019	Beta	($\alpha = 5$, $\beta = 263$)	Follow-up studies
Probability of non fatal PE	0.093	Beta	($\alpha = 25$, $\beta = 243$)	Follow-up studies
Probability of PTS	0.33	Beta	($\alpha = 5.21$, $\beta = 10.57$)	Expert opinion
Risks of treatment				
Probability of non-fatal intracranial haemorrhage	0.001	Dirichlet	(13, 37, 226, 10 481) where each parameter refers to the proportion of persons in each category. The fourth category is 'no bleeding'	Linkins[13]
Probability of fatal haemorrhage	0.003			
Probability of non-fatal, non-intracranial haemorrhage	0.021			

Table 6 Diagnostic test parameters

Test	Variable description	Mean value	Probability distribution	Parameters		
Wells test	Proportion of proximal DVT categorized as high risk	0.68	Dirichlet	A	B	C
	Proportion of proximal DVT categorized as moderate risk	0.25	Dirichlet	105.61	38.83	10.87
	Proportion of proximal DVT categorized as low risk	0.07	Dirichlet			
	Proportion of distal DVT categorized as high risk	0.34	Dirichlet	A	B	C
	Proportion of distal DVT categorized as moderate risk	0.48	Dirichlet	26.60	37.56	14.08
	Proportion of distal DVT categorized as low risk	0.18	Dirichlet			
	Proportion without DVT categorized as high risk	0.11	Dirichlet	A	B	C
	Proportion without DVT categorized as moderate risk	0.41	Dirichlet	40.78	151.99	177.94
	Proportion without DVT categorized as low risk	0.48	Dirichlet			
Ultrasound	Sensitivity for proximal DVT	0.95	Beta	1732.57	91.19	
	Sensitivity for distal DVT	0.65	Beta	630.55	339.52	
	Specificity	0.94	Beta	2035.72	129.94	
ELISA D-dimer	Sensitivity for proximal DVT	0.98	Beta	736.91	15.04	
	Sensitivity for distal DVT	0.86	Beta	993.58	161.75	
	Specificity, Wells high	0.34				
	Specificity, Wells moderate	0.45	Beta	4278.13	5228.83	
	Specificity, Wells low	0.52				
Latex D-dimer	Sensitivity for proximal DVT	0.94	Beta	2035.72	129.94	
	Sensitivity for distal DVT	0.79	Beta	313.89	83.44	
	Specificity, Wells high	0.42				
	Specificity, Wells moderate	0.55	Beta	5228.83	4278.13	
	Specificity, Wells low	0.64				
SimpliRED D-dimer	Sensitivity for proximal DVT	0.84	Beta	270.22	51.47	
	Sensitivity for distal DVT	0.64	Beta	69.29	38.98	
	Specificity, Wells high	0.52				
	Specificity, Wells moderate	0.68	Beta	5683.66	2674.66	
	Specificity, Wells low	0.79				

Table 7 Costs

Variable description	Mean value	Probability distribution	Parameters	Source
Clinical risk stratification	£6.83	None		Assumption
D-Dimer (SimpliRED)	£12.16	None		Axis Shield[26]
D-Dimer (Laboratory)	£13.11	None		NHS Trust figures[20]
Full leg ultrasound	£112.06	Normal	SE = 3.99	NHS reference costs[21]
Above knee ultrasound	£59.36	Normal	SE = 3.28	NHS reference costs[21]
Venogram	£192.00	Normal	SE = 4.82	NHS reference costs[21]
Treatment of DVT (total)	£721			

continued.

Table 7 Continued

Variable description	Mean value	Probability distribution	Parameters	Source
Based on:				
Days of heparin	8.6	Log normal	SE = 5.2	Boccalon[23]
Unit cost per dose of low molecular weight heparin (Enoxaparine)	£12.77	None		BNF[24]
Number of anticoagulant clinic reviews	4	None		Assumption
Unit cost per anticoagulant clinic review	£34	None		NHS reference costs[21]
Number of nursing visits during anticoagulation	17.2	None		Boccalon[23]
Unit cost per nursing visit	£20	None		Netten and Curtis[22]
Number of GP visits during anticoagulation	2	None		Assumption
Unit cost per GP visit	£61	None		Netten and Curtis[22]
Cost of 90 days warfarin treatment	£5.46	None		BNF[24]
Treatment of fatal PE	£1167	Normal	SE = 35.81	NHS reference costs[21]
Treatment of non-fatal PE	£1132	Normal	SE = 16.34	NHS reference costs[21]
Lifetime costs for post-thrombotic syndrome	£3866.59			
Based on:				
Unit cost for new vascular surgery out-patient	£85	Normal	SE = 2.53	NHS reference costs[21]
Unit cost for follow-up vascular surgery out-patient	£122	Normal	SE = 3.96	NHS reference costs[21]
GP visits	40	None		Netten and Curtis[22]
Treatment of severe bleeding, first year	£10 273.10	None		Sandercock[25]
Treatment of severe bleeding, subsequent years	£4662.10	None		Sandercock[25]
Treatment of fatal bleeding	£6600	None		Sandercock[25]
Treatment of non-IC haemorrhage	£569.38	Normal	9.85	NHS reference costs for gastro-intestinal bleeding[21]

Table 8 QALYs

Variable description	Mean value	Probability distribution	Parameters	Source
Normal age-specific, discounted quality-adjusted life expectancy	11.58	None		Government Actuary's Department,[17] Kind[18]
Severe post-thrombotic syndrome	0.977	Beta	(a = 232.64, b = 5.48)	O'Meara[19]
Non-fatal intracranial haemorrhage	0.29	Beta	(a = 8.34, b = 20.41)	O'Meara[19]
Non-fatal pulmonary embolism	0.94	Beta	(a = 19.43, b = 1.24)	Expert opinion