Two point-of-care test-based approaches for the exclusion of deep vein thrombosis in general practice: a cost-effectiveness analysis

Jorn Heerink (✉ j.s.heerink@utwente.nl)

University of Twente

Ruud Oudega

Jeroen Bosch Hospital

Hendrik Koffijberg

University of Twente

Ron Kusters

University of Twente

Joanne Nies

GGD Twente

Michelle Kip

University of Twente

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Abstract

Background

In the diagnostic work-up of deep vein thrombosis (DVT), the use of point-of-care-test (POCT) D-dimer assays is emerging as a promising patient-friendly alternative to regular D-dimer assays, but their cost-effectiveness is unknown. We compared the cost-effectiveness of two POCT-based approaches to the most common, laboratory-based, situation.

Methods

A patient-level simulation model was developed to simulate the diagnostic trajectory of patients presenting with symptoms of DVT at the general practitioner (GP). Three strategies were defined for further diagnostic work-up: one based on current guidelines ('regular strategy') and two alternative approaches where a POCT for D-dimer is implemented at the 1) phlebotomy service ('DVT care pathway') and 2) GP practice ('fast-POCT strategy'). Probabilities, costs and health outcomes were obtained from the literature. Costs and effects were determined from a societal perspective over a time horizon of six months. Uncertainty in model outcomes was assessed with a one-way sensitivity analysis.

Results

The Quality-Adjusted Life Years (QALYs) scores for the three DVT diagnostic work-up strategies were all around 0.43 across a six month-time horizon. Cost-savings of the two POCT-based strategies compared to the regular strategy were €103/patient for the DVT care pathway (95% CI: -€117-89), and €87/patient for the fast-POCT strategy (95% CI: -€113-67).

Conclusions

Point-of-care-based approaches result in similar health outcomes compared with regular strategy. Given their expected cost-savings and patient-friendly nature, we recommend implementing a D-dimer POCT device in the diagnostic DVT work-up.

Background

Annually, 1-2 per 1000 persons suffer from deep vein thrombosis (DVT) making it the third most prevalent cardiovascular disease according to an extensive Canadian study (1, 2). Deep vein thrombosis is associated with short and long-term morbidity and mortality, and recurrence of DVT episodes is common. Severe complications such as pulmonary embolism (PE) or post-thrombotic syndrome (PTS) can occur (3, 4); these are known to reduce quality of life (5, 6). Hence, appropriate disease detection is vital to timely initiating effective treatment possibilities. These include oral anticoagulation, in some cases

preceded by heparin injections, and compression stockings, depending on the symptoms and other patient characteristics.

As DVT cannot be discriminated from other diseases based on clinical judgment alone, in the Netherlands a specific diagnostic DVT work-up is initiated when a general practitioner (GP) suspects a DVT. A clinical decision rule (CDR) is initially applied to discriminate low (CDR <4) from high (CDR ≥4) risk patients (Table 1).

Table 1

Clinical decision rule for deep vein thrombosis according to the Dutch Committee of General Practitioners (7)

Risk factors		Weight
1.	Male gender	1
2.	Use of systemic estrogens (such as contraceptive pills, hormone rings/patches or needles)	1
3.	Presence of malignancy	1
4.	Surgery in the last month	1
5.	Absence of trauma explaining swelling in the calf	1
6.	Expanded veins of the limb	1
7.	Difference in maximal calf size ≥ 3 cm	2

High-risk patients immediately undergo a compression ultrasonography (CUS) in the hospital, while a laboratory test (D-dimer) is performed in low-risk patients. A negative (non-elevated) D-dimer rules out DVT, obviating the need for performing a relatively expensive CUS (8–10).

Deviations from this approach occur in current practice for a number of reasons. A recent publication reported that a CDR is correctly applied by 79.3% of Dutch GPs; this can be explained by the use of empirical probability estimates ('gestalt') as an alternative for CDRs (11, 12). Sensitivity of gestalt as a screening tool appears to be similar, but the specificity is substantially decreased compared to a CDR-based approach, leading to unnecessary referrals and an increase in health care costs (13, 14). Another deviation to the standard approach arises when results of a laboratory D-dimer assay are expected to be received after GP working hours. In these cases, patients are referred directly to the radiology or emergency department, causing unnecessary health care expenditures and discomfort of patients (15); 98.6% of patients assigned a low CDR score did not have DVT (8).

These undesirable phenomena could be avoided by introducing a point-of-care test (POCT) for D-dimer analysis carried out on low-risk patients. Point-of-care devices can be located at a phlebotomy service to accelerate diagnostic work-up. Patients with positive (elevated) D-dimer results are directly referred to undergo a CUS, while patients with a low CDR and negative POCT D-dimer test are discharged without

further involving the GP. As an upcoming alternative, novel quantitative capillary (whole-blood) POCT D-dimer assays could be positioned in the GP practice, requiring only a finger-prick instead of a venipuncture, providing results in less than 15 minutes (16). To our knowledge, the impact of both POCT strategies on health outcomes and costs, remains unknown. We therefore assessed the cost-effectiveness of two POCT-based approaches, comparing them to the most common, laboratory-based, situation in the Netherlands.

Methods

Model description

We developed a patient-level simulation model in Microsoft Excel (version 16.0.14228.20288). It represents the diagnostic pathways of patients with symptoms of DVT from the moment of presentation at the GP until the (correct) diagnosis is established. We applied this health-economic model to analyze the cost-effectiveness of two POCT-based approaches compared to the most common, laboratory-based, situation. Data for the input parameters was obtained from the literature. The outcome measures are the incremental costs, the incremental health effects expressed in Quality-Adjusted Life Years (QALYs), and if these are non-negligible, the incremental cost-effectiveness ratio (ICER) for the two POCT-based approaches compared to the laboratory-based situation.

Diagnostic strategies

Three different strategies of diagnosing DVT in primary care in the Netherlands were defined. An overview of these strategies is given in figure 1.

(Separate file) Figure 1

Schematic overview of diagnostic strategies of suspected deep venous thrombosis.

CDR = clinical decision rule, CUS: compression ultrasonography, D+ = Disease present, D- = Disease absent, DVT = Deep venous thrombosis, GP = General practitioner, POCT = Point-of-care test, T+ = test with positive result after D-dimer assay or CUS, T- = negative test result after D-dimer assay or CUS.

The regular strategy -the laboratory-based situation- is based on the Dutch College of General Practitioners policy guidelines. These recommend that a CDR and a subsequent quantitative D-dimer assay should be used to rule out DVT (17). In addition, we took into consideration whether the laboratory D-dimer result would be received during normal GP business hours. If so, only in case of a positive D-dimer would the patient be referred to undergo a CUS, as DVT is directly ruled-out if the D-dimer result is negative. However, should the result not be on time, the patient would be directly referred to undergo a CUS without a preceding laboratory D-dimer assay.

In an alternative approach, the DVT care pathway, patients are referred to the phlebotomy service at the hospital if, based on their CDR score, they are categorized as low risk. A quantitative D-dimer assay is

then performed on a POCT device present at the phlebotomy service. If the D-dimer results are positive, patients will directly undergo a CUS. Accordingly, the radiologist will, depending on the results, refer the patient to the internist without intervention of the GP. Those with a negative D-dimer are discharged and left to the attention of the GP.

A third strategy involves the introduction of a POCT D-dimer device at the GP practice; this approach is referred hereafter as the fast-POCT strategy. If the patient is categorized as low-risk according to the CDR score, the GP determines the patient's D-dimer value during the consultation. If the D-dimer value is positive, the patient is referred to undergo a CUS; if negative, the patient is discharged.

In all three strategies GPs can deviate from the current guidelines and may or may not apply the CDR. Given that some GPs may choose not to use a CDR, we also accounted for this scenario.

Model inputs

Of patients presenting at the GP with suspected DVT, 38.4% are male with an average age of 56.9 (8, 10, 18, 19). In our model we assumed that 79.3% of GPs correctly apply a CDR (11). On the basis that patients arriving after 13:00h are directly referred for a CUS, we assumed that 70.8% of patients would arrive in time for a laboratory D-dimer assay (20–23). The probabilities of a positive or negative D-dimer test or CUS result were obtained from multiple studies (8, 14, 18, 19, 24–26). A weighted estimate of sensitivity (S_n) and specificity (S_p) was obtained from a series of POCT and laboratory D-dimer assays in order to get a representative performance estimate of these two D-dimer assays (16, 24, 27–30).

Quality adjusted life years were used as effectiveness outcome. The health states incorporated in the model were: healthy, suffering from DVT, suffering from DVT complicated by PTS, PE, major bleeding or recurrence (5, 31–34). As a patient can only have a maximum of one quality of life score per year, the maximum per half year, and thus the upper limit of the 95% CI, was set at 0.5.

In accordance with the Dutch costing manual, we considered all costs from a societal perspective. These start from the moment a patient arrives at a GP until (correct) diagnosis up to six months of anticoagulant treatment or the occurrence of potential complications. Costs of both office and phone consultations were obtained from the Dutch costing manual (35). Diagnostic costs from a blood draw, a laboratory D-dimer test and a CUS were derived from the Dutch Health Care Authority (20). Procurement costs of a POCT device and prices per test were retrieved from sales brochures and retailers. We also included travel and parking costs (20). The number of production hours lost due to (diagnosing) DVT and potential complications were derived from literature and were both based on age group, gender and the net labor participation (17, 32, 36, 37). These were then multiplied by the costs per production hour lost determined based on the net labor participation classified per gender and age group of Dutch society (17). To determine treatment costs and costs of potential complications, we derived an average from the literature (20, 38–41). The cost estimation was then converted to 2021 Euros based on the Dutch consumer price index, (42).

An overview of the model input parameters for each of the three patient strategies used in the model, costs and quality of life score (i.e., utility values) with their corresponding CIs can be found in Tables 2, 3 and 4, respectively. Assumptions for the model are provided as supplementary material.

Table 2: Model input parameters for strategies used, showing the parameter, the value (probability) used in the model, the 95% CI interval, the distribution used and the data source.

Model input parameters	Category	Probability	Lower limit 95% CI	Upper limit 95% CI	Distribution	Reference
Patient Demographics	Sex (male)	38.4%	37.0%	39.8%	Beta	(10,46–48)
Age group	<34	9.8%	8.9%	10.6%	Dirichlet	(10,46–48)
	35-44	14.3%	13.3%	15.4%	Dirichlet	(10,46–48)
	45-54	21.5%	20.3%	22.7%	Dirichlet	(10,46–48)
	55-64	26.9%	25.7%	28.2%	Dirichlet	(10,46–48)
	65-75	11.9%	11.0%	12.8%	Dirichlet	(10,46–48)
	>75	15.5%	14.5%	16.5%	Dirichlet	(10,46–48)
Probability DVT	Prevalence DVT	15.8%	14.2%	17.4%	Beta	(12,24,46)
CDR	GP applies CDR	79.3%	76.7%	81.8%	Beta	(11)
	CDR ≥ 4	42.6%	40.4%	44.8%	Beta	(12,24,46)
Arrival patient at GP	Arrival patient before 13:00h	70.8%	33.1%	100.0%	Beta	(1,21–23,49)
Regular strategy (CDR not applied)	Prevalence DVT regular CUS	15.8%	14.2%	17.4%	Beta	(12,24,46)
	Sensitivity regular CUS	93.8%	81.9%	100.0%	Beta	(12,24,46)
	Specificity regular CUS	97.8%	94.7%	100.0%	Beta	(12,24,46)
	Prevalence DVT regular D-di	15.8%	14.2%	17.4%	Beta	(12,24,46)
	Sensitivity regular D-di	97.9%	90.9%	100.0%	Beta	(12,24,46)
	Specificity regular D-di	54.2%	43.6%	64.9%	Beta	(12,24,46)
	Prevalence DVT regular CUS after D-di	28.6%	16.5%	40.6%	Beta	(12,24,46)

Table 2: Model input parameters for strategies used, showing the parameter, the value (probability) used in the model, the 95% CI interval, the distribution used and the data source.

	Sensitivity regular CUS after D-di	93.8%	81.8%	100.0%	Beta	(12,24,46)
	Specificity regular CUS after D-di	97.8%	93.2%	100.0%	Beta	(12,24,46)
POCT-based approaches (CDR not applied)	Prevalence DVT CUS	35.7%	21.1%	50.4%	Beta	(12,24,46)
	Sensitivity CUS	93.8%	81.5%	100.0%	Beta	(12,24,46)
	Specificity CUS	97.8%	92.2%	100.0%	Beta	(12,24,46)
	Prevalence DVT D-di	15.8%	14.2%	17.4%	Beta	(12,24,46)
	Sensitivity D-di	93.2%	80.5%	100.0%	Beta	(12,24,46)
	Specificity D-di	68.6%	58.7%	78.5%	Beta	(12,24,46)
Regular strategy (CDR applied)	Prevalence DVT >13:00h CUS	3.8%	2.7%	4.9%	Beta	(12,24,46)
	Sensitivity >13:00h CUS	93.8%	69.5%	100.0%	Beta	(12,24,46)
	Specificity >13:00h CUS	97.8%	94.9%	100.0%	Beta	(12,24,46)
	Prevalence DVT <13:00h D-di	3.8%	2.7%	4.9%	Beta	(12,24,46)
	Sensitivity <13:00h D-di	97.9%	83.7%	100.0%	Beta	(12,24,46)
	Specificity <13:00h D-di	54.2%	44.3%	64.2%	Beta	(12,24,46)
	Prevalence DVT <13:00h CUS after D-dim	7.8%	6.2%	9.3%	Beta	(12,24,46)
	Sensitivity <13:00h CUS after D-dim	93.8%	69.3%	100.0%	Beta	(12,24,46)
	Specificity <13:00h CUS after D-dim	97.8%	93.5%	100.0%	Beta	(12,24,46)
POCT-based approaches (CDR applied)	Prevalence DVT POCT D-di	3.8%	2.7%	4.9%	Beta	(12,24,46)
	Sensitivity POCT D-di	93.2%	68.0%	100.0%	Beta	(12,24,46)

Table 2: Model input parameters for strategies used, showing the parameter, the value (probability) used in the model, the 95% CI interval, the distribution used and the data source.

	Specificity POCT D-di	68.6%	59.3%	77.9%	Beta	(12,24,46)
	Prevalence DVT CUS after POCT D-dim	10.5%	0.1%	20.8%	Beta	(12,24,46)
	Sensitivity POCT CUS after POCT D-dim	93.8%	68.7%	100.0%	Beta	(12,24,46)
	Specificity POCT CUS after POCT D-dim	97.8%	92.6%	100.0%	Beta	(12,24,46)
	Prevalence CUS after >4 CDR	31.5%	28.4%	34.7%	Beta	(12,24,46)
	Sensitivity CUS after >4 CDR	93.8%	69.5%	100.0%	Beta	(12,24,46)
	Specificity CUS after >4 CDR	97.8%	94.9%	100.0%	Beta	(12,24,46)
Complications	PE	27.0%	13.6%	40.4%	Beta	(47)
	PTS	6.0%	3.1%	9.0%	Beta	(50)
	Major Bleeding	3.5%	1.8%	5.2%	Beta	(44,51)
	Recurrence	5.0%	2.6%	7.5%	Beta	(52)

DVT = Deep venous thrombosis, CDR = Clinical Decision Rule, CUS = Compression Ultrasonography, D-di = D-dimer assay, GP = General practitioner, POCT = Point-of-care Test, PE = Pulmonary Embolism, PTS = Post Thrombotic Syndrome.

Table 3

Model input parameters for costs, showing the parameter, the value (amount) used in the model, the 95% CI interval, the distribution used and the data source.

Cost parameters	Category	Cost	Lower limit 95% CI	Upper limit 95% CI	Distribution	Reference
Consultation	Appointment at GP practice	€ 36.45	€ 18.60	€ 54.32	Gamma	(35)
	Consult by phone	€ 18.78	€ 9.58	€ 27.98	Gamma	(35)
Diagnostics	Blood draw	€ 6.30	€ 3.21	€ 9.39	Gamma	(20)
	D-di POCT at office (fast-POCT strategy)	€ 32.83	€ 16.74	€ 48.90	Gamma	Company info
	D-di POCT including AQT (DVT care pathway)	€ 8.83	€ 4.50	€ 13.15	Gamma	Company info
	D-di assay on STA-Liatest	€ 5.81	€ 2.96	€ 8.65	Gamma	(20)
	CUS	€ 92.19	€ 47.02	€ 137.37	Gamma	(20)
Travel	To GP	€ 0.23	€ 0.11	€ 0.34	Gamma	(35)
	To phlebotomy service	€ 4.79	€ 2.44	€ 7.13	Gamma	(35)
Treatment	Treatment costs	€ 580.79	€ 269.20	€ 865.37	Gamma	(20,38,39,41)
Complication	Cost PE	€ 4,501.04	€ 2,259.53	€ 6,706.54	Gamma	(20,38,39,41,43)
	Cost PTS	€ 4,001.12	€ 2,040.57	€ 5,961.67	Gamma	(20,41,43)
	Cost major bleeding	€ 7,174.99	€ 3,659.25	€ 10,690.73	Gamma	(20,38,39,41,43)
	Cost recurrence	€ 673.78	€ 346.38	€ 1,012.87	Gamma	(20,38,39,41)
Male productivity costs per hour	<34	€ 30.61	€ 15.61	€ 45.61	Gamma	(17)
	35-44	€ 37.25	€ 19.00	€ 55.50	Gamma	(17)

DVT = Deep venous thrombosis, CUS = Compression Ultrasonography, D-di = D-dimer assay, GP = General practitioner, POCT = Point-of-care Test, PE = Pulmonary Embolism, PTS = Post Thrombotic Syndrome.

Cost parameters	Category	Cost	Lower limit 95% CI	Upper limit 95% CI	Distribution	Reference
	45-54	€ 37.16	€ 18.97	€ 55.38	Gamma	(17)
	55-64	€ 32.88	€ 16.76	€ 48.99	Gamma	(17)
	65-75	€ 7.49	€ 3.82	€ 11.16	Gamma	(17)
	>75	€ 2.08	€ 1.06	€ 3.10	Gamma	(17)
Female productivity costs per hour	<34	€ 27.57	€ 14.06	€ 41.08	Gamma	(17)
	35-44	€ 30.56	€ 15.59	€ 45.55	Gamma	(17)
	45-54	€ 30.34	€ 15.47	€ 45.21	Gamma	(17)
	55-64	€ 23.81	€ 12.14	€ 35.48	Gamma	(17)
	65-75	€ 3.47	€ 1.77	€ 5.17	Gamma	(17)
	>75	€ 0.76	€ 0.39	€ 1.13	Gamma	(17)
DVT = Deep venous thrombosis, CUS = Compression Ultrasonography, D-di = D-dimer assay, GP = General practitioner, POCT = Point-of-care Test, PE = Pulmonary Embolism, PTS = Post Thrombotic Syndrome.						

Table 4

Model input parameters for quality of life, showing the parameter, the value (utility) used in the model, the 95% CI interval, the distribution used and the data source.

Quality of life estimates	Category	Utility	Lower limit 95% CI	Upper limit 95% CI	Distribution	Reference
Average quality of life in 6 months	Healthy	0.4345	0.2163	0.5	Beta	(34)
	Treated DVT	0.3924	0.1961	0.5	Beta	(5,31)
	DVT with PE	0.3880	0.1940	0.5	Beta	(5,31,33)
	DVT with PTS	0.3901	0.1950	0.5	Beta	(5,31)
	DVT with major bleeding	0.3874	0.1937	0.5	Beta	(5,31,44)
	DVT with recurrence	0.3762	0.1883	0.5	Beta	(5,31)
DVT = Deep venous thrombosis, PE = Pulmonary Embolism, PTS = Post Thrombotic Syndrome.						

Probabilistic sensitivity analysis

A probabilistic sensitivity analysis (PSA) was performed by means of a Monte Carlo simulation (10,000 iterations of from 10,000 patients) to demonstrate the effect of joint uncertainty in the input parameters

on the outcomes of the model. An incremental cost-effectiveness plane was used to display the uncertainty in model outcomes.

One-way sensitivity analysis

A one-way sensitivity analysis was performed to determine which parameters substantially influence model outcomes. The impact on the output of each strategy was analyzed by applying the lower and upper limit of the corresponding 95% confidence intervals (CIs) of each parameter in the model. Results are presented in tornado diagrams.

Results

The average costs per patient were € 827 (95% CI: €750-909) for the regular strategy, €724 (95% CI: € 656-798) for the DVT care pathway, and € 740 (95% CI: €674-812) for the fast-POCT strategy. Average cost-savings for the DVT care pathway and for the fast-POCT strategy compared with the regular strategy were € 103/patient (95% CI: -€117-89, a relative reduction of 12.4%) and € 87/patient (95% CI: -€113-63, a relative decrease of 10.5%), respectively. As the difference in QALYs was approximately -0.0002, equal to less than two hours in full health, this was considered clinically irrelevant. Therefore, no ICER was determined, as the ICER would be unstable with this low denominator. The use of the DVT care pathway instead of the regular strategy could result in health care savings of approximately € 2,575,000 half-yearly (€ 103 * 25,000 patients), thus € 5,150,000 annually. The fast-POCT strategy could save approximately € 2,175,000 half-yearly (€ 87 * 25,000 patients), € 4,350,000 annually.

(Separate file) Figure 2a: Incremental cost-effectiveness plane of the DVT care pathway versus the regular strategy.

(Separate file) Figure 2b: Incremental cost-effectiveness plane of the fast-POCT strategy versus the regular strategy.

Figures 2a and 2b show an incremental cost-effectiveness plane, presenting the results of the PSA. These figures show cost savings of 100% when comparing the DVT care pathway and the fast-POCT strategy to the regular strategy.

(Separate file) Figure 3a: Tornado diagram showing the impact of varying input parameters on model outcome when the regular strategy is compared to the DVT care pathway. CUS: compression ultrasonography. POCT: point-of-care. CDR: clinical decision rule.

(Separate file) Figure 3b: Tornado diagram showing the impact of varying input parameters on model outcome when the regular strategy is compared to the fast-POCT strategy. DVT: deep vein thrombosis. CUS: compression ultrasonography. POCT: point-of-care. CDR: clinical decision rule.

The tornado diagrams shown in figure 3a and 3b demonstrate the influence of the uncertainties of the input parameters on the incremental costs. Comparing the DVT care pathway and the fast-POCT strategy

to the regular strategy shows the time of arrival of patients has the greatest impact on the differences in costs, as more patients are referred directly to undergo a CUS. All outcomes of the univariate sensitivity analyses show that the DVT care pathway and the fast-POCT strategy result in cost-savings compared to the regular strategy.

An additional sensitivity analysis was performed to determine the extent of influence of arrival time of patients at the GP practice on the outcome of the model. Table 5 shows that the arrival time did not influence model outcomes.

Table 5
Additional sensitivity analysis for arrival time parameter

Probability patient arriving in time (%)	Incremental costs regular strategy vs. DVT care pathway (€)	Incremental costs regular strategy vs. fast-POCT strategy (€)
0.0	90.92	66.44
70.8	65.49	33.81
100.0	54.52	30.04

Discussion

We demonstrated that both POCT-based approaches in this study, if implemented, reduce costs from a societal perspective when compared to the regular strategy. The loss of QALYs (<0.0002 QALYs loss over a 6-month time horizon) was considered not to be clinically relevant. In view of these results, using a POCT D-dimer test is the most advantageous option, despite the relatively high costs of POCT devices in terms of purchase and maintenance.

Data from the latest quantitative POCT devices were used in this study. These test systems are considered to be patient and user-friendly as they only require a capillary finger prick of blood, facilitating the application of these devices in settings outside the laboratory (16). More studies on this topic have been performed on past-generation POCT devices, but none, to our knowledge, have incorporated productivity losses per health state or fully considered production costs and complication losses as detailed as in our study. Neither have they incorporated alternative scenarios like the hybrid approach of a DVT care pathway, or sub-scenarios in which physicians do not follow current guidelines. Our results are in line with earlier studies on now-deprecated POCT devices which demonstrate that POCT-based approaches are less expensive than the regular strategy. (41, 43)

In the near future, the rapid evolution of quantitative capillary POCT devices is expected to improve their diagnostic accuracy, further improving health-related outcomes. The false-negative rate is expected to be further reduced with fewer cases being missed. This will lead to a decline of complications in the DVT care pathway and fast-POCT strategy, compared to current model outcomes.

Strengths

The main strength of this study is that it was set up to provide an accurate and detailed illustration of diagnostic work-up after a patient with DVT symptoms presents to the GP. In order to achieve this, we incorporated two important real-life input parameters in our model. The first parameter is the estimated production cost loss per health state based on the literature. (32, 36, 37, 45) Net labor participation per complication and associated health-state, sex and age group were used to accurately represent production losses and related costs in real-life DVT patients in the 6-month time horizon during and after DVT diagnosis. The second parameter is the arrival time of patients at the GP as this can greatly affect the chosen diagnostic strategy. As these parameters have an impact on the costs, they form significant factors.

A further strength is the conservative assumptions made in the model regarding treatment costs, thus possibly underestimating cost savings. For example, treatment and complication costs were based on treatment for six months based on available data, even though only three months were suggested by the Dutch College of General Practitioners (7). Moreover, as the Sn and Sp of the current POC test devices are lower than their conventional counterparts, more complications were found in the POCT-based approaches. Furthermore, the diagnostic performance of D-dimer POC tests is expected to improve in the near future, so current assumptions about their diagnostic values will probably underestimate the cost-savings of POCT-based strategies. Combining these factors, we expect further cost savings and health losses using the POCT-based approaches. Furthermore, in our model we assumed that a POC test at the GP practice would lead to a more time-consuming consultation in the fast-POCT strategy. However, if this test could be embedded in the first consultation, this would reduce consultation costs, resulting in additional cost-savings when using the fast-POCT strategy.

Limitations

Several limitations need to be addressed. First, some input parameters used in the model were obtained from the literature, while others were based on assumptions. One of these assumptions is the time of arrival at the GP of a patient experiencing symptoms that could indicate a DVT. There is no specific data available on how many patients arrive too late for the GP to obtain laboratory D-dimer results before the end of the working day. This is relevant as the follow-up cannot be done on the same day. Because of this, arrival time greatly affects the GP's strategy so we chose to include this variable in our model. We performed a scenario analysis in which all patients arrived on time vs. another scenario in which they were directly referred to undergo a CUS. This analysis showed no substantial change in model outcomes. Therefore, it is unlikely that this limitation has affected our conclusions.

A second limitation is that a full cost-effectiveness study could not be performed due to the small differences in QALYs between the three different strategies. These can be explained by the small difference in Sn and Sp between the laboratory and POCT-based D-dimer assays. Instead, we performed a cost-minimization analysis, which provided insights into the considerable cost savings of the POCT-based approaches.

Implications for practice

Patient-friendliness is an important factor in health care. We were unable to include patient-friendliness in our model, as no quantitative measures are currently available for this item. However, waiting time can be reduced, resulting from (i) a POCT assay being performed during the GP consultation in the fast-POCT strategy and (ii) direct referral to the radiologist and internist in the DVT care pathway. These both substantially contribute to patient-friendliness. Furthermore, once the consultation is completed in the two POCT-based approaches, GPs are no longer responsible for follow-up of their patients, so this will also reduce the risk of errors.

We show that both the DVT care pathway and the fast-POCT strategy save costs when compared to the regular strategy. If a final choice between these two strategies has to be made, the size and location of the GP practice should be taken into consideration. Larger practices in remote areas may benefit more from the fast-POCT strategy as the majority of (mostly negative-D-dimer) patients will not be referred; this would greatly reduce their travel time. Moreover, costs per patient per test are limited as POCT device procurement costs can be spread over more patients. For the same reason, smaller practices may benefit more from the DVT care pathway.

Conclusions

In conclusion, both POCT-based approaches showed cost-savings, with a negligible loss of QALYs compared to the most common current strategy. We are convinced that with the demonstrated cost savings and the added patient and user-friendliness, the DVT care pathway and the fast-POCT strategy should be introduced in clinical practice.

Abbreviations

DVT
Deep vein thrombosis
PE
Pulmonary embolism
PTS
Post-thrombotic syndrome
GP
General practitioner
CDR
Clinical decision rule
CUS
Compression ultrasonography
Sn
Sensitivity
Sp
Specificity

POCT
Point-of-care test
QALY
Quality-adjusted life years
ICER
Incremental cost-effectiveness ratio
PSA
Probabilistic sensitivity analysis

Declarations

Ethics approval and consent to participate

All methods were performed in accordance with the relevant guidelines and regulations. 'Consent to participate' is not applicable, as no patient level data was included in this study.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary files.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

MK, JH, JN and RK were involved in final study design. JN and MK were involved in data acquisition and model analysis. JN and JH wrote the first draft of the manuscript. All authors have reviewed and edited the manuscript and approved the final version.

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Figures

Figure 1

Figure 1

Schematic overview of diagnostic strategies of suspected deep venous thrombosis.

CDR = clinical decision rule, CUS: compression ultrasonography, D+ = Disease present, D- = Disease absent, DVT = Deep venous thrombosis, GP = General practitioner, POCT = Point-of-care test, T+ = test with positive result after D-dimer assay or CUS, T- = negative test result after D-dimer assay or CUS.

Figure 2

2a: Incremental cost-effectiveness plane of the DVT care pathway versus the regular strategy.

2b: Incremental cost-effectiveness plane of the fast-POCT strategy versus the regular strategy.

Figure 3

3a: Tornado diagram showing the impact of varying input parameters on model outcome when the regular strategy is compared to the DVT care pathway. CUS: compression ultrasonography. POCT: point-of-care. CDR: clinical decision rule.

3b: Tornado diagram showing the impact of varying input parameters on model outcome when the regular strategy is compared to the fast-POCT strategy. DVT: deep vein thrombosis. CUS: compression ultrasonography. POCT: point-of-care. CDR: clinical decision rule.

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