



# THE NEW FRONTLINE OF DVT ASSESSMENT

## A multisite review of clinical D-dimer testing in primary care

### ABSTRACT/OVERVIEW

Every year, secondary care facilities across the UK are inundated with patients referred from primary care with suspected cases of deep vein thrombosis (DVT), more than 70% of whom are later found to be negative for the condition and sent home with no need of further treatment. In an effort to reduce the number of these referrals and improve the diagnostic accuracy of DVT in primary care, a number of NHS GP facilities have begun to use a new, rapid D-dimer assay that can eliminate more than a third of these suspect cases directly from a GP's office. By revising the accepted diagnostic algorithm for DVT assessment, NHS facilities stand to significantly reduce their spending on this condition and minimise the amount of time lost by radiologists and staff diagnosing it. The benefits to patients are also considerable and include reducing stress over uncertain diagnosis, minimising carer time and eliminating unnecessary journeys to secondary care.

Deep vein thrombosis (DVT) is one of the most notoriously difficult conditions to confirm or rule out in primary care due to the wide variety of non-thrombotic disorders with a similar clinical presentation and the limited number of diagnostic tools available to assess the condition.<sup>1</sup> Instead, primary care physicians must rely on clinical prediction methods such as Wells scoring (see Box 1) to gauge the likelihood of lower-limb DVT and whether a patient should be referred to secondary care for evaluation by ultrasound and laboratory blood tests.<sup>2</sup> As a result, between 70% to 80% of cases referred to secondary care are later found to be negative for DVT.<sup>3,4</sup> Accurate diagnosis and the need for a reliable empirical testing method at the frontline of patient care have thus become increasingly important issues in the budget-conscious NHS. Not only are untreated patients at risk for developing pulmonary embolism (as unjustified treatment with anticoagulants is a risk factor for bleeding), but the financial cost and lost time for the additional diagnoses pose

excessive and unnecessary burdens to hospital Trusts.

In an effort to minimise the number of suspect cases received annually by secondary care, a number of healthcare facilities across the UK are investigating the use of D-dimer tests in primary care. D-dimer is a specific degradation product of the thromboembolic process, commonly detected using clinical screening methods such as latex agglutination and enzyme-linked immunosorbent assays (ELISA). Such tests, however, require specialised equipment and/or training to perform, making them generally reserved for use in hospital laboratories. The alternative has been for GPs to send blood samples to their local laboratories but the delays associated with mailing samples and results processing are generally too long to be of practical use for a condition where urgent diagnosis is considered essential.

A recently developed rapid test kit suitable for use by non-laboratory personnel (Clearview Simplify D-dimer, see Box 2) is changing this outlook, offering the possibility of significantly reducing the number of suspect DVT and PE cases requiring further diagnosis. Like other D-dimer assays using the 3B6 antibody, the test is highly specific and 100% sensitive, with a correspondingly high negative predictive value. That is, when used in conjunction with a validated pre-test probability scoring method, it can conclusively and safely rule out DVT in low and moderate risk patients.

A number of healthcare facilities, both in primary and secondary care, have adopted the new assay and begun to promote its use as a means of excluding suspected DVT when scoring methods alone would provide otherwise ambiguous results. Among those

facilities are the Windrush Health Centre (WHC), an NHS primary care facility in Oxfordshire, and the East Sussex Downs & Weald PCT (ESDW PCT), which organised a roll-out of the test to local practices under a Local Enhanced Service (LES). Over a matter of months, each of these sites demonstrated a dramatic reduction in the number of suspect DVT requiring ultrasound evaluation and a corresponding spending cut by their local PCTs.

### INITIAL ASSESSMENT

In mid-2006, the EDH Trust was exploring different opportunities for new, more cost-effective treatment pathways that could facilitate practice based commissioning. An audit was conducted of their medical assessment unit (MAU) data to determine what conditions would make the best targets for streamlining. It was quickly found that query

DVT cases represented nearly half (48% of sampled case reports) of incoming patients to the unit. This created some confusion as the corresponding hospital discharge and national activity data sets showed DVT to represent a much smaller proportion of final diagnoses. The reviewing panel also found that with the introduction of Payment by Results, there had been a significant increase in the number of short-stay (less than 24 hours) patients. In particular, many patients were coming in for periods of only two to four hours for which the Primary Care Trust was paying full acute admissions costs.

As described by Paul Trevethick, Assistant Director of Commissioning & Development, "Initially, like other PCT's, we had only the top level management data to work with, in which only the final patient diagnoses are recorded. When we

**PCT's show a reduction in DVT admissions with the use of D-dimer tests in primary care**

lined this up with detailed audit results, there was large incongruity that was overwhelmingly related to the volume of patients that had originally arrived as query DVT admissions. The financial impact of these cases was enormous, as each of these acute admissions cost the PCT £400-500 at a minimum, regardless of their final diagnosis. When one considers that we had, on average 50 to 60 such cases per month, this amounted to a substantial sum of money."

Around the same time, Dr. Stephen Bright, a GP partner at the WHC was examining the same scenario from the perspective of a primary care physician, looking at ways to reduce the number of patients he and his colleagues sent for evaluation at their local DVT service. "In the absence of a chemical or other empirical testing method, the clinical evaluation of DVT leaves a lot of grey areas, particularly when dealing with low and moderate risk patients," said Dr. Bright. "For obvious safety reasons, virtually all of these patients must then be sent on to secondary care or our local DVT clinic for further evaluation, which then of course leads to high rate of negative results. Not only does this become a burden to patients, but the cost to the PCT is a minimum of £270 per patient (for patients with a negative diagnosis). From our point of view as GPs, it made sense that we find a method of more accurately diagnosing or discounting DVT directly from the clinic. It was then that we came across the Clearview Simplify D-dimer kit."

**TRIALING THE NEW ASSAY**

At ESDW PCT a new clinical pathway was designed in which the Simplify D-dimer test (already in use in the hospital itself) was moved out into the community for use in all primary care practices who referred query DVT cases to the Trust. A direct booking system was also established for the hospital's Doppler facilities, enabling GPs to reserve ultrasound slots for their patients directly from their own offices. As Mr. Trevethick continued, "We worked out a pathway with our consultants and local GPs based on some existing models established by other trusts that we could adapt to our purposes (see Box 3). The biggest change was that suspect DVT patients are now given a D-dimer test as part of the clinical assessment by their local GP, who can then, if it's needed, refer patients directly into the hospital for Doppler ultrasound. We deliberately ran a test of the new protocol on a

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| <b>Wells probability scoring<sup>2</sup></b>  |           |
| <b>Wells criteria and scoring system (possible score range: -2 to 9):</b>                         |           |
| 1) Active cancer (treatment within last 6 months or palliative):                                  | 1 point   |
| 2) Paralysis, paresis or recent cast immobilization of lower extremities:                         | 1 point   |
| 3) Recently bedridden for >3 days or major surgery in the past 12 wks:                            | 1 point   |
| 4) Calf swelling >3cm compared to the asymptomatic leg:   | 1 point   |
| 5) Collateral superficial veins (non-varicose):   | 1 point   |
| 6) Pitting oedema confined to the symptomatic leg:  | 1 point   |
| 7) Swelling of entire leg:  | 1 point   |
| 8) Localized tenderness along distribution of deep venous system:                                 | 1 point   |
| 9) Previously documented DVT  | 1 point   |
| 10) Alternative diagnosis as likely or more possible than DVT:                                    | -2 points |
| <b>Interpretation:</b>  |           |
| A score of 2+: DVT is likely; consider imaging the leg veins.                                     |           |
| A score of less than 2: - DVT is unlikely; consider a d-dimer blood test to further rule out DVT. |           |
| <b>Box 1</b>  |           |

normal day of the week basis, rather than out-of-hours, to assess its practicality. Within just five months of running the programme, we had cut the number of query DVT admissions arriving to the EDH by more than half and after a year, DVT admissions had fallen to one-fifth of their previous monthly volumes."

At the Windrush clinic, Dr. Bright and his colleagues had a similar experience during a recent evaluation of Clearview Simplify D-dimer, greatly reducing the number of patients they refer to secondary care and noting a significant improvement in patient well-being. "If you look at a pool of 100 suspect DVT cases," said Dr. Bright, "you can usually exclude only about 10 of these through Wells scoring alone – and that's if you're prepared to take that risk. With Clearview Simplify D-dimer, however, we can raise this figure significantly to exclude 40 or more patients. This can lead to considerable

savings for the PCT as the test costs only a few pounds to administer, compared to the £270 charge for outpatient assessment or £1070 for an inpatient assessment. More importantly, the test has improved the quality of care we're able to offer our patients, providing results and peace of mind in just 10 minutes."

Such benefits have not gone unnoticed by Dr. Bright's patients, many of whom have been surprised at how smoothly the care pathway has been at Windrush. As Dr. Bright continues, "It's not uncommon for our patients to have done some of their own research on DVT online and many will thus be aware that they may need to go for an ultrasound and of the long waiting queues associated with this. These patients really feel quite fortunate to be part of this new generation of testing and, whether they are positive or negative for D-dimer, as simply being shown visible results instils a certain confidence that they are being given the

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| <b>Clearview Simplify D-dimer: How the test works</b>  |  |
| Clearview Simplify D-dimer is a newly developed assay for D-dimer, similar to existing immunochromatographic tests for DVT, using the murine monoclonal antibody 3B6/22, conjugated to colloidal gold particles, to bind soluble D-dimer in sample blood. The test cartridge itself is a slide similar in appearance to a professional use pregnancy test and requires only a drop of finger prick blood, venous blood or plasma, followed by two drops of a buffer solution, to complete. Should the sample blood contain elevated levels of D-dimer, an immune complex will form and be carried by chromatographic flow to the test domain area. There, a second antibody specific for D-dimer will fix the complex to form a clearly visible monolayer, indicating a positive result for the presence of D-dimer at concentrations of ≥80ng/mL. |  |
| <b>Box 2</b>   |  |

**Revised DVT assessment protocol developed at the EDH Trust**

Under the new Local Enhanced Service Arrangement effected by the EDH, the diagnostic work-up of suspect DVT patients is performed in three stages:

1. Patient histories are taken, their Wells score is determined and a D-dimer is administered. The Trust pays GPs £25 for each of these initial assessments.
2. Patients not excluded for DVT in the first stage are referred to the EDH and administered an interim course of Clexane. The Trust pays GPs an additional £50 at this stage.
3. If patients are found to be positive for DVT, then GPs can choose to initiate anti-coagulation therapy for an additional £200 reimbursement from the Trust. Alternatively, GPs can refer patients back to the hospital for treatment in secondary care.

As a result of this new stratagem, the maximum charge to Trust for each positive case of DVT is £275 and just £25-75 if patients are found to be negative. When combined with the reduction of acute care admissions, the EDH Trust was thus able to save in excess of £180,000 in the trial year of the programme, including the cost of establishing the LES (Source: internal data from the EDH).

**Box 3**

best possible care. When presented at our patient participation group [June 23, 2007], they were highly supportive of this system and surprised that it was not more widely available.

We have also used the Simplify D-Dimer assay for patients in whom a pulmonary embolism is a possibility, which previously we would have been mandated to refer for inpatient assessment (although a pulled muscle or chest infection were also likely). Just last month we had two patients in this group for which we excluded PE through a negative D-dimer test and low Wells PE score. This saved each patient at least a day at hospital and the PCT £2320."

**BEYOND THE FINANCIAL BENEFITS**

With the new care pathway and LES protocols having been in place throughout Eastbourne for more than 12 months, Mr.

Trevethick and his colleagues have been able to assess the programme. In addition to the inherent economical advantages of the new care pathway, there have been a number of supplementary benefits to the system. As Mr. Trevethick continued, "Whenever you're able to streamline a treatment pathway, there will be a number of knock-on effects. By reducing the number of unnecessary admissions, the MAU staff has been better able to prioritise it's time and get to other patients faster, while reducing the administrative burden associated with DVT cases. Referral to ultrasound is also now an immediate booking from the GP's office, rather than the 36-48 hour waiting period patients would previously have to cope with."

These observations were echoed by Dr. Bright at the WHC, "Using a rapid D-dimer test in primary care creates a more secure framework for practitioners, enabling

greater confidence in diagnoses. It also reduces the amount of hassle patients have to go through, particularly for those in whom we can safely rule out DVT on the spot. This all sums up to faster and better quality healthcare and reduced PCT costs. Looking at the pros and cons of the system, hopefully it is only a matter of time before D-dimer testing in primary care becomes part of the routine protocol for DVT assessment."

Mr. Trevethick agreed with this analysis concluding, "The assessment protocol we've been using isn't particularly complex, and could quickly be adapted to a number of primary care service groups and facilities. Broad scale or Trust-wide implementation simply requires that all the players involved in the traditional treatment pathway, from GPs and radiologists, to haematologists and hospital doctors, are involved at the initiation of the programme and that they are familiar with the test. Once in place, it is relatively easy to demonstrate that clinical testing of D-dimer in primary care forms the core of a more cost-effective algorithm for non-invasive DVT diagnosis." ■

**For more information on Clearview Simplify D-dimer and primary care testing visit: [www.clearview.com](http://www.clearview.com) or contact Inverness Medical UK on 0161 483 5884**

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