The DESTINY Study

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Introduction

Deep vein thrombosis (DVT) is a potentially life-threatening condition characterised by the formation of blood clots within the deep veins, most commonly in the lower extremities. Timely and accurate diagnosis of DVT is crucial to initiate appropriate treatment and prevent complications such as a pulmonary embolism (PE). Traditional diagnostic methods, for instance, a venous ultrasound, can be time-consuming and require specialised equipment. Point of care testing (POCT) has emerged as a promising approach for rapid and efficient DVT diagnosis, with diagnostic sensitivities comparable to laboratory methods.

Aim

DESTINY D-dimer was observational feasibility study that aimed to determine whether POC Dimer can safely exclude potential DVT's at primary care. The study compared the sensitivity of the Roche Cobas H232 and LumiraDx D-dimer assays to the laboratory D-dimer assay.

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Methodology

Healthy males and females (≥18) with suitable venous access were recruited to provide an aliquot of venous blood that is sent to secondary care, as part of their regular consultation for suspected DVT. An aliquot of venous blood was analysed on the POC Roche Cobas H232 D-dimer assay (150µl), whilst a finger-prick blood sample was obtained and analysed on the Lumira Dx D-dimer assay (20µl). A Well' Risk score is performed by a practice nurse and recorded with the patients POC D-dimer results (Figure 1). Results of the laboratory D-dimer assay (Sysmex CS2100i INNOVANCE) were compared to the POC D-dimer and alongside final diagnosis by Doppler ultrasound at secondary care. An age-adjusted D-dimer was applied to the result analysis to determine any improvements to D-dimer accuracy at the 500 µg/L cut-off.

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Clinical feature	Points
Active cancer* (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation on the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confirmed to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score	Points
DVT likely	2 points or more
DVT unlikely	1 point or less

Figure 1. Well's Risk Criteria

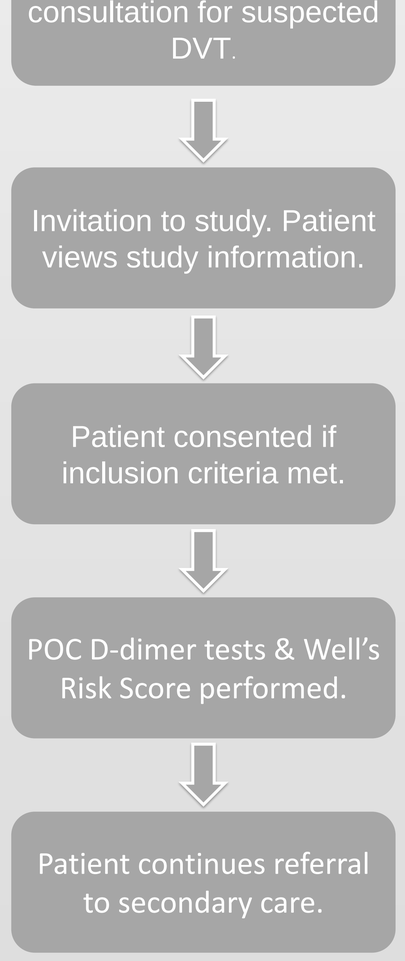

Figure 2. DESTINY patient pathway

Figure 3. Operating the LumiraDx D-dimer assay, capillary sample

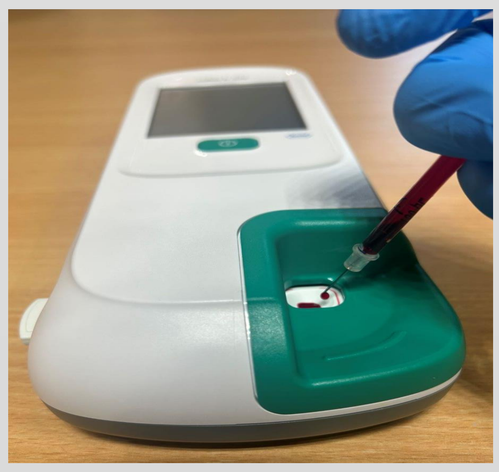

Figure 4. Operating the Roche Cobas H232 D-dimer assay, venous sample

Results

A total of 118 patients were tested in the DESTINY study who were all suspected of having a DVT, with a D-dimer concentration greater than 500 µg/L indicating a positive result. 73 (66%) tested positive using the Lumira Dx, with a mean ± SD of 927 ± 810 (range 190-4000). 20 (31%) tested positive using the Roche Cobas H232, with a mean ± SD of 597 ± 718.4 (range 100-2784). 63 (56%) tested positive using the lab LPIA assay, with a mean ± SD of 725 ± 787 (range 180-4480), (Figure 5).

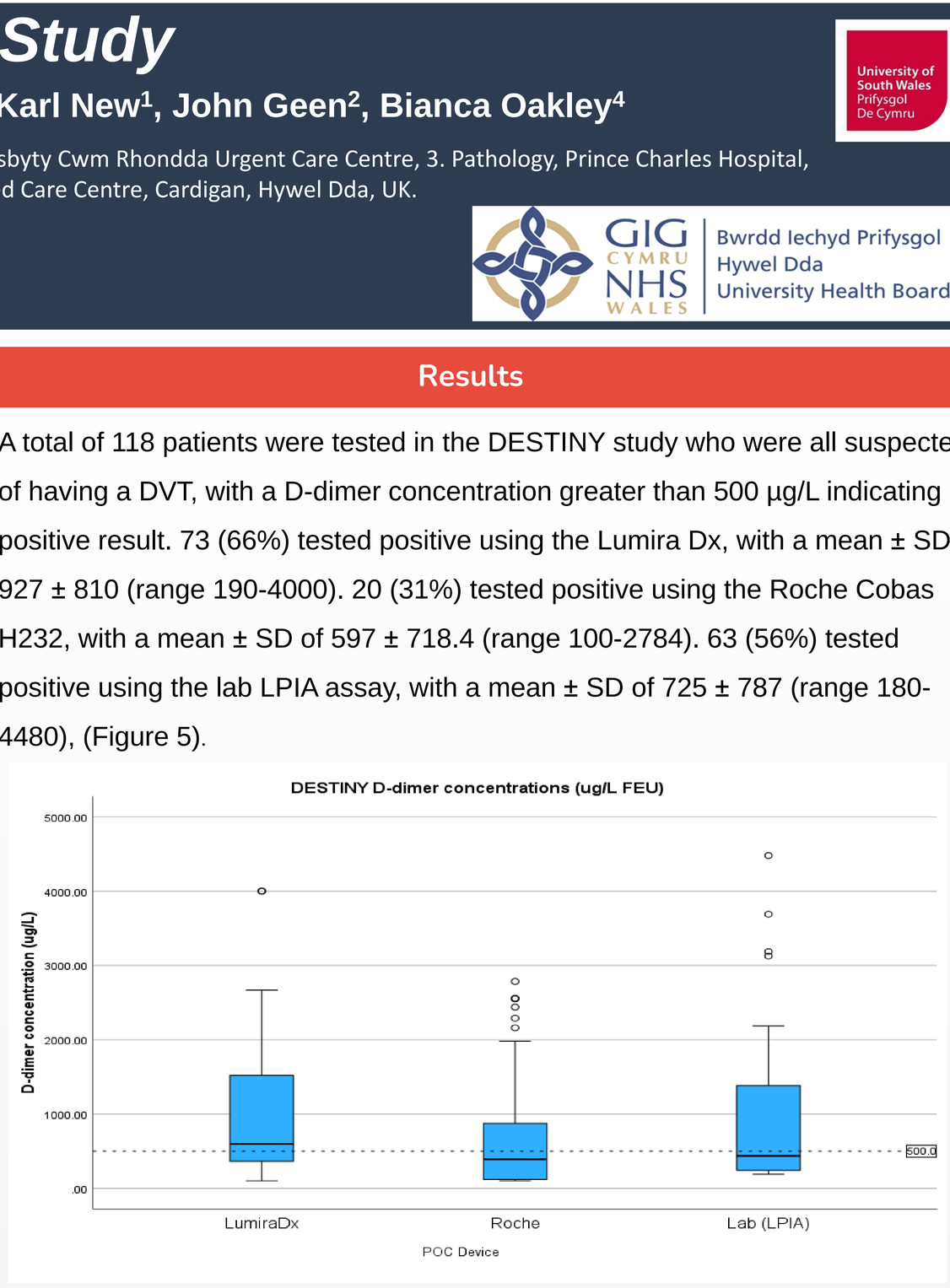

Figure 5. *Graph to show mean D-dimer concentration with reference to 500 µg/L D-dimer cut-off*

The sensitivity and specificity of the POC assays were comparable to that of the laboratory LPIA D-dimer assay. Relative to a positive DVT confirmed by Doppler, the Lumira Dx (n=109) test sensitivity was 100%, specificity was 39.2%, positive predictive value (PPV) was 20.5%, and negative predictive value (NPV) 100%. The Roche Cobas H232 (n=64) test sensitivity was 100%, specificity was 75.4%, PPV value 33.3%, and NPV value of 100%. The laboratory LPIA (n=113) test sensitivity was 100%, specificity 62.0%, PPV value of 28.3%, and NPV of 100%.

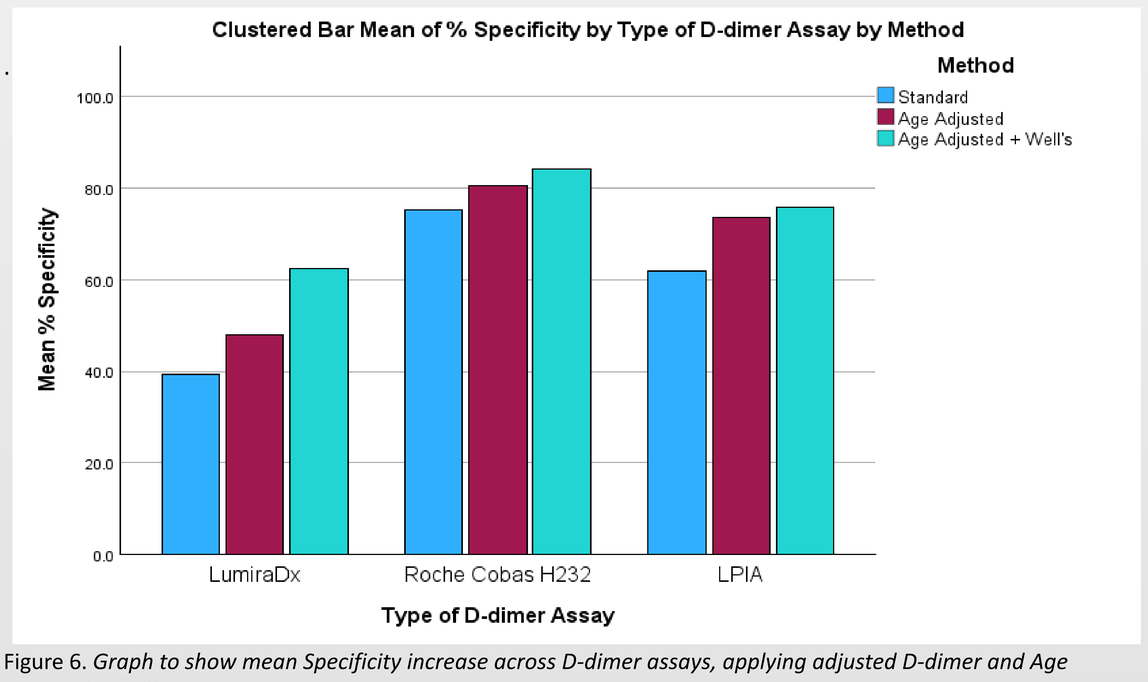

Figure 6. *Graph to show mean Specificity increase across D-dimer assays, applying adjusted D-dimer and Age Adjusted +Well's Score*

Using an age-adjusted D-dimer cut-off (patients 50 years or older calculated as age × 10 µg/L) significantly improved the specificity of all assays and PPV, while the sensitivity remained at 100% for the POC assays (Figure 6).

The mean Wells risk score for suspected DVT patients was 1.5 ± SD 1.4. Applying a Wells risk score of >2 in combination with an age adjusted D-dimer to rule out potential DVT's further improved the assay sensitivity, specificity, PPV and NPV (Figure 6).

Conclusion

The high sensitivity and 100% NPV of the POC D-dimer assays indicate their potential to safely reduce DVT referrals to secondary care. Mean D-dimer values from POC assays were comparable to the lab (P=0.12), though variability between devices (P=0.04) suggests challenges in standardisation. Incorporating age-adjusted D-dimer thresholds and Wells scores of >2 further improved both sensitivity and specificity, enhancing predictive accuracy.

These findings support the integration of POC D-dimer testing in primary care to optimise DVT detection and reduce unnecessary referrals, though Doppler ultrasound remains necessary for confirmatory diagnosis due to the low specificity of D-dimer tests.

Acknowledgements

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