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Point-of-care INR coagulometers for self-management of oral anticoagulation:

primary care diagnostic technology update

Clinical Question

In patients who require long-term anticoagulation treatment, how accurate and effective is self-management using a home monitoring device for INR, compared to standard practice?

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Submitted: 1 June 2012; **final acceptance:** 28 June 2012.

©British Journal of General Practice

This is the full-length article (published online 29 Oct 2012) of an abridged version published in print. Cite this article as: **Br J Gen Pract** 2012; DOI: 10.3399/bjgp12X658476

ADVANTAGES OVER EXISTING TECHNOLOGY

Devices to measure international normalised ratio (INR) are intended for both professional use and patient self-testing to monitor oral anticoagulant therapy. INR is a standardised measurement of the prothrombin time, which is the time it takes blood to clot after addition of tissue factor. Point-of-care (POC) INR testing within primary care settings eliminates delays in waiting for the result of prothrombin time measurement to be processed by the hospital laboratory, and the subsequent delay in adjustment of anticoagulation dosing. It also avoids the need to attend hospital anticoagulation clinics.

DETAILS OF TECHNOLOGY

The POC devices use electrochemical methods or function by drawing a precise amount of blood into a micro-channel and detect clot formation when the blood movement decreases below a predetermined rate. Currently there are three coagulometers on the market which are suitable for self-testing as they use capillary whole blood obtained from a finger prick. The measuring ranges of these devices vary slightly: INR of 0.6 to 8.0 for CoaguChek® XS (Roche Diagnostics), 0.8 to 8.0 for INRatio® (Hemosense), and 0.8 to 9.9 for ProTime®/ProTime 3 (International Technidyne Corporation). The sample volume required is very small (15–30 µL) with few user dependent steps. The results are typically available in less than 5 minutes.¹

PATIENT GROUP AND USE

Patients requiring long-term anticoagulation therapy, for atrial fibrillation, venous thromboembolism, prosthetic heart valves, or myocardial infarction and a number of pro-thrombotic conditions.

IMPORTANCE

Oral anticoagulation therapy, usually with warfarin, aims to reduce the risk of thromboembolic events, but requires regular

and frequent monitoring to not only ensure INR is within the therapeutic range, but also to reduce the risk of haemorrhage due to over-anticoagulation. An estimated 950 000 people are receiving oral anticoagulation therapy in the UK.²

PREVIOUS RESEARCH

Accuracy compared to existing technology

A recent systematic review on the precision and accuracy of POC coagulometers reviewed the evidence for CoaguChek XS, INRatio, and ProTime/ProTime 3.³ Across 14 studies on the accuracy of CoaguChek, the correlation coefficient varied from 0.81 to 0.95. Three studies on the accuracy of INRatio reported correlation coefficients from 0.92 to 0.95 and four studies on the accuracy of ProTime/ProTime 3 reported correlation coefficients from 0.72 to 0.90. The review concluded that accuracy of POC coagulometers was comparable to laboratory measures and generally adequate for clinical use. A multicentre user study tested CoaguChek XS compared to CoaguChek S and found that results were similar with mean relative bias <1%.⁴

Impact compared to existing technology

Evidence on patient self-monitoring of oral anticoagulation therapy shows improvement in anticoagulant control and reduced risk of thrombosis compared to clinic-based care. A systematic review of self-monitoring and self-management of oral anticoagulation concluded that self-management (that is, self-testing and self-adjusting warfarin) provided significant reductions in thromboembolic events (relative risk [RR] 0.47, 95% CI = 0.31 to 0.70) and all-cause mortality (RR 0.55, 95% CI = 0.36 to 0.84), while self-monitoring (that is, self-testing and adjustment by clinician) reduced major haemorrhages (RR 0.56, 95% CI = 0.35 to 0.91), but not thrombotic events (RR 0.57, 95% CI = 0.32 to 1.00), or mortality (RR 0.84, 95% CI = 0.50 to 1.41).⁵ Several subsequent randomised controlled trials have shown that

anticoagulation self-management was at least as good as or in some cases better than conventional management with INR values showing smaller variance and fewer major thromboembolic and bleeding complications in older people.⁶⁻⁸ The most common testing frequency is weekly, but lower frequency of testing can be justified based on the patient's condition. Trials carried out in the UK suggest that 24% of patients would agree to carry out self-monitoring, of these 70% could be successfully trained and able to conduct self-monitoring.⁹ A UK-based study suggests that self-monitoring patients were significantly more likely to have INR within therapeutic ranges than those receiving routine hospital anticoagulation clinic care (INR range 71% versus 60%, respectively [$P = 0.003$]) and significantly less time outside critical limits.¹⁰

A recent systematic review and meta-analysis of individual patient data¹¹ that had 5 years of follow-up data found a significant reduction in thromboembolic events in patients who self-monitored their INR (hazard ratio 0.51, 95% CI = 0.31 to 0.85), but not for major haemorrhagic events or death. Participants aged <55 years showed greater reductions in thromboembolic events (hazard ratio 0.33, 95% CI = 0.17 to 0.66), as did participants with mechanical heart valves (hazard ratio 0.52, 95% CI = 0.35 to 0.77).

Cost-effectiveness and economic impact

A Health Technology Assessment report in 2007, which is somewhat out of date, on the clinical effectiveness and cost-effectiveness of different INR models suggests that self-monitoring is effective and safe for long-term oral anticoagulation therapy in selected and successfully-trained patients.⁹ However, the economic evaluation found that patient self-management was more expensive than available routine care (£417 versus £122 per patient-year, respectively). Using UK based Self-Monitoring, Analysis, and Reporting Technology (SMART) trial data² and pooled results from all available trials, the incremental cost per QALY of self-monitoring versus usual care was £47 387 after 5 years and £19 617 after 10 years. The report concluded that patient self-management is unlikely to be more cost-effective than the current high-quality care provided by specialised UK anticoagulation clinics. In contrast, more recent evidence from a Canadian health technology assessment report¹² indicates that the ICER (cost per QALY) for self-managing dominates both standard care and self-testing, which means that self-monitoring resulted in significantly more QALYs gained than standard care and is on average cost-saving. A Belgian

HTA report reached similar conclusions,^{13,14} where in all scenarios investigated, the ICER (cost per life-year) of self-monitoring compared to usual care is on average the dominant strategy (less costly and more effective) or highly cost-effective compared to usual care. It should be noted that more recent and more favourable evidence of INR effectiveness was used in the Belgian¹⁵ and Canadian cost-effectiveness models. Patient level data was not available for these reviews and the probabilities used in the models were driven by literature findings and expert opinion.

Relevant Guidelines

National Institute of Health and Clinical Excellence. *Atrial fibrillation*. NICE guidance CG36. London: NICE, 2006. (<http://publications.nice.org.uk/atrial-fibrillation-cg36/guidance#antithrombotic-therapy>)

Keeling D, Baglin T, C Tait, *et al*. British Committee for Standards in Haematology (BCSH). *Guidelines on oral anticoagulation with warfarin — fourth edition*. Br J Haematol 2011; **154**(3): 311–324. doi: 10.1111/j.1365-2141.2011.08753.x. Epub 2011 Jun 14.

Scottish Intercollegiate Guidelines Network. *Antithrombotic therapy section 13: oral anticoagulants*. SIGN guideline no 36. Edinburgh: SIGN, 2012. (<http://www.sign.ac.uk/guidelines/fulltext/36/section13.html>).

What this technology adds

Point-of-care tests for INR are as accurate as laboratory-based measurements. There is good evidence that self-monitoring to adjust warfarin significantly reduces the rate of thromboembolic events, but not risk of major haemorrhage or death. Self-management of INR may be cost effective based on recent estimates. Translation of evidence into primary care settings is limited.

Methodology

Standardised methodology was applied in writing this report, using prioritisation criteria and a comprehensive, standardised search strategy, and critical appraisal. Full details of these are available from madox.org.

Funding

This article presents independent research commissioned by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research funding scheme (RP-PG-0407-10347). The views expressed in this article are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

Acknowledgements

The authors would like to thank Nia Roberts and Ibrat Djabbarov for their contribution.

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