

Horizon Scan Report 0012

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Diagnostic Technology: Point-of-Care International Normalised Ratio coagulometers for self-management of oral anticoagulation.

Clinical Question: In patients who require long-term anticoagulation treatment, what is the accuracy and acceptability of self-management using home International Normalised Ratio (INR) devices, compared to standard practice?

Devices:

CoaguChek XS (Roche Diagnostics), Hemosense INRatio (Hemosense Inc) and Protime 3 (ITC) are the devices currently identified in the UK market. These devices have been evaluated and compared in a Buyers' guide prepared by the NHS Purchasing and Supplies Agency (PASA) in January 2008 (1). Other similar devices have been available until recently: CoaguChek S, which has been replaced by its updated version CoaguChek XS, and SmartCheck INR (Unipath Ltd), which has been recalled by the manufacturer due to faults found with the device.

Advantages over Existing Technology:

INR devices are intended for both professional use and patient self-testing in the monitoring of oral anticoagulant therapy. International normalised ratios (INR) are a standard measurement of the prothrombin time. The prothrombin time is the time it takes plasma to clot after addition of tissue factor. Point-of-care (POC) INR testing within the primary care setting eliminates the delay in waiting for the result of prothrombin time to be processed by the hospital laboratory, and the subsequent delay in adjustment of anti-coagulation dosing and avoiding the need to attend hospital (2). Locating INR test equipment near the patient produces a faster result and this could be important in the management of long-term conditions, in acute haemorrhagic cases, or where the results can inform the decision on treatment. Providing patients with the opportunity to be more involved in the management of their own condition is an important factor highlighted by the NHS Next Stage Review (33). With structured training, motivated patients with sufficient manual skills and eyesight are able to manage their own long-term, oral anticoagulation therapy (3).

Details of Technology:

The instrument detects the clot formation when the blood movement decreases below a predetermined rate. The measuring ranges of these devices vary: INR of 0.6 – 8.0 for CoaguChek XS, 0.8 – 8.0 for Hemosense INRatio, and 0.8 – 9.9 for Protime 3. Patients can perform self-testing which uses capillary whole blood obtained from a finger prick. The sample volume can be very small (15-30 μ L) with few user dependent steps. The results are typically available in less than 5 minutes.

Patient Group and Use:

- Patients who require long-term anticoagulation therapy, in the clinical context of atrial fibrillation, venous thromboembolism, prosthetic heart valves or myocardial infarction.

Importance:

Common cardiac conditions are linked to increased risk from thrombosis and require anticoagulation therapy. Oral anticoagulation therapy, usually with warfarin, which aims to reduce the chance of unwanted thromboembolism, requires regular and frequent monitoring to avoid decreased clotting which may increase bleeding. It is estimated that 950,000 people are receiving oral anticoagulation therapy in the UK (4).

Previous Research:

Accuracy compared to existing technology

In samples from 397 warfarin-treated adult patients, a comparison between INR values from capillary samples using CoaguChek XS and venous plasma samples using the Owren prothrombin time assay in a hospital setting showed a

correlation of $r = 0.94$ (7). In a cardiac outpatient clinic, a study of 93 adult patients with atrial fibrillation receiving oral anti-coagulant therapy compared CoaguChek XS with the central laboratory coagulation analyser and results showed a close correlation of $r = 0.96$ (11). Data from 41 adult patients on long-term anticoagulation therapy without previous self-monitoring experience comparing CoaguChek XS versus standard laboratory measurements showed a Pearson correlation of 0.95 (8). These data were confirmed by a study in a community setting in Australia on patients starting warfarin therapy, where 337 CoaguChek XS results from 98 patients showed a correlation of $r^2 = 0.95$ when compared to standard laboratory analysis. A total of 93.5% of CoaguChek XS INRs were within 0.5 units of laboratory INR and 99.4% were within 0.8 units of laboratory INR. A UK study of 84 patients on long-term anticoagulation therapy also showed a high correlation between laboratory testing and self-testing using CoaguChek ($r = 0.95$) (26). An evaluation of the accuracy and ease of use of CoaguChek XS in a trial of warfarin home monitoring in 17 patients in Australia showed a high correlation ($r = 0.91$) between the POC monitor and the laboratory measurements and patients and doctors found the device to be easy to use (12).

A study investigating the accuracy of CoaguChek XS in 35 paediatric patients (aged 4 months to 18 years old) showed a mean difference in venous and capillary INR value of -0.13 (-0.57 to 0.55) and the Pearson correlation coefficient was 0.95 (5). When comparing the accuracy of CoaguChek XS with a laboratory reference method in another study on 26 paediatric samples, the correlation using capillary samples was $r = 0.95$. In this study correlation between venous and capillary samples was $r = 0.81$ (6).

One study comparing the accuracy of ProTime 3 with central laboratory results showed that INR were 0.8 ± 0.68 units higher than plasma INR values and correlation with plasma for the ProTime 3 device was $r^2 = 0.73$ (15). Another study comparing several POC INR monitors with a standard laboratory test showed a correlation coefficient of $r^2 = 0.96$ for ProTime 3 and $r^2 = 0.8$ for INRatio (14). A further study showed a correlation of $r = 0.94$ between ProTime and laboratory analysis (16). Samples from 19 paediatric patients showed a correlation of 0.89 when comparing this POC device with a laboratory test (17).

Impact compared to existing technology

Self-management coagulation monitors are simple to use and have few operator dependent steps. Nurse-led primary care anticoagulation clinics using point-of-care testing (POCT) had comparable outcomes in terms of INR control with routine hospital outpatient management (18). A study in Singapore of POC INR testing using CoaguChek SX in a hospital-based anticoagulation clinic (1332 clinic visits) showed a reduction of clinic visit duration by 35 min without cost increments to patients or the laboratory and in a survey of 323 patients, 87.5% (95% CI 82.5-91.5%) preferred POC INR monitoring (10). In a study of self-testing in the UK of 84 patients, 87% of patients found the self-testing straightforward and 77% preferred self-testing (26).

In terms of the usability of self-monitoring devices, one study of ProTime 3 showed that trained patients yielded equivalent INR results to professional operators ($r = 0.92$) and that patient satisfaction and compliance increased when a training programme was implemented (13). A UK based randomised control trial suggests that self-management of anticoagulation therapy is as safe as management in a nurse-led general practice clinic (19). Evidence on patient self-management of oral anticoagulation therapy shows improvement in anticoagulant control and reduced risk of bleeding and re-thrombosis. The most frequent 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 and 80% of the latter would conduct long-term self-monitoring (20). A UK based study suggests that self-monitoring patients had significantly better anticoagulant control than those receiving routine hospital anticoagulation clinic care of therapeutic INR range 71% vs 60%, respectively ($p=0.003$) and significantly less time outside critical limits (21). A systematic review has shown that patients capable of self-monitoring and self-adjusting therapy have fewer thromboembolic events and lower mortality than those who self-monitor alone (22). Subsequent to this review, several further randomised controlled trials have shown that anticoagulation self-management was as least as good or in some cases better than conventional management (24, 28), with INR values showing smaller variance (25) and fewer major thromboembolic and bleeding complications in the elderly (27).

A recent systematic review on self-monitoring and self-management of oral anticoagulation concluded that self-management showed significant reductions in thromboembolic events (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 reduced major haemorrhages (RR 0.56, 95% CI 0.35 to 0.91). The study concluded that patients who self-monitor or self-manage can improve the quality of their anticoagulation therapy, reducing the number of thromboembolic events and mortality without increase in harms. However, for up to half of the patients, self-monitoring or self-management were not feasible due to patient refusal, exclusion by the general practitioner or inability to complete training.

Guidelines and Recommendations

Several guidelines and recommendations have been published in the UK (30, 31). The International Self-Monitoring Association for Oral Anticoagulation's guideline suggests that "patient self-testing and patient self-management are effective methods of monitoring oral anticoagulation therapy, providing outcomes at least as good as, and possibly better than, those achieved with an anticoagulation clinic", adding that "all patients must be appropriately selected and trained" (23). The NICE clinical guideline on atrial fibrillation recommends the following (29):

"In patients with AF who require long-term anticoagulation, self-monitoring should be considered if preferred by the patient and the following criteria are met:

- the patient is both physically and cognitively able to perform the self-monitoring test, or in those cases where the patient is not physically or cognitively able to perform self-monitoring, a designated carer is able to do so
- an adequate supportive educational programme is in place to train patients and/or carers
- the patient's ability to self-manage is regularly reviewed
- the equipment for self-monitoring is regularly checked via a quality control programme."

Patient Resource:

A good patient information resource, providing accounts of patients' experiences, news, advice and information can be found at <http://www.anticoagulationeurope.org/>.

Cost-effectiveness and economic impact:

Prices for the INR devices available on the UK market vary from £399 for CoaguChek XS and Hemosense INRatio to £884 for ProTime 3 (1). Consumables are available on prescription and national prescription pricing rates apply.

The Health Technology Assessment report (2007) 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 (20). The economic evaluation found that patient self-management (PSM) was more expensive than available routine care (£417 vs £122 per patient-year, respectively). Using a cost-effectiveness threshold of £30,000 per quality-adjusted life-year (QALY) gained, patient self-monitoring does not seem to be a cost-effective approach. The incremental cost per QALY gained by patient self-monitoring is £122,365 over 5 years and £63,655 over 10 years. The estimated probability that patient self-monitoring is cost-effective (up to £30,000/QALY) is 44% over a 10-year period. This was based on data from the Birmingham based SMART study. Using pooled results from all available trials resulted in an incremental cost per QALY of PSM versus usual care was £47,387 after 5 years and £19,617 after 10 years. Self-monitoring may enhance the quality of life for some patients who are frequently away from home, who are in employment or education, or who find it difficult to travel to clinics. The report concludes that patient self-management is unlikely to be more cost-effective than the current high-quality care provided by specialised UK anticoagulation clinics. More recent evidence comes in the form of the Ontario based HTA report (37), where the ICER (cost per life-year) for self-managing dominates both standard care and self-testing (which means that PSM resulted in significantly more QALYs gained than standard care and is on average cost-saving), and the Belgian based HTA report (38), where in all scenarios investigated, the ICER of PSM compared to usual care is on average the dominant strategy compared to usual care, except in the scenario of 100% of GP consultations maintained and 52 tests/year. It must be noted that patient level data was not available for these reviews and the probabilities used in the model were driven by literature findings and expert opinion. Individual patient data evidence will be forthcoming.

Policy context comments:

The five-year plan for the NHS published in December 2009 identifies the need for enabling patients to manage their own conditions and treating them closer to home, thereby avoiding unnecessary hospital visits (32). The report states that this would release annual savings of up to £2.7 billion. According to the report, hospital-based care will be re-structured to concentrate on the sickest patients and more care will be provided closer to people's homes.

Research Questions:

Multi-centre randomised trials of home based INR use within the UK are required. In addition for those patients in whom it is considered that self-management is not possible then alternative strategies should be explored e.g. primary care and community pharmacy clinics

Research is needed in the clinical effectiveness and cost-effectiveness of patient education and training in long-term oral anticoagulation therapy.

Assessment of the effectiveness of patient self-management in children is needed.

Suggested next step:

Further randomized studies should await the publication of two studies due to be published this year, namely an individual patient meta-analysis (35) and a study on the impact of patient self-testing (36).

The current focus should be on health economic analyses to address the disparities in cost-effectiveness reports.

Expected outcomes:

Patients provided with sufficient training can self-monitor and self-manage their anticoagulation therapy, reducing the number and duration of clinic visits.

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This report was prepared by the Primary Care Diagnostic Horizon Scanning Centre Oxford

Authors: I. Djabbarov, A. Plüddemann, C. Heneghan, M. Thompson, C. P. Price

Contact details: Dr. Annette Plüddemann; [Email: horizonscanning@dphpc.ox.ac.uk](mailto:horizonscanning@dphpc.ox.ac.uk)