Is patient self-monitoring (including self-testing and self-management) of oral anticoagulation therapy safe, efficacious and cost-effective?

What is an evidence note

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions and are produced in an approximately 3 month period. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The reports are subject to peer review. Evidence notes do not make recommendations for NHSScotland.

Key definitions

Patient self-testing (PST): involves patients performing blood sampling and analysis at home using a portable, battery operated International Normalised Ratio (INR) testing machine. Results are communicated to a healthcare professional who then decides on dose adjustment.

Patient self-management (PSM): here the patient not only performs the blood sampling and analysis but also makes any vitamin K antagonist dose adjustment required.

Patient self-monitoring: In this evidence note, PST and PSM strategies are collectively referred to as patient self-monitoring.

Introduction

Oral anticoagulation therapy (OAT) is indicated for a range of conditions, including venous thromboembolism, atrial fibrillation, valvular heart disease and prosthetic heart valves. While newer anticoagulant drugs such as direct thrombin inhibitors like dabigatran are being introduced for specific patient groups, the most commonly used agents are the vitamin K antagonists, predominantly

Key points

- Around 1% of the 74,000 patients prescribed warfarin in Scotland are also in receipt of International Normalised Ratio (INR) self-testing strips.
- There is considerable heterogeneity in the evidence base for patient self monitoring with respect to the indications for therapy, patient selection, the intensity of education and support provided, and the frequency of testing. There is also variation in the format and quality of the ‘usual care’ comparison.
- Meta-analyses of randomised controlled trials (RCT) data in patients receiving long-term oral anticoagulation therapy with vitamin K antagonists report that self-monitoring of INR reduces the rate of thromboembolic events, compared with usual care, without affecting the rate of major bleeding events or mortality. This finding is challenged by the largest and most recent RCT in the analyses which examined self testing and found no benefits in time to stroke, major bleeding episode or death.
- In subgroup analysis, self-management was more effective than self-testing.
- Analyses of outcomes by age and indication for therapy highlighted that there were reductions in thromboembolic events in those aged <55 years and in participants with a mechanical heart valve.
- Patient quality of life is examined in the clinical effectiveness literature as a secondary outcome. Where it is reported, the majority of studies record beneficial effects.
- Economic analyses suggest that in the United Kingdom (UK) healthcare setting, INR self-monitoring is unlikely to be cost effective when compared with usual care.
Warfarin has narrow therapeutic index and ongoing monitoring of the level of anticoagulation of the blood using the INR is required to determine the safest and most effective dose for individual patients. Treating to a therapeutic target INR for each condition (commonly 2.5) addresses the variability in the action of vitamin K antagonists which is dependent on a range of environmental factors including diet, changes in metabolism and concomitant illness and medication use. Current models of OAT monitoring involve patients attending a hospital outpatient clinic or community-based service.

**Health technology description**

Patient self-testing (PST) involves patients performing blood sampling and analysis at home using a portable, battery operated INR testing machine. Results are communicated to a healthcare professional who then decides on dose adjustment. In patient self-management (PSM), the patient not only performs the blood sampling and analysis but also makes any vitamin K antagonist dose adjustment required. In this evidence note, these two strategies are collectively referred to as patient self-monitoring.

Three self-testing devices are available for use by patients in the UK: CoaguChek XS®, INRatio®, and Protime 3® (2009 information). Each uses a different methodology. The test strips and lancets are available on prescription. Devices cost from £275 to £399 (2013 prices, excluding VAT) and are not provided by the NHS (personal communication with manufacturers, May 2013). The test strips and lancets are available on prescription (£2.60 to £2.81 per test strip) and in 2011–2012 national spend on test strips dispensed in the community was £127,221 (J Vize, Senior Information Analyst, ISD Scotland. Personal Communication, 09 May 2013).

The National Institute for Health and Care Excellence (NICE) is currently developing diagnostics technology guidance for the CoaguChek XS® system (and other alternative technologies identified during scoping) to monitor the coagulation status of people receiving long-term vitamin K antagonist therapy (http://guidance.nice.org.uk/DT/16). It is anticipated that the guidance will be published in July 2014.

**Epidemiology**

In Scotland, in 2011–2012 around 74,000 individuals were prescribed warfarin. The number of people prescribed warfarin is increasing; in year 2008–2009 there were around 65,000 patients prescribed the medication. Approximately 1% (739) of people prescribed warfarin also receive testing strips on prescription, with the number of items dispensed per 100,000 population highest in NHS Western Isles, NHS Orkney and NHS Shetland (J Vize, Senior Information Analyst, ISD Scotland. Personal Communication, 15 January 2013 and 09 May 2013).

**Clinical effectiveness**

**Adults**

The evidence base for INR self-monitoring is heterogeneous with respect to the patient groups, parameters of the interventions and the usual care comparator. Most studies incorporate patients with a range of indications for oral anticoagulation. Study participants require motivation, confidence and sufficient mental and physical capabilities to perform the checks. Patient perspectives on the utility of the technology are likely to vary widely. Interventions are heterogeneous in terms of testing protocols and the intensity and quality of education and support provided. There is little consistency in control interventions which vary from highly specialised anticoagulation clinics or more general outpatient clinics through to routine primary care.

Primary outcome measures in randomised controlled trials (RCTs) examining the clinical effectiveness of self-monitoring of oral anticoagulation therapy include: rates of thromboembolic events such as stroke; rates of severe haemorrhagic events, the precise definition of which varies between studies; and mortality. Secondary outcomes include time spent in therapeutic range, patient satisfaction and quality of life.

Two meta-analyses summarise the evidence base in adults. The first identified 22 RCTs of self-monitoring (n=8,413, mean age 65 years), of which 13 studies had duration of follow up of less than 12 months. Based on data from 14 trials, the analysis reported a reduction in major thromboembolic events, odds ratio (OR) 0.58 (95% confidence interval (CI) 0.45 to 0.75;
p<0.001). Based on data from 16 trials there was no evidence of an increase in major bleeding events, OR 0.89 (95% CI 0.75 to 1.05; p=0.169). There was lower all-cause mortality in the self-monitoring group, based on 13 trials, OR 0.74 (95% CI 0.63 to 0.87; p<0.001) and this was statistically significant. Strength of evidence, based on the quality of the included studies, for the thromboembolism and bleeding outcomes was appraised as moderate while for the mortality outcome, strength of evidence was appraised as low due to heterogeneity between trials. There was no statistically significant difference between study groups in the mean percentage of INRs in the therapeutic range. Of 11 studies in the review measuring patient quality of life, eight reported that patient satisfaction, quality of life or both were better in the patient self-monitoring group. Meta-analysis for this outcome was not possible due to the diversity of outcome measures. In 11 of the 22 studies in the review, fewer than half of the patients who met the eligibility criteria completed the training and agreed to be randomly assigned.

A subsequent meta-analysis was based on individual patient data (n=6,417, mean age 65 years) obtained from 11 trials. More than half of the participants had atrial fibrillation and over a third had a mechanical heart valve. The study reported a statistically significant reduction in thromboembolic events in the self-monitoring group, hazard ratio (HR) 0.51 (95% CI 0.31 to 0.85; p=0.010). There was no statistically significant difference between the study groups in rates of major haemorrhagic events HR 0.88 (95% CI 0.74 to 1.06; p=0.18) or in deaths HR 0.82 (95% CI 0.62 to 1.09; p=0.18). The use of individual patient data facilitated the identification of subgroup effects. For the thromboembolic events outcome, participants who self-managed had significantly fewer events than control, while those who self-tested did not. Participants younger than 55 years of age and those with a mechanical heart valve had statistically significant reductions in thromboembolic events. Full analysis of time in therapeutic range and number of tests conducted was not reported.

Both these analyses incorporated the findings of the largest RCT of PST. The Home International Normalised Ratio Study (THINRS), published in 2010, randomised 2,922 patients to weekly home self-testing or to monthly high-quality testing in a specialist clinic. Follow up was undertaken for a minimum of 2 years (mean follow up 3 years, range 2.0–4.75). There were no statistically significant differences between study groups for the three primary end points: stroke, major bleeding or death. This study was identified by both the meta-analyses as a major source of heterogeneity due to it having both a longer follow up period and a higher quality intervention in the usual care arm compared with previous trials.

Children

A systematic review of studies of INR self-monitoring in children identified 11 studies, all but one of which were small uncontrolled case series with limited follow up. One small RCT (n=28) was identified which randomised children undertaking PST to continued PST or to PSM. At 1-year follow up there was no difference between the groups in time in INR target range but the PSM group reported higher quality of life. No meta-analysis was possible.

Cost effectiveness

Two systematic reviews and one cost effectiveness analysis summarise the economic evidence comparing patient self-monitoring strategies with usual care. The findings of the analyses within these reports are dependent on the effectiveness of usual care in the specific healthcare setting and the range of provider and societal costs which are incorporated. Self-monitoring has been reported to be cost effective in Canadian, German and Belgian healthcare settings.

Two economic analyses from the United Kingdom (UK) have concluded that, compared with usual care, PSM is unlikely to be a cost-effective strategy at a threshold of £30,000 per quality adjusted life year (QALY). The first of these, a cost-utility study conducted alongside a 2005 UK RCT, found that costs over a 1-year period were significantly higher in the PSM arm even when estimates of potential societal cost savings (such as patient transport and lost productivity) for the PSM arm were included. At a threshold of £30,000 per QALY gained the probability that PSM was cost effective ranged from 26–49% depending on which cost estimates were included.
Following on from this and using the same RCT data, a separate economic evaluation was carried out\(^ {14}\). A Markov state-transition model was constructed with a cycle length of 1 year that compared health costs and outcomes of patient self-monitoring with hospital or practice-based clinic monitoring. The estimated incremental cost per QALY gained by self-monitoring was £122,365 over 5 years and £63,655 over 10 years. The probability that patient self-monitoring would be cost effective (at a £30,000/QALY threshold) was 44% over 10 years\(^ {14}\).

**Safety**

A review concluded that portable coagulometers have acceptable accuracy and precision when compared with laboratory measures of INR but that external quality control is essential\(^ {1,16}\).

In the largest RCT of PST (n=1,463 in treatment arm, 4,495 patient years of weekly testing) no participants recorded any adverse event related to operation of the blood testing device\(^ {8}\).

**Conclusion**

Meta-analyses report that, for patients requiring long-term oral anticoagulation with vitamin K antagonists, PST or PSM of INR reduces the rate of thromboembolic events when compared with usual care without increasing the rate of major bleeding events or all-cause mortality. Certainty around this finding is reduced in view of a recent, large and well conducted multi-centre RCT, with long-term follow up, reporting no benefit in a comparison of PST with care in a specialist clinic meeting guidelines for high quality anticoagulation management.

Health economic evidence is inconsistent between countries. Findings are likely to be highly specific to the healthcare structures which are in place and particularly the frequency of testing in usual care. UK economic analyses report that self-monitoring is unlikely to be cost effective.

**Equality and diversity**

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The evidence note process has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

**About evidence notes**

Evidence notes are routinely considered for review 2 years post-publication, and at 2-yearly intervals thereafter. However, in the light of the consideration of this technology within the NICE diagnostics assessment process and expected publication of NICE guidance in 2014, this evidence note will be considered for review again in 12 months. For further information about the evidence note process see http://www.healthcareimprovementscotland.org/our_work/clinical__cost_effectiveness/shtg/standard_operating_procedures.aspx

To propose a topic for an evidence note, email evidencenotes.HCIS@nhs.net

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network http://www.knowledge.scot.nhs.uk, or by contacting your local library and information service.
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Healthcare Improvement Scotland development team

• Lorna Thompson, Lead Author/Health Services Researcher
• Jenny Harbour, Information Scientist
• Susan Downie, Medical Writer
• Doreen Pedlar, Project Co-ordinator
• Marina Tudor, Team Support Administrator
• Members of the SHTG evidence review committee

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References


