Evidence Review for Prescribing Clinical Network

Treatment: Self-testing with Coaguchek point of care testing (POCT) device and test strip prescribing in the community

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Summary page

- How strong is the evidence for claimed efficacy? - Grade A

- Potential advantages in terms of: efficacy, compliance, pharmacokinetics, drug interactions and adverse effects? **Improved patient experience and potential for improved anticoagulant control in selected patients**

- Is there a clear place in therapy / treatment pathway? **Yes**

- Is monitoring for efficacy required? – **Yes – follow up of patient to ensure quality of testing maintained and INR control optimal.**

- Is monitoring for toxicity required? – **Yes but only as usual treatment - the anticoagulant effect and side effects need to be reviewed every 6 to 12 months.**

- Is dose titration required? **If Self-testing yes, as with usual treatment, regular dose titration of anticoagulant on test results advice by anticoagulant clinic remotely, e.g.by 'phone. If self-managing the patient will adjust the dose and the clinic will review this at 3 to 6 monthly intervals.**

- Traffic light status for prescribing test strips **Red or from clinic supply proposed**

- Role of the specialist **Education and training of patient in use of POCT device, monitoring of INR control, advising on dose if appropriate, review of positive and negative effects of anticoagulants and on-going need for anticoagulation**

- Role of GP **ensuring the INR is being monitored and in range before prescribing anticoagulant drugs**

- Financial implications- Estimated cost or saving per 100 000 population:
  Potential increase in prescribing budget due to prescribing of test strips, but this should be transferred from the anticoagulant clinic.
  Current spend on test strips is approx £3,300 per 100,000 population

The Cochrane review in 2010 proposes savings may be generated from a reduction in major haemorrhages in patients who self-test and reductions in thrombosis in patients who self-test and self-manage, the increased education and training may also have contributed to these reductions. (1,2)

- Other issues
  Anticoagulation is an area of high risk and requires excellent clinical governance arrangements.

Recommendations:

Patient self-testing should be considered if preferred by a patient and where a clinical need has been identified by the GP/Consultant and certain criteria are met, including patient competency.
There must be a formal arrangement established to support self-testing between the anticoagulant clinic and the patient and their usual GP must be kept fully informed.

The current funding for anticoagulant monitoring should be used to support any supply of test strips.

For community based clinics under the Local Enhanced Service (LES) the contract states that strips will be given by the clinic (NOT on prescription) at clinic appointments from clinic stock. Clinic appointments for INR monitoring are typically at intervals of 4 to 10 weeks, more often when the patient is unwell or a new medicine is started. If a patient is self-testing every 7 to 14 days one pack of 48 strips will be sufficient for 12 months. This would allow for test failures, QC and EQA samples. For a patient with a stable INR a pack of 24 would be suitable.

For hospital based clinics the strips should be supplied by the hospital managing the anticoagulation. This ensures the quantity of strips supplied meets the clinical need.

If GPs were to prescribe for their patients managed by hospital clinics, there would need to be excellent communication regarding the quantities required.

1. Purpose of the Review

To evaluate the use of patient self-testing for INR monitoring and the associated responsibilities of the patient, their anticoagulant clinic and general practitioner.

2. Appropriateness

2.1 The patient: - Patients taking long-term anticoagulant medication, typically warfarin, and wishing to monitor their INR at home using a POCT device and test strips. Self-testing is not suitable for everyone, but can result in greater patient satisfaction and enhanced quality of life. To self-monitor patients must be manually dexterous, have reasonable eyesight and reliable access to a telephone or other devices to communicate with the anticoagulant clinic between visits. Some patients may also wish to self-manage, deciding their dose without referral to the anticoagulant clinic.

2.2 The problem:

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

Self-testing may be particularly beneficial for:

- Those with particular risk factors for bleeding, such as being older than 65 years, having other major medical conditions or taking medicines aside from warfarin.
- Those with highly variable INRs, perhaps also enabling individuals to correlate factors such as specific foods with alterations in their INR results.
- Those with difficulties travelling to clinics due to distance, disabilities or work/family commitments.

Effects and prognosis: 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.

2.3 The Intervention:

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-Testing (POCT) for INR 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 anti-coagulant dosing. It also avoids the need to attend hospital anticoagulation clinics.

How does it work: The POCT devices function by drawing a precise amount of blood into a micro-channel and detecting clot formation when the blood movement decreases below a predetermined rate. The sample volume required is very small (10–30µL) with few user dependent steps. The results are typically available in less than 5 minutes.

Care setting: Where is the intervention given? - Primary care, patient's home.

Frequency: How often is the intervention given – Life long, testing frequency dependent on clinical factors from weekly to every 12 weeks, but typically every 4 to 8 weeks.

2.4 Alternative treatments:

a. Hospital clinic testing – out patient appointment with haematology team to have a test, know the result and be advised on dosage.
b. Hospital lab testing (postal service)– phlebotomy appointment for test, results done later and patient called if any change to therapy required. Instructions posted to patient. Less opportunity for communication regarding the result, lifestyle advice and dosage instuctions.
c. Community clinic – POC testing by a professional at a community based clinic appointment - have a test, know the result and be advised on dosage.

3. Effectiveness

3.1 Expected benefits

Evidence on patient self-testing of oral anticoagulation therapy shows improvement in anticoagulant control and significantly reduced major haemorrhages compared to clinic-based care. Self-management showed significant reductions in thromboembolic events and all-cause mortality. (1,2)

3.2 Is there a plausible biological basis for effectiveness?

Within the critical range of interest, point-of-care tests for INR are as accurate as laboratory-based measurements. There is good evidence that Self-testing to adjust warfarin significantly reduces the rate of thromboembolic events, but not risk of major haemorrhage or death.

3.3 Side-effects/complications N/A

3.4 Review of evidence

An independent research paper last year: **Point-of-care INR coagulometers for self-management of oral anticoagulation** published in the British Journal of General Practice, Nov 2012, produced the following findings:

Evidence on patient Self-testing of oral anticoagulation therapy shows improvement in anticoagulant control and reduced risk of thrombosis compared to clinic-based care. A systematic review of Self-testing 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-testing (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). 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. 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-testing, of these

70% could be successfully trained and able to conduct Self-testing. A UK-based study suggests that Self-testing 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.
A recent systematic review and meta-analysis of individual patient data 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).

Local clinics wishing to start patients on self-management or Self-testing would require clear management plans, clinical governance and quality control arrangements, training and signed agreement with the patient. See Appendix 1

4. Summary of Key Points for Consideration

4.1 National guidance:

MHRA - Management and Use of point of care testing (POCT) in vitro diagnostic (IVD) devices; 2010
The key issues addressed in this guidance include:

- A clinical need must be identified before the implementation of a POCT service.
- Consider involving the local hospital laboratory in the management of POCT services.
- Lines of accountability for POCT management must be clear.
- Managers of POCT services must be aware of their responsibilities under clinical governance.
- Arrangements for training, management, quality assurance (QA) and quality control (QC), health and safety policy and the use of standard operating procedures (SOPs) must be made and reviewed at frequent specified intervals.
- Assessment of the service by an external accreditation body is recommended.
- You should consider the available evidence for the performance of the test.
- Adverse incidents must be reported to the MHRA.
- Clear, comprehensive record keeping and documentation is vital.
- Everyone involved in POCT should know what to do in the event of any abnormal result or unsatisfactory QC result.

National Institute of Health and Clinical Excellence.
Venous thromboembolic diseases: NICE Clinical Guideline June 2012
Indicates there is insufficient evidence to support the cost effectiveness of routinely offering self-testing or Self-testing.
Atrial fibrillation. NICE guidance CG36. London: NICE, 2006.
Recommends Self-testing should be considered if preferred by a patient and if certain criteria are met. This guideline is being updated and the scope indicated it will reflect the recommendations of the VTE guideline.
Support for commissioning: anticoagulation therapy, NICE May 2013
Commissioners should work with clinicians to develop local protocols to support individuals who request to self-monitor or self-manage. This should include funding arrangements for testing equipment and testing strips.

British Committee for Standards in Haematology (BCSH).Keeling D, Baglin T, C Tait, et al. Guidelines on oral anticoagulation with warfarin — fourth edition. Br J Haematol 2011

Individuals on warfarin can adopt one of two separate anticoagulant self-testing programmes: Individuals may elect to check their own INR using one of the commercially available INR monitors (Perry et al, 2010) and then report their INR to a healthcare professional who is then responsible for dosing advice. Such advice can be given verbally initially but should also be sent in writing or electronically (Ryan et al, 2009). Alternatively, patients may be trained to both monitor their INR and adjust their dose of warfarin based upon the result. In a recent Cochrane systematic review, patients who self-monitored or self-managed their anticoagulants improved the overall quality of their oral anticoagulation therapy compared to standard monitoring (Garcia-Alamino et al, 2010). The number of thromboembolic events and overall mortality was decreased without any increase in bleeding. However, Self-testing or self-management may not be appropriate for most patients e.g. in those unable to complete the training programme, with no wish to participate in such a programme or with a lack of support from their general practitioner. Guidelines for patients self-testing have been published (Fitzmaurice et al, 2005) and that paper, the review by Perry et al (2010) and a BCSH guideline (Briggs et al, 2008) cover the important issue of quality assurance for point-of-care machines.

Scottish Intercollegiate Guidelines Network. **SIGN 129 • Antithrombotics: indications and management**, June 2013.

A range of models of care for long term management of anticoagulation with VKAs is available including hospital based anticoagulant clinics, community based clinics with INR measurement in a hospital laboratory, community based clinics with point of care (POC) testing, patient self-testing of INR and patient self-testing and dosing, both using POC equipment. In addition, dosing decisions may be made by a range of health professionals and/or computer-assisted dosing programmes .

The use of POC testing is associated with improved time in the INR target range and a significant reduction in risk of thromboembolic events and death.[233-236] These benefits were most marked in studies undertaken outside the UK and may not be evident when compared to specialised anticoagulant clinic services. Self-testing and management may not be applicable for the majority of patients and the apparently improved outcomes may reflect better patient education.

Point of care testing is likely to be more expensive than monitoring by specialised anticoagulant clinic
services in the UK. One RCT indicated that computer-assisted dosing may be associated with a slight further improvement in time-in-range, above that achievable by manual dosing.[237]

An analysis of the clinical and cost effectiveness of different models of managing long term oral anticoagulation therapy suggests that self-testing is unlikely to be more cost effective than current usual care in the UK.[233]

Self-testing and self-dosing are safe and effective and can be considered for some patients.

- For patients who are self-testing, appropriate education and training should be provided, clinical advice should be available on request, and provision should be made for quality assurance.
- Healthcare professionals providing dosing advice on INR should be appropriately trained and able to provide documented evidence of competence.
- Healthcare professionals undertaking POC testing should be trained in its operation and maintenance prior to use, including the requirement for robust quality assurance of the INR measurements.

4.2 Efficacy

Patients should only conduct self-testing, with or without self-management, within a managed programme. The same standards of total quality management as practiced in hospital-based clinics should be adhered to. Patients should be assessed for capability: only patients considered competent to follow total quality management procedures should complete training and undertake self-testing.

Patient self-testing programmes should be reviewed and audited at regular intervals for both technical (INR measurement) and clinical utility. Quality assurance procedures should include regular review of the proportion of INRs in range and the incidence of over anticoagulation, bleeding and thrombotic adverse events.

4.3 Potential Benefits over existing therapy

Improved quality of anticoagulant therapy. Improved patient satisfaction

4.4 Potential disadvantages

- Poor quality of analysis.
- Poor record keeping.
- Lack of result interpretation.
- Failure to detect erroneous results.
- The availability of self-testing may tempt users to perform unnecessary or inappropriate tests leading to increased use and expenditure on test strips.
- Data recording may be complex and less robust – less recording of results in patient records.

4.5 Budgetary Impact

4.5.1 Cost:

Patients self-testing can be expensive - patients who self-test tend to test at a higher frequency than those monitored within a hospital or community clinic.
It is the experience of local clinics that, done properly, supporting a self-testing patient requires at least as much time as for usual appointment monitoring, this is due to the increased education and telephone advice provided.

Roche Diagnostics offer a 28% discount on list price for the CoaguChek XS test strips and controls and 34% on Accu-check lancets to practices signed up to the Anticoagulation LES. This discount is available to practices purchasing directly from Roche and may be renegotiated on a CCG basis. Supply by FP10 is therefore considerably more expensive:

2013-4 discount deal	List price	Discount price
CoaguChek XS test strips (48)	£131.75	£94.86
CoaguChek XS test strips (24)	£67.39	£48.52
CoaguChek XS Plus PT Controls	£15.00	£10.80
Accu-chek Safe-T-pro Plus Lancet (200)	£28.99	£19.13

All prices are excluding VAT

Despite the LES specifying strips must be purchased by the practice, current spend on test strips via FP10 prescribing is £33,111 per annum across Surrey.

<u>Cost comparison of anticoagulant monitoring and new oral anticoagulants</u>

Monitoring in community via LES : £211.88 per annum per patient. This covers supporting a minority of patients in self-testing and providing test strips from clinic supplies.
For patients who need to test very two weeks or less, packs of 24 strips are given.

Monitoring in hospital - £unknown (included within block contract)
Prescribing of test strips to monitor every 7 to 14 days (1 x 48) - £158.10 inc VAT

Prescribing new-oral anticoagulants that do not require INR monitoring (Apixaban, Rivaroxaban or Dabigatran) approx £800 per annum.

4.5.2 Precedent setting:
Approximately 2.4% of the population will require anticoagulation (2400 per 100,000). An unknown number of these are already Self-testing with variable levels of governance and quality control. Trials in the UK suggest that 25% of patients on warfarin are willing to self-monitor and 70% of these would be suitable. This would equate to a maximum of 420 per 100,000 if offered to all.

5. Conclusions and Recommendations

Patient self-testing should be considered if preferred by a patient and where a clinical need has been identified by the GP/Consultant if certain criteria are met. There must be a formal arrangement established to support Self-testing between the anticoagulant clinic, the patient and their usual GP.
It should be noted that in general, patient Self-testing is unlikely to be more cost-effective than the current high quality care provided by specialised anticoagulation clinics in the UK. Only patients with indications for long term anticoagulant therapy should be considered for Self-testing, due to the time taken for patients to familiarise themselves with the processes involved in Self-testing and due to the cost of the equipment which is not available at NHS expense. The testing machine is usually purchased by the patient. The current cost for a patient held Coaguchek machine is £299.

Clinics wishing to support patients in Self-testing need to ensure the following:

- An adequate supportive educational programme is in place to train patients and/or carers.
- The patient's ability to self-monitor is regularly reviewed.
- The equipment for Self-testing is regularly checked via a quality control and External Quality Assessment programme.
- Patients and/or their carers must give informed consent to the clinician responsible for their Self-testing.
- Prior to commencement of Self-testing, competence to perform an INR test must be assessed and signed off by an experienced and appropriately trained healthcare professional.
- Prior to commencement of Self-testing the patient is aware of the accepted frequency of testing and that any excessive testing will not be funded by the NHS
- The patient's usual GP will be sent copies of the agreement and informed of the process for the patient to obtain test strip supplies

Self-testing should not be commenced in patients where treatment compliance is an issue e.g. non-attendance at clinics or failure to take their medication as prescribed.

Only portable coagulometers that have undergone acceptable evaluations by an expert body e.g. the MHRA should be used for INR Self-testing and internal quality control should be performed in accordance with the individual manufacturer's

recommendations at least every one to three months or with every new box of test strips or if an unusual result is obtained or if there is an unusual occurrence that may affect the results.

External Quality Assessment should also be carried out every three to six months either by the patient attending a clinic which participates satisfactorily in an accredited EQA programme e.g. NEQAS, testing a sample on the patient's monitor and the monitor in the clinic, INR results >2.0 should be within 0.5 INR units of each other. Alternatively a venous sample can be collected at the same time as the patient's Self-testing test, and analysed in an appropriate hospital laboratory. However, it is important to note that INR measurements may deviate according to the technique used for measurement, an INR deviation of +/- 10% has been considered acceptable for clinical purposes.

Appendix 1: Evidence search

Search terms used:

Resource	Used in this review?
National Library for Health (NHL) http://www.library.nhs.uk/Default.aspx A gateway site with access to other resources such as Reviews (Bandolier, Cochrane, CRD etc), Guidelines (e.g. NICE), Clinical Knowledge Summaries (CKS) and Journals including AMED, British Nursing Index, CINAHL, E-books, EMBASE, HMIC, MEDLINE, My Journals, PsycINFO, PubMed, Databases from Dialog.	✓
National Institute of Health and Clinical Excellence (NICE) http://www.nice.org.uk/ NICE produces national guidance in three areas of health: 1. Public health - guidance on the promotion of good health and the prevention of ill health 2. Health technologies - guidance on the use of new and existing medicines, treatments and procedures within the NHS 3. Clinical practice - guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.	✓ (through NHL)
Bandolier http://www.medicine.ox.ac.uk/bandolier/index.html Bandolier is a website about the use of evidence in health, healthcare, and medicine. Information comes from systematic reviews, meta-analyses, randomised trials, and from high quality observational studies.	✓(through NHL)
Centre for Reviews and Dissemination http://www.york.ac.uk/inst/crd/ CRD undertakes high quality systematic reviews that evaluate the effects of health and social care interventions and the delivery and organisation of health care. Databases maintained by CRD include Database of Abstracts of Reviews of Effects (DARE), NHS Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA) Database	✓(through NHL)
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/ Scottish equivalent of NICE	✓
Medical Services Advisory Committee (Australia)	✓

http://www.msac.gov.au/internet/msac/publishing.nsf/Content/home-1 The principal role of the Medical Services Advisory Committee (MSAC) is to advise the Australian Minister for Health and Ageing on evidence relating to the safety, effectiveness and cost-effectiveness of new medical technologies and procedures.	
Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/index.php/en/home The Canadian Agency for Drugs and Technologies in Health (CADTH) is a national body that provides Canada's federal, provincial and territorial health care decision makers with credible, impartial advice and evidence-based information about the effectiveness and efficiency of drugs and other health technologies.	✓

References

1. Point-of-care INR coagulometers for self-management of oral anticoagulation: A Plüddemann et al; British Journal of General Practice, November 2012 e798

2. Self-monitoring and self-management of oral anticoagulation (Cochrane Review 2010) Garcia-Alamino JM, Ward AM, Alonso-Coello P, Perera R, Bankhead C, Fitzmaurice D, Heneghan CJ
3. Anticoagulation: Self-testing – Patient information David Fitzmaurice et al; Atrial Fibrillation Association
4. Point of care testing for INR monitoring: where are we now? E. T. Murray et al. British Journal of Haematology, 2004 127, 373–378
5. Venous Thromboembolic Diseases NICE Clinical Guideline June 2012
6. SIGN 129 • Antithrombotics: indications and management a National Clinical Guideline, Updated June 2013

The links below provide additional information / patient perspective

http://www.acsma.org.uk/

http://www.anticoagulationeurope.org/