bjh guideline

An evidence-based review and guidelines for patient self-testing and management of oral anticoagulation

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Summary

There is a limited evidence base for self-testing and -management for oral anticoagulation management. Available data suggest that these are credible models for a significant minority of patients if underpinned by structured training and follow-up. The guidelines presented are necessarily consensual and outline procedures for patient selection, training, product procurement, product maintenance, quality assurance procedures, dosage adjustment and clinical supervision. The cost-effectiveness of these models remains to be elucidated within the UK. Further data on both health economic and clinical outcomes are required from UK based studies before widespread implementation of self-testing and management can be recommended on a wider scale.

Keywords: anticoagulation, self-testing, self-management, guidelines.

These guidelines are derived from the evidence available regarding clinical effectiveness and health economics of patient self-testing and self-management of oral anticoagulation therapy. The guidelines cover patient self-management, where patients measure their own international normalised ratio (INR) and interpret the result themselves, as well as patient self-testing, whereby patients measure their own INR but contact a health professional for interpretation. These guidelines follow the format of the British Committee for Standards in Haematology evidence-based guidelines (British Society for Haematology, British Committee for Standards in Haematology Haemostasis and Thrombosis Task Force, 1998) for therapeutic management of warfarin.

The expansion of clinical indications for oral anticoagulation therapy (primarily warfarin in the UK) (Lowe, 1992; Sweeney *et al*, 1995), particularly non-rheumatic atrial fibrillation, (Gustafson *et al*, 1992; Sandercock *et al*, 1992) has raised concerns over how therapeutic monitoring should be undertaken (Taylor *et al*, 1993; Sudlow *et al*, 1995). It is estimated that around 950 000 people in the UK are currently taking warfarin (Gardiner *et al*, 2004). These guidelines provide updated, evidence-based guidance for self-management and self-testing of oral anticoagulation therapy and supercede previous recommendations (Fitzmaurice & Machin, 2001).

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1. Reliability of point of care testing for self-management

The use of point of care (POC) testing for INR estimation affords the possibility of selected patients undertaking either self-testing or -management (Rink *et al*, 1993; Hobbs, 1996). Reliable, portable machines are available that have been subject to rigorous laboratory evaluation (Oberhardt *et al*, 1991; Kapiotis *et al*, 1995; Machin *et al*, 1996). Two portable, battery-driven, prothrombin time coagulometers have had satisfactory evaluations performed by the UK Medicines and Healthcare Products Regulatory Agency (MHRA, previously the Medical Devices Agency, MDA) Coagulation Evaluation Centre, showing acceptable precision and comparable INR values across the therapeutic range (Table I) (England *et al*, 1995). Two further portable coagulometers are awaiting MHRA evaluation at the time of writing. Good performance has been demonstrated with commercially available POC coagulometers, in terms of accuracy, reproducibility and long-term reliability, when used by selected patients (Hasenkam *et al*, 1997a; Gardiner *et al*, 2004).

Healthcare professionals working within a National Health Service (NHS) Trust should discuss the potential use of POC devices (whether within the 'trust', or by patients outside the trust) with their local POC committee. Every NHS trust is required to have a POC committee, whose objective is to ensure acceptable analytical and clinical quality standards. They may also offer advice on device selection and procurement.

doi:10.1111/j.1365-2141.2005.05739.x

Table I. Characteristics of Medicines and Healthcare Products Regulatory Agency evaluated coagulometers.

Name of POC testing device (Diagnostic Company)	Coaguchek (Roche)*	Protime (ITC)
Specimen collection	Test strip/iron oxide particles/ thromboplastin	Test cuvette/Tenderlett device/ cuvette containing thromboplastin
Quantity of blood (μl)	10	27
Detection principle	Iron oxide particles/photoreflection	Photoptic detection of decreased blood flow
Type of blood	Whole blood – venous or capillary	Whole blood – venous or capillary
Thromboplastin (ISI)	Rabbit brain	Recombinant
Memory store	30 Test results	39 Test results
IQC	Supplied by manufacturer	Integral to test cuvette
Calibration	Lot-specific code chip new test strips.	Instrument and cuvettes pre-calibrated

*Coaguchek plus is also available, which also performs an activated partial thromboplastin time test.

2. A review of the evidence for patient self-testing and management of oral anticoagulation

The move towards patient self-testing and -management has grown out of problems inherent to clinic models, with patients demanding more autonomy and control over their condition (Kurnitz, 1998). Whilst convenience and patient autonomy are undoubtedly important, the relative clinical safety and effectiveness of patient self-management in comparison with the existing models of care must be established.

Papers presenting original data for patients undertaking self-monitoring identified from a MEDLINE search from 1965 to November 2003, using a variety of search terms, and also by contacting experts in the field have been included within this analysis. Because of the relative lack of research in this area, observational data have been included as well as controlled trials. From published data, six prospective randomised controlled trials (White *et al*, 1989; Sawicki, 1999; Cromheecke *et al*, 2000; Korfer & Kortke, 2001; Sidhu & O'Kane, 2001; Gadisseur *et al*, 2003), three matched controlled (Ansell *et al*, 1995; Hasenkam *et al*, 1997b; Cosmi *et al*, 2000) and three observational studies (Anderson *et al*, 1993; Barnado, 1995; Massicotte *et al*, 1995) were identified (Table II). Early studies addressed the feasibility of allowing patients receiving oral anticoagulation to undertake self-management and were predominantly undertaken in North America (Stamper & Toth, 1996).

White *et al* (1989) randomised 46 patients to either home monitoring or clinical management. Patients were required to be commencing warfarin for the first time, to have an indication requiring at least 8-week therapy (the duration of follow-up), to have access to a telephone, to live within 150 miles of the study centre (Sacramento, CA, USA), and to be willing to have given informed consent. The training process was not adequately described but included observation of the patients determining at least one prothrombin time success-

Table II. Summary of studies included in the literature review.

Study	Country	Nature of study	Patient numbers intervention/control	Results intervention *versus* control
White *et al* (1989)	USA	RCT	23/23	93% vs. 75%*
Sawicki (1999)	Germany	RCT	90/89	53% vs. 34%**
Cromheecke *et al* (2000)	Holland	RCT	25/25 (cross-over trial)	55% vs. 49%*
Korfer and Kortke (2001)	Germany	RCT	279/303	80% vs. 54%***
Sidhu and O'Kane (2001)	UK	RCT	41/49	77% vs. 64%*
Gadisseur *et al* (2003)	Holland	RCT	47/60	66% vs. 59%*
Hasenkam *et al* (1997b)	Denmark	Matched	21/20	77% vs. 55%*
Ansell *et al* (1995)	USA	Matched	20/20	89% vs. 68%*
Cosmi *et al* (2000)	Italy	Matched (self-testing)	78/78	80% vs. 80%*
Anderson *et al* (1993)	Canada	Observational	40/self-control	74%***
Barnado (1995)	Germany	Observational	216/no control	83·1%***
Massicotte *et al* (1995)	Canada	Observational	23/no control	63%***

RCT, randomised controlled trial; *, % time in range; **, % patients in range; ***, % tests in range.

fully. The self-monitoring group showed a greater percentage of time within therapeutic range (93% vs. 75%, $P = 0{\cdot}003$) with control patients having significantly more time spent below range (data not stated, $P < 0{\cdot}001$). The coagulometer used was a Coumatrack (Dupont Inc., Wilmington, DE, USA).

Sawicki (1999) reported a randomised controlled trial of patient self-management *versus* routine care, which showed modest improvement in the self-management group in terms of deviation from target INR (squared INR deviation 0·65 vs. 0·83, $P = 0{\cdot}03$). This German study randomised 179 patients who were each followed up for 6 months. All consecutive patients who had not previously been treated within the study centres, who required life-long anticoagulation and agreed to participate, were enrolled. The intervention comprised a structured educational programme consisting of three consecutive weekly teaching sessions of 60–90 min for groups of three to six patients provided by trained nurses or physicians. The coagulometer used was the Coaguchek (Roche Diagnostics, Mannheim, Germany). Control patients had INR estimation every 2 weeks; intervention patients were advised to check every 1 or 2 weeks depending on the INR result. Unfortunately, neither group performed particularly well, with only around 50% of patients achieving therapeutic INRs. Adverse events were similar in both groups with one major haemorrhage in each group and one ischaemic stroke in the routine care group. This is not surprising given the small scale and short period of follow-up (3 months).

A study from Holland included 50 patients (consecutive ambulant patients with a long-term indication for warfarin) in a randomised crossover trial between self-management and anticoagulation clinical management (3 months of each) (Cromheecke *et al*, 2000). The coagulometer used was Coaguchek. There was no significant difference in the percentage of time spent within therapeutic range (self-managed 55% *versus* clinic 49%, $P = 0{\cdot}06$). Training was provided in groups in two, 2-h sessions, 10 d apart. The frequency of testing in the self-management period was once every 8·6 d compared with a test frequency of once every 9·0 d in the clinical period. There was no difference in adverse event rates, again not surprising given the small number and short follow-up period.

The study by Korfer and Kortke (2001), of the Early Self-Controlled Anticoagulation Trial from Germany reported data on 600 patients, with 305 using POC testing (Coaguchek Plus; Roche Diagnostics) to perform self-management following heart valve replacement and 295 managed by a doctor. It is not clear whether the control group were managed within specific clinics or within the physician office system. The self-management group were given standardised training in home prothrombin estimation using POC testing and asked to monitor their INR every third day. The physicians managed the other group with no recommendation for interval of INR measurement. Patients were asked to inform the doctor if the INR was measured 0·5 below or above the target range. A total of 23 693 readings were analysed for the self-management group compared with only 4599 for the conventionally managed patients. Seventy-nine per cent of self-managed INRs were within the therapeutic range compared with 62% from the control group. Patients randomised to self-management withdrew was 8·3% and the authors concluded that 80% of patients with mechanical cardiac valves could undertake self-monitoring of their INR.

In Northern Ireland, Sidhu and O'Kane (2001), successfully trained 41 patients with heart valve replacement from 51 patients randomised with 49 control patients managed conventionally; both groups were followed up for 2 years. Training was undertaken in groups of two to five patients and was delivered in two, 3-h sessions. The coagulometer used was the Coaguchek. Self-managed patients demonstrated better control in terms of both proportion of tests in range (67·6% vs. 58·0%, $P < 0{\cdot}0001$), and time within therapeutic range (76·5% vs. 63·8%, $P < 0{\cdot}0001$). There were no significant differences in mortality or morbidity between the two groups.

Gadisseur *et al* (2003) recruited patients from Dutch anticoagulation clinics. Only 25% of patients agreed to participate in the study. Patients performed weekly INR tests using a Coaguchek S. In a complicated design, patients were trained to either self-manage or self-test in three sessions a week apart, in groups of four to five patients. Patients were followed for 26 weeks. There was a non-significant improvement in therapeutic control (% time in range) for both self-testing (64%) and self-managing patients (66%) compared with patients managed through the anticoagulation clinic (59%).

Hasenkam *et al* (1997b) enrolled 21 patients following heart valve replacement. Inclusion criteria were: implantation of a bileaflet mechanical heart valve, aged between 18 and 70 years, residence within 100 km of the study centre (Aarhus, Denmark) with a high level of patient compliance anticipated from interview. Exclusions were, coagulopathies, addiction to drugs or alcohol and liver disease. The control group were matched retrospectively ($n = 20$). The Coaguchek was used for INR estimation. Training for intervention patients took place over 6 weeks and was undertaken on both an inpatient and outpatient basis. The content and intensity of the training was not specified. Patients were considered to be fully capable of self-management after 30 weeks. Nineteen of 21 patients continued self-management beyond 9 months (the minimum follow-up). The median INR value was within therapeutic range for all study patients but for only 15 of 20 controls. Similarly the intervention patients were within therapeutic range 77% of the time compared with 55% for the control patients.

In a similar study in North America, Ansell *et al* (1995) recruited 20 patients with stable INRs (undefined) who had been taking oral anticoagulation for at least 1 month and were willing to undertake self-monitoring. Training in both monitoring and dose-adjustment took place over a 2-week period; however, the content and intensity of training were not specified. The study used the Coumatrak monitor. Study patients monitored their prothrombin time 2153 times during a mean interval of 44·7 months compared with 1608 measurements in the 20 matched controls over 42·5 months. Study

patients had therapeutic prothrombin times 88·6% of the time compared with 68·0% in the control group. There were no significant differences in complication rates between the groups.

An Italian study (Cosmi *et al*, 2000) recruited 78 patients on stable oral anticoagulation therapy (warfarin and acenocoumarol) from four centres. This was a self-testing rather than self-management trial. Patients were enrolled on a volunteer basis after passing an abbreviated mental test and providing consent. A total of 78 controls were selected, matched for age, gender and therapeutic range. After three instruction sessions on the use of the coagulometer (Coaguchek) subjects measured their INR at home and communicated the result to a central office and suggested dose adjustment and date for next test. However, they were requested to follow the prescription made by the central office. The dose suggested by subjects was equal to or within ±6% of the mean weekly dose in over 80% of cases. Both subjects and controls achieved 80% time within therapeutic range.

Anderson *et al* (1993) reported on 40 patients receiving long-term warfarin therapy who were willing to undertake self-monitoring. The selection process and training were not well described. The coagulometer used was a Biotrak (Ciba Corning, Mountain View, CA, USA). Patients were followed up for 6–24 months and showed good therapeutic control although the outcomes stated were principally related to agreement between patient-measured INR and contemporaneous laboratory-measured INR.

Barnado (1995) reported on 216 (out of 600) patients who had been trained in self-monitoring between 1986 and 1992 using the Coaguchek device. The training programme consisted of three, 1-h sessions with a nurse to learn how to use the coagulometer with an additional 5 h of theoretical training with a physician. Eligibility criteria were: the ability to participate in a patient-orientated programme (not defined); adequate eyesight (not defined); adequate motor co-ordination (not defined); and sufficient manual dexterity to comply with all aspects of the self-management programme (not defined). Prothrombin time determinations of 83·1% were within target range with no major bleeding or thrombotic episodes reported. One major weakness of this study is the poor level of follow-up with only 216 of 600 patients reported.

In Canada, Massicotte *et al* (1995) reported on 23 children who undertook home testing using a Biotrak with testing performed by their parents. This was essentially a feasibility study but showed that of 599 home measurements, 63% were within the therapeutic range. This was stated to be similar to patients managed in a clinic but the original data were not given. The average duration of follow-up was 13 months. One subdural haematoma and one catheter-related thrombotic event were reported.

It can be concluded that, while self-testing and -management appear credible alternatives to existing models of care, there are currently few data from the UK to support its use (Fitzmaurice *et al*, 2002; Gardiner *et al*, 2004). There are no reliable clinical outcome data in any of the published studies to support its use either. Evidence is required from the UK trials regarding both clinical and cost-effectiveness before it can be widely promoted within the UK. Standard care within several studies was poor in comparison with the previously published UK data (Fitzmaurice *et al*, 1996; Rose, 1996). Consequently, improvement in therapeutic control and associated reductions in serious adverse events associated with self-management will be exaggerated in comparison with the UK models of care. Until robust UK data were available from randomised controlled trials of patients deemed eligible for self-management allocated to either an intervention or a standard care group, caution must be applied in allowing patients to undertake patient self-management. In addition, none of these studies apparently considered whether the patient should regularly employ some form of external quality control to test the reliability of their INR results.

3. Costs

The cost effectiveness of patient self-management needs further investigation. One USA study which investigated cost was identified (Anderson *et al*, 1993). The cost of home monitoring was approximately half that of routine care over an 8-week period with costs based only on cost of monitor and test cartridges against hospital laboratory tests. Other costs, such as transport for the patient and clinic overheads, were not included. The authors stated that if improved control reduced the risk of thromboembolic or haemorrhagic complications the cost savings associated with home monitoring would be substantial.

One German study demonstrated a 50% reduction in costs associated with self-management compared with routine care (Taborski *et al*, 1999). However, routine care comprised physician office attendance with poor control and high rates of complications, which were included in the analysis.

No cost-effectiveness data have been published from the UK perspective, comparison with both hospital clinic attendance and primary care based management must be considered.

4. Training for self-management

In Germany it is estimated that around 400 000 patients currently manage their own anticoagulation and there is a nationally approved, formalised training programme for anticoagulation. As such it is similar in concept to the National Asthma Training centre in the UK, which provides training for health professionals who then disseminate this training to patients (Bisley, 1997).

The Association of Self Management of Anticoagulation (ASA) has established a series of training centres across Germany. The association organises seminars to train the trainers, namely the doctors and nurses establishing home monitoring with their patients, and also to train patients. For the trainers, the content of these courses covers: theoretical and pharmaceutical aspects of anticoagulation; a training outline demonstrating the equipment to be used by the patients; and a

practical session using the POC testing systems. The patient programme comprises: (i) theoretical aspects of anticoagulation management; (ii) indications for anticoagulation, how to monitor the blood; (iii) frequency of coagulation monitoring; (iv) problems with monitoring; (v) interaction between anticoagulants and other medications; (vi) influences of nutrition, alcohol, intercurrent illness and travel; (vii) recording of test results; (viii) recognising and treating complications; (ix) overlapping heparin therapy; (x) vaccinations; and (xi) endocarditis prophylaxis. The practical session includes: (i) operating the coagulation monitor; (ii) practising a coagulation test; (iii)practising an internal quality control (IQC) test; (iv) correct fingerstick procedure; (v) possible sources of error; (vi) recording test results.

Currently in the UK there are no formal training programmes for patients and it is clear that standardisation of training is a pressing requirement. Recent UK studies have trained more than 300 patients in self-management using a programme adapted from the ASA training. This programme was found to be sufficient for the majority of patients (Fitzmaurice *et al*, 2002; Murray *et al*, 2004). The programme involved two training sessions a week apart undertaken by a nurse experienced in anticoagulation management.

The aims of the training were to ensure theoretical understanding of oral anticoagulation and INR monitoring; that patients (or carers) were able to measure INR reliably using a near patient testing system and were able to interpret the INR in terms of appropriate warfarin dose. Session 1 (2 h) was a group session for up to six people. At session 2, patients were assessed individually for competence in undertaking PSM in terms of: accurately performing an INR test using the near-patient testing system; quality control issues, dosing algorithm and dosage adjustment, and documenting INR results and adverse events. Some patients required a third training session to ensure competence, particularly in dosage adjustment. Patients were given a training video and the facility to practice using the near-patient testing system at home between training sessions, which was valuable in increasing the level of competency. There are now regular 'train the trainers' courses for nurses to train patients and this will hopefully lead to standardisation of training.

5. Implications for patient self-monitoring of oral anticoagulation in the UK

Although there is evidence from outside the UK to suggest that patient self-management is a valuable model of care for long-term anticoagulation management, in terms of reliability, convenience and reduced risks, further multicentre randomised trials within the UK are required. This is particularly true given the apparent poor therapeutic control found within other healthcare systems where physician office testing remains routine practice and anticoagulation hospital clinics are not as well established or widespread as they are in the UK.

6. Quality assurance

Whilst quality assurance is deemed essential for hospital laboratories and primary care clinics undertaking INR measurements, the whole issue of both internal and external quality control for patients measuring their own INR does not seem to have been addressed. Massicotte *et al* (1995) included data on the comparative results obtained using POC testing and laboratory technology but did not address the issue of quality assurance. Therefore, the following discussion is based on level IV evidence only.

Quality assurance of POC monitors is required to ensure that results are reliable. For POC determinations made by health care professionals, guidelines recommend both IQC testing and also external quality assessment (EQA) (Medical Devices Agency, 2002, The National Committee for Clinical Laboratory Standards (NCCLS, 2004). Electronic quality control is available for some POC devices. With these monitors an electronic device is inserted in place of a test strip and the signal produced tests the optical/electronic systems and mimics the analysis of a genuine blood sample. Where available, electronic IQC should be used each time the monitor is used, but does not constitute sufficient IQC alone.

Where available, manufacturers liquid control material that involves analysis with a test strip should be used. One of the acceptance criteria for patients to self-test (or self-manage) should be the ability to analyse IQC material successfully. The frequency of IQC testing required to ensure effective anticoagulant control by patients self-testing with POC devices has no evidence base but we previously recommended that IQC is tested in the following situations: (i) when introducing a new batch/lot number of test strips; (ii) when commencing use of newly delivered test strips (even when they are the same lot number as used previously); (iii) if there is any doubt about the storage conditions of test strips; (iv) if an unexpectedly high or low result occurs; (v) at least once per month. Monthly testing may be impractical and adds expense for patients, and we have revised this recommendation between 1 and 3 months.

The IQC material should have a mean/target INR in the range 2·0–4·0 and for any particular batch/lot of IQC samples the range of INR results obtained on different occasions should not vary by more than ±0·5 INR units (e.g. target/mean INR 3·0, acceptable limits 2·5–3·5). A wider target range, such as those for some commercial IQC materials that have allowed variability of ±1·0 INR units, should not be considered acceptable.

If the INR result of an IQC lies outside the target a second IQC sample should be tested. If the second result is also out of range then patient testing must be suspended until the cause has been identified and the problem rectified.

Some devices have inbuilt IQC within the test strips. This alone may not be acceptable as the sole means of IQC, particularly where the result of the IQC analysis is not displayed as INR. Where possible, a liquid control should be used for IQC for these particular monitors as described above.

Some form of external assessment of INRs determined with POC monitors is recommended (Medical Devices Agency, 2002). This should involve an accredited EQA programme such as the UK National External Quality Assessment Scheme (NEQAS) (Kitchen *et al*, 2005). For health care professionals EQA has been successful using proficiency testing with plasma samples similar to that available for conventional laboratory INR testing (Tripodi *et al*, 2004). In the UK NEQAS programme, results from users of the same type of monitor are grouped together and any individual result within 15% of the median result (above or below) is considered to be within consensus. Pilot data have confirmed that patients capable of self-managing oral anticoagulation can also successfully participate in this type of programme, involving freeze-dried plasma samples despatched through the post every 3–4 months (Murray *et al*, 2003) Patients were able to perform such EQA tests competently, obtaining similar results to those obtained by healthcare professionals who had analysed the same test samples. A UK NEQAS programme specifically for patient selftesting is now available. If a patient has results that are persistently outwith the consensus the clinician with overall responsibity for managing the patients anticoagulation is informed. If problems remain unresolved, the monitor and test strips should be assessed by the training centre where possible, or if not by the manufacturer. Patient self-testing should be suspended when such persistent problems are unresolved.

There are at least two other alternative methods for EQA of patient self-testers. One option is for the patient to be assessed in a centre that participates satisfactorily in an accredited EQA programme, such as NEQAS. In this case the patient should test their blood on their monitor and the monitor in the clinic and INR results >2·0 should be within 0·5 INR units of each other.

Another approach to EQA for POC INR results is to collect a venous sample at the same time as the POC test, which is then analysed in an appropriate hospital laboratory. This approach was used by Tripodi *et al* (2004). This could be carried out every 6–12 months for stabilised patients. INR results of stabilised patients should be within 0·5 of each other. There are difficulties with this approach because the quality of hospital laboratory INR results may vary (Kitchen *et al*, 1994). If this approach is used it should be noted that INRs of over-anticoagulated patients vary according to the technique used for measurement, and even for stabilised patients within the therapeutic range, an INR deviation of ±10% between methods has been considered acceptable for clinical purposes (Kitchen & Preston, 1996). When an INR result between 4·5 and 8·0 is obtained with a POC device this should be repeated with the same technique to ensure that the prolonged result is not a consequence of poor sample quality. The second result should be within 0·5 of the first. If a result of >8·0 occurs, a venous sample should be sent to a hospital laboratory for testing.

One striking feature of all the papers reviewed is the high frequency of testing encouraged by the self-management model. Testing is recommended between every 3 and 7 d, with increased frequency of testing should control deteriorate. This level of testing would be extremely costly and it is not clear why this frequency of testing is required. In comparison, stable patients in the clinic setting may only be tested at 10- to 13-week intervals.

Cost is obviously an extremely important element to the patient self-management model. The German and US health systems are insurance-company led. Insurers appear convinced of the therapeutic effectiveness of this model and are willing to fund it once individual competence has been established. This is due, in part, to the improved therapeutic control found with patient self-management compared with standard care in these countries. It is not clear whether this level of improvement, i.e. sufficient to reduce major adverse events, is possible in the UK. If it is not, then the increased capital costs associated with individual coagulometers, increased frequency of testing and the cost of training would need to be offset against the reduced costs because of reduced patient contact with health professionals. Some test strips are currently available on the drug tariff in the UK although patients still have to meet the capital cost of buying the coagulometer. It is not clear how self-testing or -management will be re-imbursed within the new General Medical Services Contract for General Practitioners (GMS), which, in its present form does not mention these forms of management (http://www.dh.gov.uk).

7. Summary statement

Using levels of evidence as defined in the British Society for Haematology guidelines (British Society for Haematology, British Committee for Standards in Haematology Haemostasis and Thrombosis Task Force, 1998, Table III) the following section summarises the evidence described above.

- There is grade A (level Ib) evidence of the effectiveness of patient self-management.
- There is grade C (level IV) evidence of the effectiveness of patient self-testing.
- Only patients with long-term (>1 year) indications for warfarin therapy should be considered for self-testing or -management.
- There is no additional evidence to guide the selection of patients or the intensity of the training and support (including quality control testing) for patients being offered self-testing or -management.
- There is grade B (level II) evidence of the cost-effectiveness of self-management within the US and German healthcare systems. This is founded on improved therapeutic control compared with routine care, however the routine care results are poor compared with the reported UK clinical data. No published evidence exists of cost-effectiveness within the UK healthcare system.
- No data are provided regarding the nature of patient interpretation of the INR and no formal dosing algorithms have been published.

Table III. Levels of evidence.

Recommendations	
Grade A (evidence levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
Grade B (evidence levels IIa, IIb, III)	Requires availability of well-conducted clinical studies but no randomised controlled trials on the topic of recommendation
Grade C (evidence level IV)	Requires evidence from expert committee re ports or opinions and/or clinical experience of respected authorities: indicates absence of directly applicable studies of good quality
Level of evidence	
Ia	Meta-analysis of randomised controlled trials
Ib	At least one randomised controlled trial
Iia	At least one well-designed study without rand-omisation
Iib	At least one well-designed quasi-experimental study
III	Well-designed non-experimental descriptive studies
IV	Expert committee reports or opinions and/or clinical experience of respected authorities

8. Implications for patient self-monitoring of oral anticoagulation in the UK

Although there is evidence from outside the UK to suggest that patient self-management is a valuable model of care for long-term anticoagulation management, in terms of reliability, convenience and reduced risks, further multi-centre randomised trials within the UK are required. This is particularly true given the apparent poor therapeutic control found within other healthcare systems where physician office testing remains routine practice and anticoagulation hospital clinics are not as well established or widespread as they are in the UK.

At this time there is no system of payment in the UK for purchasing monitors although some test strips are now available on prescription in a similar way to glucose monitor strips.

9. Guidelines for patient self-testing or -management of oral anticoagulation

Given the relative lack of evidence, the following recommendations are necessarily consensual (evidence level C).

1. Only patients with long-term indications for warfarin therapy should be considered for self-testing or -management. In exceptional circumstances, patients with short-term indications (e.g. first deep vein thrombosis) may be considered for self-testing, however, it should be noted that it can take 2–3 months before a patient becomes fully accustomed to this method of therapy management.
2. Only conformite europeen-marked devices that have undergone acceptable evaluations by an expert, independant body (e.g. the MHRA in the UK) subject to external peer-review, are to be used for self-testing. Discussions should be held with the local haematologist (where appropriate) and with the Trust POC committee before initiating patient self-testing. Local guidelines and procurement rules should also be checked.
3. Patients (or patient carers) must give informed consent to undertake patient self-management. This will include agreement to attend clinic regularly and to record results accurately.
4. Competence to perform an INR must be assessed by a trained healthcare professional prior to allowing home testing.
5. Competence to correctly interpret an INR result must be assessed by a healthcare professional prior to allowing self-management. This must be based on an individualised patient algorithm (Table IV).
6. Previous stability of INR is not a prerequisite to home testing as unstable patients may benefit from increased autonomy and the possibility of increased frequency of testing.
7. Patients considered for self-testing or -management must have a documented INR target in line with accepted guidelines and clinical practice.
8. Contraindications for patient self-testing or -management will include previous non-compliance, in terms of either attendance at clinic or taking of medication.
9. Patients undertaking self-testing or -management must retain contact with a named clinician. This will, in most

Table IV. An example of a hypothetical individual patient algorithm.

Name (Betty Smith)	Indication for warfarin (atrial fibrillation)	Therapeutic range (2–3)	Current warfarin dose (3 mg)
Date (1 November 2004)			
INR result		Next test due (weeks)	
	Warfarin dose (mg)		
<1		Contact health	
	–	professional	
1–1·5		1	
	4		
1·5–2		1	
	3·5		
2–3		2	
	3		
3–4		1	
	2·5		
4–5		1	
	2		
>5		Contact health	
	Stop warfarin	professional	

cases, be a consultant haematologist who will be clinically responsible. In all cases the patient's GP and the clinician who initiated the warfarin therapy must be informed.

10. Patients undertaking self-management must be reviewed at least every 6 months by the responsible clinician.
11. Electronic QC where available should be used each time the monitor is used.
12. The IQC material should be analysed when introducing a new batch/lot number of test strips or when commencing use of newly delivered test strips (even when they are the same lot number as used previously).
13. The IQC material should be re-tested if an unexpectedly high or low result occurs.
14. The IQC should be tested every 1 and 3 monthly, or with each test if the interval between testing exceeds 12 weeks.
15. Patients who are self-testing should participate in at least one form of EQA, i.e. one of a, b or c below. If a patient has persistent problems the monitor should be assessed in a centre that participates satisfactorily in a formal EQA programme and patient self-testing should be suspended if persistent problems are unresolved. This is the case whichever option is employed.
    (a) Patients may participate in a formal EQA programme, such as UK NEQAS, Common External Quality Assessment System (CEQAS) or other accredited programme.
    (b) The patients' monitor may be assessed in a centre that participates satisfactorily in an accredited EQA programme, such as NEQAS. In this case, the patient should test their own blood on their own monitor/test strips and the monitor/test strips routinely used in the clinic; the INR results should be within 0·5 INR units of each other.
    (c) A venous sample may be collected at the same time as the POC test and sent to an appropriate hospital laboratory far analysis. This could be carried out every 6 months for stabilised patients. In this case, INR results are acceptable if within 0·5 INR units of each other.
16. Any INR result between 4·0 and 8·0 should be repeated with the POC device to ensure that the prolonged result is not a consequence of poor sample quality. Repeat analysis should be within 0·5.
17. If an INR of >8·0 or sample error is obtained, a venous sample should be collected and analysed in an appropriate hospital laboratory.

Funding

The creation of these guidelines was unfunded. DF is funded by a National Primary Care Career Scientist award.

Conflict of interests

DF has received funding from Roche Diagnostics to attend research symposia.

Expiry date April 2008

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