A randomised controlled trial of patient self management of oral anticoagulation treatment compared with primary care management

D A Fitzmaurice, E T Murray, K M Gee, T F Allan, F D R Hobbs

Background: The increase in numbers of patients receiving warfarin treatment has led to the development of alternative models of service delivery for oral anticoagulant monitoring. Patient self management for oral anticoagulation is a model new to the UK. This randomised trial was the first to compare routine primary care management of oral anticoagulation with patient self management. 

Aim: To test whether patient self management is as safe, in terms of clinical effectiveness, as primary care management within the UK, as assessed by therapeutic international normalised ratio (INR) control.

Method: Patients receiving warfarin from six general practices who satisfied study entry criteria were eligible to enter the study. Eligible patients were randomised to either intervention (patient self management) or control (routine primary care management) for six months. The intervention comprised two training sessions of one to two hours duration. Patients were allowed to undertake patient self management on successful completion of training. INR testing was undertaken using a CoaguChek device and regular internal/external quality control tests were performed. Patients were advised to perform INR tests every two weeks, or weekly if a dose adjustment was made. Dosage adjustment was undertaken using a simple dosing algorithm.

Results: Seventy eight of 206 (38%) patients were eligible for inclusion and, of these, 35 (45%) declined involvement or withdrew from the study. Altogether, 23 intervention and 26 control patients entered the study. There were no significant differences in INR control (per cent time in range: intervention, 74%; control, 77%). There were no serious adverse events in the intervention group, with one fatal retroperitoneal haemorrhage in the control group. Costs of patient self management were significantly greater than for routine care (£90 v £425/patient/year).

Conclusion: These are the first UK data to demonstrate that patient self management is as safe as primary care management for a selected population. Further studies are needed to elucidate whether this model of care is suitable for a larger population.
patient attitude towards patient self management, and quality of life issues.

METHODS
Six general practices in the West Midlands using the Birmingham model of anticoagulation management were recruited for our study. Before the original near patient testing and computerised decision support software trial, those practices had not been involved in anticoagulation monitoring and were typical of service practice. Clinics were nurse led and used a Coaguchek near patient testing device (Roche Diagnostics Lewes, Sussex, UK) for INR measurement and computerised decision support software (BAP-PC; University of Birmingham) for the interpretation of the results.

All patients attending the clinic, over the age of 18, receiving long term anticoagulation treatment for a period of at least six months, with sufficient vision and manual dexterity to operate a Coaguchek near patient testing system, and with satisfactory INR control, defined as achieving INR within 0.5 of the target value for at least 60% of the time in the previous 12 months, were identified. From this list, the practice nurse was asked to select patients who would be capable of performing patient self management, following the criteria of previous treatment adherence, physical well being, anxiety, cognitive ability, visual acuity, and ability to follow simple instructions. These selected patients were invited to an informal talk about the study and asked to give written consent. Patients who consented to participate in the study were randomly allocated using computer generated coding into either intervention (patient self management) or control (routine clinic management).

Intervention group (patient self management)
Those in the self management group of patients were required to attend a training course involving two workshops of one to two hours, one week apart. Workshops, based within individual practices, were organised by research staff and attended by practice staff. Sessions covered theoretical and practical aspects of anticoagulation management, including the procedure for performing a blood test using the near patient testing device, quality control procedures, and managing the INR result using a specified algorithm (fig 1).

After the first training session, patients were given a near patient testing device and test strips to practice blood tests at home. They were asked to record at least six results and highlight any problems. At the second session they were given a series of clinical vignettes to assess their understanding of INR management. Patients were individually assessed by the research team and if it was felt that they were competent to carry out self management, sufficient test strips and quality control vials were provided for home use.

For a six month period, patients were required to perform an INR test every two weeks or after one week following dosage adjustment. Batch numbers and expiry dates of test strips and quality control vials distributed to patients were recorded centrally. Daytime access to medical advice was provided via a pager and patients were instructed that the dosing algorithm could be overridden only after consultation with the research team. Support was also available from their practice nurse and general practitioner, and a record kept describing all contacts made by the patients. Self management patients were provided with a clinical report form (CRF) to record INR measurement. Practice nurses entered data on INR, warfarin dose, number of test strips used and any adverse events on to the CRF at each visit.

Control group
Control patients were managed as before in routine practice clinics using the Coaguchek near patient testing device for INR measurement. Practice nurses entered data on INR, warfarin dose, number of test strips used, and any adverse events on to the CRF at each visit.

Collection of patients' responses to self management
At study conclusion, a random sample of patients (eight patient self management and eight control) were given a semistructured interview covering relevant themes generated from a series of focus groups, which involved professionals involved in anticoagulation management. Material was pooled from a previously validated questionnaire regarding warfarin treatment were also used, in addition to the SEIQoL tool for quality of life estimation. Interviews were audiotaped and transcribed. Content analysis of the questionnaires was used to draw out common themes and valid comment.

<table>
<thead>
<tr>
<th>INR result</th>
<th>Warfarin dose</th>
<th>Next test due</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.1</td>
<td>Contact nurse</td>
<td></td>
</tr>
<tr>
<td>1.1–1.9</td>
<td>Increase by ... mg</td>
<td>1 week</td>
</tr>
<tr>
<td>2–3</td>
<td>Same dose</td>
<td>2 weeks</td>
</tr>
<tr>
<td>3.1–3.9</td>
<td>Decrease by ... mg</td>
<td>1 week</td>
</tr>
<tr>
<td>&gt;4</td>
<td>Contact nurse</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current warfarin dose</th>
<th>Change of dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 mg</td>
<td>↑/↓ 0.5 mg</td>
</tr>
<tr>
<td>3–6 mg</td>
<td>↑/↓ 1.0 mg</td>
</tr>
<tr>
<td>6–9 mg</td>
<td>↑/↓ 1.5 mg</td>
</tr>
<tr>
<td>9 mg or over</td>
<td>↑/↓ 2.0 mg</td>
</tr>
</tbody>
</table>

Figure 1 Patient algorithm.
Table 1 Resource items and unit costs

<table>
<thead>
<tr>
<th>Resource item</th>
<th>Cost (£)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow up attendance at anticoagulation clinic</td>
<td>8.84</td>
<td>Parry et al24</td>
</tr>
<tr>
<td>Intervention group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test strip (for each strip)</td>
<td>2.30</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>Advice by practice nurse (for each 15 minute consultation)</td>
<td>5.75</td>
<td>Netten25</td>
</tr>
<tr>
<td>Internal quality control (for each assessment)</td>
<td>2.30</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>External quality control (for each assessment)</td>
<td>30.00</td>
<td>NEQAS</td>
</tr>
<tr>
<td>Training session (for each patient)*</td>
<td>6.00</td>
<td>Parry et al24</td>
</tr>
<tr>
<td>Room hire</td>
<td>20.00</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>Staff time</td>
<td>23.00</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>Quality control</td>
<td>1.46</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>Equipment (per machine)</td>
<td>400.00</td>
<td>Manufacturer</td>
</tr>
</tbody>
</table>

*Assuming 5 patients for each training session.
NEQAS, National External Quality Assessment Scheme.

Data analysis
Data were collated on to an SPSS database for analysis. Townsend scores of home addresses were compared. Individual statistical tests included McNemar's test for dependent proportions, $\chi^2$, and log linear modelling.

Cost data were collected over the six month follow up period on a per patient basis, allowing the estimation of health service costs for each study patient. The data focused on key resource use items where variation by trial arm was hypothesised a priori. These items, along with the unit costs used in this analysis, are listed in table 1. The mean cost each year for each group (control versus intervention) was compared using standard parametric methods ($t$ test), given that the cost distributions were not highly skewed.

RESULTS
Two hundred and six of a total of 298 (70%) patients attending the anticoagulation clinics at six study practices fulfilled preliminary requirements for study entry. One hundred and twenty eight of 206 (62%) were considered inappropriate for patient self management by practice nurses, and 22 of 78 (28%) of the remaining patients refused to enter the study. Reasons for exclusion included; problems with manual dexterity (13%), anxiety (12%), lack of cognitive ability (8%), non-compliance (6%), physically unwell (8%), or too elderly for patient self management (12%). Fifty six of 206 (27%) patients entered the study (26 controls, 30 patient self management). Seven patients randomised to patient self management were not included for analysis: three did not attend the training sessions, one failed the assessment, and three dropped out within the first month of the study (two because of a loss of confidence and one because of problems with manual dexterity). Therefore, 23 patients randomised to the patient self management group were included in the trial analysis.

There were no significant differences in mean age (patient self management, 63 years; controls, 69 years) or Townsend scores between the two groups. A larger proportion of men than women took part in the study (37 men, 12 women). Twenty one of the 23 participants were white and 17 of 23 were retired.

Clinical indications for warfarin treatment were similar between the two groups, with most patients receiving warfarin for atrial fibrillation (27 of 49).

INR control and adverse events
There was no significant difference in prestudy (six months) INR percentage time in range (66% patient self management versus 76% controls). There were no significant differences between the two groups in the percentage time in range (74% patient self management versus 77% controls) or the proportion of tests in range (66% patient self management versus 72% controls) for the study period (table 2), and no significant change between prestudy and study data for either group.

There were seven self reported minor adverse events (two breathlessness, two unexplained bruising, one haematuria, and one menorrhagia) and no serious events in the intervention group. There was one serious adverse event in the control group, a fatal retroperitoneal haemorrhage. There were no recorded minor adverse events in the control group. Control patient data were abstracted from clinical records, whereas intervention patients were asked directly at follow up regarding adverse events. The need for telephone support was minimal.

External quality assurance
The EQA results from the study participants were compared with the results from 75 health care professionals using the CoaguChek near patient testing device. There were no significant differences in median INRs between the patients and the professionals (table 3).

INR, international normalised ratio.

Table 2 International normalised ratio results

<table>
<thead>
<tr>
<th></th>
<th>Percentage time in range (95% CI)</th>
<th>Percentage of tests in range (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self management (n=23)</td>
<td>74 (67–81)</td>
<td>66 (61–71)</td>
</tr>
<tr>
<td>Control (n=26)</td>
<td>77 (67–86)</td>
<td>72 (65–80)</td>
</tr>
</tbody>
</table>

CI, confidence interval.

Table 3 National External Quality Assessment Scheme results

<table>
<thead>
<tr>
<th></th>
<th>Sample 1 Median INRs</th>
<th>Sample 2 Median INRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n=23)</td>
<td>3.6, 3.8, 3.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Professionals (n=75)</td>
<td>3.4</td>
<td>2.8</td>
</tr>
</tbody>
</table>

INR, international normalised ratio.
weeks for the control group. Sixty one of 336 (18%) of INR tests performed by the patients in the self management group during the study period were outside protocol criteria. The reasons given for extra tests were: concurrent antibiotic treatment, tooth extraction, and working abroad.

The mean cost each year for patients in the intervention arm was £425 compared with £90 for patients in the control arm (p < 0.001). Intervention costs were based on capital costs (spread over five years at a rate on interest of 6%) and running costs of the equipment, quality control, training, and support from the practice. Control costs were based on average cost for each patient attending a primary care clinic. These costs included capital costs of equipment, training of the general practitioner and practice nurse (spread over five years at a rate on interest of 6%), running costs to include time spent by practice nurse in running the clinic, general practitioner support, test strips, and service charge for room usage (table 4).

Indirect costs to the patient were not included.

**Table 4** Total cost for each patient calculated for each year

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>23</td>
<td>26</td>
</tr>
<tr>
<td>Mean</td>
<td>425.23*</td>
<td>89.71*</td>
</tr>
<tr>
<td>SD</td>
<td>52.65</td>
<td>38.58</td>
</tr>
<tr>
<td>Median</td>
<td>413.53</td>
<td>88.40</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>388.23–459.53</td>
<td>53.04–123.76</td>
</tr>
<tr>
<td>Range</td>
<td>342.23–563.03</td>
<td>17.68–141.44</td>
</tr>
</tbody>
</table>

*p<0.001, t test.

For our study, patients successfully performed EQA on four separate occasions and these results will contribute to the debate concerning patients’ ability to manage EQA.14 IQC is considered by some to be an adequate performance test for the reliability of the result, but although it is a useful test to assess day to day precision it could be argued that the target range is unacceptably wide. In addition, if EQA is deemed essential for hospital and primary care clinics undertaking INR measurement, the same conditions must apply to patient self management, although this has not been referred to in previous patient self management studies.

In conclusion, patient self management is in an embryonic phase in the UK, and these are the first data to suggest that it is as clinically effective as routine care, in this case primary care management of oral anticoagulation. Evidently patient self management is more costly than practice based management as a result of increased use of the near patient testing device, test strips, quality assurance, and training. Some of these excess costs may not prove necessary. Nevertheless, if patient self management costs are confirmed as higher than routine care they could only be recouped within the National Health Service. However, on current evidence, a more conventional approach to the management of patients receiving anticoagulation is by far the cheapest option.

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Before consideration can be given to widespread adoption of this model further UK research is needed. This will need to deal with issues around the nature of training, the definition of patient eligibility, the frequency of testing, and costs. Although cost effectiveness appears unlikely considering these preliminary data, patient self management has been
shown to be safe and effective for the minority of patients who might select it.

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Authors’ affiliations

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REFERENCES

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