

## Self management of oral anticoagulation: randomised trial

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### Abstract

**Objective** To determine the clinical effectiveness of self management compared with routine care in patients on long term oral anticoagulants.

**Design** Multicentre open randomised controlled trial.

**Setting** Midlands region of the UK.

**Participants** 617 patients aged over 18 and receiving warfarin randomised to intervention (n = 337) and routine care (n = 280) from 2470 invited; 193/337 (57%) completed the 12 month intervention.

**Intervention** Intervention patients used a point of care device to measure international normalised ratio twice a week and a simple dosing chart to interpret their dose of warfarin.

**Main outcome measure** Percentage of time spent within the therapeutic range of international normalised ratio.

**Results** No significant differences were found in percentage of time in the therapeutic range between self management and routine care (70% v 68%). Self managed patients with poor control before the study showed an improvement in control that was not seen in the routine care group. Nine patients (2.8/100 patient years) had serious adverse events in the self managed group, compared with seven (2.7/100 patient years) in the routine care arm ( $\chi^2(df=1)=0.02, P=0.89$ ).

**Conclusion** With appropriate training, self management is safe and reliable for a sizeable proportion of patients receiving oral anticoagulation treatment. It may improve the time spent within the therapeutic range for patients with initially poor control.

**Trial registration** ISRCTN 19313375.

### Introduction

Around 950 000 people in the United Kingdom take warfarin,<sup>1-3</sup> and the service load for monitoring anticoagulation is predicted to increase by a factor of five over the next decade.<sup>4</sup> The international normalised ratio (INR) measures the level of the anticoagulation induced clotting defect,<sup>5</sup> and point of care devices have been shown to be reliable for estimating INR.<sup>6</sup> Small observational and randomised studies suggest that point of care testing is an appropriate way to enable self management of oral anticoagulation by patients.<sup>7-9</sup> However, these studies are small and in select populations, and more data from large scale

randomised controlled trials are needed.<sup>10-12</sup> This paper reports clinical outcomes of the first UK, and the largest worldwide, study of self management of oral anticoagulation.

### Methods

We identified patients from primary care centres within the UK Midlands Research Consortium (MidReC). Centres covered rural and suburban areas with a socioeconomic range of patients. Eligible patients were aged 18 or over, with a long term (greater than 12 months) indication for oral anticoagulation,<sup>13</sup> who had taken warfarin for at least six months with a target INR of 2.5 or 3.5. We randomly allocated consenting patients to intervention or routine care. We asked intervention patients to attend two nurse led training sessions<sup>14</sup> covering the theory of anticoagulation, the INR, INR targets, how to measure and interpret INR, how to adjust dose, and quality control. After the training, patients considered capable of self management were given home testing equipment (CoaguChek S, Roche Diagnostics). Intervention patients managed their own anticoagulation for 12 months, testing INR every two weeks. They adjusted dosage by using a dosing schedule based on a traffic light system (see [bmj.com](http://bmj.com)). Patients were instructed to do internal quality control tests if they got an unusual INR result, and were reviewed every three months to assess progress. Routine care patients continued attending either hospital or practice based anticoagulant clinics.

The primary outcome measure was therapeutic INR control determined by the percentage of time spent within the therapeutic range.<sup>15</sup> We collected adverse event data from general practice records. We defined serious adverse events as those needing treatment or medical evaluation.

### Analysis plan

We did analyses by intention to treat (all patients randomised to intervention group), on treatment (patients actually receiving intervention), and off treatment (intervention data from patients who discontinued the intervention early). We compared patients'

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**Table 1** Percentage of time (95% confidence interval) within therapeutic range for international normalised ratio and number of patient years

Patient group	Pre-study	Study	Change	Patient years
Intervention total (n=337)	68 (64.3 to 70.7)	70 (68.1 to 72.4)	2.50 (-0.64 to 5.65)	318
Routine care (n=280)	69 (65.2 to 72.1)	68 (65.2 to 70.6)	-0.69 (-4.35 to 2.96)	264
On treatment (n=242)	69 (65.2 to 72.6)	72 (69.5 to 73.7)	2.29 (-1.26 to 5.85)	214
On-treatment dropouts (n=34)	61 (51.3 to 70.9)	61 (53.2 to 68.7)	-0.13 (-10.4 to 10.2)	17

quantitative results between the pre-study and study periods and made comparisons between the intervention and routine patients.

## Results

In all, 2530 patients from 49 practices were eligible. Only 60 (2%) patients were excluded by their general practitioner, leaving 2470 patients invited to participate, of whom 1888 (76%) responded; 1156 declined to participate, and 732 agreed to attend an information session. Of those who initially agreed to attend the information session, 115 (16%) were excluded or failed to attend and 617 (84%) gave written informed consent and were randomised to the intervention or routine care arm of the study (337 intervention, 280 routine care). Of all patients invited to take part, 617/2470 (25%) were recruited. Significantly more men than women were randomised into the study (400 (65%) male *v* 217 (35%) female,  $P < 0.001$ ). Routine care patients were older than intervention patients (66 *v* 64,  $P = 0.015$ ).

Clinical indications for warfarin in rank order were atrial fibrillation, mechanical prosthetic heart valves, recurrent pulmonary embolism or deep vein thrombosis, cardiomyopathy, and transient ischaemic attack or stroke. We found no significant differences between intervention and routine care in terms of coronary risk factors.

Of 337 patients randomised to intervention, 242 (72%) attended and successfully completed training and 193 (80%) completed the intervention (see [bmj.com](http://bmj.com)). Of the 280 patients randomised to routine care, 250 (89%) completed 12 months.

## Adverse events

### Intention to treat analysis

We had 582.1 patient years of follow-up for the intention to treat analysis. The overall incidence of serious adverse events was 2.8/100 patient years (16 events), comprising 2.8/100 patient years (nine events) in the intervention arm and 2.7/100 patient years (seven events) in routine care ( $\chi^2(df=1) = 0.02$ ,  $P = 0.89$ ). The overall rate of serious bleeding was 1.5/100 patient years (1.6 intervention *v* 1.5 routine care). The overall rate of serious thrombosis was 1.2/100 patient years (1.3 *v* 1.1).

### Intervention: on-treatment analysis

We had 214 patient years of follow-up for the on-treatment analysis. The incidence of serious adverse events was 1.8/100 patient years (four events). The incidence of bleeding episodes was 0.45/100 patient years, and the incidence of thrombotic events was 1.4/100 patient years.

### Intervention: off-treatment analysis

We had 103 patient years of follow-up for the off-treatment analysis. The incidence of serious adverse events was 4.83/100 patient years (five events). The incidence of bleeding episodes was 3.86/100 patient years. The incidence of thrombotic events was 0.97/100 patient years.

## Therapeutic INR control

In the intention to treat analysis, we found no significant differences in mean percentage of time within the therapeutic range for INR between pre-study and study periods in either the intervention arm ( $t_{320} = 1.57$ ,  $P = 0.12$ ) or the routine care arm ( $t_{255} = -0.37$ ,  $P = 0.71$ ) (table 1). INR control based on mean percentage of time within the therapeutic range during the study did not differ significantly between the intervention and routine care groups (70% *v* 68%;  $t_{575} = 1.35$ ,  $P = 0.18$ ).

In the intention to treat patients, we found a significant difference in the percentage of time within the therapeutic range for INR in pre-study and study periods between patients with therapeutic targets of 2.5 and 3.5 in both groups. Intervention group: pre-study 74% versus 45% ( $t_{319} = 7.46$ ,  $P < 0.001$ ); study 74% versus 55% ( $t_{319} = 7.48$ ,  $P < 0.001$ ). Routine care: pre-study 72% versus 52% ( $t_{254} = 3.70$ ,  $P < 0.001$ ); study 71% versus 53% ( $t_{254} = 4.70$ ,  $P < 0.001$ ).

In the intervention group patients with a target of 3.5, a significant improvement occurred between pre-study and study (45% *v* 55%;  $t_{65} = 2.77$ ,  $P = 0.007$ ). No significant difference occurred in intervention group patients with a target of 2.5 (73% *v* 74%;  $t_{254} = 0.29$ ,  $P = 0.77$ ) or the routine care patients with either a target of 2.5 (72% *v* 71%;  $t_{217} = -0.44$ ,  $P = 0.66$ ) or a target of 3.5 (52% *v* 53%;  $t_{37} = 0.07$ ,  $P = 0.94$ ) (table 2).

If we examine the distributions of percentage of time in range by centiles, patients in the intervention group who were poorly controlled at baseline (defined as time in range below the median) showed a significant increase from pre-study to study, whereas those in the routine care group did not. The magnitude of this improvement was approximately 20% (95% confidence interval 9% to 32%) for the 3.5 target group and around 15% (6% to 24%) for the 2.5 target group. In the routine care group a change of 3-5% occurred in both 2.5 and 3.5 target groups.

**Table 2** Percentage of time (95% confidence interval) within therapeutic range for international normalised ratio, by therapeutic target

Patient group	Pre-study	Study	Change	P value
Intervention, target 2.5 (n=255)	74 (70.7 to 77.2)	74 (72.3 to 76.6)	0.51 (-2.94 to 3.96)	0.77
Intervention, target 3.5 (n=66)	45 (37.3 to 51.7)	55 (50.0 to 60.0)	10.21 (2.84 to 17.59)	0.007
Routine care, target 2.5 (n=218)	72 (68.0 to 75.3)	71 (67.8 to 73.7)	-0.88 (-4.78 to 3.02)	0.66
Routine care, target 3.5 (n=38)	52 (42.2 to 62.1)	53 (45.3 to 60.0)	0.38 (-10.35 to 11.11)	0.94

## Discussion

This study is the largest to evaluate the clinical effectiveness of patient self management of oral anticoagulation compared with routine care. Study recruitment was non-selective; the comparator provided good control of INR, both enhancing generalisability and reflecting real life. Overall, only 25% of eligible patients were randomised. A recent smaller Dutch study had a similar recruitment rate,<sup>16</sup> although a Spanish study recruited nearly 50% of eligible patients.<sup>17</sup>

Of those patients who were randomised to self management most (72%) were able to complete training, and 78% of those who started self management were able to complete 12 months. Self management is therefore a feasible model of care for an appreciable proportion of patients.

We found no overall significant differences between the study arms for the primary outcome measure. Therapeutic INR control was good in both arms; both groups spent around 70% of time within their therapeutic range, which is comparable to the Dutch study (68.6% in the self management group) and significantly better than the Spanish group (58.6%).<sup>16, 17</sup> Examining the change from pre-study to study for self managed patients for those with targets of 2.5 and 3.5 revealed that those with poorer control improved from pre-study to study. The improvement was approximately 15% in the 2.5 target group and 20% in the 3.5 target group. This was not the case in the routine care group. Self management is thus effective and safe and may even represent the model of choice for patients who are poorly controlled in routine care. The therapeutic control and adverse event rates compared favourably with previously published data.<sup>3</sup>

### Limitations

The study was limited by the parameters set for self management. Patients were asked to do an INR test every two weeks, with weekly testing after a dose change. Although this makes comparison with routine care problematic, it reflects the reality of the current models of service provision. A few patients had difficulty attending the three month clinical review sessions.

That only 25% of patients agreed to participate probably reflects reluctance to participate in a trial and a high level of satisfaction with current services rather than a reluctance to self manage. A quarter of patients did not complete training, and a further fifth withdrew prematurely, suggesting that barriers to self management exist. The findings warrant further research before self monitoring is commissioned more widely in the UK, as demand from patients may be limited.

### Conclusions

For an appreciable number of motivated patients on oral anticoagulation, self management is a safe and realisable alternative to existing models of care. This model is particularly effective for treating patients with poor INR control, who are a difficult population to manage and are at risk of adverse events. Now that self management for anticoagulation has been shown to be as safe and effective as routine care, it would be valid to test whether this reassurance alters patients' and health

## What is already known on this topic

Self management for oral anticoagulation has been shown to be effective in highly selected populations within healthcare environments not comparable to the UK

## What this study adds

Self management for oral anticoagulation is safe and effective for a sizeable minority of patients receiving warfarin

For patients who have been appropriately trained, self management is as clinically effective as routine care provided by UK oral anticoagulation clinics

Fewer patients than anticipated wished to self manage their oral anticoagulation

professionals' equipoise in accepting self management in this context.

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