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Assessing the utility of an online registry for patients monitoring their own warfarin therapy

Short title: Self report registry for PSM of warfarin

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Abstract

Objective: To evaluate the utility of an online self-report registry for patient self monitoring and management (PSM) of warfarin therapy.

Methods: A prospective observational study of UK based patients undertaking PSM and recording their INR data via an online registry. Consenting participants recorded INR test dates, results and warfarin dosages using the online registry for a period of 12 months. Participants reported demographic data, disease characteristics and treatment-related adverse events and provided feedback via a survey. Data accuracy was assessed through comparison of INR results recorded online with results stored on 19 INR testing devices. Percentage time spent within therapeutic range (TTR) was also examined.

Results: Eight seven percent (39/45) completed the study period. Age ranged from 26-83 years, 44% had undertaken PSM for >5 years. Sixty six percent (25/38) reported that the registry was easy to navigate and use. Forty two participants contributed a total of 1669 INR results. Agreement between self-reported INR results and source INR data was high (99%). Mean therapeutic time in range (TTR) was 76% (SD 18.58) with 83% having >60% TTR.

Conclusion: Findings suggest that an online PSM registry is feasible, accurate and acceptable to patients. These findings require confirmation in a larger cohort of PSM patients. An online self report registry could provide a valuable resource for gathering real world evidence of clinical effectiveness and safety of these developing models of care.

Key words: Oral anticoagulation, Warfarin, Self-monitoring, Patient registry, self-reporting.

Introduction

Patient self monitoring and self management of oral anticoagulation therapy with vitamin K antagonists (mainly warfarin in the UK) involve the patient being responsible for testing their International Normalised Ratio (INR) using a finger prick, blood sample and a point of care (POC) coagulometer device ¹. Patients self managing their warfarin therapy interpret their INR test result themselves and adjust their warfarin dose and test frequency accordingly. In the patient self monitoring model, the patient contacts a health professional for advice on warfarin dose and INR test frequency.

The clinical effectiveness of patient self monitoring and self management of oral anticoagulation has been demonstrated in a number of controlled trials ²⁻⁴. A systematic review and meta-analysis demonstrated that self monitoring and self management are associated with a significant one-third reduction in major haemorrhage and self management with a significant reduction in death ⁵. Current NICE guidelines related to the use two point of care coagulometers for self-monitoring of anticoagulation state that self-monitoring and self-management are likely to be clinically effective and that self management is highly cost effective whereas self monitoring is not ⁶.

Whilst there is a large body of trial evidence supporting patient self monitoring and management of warfarin therapy, little is known, about the effectiveness and safety of these models of care outside trial conditions apart from small follow up studies ^{7;8}. The findings of the follow up studies are limited as patient populations are highly selected and as such unrepresentative of the wider population undertaking self monitoring or management. A recent Cochrane review of self-monitoring and management compared to standard management acknowledged a lack of generalisability of trial findings and suggested that large population-based observational studies are required to confirm the safety and effectiveness of these models of care in routine clinical practice ⁹.

In the UK, it is estimated that around 1-2% of the 1.2 million patients receiving warfarin therapy are undertaking self monitoring or self management of warfarin therapy ¹⁰. Of concern is the difficulty with systematically collecting data related to the utility of this model of care to reflect typical self management practices and patient characteristics, as patients undertaking self management keep their own records and do not necessarily fully engage with oral anticoagulation services.

One approach to overcoming this problem would be through a registry which offers the opportunity to gather data to better reflect real world practices and outcomes. Registries have previously been utilised for population based epidemiological research as they typically involve larger, more diverse populations than trials ^{11;12}.

Online registries have been successfully developed to track patient satisfaction with chronic medication and to report upon real-world side effects of medications ¹³. Also self-reported data from internet based patient communities have been developed for planning and developing effective research proposals ^{14;15}. Substantial patient benefits have been shown in other studies utilising the internet to deliver education and interventions for self care of chronic disease and for electronic symptom reporting clearly demonstrating the potential of the internet to improve patient outcomes ¹⁶⁻¹⁸. Internet based, direct-to-patient systems which utilise a combination of decision support software and expert supervision have been shown to facilitate patient self monitoring of warfarin therapy and improve INR control. ¹⁹⁻²²

Therefore an online patient self-report registry would offer a practical way to capture data related to self- monitoring/management and further extend the clinical effectiveness and safety evidence base for these models of care. The usefulness of such a registry depends upon the quality of the data recorded. It is unclear, whether patients would be willing and able to contribute data using an online registry.

The aim of the current study was therefore to evaluate the utility of an online self-report register for patients self managing their oral anticoagulation and explore patient outcome data.

Methods

Study design

A prospective observational study of patients undertaking self- management of oral anticoagulation therapy and recording their INR data via an online registry was conducted between December 2010– December 2011. Ethical review and approval for the study was provided by the institutions ethical review board.

Recruitment and eligibility

Participants were recruited via advertisement i) in an electronic newsletter, ii) a quarterly magazine, iii) on two websites and iv) at a conference. Individuals managing their warfarin therapy, aged >18 years with internet access were eligible to participate. The study information sheet was available via the online registry or from the research team. Those wishing to participate completed a consent form and registered their name and contact details using the online registry.

Collection of data

Consenting participants were asked to record INR test dates, results and warfarin dosages using the online registry for a 12 month period. Participants also recorded demographic data, disease characteristics; methods used for quality control and dosing and treatment related bleeding or thrombotic events. To reduce missing data, weekly data checks were undertaken to identify missing INR results and generate reminder emails. Participants providing their email contact details were invited to complete a survey to ascertain their opinions and experience of using the online registry and suggestions of how the registry could be improved. Participants continued to receive dosing advice and clinical supervision as previously arranged with their direct care team. The online register was used for reporting of data only. No advice on dosage adjustment and frequency of testing was provided via the online registry. The research team and the participants had access to the registry data. The participants' clinical supervisors and direct care team were not provided with access to the registry.

Structure and content of the online registry

The design and development of the online self-report registry was informed by patients, health professionals and review of websites designed for by older people.²³ The registry home page contained links to study information and demonstrations of how to provide consent and data. The data collection forms each comprised i) a header; describing the type of data to be recorded ii) a bookmark; detailing the current question to be answered and iii) a map; detailing how many more questions were to be answered. Guides to aid interpretation of questions were provided.

Data analysis

The quality of the self-reported data was evaluated through comparison of the INR test results and dates recorded online with the results and dates downloaded directly from the POC devices of 19 randomly selected participants. These data were also used to determine therapeutic INR control defined by percentage time spent within therapeutic range for each participant (TTR). TTR was calculated using the Rosendaal equation which assumes a linear change between INR test results²⁴. The paired t test was used to compare TTR derived from the INR data stored on the POC device with TTR calculated from the INR data recorded online.

Patient reported treatment related bleeding or thrombotic events were categorized as serious and non serious adverse event. Serious adverse bleeding events were defined as clinically overt bleeding associated with hospitalization; a blood transfusion; or a fatal outcome. Non serious adverse bleeding events were defines as overt bleeding associated with medical intervention, unscheduled contact (visit or telephone call) with a physician, or associated with discomfort for the subject such as pain or impairment of activities of daily life. A diagnosis of deep vein thrombosis, pulmonary embolism or stroke constituted serious thrombotic events.

Results

The online consent form was completed by 45 patients. Thirteen percent (6/45) did not contribute all study data points or complete the 12 month study period (figure 1). One participant used the register to record data related to age and gender only. Two participants used the register to record demographic data, indication for and duration of warfarin therapy and model of care utilised however, did not record INR data. Three participants discontinued using the online register after recording; demographic data, indication for and duration of warfarin therapy, model of care utilised and INR data for a period of 3 months. A total of 39/45 (87%) completed the 12 month study period and provided all study data points.

Sixty nine percent (31/45) were male (table 1). Age ranged from 26 to 83 years with 29/45 (64%) 60 years or more. The main indications for warfarin were; mechanical heart valve 21/44 (48%), atrial fibrillation 11/44 (25%) and pulmonary embolism 5/44 (11%). The length of time participants had been taking warfarin ranged from less than 12 months 1/44 (2%) to more than 5 years 24/44 (55%). In terms of model of care utilised, 25/44 (57%) of the cohort were self managing their warfarin therapy and 19/44 (43%) were self monitoring their INR.

Therapeutic time in range and adverse events

Forty two of the forty five (93%) participants recorded 1669 INR results and contributed 36.9 patient years of data. The mean frequency of INR testing was 16 days (range 3-92 days). The mean TTR of the cohort was 76% (SD 18.58), TTR ranged from 22-100% with 83% spending more than 60% time in range (the standard recommended by the British Society for Haematology)²⁵. A total of 58 adverse events were reported by 17/ 42 (40%) participants. Four were categorised as serious adverse events (11.5 per 100 patient years) and included one post-operative bleed, one suspected pulmonary embolism, one suspected deep vein thrombosis and one transient ischemic attack.

Quality control results

The methods of external quality assurance (EQA) used by the cohort varied, 17/44 (38.6%) compared INR results obtained on two POC devices (their own device and a clinic owned device) using simultaneous capillary blood samples. Ten (22.7%) compared the INR result obtained using a capillary blood sample and their POC device with the INR result obtained by the hospital laboratory using a venous blood sample. Eight (18.2%) reported that they had used both methods of EQA and 9/44 (20.5%) stated that they had not used any method of EQA.

Administration of the online registry

Two hundred and fifty one telephone helpline queries were logged. Sixteen percent of calls were received during the initial three months from 17/42 (40%) participants requiring help using the online registry to record their data. Overall, 25/42 (60%) did not use the helpline.

Data quality

A total of 926 INR test results and dates were downloaded from 19 POC devices. Of these 118/926, (13%) were not recorded online. (Figure 2) The paired t test showed no significant differences in individual participants online TTR compared with the TTR derived from INR results stored on the

POC device (p=0.999). 805/808 (99.6%) of the INR results reported online were accurately recorded.

Participant evaluation

Participant surveys were returned by 38/44 (86%), of which 37/44 (84%) were fully completed. Eighty nine percent (33/37) reported that they had not experienced any problems accessing the register and 66% (25/38) found the online system easy to navigate and use. Seventy one percent (27/38) stated they would be happy to carry on recording data. Fifty five percent reported that they would like to be able to review their past INR results, 50% to review their previous warfarin doses, 24% would have liked dosing advice and 18% would have liked to access education materials.

Discussion

This paper reports the utility of an online self-report register for patients self managing their oral anticoagulation and explores patient outcome data. The high study completion rate, accuracy of reporting and positive participant feedback observed in this study suggest that internet based data acquisition techniques can be used to enable sharing of patient outcomes data and confirm the feasibility of a longitudinal online PSM registry.

Participants recorded their INR data, warfarin dosage and treatment associated adverse events via an online self-report registry for a period of 12 months. To our knowledge this is the first study to examine the feasibility of an online self- report PSM registry to gather real world data related to the clinical effectiveness and safety of this developing model of care.

In general, participants required very little support when recording their data online and few queries were received via the helpline. In addition, participant feedback indicated that the majority were willing to continue recording their data online.

The online registry allowed recruitment and collection of data from a cohort of patients undertaking PSM across the UK with 87% of those recruited completing the 12 month study period. The cohort comprised a diverse group of patients in terms of age, indication for and duration of warfarin therapy and experience of PSM. More men than women were recruited however; the proportion of male to female participants was similar to that observed in trials of PSM ^{2;7}. All age groups were represented in the current study, although the majority of the population were aged 60 years or more, which reflects PSM trial findings. A reason for this may be that older people typically use the internet for health related activities and anecdotal evidence suggests older people are more likely to self monitor or manage their anticoagulation ⁹. It has been suggested that internet based medical registries are subject to selection bias based upon internet accessibility and use ^{26;27}. Recently published data, however, demonstrate that 83% of households now have access to the internet and 72% of adults in the UK have shopped online ²⁸.

In contrast to trials of PSM, the study population comprised a greater proportion of patients with a mechanical heart valve than with atrial fibrillation ^{2;3;7}. Further research in the real world setting is

required to confirm the characteristics of this patient group. It would be interesting to also include children in further work as they are a group who benefit from PSM in terms of missed school days and are likely to be highly motivated to use an online system.

It was encouraging to see that the data entered was 99% accurate when comparing INR results recorded online with source data obtained from the POC device. Some incomplete data reporting was observed, however, this did not have a statistically significant impact upon overall percentage time spent within therapeutic range (TTR) during the study period. The reminder emails were effective in improving INR data capture. The reasons for incomplete INR data recording were not collected therefore it is difficult to suggest additional strategies to improve reporting of INR data.

Therapeutic INR control varied in the patient cohort. However, in accordance with studies of PSM outside of trial conditions,^{7:8} around 80% of the current PSM cohort was within therapeutic range more than 60% of the time. These findings indicate that PSM can be effective in the real world setting. Due to the small sample size, calculation and comparison of therapeutic control between the groups self managing and self testing was not undertaken.

One concern related to PSM is that INR tests would be undertaken too frequently which may reduce both clinical and cost effectiveness. This study showed an average testing frequency of 16 days, equating to around 23 tests per year which is similar to the number of tests per year for self monitoring reported in the NICE guideline document currently out for consultation²⁹.

The overall incidence of serious adverse events, mainly thrombotic episodes, was higher than that reported in trials of PSM patients receiving long term anticoagulation for any indication² and after mechanical heart valve insertion³⁰. The reasons for this are unclear and need further investigation. A limitation of this study was that verification of self-reported treatment related adverse events with the clinical records was not possible. If an online self-report registry is to be a useful resource, research to evaluate the validity of self-reported warfarin related adverse events and/or strategies to verify patient recorded treatment associated adverse events are required. Further limitations of the current study are the small sample size and relatively short duration of follow-up.

In the current study dosing advice was not provided to participants via the online registry. For those undertaking self testing, specific details of the arrangements for adjustment of dosage were not

captured. Several studies have however shown improvements in therapeutic control in patients that self-test and have direct access to an internet based decision support system or clinical supervisor for dosing advice.^{19;21;22} In a prospective, single-group, before and after study, O' Shea et al demonstrated an increase in therapeutic time in range from 63% in the anticoagulation clinic to 74% during internet-supervision.²¹ Similarly, a subsequent randomized, cross over study, using the same internet based system, reported an improvement in therapeutic control from 59% to 74%.¹⁹ More recently, significant improvements in TTR (66% to 78%) have been observed in older (mean age 70 years) self testing patients using online decision support.²² Although these finding are from selected groups of patients and may not be generalisable to a broader population, it is reasonable to suggest that provision of a decision support system for dosing within an online register may lead to additional patient benefits. The function of the online registry could be further extended to provide training and educational materials and an advice and support forum for patients undertaking PSM including those people traveling abroad who can access the database from anywhere in the world. Furthermore, the online registry offers the option to prospectively collect additional outcomes such as health related quality of life and patient satisfaction. Addition of these features may further encourage patients to firstly, undertake this model of care and secondly, contribute longitudinal PSM data to an online registry.

Conclusions

The results of this study essentially indicate that an online registry for PSM of oral anticoagulation is feasible, acceptable and accurate although a larger cohort of participants is required to confirm these results. Based upon these findings, an online registry for this developing model of care could provide a valuable tool to gather real world clinical effectiveness and safety evidence.

Take home messages

- Clinical efficacy of Patient Self Monitoring (PSM) of warfarin therapy has been demonstrated in trials. The effectiveness of PSM outside of trial condition is however difficult to capture.
- PSM patients are willing and able to contribute their data to an online self report registry.
- A simple online self-report registry could provide an opportunity to gather real world effectiveness and safety data related to PSM of warfarin therapy.

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Disclosure

The authors report no conflict of interest

Authorship

The study was designed by DAF and ETM and funding was secured by DAF. JB undertook management of the study, data collection, data management and all analyses. All authors contributed to data interpretation. DM wrote the first draft of this paper and all authors were responsible for subsequent critical revision of the manuscript. DM is the corresponding author for this paper.

Informed consent and patient details

I confirm all patient/personal identifiers have been removed or disguised so the patient/person(s) described are not identifiable and cannot be identified through the details of the story.

Table 1. Participant characteristics

Age at consent, years (n=45)	n (%)
18-39	3 (7)
40-59	13 (29)
60-79	28 (62)
80 plus	1 (2)
Gender (n=45)	
Male	31 (69)
Female	14 (31)
Condition requiring warfarin (n=44)	
Mechanical Heart Valve	21 (48)
Atrial Fibrillation	11 (25)
Deep Vein Thrombosis (DVT)	4 (9)
Pulmonary Embolism (PE)	5 (11)
Antiphospholipid syndrome (APS)	2 (5)
DVT / PE / APS	1 (2)
Regularly receiving the following medication (n=44)	
Aspirin	4 (9)
Amiodarone	1 (2)
NSAIDS	2 (5)
No	37 (84)
Duration of warfarin, years (n=44)	
<1	1 (2)
1 – 2	4 (9)
2 – 3	6 (14)
3 – 4	8 (18)
4 – 5	1 (2)
>5	24 (55)
Model of care	
Self management [*]	25 (57)
Self monitoring [#]	19 (43)
With dosage adjustment advice provided by a Hospital based oral anticoagulation clinic	13 (68)
Primary care based oral anticoagulation clinic	6 (32)
Duration of self management,[*] years (n=25)	
<1	4 (16)
1 – 2	3 (12)
2 – 3	3 (12)
3 – 4	1 (4)
4 – 5	3 (12)
>5	11 (44)
Duration of self monitoring,[#] years (n=19)	
<1	3 (16)
1 – 2	3 (16)
2 – 3	7 (37)
3 – 4	6 (31)

^{*} Self testing and self dosing, [#] Self testing only

Figure 1. Flow diagram showing how many patients used the online register to record each of the study data points

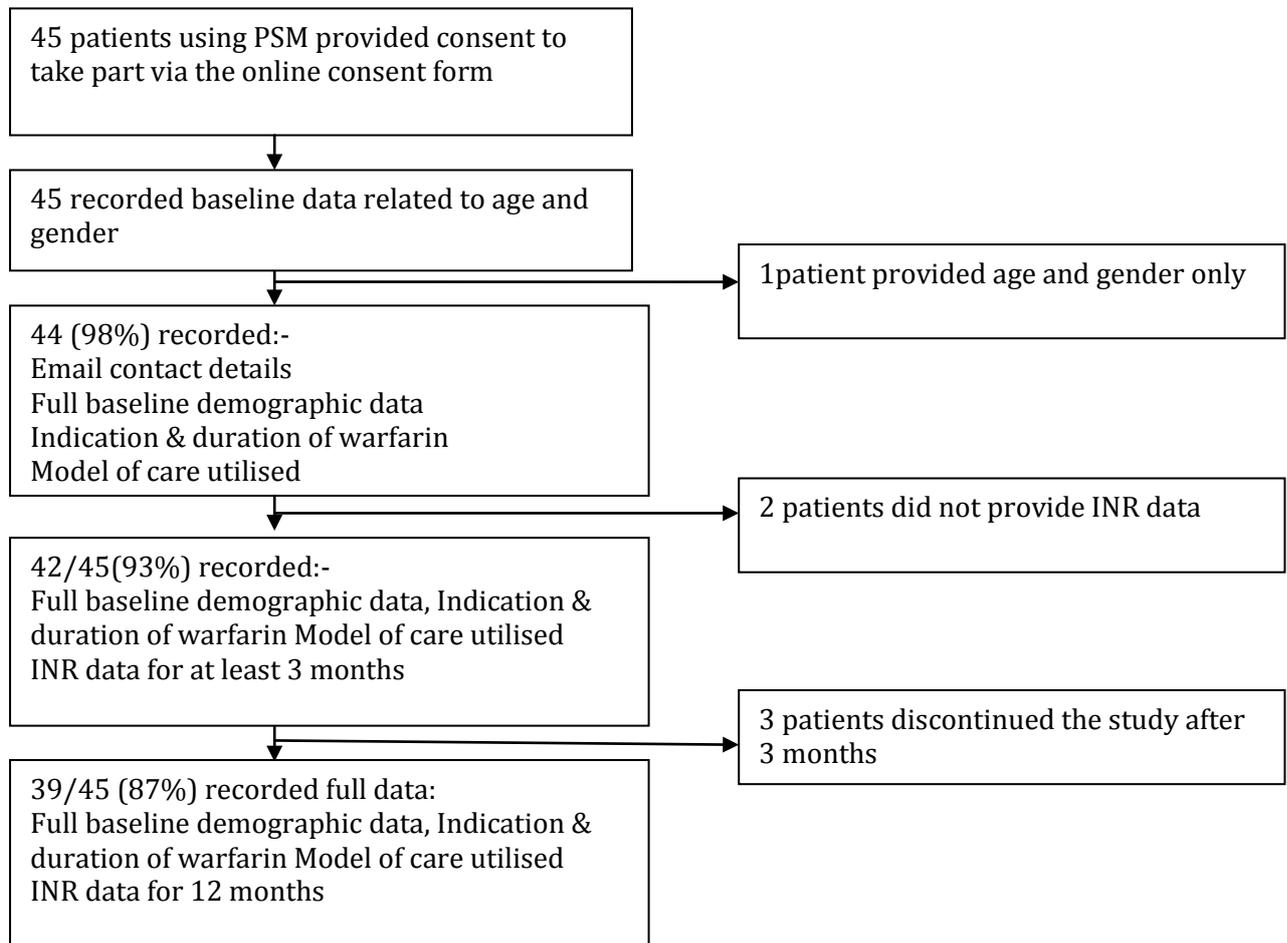
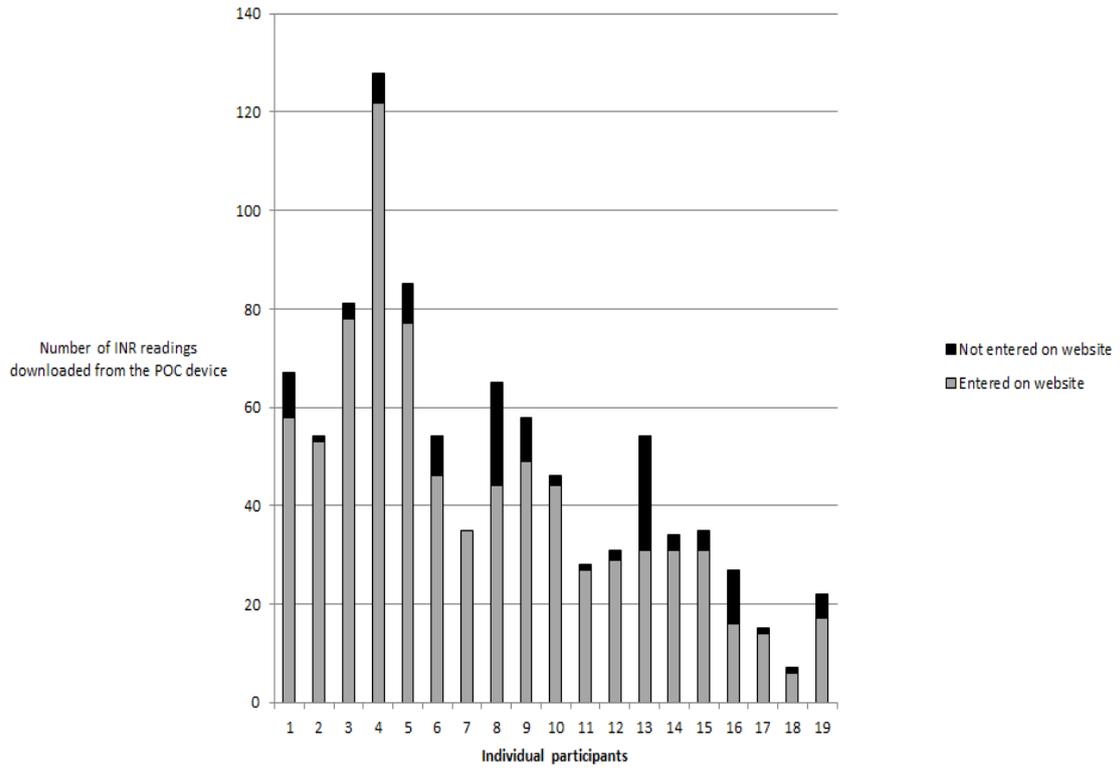


Figure 2. Number of INR test results downloaded from the POC device and reported via the online registry



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