Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation (Review)

Clarkesmith DE, Pattison HM, Lane DA

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TABLE OF CONTENTS

[Intervention Review]

Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation

Danielle E Clarkesmith[1], Helen M Pattison[2], Deirdre A Lane[1]

[1]University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, UK. [2]School of Life and Health Sciences, Aston University, Birmingham, UK

Contact address: Deirdre A Lane, University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Dudley Road, Birmingham, B18 7QH, UK. deirdrelane@nhs.net.

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ABSTRACT

Background

Current guidelines recommend oral anticoagulation therapy for patients with atrial fibrillation who are at moderate-to-high risk of stroke, however anticoagulation control (time in therapeutic range (TTR)) is dependent on many factors. Educational and behavioural interventions may impact on patients' ability to maintain their International Normalised Ratio (INR) control.

Objectives

To evaluate the effects on TTR of educational and behavioural interventions for oral anticoagulation therapy (OAT) in patients with atrial fibrillation (AF).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) in *The Cochrane Library* (2012, Issue 7 of 12), MEDLINE Ovid (1950 to week 4 July 2012), EMBASE Classic + EMBASE Ovid (1947 to Week 31 2012), PsycINFO Ovid (1806 to 2012 week 5 July) on 8 August 2012 and CINAHL Plus with Full Text EBSCO (to August 2012) on 9 August 2012. We applied no language restrictions.

Selection criteria

The primary outcome analysed was TTR. Secondary outcomes included decision conflict (patient's uncertainty in making health-related decisions), percentage of INRs in the therapeutic range, major bleeding, stroke and thromboembolic events, patient knowledge, patient satisfaction, quality of life (QoL), and anxiety.

Data collection and analysis

The two review authors independently extracted data. Where insufficient data were present to conduct a meta-analysis, effect sizes and confidence intervals (CIs) of the included studies were reported. Data were pooled for two outcomes, TTR and decision conflict.

Main results

Eight trials with a total of 1215 AF patients (number of AF participants included in the individual trials ranging from 14 to 434) were included within the review. Studies included education, decision aids, and self-monitoring plus education.

For the primary outcome of TTR, data for the AF participants in two self-monitoring plus education trials were pooled and did not favour self-monitoring plus education or usual care in improving TTR, with a mean difference of 6.31 (95% CI -5.63 to 18.25). For the secondary outcome of decision conflict, data from two decision aid trials favoured usual care over the decision aid in terms of reducing decision conflict, with a mean difference of -0.1 (95% CI -0.2 to -0.02).

Authors' conclusions

This review demonstrated that there is insufficient evidence to draw definitive conclusions regarding the impact of educational or behavioural interventions on TTR in AF patients receiving OAT. Thus, more trials are needed to examine the impact of interventions on anticoagulation control in AF patients and the mechanisms by which they are successful. It is also important to explore the psychological implications for patients suffering from this long-term chronic condition.

PLAIN LANGUAGE SUMMARY

Educational and behavioural interventions to increase the time in the therapeutic range for patients with atrial fibrillation on anticoagulant therapy

Atrial fibrillation is a chronic condition that is characterised by an irregular heart beat. This irregularity of the heart rhythm places people with atrial fibrillation at greater risk of forming blood clots and subsequently increases their risk of stroke. The most common treatment for reducing the risk of stroke is medication with oral drugs that 'thin' the blood, known as oral anticoagulants, to reduce the risk of blood clots forming. People taking warfarin are regularly monitored to assess the time it takes for their blood to clot, known as the International Normalised Ratio (INR), to ensure that the INR is within the target therapeutic range of 2.0 to 3.0. This narrow therapeutic range is often difficult to achieve due to the many factors that can affect INR control such as alcohol intake, other medications, and food intake.

Educational and behavioural interventions may play an important role in improving the ability of people with atrial fibrillation to maintain their INR control, by increasing their knowledge and understanding about warfarin and atrial fibrillation. The objectives of this review were to assess the effects of educational and behavioural interventions for people with atrial fibrillation who were on warfarin to maintain a therapeutic INR range.

Eight studies were finally included within the review. Interventions included patient education, decision aids, and self-monitoring plus education. The primary outcome for the review was the percentage of time the INR was within the therapeutic range. Decision conflict, measuring patients' uncertainty in making health related decisions and factors contributing to that uncertainty, was also a common outcome for decision aid trials. Other outcomes included the percentage of INRs in the therapeutic range, major bleeding, stroke, thromboembolic (clotting) events, knowledge, patient satisfaction, quality of life, and anxiety.

Three self-monitoring plus education trials reported the time in the therapeutic range; the pooled data did not favour either self-monitoring or usual care. Data from two decision aid trials favoured usual care in terms of reducing people's decision conflict surrounding treatment uptake and adherence.

The review authors concluded that more trials are needed to examine the impact of educational and behavioural interventions on anticoagulation control in people with atrial fibrillation. We now have novel oral anticoagulants that do not require monitoring of INR as warfarin does. Education is particularly important to provide safety information and ensure patients are able to make informed decisions about treatment options and to manage their oral anticoagulation therapy. However, more disease-specific theory-driven interventions need to be trialled to understand the mechanisms by which such interventions can be successful.

BACKGROUND

Description of the condition

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice (Fuster 2006). The lifetime risk of developing AF is approximately one in four among people aged 40 years or older (Lloyd-Jones 2007). The incidence and prevalence of AF is rising. One US population-based study (n = 4618) found the age and sex-adjusted incidence of AF per 1000 person-years was 3.04 (95% CI 2.78 to 3.31) in 1980, increasing to 3.68 (95% CI 3.42 to 3.95) in 2000; amounting to a relative increase of 12.6% (Miyasaka 2006). Similar findings in the European Rotterdam Study (n = 6806) found that the overall prevalence of AF was 5.5% to 6.0% in men and 5.1% in women (Heeringa 2006). The prevalence of AF dramatically increases with age, rising from 0.5% at 40 to 50 years of age to 5% to 15% at 80 years (Go 2001; Heeringa 2006; Lloyd-Jones 2004; Miyasaka 2006; Stewart 2001), with the prevalence being slightly higher in men than in women (Lloyd-Jones 2004). AF is associated with a five-fold greater risk of stroke and thromboembolism (Wolf 1991), and the incidence of stroke attributable to AF also increases with age (Lip 2006). When including hospital admissions, treatment costs, and long-term nursing home care, AF accounts for 0.62% of the total UK healthcare expenditure, with a projected cost of 0.88% of the total expenditure in 2000 (Stewart 2004). Given the increasing incidence and prevalence of AF these figures are likely to rise.

Patients with an increased risk of stroke (as determined by stroke risk stratification models) should receive long-term oral anticoagulant therapy (OAT), unless contraindicated. In a meta-analysis, dose-adjusted OAT, within the International Normalized Ratio (INR) range of 2.0 to 3.0, significantly reduced the risk of ischaemic stroke or thromboembolism in patients with non-valvular AF by 39% (95% CI 22% to 52%) and 64% (95% CI 41% to 62%), respectively, compared with both either aspirin or placebo (Hart 2007). Whilst OAT dramatically reduces stroke risk, the therapeutic range of the INR is narrow and must be maintained. This can be problematic, with INRs greater than 3.0 increasing the risk of major and minor bleeding and INRs less than 2.0 increasing the risk of thromboembolism (Lip 2006). Regular INR monitoring is essential and patients need to carefully adhere to dietary and lifestyle restrictions (Ansell 2004). A retrospective analysis of OAT in the UK demonstrated that only patients with the greatest INR control increased their time to stroke occurrence, with only patients spending over 71% of their time in the target therapeutic range (TTR) benefiting (Morgan 2009). In practice, 51% of patients at high risk of stroke ($CHADS_2$ score 2 or more) remained outside of the target therapeutic range for at least 50% of the time (Morgan 2009). Further, a post hoc analysis of patients enrolled in the 'Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events' (ACTIVE), which randomised AF patients with one additional stroke risk factor to receive clopidogrel 75 mg/d plus aspirin (75 to 100 mg/d recommended dose) or OAT, found that patients with a TTR less than 58% gained no benefit from OAT. The INR must be within the therapeutic range for at least 58% of the time to confer benefit in terms of stroke risk reduction (Connolly 2008). Thus, maintenance of INR is a major concern for both AF patients and healthcare professionals. Furthermore, whilst interventions targeting this patient group ultimately aim to reduce the risk of stroke, patients' TTR is a good short-term indicator of whether the patients will experience adverse events in the long-term, thus presenting a useful trial endpoint.

The inherent difficulties associated with warfarin (narrow therapeutic range; drug, alcohol, and food interactions; regular blood tests) have led to the development of novel oral anticoagulant drugs, which have sought to overcome these problems by providing an efficacious and safe alternative treatment that does not require regular monitoring. Several new oral anticoagulant drugs have been tested in clinical trials, some of which have been completed (Connolly 2009; Connolly 2011; Granger 2011; Patel 2011) while others (Ruff 2010) are still ongoing. Whilst the use of novel antithrombotics may shift the focus of interventions for this patient group, it is important investigate ways in which we can improve the outcomes of patients still taking warfarin and whether the principles used for interventions with this group are also relevant for the new oral anticoagulants.

Given that AF is a chronic condition that places patients at increased risk of mortality and morbidity, particularly from stroke, and often requires life-long treatment, including long-term OAT, the educational materials and the support given to patients when they are first prescribed OAT are crucial for the maintenance of their treatment regimens.

Description of the intervention

Attempts to support behaviour change can take numerous forms. At the individual level they almost always fall into the category of 'education or communication' and may use one or more behaviour change techniques (NICE 2007). Patient education for OAT has attempted to influence patient behaviour and improve knowledge, attitudes, and practices that are necessary to improve health outcomes (Wofford 2008). Techniques used in delivering patient education cover a wide spectrum, including the use of booklets and videos as media to transmit additional information either alone or in addition to self-management interventions (such as INR self-monitoring) and interventions which use decision aids (Khan 2004a; Man-Son-Hing 1999). Patient knowledge surrounding OAT varies with age (Tang 2003). Elderly patients (> 75 years) demonstrate poorer knowledge. In one study less than half of one patient sample were able to name even one specific benefit, risk, or lifestyle change associated with warfarin (Coehlo-Dantas 2004). In several cases spouses were more knowledgeable than the patients and appeared to play a vital role in monitoring the indi-

vidual's treatment regime (Coehlo-Dantas 2004). Therefore, educational interventions for this particular patient group may prove to be particularly beneficial.

Other interventions focus on behavioural and practical aspects of lifestyle change and treatment. Behavioural interventions aim to modify patients' behaviour towards treatment and symptoms (NICE 2007). Interventions that use these principles to promote change include cognitive behavioural therapy (CBT), motivational interviewing, and heart rate variability biofeedback. CBT is a goal-oriented, systematic procedure which aims to solve problems concerning dysfunctional emotions, behaviours, and cognitions and to promote positive attitude, self efficacy, and planning. However, with any complex intervention it is difficult to determine which component has influenced the behavioural outcome. Interventions vary in duration and levels of support. Clearly it is important for trials to be explicit about the content and delivery of their interventions and to choose appropriate evaluation tools in order to examine how and why their interventions are successful.

How the intervention might work

Interventions for patients with AF who receive OAT should ultimately aim to improve clinical outcomes, primarily reducing the prevalence of stroke and mortality. However, in the short-term we can aim to increase patients' time in the therapeutic range (TTR) by focusing on factors that affect treatment adherence. Many factors can affect INR control, such as drug-drug interactions and variable dietary vitamin K intake (Holbrook 2005), but with adequate knowledge surrounding treatment and lifestyle factors interventions should aim to encourage behaviour change through education. It has been suggested that several factors influence adherence, and these factors are either intentional or unintentional. Intentional non-adherence can occur when patients make a decision not to take their treatment as a result of their personal motivations or beliefs, or both. Unintentional non-adherence refers to an individual's skills or ability to take his or her medications (for example problems with remembering to take tablets).

Based on the literature surrounding patient adherence, poor INR control could result from both unintentional and intentional non-adherence. Where patients' knowledge of their condition and their OAT is limited, this may impact on their practical ability to manage treatment (unintentional) and their perceptions surrounding treatment necessity (intentional). Several studies have demonstrated that patients have poor knowledge of AF and its treatment (Lane 2006; Lip 2002; Nadar 2003; Tang 2003). There is evidence that patient knowledge correlates significantly with TTR (Tang 2003), with more knowledgable patients having a greater TTR. Thus by improving patient knowledge of factors affecting their TTR and how to manage OAT treatment, patients may be more able to adhere to the treatment regimen. In clinical terms, if education can demonstrate an improvement in TTR, it could have important clinical benefits (that is the reduction of adverse events such as stroke and major bleeding). Decision aids are informative interventions designed to help people make specific choices surrounding their medications, and they may also increase patient knowledge. These interventions aim to reduce decision conflict, which refers to the patient's uncertainty in making health-related decisions and the factors relating to that uncertainty, which may subsequently impact on treatment uptake and adherence.

Intentional non-adherence may be more difficult to target and interventions need to focus on inaccurate perceptions of medications. The common sense model (Leventhal 1992) suggests that patients hold beliefs about the necessity of their prescribed medication (Specific-Necessity) and concerns about prescribed medication based on beliefs about the danger of dependence and long-term toxicity as well as the disruptive effects of the medication (Specific-Concerns). The model also describes general beliefs about medication, assessing beliefs that medicines are addictive and harmful (General-Harm) and that medicines are over-prescribed by doctors (General-Overuse). These beliefs, and the way in which patients balance their concern about medications, have been widely used in predicting medication adherence in a variety of chronic conditions including rheumatoid arthritis (Neame 2005), asthma (Jessop 2003), type II diabetes (Farmer 2006), and depression (Aikens 2005).

A comparison of beliefs about medications between adherent, unintentional non-adherent, and intentionally non-adherent patients found significant differences in medication-related beliefs in patients with a range of chronic illnesses after being newly prescribed medication for the last 10 days (Clifford 2008). Compared with adherers, intentional non-adherers had significantly lower scores on the necessity subscale of the Beliefs about Medication Questionnaire (P value 0.012), higher scores on the concerns subscale (P value 0.008), and lower scores on the necessity-concerns differential (P value 0.001). There were no significant differences between adherers and unintentional non-adherers (Clifford 2008). Evidently, whilst unintentional non-adherers may benefit from memory aids (that is reminders, tablet dosettes), intentional non-adherers may need to address both their perceptions of their medication and misinformation, which may be achieved by increasing patient education surrounding their treatment. Intentional non-adherers appear to doubt their personal need for their medication and have concerns about taking it when compared to adherers. Thus focusing on the necessity of warfarin for stroke risk reduction and alleviating concerns surrounding warfarin treatment may change inaccurate perceptions and potentially lead to increased patient adherence.

Why it is important to do this review

AF is a condition that is increasing in prevalence (Miyasaka 2006) and requires treatment with OAT to reduce associated stroke risk. However, patients on warfarin need to to maintain a narrow therapeutic INR range, which may be difficult to achieve in practice

(Morgan 2009). Patients need sufficient information to make informed choices and actively participate in the management of their own treatment (Thrall 2004). Patient education aims to influence patient behaviour and improve knowledge, attitudes, and practices that are necessary to improve health outcomes (Wofford 2008), but the efficacy of patient interventions designed to improve AF patient adherence to OAT is not clear. By increasing patient knowledge and understanding surrounding AF and OAT we may reduce the prevalence of intentional and unintentional non-adherence, subsequently increasing TTR. TTR is important and has been shown to be a predictor of thromboembolic or haemorrhagic complications, although it is a surrogate for the hard endpoints such as reductions in mortality and stroke that OAT is aimed at achieving. TTR does give an indication as to whether patients are adhering to medication, which should translate into a reduction in stroke and major bleeding events. This review evaluated the value of educational and behavioural interventions for patients with AF who were currently prescribed warfarin, including the impact on TTR and secondary outcomes such as decision conflict, patient knowledge, and quality of life.

OBJECTIVES

To evaluate the effects on TTR of educational and behavioural interventions for oral anticoagulation therapy (OAT) in patients with atrial fibrillation (AF).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of educational or behavioural interventions with any length of follow-up and in any language were included.

Types of participants

Adults (aged 18 years or older) with AF, categorised according to the European Society of Cardiology (ESC) guidelines (ESC 2010), including:

- newly diagnosed AF,
- paroxysmal AF, defined as episodes that usually terminate spontaneously (usually in less than 48 hours), but may last for up to seven days,
- persistent AF, characterised by an episode lasting more than seven days or requiring termination via cardioversion,
- long-standing persistent AF, where AF has been present for > one year (i.e. permanent AF) but where a rhythm control strategy is adopted,
- permanent AF, where AF has been continuous for more than one year and accepted as the 'normal' heart rhythm by the patient and the physician (hence no rhythm control adopted).

AF was diagnosed and documented by electrocardiogram (12-lead or Holter monitoring). Patients that were eligible for, or currently receiving, OAT were considered for inclusion in this review. Studies which included AF patients with other medical conditions were also included in this review. The studies were RCTs comparing at least one intervention with a control group, and including patients with AF as either the study population or a specified subgroup. Studies were only included where patients were grouped per indication, that is for patients taking oral anticoagulants for AF, deep vein thrombosis or pulmonary embolism (DVT or PE), valve replacements etc, only AF patient data were included within the analysis.

Types of interventions

All types of educational and behavioural interventions given to AF patients who were taking OAT were considered for this systematic review. Educational interventions included those that delivered patient information, such as:

- educational booklets;
- videos as media to transmit additional information;
- self-management interventions (such as INR self-monitoring) that also educated patients;
- decision aids;
- talking interventions.

Behavioural interventions included techniques that attempted to modify patients' behaviour towards treatment and symptoms, such as:

- cognitive behavioural therapy (CBT);
- self-monitoring or management interventions that include significant educational components;
- motivational interviewing;
- heart rate variability biofeedback.

Interventions could target adults on the individual level or as a group. The intervention may have taken place in the emergency department, a hospital, the home, or in the community and could have been delivered by a nurse, pharmacist, educator, health or medical practitioner, or a multidisciplinary team associated with the hospital or referred to by the hospital. The intervention could have been undertaken at any time point from diagnosis of AF or initiation of OAT (that is not only newly diagnosed AF patients or those newly referred for anticoagulant therapy). Trials were only considered where the comparison groups were usual care, no intervention, or the intervention in combination with other self-management techniques. Usual care was defined as standard

anticoagulation clinic practice, where patients attended routine INR checks (defined as usual care by the author). Any length of follow-up was included. We have endeavoured to ensure that our review is clearly distinct from the Garcia-Alamino 2010 review. In particular, we have only included self-monitoring interventions where they include a clear and distinct educational component (in addition to training on the use of the self-monitoring device); this should include topics in addition to self-testing, such as risk information, lifestyle changes, and information pertaining to their condition.

Types of outcome measures

Primary outcomes

The primary outcome measure was the percentage of time spent within the therapeutic range (TTR), as defined by Rosendaal and colleagues (Rosendaal 1993) (INR 2.0 to 3.0).

Secondary outcomes

The secondary outcomes were:

- major bleeding (defined as bleeds that result in death, are life threatening, cause chronic sequelae, or consume major healthcare resources) and minor bleeding (Schulman 2004);
- stroke and thromboembolic events;
- increased knowledge with regard to AF and anticoagulation therapy;
- patient satisfaction;
- acceptability of the anticoagulant therapy;
- quality of life; psychological well-being;
- changes in perception towards AF and INR control;
- changes in the patients' illness beliefs and illness representations;
- self-reported adherence to treatment and a change in the patients' beliefs about medications;
- economic costs of the intervention (cost-effectiveness);
- decision conflict*.

*Decision conflict was included as a secondary outcome in the final analysis. Whilst not specified as an outcome of interest in the original protocol, it was highlighted as a common secondary outcome measure in three of the studies included in the final review. For this reason, the authors decided to include these data within the results.

These outcomes were quantified using validated or non-validated questionnaires, ratings, or scales.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) in *The Cochrane Library* (2012, Issue 7 of 12), MEDLINE Ovid (1950 to week 4 July 2012), EMBASE Classic + EMBASE Ovid (1947 to Week 31 2012), PsycINFO Ovid (1806 to week 5 July 2012) on 8 August 2012 and CINAHL Plus with Full TEXT EBSCO (to August 2012) on 9 August 2012. See Appendix 1 for the search strategies.

Searching other resources

Abstract books from national and international cardiology, psychology, and psychiatry conferences were handsearched, to include meetings relating to AF and meetings that discussed the development of educational and behaviour change interventions, including:

- European Society of Cardiology;
- American College of Cardiology;
- American Heart Association;
- Society for Behavioural Medicine and the Division of Health Psychology Conference;
- European Health Psychology Conference;
- Royal College of Psychiatrists Annual Meeting.

Dissertation abstracts (UMI ProQuest Digital Dissertations) were also searched. Reference lists of all relevant papers were searched to identify other potentially relevant articles.

No language restrictions were applied to the searches.

Data collection and analysis

Selection of studies

Two authors (Clarkesmith and Lane) independently scrutinised the titles found from the search and decided on inclusion or exclusion. From the included titles these two authors (Clarkesmith and Lane) then independently selected the abstracts and papers for inclusion and exclusion. We used Cohen's kappa statistic to assess agreement between the two authors on the selection of articles for inclusion. At the first review stage (June 2010), the kappa coefficient was 98.4%. Following the updated search in 2012, the kappa coefficient was 95%. Where disagreements arose the full-text article was accessed to determine whether the study met the inclusion and exclusion criteria. The authors discussed the article and agreement was reached by consensus.

Data extraction and management

Two review authors independently extracted the data. For each trial, the following data were extracted (where available) using a specially designed data extraction form: participants (sample size,

age, sex, ethnicity, marital status, type of AF); type of anticoagulation therapy (warfarin, other); type and duration of the interventions (intervention versus usual care or no intervention, other combinations); primary (TTR) and secondary outcomes (increase in knowledge with regard to AF and anticoagulation therapy, decision conflict, time within the therapeutic INR range, patient satisfaction, acceptability of the anticoagulant therapy, quality of life, changes in perception towards AF and INR control, changes in the patients' illness beliefs and illness representations, changes in the patients' beliefs about medications, self-reported adherence, psychological well-being); length of follow-up; statistical methods employed; the effect size and its precision. Studies were included in this review if they reported any of the primary or secondary outcomes of interest, regardless of whether the original study's primary or secondary outcomes corresponded with the review's primary or secondary outcomes. For example, if a study reported TTR as a secondary outcome the TTR was included in this review but as the primary outcome.

Assessment of risk of bias in included studies

Two review authors independently assessed the methodological quality of each trial in accordance with guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Each study was assessed in several areas of bias (sequence generation, allocation concealment, degree of blinding particularly of the outcome assessors, patient attrition rate, selective reporting bias). The risk of bias was determined using the Cochrane Collaboration's risk of bias tool.

We asked if the domains listed below were considered to be adequate. There were three possible responses: low risk, high risk, or unclear risk. The criteria for responses are outlined below.

Sequence generation

- Low risk, if the allocation sequence was generated using techniques such as a random number table; a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; or cluster randomisation.
- High risk, if the allocation sequence was generated using techniques such as odd or even date of birth; date (or day) of admission; hospital or clinic record number.
- Unclear risk, if there was insufficient information about the sequence generation process to permit judgement.

Allocation concealment

- Low risk, if the allocation concealment used methods such as central allocation (including telephone, web-based, and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered opaque, sealed envelopes.
- High risk, if the participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque, or not sequentially numbered); alternation or rotation; date of birth; case record number.
- Unclear risk, if there was insufficient information to permit judgement of 'Yes' or 'No'. If the method of concealment was not described or not described in sufficient detail to allow a definite judgement (e.g. if the use of assignment envelopes was described but it remained unclear whether envelopes were sequentially numbered, opaque and sealed).

Where the method of allocation was unclear, we contacted study authors to provide further details.

Blinding

- Low risk, if there was no blinding but the review authors judged that the outcome and the outcome measurement were not likely to be influenced by lack of blinding; if blinding of participants and key study personnel was ensured and it was unlikely that the blinding could have been broken; if either participants or some key study personnel were not blinded but outcome assessment was blinded and the non-blinding of others was unlikely to introduce bias.
- High risk, if there was no blinding or incomplete blinding and the outcome or outcome measurement was likely to be influenced by lack of blinding; if blinding of key study participants and personnel was attempted but it was likely that the blinding could have been broken; if either participants or some key study personnel were not blinded and the non-blinding of others was likely to introduce bias.
- Unclear risk, if there was insufficient information to permit judgement of 'Yes' or 'No' or the study did not address this outcome (e.g. where the blinding was described only as double-blind without any other details).

Incomplete data assessment (loss of participants, for example with withdrawals, dropouts, protocol deviations)

- Low risk, if there were no missing outcome data; reasons for missing outcome data were unlikely to be related to the true outcome; missing outcome data were balanced in numbers across intervention groups with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes was not enough to have a clinically relevant impact on observed effect size; missing data were imputed using appropriate methods; for cluster randomised trials, an error

made in statistical analysis when the analysis does not take account of the unit of allocation. In some studies, the unit of allocation is not a person but is instead a group of people. Sometimes the data from these studies are analysed as if people had been allocated individually. Using individuals as the unit of analysis when groups of people are allocated can result in overly narrow confidence intervals. Thus, where included in meta-analysis, it can result in studies receiving more weight than is appropriate and this must be accounted for.

- High risk, if the reasons for missing outcome data were likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk was enough to introduce clinically relevant bias in the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes was enough to introduce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.
- Unclear risk, if there was insufficient reporting of attrition or exclusions to permit judgement of 'Yes' or 'No' (e.g. numbers randomised were not stated, no reasons for missing data were provided); or the study did not address this.

Selective outcome reporting

- Low risk, if the study protocol was available and all of the study's pre-specified (primary and secondary) outcomes that were of interest in the review were reported in the pre-specified way; the study protocol was not available, but it was clear that the published reports included all expected outcomes including those that were pre-specified.
- High risk, if not all of the study's pre-specified primary outcomes were reported; one or more primary outcomes were reported using measurements, analysis methods, or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting was provided, such as an unexpected adverse effect); one or more outcomes of interest in the review were reported incompletely so that they could not be entered in a meta-analysis; the study report failed to include results for a key outcome that would be expected to have been reported for such a study.
- Unclear risk, if there was insufficient information to permit judgement of 'Yes' or 'No'.

Other sources of bias

- Yes, if the study appeared to be free of other sources of bias.
- No, if there was at least one important risk of bias (e.g. the study had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal stopping rule); had extreme baseline imbalance; had been claimed to be fraudulent; had some other problem).
- Unclear, if there was either insufficient information to assess whether an important risk of bias existed or if there was insufficient rationale or evidence that an identified problem would not introduce bias.

Measures of treatment effect

Statistical analyses were undertaken as follows. For continuous variables (for example changes in illness perception questionnaire or changes in TTR), the weighted mean difference was used. As a summary measure of effectiveness, odds ratios with 95% confidence intervals (CIs) were calculated for dichotomous variables.

Dealing with missing data

Where the article indicated inclusion of AF patients, but data was not included by subgroup, we contacted the authors of the included studies to gather AF-specific data. We also contacted authors where there was insufficient detail on the demographic data for AF patients or the content of the intervention. We received responses and additional data from several authors (Beyth 2000; Christensen 2007; Gadisseur 2003; Polek 2012; Thomson 2007). For nine studies the authors could not be contacted (Sawicki 1999; Stone 1989; Watzke 2000) or did not respond to e-mail or written requests for unpublished data (Barcellona 2006; Chan 2006; Gardiner 2006; Menendez-Jandula 2005; Ryan 2009; Siebenhofer 2007). For one study (Machtinger 2007) the author was successfully contacted but the data were unavailable. If authors responded with data that were incomplete they were contacted again for further details.

Assessment of heterogeneity

Assessment of heterogeneity of studies included in the meta-analysis were carried out using the I^2 statistic, to describe the proportion of the variability in the results not due to chance. Whilst there was no significant heterogeneity between the studies included in the meta-analysis, the studies varied substantially in their intervention design and cohort demographics, thus a random-effects statistical model was adopted for the analysis. In addition, the Chi^2 test for heterogeneity was performed and the data were considered heterogenous if the P value was less than 0.10.

Assessment of reporting biases

There were not enough studies in this review to test for reporting bias, thus the findings were discussed as a narrative review. However, future revisions will test for bias using a funnel plot based on

the data for the primary outcome of time spent within therapeutic INR range (TTR). Asymmetry of the funnel plot will be taken as an indication of publication bias. Other causes of asymmetry of the funnel plot will also be looked at, such as clinical heterogeneity between studies (for example different control event rates) or methodological heterogeneity between studies (for example failure to conceal allocation). A summary of who was blinded during both the conduct and analysis of the study was summarised in a narrative review and the conclusions informed the risk of bias tool. The completeness of the data was summarised and any concerns over the exclusion of participants or excessive dropouts were reported. Concerns over the selective reporting of outcomes, time points, or subgroups were also reported.

Data synthesis

Results of individual studies were combined within a narrative review. Where possible and appropriate, meta-analysis was used to statistically combine results. TTR data were included if directly reported using the Rosendaal method (Rosendaal 1993) of calculation or where available from personal communication with the authors. For the analysis we used Review Manager (Version 5.1). For the statistical analysis we calculated mean differences and 95% CIs as the summary statistics. We examined heterogeneity using the Chi^2 and the I^2 statistics (Higgins 2011). We used a random-effects model to calculate a pooled mean difference where significant heterogeneity existed between studies.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses were carried out looking at the type of intervention (educational alone, behavioural alone, and a combination of education and behavioural versus usual care). Future revisions may also examine frequency (one session versus multiple sessions) and duration (less than six months versus more than six months) of the intervention, length of time on OAC, men versus women, individual versus group interventions, and age of participant groups dependant upon the availability of such data in the included study reports.

Sensitivity analysis

There were insufficient studies to carry out sensitivity analyses. However, future revisions of the review may employ sensitivity analyses to examine factors that may lead to differences between the results of individual trials: poor quality versus good quality trials.

RESULTS

Description of studies

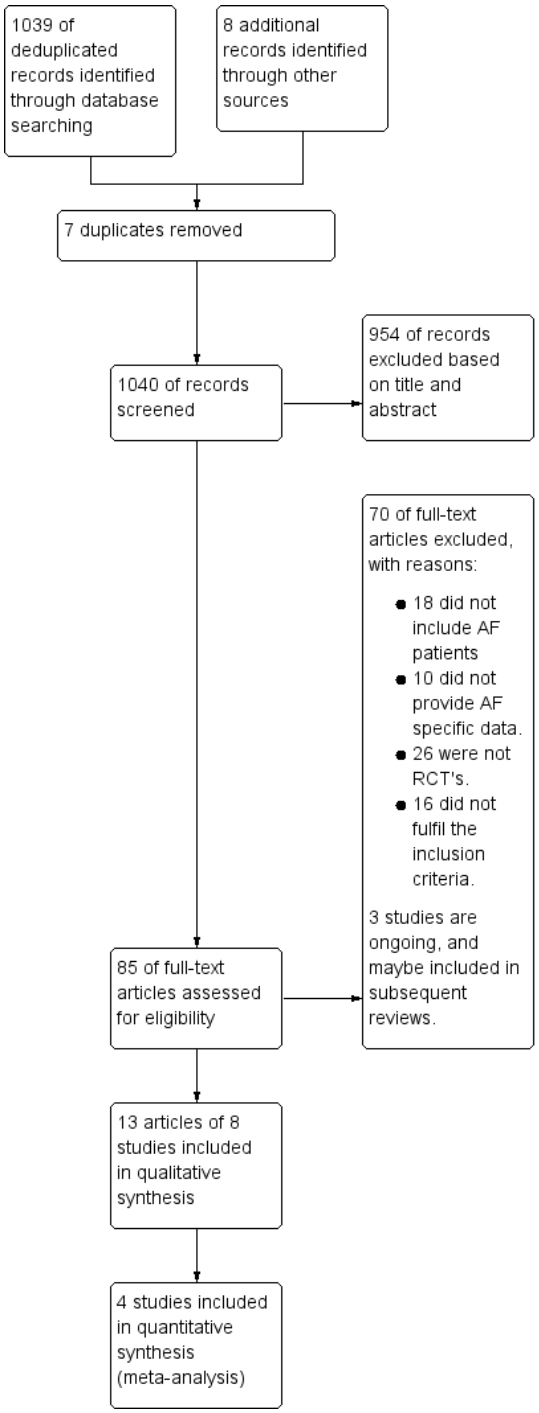
Results of the search

The search retrieved 1040 de-duplicated articles from all sources. Of these, 954 were excluded by assessing the titles and abstracts. We obtained 86 full-text articles for consideration. Seventy articles were excluded based on the review of the full-text article. Three studies were included as ongoing trials. Thirteen articles reporting on eight studies were included in the final review.

Included studies

Thirteen articles reporting on eight studies were included in this review (Beyth 2000; Christensen 2007; Gadisseur 2003; Man-Son-Hing 1999; McAlister 2005; Polek 2012; Thomson 2007; Voller 2005). Features of the interventions are included in the study tables (Characteristics of included studies). See the PRISMA flow chart for the inclusion process (Figure 1).

Figure 1. Study flow diagram.



Methods

All eight included studies were randomised controlled trials. Four of the studies specifically recruited AF patients (Man-Son-Hing 1999; McAlister 2005; Thomson 2007; Voller 2005). A further four 'mixed' trials recruited patients with a range of indications for OAT (for example AF, venous thromboembolism, cardiovascular disease, heart valve prosthesis, peripheral vascular disease, myocardial infarction) and provided unpublished data on the AF patients (Beyth 2000; Christensen 2007; Gadisseur 2003; Polek 2012). One trial was a cluster randomised study (McAlister 2005) and one (Gadisseur 2003) used a Zelen design.

Participants

The total sample size of AF patients, including published and unpublished data, varied from 14 (Polek 2012 unpublished) to 434 (McAlister 2005) participants. The mean age of the trial participants ranged from 59 to 75 years. One trial did not provide any demographic information for their AF patients (Gadisseur 2003). Patients were included if they had AF (McAlister 2005; Thomson 2007; Voller 2005); were receiving intravenous heparin (Beyth 2000); were aged 18 years or over (Christensen 2007; McAlister 2005), 65 years or over (Beyth 2000), 60 years or over (Thomson 2007), 18 to 75 years (Gadisseur 2003); planned to start warfarin (Beyth 2000; Gadisseur 2003; Polek 2012; Thomson 2007); had been taking warfarin (Thomson 2007) for > three months (Gadisseur 2003), > eight months (Christensen 2007); were accessible via telephone (Polek 2012).

Patients were excluded if they had been treated with warfarin at any time in the previous six months (Beyth 2000); were admitted from a nursing home (Beyth 2000; Polek 2012); were enrolled in another clinical trial (Beyth 2000; Voller 2005); were too ill to give consent (Beyth 2000) or did not speak English (Beyth 2000; McAlister 2005; Polek 2012; Thomson 2007); had previously used self-management (Christensen 2007); had antiphospholipid syndrome (Gadisseur 2003), a life threatening illness (Gadisseur 2003), life expectancy $\leq$ one year (Gadisseur 2003; McAlister 2005), cognitive impairment (Gadisseur 2003; McAlister 2005; Polek 2012; Thomson 2007) and physical limitations making successful participation impossible (Gadisseur 2003), poor hearing or eyesight (Voller 2005), a major haemorrhage in a previous trial (Man-Son-Hing 1999); were taking warfarin for another condition (McAlister 2005; Thomson 2007; Voller 2005), scheduled for cardioversion (McAlister 2005; Thomson 2007); had a history of psychotic disorder (Polek 2012), previous stroke or transient ischaemic attack (TIA) (Thomson 2007), or alcohol or other addiction (Voller 2005).

Types of studies

Of the eight studies that were identified, two compared education with usual care (Gadisseur 2003; Polek 2012), four compared self-monitoring plus education with usual care (Beyth 2000; Christensen 2007; Gadisseur 2003; Voller 2005), and one also included a self-management group (Gadisseur 2003). A further three trials focused on the use of a decision support aid versus usual care (Man-Son-Hing 1999; McAlister 2005) or a 'guideline evidence' comparison group (Thomson 2007).

Types of interventions

Interventions were either one to one (Beyth 2000; McAlister 2005; Polek 2012) or group training session(s) (Gadisseur 2003; Voller 2005). Three of the trials did not explicitly specify a group or individual intervention type (Christensen 2007; Man-Son-Hing 1999; Thomson 2007).

All of the interventions included an educational element, usually consisting of a description of the consequences of minor or major stroke and major haemorrhage, the blood monitoring required for warfarin, and the probability of stroke and major haemorrhage for patients taking warfarin. Most interventions also included information regarding the lifestyle factors influencing warfarin control. Self-monitoring interventions included training on the use of INR monitoring devices (Beyth 2000; Christensen 2007; Gadisseur 2003; Voller 2005).

Decision aid interventions offered more detailed information on the risks of bleeding and thromboembolism (Man-Son-Hing 1999; McAlister 2005; Thomson 2007). All three trials using a decision support aid employed pictograms to depict the risk of stroke and bleeding on either placebo, aspirin, or warfarin; two utilised paper-based charts (Man-Son-Hing 1999; McAlister 2005) and the third (Thomson 2007) used a computerised version. The decision aid was presented and patients were asked to select which treatment they would prefer on the basis of the risk information presented in the pictogram (probability trade-off technique). For example, the consequences of a minor stroke, a major stroke, minor and major bleeding were described along with the probability of those events occurring whilst taking different treatment options. This gave patients the opportunity to make informed decisions (Man-Son-Hing 1999); in this trial patients completed a worksheet which summarised the information following the decision aid.

Duration of the intervention

The duration of the educational training element of the interventions varied. Four trials reported a one-off consultation of 30 to

60 minutes (Beyth 2000; Thomson 2007) or three sessions each lasting 60 to 120 minutes (Gadisseur 2003; Voller 2005). The other four trials did not specify how long the intervention lasted or the number of sessions (Christensen 2007; Man-Son-Hing 1999 McAlister 2005; Polek 2012).

Intervention facilitator

Two studies did not specify the type of facilitator (Christensen 2007; Voller 2005). Of those that did, facilitators included a lay educator (Beyth 2000); a physician, pharmacist, or healthcare professional (Gadisseur 2003; McAlister 2005; Polek 2012); and a computerised audio tool (Man-Son-Hing 1999; Thomson 2007).

Country

The geographical settings of the studies were: Denmark (Christensen 2007), Netherlands (Gadisseur 2003), Germany (Voller 2005), USA (Beyth 2000; Man-Son-Hing 1999; Polek 2012), Canada (McAlister 2005), and the UK (Thomson 2007).

Setting for the intervention

Most of the interventions were conducted in a hospital or anticoagulation clinic setting (Beyth 2000; Christensen 2007; Gadisseur 2003; Man-Son-Hing 1999; Polek 2012). One of the trials took place in general physician (GP) practices (McAlister 2005), another in a research clinic with patients from general practices (Thomson 2007). One of the trials did not describe the intervention setting (Voller 2005).

Follow-up

Assessment of the impact of the intervention on outcomes was at three (Polek 2012), six (Beyth 2000; Christensen 2007; Gadisseur 2003; Man-Son-Hing 1999), and 12 months (McAlister 2005; Thomson 2007).

Funding

Three of the trials declared some funding input by drug companies (Gadisseur 2003; Man-Son-Hing 1999; Voller 2005).

Outcome measures

Primary outcome

The percentage of time spent within the therapeutic range (TTR), an INR of 2.0 to 3.0, was reported by three trials (Beyth 2000; Christensen 2007; Gadisseur 2003) as outlined by the Rosendaal method. One trial reported the TTR in days (Voller 2005). Three trials reported other indicators of INR control: percentage of in-range INRs (McAlister 2005; Voller 2005), and combined INR and complications outcomes (Christensen 2007). Of those studies reporting TTR, all tested self-monitoring plus education or education only interventions, but only one published AF-specific data (Voller 2005) and this trial did not use the Rosendaal method. Thus, the remaining trial authors were contacted for AF-specific data, which were provided by two of the authors (Christensen 2007; Gadisseur 2003). AF-specific data were not requested for outcomes that were not comparable, that is combined INR and complications outcomes (Christensen 2007).

Secondary outcomes

One study reported major bleeding, stroke, and thromboembolic events and provided unpublished AF-specific data (Beyth 2000). None of the studies reported on minor bleeding. Four trials reported on patient knowledge (Man-Son-Hing 1999; McAlister 2005; Polek 2012; Thomson 2007). Two trials assessed knowledge before and after the intervention (Man-Son-Hing 1999; Thomson 2007), two only tested after the intervention (McAlister 2005; Polek 2012). Three trials included patient satisfaction as a specified outcome (Gadisseur 2003; Man-Son-Hing 1999; McAlister 2005). However, one trial did not report on this outcome (McAlister 2005), thus the data were not included. One study reported on quality of life (QoL) as an outcome (Gadisseur 2003) using a questionnaire originally validated by Sawicki (Sawicki 1999). Further, one of the trials did not publish AF-specific data (Gadisseur 2003). Three studies reported decision conflict (Man-Son-Hing 1999; McAlister 2005; Thomson 2007), which measures (1) healthcare consumers' uncertainty in making a health-related decision; (2) the factors contributing to the uncertainty; and (3) healthcare consumers' perceived effective decision making. However, one of the studies did not have a usual care arm (Thomson 2007) and therefore was not included in the pooled data analysis. One study reported self-efficacy (Polek 2012) and one other study reported patient anxiety (Thomson 2007). Another study reported mortality (Beyth 2000) but did not specify if death was due to a cardiovascular cause or any cause. One study reported the number of thromboembolic or haemorrhagic complications requiring medical treatment (Voller 2005).

None of the studies reported on:

- patient acceptability of anticoagulant therapy;
- changes in perception towards AF and INR control;
- changes in illness beliefs;
- illness perceptions;
- self-reported adherence to treatment;
- beliefs about the medication;

- economic costs of the intervention.

Excluded studies

See the table 'Characteristics of excluded studies'.
Seventy studies were excluded for the following reasons.
1. Eighteen studies were excluded: four did not provide a breakdown of a mixed indication cohort per indication (McCahon 2011; Nilsson 2011; Vadher 1996; Vadher 1997), 14 studies did not include AF patients (Baker 1991; Bump 1977; Claes 2005; Claes 2006; Cordasco 2009; Cromheecke 2000; Cromheecke 2001; Fitzmaurice 2005; Holbrook 2007; Landefeld 1992; Mazor 2007; Pernod 2008; Waterman 2001).
2. Ten studies were eligible for inclusion but the data were inadequate as AF-specific findings were not presented, and attempts to obtain the specific data from the authors were unsuccessful. For nine of these studies: the authors could not be contacted (Stone 1989; Sawicki 1999; Watzke 2000), or did not respond to e-mail or written requests for unpublished data (Barcellona 2006; Chan 2006; Gardiner 2006; Menendez-Jandula 2005; Ryan 2009; Siebenhofer 2007). For one study (Machtinger 2007) the author was successfully contacted but the data were unavailable.
3. Twenty-six studies were not RCTs (Armstrong 2011; Bajorek 2005; Blaise 2009; Bloomfield 2011; Burns 2009; Castelino 2010; Corbella 2009; Davis 2005; Duran-Parrondo 2011; Fraenkel 2011; Hasan 2011; Krause 2010; Leger 2004; Megden 1999; Nedaz 2002; Polzien 2007; Reverdin 2011; Saokaew 2010; Satger 2009; Sawicki 2003; Taylor 1997; Tuiskula 2011; Winans 2010; Witt 2005; Woodend 2005; Wurster 2006).
4. Sixteen studies did not fulfil our predefined inclusion criteria. Four did not include an educational or behavioural intervention (Field 2010; Fitzmaurice 1996; Fitzmaurice 2000; Gouin-Thibault 2010; Matchar 2005; Trivalle 2010; Waterman 2001 b). Five studies provided education on self-monitoring alone with no additional education on AF and the risks and benefits of OAT (Christensen 2011; Dolor 2010; Grunau 2011; Matchar 2010; Sunderji 2005). None of the studies were excluded for including participants < 18 years of age. Three studies did not report any of the pre-specified outcomes (Batty 2001; Jackson 2004; PRISM Study group 2003). One of the studies did not randomise their usual care group (Khan 2004).
Three studies were eligible for inclusion but are ongoing trials and their results are not yet available (Hua 2011; Smith 2010; Stafford 2011).

Risk of bias in included studies

See the table 'Characteristics of included studies'.
Risk of bias was assessed independently by two review authors (DEC, DAL) in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5 (Higgins 2011). The risk of bias for each of the included studies is summarised in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

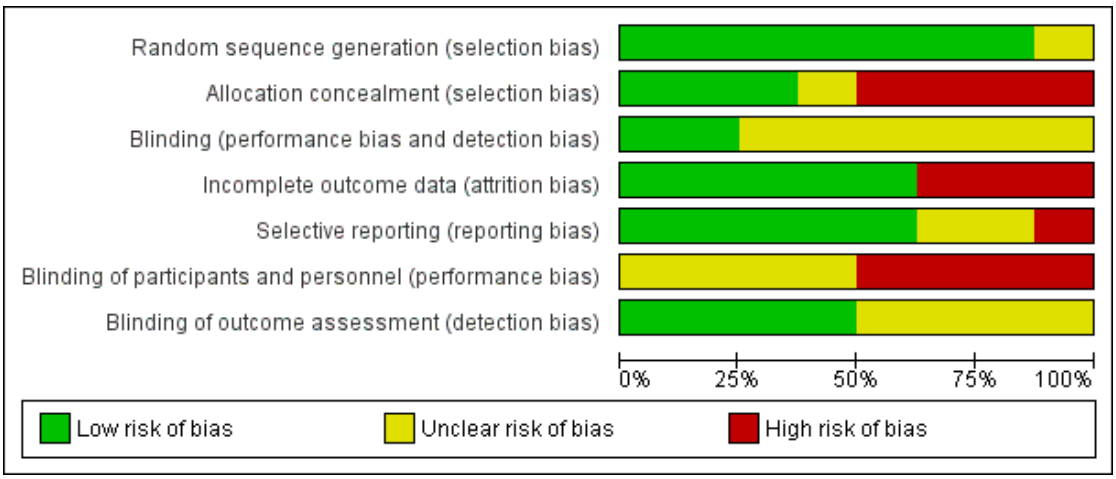
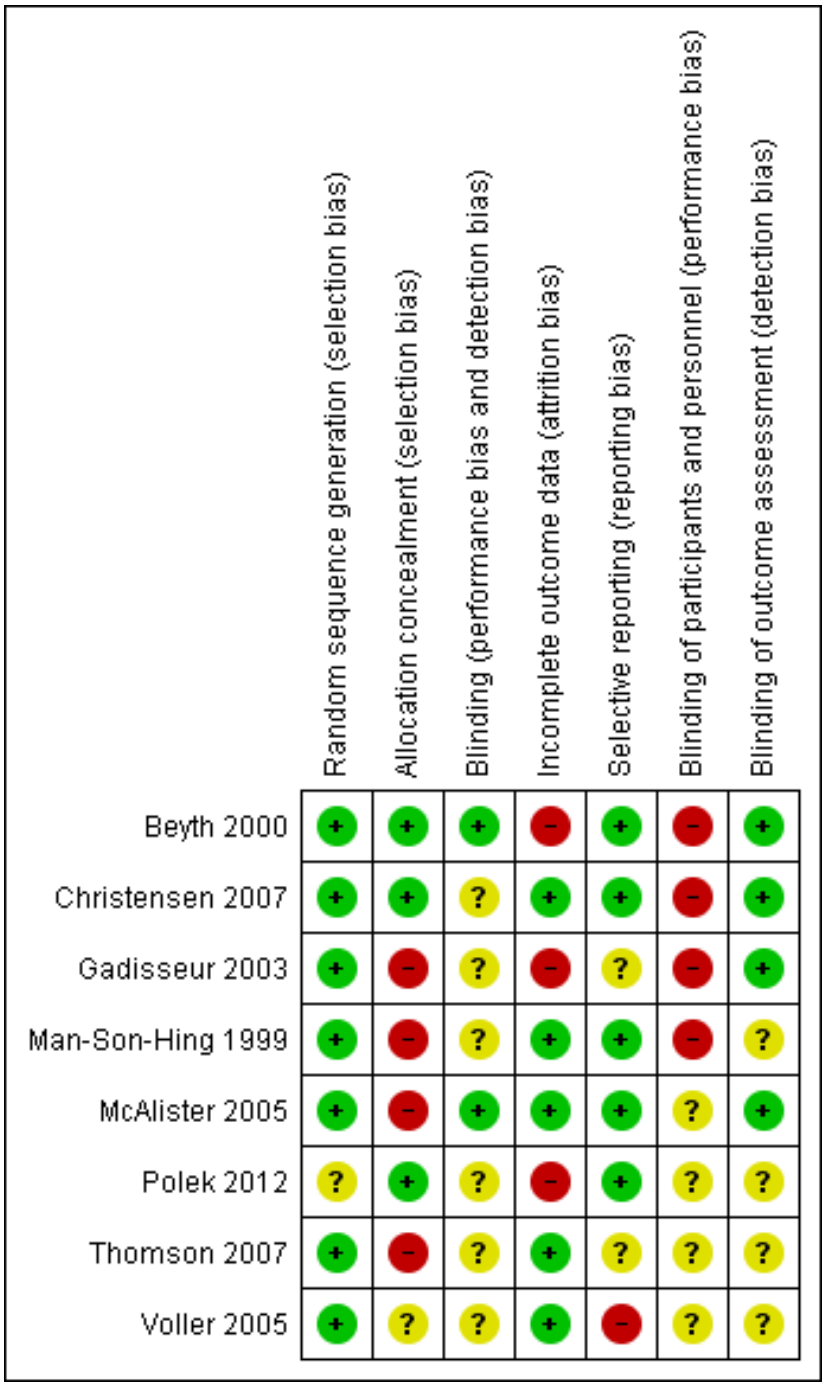


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Six of the included trials provided information about adequate sequence generation. For the majority of trials this consisted of randomisation to the intervention or usual care: according to a computer-generated sequence using block randomisation (Christensen 2007; Man-Son-Hing 1999; McAlister 2005; Thomson 2007), a random numbers table (Voller 2005), or a two-step partial-Zelen design (Gadisseur 2003). The other two trials did not provide details of sequence generation (Beyth 2000; Polek 2012). One study used cluster randomisation at the level of the family physician (McAlister 2005). All eligible patients within any one physician's practice were allocated to the intervention (50 practices) or usual care (52 practices). This process avoided contamination that may have occurred if the same physician delivering the intervention also delivered usual care. This trial also accounted for their randomised clusters in their analysis, weighting the analysis accordingly, thus their allocation was considered low risk of bias.

All of the studies reported the number of eligible participants. However, for the mixed cohort trials it was difficult to retrospectively assess which of the screened patients had AF. Of those trials specifically recruiting AF patients, the percentage of eligible patients randomised ranged from 7% (Khan 2004a), 30% (Thomson 2007), to 49% (McAlister 2005). In the mixed indication cohort trials this percentage ranged from 18% (Gadisseur 2003) to 95% (Christensen 2007). Thus some of the trials were more representative than others. Those trials that included a small percentage of eligible participants were at risk of selection bias whereby patient characteristics may affect the study outcomes. For example, those patients that participated may have been more motivated or willing to participate.

Blinding

Blinding patients to the intervention they were receiving was not possible with this type of intervention, nor was it possible to blind the intervention facilitator to which arm the patients were in. This inevitably raises the risk of bias for all studies. Experimenter bias could have occurred in these trials, whereby the individuals delivering the intervention and usual care could behave differently towards a group inadvertently affecting the study outcome. However, blinding the data analyst or researcher to which intervention arm the patient was assigned to was possible, in principle, and was undertaken in four trials (Beyth 2000; Christensen 2007; Gadisseur 2003; McAlister 2005). Four trials did not state whether their data analyst was blinded to which group the patients were randomised to (Man-Son-Hing 1999; Polek 2012; Thomson 2007) or indeed whether the individual delivering the intervention also carried out the analysis, which inevitably increases the risk of bias.

Incomplete outcome data

The percentage of patients completing the final follow-up ranged from 63% (Man-Son-Hing 1999) to 100% (Voller 2005). Where attrition was greater than 20% this was considered a risk of bias. If attrition is related to any feature of the study design, the instrumentation, or leads to bias between groups, this will increase the risk of bias. Some of the self-monitoring and decision aid studies reported participants as lost to follow-up due to an inability to perform the tests or to understand the decision aid. Other reasons included discontinuing warfarin, death, illness, and hospitalisation. Where patients were unable to use the intervention this could lead to a high risk of bias, with a more 'capable' sample.

Selective reporting

Two of the studies published a protocol paper (McAlister 2005; Voller 2005). McAlister reported on all but one of the pre-specified outcomes (patient satisfaction). Voller and colleagues reported on all of their pre-specified outcomes, although the trial was ended early due to insufficient participant numbers to power the primary outcome (Voller 2005). A further six studies did not publish protocol papers (Beyth 2000; Christensen 2007; Gadisseur 2003; Man-Son-Hing 1999; Polek 2012; Thomson 2007), but reported on all the outcomes specified within their method section.

Other potential sources of bias

Over the course of the study participants may change. With increasing age the participants in these studies were likely to have suffered from additional comorbidities and started taking new medications. These trial designs cannot control for the impact of concomitant medications or the additional burden of new medication regimes across the study period, thus this may have increased the risk of bias for all trials.

Effects of interventions

Various methods of measuring outcomes were employed and this was the main obstacle when comparing study findings. This was further complicated by the different time points at which measurements were taken, depending on the length of the trial. Further, the included studies differed in type (behavioural and decision aids) and in their comparator group. Where data were comparable, that is using the same measurement tool and type of intervention, AF-specific data were requested.

Education

Percentage of time spent within the therapeutic range (TTR)

Two of the included trials compared education only and usual care (Gadisseur 2003; Polek 2012). One of these trials reported TTR (Gadisseur 2003).

Gadisseur et al (Gadisseur 2003) studied a cohort with a mixed indication for OAT and provided additional unpublished data on the AF cohort. They found that the TTR (SD) in the education only group was higher than TTR in the usual care arm: 75.0% (18.5) versus 67.1% (26.4), respectively; mean difference 7.9 (95% CI -3.9 to 19.7).

Patient satisfaction

One education trial reported patient satisfaction (Gadisseur 2003). However, the authors did not provide AF-specific data on patient satisfaction for the education only group, thus it could not be included within this narrative review.

Knowledge

One trial provided unpublished AF data on knowledge outcomes (Polek 2012). They found slightly higher knowledge scores in the intervention group than the usual care group at the 12-week follow-up: 11.2 (1.6) versus 10.1 (1.7) respectively. However, the number of AF patients in this mixed cohort was too small to draw definitive conclusions.

Self-monitoring plus education

Percentage of time spent within the therapeutic range (TTR)

Four trials examined the impact of self-monitoring plus education (Beyth 2000; Christensen 2007; Gadisseur 2003; Voller 2005).

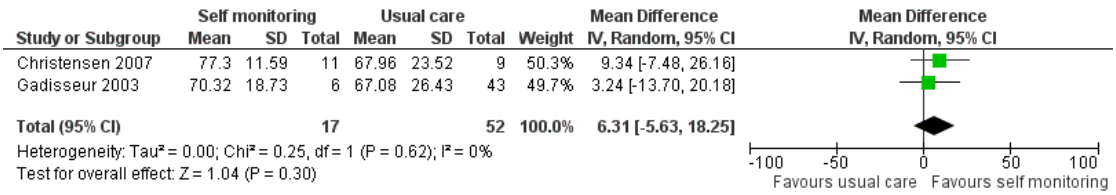
Christensen (Christensen 2007) recruited patients with multiple indications for OAT, with only 20 AF patients: 11 receiving self-management plus education and nine in the usual care group. INR control in the intervention group (mean (SD)) was slightly higher in the intervention group than the usual care group: 77.3% (11.6) versus 67.9% (23.5), respectively; mean difference 9.3 (95% CI -7.5 to 26.2).

Gadisseur (Gadisseur 2003) was also a mixed cohort trial that provided unpublished data on AF patients. TTR (mean (SD)) in the self-monitoring plus education group was slightly higher than in the usual care group: 70.3% (18.7) versus 67.1% (26.4), respectively; mean difference 3.2 (95% CI -13.7 to 20.2).

Beyth et al (Beyth 2000) did not provide AF-specific data on TTR outcomes and thus could not be included in these analyses.

The pooled analysis of the two studies reporting TTR using the Rosendaal method of calculation (Christensen 2007; Gadisseur 2003) demonstrated that self-monitoring plus education did not significantly improve TTR when compared to usual care, mean difference of 6.3 (95% CI -5.63 to 18.25) (Analysis 1.1; Figure 4).

Figure 4. Forest plot of comparison: 1 Time in therapeutic INR range, outcome: 1.1 Time in therapeutic INR range.



Major bleeding, stroke and thromboembolic events

One study provided unpublished AF data on major bleeding, stroke and thromboembolic events (Beyth 2000). Beyth and colleagues found the number of cases of major bleeding in the self-monitoring plus education group (n = 1, 1.8% of total AF cohort) was similar to the number of cases in the usual care group (n = 2, 3.7% of total AF cohort). There were also very few cases of stroke and thromboembolic events in the self-monitoring plus education (n = 1, 1.8% of total AF cohort) and usual care (n = 2, 3.7% of total AF cohort) groups (Beyth 2000). Voller (Voller 2005) measured thromboembolic and bleeding events. Two severe haemorrhages occurred in one patient in the self-monitoring group, and one thromboembolic event occurred in the usual care group.

Time of INR values in therapeutic range

Voller (Voller 2005) measured time within range (in days) and percentage of time in the INR target range, but did not calculate TTR using the Rosendaal method. Values were in the target range significantly more frequently (P < 0.01) in the patients under self-management (67.8%) than in the family doctor group (58.5%). There was a trend, but no significant difference, with regard to the number of days within the target range (178 ± 126 days as compared to 155.9 ± 118.4 days).

Education versus self-monitoring (plus education)

Percentage of time spent within the therapeutic range (TTR)

One trial compared self-monitoring plus education with education only (Gadisseur 2003).

Gadisseur (Gadisseur 2003) provided unpublished data on AF patients that suggested the TTR was slightly higher (mean (SD)) in the self-monitoring group than in the education only group: 71.1% (14.5) versus 70.4% (24.5); mean difference of 0.7 (95% CI -7.9 to 9.3).

Decision aids

Percentage of INRs in range

One trial reported the percentage of INRs in range (McAlister 2005). Percentage of INRs within the therapeutic range differed from TTR as the outcome was not calculated using the Rosendaal method (Rosendaal 1993). McAlister (McAlister 2005) found that INR control deteriorated in the usual care arm over time (INRs were between 2 and 3 on 66% of the days at 3 months versus 70% of the days at baseline), while INR control improved in the intervention arm (INRs were between 2.0 and 3.0 on 72% of the days at 3 months versus 65% at baseline) over time. The between group difference was statistically significant (P = 0.02). By 12 months, INR control in both arms had regressed back to baseline levels.

Increased knowledge

Two trials reported on patient knowledge (Man-Son-Hing 1999; Thomson 2007). Thomson (Thomson 2007) used an extension of the decision conflict scale (O'Connor 1995) and found that although knowledge scores after the intervention had improved slightly, by three-month follow-up they had returned to pre-intervention levels. There was no significant difference between the decision aid and guidelines groups at any point.

The second trial used a non-validated scale and demonstrated that patients in the decision aid group had significantly greater knowledge of treatment-related information: aspirin-related difference 15.9 (95% CI 4.6 to 27.2, P < 0.001); warfarin-related 14.9 (95% CI 4.6 to 25.2, P < 0.001) than those in the usual care group (Man-Son-Hing 1999).

Patient satisfaction

One trial using a decision aid intervention reported patient satisfaction as an outcome (Man-Son-Hing 1999). They found that the use of the decision aid did not significantly affect patients' satisfaction with their physician consultations.

Decision conflict

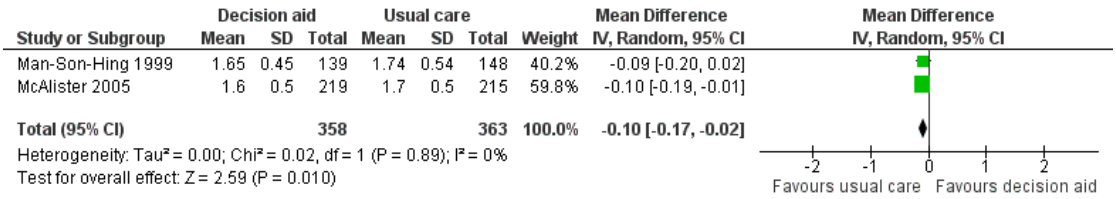
Three studies (Man-Son-Hing 1999; McAlister 2005; Thomson 2007) reported decision conflict, and all used the decision conflict scale (O'Connor 1995).

Man-Son-Hing (Man-Son-Hing 1999) found that the usual care arm scored slightly higher (mean (SD)) on decision conflict than the decision aid arm: 1.74 (0.5) versus 1.6 (0.4); mean difference -0.09 (95% CI -0.2 to 0.02).

McAlister (McAlister 2005) found that the usual care arm scored slightly higher (mean (SD)) on decision conflict that the decision aid arm: 1.7 (0.5) versus 1.6 (0.5); mean difference -0.10 (95% CI -0.19 to -0.01).

Although three studies reported decision conflict as an outcome (Man-Son-Hing 1999, McAlister 2005; Thomson 2007), only two compared differences in the usual care and decision aid intervention groups (Man-Son-Hing 1999; McAlister 2005). The third compared the decision aid with a guideline comparison group (Thomson 2007) and therefore was not included in the meta-analysis. Data from the two trials (Man-Son-Hing 1999; McAlister 2005) were pooled and the analysis favoured usual care in terms of reducing decision conflict: mean difference -0.10 (95% CI -0.17 to -0.02) (Figure 5; Analysis 2.1).

Figure 5. Forest plot of comparison: 2 Decision conflict, outcome: 2.1 Decision conflict.



Anxiety

Only one trial reported anxiety as an outcome (Thomson 2007). Anxiety fell significantly in both groups pre- to post-clinic, mean change -4.57 (95% CI -6.30 to -2.84), but there was no evidence of a significant difference in anxiety between the two groups (F (1, 95) = 0.001; P = 0.98).

DISCUSSION

Summary of main results

This review found eight RCTs (Beyth 2000; Christensen 2007; Gadisseur 2003; Man-Son-Hing 1999; McAlister 2005; Polek 2012; Thomson 2007; Voller 2005) of behavioural and educational interventions for anticoagulant therapy in patients with AF. Two trials compared education with usual care (Gadisseur 2003; Polek 2012), four compared self-monitoring plus education with usual care (Beyth 2000; Christensen 2007; Gadisseur 2003; Voller 2005), and one trial also compared a self-management group (consisting of self-testing and self-dosing) (Gadisseur 2003). Three trials focused on the use of a decision support aid versus usual care (Man-Son-Hing 1999; McAlister 2005) or a comparison group (Thomson 2007). The analyses included a small number of trials with small sample sizes, thus more evidence is needed to draw definitive conclusions.

Self-monitoring plus education versus usual care

Two self-monitoring plus education trials reported TTR (Christensen 2007; Gadisseur 2003). Pooled data for the AF patients demonstrated that self-monitoring plus education did not significantly improve TTR when compared to usual care (OR 6.3, 95% CI -5.63 to 18.25) (Analysis 1.1). One previous Cochrane review compared self-management (monitoring and dosing) and self-monitoring (monitoring only) interventions for mixed indication patients taking OAC. In their pooled data analysis, self-management interventions showed significant reductions in both thromboembolic events (RR 0.50, 95% CI 0.36 to 0.69) and all-cause mortality (RR 0.64, 95% CI 0.46 to 0.89), but self-monitoring did not (Garcia-Alamino 2010). The findings from the current review support those by Garcia-Alamino and colleagues that in an AF cohort self-monitoring is no more successful in increasing INR control than usual care.

Decision aids

Decision aid trials favoured usual care over the intervention in minimising decision conflict (mean difference -0.10, 95% Cl -0.17 to -0.02). The use of a decision aid did not have a significant impact on AF patients' anxiety levels (Thomson 2007) or patient satisfaction (Man-Son-Hing 1999). This suggests that patients that took part in the decision aid trial were uncertain about the decision as to which treatment choice they were going to make.

Overall completeness and applicability of evidence

Four of the included trials had mixed indication cohorts (Beyth 2000; Christensen 2007; Gadisseur 2003; Polek 2012), and 10 further trials were excluded as they did not provide AF-specific data (Barcellona 2006; Chan 2006; Gardiner 2006; Machtinger 2007; Menendez-Jandula 2005; Ryan 2009; Sawicki 2003; Siebenhofer 2007; Stone 1989; Watzke 2000). Recruiting patients with mixed indications for warfarin can be problematic. Patients often have different INR ranges (for example with valve replacements) and each patient group is unique in their lifestyle and treatment recommendations. AF patients are often older (Kannel 1998), prescribed treatment on a long-term basis (NICE 2006), and susceptible to inaccurate beliefs surrounding their illness (Steed 2010) due to their symptoms being irregular and often unrecognised (Fuster 2006). Thus it is essential that interventions are disease specific, yet only one of the included trials specifically mentioned educating the patients about AF (McAlister 2005). Without discussing the illness itself patients may not understand the need for treatment and the associated risks of their condition. Those interventions

that are disease specific may prove more successful in targeting the particular concerns of the target population.

A further consideration is that the participants in these trial cohorts may exhibit a number of co-morbidities which have not been accounted for, thus they may have received similar behaviour change interventions in the past for conditions such as diabetes potentially increasing their knowledge and awareness of risk. Therefore, the results of these trials may not be representative of the effect a behavioural or educational intervention may have on a sample of warfarin-naive AF only patients, and we cannot draw conclusions on the use of interventions for newly referred patients who are at greatest risk of complications.

Patients that self-monitor are also educated to ensure they are able to perform the tests accurately and safely. It is therefore difficult to determine whether the education or the self-monitoring is improving health outcomes. Further, patients selected for self-monitoring tend to be younger, healthier, and better educated. Thus they may not be representative of a general AF population (Garcia-Alamino 2010). Similarly, decision aids provide patients with education regarding treatment choices thus it is difficult to determine whether increases in knowledge alone may have the same effect. The delivery of the intervention could also influence the outcomes; a group-based intervention provides opportunity for social comparison, which influences patient attitudes towards their treatment and their perception of social norms.

All of the trials recruited patients that had been previously taking OAT. Whilst some trials included warfarin-naive patients (Thomson 2007) or inpatients starting OAT (Beyth 2000; Polek 2012), none of the trial cohorts were exclusively warfarin-naive. Experience of taking warfarin could increase the risk of poor internal validity as patients may had been receiving OAT treatment long term, for up to 5.5 years (Christensen 2007) prior to receiving the intervention, and may be influenced by their treatment history (for example side effects). Previous experience of the treatment may also influence their levels of adherence to recommendations, and a patient's decision to start taking the treatment in the first place (Holbrook 2005; Lip 2011). Patients may develop specific beliefs about their medications that influence the decision making process, such as the inconvenience of regular blood tests, need for reductions in or abstinence from alcohol, and dietary restrictions (Dantas 2004; Lane 2006; Lip 2007; Lip 2011). Patients may also feel a level of protection from harm by taking a treatment (Lip 2011), thus increasing their likelihood of adopting one treatment over another. One of the trials in this review recruited patients that had previously taken part in the Stroke Prevention in Atrial Fibrillation (SPAF) trial (Man-Son-Hing 1999). All of these patients had previously taken either an antiplatelet drug (60% of decision aid group versus 60% of the usual care group) or OAT (37% of the decision aid group versus 38% of the usual care group). The participants within this trial are unlikely to be representative of patients that are making treatment decisions for the first time. Firstly, they are ex-trial patients and may be more likely to have had prior treatment-related education and, secondly, they have had first-hand experience of one or both treatments. One study found that more patients chose warfarin in a decision aid trial when the drug name was blinded than when it was unblinded (Holbrook 2007), suggesting that patients are influenced by prior knowledge, beliefs surrounding medications, and perhaps any adverse events they may have suffered from. Research suggests that patients are more likely to choose their current treatment over and above another; it has been suggested that this act prevents cognitive dissonance (that is the stress of choosing a preferred treatment over actual treatment choice) (Fuller 2004; Holbrook 2007; Howitt 1999; Protheroe 2000).

Quality of the evidence

Two types of bias were most prevalent within the studies. Firstly, blinding of patients to the intervention received was not possible, nor was it possible to blind the intervention facilitator, inevitably raising the risk of bias. It is unclear whether the researchers may have biased patient outcomes by treating the patients in the intervention arm differently from those in the control group. Blinding the data analyst or researcher to which intervention arm the patient was assigned to was undertaken in four trials (Beyth 2000; Christensen 2007; Gadisseur 2003; McAlister 2005). Trials must be explicit when reporting their methods and procedures to ensure accurate assessment of blinding bias and enable comparison of trials.

Inclusion bias was also evident in many studies, where the trial participants may not have been representative of the eligible participants. The percentage of eligible patients randomised was as low as 18% (Gadisseur 2003) in one of the mixed cohort trials. Perhaps the reluctance of individuals to participate may relate to the extensive training required, particularly for self-monitoring trials. Furthermore, many patients may refuse consent due to physical limitations, the time commitment associated with multiple training sessions, or psychological barriers to performing self-monitoring. AF patients in particular are mostly elderly (Kannel 1998), and often highly symptomatic (Lip 2011), thus trial participation may be a burden. This could explain the small AF sample sizes in the included mixed OAT indication trials, as patients with other indications may be younger and with fewer co-morbidities.

The quality of care in the control groups may vary, affecting the benefit and control of standard anticoagulation monitoring. The educational element of the intervention may be one of the key factors in improving TTR. However, trials vary in the intensity, duration, and number of education sessions, thus we cannot draw conclusions about the influence of each of the educational components of these interventions.

Five studies did not record patients' level of education (Christensen 2007; Gadisseur 2003; Polek 2012; Thomson 2007; Voller 2005), a factor which may impact on knowledge uptake and treatment control. Research suggests that patients with greater knowledge of

their treatment spend more time in the therapeutic range (Tang 2003). Thus the results of the trials that do not indicate education level may be influenced by individual differences in educational achievement between trial groups.

Whilst the educational components of the interventions did focus on important areas of risk (that is side effects, medication recommendations), they did not include education specific to the patient's indication for treatment. Studies suggest that AF patients have limited knowledge of their condition (Coehlo-Dantas 2004; Lane 2006; Nadar 2003; Tang 2003), which may influence the perceptions they form about their illness and their treatment (Steed 2010). Thus it is essential that patients form accurate concepts of their illness and make appropriate lifestyle changes.

Few studies provided AF-specific data on psychological outcomes such as anxiety, depression, and quality of life. Those that did found no significant differences between groups. Only one decision aid trial reported anxiety as an outcome (Thomson 2007). Thomson found that anxiety fell significantly in both groups from pre- to post-clinic, mean change -4.57 (95% CI -6.30 to -2.84), but there was no evidence of a significant difference in anxiety between the two groups (F (1, 95) = 0.001; P = 0.98). None of the self-monitoring trials measured anxiety, a factor which may have an influence on patients' self-efficacy to perform regular blood tests. Numerous studies suggest that AF patients suffer from high levels of anxiety (Thrall 2004), yet none of the interventions were designed with this in mind. As evidence suggests that AF patients often have inaccurate illness representations (Steed 2010), trials of interventions that include psychological components and outcome measures are needed.

Potential biases in the review process

Our search strategy included a comprehensive search of several electronic databases, meticulous handsearching of reference lists of included and excluded papers, recent conference proceedings, and personal communications with experts in this area. In addition, we wrote to all the authors of included studies requesting AF-specific data and further demographic and clinical details on the included cohorts. Further, the titles and abstracts of all studies identified by the search strategy were reviewed independently by two review authors and disagreements were resolved by consensus. Data extraction of the included studies was also undertaken independently by two review authors. Therefore, we believe that the potential for bias in the review process was minimal and that it unlikely that we have missed important studies.

AUTHORS' CONCLUSIONS

Implications for practice

Patients participating in both educational interventions and self-monitoring interventions (with education) appear to spend more time within the therapeutic INR range, but pooled analyses of the AF data did not favour self-monitoring plus education over usual care. Evidence is limited as only a few trials with small samples of AF patients were included. More trials are needed to examine the impact of intensive educational interventions on anticoagulation control in AF patients and the impact on TTR. Self-monitoring may not be a feasible option for many patients, particularly as it requires additional training (Fitzmaurice 2000), is costly (Fitzmaurice 2000), and new anticoagulants are now available which do not require monitoring (Lip 2011; Shantsila 2010). Further, one of the newer oral anticoagulants (NOAC) trials, where dabigatran was compared with warfarin, examined the TTR of those patients taking warfarin and compared the event rates by quartile of centre TTR (cTTR) (Wallentin 2010) and demonstrated that despite very good cTTR (> 72.6%) both doses of dabigatran were associated with fewer adverse events than warfarin. However, there will still be some patients for whom the NOACs are not suitable (for example those with severe renal impairment), where warfarin would be the only alternative OAC treatment. However, no study to date has compared self-monitoring with warfarin to treatment with dabigatran on adverse events (stroke and major bleeding) and therefore it is unclear whether there would be a benefit of self-monitoring with warfarin (in the appropriate patient) over treatment with dabigatran.

Implications for research

This review highlights the need for AF-specific trials in larger cohorts and among warfarin-naive AF patients. The number of AF patients within the trials was limited with most patients being warfarin-experienced. Furthermore, the trials that were included primarily focused on self-monitoring plus education or decision aids. None of the trials specifically looked at other types of interventions such as intensive education or behaviour change interventions that are driven to improve psychological outcomes (that is motivational interviewing and cognitive behavioural therapy). Trials also need to consider the use of disease-specific measuring tools, which may provide a more accurate assessment of the impact of the intervention. In addition, such trials should account for the potential confounding effects of level of education and the quality of the care in the control group.

Ongoing trials

A trial currently being undertaken by the review authors has recruited warfarin-naive AF patients and has specifically examined the effects of an intensive educational intervention to gain an understanding of the impact of an intervention during this 'high risk' phase of treatment (Smith 2010). Other ongoing trials have

focused on education (Hua 2011) and an enhanced patient discharge system (Stafford 2011). These trials may provide additional evidence and insight for later review updates. We will update this review once the results from these studies are published. In addition, for the results to be generalisable to the AF population there is a need for population-based studies that collect data on adverse event rates, time in range, and cost effectiveness, factors that impinge on successful educational and behavioural interventions. Future studies should set out to understand the mechanisms by which interventions are successful by exploring the psychological and practical implications for AF patients commencing OAC treatment.

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REFERENCES

References to studies included in this review

Beyth 2000 *{published data only}*

Beyth RJ, Landefeld CS. Multicomponent comprehensive care was as effective as usual care for decreasing major bleeding in older patients on warfarin. *Evidence Based Medicine* 2001;**6**:116.

* Beyth RJ, Quinn L, Landefeld S. A multicomponent intervention to prevent major bleeding complications in older patients receiving warfarin. *Annals of Internal Medicine* 2000;**133**(9):687–95.

Christensen 2007 *{published data only}*

Christensen TD, Maegaard M, Sorensen HT, Hjortdal VE, Hasenkam. Self-versus conventional management of oral anticoagulant therapy. *American Journal of Cardiovascular Drugs* 2007;**7**(3):191–7.

* Christensen TD, Maegaard M, Sorensen HT, Hjortdal VE, Hasenkam JM. Self-management versus conventional management of oral anticoagulant therapy: A randomised, controlled trial. *European Journal of Internal Medicine* 2006; **17**:260–6.

Gadisseur 2003 *{published data only}*

Gadisseur APA, Breukink-Enghers WGM, van der Meer FJM, van den Besselaar AMH, Sturk A, Rosendaal FR. Comparison of the quality of oral anticoagulant therapy through patient self-management by specialized anticoagulation clinics in the Netherlands. *Archives of Internal Medicine* 2003;**163**(24):2639–46.

Gadisseur APA, Kaptein AA, Breukink-Engbers WGM, Van der meer FJM, Rosendaal FR. Patient self-management of oral anticoagulant care vs. management by specialized anticoagulation clinics: positive effects on quality of care. *Journal of Thrombosis and Haemostasis* 2004;**2**:584–91.

Man-Son-Hing 1999 *{published data only}*

Man-Son-Hing M, Laupacis A, O'Connor AM. A patient decision aid regarding antithrombotic therapy for stroke prevention in atrial fibrillation: A randomized controlled trial. *JAMA* 1999;**282**(8):737–43. [DOI: 10.1001/jama.282.8.737]

McAlister 2005 *{published data only}*

McAlister FA, Man-Son-Hing M, Straus SE, Ghali WA, Anderson D, Majumdar SR, et al.for the Decision Aid in Atrial Fibrillation (DAAFI) Investigators. Impact of a patient decision aid on care among patients with nonvalvular atrial fibrillation: a cluster randomised trial. *Canadian Medical Association Journal* 2005;**173**(5):496–501.

McAlister FA, Man-Son-Hing M, Straus SE, Ghali WA, Gibson P, Anderson D, et al.A randomised trial to assess the impact of an antithrombotic decision aid in patients with nonvalvular atrial fibrillation: the DAAFI trial protocol [ISRCTNI4429643]. *BMC Cardiovascular Disorders* 2004; **4**:5.

Polek 2012 *{published data only}*

Polek C, Hardie T. Warfarin use post hospitalization: pilot comparative effectiveness of telephone follow-up. *Rehabilitation Nursing* 2012;**37**(2):80–7.

Thomson 2007 *{published data only}*

Thomson RG, Eccles MP, Steen IN, Greenaway J, Stobbart L, Murtagh MJ, May CR. A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: a randomised controlled trial. *Quality and Safety in Health Care* 2007;**16**:216–23. [DOI: 10.1136/qshc.2006.018481; :]

Voller 2005 *{published data only}*

Voller H, Glatz J, Taborski U, Bernado A, Dovifat C, Bunkard G, Heidinger K. [Hintergrund und Prufplan der studie zum Selbstmanagement der Antikoagulation bei Patient mit nichtvalvularem Vorhofflimern (SMAAF–studie)]. *Zeitschrift fur Kardiologie* 2000;**89**: 284–8.

Voller H, Glatz J, Taborski U, Bernardo A, Dovifat C, Heidinger K. Self-management of oral anticoagulation in nonvalvular atrial fibrillation (SMAAF study) [Selbstmanagement de antikoagulation bei patienten mit nichtvalvularem vorhofflimmern]. *Zeitschrift fur Kardiologie* 2005;**94**(3):183–6.

References to studies excluded from this review

Armstrong 2011 *{published data only}*
Armstrong EP, Chemodurow L, Christensen S, Johnson ES. A pre- post-evaluation of implementing an inpatient monitoring and education program. *Pharmacy Practice* 2011;**9**(2):101–5.

Bajorek 2005 *{published data only}*
Bajorek BV, Krass I, Ogle SJ, Duguid MJ, Shenfield GM. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: A pharmacist-led mutlidisciplinary intervention. *Journal of the American Geriatrics Society* 2005;**53**:1912–20. [DOI: 10.1111/j.1532-5415.2005.53564.x]

Baker 1991 *{published data only}*
Baker D, Roberts DE, Newcombe RG, Fox KAA. Evaluation of drug information for cardiology patients. *British Journal of Clinical Pharmacy* 1991;**31**:525–31.

Barcellona 2006 *{published data only}*
Barcellona D, Contu P, Marongiu F. A two-step educational approach for patients taking oral anticoagulants does not improve therapy control. *Journal of Thrombosis and Thrombolysis* 2006;**22**:185–90. [DOI: 10.1007/s11239-006-9027-2]

Batty 2001 *{published data only}*
Batty G, Oborne CA, Hooper R, Jackson S. Investigation of intervention strategies to increase the appropriate use of antithrombotics in elderly hospital inpatients with atrial fibrillation. *The Journal of Clinical Governance* 2001;**9**:115–22.

Blaise 2009 *{published data only}*
Blaise S, Satger B, Fontaine M, Yver J, Rastel D, Toffin L, et al.Evaluation of an education program for patients taking oral anticoagulants: Experience of the GRANTED network in Isere [Evaluation d'un programme d'education therapeutique pour les traitments anticoagulants oraux: exerience du reseau Ville–Hopital GRANTED du secteur Sud–Isere]. *Journal des Maladies Vasculaires* 2009;**34**:346–53. [DOI: 10.1016/j.jmv.2009.07.088]

Bloomfield 2011 *{published data only}*
Bloomfield HE, Krause A, Greer N, Taylor BC, MacDonald R, Rutks I, et al.Meta-analysis: effect of patient self-testing and self-management of long-term anticoagulation on major clinical outcomes. *Annals of Internal Medicine* 2011;**154**(7):472–w-160.

Bump 1977 *{published data only}*
Bump CM, Campbell JG. The relationship of patient education to the clinical course of patients receiving anticoagulants. *Abstracts of Hospital Management Studies* 1977;**14**(2):18091.

Burns 2009 *{published data only}*
Burns S. Application of the theory of planned behavior to oral anticoagulation therapy. *Nursing and Health Sciences* 2009;**11**:98–101. [DOI: 10.1111/j.1442-2018.2009.00426.x]

Castelino 2010 *{published data only}*
Castelino RL, Chen TF, Guddattu V, Bajorek BV. Use of evidence-based therapy for the prevention of cardiovascular events among older people. *Evaluation & the Health Professions* 2010;**33**(3):276–301.

Chan 2006 *{published data only}*
Chan FWH, Wong RSM, Lau WH, Chan TYK, Cheng G, You JHS. Management of Chinese patients on warfarin therapy in two models of anticoagulation service - a prospective randomized trial. *British Journal of Clinical Pharmacology* 2006;**62**(5):601–9. [DOI: 10.1111/j.1365-2125.2006.02693.x]

Christensen 2011 *{published data only}*
Christensen H, Lautertein JJ, Sorensen PD, Petersen ERB, Madsen JS, Brandslund I. Home management of oral anticoagulation via telemedicine versus conventional hospital-based treatment. *Telemedicine and e-Health* 2011;**17**(3):169–76. [DOI: 10.1089/tmj.2010.0128]

Claes 2005 *{published data only}*
Claes N, Buntinx F, Vijgen J, Arnout J, Vermylen J, Fieuws S, Van LH. The Belgian improvement study on oral anticoagulation therapy: a randomized clinical trial. *European Heart Journal* 2005;**26**(20):2159–65.

Claes 2006 *{published data only}*
Claes N, Moeremans K, Frank B, Jef A, Jos V, Herman VL, Lieven A. Estimating the cost-effectiveness of quality-improving interventions in oral anticoagulation management within general practice. *Value in Health* 2006;**9**(6):369–76. [DOI: 10.1111/j.1524-4733.2006.00129]

Corbella 2009 *{published data only}*
Corbella A, Bottari L, Cevasco I, Giacobbe S, Roba I, Rossini S, Tognarelli M. Patients in chronic anticoagulation therapy: the organization of an educational program run by nurses and the assessment of patients' satisfaction [Le persone in Terapia Anticoagulante Orale (TAO): costruzione di un intervento gestito dagli infermieri e valutazione del gradimento]. *Assistenza Infermieristica e Ricerca* 2009;**28**(2):65–72.

Cordasco 2009 *{published data only}*
Cordasco KM, Asch SM, Bell DS, Guterman JJ, Gross-Schulman S, Ramer L, et al.A low-literacy medication education tool for safety-net hospital patients. *American Journal of Preventative Medicine* 2009;**37**(6 Suppl 1):S209–16. [DOI: 10.1016/j.amepre.2009.08.018]

Cromheecke 2000 *{published data only}*
Cromheecke ME, Levi M, Colly LP, de Mol BJM, Prins MH, Hutten BA, et al.Oral anticoagulation self-management and management by a specialist anticoagulation clinic: a randomised cross-over comparison. *Lancet* 2000;**356**(8):97–102.

Cromheecke 2001 *{published data only}*
Cromheecke ME, Levi M, Colly LP. Self management of long term oral anticoagulation was as effective as specialist anticoagulation clinic management. *Evidence-Based Medicine* 2001;**6**(2):41.

Davis 2005 *{published data only}*
Davis NJ, Billett HH, Cohen HW, Arnsten JH. Impact of adherence, knowledge, and quality of life on anticoagulation control. *Annals of Pharmacotherapy* 2005;**39**(4):632–6.

Dolor 2010 *{published data only}*
Dolor RJ, Ruybalid RL, Uyeda L, Edson RG, Phibbs C, Vertrees JE, et al.and the THINRS site investigators. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA cooperative study #481 - The home INR study (THINRS). *Journal of Thrombosis and Thrombolysis* 2010;**30**:263–75.

Duran-Parrondo 2011 *{published data only}*
Duran-Parrondo C, Vazquez-Lago JM, Campos-Lopez AM, Figueras A. Impact of a pharmacotherapeutic programme on control and safety of long-term anticoagulation treatment. *Drug Safety* 2011;**34**(6):489–500.

Field 2010 *{published data only}*
Field TS, Tjia J, Mazor KM, Donovan JL, Kanaan AO, Harrold LR, et al.Randomized trial of a warfarin communication protocol for nursing homes: an SBAR-based approach. *The American Journal of Medicine* 2011; **124**:2.

Fitzmaurice 1996 *{published data only}*
Fitzmaurice DA, Hobbs FDR, Murray ET, Bradley CP, Holder R. Evaluation of computerized decision support for oral anticoagulation management based in primary care. *British Journal of General Practice* 1996;**46**:533–5.

Fitzmaurice 2000 *{published data only}*
Fitzmaurice DA, Hobbs FD, Murray ET. A nurse led clinic and computer decision support software for anticoagulation decisions were as effective as a hospital clinic. *Evidence Based Medicine* 2001;**6**:61.
* Fitzmaurice DA, Hobbs FD, Murray ET, Holder RL, Allan TF, Rose PE. Oral anticoagulation management in primary care with the use of computerized decision support and near-patient testing: a randomised, controlled trial. *Archives of Internal Medicine* 2000;**160**(15):2343–8.

Fitzmaurice 2005 *{published data only}*
Fitzmaurice DA, Murray ET, Gee KM. A randomised controlled trial of patient self management of oral anticoagulation treatment compared with primary care management. *Journal of Clinical Pathology* 2002;**55**:845–9. [DOI: 10.1136/jcp.55.11.845]
* Fitzmaurice DA, Murray ET, McCahon MD, Holder R, Raferty JP, Hussain S, et al.Self management of oral anticoagulation: randomised trial. *BMJ* 2005;**331**(7524): 1057. Erratum in: BMJ 2005 331(7528):1330. [DOI: 10.1136/bmj.38618.580903.AE; : ISRCTN 19313375]
Murray E, Fitzmaurice D, MaCahon D, Fuller C, Sandhur H. Training for patients in a randomised controlled trial of self management of warfarin treatment. *BMJ* 2004;**328** (21):437.

Fraenkel 2011 *{published data only}*
Fraenkel L, Street RL, Fried TR. Development of a tool to improve the quality of decision making in atrial fibrillation. *BMC Medical Informatics and Decision Making* 2011;**11**:59.

Gardiner 2006 *{published data only}*
Gardiner C, Williams K, Longair I, Mackie IJ, Machin SJ, Cohen H. A randomised control trial of patient self-management of oral anticoagulation compared with patient self-testing. *British Journal of Haematology* 2006;**132**: 598–603. [DOI: 10.1111/j.1365-2141.2005.05899]

Gouin-Thibault 2010 *{published data only}*
Gouin-Thibault I, Levy C, Pautas E, Cambus JP, Drouet L, Mahe I, et al.Improving anticoagulation control in hospitalized elderly patients on warfarin. *Journal of the American Geriatrics Society* 2010;**58**:242–7.

Grunau 2011 *{published data only}*
Grunau B, Wiens MO, Harder KK. Patient self-management of warfarin therapy. *Canadian Family Physician* 2011;**57**:292–8.

Hasan 2011 *{published data only}*
Hasan SS, Sharmala R, Syed IA, Basariah N, Chong DWK, Mei TK, Chin OH. Factors affecting warfarin-related knowledge and INR control of patients attending physician- and pharmacist-managed anticoagulation clinics. *Journal of Pharmacy Practice* 2011;**24**(5):485–93.

Holbrook 2007 *{published data only}*
Holbrook A, Labiris R, Goldsmith CH, Ota K, Harb S, Sebaldt RJ. Influence of decision aids on patient preferences for anticoagulant therapy: a randomized trial. *Canadian Medical Association Journal* 2007;**176**(11):1583–7.

Jackson 2004 *{published data only}*
Jackson SL, Peterson M, Vial JH. A community-based educational intervention to improve antithrombotic drug use in atrial fibrillation. *The Annals of Pharmacotherapy* 2004;**38**:1794–9. [DOI: 10.1345/aph.1E152]

Khan 2004 *{published data only}*
Khan TI, Kamali F, Kesteven P, Avery P, Wynne H. The value of education and self-monitoring in the management of warfarin therapy in older patients with unstable control of anticoagulation. *British Journal of Haematology* 2004; **126**:557–64.

Krause 2010 *{published data only}*
Krause A, Bloomfield H, Wilt T. Safety and effectiveness of patient-managed outpatient anticoagulation: A systematic review. *Journal of General Internal Medicine* 2010;**25**:S387.

Landefeld 1992 *{published data only}*
Landefeld CS, Anderson PA. Guideline-based consultation to prevent anticoagulation-related bleeding. *Annals of Internal Medicine* 1992;**116**(10):829–37.

Leger 2004 *{published data only}*
Leger S, Allenet B, Pichot O, Figari G, Calop J, Carpentier P, Bosson JL. Impact of an education program on patient behaviour favoring prevention of drug-related adverse events: a pilot study in patients receiving oral anticoagulants for thromboembolic venous disease [Impact d'un pragramme d'education therapeutique sur les attitudes de prevention vis–s–vis du risque iatrogene: etude pilote controlee visant les patients sous–anticoagulants oraux pour maladie thromboembolique veineuse]. *Journal des Maladies Vasculaires* 2004;**29**(3):152–8.

Machtinger 2007 *{published data only}*

Machtinger EL, Wang F, Chen LL, Rodriguez M, Wu S, Schilinger D. A visual medication schedule to improve anticoagulation control: A randomised controlled trial. *The Joint Commission Journal on Quality and Patient Safety* 2007; **33**(10):625–35.

Matchar 2005 *{published data only}*

Matchar DB, Jacobson AK, Edson RG, Lavori PW, Ansell JE, Ezekowitz MD, et al.The impact of patient self-testing of prothrombin time for managing anticoagulation: Rationale and design of VA cooperative study #481 - the home INR study (THINRS). *Journal of Thrombosis and Thrombolysis* 2005;**19**(3):163–72.

Matchar 2010 *{published data only}*

Matchar DB, Jacobson A, Dolor R, Edson R, Uyeda L, Phibbs CS, et al.Effect of home testing of international normalised ratio on clinical events. *The New England Journal of Medicine* 2010;**363**(17):1608–20.

Mazor 2007 *{published data only}*

Mazor KM, Baril J, Dugan E, Spencer F, Burgwinkle P, Gurwitz JH. Patient education about anticoagulant medication: Is narrative evidence or statistical evidence more effective?. *Patient Education and Counseling* 2007;**69**: 145–57. [DOI: 10.1016/j.pec.2007.08.010]

McCahon 2011 *{published data only}*

McCahon D, Fitzmaurice DA, Murray ET, Fuller CJ, Hobbs RFD, Allan TF, Raferty JP. SMART: Self-management of anticoagulation, a randomised trial. *BMC Family Practice* 2003;**4**:11.

* McCahon D, Murray ET, Murray K, Holder RL, Fitzmaurice DA. Does self-management of oral anticoagulation therapy improve quality of life and anxiety?. *Family Practice* 2011;**28**(2):134–40.

Megden 1999 *{published data only}*

Megden TH, Heidgen FJ, Vetter H. Optimization of long term control of oral anticoagulation by patient self-management [Verbesserung der langzeitkontrolle der oralen antikoagulation durch patienten–selbstmanagement]. *Herz Kreislauf* 1999;**31**(10):393–7.

Menendez-Jandula 2005 *{published data only}*

* Menendez-Jandula B, Souto J, Oliver A, Monserrat I, Quintana M, Gich I, Bonfill X, Fontcuberta J. Comparing self-management of oral anticoagulant therapy with clinic management. *Annals of Internal Medicine* 2005;**145**:1–10. Menendez-Jandula B, Souto JC, Oliver A. Patient self management of anticoagulants resulted in fewer major complications than clinic-based management. *Evidence Based Nursing* 2005;**142**:1–10.

Nedaz 2002 *{published data only}*

Nedaz M. Atrial fibrillation, anticoagulation and shared decision making [Fibrillation auriculaire et partage avec le patient de la decision d'anticoaguler]. *Medecine et Hygiene* 2002;**60**(2412):2054–8.

Nilsson 2011 *{published data only}*

Nilsson N, Eide TH, Kjeldhy C, Refsum N, Dahle G. What knowledge do patients on warfarin have about their treatment, and may patient education by a pharmacist improve their knowledge?. *International Journal of Clinical Pharmacy* 2011;**33**:418.

Pernod 2008 *{published data only}*

Pernod G, Labarere J, Yver J, Satger B, Allenet B, Berremili T, et al.EDUC'AVK: Reduction of oral anticoagulant-related adverse events after patient education: A prospective multicenter open randomized study. *Journal of General Internal Medicine* 2008;**23**(9):1441–6. [DOI: 10.1007/s11606-008-0690-1]

Polzien 2007 *{published data only}*

Polzien G. Prevent medication errors: a new year's resolution. *Home Healthcare Nurse* 2007;**25**(1):59–62.

PRISM Study group 2003 *{published data only}*

Lees KR, Sim I, Wier CJ, Erwin L, McAlpine C, Rodger J, et al.Cluster-randomized, controlled trial of computer-based decision support for selecting long-term anti-thrombotic therapy after acute ischaemic stroke. *QJM: An International Journal of Medicine* 2003;**96**:143–53. [DOI: 10.1093/qjmed/hcg019]

Reverdin 2011 *{published data only}*

Reverdin S, Schnetzler B, Gagneux G, Gavignet C, Boehlen F, Moerloose P. Implementation of an INR self-testing and self-management programme in common ambulatory private practice: our experience with 90 patients. *Swiss Medical Weekly* 2011;**141**:w13199.

Ryan 2009 *{published data only}*

Ryan F, Byrne S, OShea S. Randomized controlled trial of supervised patient self-testing of warfarin therapy using an internet-based expert system. *Journal of Thrombosis and Haemostasis* 2009;**7**:1284–90.

Saokaew 2010 *{published data only}*

Saokaew S, Permsuwan U, Chaiyakunapruk N, Nathisuwan S, Sukonthasarn A. Effectiveness of pharmacist-participated warfarin therapy management: a systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis* 2010; **8**:2418–27.

Satger 2009 *{published data only}*

Satger B, Blaise S, Fontaine M, Yver J, Allenet B, Baudrant M, et al.Therapy education for patients receiving oral anticoagulants vitamin K antagonists [Education therapeutique des patients traites par anticoagulants oraux antivitamines k]. *La Presse Medicale* 2009;**38**(12):1780–7. [DOI: 10.1016/j.lmp.2009.07.019]

Sawicki 1999 *{published data only}*

Sawicki PT, for the working group for the study of patient self-management of oral anticoagulation. A structured teaching and self-management program for patients receiving oral anticoagulation. *JAMA* 1999;**281**(2):145–50.

Sawicki 2003 *{published data only}*

Sawicki PT, Blaser B, Didjurgeit U, Kaiser T, Kleepies C, Schmitz N, Stubbe J. Long-term results of patient's self-management of oral anticoagulation. *Journal of Clinical and Basic Cardiology* 2003;**6**(1-4):59–62.

Siebenhofer 2007 *{published data only}*
Siebenhofer, A, Rakovac I, Kleepies C, Piso B, Didjurgeit U. Self-management of oral anticoagulation in the elderly: Rationale, design, baselines and oral anticoagulation control after one year follow-up. *Blood Coagulation, Fibrinolysis and Cellular Haemostasis* 2007;**97**:408–16. [DOI: 10.1160/TH06-08-0482]

Stone 1989 *{published data only}*
Stone S, Holden A, Knapic N, Ansell J. Comparison between videotape and personalized patient education for anticoagulant therapy. *The Journal of Family Practice* 1989;**29**(1):55–7.

Sunderji 2005 *{published data only}*
Sunderji R, Gin K, Shalansky K, Carter C, Chambers K, Davies C, et al.Clinic impact of point-of-care vs laboratory measurement of anticoagulation. *American Journal of Clinical Pathology* 2005;**123**:184–8.

Taylor 1997 *{published data only}*
Taylor FC, Gray A, Cohen H, Gaminara L, Ramsay M. Costs and effectiveness of a nurse specialist anticoagulant service. *Journal of Clinical Pathology* 1997;**50**:823–8. [DOI: 10.1136/jcp.50.10.823]

Trivalle 2010 *{published data only}*
Trivalle C, Cartier T, Verny C, Mathieu AM, Davrinche P, Agostini H, et al.and the IMEPAG Group. Identifying and preventing adverse drug events in elderly hospitalised patients: a randomised trial of a program to reduce adverse drug effects. *The Journal of Nutrition, Health and Ageing* 2010;**14**(1):57–61.

Tuiskula 2011 *{published data only}*
Tuiskula KA, Sullivan KM, Abraham G, Lahoz MR. Revising warfarin patient education materials to meet a national patient safety goal. *American Journal Health-System Pharmacy* 2011;**68**:974–6.

Vadher 1996 *{published data only}*
Vadher B, Patterson DLH, Leaning M. Comparison of oral anticoagulant control by nurse-practitioner using a decision-aid with that by clinicians. *British Journal of Haematology* 1996;**93**(1):31.

Vadher 1997 *{published data only}*
Vadher B, Patterson DLH, Leaning M. Evaluation of a decision support system for initiation and control of oral anticoagulation in a randomised trial. *BMJ* 1997;**314**:1252–6.

Waterman 2001 *{published data only}*
Waterman AD, Miligan PE, Banet GA, Gatchel SK, Gage BF. Establishing and running an effective telephone-based anticoagulation service. *Journal of Vascular Nursing* 2001;**19**:4.

Waterman 2001 b *{published data only}*
Waterman AD, Banet G, Miligan PE, Frazier A, Verzino E, Walton B, Gage BF. Patient and physician satisfaction with a telephone-based anticoagulation service. *Journal of General Internal Medicine* 2001;**16**:460–3.

Watzke 2000 *{published data only}*
Watzke HH, Forberg E, Svolba G. A prospective controlled trial comparing weekly self-testing and self-dosing with the standard management of patients on stable oral anticoagulation. *Thrombosis and Haemostasis* 2000;**83**:661–5.

Winans 2010 *{published data only}*
Winans ARM, Rudd KM, Triller D. Assessing anticoagulation knowledge in patients new to warfarin therapy. *The Annals of Pharmacotherapy* 2010;**44**:1152–7.

Witt 2005 *{published data only}*
Witt DM, Sadler MA, Shanahan RL, Mazzoli G, Tillman DJ. Effect of a centralized clinical pharmacy anticoagulation service on the outcomes of anticoagulation therapy. *Chest* 2005;**127**:1515–1522. [DOI: 10.1378/chest.127.5.1515]

Woodend 2005 *{published data only}*
Woodend AK. Patient self management of anticoagulants resulted in fewer major complications than clinic-based management. *Evidence-Based Nursing* 2005;**8**(3):87.

Wurster 2006 *{published data only}*
Wurster M, Doran T. Anticoagulation management: A new approach. *Disease Mangement* 2006;**9**(4):201–9.

References to ongoing studies

Hua 2011 *{published data only}*
Hua TD, Vormfelde SV, Abed MA, Schneider-Rudt H, Sobotta P, Friede T, Chenot JF. Practice nurse-based, individual and video assisted patient education in oral anticoagulation - Protocol of a cluster-randomized controlled trial. *BMC Family Practice* 2011;**12**:17.

Smith 2010 *{published data only}*
Smith DE, Borg Xuereb C, Pattison HM, Lip GYH, Lane DA. TRial of an Educational intervention on patients' knowledge of Atrial fibrillation and anticoagulant therapy, INR control and outcome of Treatment with warfarin (TREAT). *BMC Cardiovascular Disorders* 2010;**10**:21.

Stafford 2011 *{published data only}*
Stafford L, Peterson GM, Bereznicki LRE, Jackson S. A role for pharmacists in community-based post-discharge warfarin management: protocol for the 'role of community pharmacy in post hospital management of patients initiated on warfarin' study. *BMC Health Services Research* 2011;**11**:16.

Additional references

Aikens 2005
Aikens JE, Nease DE, Nau PD, Klinkman MS, Schwenk TL. Adherence to maintenance-phase antidepressant medication as a function of patient beliefs about medication. *Annals of Family Medicine* 2005;**3**:23–30.

Ansell 2004
Ansell J, Hirsh J, Poller L, Bussey H, Jacobsen A, Hylek E. The pharmacology and management of the vitamin K antagonists. *Chest* 2004;**126**:204–33.

Clifford 2008
Clifford S, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional non-adherers: application of the necessity-concerns framework. *Journal of Psychosomatic Research* 2008;**64**:41–6.

Coehlo-Dantas 2004
Coehlo-Dantas G, Thomson BV, Manson JA, Tracy CS, Upshur REG. Patients' perspectives on taking warfarin: qualitative study in family practice. *BMC Family Practice* 2004;**5**:15. [DOI: 10.1186/1471-2296-5-15]

Connolly 2008
Connolly SJ, Pogue J, Eikelboom J, Flaker G, Commerford P, Franzosi MG, et al.Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalised ratio control achieved by centres and countries as measured by time in therapeutic range. *Circulation* 2008;**118**:2029–37.

Connolly 2009
Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A. Dabigatran versus warfarin in patients with atrial fibrillation. *The New England Journal of Medicine* 2009;**361**(12):1139–51.

Connolly 2011
Connolly SJ, Eikelboom J, Joyner C, Diener HC, Hart R, Golitsy S. Apixaban in patients with atrial fibrillation. *The New England Journal of Medicine* 2011;**364**:806–17.

Dantas 2004
Dantas GC, Thomson BV, Manson JA, Tracy CS, Upshur RE. Patients' perspectives on taking warfarin: qualitative study in family practice. *BMC Family Practice* 2004;**5**:15.

ESC 2010
ESC. Guidelines for the management of atrial fibrillation. *European Heart Journal* 2010;**278**:1–61.

Farmer 2006
Farmer A, Kinmonth AL, Sutton S. Measuring beliefs about taking hypoglycaemic medication. *Diabetic Medicine* 2006; **23**:265–70.

Fuller 2004
Fuller R, Dudley N, Blacktop J. Avoidance hierarchies and preferences for anticoagulation-semi-qualitative analysis of older patients' views about stroke prevention and the use of warfarin. *Age and Ageing* 2004;**33**:608–11.

Fuster 2006
Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al.ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *Circulation* 2006;**114**:257–354.

Garcia-Alamino 2010
Garcia-Alamino JM, Ward AM, Alonso-Coello P, Perera R, Bankhead C, Fitzmaurice D, Heneghan CJ. Self-monitoring and self-management of oral anticoagulation: Review. *The Cochrane Library* 2010, (7).

Go 2001
Go AS, Hylek EM, Philips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: the anticoagulation and risk factors in atrial fibrillation (ATRIA) study. *JAMA* 2001;**285**(18): 2370–5.

Granger 2011
Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek E, Hanna M. Apixaban versus warfarin in patients with atrial fibrillation. *The New England Journal of Medicine* 2011;**365**:981–92.

Hart 2007
Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have non-valvular atrial fibrillation. *Annals of Internal Medicine* 2007;**146**:857–67.

Heeringa 2006
Heeringa J, van der Kuip DA, Hofman A, van Herpen G, Stricker BH, Stijnen J, et al.Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *European Heart Journal* 2006;**27**:949–53.

Higgins 2011
Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0*. The Cochrane Collaboration, March 2011.

Holbrook 2005
Holbrook AM, Pereira JA, Labiris R, McDonald H, Douketis JD, Crowther M. Systematic overview of warfarin and its drug and food interactions. *Archives of Internal Medicine* 2005;**165**:1095–106.

Howitt 1999
Howitt A, Armstrong D. Implementing evidence based medicine in general practice: audit and qualitative study of antithrombotic treatment for atrial fibrillation. *BMJ* 1999; **318**:1324–7.

Jessop 2003
Jessop DC, Rutter DR. Adherence to asthma medications: the role of illness representations. *Psychology and Health* 2003;**18**(5):595–612.

Kannel 1998
Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *American Journal of Cardiology* 1998;**82**(8A):2–9.

Kumar 1989
Kumar S, Haigh JR, Rhodes LE, Peaker S, Davies JA, Roberts BE, et al.Poor compliance is a major factor in unstable outpatient control of anticoagulant therapy. *Journal of Thrombosis and Haemostasis* 1989;**62**:729–32.

Lane 2006
Lane DA, Ponsford J, Shelley A, Sirpal A, Lip GYH. Patient knowledge and perceptions of atrial fibrillation

ans anticoagulant therapy. *Journal of Thrombosis and Haemostasis* 2006;**110**:354–8.

Leventhal 1992
Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence affect on cognitive interactions. *Cognitive Therapy and Research* 1992;**16**:143–63.

Lip 2002
Lip GYH, Kamath S, Jafri M, Mohammed A, Bareford D, McAlister FA. Ethnic differences in patient perceptions of atrial fibrillation and anticoagulation therapy: the West Birmingham Atrial Fibrillation Project. *Stroke* 2002;**33**: 238–44.

Lip 2006
Lip GY, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. *Thrombosis Research* 2006;**118**:321–33.

Lip 2007
Lip GYH, Agnelli G, Thach AA, Knight E, Rost D, Tangelder MJ. Oral anticoagulation in atrial fibrillation: a Pan-European Patient Survey. *European Journal of Internal Medicine* 2007;**18**:202–8.

Lip 2011
Lip GYH, Andreotti F, Fauchier L, Huber K, Hylek E, Knight E, et al.Bleeding risk assessment and management in atrial fibrillation patients: a position document from the European Heart Rhythm Association, endorsed by the European Society of Cardiology Working Group on Thrombosis. *Europace* 2011;**13**:723–46. [DOI: 10.1093/europace/eur126]

Lloyd-Jones 2004
Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al.Lifetime risk for developing atrial fibrillation: The Framingham Heart Study [1042–1046]. *Circulation* 2004;**110**.

Lloyd-Jones 2007
Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al.Lifetime risk for developing atrial fibrillation: The Framingham Heart Study. *Circulation* 2007;**110**:1042–6.

Miyasaka 2006
Miyasaka Y, Barnes ME, Gersh BJ. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation* 2006;**114**: 119–25.

Morgan 2009
Morgan CL, McEwan P, Tukiendorf A, Robinson PA, Clemens A, Plumb JM. Warfarin treatment in patients with atrial fibrillation: Observing outcomes associated with varying levels of INR control. *Thrombosis* 2009;**124**:37–41.

Nadar 2003
Nadar S, Begum N, Kaur B, Sandhu S, Lip GYH. Patients understanding of anticoagulation therapy in a multiethnic population. *Journal of the Royal Society of Medicine* 2003; **96**:175–9.

Neame 2005
Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. *Rheumatology* 2005;**44**:762–7.

NICE 2006
National Collaborating Centre for Chronic Conditions. Atrial fibrillation: national clinical guideline for management in primary and secondary care. London: Royal College of Physicians 2006.

NICE 2007
Behaviour change at population, community and individual levels. NICE Public Health Guidelines 6 2007.

O'Connor 1995
O'Connor AM. Validation of a decision conflict scale. *Medical Decision Making* 1995;**15**(1):25–30. [DOI: 10.1177/0272989X9501500105]

Patel 2011
Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *The New England Journal of Medicine* 2011; **365**:883–91.

Protheroe 2000
Protheroe J, Fahey T, Montgomery AA, Peters TJ. The impact of patients' preferences on treatment of atrial fibrillation: observational study of patient based decision analysis. *BMJ* 2000;**320**:1380–4.

Rosendaal 1993
Rosendaal FR, Cannegieter SC, van der Meer FJM, Briet E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thrombosis and Haemostasis* 1993;**69** (3):236–9.

Ruff 2010
Ruff CT, Giugliano RP, Antman EM, Crugnale SE, Bocanegra T, Mercuri M, et al.Evaluation of the novel factor Xa inhibitor edoxaban compared with warfarin in patients with atrial fibrillation: design and rationale for the effective anticoagulation with factor Xa next generation in atrial fibrillation. *American Heart Journal* 2010;**160**(4):635–41.

Schulman 2004
Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *Journal of Thrombosis and Haemostasis* 2005;**3**:692–4.

Shantsila 2010
Shantsila A, Lip GYH. Towards (cost) effective cardiovascular risk management: using new drugs vs. the better use of available ones. *International Journal of Clinical Practice* 2009;**64**(2):138–40. [DOI: 10.1111/j.1742-1241.2009.02233.x]

Steed 2010
Steed L, Newman SP, Hardman SMC. An examination of the self-regulation model in atrial fibrillation. *British Journal*

of Health Psychology 2010;**4**(4):337–47. [DOI: 10.1348/135910799168687]

Stewart 2001

Stewart S, Hart CL, Hole DJ. Population prevalence, incidence, and predictors of atrial fibrillation in the Renfew/Paisley study. *Heart* 2001;**86**(5):516–21.

Stewart 2004

Stewart S, Murphy N, Walker A, McGuire A, McMurray JJV. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart* 2004;**90**:286–92.

Tang 2003

Tang E, Lai C, Lee K, Wong RSM, Cheng G, Chan TYK. Relationship between patients warfarin knowledge and anticoagulation control. *Annals of Pharmacotherapy* 2003;**37**:34–9.

Thrall 2004

Thrall G, Lip GYH, Lane D. Compliance with pharmacological therapy in hypertension: can we do better, and how?. *Journal of Human Hypertension* 2004;**18**:595–7.

Wallentin 2010

Wallentin L, Yusuf S, Ezekowitz MD, Alings M, Flather M, Franzosi MG, et al.Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: analysis of the RE-LY trial. *Lancet* 2010;**376**(9745):975–83.

Ware 1992

Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). *Medical Care* 1992;**30**(6):473–83.

Wofford 2008

Wofford JL, Wells MD, Singh S. Best strategies for patient education about anticoagulation with warfarin: a systematic review. *BMC Health Service Research* 2008;**8**:40.

Wolf 1991

Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991;**22**(8):983–8.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Beyth 2000

Methods	Randomised, controlled, parallel-groups design
Participants	**N randomised:** 132 versus 162 usual care **Diagnosis of ppts:** AF n=54 (16.6%) for the intervention group and usual care groups. Other indications include venous thromboembolism, cerebrovascular disease, heart valve prosthesis, peripheral vascular disease, myocardial infarction **Demographics for total cohort:** Age:74.9±6.9 versus 74.5±6.6 % female: 55 versus 59% usual care % white: 69% versus 65% usual care Mean number of school years 12.1±4.4 [intervention], 12.1±4.1 [usual care] **Demographics for AF patients:** Age: 74.6±6.8 intervention versus 75.5± 6.2 usual care % female: 40% versus 66% usual care % white: 77% versus 77% usual care Mean number of school years 14.5±4.9 [intervention], 12.0±3.9 [usual care] **Inclusion/exclusion criteria:** Patients hospitalised and receiving 10000 units or more of intravenous heparin, were 65 years or over, for whom warfarin treatment was planned for 10 days or more. Patients were excluded if they had been treated with warfarin at any time in the previous 6 months, were admitted from a nursing home, were enrolled in another clinical trial, were too ill to give consent or did not speak English
Interventions	**Type:** Guideline-based consultation, Education and self-monitoring **Content:** A consultation that assessed the patients indication for therapy and potential risks for warfarin related bleeding (a method used by the researchers previously). This included specific recommendations about modifiable risk factors, such as use of non-steroidal anti-inflammatory drugs.The other component included patient education, coaching and self monitoring. Patient education consisted of one to one teaching by a lay educator using a specifically formatted workbook for older adults to teach them about warfarin, indications for its use, drug and food interactions, and the signs and symptoms of bleeding. Coaching aimed to increase patients participation in their care and improve information seeking-skills. Self-monitoring of prothrombin time (grounded in social learning theory). Patients were taught to self-monitor prothrombin time. Patients instructed to use monitor 3 times in first week and once weekly after that **Duration:** 30 minutes-1 hour (consultation) **Facilitator:** lay educator **Setting:** hospital
Outcomes	Incidence of major bleeding Excessive anticoagulation Rates of VTE
Country	Cleveland, Ohio, USA

Beyth 2000 (*Continued*)

Comparison	Usual care group	
Length follow-up	6 months	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were stratified according to their baseline risk for major bleeding by using the outpatient bleeding risk index. The index includes 4 independent risk factors for major bleeding: age 65 or older, history of gastrointestinal bleeding, history of stroke, and one or more of four specific comorbid conditions (myocardial infarction, hematocrit<30%, creatinine concentration> 133µmol/L (1.5mg/dL), or diabetes mellitus). Patients with one or two risk factors were classified as intermediate risk, and those with 3 or more risk factors were classified as high risk; estimated frequencies of major bleeding in 6 months were 6% and 35% respectively
Allocation concealment (selection bias)	Low risk	426 eligible patients were identified, 294 (69.0%) received either usual care or the intervention. This indicates low risk of selection bias
Blinding (performance bias and detection bias) All outcomes	Low risk	The educational intervention was delivered by a lay educator that was not involved in the treatment of the patients
Incomplete outcome data (attrition bias) All outcomes	High risk	81% (n=132) of the 163 patients assigned to the intervention group participated in the intervention. 12 patients felt more comfortable with venipuncture, 3 stopped warfarin during hospitalisation, and 1 was discharged to a nursing home that precluded the use of a portable monitor. At 6 months 21 patients (13%) in the intervention group and 26 (16%) of the usual care group had died

Beyth 2000 (*Continued*)

Selective reporting (reporting bias)	Low risk	The method section describes the primary outcome as first major bleeding event during the 6 month intervention period. Secondary outcomes were death and recurrent VTE at 6 months; major bleeding after 6 months and INR control during the first 6 months of therapy. The authors report data on all of these outcomes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants cannot be blinded to which arm of the trial they receive. Neither can the personnel delivering the intervention be blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Trained abstractors who were not involved with the intervention component of the study collected data from the medical chart at the start of OAC, and by blinded interview at enrolment at 1, 3, 6 months after enrolment and every 6 months thereafter. Whenever an event was reported, the clinical characteristics of the bleeding or thromboembolic episode were determined by review of the relevant medical record and abstracted without identifying the patient onto a standard form

Christensen 2007

Methods	Open-label randomised controlled trial, cross-over (6 months)
Participants	**N randomised:** 47 versus 45 (usual care/conventional management) **AF:** n=11 versus n=9 (usual care), other indications include mechanical heart valve, coagulopathies, VTE, synthetic vascular graft **Demographics for total cohort:** Age: 51.5±14.4 versus 46.3±13.4 (usual care) % female: 23% versus 44% (usual care) % white: not stated % education above primary level: not stated **Demographics for AF cohort:** Age (SD): 59 (18) versus 51 (12) % female: 0% intervention versus 7% usual care % white: 100% in both groups % high school or greater: 4% versus 3% usual care **Inclusion/exclusion criteria:** Patients were eligible if they were referred for patient self-management by a general practitioner or hospital department, treated with oral anticoagulants >8 months, 18 years or over, willing to be randomised. Patients were excluded if they had previously used

	self-management or lived abroad
Interventions	**Type:** Teaching lesson (not explained in detail) and patient self-management (PSM) Content: The group used Coagucheck, which displays the INR value after the application of a drop of blood. Self-management training included patient practicing analysis of blood specimens. The patient gradually assumed management of OAC. After 27 weeks patients took an exam, if passed patient went on to self-manage. After 6 months the conventional management group started the same training **Duration:** not stated **Facilitator:** not stated **Setting:** hospital
Outcomes	Major complications (bleeding and thromboembolism requiring intervention) Death and/or discontinuation of the study Primary endpoint: variance of INR in trial and control samples TTR
Country	Aarhus, Denmark
Comparison	Conventional management
Length follow-up	0bservation period 1) 8-12 months before randomisation 2) primary observation period (6 months of either patient self-management or conventional management) 3) patient self-management training (27 weeks)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned to patient self-management using a computerised, prospective, randomisation schedule. Randomisation in blocks with various sizes in numbers of 2,4, and 6 was used
Allocation concealment (selection bias)	Low risk	105 patients were eligible to take part in the study and 100 patients were randomised (95%), therefore there is a low risk of selection bias
Blinding (performance bias and detection bias) All outcomes	Unclear risk	It was unclear whether the personnel delivering the intervention was also involved in treating the usual care arm

Christensen 2007 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	In the self-management arm three patients dropped out, two during the training period, and one died. In the usual care arm of the study one patient was withdrawn by the physician and four dropped out during the self-management training. Thus 92% of original cohort participants were included in the analysis
Selective reporting (reporting bias)	Low risk	The endpoints were the variance (mean square of standard deviation) of the INR value, the median INR value (using a blinded control sample analysed monthly by a reference laboratory) and the coumarin dose. All outcomes were reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Due to the nature of the intervention, the participants receiving the intervention and the personnel delivering it cannot be blinded to which arm of the intervention they are in
Blinding of outcome assessment (detection bias) All outcomes	Low risk	External control blood samples were blinded. The results of the INR analysis was blinded for all except one secretary who would ensure the safety of the patient by contacting the managing physician if the INR value was below 1.5 or above 4.5

Gadisseur 2003

Methods	Multicentre randomised study, 4 arms
Participants	**N randomised:** A) weekly self-measurement n=52; B) weekly self measurement and self-dosing n=47; C) educated routine care n=60; D) existing routine care (not trained) n=161. This study used a Zelen design Diagnosis of ppts: number of AF patients in group A=6 (11.6%), group B=9 (19.2%), group C=10 (16.6%), and group D=43 (26.7%). Other indications included DVT, PE, artificial heart valves, vascular prosthesis **Demographics for total cohort:** Age: mean age A=54.8 (25-74), B=53.9 (24-75), C=56 (21-73), D=62 (32-75) % female: A=23%, B=32%, C=40%, D=46% % white: not stated % education above primary level: not stated **Demographics for the AF patients:** not provided **Inclusion/exclusion criteria:** At least >3 months of OAT experience, need for long-term OAT, aged 18-75. Patients were excluded if they had antiphospholipid syndrome, a life threatening illness, life ex-

	pectancy ≤1 year, diminished understanding, and physical limitations making successful participation impossible	
Interventions	**Type:** self-management and self-dosing including education **Content:** They received information about the study, the blood coagulation system, OAT, and the effects of some substances (eg. alcohol, certain medications and foods rich in vitamin K) on OAT; then they were also taught how to use Coagucheck device, and instructed on oral self-dosing of phencoumon and acenocoumarol. This also contained practical information about working with the Coagucheck, information about the coagulation system, theoretical and practical self-dosing training. They were also given written information on all the topics discussed Group A: weekly INR self-measurement, but dosing was performed by anticoagulation clinic physicians. Patients reported their INR values by telephone to the anticoagulation clinics. Dosing schedules communicated via telephone Group B: this group self-managed their OAT, patients informed the anticoagulation clinic of their INR measurements, proposed dosing schedules and reported any relevant information or complications. Patients were contacted via telephone to confirm whether they could adhere to their proposed dosing schedule or if they needed to adjust it Group C: patients were trained for inclusion in groups A or B but stayed with the routine care system. Measurements of INR and dosing were done by anticoagulation clinic physicians, and the interval between INR measurements depended on the stability of the INR values Group D: patients in this group were unaware of their participation in the study, representing the existing care system **Duration:** 3 training sessions, groups of 4-5, 90-120 minutes **Facilitator:** delivered by physician, paramedical person **Setting:** hospital	
Outcomes	Quality of life (questionnaire developed by Sawicki et al), 32 items, validated. The questionnaire was meant to measure patient concerns, the impact of self-monitoring of INR, and the possibility of increased education. Translated from German to Dutch and marginally altered for relevance in the Netherlands	
Country	Netherlands	
Comparison	A) weekly self-measurement B) weekly self-measurement and self-dosing C) educated routine care D) existing routine care (not trained)	
Length follow-up	Mean follow-up time 24.5 weeks	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	Low risk	The patients were selected by groups of 40 and randomised to 4 treatment groups (A, B, C and D) following a 2-step partial zelen design
Allocation concealment (selection bias)	High risk	Of the 881 eligible participants, 159 (18%) were randomised, therefore this study is at high risk of inclusion bias. 916 patients were randomly selected by a computer, 35 (3.9%) were excluded because of intellectual or physical limitations or because of a life expectancy of < 1 year
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The authors do not state whether those physicians delivering the intervention also treated the usual care arm
Incomplete outcome data (attrition bias) All outcomes	High risk	116 (64%) of the original 180 patients randomised to the study completed the quality of life questionnaires at baseline and follow-up. 21 patients were withdrawn or ineligible and the remainder were lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Pre-specified endpoints were (1) quality of OAT represented by the number of INR readings within target range (TTR); (2) patients ability to independently perform anticoagulant self-dosing, by number of dosage corrections made. All specified outcomes were reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Patients who were not randomised to group D were sent a letter with written information about the study (thus not blinded). Knowledge of the composition of the different groups was restricted to a few nurses who were also responsible for anonymously transferring the dosing schedules for group A and group B patients to standard forms and faxing them to the other participating anticoagulation clinics. The patients and staff could not be blinded to which arm of the trial participants were assigned to
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The physicians evaluating and correcting the proposed dosing schedules for group A and B were unaware of the originators of these schedules. The INR values of the patients in routine care groups C and D were entered into the routine computerised system in such a way that the dosing physicians could not distinguish be-

		tween these and the general patient population

Man-Son-Hing 1999

Methods	Randomized controlled trial 20 possible SPAF trial centres invited, 14 participated
Participants	**N randomised:** intervention n= 139 (10 lost to follow-up); control n=148 (14 lost to follow-up) Diagnosis of ppts: all atrial fibrillation **Demographics of cohort:** Age: intervention mean=65, control mean=65 % female: intervention 24%, control 24% % white: not stated % education above primary level: intervention 90% high school education or greater, control 91% high school education or greater **Inclusion/exclusion criteria:** all participants were in the SPAF III aspirin cohort study and were eligible unless they had high risk criteria or had a major haemorrhage during the study
Interventions	**Type:** decision aid **Content:** 29 page booklet, a personal worksheet (complete pre-intervention), 20-minute audiotape that guided the patient through the booklet and worksheet. The intervention included a description of the consequences of minor/major stroke and major haemorrhage, the blood monitoring required for warfarin and the 2-year probability of stroke and major haemorrhage for patients taking aspirin/warfarin using pictograms **Duration:** not stated **Facilitator:** physician/audio tape **Setting:** hospital
Outcomes	1-4 days after meeting with their physicians patients completed questionnaires Patient choices (strength of their decisional input, 5-point Likert scale, unvalidated) Knowledge (23 questions about AF, stroke and treatment, unvalidated) Expectations (4 questions regarding patient expectations of stroke/haemorrhage, unvalidated) Decisional conflict (decisional conflict scale, ref: O'Connor 1995) Satisfaction (6 questions, 5-point Likert scale, unvalidated) Six-month adherence to their treatment decisions (self-report brief questionnaire, administered via telephone, unvalidated)
Country	US
Comparison	Control group, usual care, i.e. no change was made to the usual manner in which each centre communicated the results of the SPAF III study or the way in which the decision regarding type of antithrombotic was made
Length follow-up	6-month follow-up

Man-Son-Hing 1999 (*Continued*)

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated scheme, administered from a central location to block sequence from previewing. Stratified by centre and the presence of a history of hypertension
Allocation concealment (selection bias)	High risk	657 patients were eligible for the trial, 287 participated (43%), giving a substantial risk of inclusion bias. 24 participants were lost to follow-up
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The authors do not state whether those physicians delivering the intervention also treated the usual care arm
Incomplete outcome data (attrition bias) All outcomes	Low risk	87 (63%) worksheets from 139 patients participating were completed. However, all of the 139 patients randomised to the decision aid were included in the study analysis of decision conflict
Selective reporting (reporting bias)	Low risk	Outcome measures were patients' ability to make choices regarding antithrombotic therapy, 6-month adherence to decision, knowledge, decision conflict and satisfaction. There was no protocol paper for this study. However, one of the pre-specified outcome variables in the method section was not reported (patient satisfaction)
Blinding of participants and personnel (performance bias) All outcomes	High risk	The authors do not state whether the researcher or personnel were blinded to which arm the participants were randomised to. However, we can assume that participants and physicians were not blinded to treatment allocation due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The authors do not state whether the personnel scoring and analysing the questionnaires were blinded to the treatment allocation

McAlister 2005

Methods	Prospective, multicentre, two-arm, cluster randomised trial.
Participants	**N randomised:** intervention n=219, control n=215 50 GP practices were randomised to the decision aid group and 52 were randomised to usual care Diagnosis of participants: All NVAF (also broken down type of AF, see paper) **Demographics of cohort:** Age: intervention 73±9; controls 71±10 % female: intervention 43%, controls 34% % white: not stated % education above primary level: completed high school: intervention n=84 (38%), usual care n=72 (33%) **Inclusion/exclusion criteria:** community-dwelling patients, over the age of 18, will be included in this study if they have a diagnosis of NVAF (intermittent or chronic) confirmed by ECG or prescription for digoxin. They were excluded if they had 1) valvular AF; 2) taking warfarin for another condition; 3) are scheduled for cardioversion; 3) have a contraindications for warfarin or aspirin; 4) cognitive impairment; 5) their life expectancy is less than 12 months; 6) cannot understand/converse in English
Interventions	**Type:** general education session plus patient decision aid and physicians manual **Content:** 30-page decision aid booklet, personal worksheet, 50-minute audiotape to guide participants through the booklet and worksheet, and a 7-page physicians manual summarising the evidence discussed in the patient booklet with a focus on the 2001 ACCP risk stratification schema and recommendations for antithrombotic therapy. 4 versions of the decision aid were available depending on patient's baseline stroke risk. All four versions provide the same background information about AF; the potential consequences of stroke and major haemorrhage, relative efficacy/bleeding risks with warfarin and aspirin therapy. Key points are further elaborated upon in the audio-tape. The 1 page worksheet is to be completed by the patient after reviewing the booklet to clarify their personal values regarding desired outcomes, the therapy they are inclined to take, their preferred role in the decision process, and any questions they have for their physician **Duration:** not stated **Facilitator:** physician **Setting:** GP practices
Outcomes	Use of appropriate antithrombotic therapy at 3 months, as defined by the 2001 ACCP recommendations. Secondary outcomes include (1) appropriate antithrombotic therapy at 6 months and 12 months, (2) patient's readiness to make a choice at baseline (previously validated questionnaire, with reference), (3) patient knowledge after the intervention (multiple-choice responses used in previous trial, with reference), (4) decisional conflict - decision conflict scale (O'Connor), (5) acceptability of decision aid (9 questions with variable responses on a 5-point Likert scale), (6) satisfaction (5-point Likert scale), (7) adherence with therapy (validated Morisky scale with modified 5-point Likert scale response)
Country	Canada
Comparison	Usual care

Length follow-up	1-year follow-up
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation to intervention or usual care is being carried out according to a computer-generated sequence using clustered block randomisation (block size of four) with allocation concealment
Allocation concealment (selection bias)	High risk	904 patients were eligible for the study. 446 patients were randomised (49%). Due to the number of patients declining screening, there is an increased risk of inclusion bias
Blinding (performance bias and detection bias) All outcomes	Low risk	Physicians that delivered the intervention did not treat the usual care arm
Incomplete outcome data (attrition bias) All outcomes	Low risk	446 eligible participants were randomised. 434 (97%) were included in the 3-month follow-up evaluation
Selective reporting (reporting bias)	Low risk	The primary endpoint was use of appropriate antithrombotic therapy, other endpoints include TTR, patients readiness to make choices, knowledge, decision conflict, acceptability of decision aid, satisfaction, and adherence. Adherence and satisfaction scales data are not explained in detail. However, authors report the majority of data from the protocol paper including key primary and secondary outcomes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The authors do not state whether the researcher or personnel were blinded to which arm the participants were randomised to. However, we can assume that participants and physicians were not blinded to treatment allocation due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The outcome assessment was carried out by an independent statistician who was blinded to group allocation

Polek 2012

Methods	Nested randomised controlled trial
Participants	**N randomised:** intervention=25, usual care = 28 Mixed indication cohort **Demographics of the cohort:** mean (SD) age = 63.71 (16.04) % female: not stated % white: not stated % educated above primary school level: not stated **Demographics of the AF patients:** N=14 Treatment group n= 5; usual care n= 9 Age, mean (SD): intervention = 73.6 (11.1), usual care = 76 (13.4) % female: intervention = 4/5 (80%), usual care = 3/9 (33%) % white: intervention = 3/5 (60%), usual care = 5/9 (55%) % educated above primary school level: not available **Inclusion criteria:** patients discharged to home on OAT, alert and orientated, able to speak and understand English, and accessible via telephone **Exclusion criteria:** patients discharged to a nursing home or rehabilitation facility, history of psychotic disorder or cognitive impairment
Interventions	**Type:** Enhanced educational intervention **Content:** face-to-face warfarin education, printed materials, instruction, medical alert bracelet. The intervention was based on Banduras social cognitive model and aimed to improve self-efficacy. Four post-discharge phone calls assessing knowledge post-intervention and correcting incorrect answers **Duration:** not stated **Facilitator:** pharmacist **Setting:** hospital
Outcomes	Warfarin knowledge Self-efficacy
Country	USA
Comparison	Usual care
Length follow-up	12 weeks
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Patients were randomly assigned to the intervention or usual care group after receiving patient education from the pharmacist. Authors do not describe the sequence generation

Polek 2012 (*Continued*)

Allocation concealment (selection bias)	Low risk	66 patients were screened and offered participation in the study. There were 53 patients included in the original randomised sample (80% of those screened), with a low risk of inclusion bias. 42 of the original sample of 53 completed the study (79%)
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The authors do not state whether the personnel delivering the intervention also treated the usual care arm
Incomplete outcome data (attrition bias) All outcomes	High risk	The final sample included 42 (79%) of the original 53 patients that were randomised to the study
Selective reporting (reporting bias)	Low risk	The authors describe two outcomes in their method section (1) warfarin knowledge and (2) self-efficacy. The authors report on both outcomes in their results section. There was no published protocol paper, thus we cannot determine whether those outcomes reported reflect those that were included in the study
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The authors do not state whether the researcher or personnel were blinded to which arm the participants were randomised to. However, we can assume that participants and physicians were not blinded to treatment allocation due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Authors do not state whether the person scoring the questionnaires was blinded to the treatment allocation

Thomson 2007

Methods	Three/2-armed open, randomised controlled efficacy trial
Participants	**N randomised:** 69 decision aid versus 67 guidelines % AF: all AF patients **Demographics of cohort:** Age: 73.1±6.7 decision aid versus 73.7±6.2 guidelines % female: 43.4 decision aid versus 44.6 guidelines % white: not stated % education above primary level: not stated **Inclusion/exclusion criteria:** patients were recruited if they were already taking warfarin or if they were considering taking warfarin for the first time. Patients were eligible if they aged 60 or over and had either chronic NVAF or PAF. Patients were excluded if they were acute onset AF requiring cardioversion, previous stroke or TIA, contraindications

	for warfarin, taking warfarin for other indications, cognitive impairment, non-English speaking, or at risk of cerebral bleed
Interventions	**Type:** decision aid **Content:** included individual risk and benefit presentation and a section to support shared decision making 2 different decision aids 1. Used explicit value elicitation employing the standard gamble method and Markov decision analysis "explicit tool" 2. Included only risk/benefit presentation "implicit tool" (computerised decision aid). The doctor was trained to use the computerised decision aid Early in the trial, the observation study (running alongside the trial) found the first decision aid to be difficult, so this arm was discontinued (gamble method) and the paper describes the results of the second arm versus evidence-based paper guidelines. The intervention arm included benefits and harms of warfarin treatment, advantages and disadvantages, personalised risk assessment (using the Framingham equation). The presentation used graphical and numerical forms of presentation **Duration:** mean 31 minutes long (range 16-41) **Facilitator:** computerised tool **Setting:** research clinic
Outcomes	Decision conflict Knowledge State trait anxiety inventory Degner's decision making preference scale
Country	Newcastle, UK
Comparison	Guideline-based consultation
Length follow-up	3 months
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomised to either: (a) computerised decision aid (intervention) or (b) evidence-based paper guidelines (control), using electronically-generated random permuted blocks via a web-based randomisation service provided by the Centre for Health Services Research
Allocation concealment (selection bias)	High risk	483 patients were eligible for the study, 145 patients were eventually randomised (30%) . Thus there is a substantial risk of inclusion

		bias
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The authors do not state whether those physicians delivering the intervention also treated the usual care arm
Incomplete outcome data (attrition bias) All outcomes	Low risk	16 (23%) of the 69 patients allocated to the decision aid tool did not receive the intervention. 11 (16%) of the 67 patients allocated to the guidelines group did not receive the intervention. In total 19% of patients randomised did not receive the intervention. Reasons included withdrawal of consent, death, illness, surgery, alcoholism, and inability to use the tool
Selective reporting (reporting bias)	Unclear risk	The primary outcome was decision conflict. Secondary outcomes were state trait anxiety, knowledge and decision making preference. Decision conflict outcomes were reported, but there was no tabulated report of the scale breakdown. All of the outcomes were reported, but mean scores and numbers of patients per group were not
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The authors do not state whether the researcher or personnel were blinded to which arm the participants were randomised to. However, we can assume that participants and physicians were not blinded to treatment allocation due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The authors do not state whether the person scoring the questionnaires was blinded to the treatment allocation

Voller 2005

Methods	Prospective multicentre randomised controlled trial
Participants	**N randomised:** 101 self-management versus 101 family doctor group All NVAF patients **Demographics of cohort:** Age: 64.6±9.6 self-management versus 64.1±8.9 family doctor % female: 28.6 self-management versus 38.6 family doctor % white: not stated % education above primary level: not stated **Inclusion/exclusion criteria:** all patients whom long-term anticoagulation was indi-

	cated because of permanent non-valvular atrial fibrillation were to be included into the investigation. Exclusion criteria were the lack of suitability for INR self-management, participation in another study, alcohol or other addiction, a mechanical heart valve replacement or anticoagulant treatment already administered for another indication and diseases such as AIDS or carcinomas. Patients with visual impairment were also excluded
Interventions	**Content:** educational session following the standards of the working group for self monitoring of anticoagulation ASA. Based on the intervention session developed my Sawicki and colleagues (ref 12). The programme consisted of three consecutive weekly teaching sessions for groups of 3 to 6 patients. Topics included anticoagulation in general, INR self-monitoring, preventing bleeding, effects of diet and other medication, reducing or increasing dose, problems that may be encountered with operations, illness, exercise, pregnancy etc **Duration:** 60-90 minutes (based on Sawicki's description) **Facilitator:** not stated **Setting:** not stated
Outcomes	**Primary endpoint:** number of thromboembolic or hemorrhagic complications requiring treatment **Secondary endpoints:** the degree of handicap after stroke, the degree of severity of haemorrhage, the proportion as well as cumulative time of the INR values in the individual target range, INR variance, time course of complications and the cost efficiency of self-measurement compared to conventional procedures
Country	Germany
Comparison	Family doctor group
Length follow-up	Overall observation period (retrospective): self-management 37.34±5.93 years family doctor 40.25±6.07 years
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation list developed before beginning of the study with SAS-procedure PROC PLAN
Allocation concealment (selection bias)	Unclear risk	Authors do not report how many participants were eligible for the study
Blinding (performance bias and detection bias) All outcomes	Unclear risk	The authors do not state whether those physicians delivering the intervention also treated the usual care arm

Incomplete outcome data (attrition bias) All outcomes	Low risk	202 patients were randomised to the study and all of these patients were included in the final analysis
Selective reporting (reporting bias)	High risk	The study was discontinued because the number of cases was too small, and the group comparison was confined to the evaluation of the number of INR values measured and the total period for which the patients remained outside, above and below the target range
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The authors do not state whether the researcher or personnel were blinded to which arm the participants were randomised to. However, we can assume that participants and physicians were not blinded to treatment allocation due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The authors do not state whether the person scoring the questionnaires was blinded to the treatment allocation

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Armstrong 2011	Not an RCT
Bajorek 2005	Not an RCT, no control group
Baker 1991	Wrong patient group, no AF
Barcellona 2006	No unpublished AF data provided on request
Batty 2001	Does not measure any of the required outcomes
Blaise 2009	Not an RCT, retrospective study
Bloomfield 2011	Meta-analysis, not an RCT
Bump 1977	No AF patients
Burns 2009	Not an RCT, review paper

(*Continued*)

Castelino 2010	Not an RCT
Chan 2006	No unpublished AF data provided on request
Christensen 2011	Limited education, specific to self-testing
Claes 2005	No AF patients
Claes 2006	No AF patients
Corbella 2009	Not an RCT
Cordasco 2009	No AF patients
Cromheecke 2000	No AF patients
Cromheecke 2001	No AF patients
Davis 2005	Not an RCT, survey
Dolor 2010	No education other than instruction to self-test
Duran-Parrondo 2011	Trial is not randomised
Field 2010	Training is for staff not patients
Fitzmaurice 1996	Not a patient intervention
Fitzmaurice 2000	Did not include an educational or behavioural intervention
Fitzmaurice 2005	No AF patients
Fraenkel 2011	Not compared to usual care, not an RCT
Gardiner 2006	No unpublished AF data provided on request
Gouin-Thibault 2010	Intervention for staff not patients
Grunau 2011	Patients were educated on self-monitoring only
Hasan 2011	Not an RCT
Holbrook 2007	No AF patients
Jackson 2004	Does not measure any of the required outcomes
Khan 2004	Randomisation procedure did not meet inclusion criteria

(*Continued*)

Krause 2010	Systematic review not an RCT
Landefeld 1992	No AF patients
Leger 2004	Not an RCT, wrong patient group
Machtinger 2007	No unpublished AF data provided on request
Matchar 2005	No education or behaviour change within the intervention
Matchar 2010	Self-monitoring only, no educational or behavioural intervention
Mazor 2007	No AF patients
McCahon 2011	No breakdown of patient group
Megden 1999	Not an RCT
Menendez-Jandula 2005	No unpublished AF data provided on request
Nedaz 2002	Not an RCT, this paper is a commentary
Nilsson 2011	Abstract only, no mention of AF patients
Pernod 2008	No AF patients
Polzien 2007	Not an RCT, commentary
PRISM Study group 2003	Does not include any of the primary or secondary outcomes
Reverdin 2011	Not an RCT
Ryan 2009	No unpublished AF data provided on request
Saokaew 2010	Systematic review and meta-analysis, not an RCT
Satger 2009	Not an RCT, review article
Sawicki 1999	No unpublished AF data provided on request
Sawicki 2003	Not an RCT, no comparison group
Siebenhofer 2007	No unpublished AF data provided on request
Stone 1989	No unpublished AF data provided on request
Sunderji 2005	Education only relates to self-monitoring

(*Continued*)

Taylor 1997	Not an RCT
Trivalle 2010	Education of staff not patients
Tuiskula 2011	Not an RCT
Vadher 1996	No breakdown of patient group
Vadher 1997	No breakdown of patient group
Waterman 2001	No AF patients, no comparison group
Waterman 2001 b	No patient intervention
Watzke 2000	No unpublished AF data provided on request
Winans 2010	Not an RCT
Witt 2005	Not an RCT, retrospective, observational cohort study
Woodend 2005	Not an RCT (commentary)
Wurster 2006	Not an RCT

Characteristics of ongoing studies *[ordered by study ID]*

Hua 2011

Trial name or title	Practice nurse-based, individual and video-assisted patient education in oral anticoagulation - Protocol of a cluster-randomized controlled trial (No trial acronym)
Methods	Cluster randomised controlled trial of 22 GP practices
Participants	All patients taking OAT (with a range of indications)
Interventions	Educational intervention including a video, brochure and individual training session versus usual care
Outcomes	Primary outcome: number of correctly answered questions from the 13-item OAT questionnaire Secondary outcomes: time spent in therapeutic range, subjective feelings of safety and complications related to OAT
Starting date	January 2011
Contact information	thanhduchua@med.uni-goettingen.de
Notes	

Smith 2010

Trial name or title	TRial of an Educational intervention on patients' knowledge of Atrial fibrillation and anticoagulant therapy, INR control, and outcome of Treatment with warfarin (TREAT)
Methods	Randomised controlled trial
Participants	Newly diagnosed AF patients
Interventions	One-off one-hour educational intervention, with DVD, consultation, worksheet and booklet
Outcomes	TTR, knowledge, illness perceptions, beliefs about medication, cost-effectiveness, hospital anxiety and depression, quality of life, stroke, thromboembolic events, major and minor bleeding
Starting date	December 2010
Contact information	d.a.lane@bham.ac.uk
Notes	

Stafford 2011

Trial name or title	A role for pharmacists in community-based post-discharge warfarin management: protocol for the 'the role of community pharmacy in post hospital management of patients initiated on wafarin' study (No acronym)
Methods	Prospective controlled cohort study
Participants	All patients discharged from hospital on warfarin
Interventions	Post-discharge warfarin management service, visits involve a home medicines review, warfarin education, provision of resources dependent on patients understanding and INR monitoring
Outcomes	Primary outcome: proportion of patients experiencing a major bleeding event in the 90 days after hospital discharge Secondary outcomes: INR control (TTR), warfarin-related adverse events, warfarin knowledge, QoL, adherence
Starting date	2011
Contact information	leanne.stafford@utas.edu.au
Notes	

DATA AND ANALYSES

Comparison 1. Time in therapeutic INR range

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time in therapeutic INR range	2	69	Mean Difference (IV, Random, 95% CI)	6.31 [-5.63, 18.25]

Comparison 2. Decision conflict

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Decision conflict	2	721	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.17, -0.02]

Analysis 1.1. Comparison 1 Time in therapeutic INR range, Outcome 1 Time in therapeutic INR range.

Review: Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation

Comparison: 1 Time in therapeutic INR range

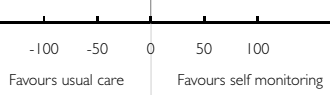
Outcome: 1 Time in therapeutic INR range

Study or subgroup	Self monitoring N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Christensen 2007	11	77.3 (11.59)	9	67.96 (23.52)		50.3 %	9.34 [-7.48, 26.16]
Gadisseur 2003	6	70.32 (18.73)	43	67.08 (26.43)		49.7 %	3.24 [-13.70, 20.18]
Total (95% CI)	**17**		**52**			**100.0 %**	**6.31 [-5.63, 18.25]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.25$, df = 1 (P = 0.62); $I^2 = 0.0\%$

Test for overall effect: Z = 1.04 (P = 0.30)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 Decision conflict, Outcome 1 Decision conflict.

Review: Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation

Comparison: 2 Decision conflict

Outcome: 1 Decision conflict

Study or subgroup	Decision aid N	Mean(SD)	Usual care N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Man-Son-Hing 1999	139	1.65 (0.45)	148	1.74 (0.54)		40.2 %	-0.09 [-0.20, 0.02]
McAlister 2005	219	1.6 (0.5)	215	1.7 (0.5)		59.8 %	-0.10 [-0.19, -0.01]
Total (95% CI)	**358**		**363**			**100.0 %**	**-0.10 [-0.17, -0.02]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.02$, df = 1 (P = 0.89); $I^2 = 0.0\%$

Test for overall effect: Z = 2.59 (P = 0.0097)

Test for subgroup differences: Not applicable

APPENDICES

Appendix 1. Search strategy

The Cochrane Library

#1 MeSH descriptor patient education as topic this term only
#2 MeSH descriptor attitude to health explode all trees
#3 MeSH descriptor patient participation this term only
#4 MeSH descriptor behavior therapy this term only
#5 MeSH descriptor cognitive therapy this term only
#6 MeSH descriptor counseling explode all trees
#7 MeSH descriptor motivation this term only
#8 MeSH descriptor goals this term only
#9 MeSH descriptor Biofeedback (Psychology) this term only
#10 MeSH descriptor decision support techniques this term only
#11 MeSH descriptor Communications Media explode all trees
#12 education in All Text
#13 (training in All Text or train in All Text)
#14 (teaching in All Text or teach in All Text)
#15 (behaviour* in All Text or behavior* in All Text)
#16 "patient knowledge" in All Text
#17 counsel* in All Text

#18 (cognitiv* in All Text near/3 therapy in All Text)
#19 (cognitiv* in All Text near/3 intervention* in All Text)
#20 motivation* in All Text
#21 contingency next management in All Text
#22 (biofeedback in All Text or bio-feedback in All Text)
#23 (goal in All Text or goals in All Text)
#24 (decision* in All Text near/3 aid* in All Text)
#25 pamphlet* in All Text
#26 booklet* in All Text
#27 video* in All Text
#28 decision next aid* in All Text
#29 "patient participation" in All Text
#30 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10)
#31 (#11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20)
#32 (#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29)
#33 (#30 or #31 or #32)
#34 MeSH descriptor warfarin this term only
#35 MeSH descriptor Coumarins explode all trees
#36 MeSH descriptor anticoagulants this term only
#37 MeSH descriptor vitamin k explode all trees with qualifiers: AI
#38 oral next anticoagula* in All Text
#39 Oral next anti-coagula* in All Text
#40 ("vitamin K" in All Text and (antagonist* in All Text or inhibitor* in All Text))
#41 "antivitamin K" in All Text
#42 "anti-vitamin K" in All Text
#43 warfarin in All Text
#44 acenocoumarol in All Text
#45 sintrom in All Text
#46 sinthrome in All Text
#47 jantoven in All Text
#48 marevan in All Text
#49 coumadin* in All Text
#50 waran in All Text
#51 phenprocoumon in All Text
#52 nicoumalone in All Text
#53 VKA in All Text
#54 coumarin* in All Text
#55 dicoumarol in All Text
#56 dicumarol in All Text
#57 (#34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43)
#58 (#44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56)
#59 (#57 or #58)
#60 (#33 and #59)

MEDLINE on Ovid

1. Warfarin/
2. acenocoumarol/
3. Coumarins/
4. Phenindione/
5. Dicumarol/
6. Anticoagulants/
7. oral anticoagula$.tw.

8. exp Vitamin K/ai [Antagonists & Inhibitors]
9. warfarin.tw.
10. acenocoumarol.tw.
11. sintrom.tw.
12. sinthrome.tw.
13. jantoven.tw.
14. marevan.tw.
15. coumadin$.tw.
16. waran.tw.
17. Phenprocoumon/
18. nicoumalone.tw.
19. (vitamin k adj3 antagonist$).tw.
20. vitamin k inhibitor$.tw.
21. oral anticoagula$.tw.
22. oral anti-coagula$.tw.
23. vka.tw.
24. antivitamin k.tw.
25. anti-vitamin k.tw.
26. or/1-25
27. Patient Education as Topic/
28. exp Attitude to Health/
29. Patient Participation/
30. ((educat$ or train$ or teach$) adj3 (program$ or intervention$)).tw.
31. (patient$ adj3 (train$ or teach$ or educat$ or inform$)).tw.
32. patient knowledge.tw.
33. Behavior Therapy/
34. Cognitive Therapy/
35. exp counseling/
36. (behavi$ adj3 (therap$ or manage$ or modif$ or chang$ or intervention$)).tw.
37. (cogniti$ adj3 (therap$ or intervention$)).tw.
38. counsel$.tw.
39. Motivation/
40. motivational interview$.tw.
41. contingency management.tw.
42. biofeedback.tw.
43. bio-feedback.tw.
44. goals/
45. (goal$ adj3 set$).tw.
46. decision support techniques/
47. decision$ aid$.tw.
48. exp communications media/
49. pamphlet$.tw.
50. booklet$.tw.
51. video$.tw.
52. or/27-51
53. 26 and 52
54. randomized controlled trial.pt.
55. controlled clinical trial.pt.
56. randomized.ab.
57. placebo.ab.
58. clinical trials as topic.sh.
59. randomly.ab.
60. trial.ti.

61. 54 or 55 or 56 or 57 or 58 or 59 or 60
62. exp animals/ not humans.sh.
63. 61 not 62
64. 53 and 63

EMBASE Ovid

RCT filter as recommended in the Cochrane Handbook (Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2 (updated September 2009). The Cochrane Collaboration, 2009. Available from www.cochrane-handbook.org.) applied.

1. phenindione/
2. antivitamin K/
3. exp coumarin anticoagulant/
4. anticoagulant agent/
5. warfarin.tw.
6. acenocoumarol.tw.
7. sintrom.tw.
8. sinthrome.tw.
9. jantoven.tw.
10. marevan.tw.
11. coumadin$.tw.
12. waran.tw.
13. nicoumalone.tw.
14. (vitamin k adj3 antagonist$).tw.
15. vitamin k inhibitor$.tw.
16. oral anticoagula$.tw.
17. oral anti-coagula$.tw.
18. vka*.tw.
19. antivitamin k.tw.
20. anti-vitamin k.tw.
21. coumarin$.tw.
22. vitamin K group/po [Oral Drug Administration]
23. or/1-22
24. patient education/
25. attitude to health/
26. patient participation/
27. ((educat$ or train$ or teach$) adj3 (program$ or intervention$)).tw.
28. (patient$ adj3 (train$ or teach$ or educat$ or inform$)).tw.
29. patient knowledge.tw.
30. behavior therapy/
31. cognitive therapy/
32. exp counseling/
33. (behavi$ adj3 (therap$ or manage$ or modif$ or chang$ or intervention$)).tw.
34. (cogniti$ adj3 (therap$ or intervention$)).tw.
35. counsel$.tw.
36. motivation/
37. motivational interview$.tw.
38. contingency management.tw.
39. biofeedback.tw.
40. bio-feedback.tw.
41. (goal$ adj3 set$).tw.
42. decision support system/
43. decision$ aid$.tw.

44. (decision$ adj3 support).tw.
45. mass medium/
46. pamphlet$.tw.
47. booklet$.tw.
48. video$.tw.
49. or/24-48
50. random$.tw.
51. factorial$.tw.
52. crossover$.tw.
53. cross over$.tw.
54. cross-over$.tw.
55. placebo$.tw.
56. (doubl$ adj blind$).tw.
57. (singl$ adj blind$).tw.
58. assign$.tw.
59. allocat$.tw.
60. volunteer$.tw.
61. crossover procedure/
62. double blind procedure/
63. randomized controlled trial/
64. single blind procedure/
65. or/50-64
66. (animal/ or nonhuman/) not human/
67. 65 not 66
68. 23 and 49 and 67

PsycINFO

1. anticoagulant drugs/
2. warfarin.tw.
3. acenocoumarol.tw.
4. coumadin$.tw.
5. waran.tw.
6. nicoumalone.tw.
7. (vitamin k adj3 antagonist$).tw.
8. oral anticoagula$.tw.
9. vka*.tw.
10. coumarin$.tw.
11. or/1-10
12. client education/
13. client participation/
14. behavior therapy/
15. cognitive therapy/
16. exp counseling/
17. motivation/
18. exp goals/
19. biofeedback/
20. decision making/
21. exp communications media/
22. ((educat$ or train$ or teach$) adj3 (program$ or intervention$)).tw.
23. (patient$ adj3 (train$ or teach$ or educat$ or inform$)).tw.
24. patient knowledge.tw.
25. health knowledge/

26. (behavi$ adj3 (therap$ or manage$ or modif$ or chang$ or intervention$)).tw.
27. (cogniti$ adj3 (therap$ or intervention$)).tw.
28. health attitudes/
29. counsel$.tw.
30. motivational interview$.tw.
31. contingency management.tw.
32. biofeedback.tw.
33. bio-feedback.tw.
34. (goal$ adj3 set$).tw.
35. decision$ aid$.tw.
36. (decision$ adj3 support).tw.
37. pamphlet$.tw.
38. booklet$.tw.
39. video$.tw.
40. or/12-39
41. 11 and 40
42. random$.tw.
43. factorial$.tw.
44. crossover$.tw.
45. cross-over$.tw.
46. placebo$.tw.
47. (doubl$ adj blind$).tw.
48. (singl$ adj blind$).tw.
49. assign$.tw.
50. allocat$.tw.
51. volunteer$.tw.
52. control*.tw.
53. "2000".md.
54. or/42-53
55. 41 and 54

CINAHL

as run on 9 August 2012:

S72 S52 and S71
S71 S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 Limiters - Published Date from: 20100501-20120931
S70 S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69
S69 cross-over*
S68 crossover*
S67 volunteer*
S66 (MH "Crossover Design")
S65 allocat*
S64 control*
S63 assign*
S62 placebo*
S61 (MH "Placebos")
S60 random*
S59 (doubl* N1 mask*)
S58 (singl* N1 mask*)
S57 (doubl* N1 blind*)
S56 (singl* N1 blind)
S55 (clinic* N1 trial?)

S54 PT clinical trial
S53 (MH "Clinical Trials")
S52 S25 and S51
S51 S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50
S50 video*
S49 booklet*
S48 pamphlet*
S47 (MH "Communications Media")
S46 (decision* aid*)
S45 (MH "Decision Support Techniques")
S44 (goal* N3 set*)
S43 (MH "Goals and Objectives")
S42 bio-feedback
S41 biofeedback
S40 contingency management
S39 motivational interview*
S38 (MH "Motivation")
S37 counsel*
S36 (cogniti* N3 (therap* or intervention*))
S35 (behavi* N3 (therap* or manage* or modif* or chang* or intervention*))
S34 (MH "Counseling")
S33 (MH "Cognitive Therapy")
S32 (MH "Behavior Therapy")
S31 patient knowledge
S30 (patient* N3 (train* or teach* or educat* or inform*))
S29 ((educat* or train* or teach*) N3 (program* or intervention*))
S28 (MH "Consumer Participation")
S27 (MH "Attitude to Health")
S26 (MH "Patient Education")
S25 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24
S24 anti-vitamin k
S23 antivitamin k
S22 vka*
S21 oral anti-coagula*
S20 oral anticoagula*
S19 vitamin k inhibitor*
S18 (vitamin k N3 antagonist*)
S17 nicoumalone
S16 "Phenprocoumon"
S15 waran
S14 coumadin*
S13 marevan
S12 jantoven
S11 sinthrome
S10 sintrom
S9 warfarin
S8 (MH "Vitamin K")
S7 oral anticoagula*
S6 (MH "Anticoagulants")
S5 "Dicumarol"
S4 "Phenindione"

S3 “Coumarins”
S2 “acenocoumarol”
S1 (MH “Warfarin”)
as run on 21 June 2010:
S76 S57 and S75
S75 S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74
S74 TX cross-over*
S73 TX crossover*
S72 TX volunteer*
S71 (MH “Crossover Design”)
S70 TX allocat*
S69 TX control*
S68 TX assign*
S67 TX placebo*
S66 (MH “Placebos”)
S65 TX random*
S64 TX (doubl* N1 mask*)
S63 TX (singl* N1 mask*)
S62 TX (doubl* N1 blind*)
S61 TX (singl* N1 blind*)
S60 TX (clinic* N1 trial?)
S59 PT clinical trial
S58 (MH “Clinical Trials+”)
S57 S17 and S56
S56 S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55
S55 (TI video*) or (AB video*)
S54 (TI booklet*) or (AB booklet*)
S53 (TI pamphlet*) or (AB pamphlet*)
S52 (MH “Communications Media+”)
S51 (TI decision* N3 support) or (AB decision* N3 support)
S50 (TI “decision* aid*”) or (AB “decision* aid*”)
S49 (MH “Decision Support Techniques+”)
S48 (TI goal* N3 set*) or (AB goal* N3 set*)
S47 (TI bio-feedback) or (AB bio-feedback)
S46 (TI biofeedback) or (AB biofeedback)
S45 (TI “contingency management”) or (AB “contingency management”)
S44 (TI “motivational interview*”) or (AB “motivational interview*”)
S43 (MH “Motivation+”)
S42 (TI counsel*) or (AB counsel*)
S41 (TI cogniti* N3 intervention*) or (AB cogniti* N3 intervention*)
S40 (TI cogniti* N3 therap*) or (AB cogniti* N3 therap*)
S39 (TI behavi* N3 intervention*) or (AB behavi* N3 intervention*)
S38 (TI behavi* N3 chang*) or (AB behavi* N3 chang*)
S37 (TI behavi* N3 modif*) or (AB behavi* N3 modif*)
S36 (TI behavi* N3 manage*) or (AB behavi* N3 manage*)
S35 (TI behavi* N3 therap*) or (AB behavi* N3 therap*)
S34 (MH “Counseling+”)
S33 (MH “Cognitive Therapy”)
S32 (MH “Behavior Therapy”)
S31 (TI “patient knowledge”) or (AB “patient knowledge”)
S30 (TI patient* N3 inform*) or (AB patient* N3 inform*)

S29 (TI patient* N3 educat*) or (AB patient* N3 educat*)
S28 (TI patient* N3 teach*) or (AB patient* N3 teach*)
S27 (TI patient* N3 train*) or (AB patient* N3 train*)
S26 (TI teach* N3 intervention*) or (AB teach* N3 intervention*)
S25 (TI teach* N3 program*) or (AB teach* N3 program*)
S24 (TI train* N3 intervention*) or (AB train* N3 intervention*)
S23 (TI train* N3 program*) or (AB train* N3 program*)
S22 (TI educat* N3 intervention*) or (AB educat* N3 intervention*)
S21 (TI educat* N3 program*) or (AB educat* N3 program*)
S20 (MH "Consumer Participation")
S19 (MH "Attitude to Health")
S18 (MH "Patient Education")
S17 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16
S16 (TI dicumarol) or (AB dicumarol)
S15 (TI dicoumarol) or (AB dicoumarol)
S14 (TI coumarin*) or (AB coumarin*)
S13 (TI VKA*) or (AB VKA*)
S12 (TI phenprocoumon) or (AB phenprocoumon)
S11 (TI coumadin*) or (AB coumadin*)
S10 (TI sintrom) or (AB sintrom)
S9 (TI acenocoumarol) or (AB acenocoumarol)
S8 (TI warfarin) or (AB warfarin)
S7 (TI "antivitamin K") or (AB "antivitamin K")
S6 (TI "vitamin K" N2 inhibitor*) or (AB "vitamin K" N2 inhibitor*)
S5 (TI "vitamin K" N2 antagonist*) or (AB "vitamin K" N2 antagonist*)
S4 (TI oral N2 anti-coagula*) or (AB oral N2 anti-coagula*)
S3 (TI oral N2 anticoagula*) or (AB oral N2 anticoagula*)
S2 (MH "Warfarin")
S1 (MH "Anticoagulants")

CONTRIBUTIONS OF AUTHORS

Data collection, paper searches, screening and appraisal, and data extraction were conducted by Drs Clarkesmith and Lane. Dr Clarkesmith wrote the initial draft of the Introduction and Methods of the review paper, which were edited by Dr Lane. Drs Clarkesmith and Lane performed the data analysis together and drafted the Results and Discussion sections. Both Dr Clarkesmith and Dr Lane revised and commented on subsequent drafts. Professor Pattison contributed to the interpretation of the analyses and provided critical revision of drafts of the review.

DECLARATIONS OF INTEREST

Dr Clarkesmith has completed a PhD studentship that was funded by an Investigator-Initiated Educational Grant from Bayer Healthcare and Aston University, but currently works as a post-doctoral researcher. Dr Lane is the principal grant holder for TREAT. Dr Clarkesmith is currently the primary investigator for the '**TR**ial of an **E**ducational intervention on patients' knowledge of **A**trial fibrillation and anticoagulant therapy, INR control, and outcome of **T**reatment with warfarin' (TREAT). The trial protocol manuscript has been published in BMC Cardiovascular Disorders (Smith 2010) and the results will be published later this year. Dr Lane and Professor Pattison were the educational supervisors of Dr Clarkesmith for the TREAT study. This review is not funded by Bayer Healthcare.

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Internal sources

- No sources of support supplied

External sources

- New Source of support, Not specified.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. Contributions of the authors

The contributions of authors has changed from the original protocol (see contributions of authors section).

2. Decision conflict as a secondary outcome

Decision conflict was included as a secondary outcome in the final analysis. Whilst not specified as an outcome of interest in the original protocol, it was highlighted as a common secondary outcome measure in three of the studies included in the final review. For this reason, the authors decided to include these data within the results.

INDEX TERMS

Medical Subject Headings (MeSH)

*International Normalized Ratio [standards]; *Patient Education as Topic; Administration, Oral; Anticoagulants [*administration & dosage; adverse effects]; Atrial Fibrillation [blood; *complications]; Chronic Disease; Decision Support Techniques; Drug Monitoring [*methods; standards]; Medication Adherence; Randomized Controlled Trials as Topic; Self Care [methods]; Stroke [blood; etiology; *prevention & control]

MeSH check words

Aged; Humans; Middle Aged