Clinical service organisation for adults with atrial fibrillation (Protocol)

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[Intervention Protocol]

Clinical service organisation for adults with atrial fibrillation

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effectiveness of different clinical service interventions for AF versus usual care for people with all types of AF.

BACKGROUND

Description of the condition

Atrial fibrillation (AF) is the most commonly occurring heart rhythm condition. Globally, the reported prevalence ranges from 2.3% to 3.4% (Ball 2013). AF is estimated to affect between 2.7 million and 6.1 million people in the US, with this number estimated to double by 2050 (January 2014). The socioeconomic burden of AF is rapidly increasing, with most of the costs primarily related to the increasing rates of hospitalisations, interventional procedures including cardiac ablation and cardioversion, and device implantation (Ball 2013; Chugh 2014). Heart failure, stroke, and dementia are common consequences of AF, with risk increasing sharply with older age. This increase in the number of people seeking care for AF creates logistical, societal, and economic challenges for the health system, healthcare professionals, patients, and their informal carers. There is diversity in current care models and service organisation for AF including care setting and provider, which contributes to the fragmentation of care. Traditionally, people with AF would be cared for and treated by a cardiologist in a cardiology clinic, or by a general practitioner or primary care physician in the outpatient setting.

However, the Atrial Fibrillation Network/European Heart Rhythm Association suggested careful examination of the optimal clinical service organisation and models of AF care (Kirchhof 2015). The association suggested that this examination should be data-driven and based on outcomes. There is strong evidence to support the use of integrated models of care for people with chronic heart failure. Such clinics using a specialised team have demonstrated improved patient outcomes including mortality and all-cause hospitalisation. Further, there is promising evidence related to collaborative multidisciplinary interventions, including nurse-led clinics and novel eHealth interventions for AF.

Structural or electrophysiological changes can alter atrial tissue to increase abnormal impulse formation, causing AF to occur. These changes can be caused by a broad range of underlying pathophysiological processes. The exact underlying mechanisms of AF are not well understood, regardless AF represents a final common phenotype for multiple disease pathways (January 2014). AF is distinguishable by "chaotic electrical atrial activation and ineffective contraction. AF is identifiable on ECG [electrocardiography] by the substitution of regular P waves with rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, associated with an irregular frequent ventricular response when AV [atrioventricular] conduction is intact" (Ferguson 2014). Typical ECG characteristics include: irregular R-R intervals (when AV conduction is present), absence of distinct repeating P waves, and irregular atrial activity (Ferguson 2014).

Description of the intervention

To date, there are a few rigorously conducted randomised controlled trials (RCTs) that have demonstrated improved outcomes for people with AF attending multidisciplinary AF clinics. One systematic review and meta-analysis found that an integrated care approach for AF management was associated with a reduction in all-cause mortality (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.32 to 0.80; P = 0.003) and cardiovascular hospitalisations (OR 0.58, 95% CI 0.44 to 0.77; P = 0.0002); however it did not significantly effect AF-related hospitalisations (OR 0.82, 95% CI 0.56 to 1.19; P = 0.29) or cerebrovascular events (OR 1.00, 95% CI 0.48 to 2.09; P = 1.00) (Gallagher 2017). Further, the 2018 Australian Clinical Guidelines for the Diagnosis and Management of Atrial Fibrillation recommended an integrated care approach to provide patient-centred, comprehensive treatment that is delivered by a multidisciplinary team (GRADE quality of evidence: high; GRADE strength of recommendation: strong) (Brieger 2018).

Integrated care can be defined as a collaborative, patient-centred care approach to the provision of healthcare that focuses on improving patients' care experiences, health outcomes, and quality of life, and creating efficiencies in the health system (Brieger 2018).

There are four fundamental components of integrated AF care (Brieger 2018). These include:

1. multidisciplinary teams including generalists;
2. patient-centred care;
3. eHealth to support the management of AF; and
4. comprehensive treatment approach to AF.

Care should aim to address quality of life and symptom burden, optimising pharmacotherapy and promoting self-care strategies, with a goal to prevent avoidable hospitalisations and reduce mortality. AF management should be patient-centred and tailored to meet the needs of the individuals. While stroke prevention is a primary goal, the potential for adverse effects of treatment (such as bleeding) needs to be balanced within the context of the most credible evidence; clinical expertise; and individual patient's circumstances, values, and treatment preferences (Ferguson 2013). Systematic review data highlighted that the prescription of oral anticoagulation for stroke prevention in AF remains poor, with more than 30% of people with known AF failing to be appropriately treated with thromboprophylaxis (Ogilvie 2010). Further, large international registries, such as the GARFIELD (Global Antithrombotic Registry in the FIELD) registry demonstrated overtreatment in people with AF at low risk of stroke, and undertreatment in people with AF at high risk for stroke is common (Kakkar 2013).

This review will include trials comparing different type of clinical service organisation for AF with usual or routine care. For the purposes of this review, integrated AF care is defined as "as collaborative, patient centred approach to the provision of healthcare that focuses on improving patients' experiences, health outcomes, and quality of life, while creating efficiencies in the health system" (Brieger 2018; page 1248). This review will evaluate different types of clinical service organisation, such as case management approaches, collaborate multidisciplinary interventions (e.g. nurse-led clinics), integrated models of care, and eHealth models of care (such as digital health, mHealth, telehealth, and structured telephone support approaches).

How the intervention might work

Enhanced clinical service organisation could lead to improved outcomes including all-cause mortality and cardiovascular rehospitalisations. These interventions are often considered complex organisational interventions. They can be delivered via structured health services across the inpatient and outpatient settings and at different stages of the care process, throughout different locations.

Many of the outlined components of care for people with AF require input from multidisciplinary healthcare professionals. No singular health discipline in isolation holds the skills or expertise to adequately manage people with these complex needs. There are many gaps in care evident from general practice and outpatient management of AF. There is mounting evidence that integrated, and skilled 'AF healthcare teams' may be the most efficient methods of optimising care for people with AF in the outpatient setting (Carter 2016; Hendriks 2012; Stewart 2016). Each health discipline offers a unique lens to optimising care for AF. For example, pharmacists are often expert in addressing issues of medication adherence; physiotherapists maintain expertise in providing physical activity advice; and dieticians in the provision of dietary recommendations. Further, nurses have key functions in providing patient education and counselling, or risk assessment or performing clinical procedures. While these examples of areas of expertise are based on quite traditional views of role function, each of the health disciplines actively contribute to achieving the pillars of AF management. Importantly, each may have a role in leading the healthcare team or care management in the outpatient setting. Therefore, it is imperative that the efficacy of these alternate models of care are closely examined against traditional models of care.

Why it is important to do this review

There is increasing need for quality management of AF in general practice, and outside of inpatient settings. However, many general practitioners may lack time to provide comprehensive AF care. Multidisciplinary healthcare professionals may offer an innovative solution to complex healthcare workforce issues. Further, advanced healthcare practitioners may be able to care for people more efficiently through an integrated chronic care organisational workforce model. To address these factors, we formulated the following research question: what is the effectiveness of different clinical service interventions for AF versus usual care, for people with all types of AF?

One systematic review focused on the evaluation of the effect of integrated care in AF (Gallagher 2017). A key limitation of this review was the sole focus on integrated care models; however, the effect of other models of care delivery in AF remains unclear. Therefore, there is need for a Cochrane Review that closely examines clinical service organisation models for people with AF. Increasingly, there is evidence to support the specialisation of healthcare teams. Advanced practitioner, specifically, nurse-co-ordinated models of care have demonstrated better outcomes for a range of other chronic conditions such as; transient Ischaemic attack (TIA) and minor stroke (O'Brien 2016), diabetes, hypertension, hypercholesterolaemia (Shaw 2014), heart failure (Rich 1995; Stewart 2012), and AF (Carter 2016; Hendriks 2012; Stewart 2016). Case management is a long-established approach to the care of people living with chronic conditions. It is a comprehensive and longitudinal approach that is often focused on a co-ordinated care approach with goal setting and attainment. Case managers are often experienced multidisciplinary clinicians who support behaviour change modification and the optimisation of medical therapies (Ma 2009). eHealth and digitally based models of AF care are increasing. The World Health Organization defines eHealth is as "the transfer of resources and healthcare by electronic means". eHealth in the context of AF may include digitally based models of care such as smartphone-delivered care, Internet-delivered care,

telehealth approaches, or structured telephone support (Hendriks 2016). There is a need for rigorous evaluation of these structured clinical service models of care in the context of AF, particularly their effect in reducing mortality and hospitalisation.

OBJECTIVES

To assess the effectiveness of different clinical service interventions for AF versus usual care for people with all types of AF.

METHODS

Criteria for considering studies for this review

Types of studies

We will include RCTs with individual parallel arm, cluster, and cross-over design. We will include studies reported as full-text, those published as abstract only, and unpublished data.

Types of participants

We will include adults (18 years of age or more) with a diagnosis of AF of any type (defined as paroxysmal, persistent, or long-term persistent AF) or aetiology (consistent with national guidelines; Brieger 2018). We will exclude studies that target general cardiac disorders rather than AF specifically. Where studies may only contain a subset of eligible participants, we will contact study authors unless data are available in published reports. If data cannot be obtained, studies with ≥ 80% of participants with AF will be included.

Types of interventions

We will include clinical service intervention directed at people with atrial fibrillation. This will include clinical service, disease-specific management interventions (inpatient, outpatient, or community-based interventions) targeted to people with AF. Interventions may include or exclude patients' families or informal carers.

Interventions may include:

1. case management;
2. collaborative multidisciplinary interventions such as disease management programmes (e.g. nurse-led clinics);
3. integrated and co-ordinated models of care; or
4. eHealth models of care (including digital health approaches, telehealth, and structured telephone support).

Usual care is defined as unrestricted, routine care.

We will exclude the following types of interventions.

1. Interventions that are primarily educational-behavioural in focus.
2. Interventions where the sole focus is lifestyle risk reduction.
3. Interventions that are targeted towards cardiovascular disease or chronic disease in general.
4. Interventions that have a sole focus on medication prescription for AF.

Types of outcome measures

Primary outcomes

1. All-cause mortality.

2. All-cause hospitalisation (number of participants with one hospitalisation, including AF-related emergency department visits).

Secondary outcomes

1. Cardiovascular mortality.
2. Cardiovascular rehospitalisation (number of participants with one cardiovascular hospitalisation).
3. AF-related emergency department visits (number of participants with at least one event).
4. Thromboembolic complications including stroke and TIA (number of participants with at least one event).
5. Minor cerebrovascular bleeding events (as defined by International Society on Thrombosis and Haemostasis (ISTH) criteria) (Kaatz 2015).
6. Major cerebrovascular bleeding events (as defined by ISTH criteria) (Kaatz 2015).
7. Minor and major bleeding events (as defined by ISTH criteria) (Kaatz 2015).
8. AF-related quality of life (using validated AF-specific quality of life instruments such as Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT), Atrial Fibrillation Quality of Life (AF-QoL) questionnaire, Quality of Life in Atrial Fibrillation (QLAF), or Atrial Fibrillation Quality of Life Questionnaire (AFQLQ)) (Aliot 2014).
9. AF symptom burden (using validated AF symptom scales and patient-reported outcome measures such as European Heart Rhythm Association (EHRA) or Atrial Fibrillation Severity Scale (AFSS)) (Heidt 2016).
10. Cost of intervention or other economic outcome.
11. Length of hospital stay.

Reporting one or more of the outcomes listed here in the trial is not an inclusion criterion for the review. Where a published report does not appear to report one of these outcomes, we will access the trial protocol and contact the trial authors to ascertain whether the outcomes were measured but not reported. Relevant trials which measured these outcomes but did not report the data at all, or not in a usable format, will be included in the review as part of the narrative. Outcomes will be measured using the longest follow-up for each study.

Search methods for identification of studies

Electronic searches

We will identify trials through systematic searches of the following bibliographic databases:

1. Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library;
2. MEDLINE (Ovid, from 1946 onwards);
3. Embase (Ovid, from 1980 onwards);
4. SCOPUS;
5. CINAHL.

We will adapt the preliminary search strategy for MEDLINE (Ovid) (Appendix 1) for use in the other databases. We will apply the Cochrane sensitivity-maximising RCT filter to MEDLINE (Ovid) and adaptations of it to the other databases, except CENTRAL (Lefebvre 2011).

We will conduct a search of ClinicalTrials.gov (www.ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch/) for ongoing or unpublished trials.

We will search all databases from their inception to the date of search, and we will impose no restrictions on language of publication or publication status.

Searching other resources

We will check reference lists of all included studies and any relevant systematic reviews identified for additional references to trials. We will also examine any relevant retraction statements and errata for included studies.

Data collection and analysis

Selection of studies

Two review authors (CF and SCI) will independently screen titles and abstracts for inclusion of all the potential studies identified by the search and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. If there are any disagreements, a third author (BB) will arbitrate. We will retrieve the full-text study reports/publication and two review authors (CF and SCI) will independently screen the full-text and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreements through discussion or, if required, we will consult a third review author (BB). We will identify and exclude duplicates and collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table (Liberati 2009).

Data extraction and management

We will use a data collection form for study characteristics and outcome data which has been piloted on at least one study in the review. One review author (CF) will extract the following study characteristics and report them in the 'Characteristics of included studies' table.

1. Methods: study design, total duration of study, and date of study.
2. Participants: number randomised, number lost to follow-up/withdrawn, number analysed, mean age, age range, gender, type of AF, history of heart failure, CHA2DS2-VASc score (Congestive heart failure; Hypertension; Age 75 years or older; Diabetes mellitus; Stroke, TIA, or TE; Vascular disease; Age 65 to 74 years; Sex category (female) risk calculator), inclusion criteria, and exclusion criteria.
3. Interventions: case management, clinic-based care, eHealth intervention, catheter ablation, non-pharmacological and pharmacological interventions.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Study setting: country of study, number of study settings.
6. Notes: funding and conflicts of interest, etc.

Two review authors (CF and SCI) will independently extract outcome data from included studies. We will resolve disagreements by consensus or by involving a third review author (BB). One review author (CF) will transfer data into the Review Manager 5 (Review Manager 2014). We will double-check that data are entered correctly by comparing the data presented in the systematic review with the those on the data extraction form. A second review author (SCI) will spot-check study characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

Two review authors (CF and SCI) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017). We will resolve any disagreements by discussion or by involving another review author (BB). We will assess the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

We will grade each potential source of bias as high, low, or unclear and provide a quote from the study report together with a justification for our judgement in the 'Risk of bias' table. We will summarise the risk of bias judgements across different studies for each of the domains listed. Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

For cluster RCTs and cross-over trials, we will use recommendation from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017).

Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will analyse dichotomous data as risk ratios (RR) with 95% confidence intervals (CI) and continuous data as mean difference (MD) or standardised mean difference (SMD) with 95% CIs. We will use the MD if studies use the same outcome measures and the SMD if studies used different outcome measures. We will enter data presented as a scale with a consistent direction of effect. We will narratively describe skewed data reported as medians and interquartile ranges.

Unit of analysis issues

We anticipate no unit of analysis issues with the studies. If we identify any non-standard design (e.g. cross-over or cluster RCTs),

we will use recommendation from the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017).

Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only). Where possible, we will use the Review Manager 5 calculator to calculate missing standard deviations using other data from the trial such as CIs (Review Manager 2014). Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Assessment of heterogeneity

We will inspect forest plots visually to consider the direction and magnitude of effects and the degree of overlap between CIs. We will use the I^2 statistic to measure heterogeneity among the trials in each analysis, but acknowledge that there is substantial uncertainty in the value of the I^2 statistic when there is only a small number of studies. We will also consider the P value from the Chi^2 test. If we identify substantial heterogeneity (I^2 greater than 50%), we will report it and explore possible causes by prespecified subgroup analysis.

Assessment of reporting biases

If we are able to pool more than 10 trials in analyses, we will create and examine funnel plots to explore possible small-study biases for the primary outcomes.

Data synthesis

We will undertake meta-analyses only where this is meaningful (i.e. if the treatments, participants, and the underlying clinical question are similar enough for pooling to make sense).

We will use a random-effects model (inverse-variance method) as we expect some heterogeneity in the interventions.

'Summary of findings' table

We will create 'Summary of findings' tables using the following outcomes; all-cause mortality; all-cause hospitalisation (number of participants with one hospitalisation, including AF-related emergency department visits); cardiovascular mortality; cardiovascular rehospitalisation; thromboembolic complications including stroke and TIA; minor cerebrovascular bleeding events; and major cerebrovascular bleeding events. We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of a body of evidence as it relates to the studies that contribute data to the meta-analyses for the prespecified outcomes. We will use methods and recommendations described in Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2017), using GRADEpro software (GRADEpro GDT). Each comparison (case management; collaborative multidisciplinary interventions; integrated models of care; eHealth models of care) will have a separate 'Summary of findings' table. We will justify all decisions to downgrade the certainty of evidence using footnotes and we will make comments to aid reader's understanding of the review where necessary.

Two review authors (CF and BB*)* will independently judge the certainty of the evidence, with disagreements resolved by discussion or involving a third review author (SCI). We will justify, document, and incorporate judgements of reporting of results for each outcome.

We will extract study data, format our comparisons in data tables, and prepare 'Summary of findings' tables before writing the results and conclusions of our review. An example 'Summary of findings' table is shown in Table 1.

Subgroup analysis and investigation of heterogeneity

We will carry out the following subgroup analyses should the number of studies and participants permit these analyses.

1. Age (more than 65 years versus under 65 years).
2. Sex (women versus men).
3. History of heart failure.
4. People who underwent AF catheter ablation versus people on medical treatment alone.
5. People with paroxysmal AF versus non-paroxysmal AF.
6. People with a CHA2DS2-VASc score of 2 or greater versus people with a score of 0 to 1.

7. Comparison of type of intervention (case management versus multidisciplinary versus integrated care versus eHealth models).

We will use the formal test for subgroup interactions in Review Manager 5 (Review Manager 2014).

Sensitivity analysis

We will carry out sensitivity analyses to test whether key methodological factors or decisions have affected the main results by only including studies with a low risk of bias. We will exclude studies that are at a high or unclear risk of bias for random sequence generation, allocation concealment, and incomplete data. Where the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Reaching conclusions

We will base our conclusions only on findings from the quantitative or narrative synthesis of included studies for this review. We will avoid making recommendations for practice and our implications for research will suggest priorities for future research and outline what the remaining uncertainties are in the area.

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ADDITIONAL TABLES

Table 1. 'Summary of findings' table

Clinical service organisation for atrial fibrillation

Patient or population:
Setting: [e.g. hospital, community]
Intervention:
Comparison:

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with treatment				
All-cause mortality	—	—	—	—	—	—
All-cause hospitalisation	—	—	—	—	—	—
Cardiovascular mortality	—	—	—	—	—	—
Cardiovascular rehospitalisation	—	—	—	—	—	—

Table 1. 'Summary of findings' table *(Continued)*

Thromboembolic complications including stroke and transient ischaemic attacks	—	—	—	—	—	—
Minor cerebrovascular bleeding events		—	—	—	—	—
Major cerebrovascular bleeding events		—	—	—	—	—

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

A P P E N D I C E S

Appendix 1. Preliminary MEDLINE (Ovid) search strategy

1 disease management/ (31372)
2 (disease* adj5 manag*).tw. (63468)
3 Patient Care Management/ (3332)
4 Medication Therapy Management/ (1654)
5 exp Patient Care Team/ (64320)
6 Patient-Centered Care/ (16724)
7 (patient* adj3 manag*).tw. (142341)
8 (patient* adj4 (care or caring)).tw. (232157)
9 (deliver* adj2 care).tw. (27151)
10 (manag* adj5 care).tw. (61398)
11 ((management or care) adj5 program*).tw. (50027)
12 (case adj5 manag*).tw. (26019)
13 Home Care Services/ (31632)
14 Home Care Services, Hospital-Based/ (1820)
15 (home adj5 (intervention* or care)).tw. (35189)
16 (home adj visit*).tw. (7825)
17 homecare.tw. (973)
18 Ambulatory Care/ (40721)
19 (ambulatory adj2 (care or caring)).tw. (11073)
20 Patient Discharge/ (26016)
21 (discharg* adj5 program*).tw. (1657)
22 (practice adj guideline*).tw. (21976)
23 Practice Guidelines as Topic/ (106741)
24 (comprehensive* adj5 (care or caring)).tw. (11985)
25 multidisciplinary.tw. (70874)
26 (treatment* adj5 plan*).tw. (74029)
27 (nurse* adj5 led).tw. (3935)
28 (discharg* adj5 plan*).tw. (5157)
29 Outpatient Clinics, Hospital/ (15308)
30 (outpatient* adj2 (clinic* or hospital*)).tw. (35947)
31 ((Outpatient* or out-patient*) adj3 (care or service*)).tw. (15339)
32 (Clinic* adj3 (visit* or special* or outpatient* or out-patient*)).tw. (67802)
33 Clinic-based care.tw. (42)

34 (Care adj3 (primary or communit* or home or integrated or nurse-led or collaborative or multidisciplin* or comprehensive)).tw. (181751)
35 Ambulatory Care Facilities/ (17291)
36 (interdisciplinary or inter-disciplinary or multidisciplinary or multi-disciplinary).tw. (105569)
37 (service* adj3 home).tw. (5761)
38 (team* adj3 (health or patient or medical or care or healthcare)).tw. (29454)
39 "Delivery of Health Care, Integrated"/ (11248)
40 (post-discharge adj3 follow-up).tw. (281)
41 ((Nurse* or pharmacist* or physio* or dietician*) adj5 (outpatient* or out-patient*)).tw. (1459)
42 (integrat* adj3 (health* or deliver*)).tw. (15967)
43 Comprehensive Health Care/ (6420)
44 (comprehensive adj2 health*).tw. (4809)
45 exp Patient Care Planning/ (60499)
46 Health Services Research/ (34837)
47 exp Community Health Services/ (283764)
48 (commun* adj2 (healthcare or health* or service*)).tw. (53764)
49 Community Health Centers/ (6717)
50 or/1-49 (1412571)
51 Atrial Fibrillation/ (48167)
52 ((atrial or auricular or atrium) adj2 fibrillation*).tw. (61208)
53 (A-fib or Afib).tw. (380)
54 or/51-53 (71362)
55 randomized controlled trial.pt. (471218)
56 controlled clinical trial.pt. (92747)
57 randomized.ab. (426434)
58 placebo.ab. (193177)
59 drug therapy.fs. (2061639)
60 randomly.ab. (300227)
61 trial.ab. (444547)
62 groups.ab. (1851139)
63 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 (4317402)
64 exp animals/ not humans.sh. (4514185)
65 63 not 64 (3732619)
66 50 and 54 and 65 (2835)

CONTRIBUTIONS OF AUTHORS

CF: responsible for the conception and design of the protocol, responsible for co-ordinating and completing the protocol, including writing the protocol.

JH: contributed to the conception, design, and writing of the protocol.

CG: contributed to the conception, design, and writing of the protocol.

BB: contributed to the conception, design, and writing of the protocol.

SCI: contributed to the conception, design, and writing of the protocol.

DECLARATIONS OF INTEREST

CF: none known.

JH: none known.

CG: none known.

BB: has been a member of the Australian Heart Foundation's working group for the development of the clinical management guidelines on Atrial Fibrillation; travel expenses with attending working group meetings were covered by the Heart Foundation.

SCI: none known.

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