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Clinical service organisation for adults with atrial fibrillation (Review)

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[Intervention Review]

Clinical service organisation for adults with atrial fibrillation

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ABSTRACT

Background

Atrial fibrillation (AF) is an increasingly prevalent heart rhythm condition in adults. It is considered a common cardiovascular condition with complex clinical management. The increasing prevalence and complexity in management underpin the need to adapt and innovate in the delivery of care for people living with AF. There is a need to systematically examine the optimal way in which clinical services are organised to deliver evidence-based care for people with AF. Recommended approaches include collaborative, organised multidisciplinary, and virtual (or eHealth/mHealth) models of care.

Objectives

To assess the effects of clinical service organisation for AF versus usual care for people with all types of AF.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and CINAHL to October 2022. We also searched ClinicalTrials.gov and the WHO ICTRP to April 2023. We applied no restrictions on date, publication status, or language.

Selection criteria

We included randomised controlled trials (RCTs), published as full texts and as abstract only, involving adults (≥ 18 years) with a diagnosis of any type of AF. We included RCTs comparing organised clinical service, disease-specific management interventions (including e-health models of care) for people with AF that were multicomponent and multidisciplinary in nature to usual care.

Data collection and analysis

Three review authors independently selected studies, assessed risk of bias, and extracted data from the included studies. We calculated risk ratio (RR) for dichotomous data and mean difference (MD) or standardised mean difference (SMD) for continuous data with 95% confidence

intervals (CIs) using random-effects analyses. We then calculated the number needed to treat for an additional beneficial outcome (NNTB) using the RR. We performed sensitivity analyses by only including studies with a low risk of selection and attrition bias. We assessed heterogeneity using the I^2 statistic and the certainty of the evidence according to GRADE.

The primary outcomes were all-cause mortality and all-cause hospitalisation. The secondary outcomes were cardiovascular mortality, cardiovascular hospitalisation, AF-related emergency department visits, thromboembolic complications, minor cerebrovascular bleeding events, major cerebrovascular bleeding events, all bleeding events, AF-related quality of life, AF symptom burden, cost of intervention, and length of hospital stay.

Main results

We included 8 studies (8205 participants) of collaborative, multidisciplinary care, or virtual care for people with AF. The average age of participants ranged from 60 to 73 years. The studies were conducted in China, the Netherlands, and Australia. The included studies involved either a nurse-led multidisciplinary approach (n = 4) or management using mHealth (n = 2) compared to usual care. Only six out of the eight included studies could be included in the meta-analysis (for all-cause mortality and all-cause hospitalisation, cardiovascular mortality, cardiovascular hospitalisation, thromboembolic complications, and major bleeding), as quality of life was not assessed using a validated outcome measure specific for AF. We assessed the overall risk of bias as high, as all studies had at least one domain at unclear or high risk of bias rating for performance bias (blinding) in particular.

Organised AF clinical services probably result in a large reduction in all-cause mortality (RR 0.64, 95% CI 0.46 to 0.89; 5 studies, 4664 participants; moderate certainty evidence; 6-year NNTB 37) compared to usual care. However, organised AF clinical services probably make little to no difference to all-cause hospitalisation (RR 0.94, 95% CI 0.88 to 1.02; 2 studies, 1340 participants; moderate certainty evidence; 2-year NNTB 101) and may not reduce cardiovascular mortality (RR 0.64, 95% CI 0.35 to 1.19; 5 studies, 4564 participants; low certainty evidence; 6-year NNTB 86) compared to usual care. Organised AF clinical services reduce cardiovascular hospitalisation (RR 0.83, 95% CI 0.71 to 0.96; 3 studies, 3641 participants; high certainty evidence; 6-year NNTB 28) compared to usual care.

Organised AF clinical services may have little to no effect on thromboembolic complications such as stroke (RR 1.14, 95% CI 0.74 to 1.77; 5 studies, 4653 participants; low certainty evidence; 6-year NNTB 588) and major cerebrovascular bleeding events (RR 1.25, 95% CI 0.79 to 1.97; 3 studies, 2964 participants; low certainty evidence; 6-year NNTB 556). None of the studies reported minor cerebrovascular events.

Authors' conclusions

Moderate certainty evidence shows that organisation of clinical services for AF likely results in a large reduction in all-cause mortality, but probably makes little to no difference to all-cause hospitalisation compared to usual care. Organised AF clinical services may not reduce cardiovascular mortality, but do reduce cardiovascular hospitalisation compared to usual care. However, organised AF clinical services may make little to no difference to thromboembolic complications and major cerebrovascular events. None of the studies reported minor cerebrovascular events. Due to the limited number of studies, more research is required to compare different models of care organisation, including utilisation of mHealth. Appropriately powered trials are needed to confirm these findings and robustly examine the effect on inconclusive outcomes. The findings of this review underscore the importance of the co-ordination of care underpinned by collaborative multidisciplinary approaches and augmented by virtual care.

PLAIN LANGUAGE SUMMARY

Are services organised to deliver care for people with atrial fibrillation (irregular heartbeat) better than usual (routine) care?

Key messages

• Organised care services for atrial fibrillation (AF) probably cause a large reduction in death from all causes and do reduce heart-related hospital admissions, but they probably make little to no difference to hospital admissions from all causes and may not reduce heart-related death compared with routine care (care provided as part of normal practice).

• Organised care services for AF may not reduce complications such as stroke and mini-stroke and major complications related to bleeding in the brain compared to routine care.

• Larger, well-designed studies are needed to give better estimates of the benefits and potential harms of organised care services for AF.

What is atrial fibrillation?

Atrial fibrillation (AF) is an irregular heartbeat that happens when the electrical signals in the heart fire quickly at the same time. This causes the heart to beat too fast or too slow, which can cause troubling symptoms and serious medical complications, including blood clots that can lead to stroke (where blood flow to the brain is blocked).

How is atrial fibrillation treated?

Atrial fibrillation is treated with lifestyle changes, medication, and procedures, including surgery, to help prevent blood clots, control the heartbeat, or restore the heart's normal rhythm.

What did we want to find out?

Organised care services for AF involve: (i) providing care that is focused on improving people's care experiences, health outcomes, and quality of life; (ii) that is delivered by a team of healthcare providers from various fields of study working together; and (iii) that uses technology to support the integrated approach. Routine care is care provided as part of normal practice.

We wanted to find out if organised care services for AF were better than usual (routine) care in reducing death and hospital admission from all causes.

We also wanted to find out if organised care services for AF were better than routine care in reducing heart-related death and hospital admissions, AF-related emergency department visits, complications such as stroke and mini-stroke, major and minor complications related to bleeding in the brain, AF-related quality of life, AF symptoms, length of hospital stay, and cost related to the services.

What did we do?

We searched for studies comparing organised care services for AF to routine care in adults diagnosed with AF. We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 8 studies involving a total of 8205 people with AF, with an average age of 60 to 73 years. The included studies were performed in China, the Netherlands, and Australia. All eight studies reported receiving individual grants or a combination of public funding and funding from industry.

Compared to routine care, organised AF care services:

- prevent one death from all causes for every 37 patients treated and followed for six years;

- prevent one hospital admission from all causes for every 101 patients treated and followed for two years;

- prevent one heart-related death for every 86 patients treated and followed for six years; and

- prevent one heart-related hospital admission for every 28 patients treated and followed for six years; but

- may make little to no difference to complications such as stroke and mini-stroke (one complication prevented for every 588 patients treated and followed for six years) and major complications related to bleeding in the brain (one bleeding complication prevented for every 556 patients treated and followed for six years).

No study assessed minor complications related to bleeding in the brain.

What are the limitations of the evidence?

Our confidence in the evidence for death and hospital admissions from all causes is only moderate because it is possible that some study participants were aware of which treatment they were getting, which could have influenced the results.

We have little confidence in the evidence for heart-related death because the ways treatment was delivered varied across studies, and it is possible that some study participants were aware of which treatment they were getting, which could have influenced the results. We are confident that organised care services for AF reduce heart-related hospital admissions.

We have little confidence in the evidence for complications and bleeding-related complications specifically because the ways treatment was delivered varied across studies, and it is possible that some study participants were aware of which treatment they were getting, which could have influenced the results. Additionally, the small number of studies prevents us from being certain about the results.

How up-to-date is the evidence?

The evidence is current to October 2022.

Summary of findings 1. Summary of findings table - Clinical service organisation compared to usual care for adults with atrial fibrillation

Clinical service organisation compared to usual care for adults with atrial fibrillation

Patient or population: adults with atrial fibrillation
Setting: primary care practices and hospitals
Intervention: clinical service organisation
Comparison: usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with clinical service organisation				
All-cause mortality follow-up: range 3 months to 5.8 years	67 per 1000	**43 per 1000** (31 to 60)	**RR 0.64** (0.46 to 0.89)	4664 (5 RCTs)	⊕⊕⊕⊖ Moderate[a]	
All-cause hospitalisation follow-up: range 12 months to 24 months	493 per 1000	**463 per 1000** (434 to 502)	**RR 0.94** (0.88 to 1.02)	1340 (2 RCTs)	⊕⊕⊕⊖ Moderate[b]	
Cardiovascular mortality follow-up: range 3 months to 5.8 years	26 per 1000	**17 per 1000** (9 to 31)	**RR 0.64** (0.35 to 1.19)	4564 (5 RCTs)	⊕⊕⊖⊖ Low[c,d]	
Cardiovascular hospitalisation follow-up: range 3 months to 5.8 years	234 per 1000	**195 per 1000** (166 to 225)	**RR 0.83** (0.71 to 0.96)	3641 (3 RCTs)	⊕⊕⊕⊕ High	
Thromboembolic complications follow-up: range 3 months to 5.8 years	17 per 1000	**19 per 1000** (12 to 29)	**RR 1.14** (0.74 to 1.77)	4653 (5 RCTs)	⊕⊕⊖⊖ Low[a,d]	
Major cerebrovascular bleeding events follow-up: range 3 months to 5.8 years	15 per 1000	**19 per 1000** (12 to 30)	**RR 1.25** (0.79 to 1.97)	2964 (3 RCTs)	⊕⊕⊖⊖ Low[c,d]	
Minor cerebrovascular events - not reported	-	-	-	-	-	

***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).

CI: confidence interval; **RR:** risk ratio

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.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_429006128031995203.

[a] Downgraded one level due to study limitations: studies had either high or unclear risk of bias for selection, performance, and/or detection bias.
[b] Downgraded one level due to study limitations: studies had either high or unclear risk of bias for selection, performance, and/or detection bias.
[c] Downgraded one level due to study limitations: studies had either high or unclear risk of bias for selection, performance, and/or detection bias.
[d] Downgraded one level due to imprecision: 95% CI contains the possibility of benefit and harm.

BACKGROUND

Description of the condition

Atrial fibrillation (AF) is the most commonly occurring heart rhythm condition. Globally, 43.6 million people were affected by AF in 2016, and the reported prevalence in the adult population ranges from 2% to 4% (Hindricks 2021). AF is estimated to affect between 2.2 million people in the USA, with this number estimated to increase to 6 to 12 million in the USA by 2050, and 17.9 million people in Europe by 2060 (Lippi 2021). AF is associated with an increased risk of thromboembolic complications such as stroke, and other cardiovascular conditions such as heart failure, with risk increasing sharply with older age. Moreover, AF is associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men (Hindricks 2021). 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).

AF is considered a chronic and complex condition. Guidelines recommend a comprehensive treatment approach, including screening and detection, treatment of AF (by applying a rate and/or rhythm control strategy), prevention of thromboembolic complications such as stroke by estimating the stroke risk in people with AF and prescribing appropriate oral anticoagulation, and the treatment of underlying cardiovascular conditions, risk factors, and modification of lifestyle behaviour. This has also been described as the ABC approach (Lip 2017). The ABC approach has three key components: 'A' Avoid stroke (with Anticoagulants); 'B' Better symptom management, with shared decision-making on rate or rhythm control; and 'C' Cardiovascular and Comorbidity risk optimisation. The complexity of AF management has called upon changes in how care is delivered: where traditionally patients with AF would be treated by a primary healthcare professional, the focus is now on novel models of care delivery where care and treatment are provided by a broader multidisciplinary team and can include virtual care.

A recent systematic review and meta-analysis examining the use of the ABC pathway on clinical outcomes found a pooled prevalence of clinical management adherent to the ABC pathway criteria equal to 21% (95% confidence interval (CI) 13% to 34%), with high heterogeneity (I^2 = 100%). Patients treated according to the ABC pathway showed a lower risk of all-cause death (odds ratio (OR) 0.42, 95% CI 0.31 to 0.56), cardiovascular death (OR 0.37, 95% CI 0.23 to 0.58), stroke (OR 0.55, 95% CI 0.37 to 0.82), and major bleeding (OR 0.69, 95% CI 0.51 to 0.94), with moderate heterogeneity (Romiti 2022). Further, bleeding was reduced with the ABC intervention when using the HAS-BLED score to mitigate modifiable bleeding risk factors, and high-bleeding risk patients were followed up (Guo 2020b).

The 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 caregivers. Current models of care, and how these are organised as clinical services, are diverse and not suitable for comprehensive care delivery by a multidisciplinary team, leading to fragmentation of care. However, the Atrial Fibrillation Network/European Heart Rhythm Association suggested careful examination of the optimal organisation of clinical services and included models of care for AF management (Hindricks 2021). 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 and AF. Within integrated models of care, specialised clinics use a multidisciplinary team approach, comprehensive treatment, and patient-centred care, which have demonstrated improved patient outcomes. These approaches have been adopted in many countries and recommended within international guidelines (Hindricks 2021). Further, there is promising evidence related to collaborative multidisciplinary interventions, including nurse-led clinics and novel electronic Health (eHealth)/mobile Health (mHealth) interventions for AF.

Description of the intervention

Collaborative, multidisciplinary interventions

This group of interventions may include disease management programmes, integrated and co-ordinated models of care. Disease management is a system of co-ordinated healthcare interventions and communications for people with a specific condition and may include self-care components. Besides providing the required treatment and care, the approach is focused on teaching patients how to manage a chronic disease (Care Continuum Alliance 2021). These approaches have been used widely in the field of diabetes mellitus.

Multidisciplinary, comprehensive interventions, such as integrated care for AF, have been recommended by international guidelines from Europe and Asia Pacific (Andrade 2020; Brieger 2018; Chao 2022; Hindricks 2021; Kirchhof 2016). Integrated care can be defined as a collaborative, patient-centred care approach to providing health care focused on improving patients' care experiences, health outcomes, and quality of life, and creating efficiencies in the health system (Brieger 2018). Integrated care consists of four fundamentals:

1. a patient-centred approach;
2. a multidisciplinary team;
3. provision of comprehensive care delivery; and
4. the use of technology to support the integrated approach.

All elements must be present to be regarded as an integrated-care approach (Brieger 2018; Hindricks 2021). Thus, models that include only a single element, for example education alone, should not be regarded as an integrated-care approach.

To date, a number of rigorously conducted randomised controlled trials have demonstrated improved outcomes for people with AF attending multidisciplinary clinics utilising an integrated-care approach. One systematic review with meta-analysis found that an integrated-care approach for AF management was associated with a reduction in all-cause mortality (OR 0.51, 95% CI 0.32 to 0.80; P = 0.003) and cardiovascular hospitalisations (OR 0.58, 95% CI 0.44 to 0.77; P < 0.001); however, it did not significantly affect 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).

eHealth and mHealth models of care

The World Health Organization defines eHealth 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). eHealth and mHealth models (also known as virtual care) are emerging, with the COVID-19 pandemic significantly contributing to this. Virtual care may be incorporated in a collaborative, multidisciplinary, and integrated approach. An example of this is the TeleCheck-AF approach, which is an on-demand mHealth intervention embedded in an integrated-care approach, to enable remotely provided, comprehensive treatment for people with AF (Linz 2020; Pluymaekers 2021).

Outcomes to be pursued in the management of AF

Care should aim to address quality of life and symptom burden, optimising pharmacotherapy in line with guideline recommendations and the needs, values, and preferences of the patient, and promoting self-care strategies, where the ultimate goal is to prevent avoidable hospitalisations and reduce mortality. AF management should be patient-centred and tailored to meet the needs of the individual. Whilst 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 the individual patient's circumstances, values, and treatment preferences (Brieger 2018; Ferguson 2013; Hindricks 2021). Findings from a systematic review highlight that the prescription of oral anticoagulation for stroke prevention in AF remains poor, with more than 30% of people not receiving appropriate thromboprophylaxis (Ogilvie 2010). Further, large international registries, such as the GARFIELD (Global Antithrombotic Registry in the FIELD) registry, have demonstrated over-treatment of people with AF who have a low risk of stroke, whilst also highlighting undertreatment of those with a high risk of stroke (Kakkar 2013).

This review included trials comparing different types of clinical service organisation for AF with usual or routine care. We evaluated different types of clinical service organisation, such as case management approaches, collaborative multidisciplinary interventions (e.g. nurse-led clinics), integrated models of care, and eHealth models of care (such as virtual care, digital health, mHealth, telehealth, and structured telephone support approaches).

How the intervention might work

Different types of clinical service organisation have the potential to improve effective and efficient care delivery, resulting in improved outcomes including a reduction of all-cause mortality and prevention of cardiovascular (re)hospitalisations. These interventions are often considered complex organisational interventions. They can be delivered via structured health services across the primary, secondary, and tertiary care settings and at different stages of the care process, throughout different locations.

Many of the components of care for people with AF require the engagement of health professionals within various disciplines. No singular health discipline holds the skills or expertise to adequately manage people with these complex needs in isolation. 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 method to optimising care for people with AF in the outpatient setting (Carter 2016; Hendriks 2012; Stewart 2015). Each health discipline offers a unique lens to optimising care for AF. For example, pharmacists are often experts in pharmacotherapeutic management and medication adherence; physiotherapists have expertise in providing physical activity advice; and dietitians in the provision of dietary recommendations and tailoring dietary plans. Further, nurses have key functions in providing patient education and counselling, risk assessment, or performing clinical procedures. Whilst these examples of areas of expertise are based on traditional views of discipline roles and functions, each health discipline actively contributes to achieving comprehensive AF management. Importantly, each discipline will have a specific role within the healthcare team or care management. It is therefore imperative that the effectiveness of these alternate models of care be robustly examined against traditional models of care.

Why it is important to do this review

Current care models for the management of AF are based on the traditional approach, where one healthcare professional would provide the required care and services. This poses a significant burden to the health system and individual practitioners and fragmentation of care from the perspective of patients and their families. Given the increasing prevalence of people with AF and associated multimorbidity, there is a pressing need for the redesign of the approach to the management of AF. Health professionals from various disciplines may offer an innovative contribution to complex healthcare workforce issues. Further, multidisciplinary teams, including advanced healthcare practitioners, may be able to provide care delivery more efficiently through an integrated organisational workforce model. To address these issues, we formulated the following research question: what is the effectiveness of different clinical service organisation versus usual care, for people with all types of AF?

One systematic review evaluated the effect of using an integrated-care approach in AF management (Gallagher 2017). A key limitation of this review was the singular focus on integrated-care models versus a broader review of other models of care. Therefore, the effect of other models of care delivery in AF remains unclear, and highlights the need for a Cochrane review that closely examines clinical service organisation models more broadly for people with AF. There is increasing evidence to support the specialisation of healthcare teams. Advanced practitioners, specifically nurse co-ordinated models of care, have demonstrated better outcomes for a range of chronic conditions such as transient ischaemic attack (TIA) and minor stroke (O'Brien 2016); diabetes, hypertension, and hypercholesterolaemia (Shaw 2014); heart failure (Rich 1995; Stewart 2012); and AF (Carter 2016; Hendriks 2012; Hendriks 2019; Stewart 2015). 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 an organised-care approach, incorporating goal-setting and attainment by patients as part of the outcomes. Case managers are often experienced clinicians from a range of health disciplines who support behaviour change modification and the optimisation of medical therapies (Ma 2009). There is a need for rigorous evaluation of these organised clinical service models of care in the context of AF.

OBJECTIVES

To assess the effects of clinical service organisation for AF versus usual care for people with all types of AF.

METHODS

Criteria for considering studies for this review

Types of studies

We included individual parallel-arm, cluster, and cross-over randomised controlled trials (RCTs), as they are more likely to provide unbiased information than other study designs. We excluded quasi-randomised trials.

We placed no restrictions on language, sample size, and duration of follow-up.

We sought help with translation or data extraction from non-English language reports of studies from volunteer assistance via Cochrane Engage platform, which is accessible to both Cochrane and non-Cochrane review teams. Where it was not possible to extract the relevant information and data from non-English language reports, readers were informed of the existence of other possibly relevant reports in 'studies awaiting classification' rather than 'excluded' studies. We included studies published as full texts and as abstract only in order to increase the comprehensiveness and precision of the review and decrease the potential impact of publication bias.

Types of participants

We included studies of adults (18 years of age or older) with a diagnosis of AF of any type (defined as paroxysmal, persistent, or long-term persistent AF) or aetiology, consistent with international and national guidelines (Brieger 2018). We excluded studies that targeted general cardiac disorders rather than AF specifically. Studies that included mixed populations were excluded unless separate results for people with AF could be identified or obtained from the study authors. We included studies where ≥ 80% of participants had AF.

Types of interventions

We included clinical service interventions directed at people living with AF. This included clinical service, disease-specific management interventions (inpatient, outpatient, or community-based interventions) targeted to people living with AF. Interventions may have included or excluded patients' families or informal carers. Clinical service interventions must have been multicomponent and involved a multidisciplinary approach to be eligible.

Interventions included:

1. case management;
2. collaborative multidisciplinary interventions such as disease management programmes;
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 excluded studies that were solely focused on the following types of interventions and that did not adopt a multidisciplinary approach.

1. Interventions that were primarily educational-behavioural in nature
2. Interventions that were described as cardiac rehabilitation programmes
3. Interventions where the sole focus was lifestyle risk reduction
4. Interventions that targeted cardiovascular disease or chronic disease in general
5. Interventions that had a sole focus on medication prescription and use, risk assessment, screening and detection of AF, and/or other individual components of disease state management

Types of outcome measures

Reporting one or more of the outcomes listed here was not an inclusion criterion. Where a published report did not appear to report one of these outcomes, we accessed the trial protocol and contacted the authors to ascertain whether the outcomes were measured but not reported. Relevant trials that measured these outcomes but did not report the data at all, or reported data in an unusable format, were included and described narratively. Outcomes were measured using the longest follow-up for each study. We evaluated the following primary and secondary outcomes.

Primary outcomes

1. All-cause mortality.
2. All-cause hospitalisation (number of participants with at least one hospitalisation).

Secondary outcomes

1. Cardiovascular mortality.
2. Cardiovascular hospitalisation (number of participants with at least one cardiovascular hospitalisation).
3. AF-related emergency department visits (number of participants with at least one event).
4. Thromboembolic complications, including stroke or TIA, or both (number of participants with at least one event).
5. Minor cerebrovascular bleeding events as defined by the International Society on Thrombosis and Haemostasis (ISTH) criteria (number of participants with at least one event) (Kaatz 2015).
6. Major cerebrovascular bleeding events as defined by ISTH criteria (number of participants with at least one event) (Kaatz 2015).
7. All bleeding events (number of participants with at least one event).
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 the 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.

Search methods for identification of studies

Electronic searches

We identified trials through systematic searches of the following bibliographic databases on 4 October 2022:

1. Cochrane Central Register of Controlled Trials (CENTRAL; 2022, Issue 10) in the Cochrane Library;
2. MEDLINE Daily, Epub Ahead of Print, In-Process & Other Non-Indexed Citations Ovid (1946 to 3 October 2022);
3. Embase (Ovid, 1980 to 2022 week 39); and
4. CINAHL Plus EBSCOhost (Cumulative Index to Nursing and Allied Health Literature; 1937 to 4 October 2022).

We adapted the preliminary search strategy for MEDLINE (Ovid) for use in the other databases (Appendix 1). The RCT filter for MEDLINE is the Cochrane sensitivity and precision-maximising RCT filter, and for Embase, terms as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* have been applied (Lefebvre 2023). For CINAHL, the Cochrane CINAHL RCT filter was used (Glainville 2019).

We also conducted a search of ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch) for ongoing or unpublished trials on 7 April 2023.

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

Searching other resources

We also checked the reference lists of all included studies and any relevant systematic reviews identified for additional references to trials, and examined any relevant retraction statements and errata for included studies.

Data collection and analysis

Selection of studies

Three review authors (AD, FS, and SA) independently screened the titles and abstracts of all studies identified by the search using Covidence (Covidence), coding them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve'. In case of disagreement, a fourth review author (CF) was asked to arbitrate. We retrieved the full-text study reports/publication, and two review authors (FS and SA) independently screened the full texts and identified studies for inclusion, and listed and recorded the reasons for exclusion of ineligible studies. We resolved any disagreements through discussion or by consulting a third review author (CF) if required. We identified and excluded duplicates and collated multiple reports of the same study so that each study, rather than each report, was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and Characteristics of excluded studies table (Page 2021).

Data extraction and management

We used a data extraction form for study characteristics and outcome data that had been piloted on at least one included study. Two review authors (FS and SA) extracted the following study characteristics and reported 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, sex, type of AF, history of heart failure, CHA_2DS_2-VASc score (Congestive heart failure; Hypertension; Age 75 years or older; Diabetes mellitus; Stroke, TIA, or thromboembolism; Vascular disease; Age 65 to 74 years; Female risk category), 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 and sites.
6. Notes: funding and conflicts of interest, etc.

We resolved any disagreements by consensus or by involving a third review author (SCI). One review author (FS) transferred the data into RevMan (RevMan 2024). We double-checked that data had been entered correctly by comparing the data presented in the systematic review with those on the data extraction form. A second review author (CF) spot-checked study characteristics for accuracy against the study report.

Assessment of risk of bias in included studies

Two review authors (FS and SA) independently assessed risk of bias in the included studies using the Cochrane RoB 1 tool (Higgins 2017). We resolved any disagreements by discussion or by involving another review author (SCI). We assessed 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, considering baseline imbalance in cluster-RCTs, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017)

We graded each potential source of bias as low, high, or unclear and provided a quote from the study report, together with a justification for our judgement, in the Risk of bias in included studies table. We summarised the risk of bias judgements across different studies for each of the domains listed. Where information on risk of bias related to unpublished data or correspondence with a trialist, we noted this in Risk of bias in included studies.

When considering treatment effects, we considered the risk of bias in the studies that contributed to that outcome.

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol (Ferguson 2019a), reporting any deviations from it in the Differences between protocol and review section of the systematic review.

Measures of treatment effect

We calculated dichotomous data as risk ratios (RRs) with 95% confidence intervals (CI) and continuous data as mean difference (MD) or standardised mean difference (SMD) with 95% CI when appropriate, using random-effects analyses; we used the MD if studies use the same outcome measures and the SMD if studies used different outcome measures. We also calculated the number needed to treat for an additional beneficial outcome (NNTB) (expected number of people who need to receive the experimental rather than the comparator intervention for one additional person to avoid an event in a given time frame) using the RR and by calculating an assumed comparator risk (baseline risk, or risk that the outcome of interest would occur with the comparator intervention) (Higgins 2023a).

We entered data presented as a scale with a consistent direction of effect. We narratively described skewed data reported as medians and interquartile ranges (IQRs).

Unit of analysis issues

We included cluster-RCTs in this review. We addressed this unit of analysis issue by conducting the analysis at the same level as the allocation, that is we analysed data as if each cluster was a single individual, using a summary measurement from each cluster (intracluster coefficients reported by the study authors).

When trials included two or more active intervention arms and only one control arm (usual care), we combined the active intervention arms to create a single, pair-wise comparison and compared this with the control arm.

These methods were based on recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2023b).

Dealing with missing data

We contacted investigators or study sponsors in order to verify key study characteristics and to obtain missing numerical outcome data where possible. We used the RevMan calculator to calculate missing standard deviations (SDs) using other data from the trial such as CIs (RevMan 2024), or contacted the study authors to request missing data. Where this was not possible, and the missing data were thought to introduce serious bias, we explored the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Assessment of heterogeneity

We inspected forest plots visually to consider the direction and magnitude of effects and the degree of overlap between CIs. We used the I^2 statistic to measure heterogeneity amongst 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 also considered the P value from the Chi^2 test. If we identified substantial heterogeneity (I^2 greater than 50%), we reported it.

Assessment of reporting biases

We were unable to assess publication bias by using a funnel plot, as too few trials were included (Page 2023).

In some cases, similarities between trial reports indicated the possibility of multiple publications from the same trial. We contacted study authors to check whether these publications were duplicates. In the absence of a response and explicit cross-referencing, we judged articles to be from the same trial if they met the following criteria: (1) evidence suggested overlapping recruitment sites, trial dates, and grant funding numbers, and (2) similar or identical patient characteristics were reported by study authors.

Data synthesis

We undertook meta-analyses only where this was meaningful, that is if the treatments, participants, and the underlying clinical question were similar enough for pooling to make sense.

We used a random-effects model (inverse-variance method), as we expected some heterogeneity in the interventions.

When we were unable to combine the data in a meta-analysis, we provided a narrative description of the results as reported by the original study authors.

Subgroup analysis and investigation of heterogeneity

An insufficient number of included studies precluded our preplanned subgroup analyses.

As heterogeneity could not be explained, we combined trials using random-effects analyses and interpreted the results cautiously, or we did not combine them at all.

Sensitivity analysis

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

Summary of findings and assessment of the certainty of the evidence

We created a summary of findings table comparing clinical service organisation for AF with usual care for the following outcomes:

1. all-cause mortality;
2. all-cause hospitalisation (number of participants with one hospitalisation);
3. cardiovascular mortality;
4. cardiovascular hospitalisation;
5. thromboembolic complications including stroke and TIA;
6. major cerebrovascular bleeding events; and
7. minor cerebrovascular bleeding events.

We used 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 followed the methods and recommendations described in Chapters 14 and 15 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2023a; Schünemann 2023b), constructing the table using GRADEpro GDT software (GRADEpro GDT). We justified all decisions to downgrade the certainty of evidence using footnotes, and made comments to aid the reader's understanding of the review where necessary.

Three review authors (CF, FS, and SA) independently judged the certainty of the evidence, with any disagreements resolved by discussion or involving a fourth review author (SCI). We justified, documented, and incorporated judgements of reporting of results for each outcome.

We extracted study data, formatted our comparisons in data tables, and prepared summary of findings tables before writing the results and conclusions of our review.

RESULTS

Description of studies

Results of the search

We identified 8459 records in total, of which 8452 were identified from the following databases:

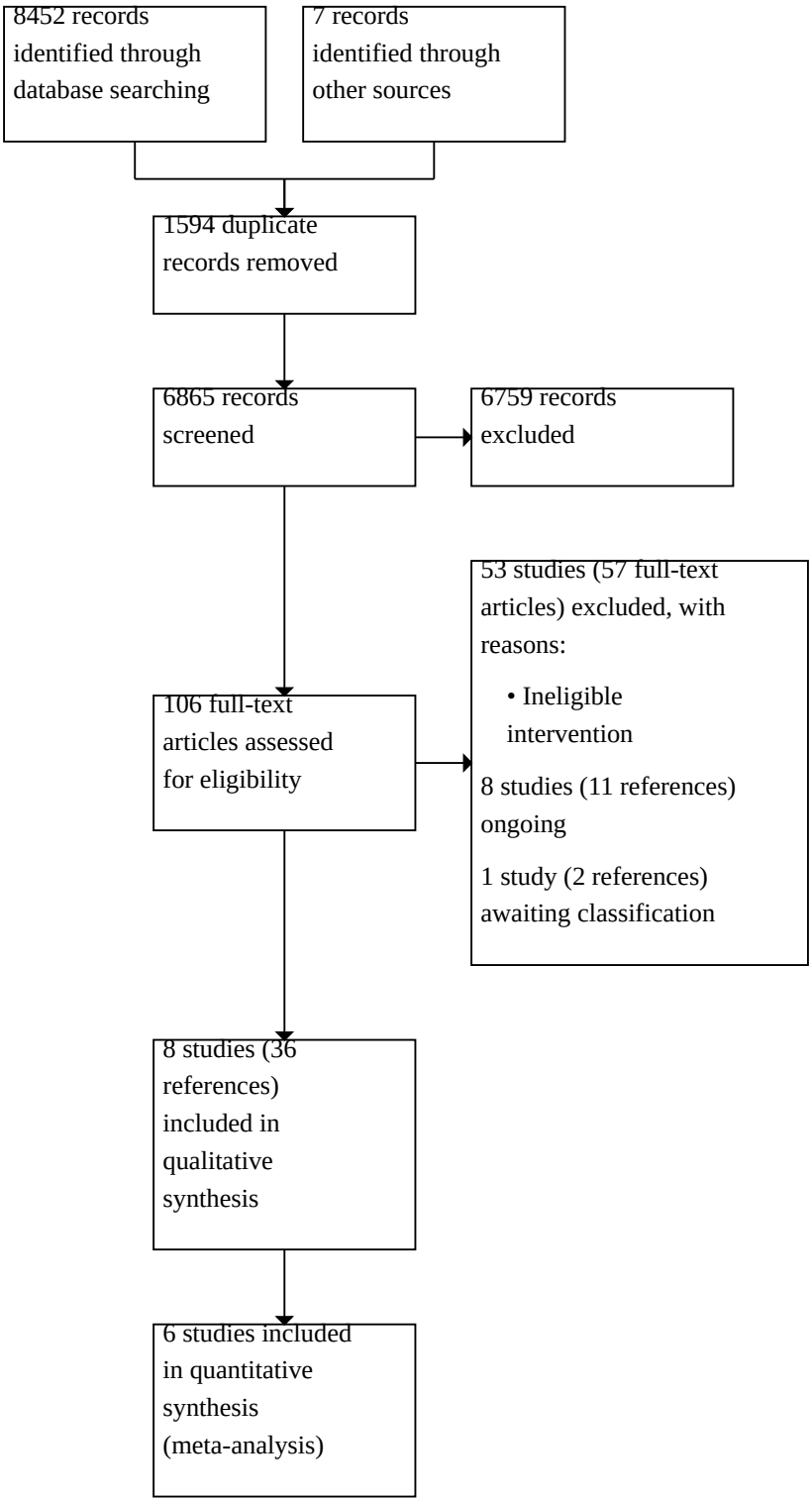
1. CENTRAL (n = 2966);
2. MEDLINE (Ovid) (n = 1282);
3. Embase (Ovid) (n = 2709);
4. CINAHL Plus (EBSCOhost) (n = 1495).

We found seven additional references by searching:

1. ClinicalTrials.gov (n = 4); and
2. WHO ICTRP (n = 3).

We excluded 1594 duplicate references. We screened 6865 titles and abstracts and excluded 6759 articles as irrelevant. We retrieved 106 full texts. After full-text review, we excluded 53 studies (57 reports) as they did not meet the review eligibility criteria. The primary reasons for exclusion are provided in Characteristics of excluded studies and Figure 1. We included a total of eight studies in the review. There is one study awaiting classification and eight ongoing studies.

Figure 1. PRISMA flow diagram.



Included studies

A total of eight studies met the inclusion criteria (Guo 2017; Guo 2020a; Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022); however, two studies could not be included in the meta-analysis (Guo 2017; Li 2023).

Detailed information regarding participants, interventions, outcomes and other key information about the studies (e.g. sources of funding, conflicts of interest, etc.) is provided in the Characteristics of included studies table.

We contacted three study authors to request major, minor, and all bleeding events data as number of participants with at least one event (Hendriks 2012; van den Dries 2020; Wijtvliet 2020). We received responses from all three authors, which enabled us to perform meta-analysis.

Design

Five studies were individual parallel-arm RCTs (Hendriks 2012; Li 2023; Stewart 2015; Wijtvliet 2020; Yan 2022), and three studies were cluster-RCTs (Guo 2017; Guo 2020a; van den Dries 2020).

Country

Three studies were conducted in the Netherlands (Hendriks 2012; van den Dries 2020; Wijtvliet 2020), three in China (Guo 2017; Guo 2020a; Yan 2022), one in Hong Kong (Li 2023), and one in Australia (Stewart 2015).

Setting

All included studies were recruited from and conducted at either a single or multiple tertiary hospitals.

Participants

The sample size of the studies included in the review ranged from 40 (Li 2023) to 3628 (Guo 2020a), giving a total of 8205 participants across all eight studies. The samples from Guo 2017 (209 participants) and Li 2023 (40 participants) were not included in the meta-analysis.

Although the specific inclusion criteria of each study varied, all of the included studies required that participants have a documented diagnosis of AF and be 18 years of age or older; the average age in both the intervention and control groups ranged from 60 to 73 years. Participants across all the included studies were generally randomised equally to both the intervention and control groups; however, van den Dries 2020 had a slightly larger proportion in the control group on analysis.

Interventions

Delivery

Two studies delivered the intervention using mHealth (i.e. mobile AF application) (Guo 2017; Guo 2020a), whilst two other studies used a decision support software such as CardioConsult AF (Curit Software; Groningen, the Netherlands), under the supervision of a cardiologist (Hendriks 2012; Wijtvliet 2020). The remaining four studies used a case management approach (Li 2023; Stewart 2015; van den Dries 2020; Yan 2022).

Content

All studies used a collaborative, multidisciplinary approach involving cardiologists, general practitioners, cardiac nurses, and allied health professionals. The majority of the studies were nurse-led (Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022). The content of the intervention varied but included the following.

1. Stroke and bleeding risk assessment: CHA_2DS_2-VASc, HAS-BLED scores, hypertension, abnormal renal/liver function, stroke, bleeding history, and overall medical history.
2. Self-care education programmes: provision of education materials or training around the pathophysiology of AF, its symptoms and possible complications, the results of the diagnostic tests and treatment options and strategies with self-care protocols.
3. Anticoagulation case management: international normalised ratio (INR) measurements in those treated with a vitamin K antagonist (VKA), special attention to drug compliance, and monitoring of kidney function in participants using a non-vitamin K antagonist oral anticoagulant (NOAC).
4. Structured postdischarge care and follow-up.
5. Psychosocial support.

Comparator

All studies compared organised care services for AF with usual care.

Outcomes

All eight included studies reported at least one of the outcomes of interest (Guo 2017; Guo 2020a; Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022); however, none of the outcomes of interest was reported by all eight studies.

Primary outcome(s)

Three studies included in the meta-analysis reported a composite of multiple outcomes (Guo 2020a; Hendriks 2012; Wijtvliet 2020), with thromboembolic/stroke events reported across all three. However, Hendriks 2012 and Wijtvliet 2020 had an additional two common outcomes, cardiovascular mortality and hospitalisation, that were part of their composite endpoint. Guo 2020a was the only study out of the three that also included all-cause mortality as part of its primary endpoint. The remaining three studies had only one or two separate primary endpoints, all-cause mortality being common between Stewart 2015 and van den Dries 2020.

Two other studies that met the inclusion criteria but were not part of the meta-analysis also had a singular primary endpoint (Guo 2017; Li 2023).

Secondary outcome(s)

Most of the included studies reported at least one secondary outcome. Approximately six secondary outcomes were commonly reported across the eight studies, although the scoring tools or definitions used by each study varied. The six common outcomes included cardiovascular hospitalisation (Guo 2020a; Stewart 2015; van den Dries 2020; Yan 2022), cardiovascular mortality (Hendriks 2012; van den Dries 2020; Yan 2022), cost-effectiveness/utility analysis (Stewart 2015; van den Dries 2020; Wijtvliet 2020), bleeding (Stewart 2015; van den Dries 2020), and AF-related quality of life (Guo 2017; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020).

Funding

All eight studies reported the sources of funding, which were either individual grants or a combination of funding from pharmaceutical/healthcare insurance companies, research foundations, research councils, academic/medical institutions, or government bodies.

Studies awaiting classification

One study is awaiting classification (see Characteristics of studies awaiting classification). We are unsure if the intervention meets the criteria for organised care services for AF.

Ongoing studies

We identified eight ongoing studies (see Characteristics of ongoing studies); all are currently in their participant recruitment phases, and were thus not available for full-text analysis.

Excluded studies

A total of 121 studies did not meet the inclusion criteria and were excluded from the analysis for the following reasons:

1. ineligible intervention (n = 100);
2. ineligible study design (n = 17);
3. ineligible patient population (n = 4).

We have provided details on 53 of these studies, all reporting ineligible interventions, in the Characteristics of excluded studies table.

Risk of bias in included studies

Overall, we assessed the risk of bias as high, as all studies had at least one domain at unclear or high risk of bias. Risk of bias summaries are presented in the risk of bias tables in Characteristics of included studies and in Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

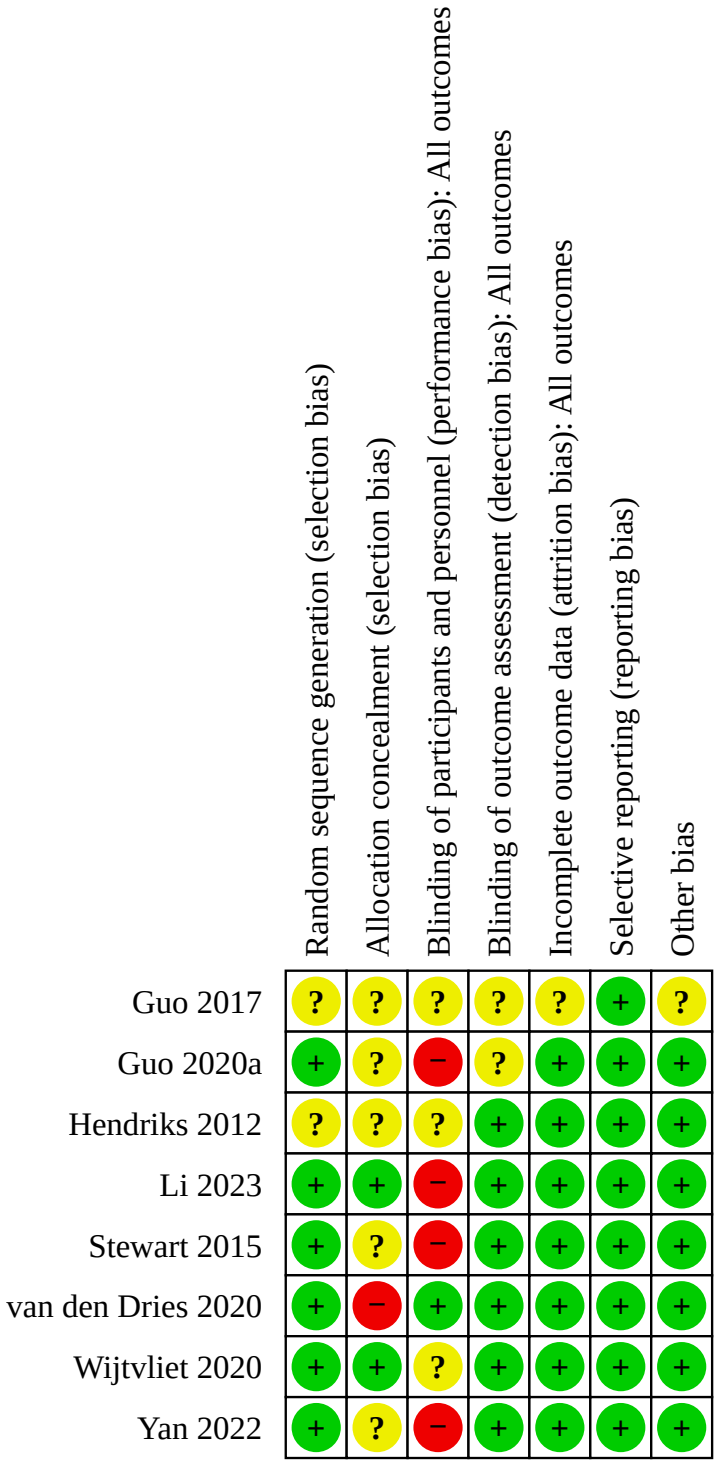
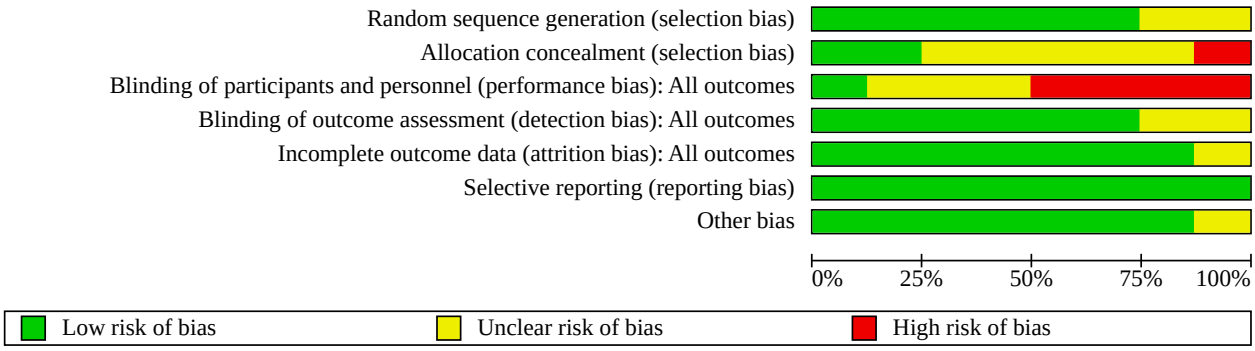


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

We assessed six studies as at low risk of bias regarding reporting of methods of random sequence generation (Guo 2020a; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022). Two studies did not report their method of random sequence generation and were therefore assessed as at unclear risk of bias (Guo 2017; Hendriks 2012).

We assessed two studies as at low risk of selection bias in relation to allocation concealment (Li 2023; Wijtvliet 2020), whilst five studies did not report their method of allocation concealment and were rated as unclear (Guo 2017; Guo 2020a; Hendriks 2012; Stewart 2015; Yan 2022). We rated one study as at high risk of bias for allocation concealment, as the study investigators and personnel could foresee the group allocation (van den Dries 2020).

Blinding

We assessed three studies as at unclear risk of performance bias, as details regarding the blinding of participants and personnel were not reported (Guo 2017; Hendriks 2012; Wijtvliet 2020). We rated four studies as at high risk of performance bias due to lack of blinding of participants and personnel (Guo 2020a; Li 2023; Stewart 2015; Yan 2022). We assessed van den Dries 2020 as at low risk of performance bias as a waiver of informed consent for anonymised data collection was approved by the Ethics Committee. This enabled assessment of undetectable possible selection bias, enhanced generalisability of the findings, and reduced the risk of contamination between groups.

We assessed six studies as at low risk of detection bias, as outcome assessors were blinded to group allocation (Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022). Two studies did not report blinding of outcome assessors (Guo 2017; Guo 2020a).

Incomplete outcome data

We assessed seven studies as having a low risk of attrition bias (Guo 2020a; Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022). We rated the Guo 2017 study as at unclear risk of bias, as insufficient information was provided to permit a judgement of whether the study had incomplete outcome data.

Selective reporting

We assessed all included studies as having a low risk of reporting bias, as the protocol was available, and the prespecified outcomes were reported in the final publications.

Other potential sources of bias

We assessed all included studies as having a low risk of other bias, apart from Guo 2017, which was judged as at unclear risk of bias due to lack of clarity regarding clusters and similarity of participants between the two clusters.

Effects of interventions

See: **Summary of findings 1** Summary of findings table - Clinical service organisation compared to usual care for adults with atrial fibrillation

Primary outcomes

All-cause mortality

All-cause mortality data were available for all five studies that were included in the meta-analysis. Clinical service organisation for AF likely resulted in a large reduction in all-cause mortality compared to usual care (risk ratio (RR) 0.64, 95% confidence interval (CI) 0.46 to 0.89; P = 0.008; I^2 = 35%; 5 studies, 4664 participants; moderate certainty evidence; Analysis 1.1). Therefore, the estimated six-year number needed to treat for an additional beneficial outcome (NNTB) for all-cause mortality with organised AF clinical services is 37.

We removed two studies in sensitivity analysis due to their unclear (Guo 2020a) or high (van den Dries 2020) risk of selection bias. The point estimate was similar, but the CI widened, and the large relative risk reduction for all-cause mortality was no longer observed. Organised AF clinical service did not reduce all-cause mortality (RR 0.71, 95% CI 0.40 to 1.24; P = 0.23; I^2 = 63%; 3 studies, 2401 participants; Analysis 1.2). Heterogeneity also increased to 63%.

All-cause hospitalisation

Two studies reported all-cause hospitalisation data. Clinical service organisation for AF likely resulted in little to no difference in all-cause hospitalisation compared to usual care (RR 0.94, 95% CI 0.88 to 1.02; P = 0.13; I^2 = 0%; 2 studies, 1340 participants; moderate

certainty evidence; Analysis 1.3). Therefore, the two-year estimated NNTB for all-cause hospitalisation is 101 compared to usual care.

We removed the study by van den Dries 2020 from the analysis due to its high risk of selection bias. As only one study remained, this precluded us from conducting a sensitivity analysis for this outcome (Analysis 1.4).

Secondary outcomes

Cardiovascular mortality

Cardiovascular mortality data were available for four studies. Clinical service organisation for AF may not have reduced cardiovascular mortality compared to usual care (RR 0.64, 95% CI 0.35 to 1.19; P = 0.20; I^2 = 33%; 5 studies, 4564 participants; low certainty evidence; Analysis 1.5). Thus, the estimated six-year NNTB for cardiovascular mortality is 86 compared to usual care.

We removed two studies from the analysis (Guo 2020a; van den Dries 2020). The relative risk for cardiovascular mortality in the sensitivity analysis did not differ. Organise AF clinical services may not have reduced cardiovascular mortality (RR 0.82, 95% CI 0.18 to 3.88; P = 0.06; I^2 = 65%; 3 studies, 2301 participants; Analysis 1.6). However, heterogeneity was increased from 33% to 65%.

Cardiovascular hospitalisation

Cardiovascular hospitalisation data were available for four studies. Guo 2020a reported the outcome as "cardiovascular rehospitalisation", hence it was removed from this analysis. Clinical service organisation for AF reduced cardiovascular hospitalisation compared to usual care (RR 0.83, 95% CI 0.71 to 0.96; P = 0.17; I^2 = 38%; 3 studies, 3641 participants; high certainty evidence; Analysis 1.7). Thus, the six-year estimated NNTB for cardiovascular hospitalisation is 28 compared to usual care.

We removed the van den Dries 2020 study from the analysis. The effect remained unchanged. Organised AF clinical services reduced cardiovascular hospitalisation compared to usual care (RR 0.79, 95% CI 0.67 to 0.94; P = 0.17, I^2 = 40%; 4 studies, 2456 participants; Analysis 1.8).

AF-related emergency department visits

Only two studies reported data on the number of AF-related emergency department visits. Clinical service organisation for AF may have had little to no effect on AF-related emergency department visits compared to usual care (RR 0.54, 95% CI 0.18 to 1.63; P = 0.28; I^2 = 69%; 2 studies, 2612 participants; Analysis 1.9).

We removed the Guo 2020a study from the analysis due to its unclear risk of selection bias. As only one study remained, this precluded us from conducting a sensitivity analysis for this outcome (Analysis 1.10).

Thromboembolic complications including stroke and/or TIA

Data relating to the number of thromboembolic complications were available for all five studies that were included in the meta-analysis. Clinical service organisation for AF may not reduce thromboembolic complications, including stroke and/or TIA, compared to usual care (RR 1.14, 95% CI 0.74 to 1.77; P = 0.55; I^2 = 0%; 5 studies, 4653 participants; low certainty evidence; Analysis 1.11). The estimated six-year NNTB for thromboembolic complications with organised AF clinical services is 588.

We removed two studies from the analysis (Guo 2020a; van den Dries 2020). The effect remained unchanged. Organised AF clinical services did not reduce thromboembolic complications (RR 1.15, 95% CI 0.66 to 2.01; P = 0.63; I^2 = 0%; 3 studies, 2401 participants; Analysis 1.12).

Minor cerebrovascular bleeding events

None of the studies reported data on the number of minor cerebrovascular bleeding events, thereby precluding meta-analysis for this outcome.

Major cerebrovascular bleeding events

Data on the number of major cerebrovascular bleeding events were available for three studies. Clinical service organisation for AF may not reduce major cerebrovascular bleeding events compared to usual care (RR 1.25, 95% CI 0.79 to 1.97; P = 0.34; I^2 = 0%; 3 studies, 2964 participants; low certainty evidence; Analysis 1.13). The six-year estimated NNTB for major cerebrovascular bleeding events is 556 compared to usual care.

We removed two studies from the analysis (Guo 2020a; van den Dries 2020). As only one study remained (Hendriks 2012), this precluded us from conducting a sensitivity analysis for this outcome (Analysis 1.14).

All bleeding events

Data relating to the number of minor and major bleeding events were available for all four studies that were included in the meta-analysis. Clinical service organisation for AF did not reduce all bleeding events compared to usual care (RR 1.13, 95% CI 0.82 to 1.55; P = 0.45; I^2 = 0%; 4 studies, 3299 participants; Analysis 1.15).

We removed two studies from the analysis (Guo 2020a; van den Dries 2020). The effect remained unchanged. Organised AF clinical services did not reduce all bleeding events (RR 1.07, 95% CI 0.66 to 1.71; P = 0.90; I^2 = 0%; 2 studies, 1047 participants; Analysis 1.16).

AF-related quality of life

Only one included study reported AF-related quality of life data using AF-specific validated outcome measures as outlined in Types of outcome measures (Li 2023). Hence, a meta-analysis could not be performed for this outcome.

The majority of included studies used various quality of life outcome measures such as the 36-item Short Form Health Survey (SF-36), EQ-5D-Y, and AFSS (Guo 2017; Hendriks 2012; Stewart 2015; van den Dries 2020; Wijtvliet 2020). We have narratively described the quality of life findings of each study.

AFEQT

The Generalised Estimating Equation analysis demonstrated better improvements in health-related quality of life scores of the intervention group than those in the usual care group six months after the intervention (β = 8.963, 95% CI 0.123 to 16.324; P = 0.045). Cohen's d values were 0.68, indicating a medium effect size (Li 2023).

AFSS

There was no difference between the mean and SD of the intervention (4.8 ± 5.2) and the usual care group (5.1 ± 5.4) using the AFSS tool (Wijtvliet 2020).

12-item Short Form Health Survey (SF-12)

There were minimal changes between baseline and follow-up for the physical and mental components of the SF-12 for all three studies. In the study by van den Dries 2020, the intervention arm had a 0.95-point decrease on the physical health component score over two years of follow-up compared to a 1.51-point decrease in the control arm (P = 0.130). For the mental health component score, there was a 2.04-point decrease in the intervention arm compared to a 0.75-point decrease (P = 0.517) in the control arm. Similarly, in the intervention group in the Stewart 2015 study, there was a mean change between baseline and follow-up of −0.5 (SD −2.4 to 1.4) in the physical component and a mean change of 1.0 (SD −1.2 to 3.2) in the mental component. In the control group, there was a mean change between baseline and follow-up of −1.0 (SD −3.0 to 1.0) in the physical component and a mean change of −1.1 (SD −3.3 to 1.0) in the mental component.

SF-36

In the study by Hendriks 2012, there was no difference between the intervention and usual care groups over time for the overall SF-36 score. However, a difference was observed between the two groups at baseline for the following subscores: physical functioning (P = 0.000), general health (P = 0.000), physical role (P = 0.010), vitality (P = 0.013), and bodily pain (P = 0.011). A difference was observed at follow-up between the two groups for the emotional role (P = 0.033) and general health (P = 0.025). A difference was also found between the two groups over time for the following subscores: physical role (nurse-led care: P = 0.062, usual care: P = 0.004); emotional role (nurse-led care: P = 0.004, usual care: P = 0.956); mental health (nurse-led care: P = 0.001, usual care: P = 0.016); vitality (nurse-led care: P = 0.008, usual care: P = 0.000); and bodily pain (nurse-led care: P = 0.633, usual care: P = 0.002).

EQ-5D-Y

The was no difference in health status between the intervention (mean difference (MD) 0.00, 95% CI −0.04 to 0.04) and the usual care (MD 0.01, 95% CI −0.03 to 0.05) group in the Stewart 2015 study. However, in Guo 2017, there was an increase (all P < 0.05) in quality of life scores in the intervention (mAF App) group (baseline: 86.5, 1 month: 87.6, 3 months: 87.2) compared with the usual care group (baseline: 71.3, 1 month: 70.1, 3 months: 69.9).

AF symptom burden

AF symptom burden data were available for only one included study (Stewart 2015), precluding meta-analysis. However, amongst the six subgroups for which AF symptom burden was assessed, a higher relative risk for palpitations was observed (RR 1.50, 95% CI 1.15 to 1.96; P = 0.003) in the usual care group compared to the intervention group (Analysis 1.17). None of the others (dyspnoea, syncope, fatigue, chest pain/discomfort, and weakness) showed evidence of an effect.

As only one study was included in the analysis, a sensitivity analysis could not be performed.

Cost of intervention or other economic outcomes

Three studies performed cost analysis. However, only the findings from two studies were presented, as findings from one study were not available at the time of writing this review (van den Dries 2020).

Hendriks 2012 found that the mean total healthcare cost per patient was lower in the nurse-led care group (EUR 2.302 + 5.506) compared with the usual care group (EUR 3.037 + 5.987). The difference in outpatient costs was attributed to lower costs for outpatient consultation (including telephone and emergency consultation) and medication costs in the nurse-led care group compared with the usual care group. At the same time, costs for interventional procedures were higher in the nurse-led care group than in the usual care group (EUR 113.31 ± 627.26 versus EUR 74.38 ± 215.04). However, the nurse-led group had an increase of 0.009 quality-adjusted life years, with a reduced cost of EUR 1109 per patient, and a gain of 0.02 life-years with a reduced cost of EUR 735 per patient.

Stewart 2015 reported that the cost per patient for the SAFETY intervention was AUD 738, compared to AUD 150 for usual care. The predicted mean healthcare cost per person was AUD 4375 less for the SAFETY intervention compared to standard management (95% CI AUD 19,585 to AUD 10,835). The total value of perfect information regarding the SAFETY intervention is estimated at AUD 50,639,794.

Length of hospital stay

Only Stewart 2015 reported length of hospital stay; both the intervention and control group had a similar average in-hospital length of stay of 4.6 ± 6.3 and 4.8 ± 7.1 days, respectively. This corresponded to a median length of stay of 7 (IQR 1 to 26) days per patient or 2.5 (IQR 1.4 to 5.2) days per event in the intervention group, compared to 9 (IQR 3 to 28) days per patient or 3 (IQR 1.6 to 7.3) days per event in the control group.

Subgroup analysis

An insufficient number of included studies precluded subgroup analysis.

DISCUSSION

Summary of main results

Hospitalisations due to AF have increased exponentially in recent decades and are known to be the costliest component of AF care delivery (Freeman 2017; Gallagher 2019; Patel 2014; Sheikh 2015). In Australia, AF is the most common cause of cardiovascular hospitalisation, outnumbering both myocardial infarction and heart failure (Brieger 2018), and is growing at a rate that is more than double that of these two conditions (Gallagher 2019). Urgent strategies are needed to stem this growing burden.

This review is the first to explore different models of care on outcomes in the AF population. We included 8 studies with a total of 8205 participants. Organisation of care for AF likely results in a large reduction in all-cause mortality (estimated six-year NNTB is 37), compared to usual care. However, this is based on moderate certainty evidence and must be considered in light of the methodological limitations of the included trials, which is validated by the results of the sensitivity analysis. When two studies were removed due to unclear or high risk of selection bias, the point estimate did not change much, but the level of heterogeneity increased and the CIs widened, touching the line of no effect.

Clinical service organisation for AF probably makes little to no difference to all-cause hospitalisation (estimated two-year NNTB of 101) based on moderate certainty evidence. However, organised AF clinical services reduce cardiovascular hospitalisation (estimated

six-year NNTB of 28) based on high certainty evidence, and validated by sensitivity analysis. AF clinical service organisation may not reduce cardiovascular mortality (estimated six-year NNTB of 86) based on low certainty evidence, and may have little to no effect on AF-related emergency department visits. Clinical service organisation for AF may make little to no difference to thromboembolic complications such as stroke (estimated six-year NNTB of 588), major cerebrovascular bleeding events (estimated six-year NNTB of 556), based on low certainty evidence. Clinical service organisation for AF had no effect on all bleeding events. None of the included studies reported minor cerebrovascular events, and only one study had AF-related quality of life data using validated outcome measures specific for AF, thereby precluding meta-analysis for these outcomes. See Summary of findings 1.

Overall completeness and applicability of evidence

The accuracy of the findings of this review and meta-analysis is based on the studies that met our inclusion criteria. The eight included studies were heterogeneous (i.e. integrated models of care versus eHealth models of care) in terms of the nature of the clinical interventions delivered within them, as well as the personnel involved. One study assessed the impact of mHealth. Whilst the results of this study are encouraging, it was undertaken in one geographical location and was delivered by physicians alone, raising uncertainty about the widespread applicability of this model.

Three studies originated in the Netherlands (Hendriks 2012; van den Dries 2020; Wijtvliet 2020), three in China (Guo 2017; Guo 2020a; Yan 2022), one in Hong Kong (Li 2023), and one in Australia (Stewart 2015). None of the studies were conducted in low-middle-income countries, therefore it is unclear whether the results would be applicable in this setting. Further evaluation in other geographical locations is required to determine the applicability of such models of care. The evidence in this review is applicable to a predominantly male population aged between 60 and 73 years. All participants were diagnosed with AF either confirmed by an electrocardiogram or cardiologist, indicating an appropriate representation of population.

All eight included studies reported at least one of the outcomes of interest (Guo 2017; Guo 2020a; Hendriks 2012; Li 2023; Stewart 2015; van den Dries 2020; Wijtvliet 2020; Yan 2022). However, none of the outcomes of interest were reported by all eight studies. Most studies reported at least one secondary outcome. There were approximately six secondary outcomes that were commonly reported across the eight studies, although the scoring tools or definition used by each study varied. Only one study, Li 2023, used a validated outcome measure specific to AF to assess AF-related quality of life, precluding meta-analysis.

The comparator was usual care. However, details on usual care were lacking in most studies. In addition, definitions of usual care varied across studies, which is likely to have influenced the size of the effect estimates.

We identified eight ongoing studies. As these studies are either in their participant recruitment phase or have not yet reported any results, our findings were limited to those studies that have reported results and could be pooled in meta-analysis. We identified only one study as awaiting classification, as we were unsure if the intervention meets the criteria for organised care services for AF. Future updates of this review will incorporate new data along with the findings of studies that are currently underway but not yet completed, or are only available as a conference abstract or awaiting classification.

Quality of the evidence

We used GRADEpro GDT software to assess the certainty of evidence for both the primary and secondary outcomes and to create Summary of findings 1 (GRADEpro GDT). The certainty of the evidence ranged from high (cardiovascular hospitalisation) to low (thromboembolic complications and major cerebrovascular events). We downgraded the certainty of the evidence by one level for all-cause mortality, all-cause hospitalisation, cardiovascular mortality, thromboembolic complications, and major cerebrovascular bleeding events due to study limitations (unclear or high risk of bias rating in some of the studies). We also downgraded by one level for cardiovascular mortality, thromboembolic complications, and major cerebrovascular bleeding events due to imprecision (wide CIs).

Potential biases in the review process

The search strategy identified all relevant studies up until October 2022. Whilst this may be viewed as a limitation, we rechecked the studies listed as awaiting classification and ongoing at the time of publication, which resulted in two more studies being included for a total of eight included studies.

Although we searched numerous key databases, it is possible that we missed some relevant publications. We were unable to assess the possibility of publication bias as there were too few studies for funnel plot construction.

We were unable to perform any subgroup analyses to investigate reasons for heterogeneity due to the inclusion of too few studies reporting on the outcome of interest. The overall risk of bias was high, as all studies were at unclear or high risk of bias related to selection, performance, and/or detection bias.

The clinical interventions delivered and the personnel involved in the included studies were heterogeneous (i.e. integrated models of care versus eHealth models of care), which makes questionable the appropriateness of combining the interventions in a meta-analysis. However, common elements in each of these studies included protocol-driven diagnostic testing, as well as education and empowerment of the patient to self-monitor and manage their condition.

Jeroen Hendriks and Celine Gallagher were lead authors of one of the primary studies included in this review (Hendriks 2012). They were not directly involved in the study selection, data extraction and analysis, and assessment of the risk of bias or certainty of evidence.

Agreements and disagreements with other studies or reviews

No other Cochrane reviews have been published on the effect of different models of care delivery on outcomes in AF populations. One prior systematic review and meta-analysis exploring the impact of integrated care on outcomes in AF populations demonstrated reduced all-cause mortality and cardiovascular

hospitalisations with this model type (Gallagher 2017). The results of the current review are consistent with that study. This Cochrane review expands upon these results by also demonstrating reduced all-cause hospitalisations by multidisciplinary models of care delivery. The evidence presented in this Cochrane review supports international guideline recommendations for clinical service organisation for AF, including models such as integrated care (Andrade 2020; Brieger 2018; Hindricks 2021; Kirchhof 2016). Other reviews have focused on adherence to the ABC pathway.

AUTHORS' CONCLUSIONS

Implications for practice

Moderate certainty evidence shows that clinical service organisation for atrial fibrillation (AF) probably results in a large reduction in all-cause mortality (one death prevented for every 37 patients treated and followed for six years) when compared to usual care. Organised AF clinical services probably make little to no difference to all-cause hospitalisation (estimated two-year number needed to treat for an additional beneficial outcome (NNTB) of 101), based on moderate certainty evidence. In contrast, clinical AF service organisation reduces cardiovascular hospitalisation (one hospitalisation prevented for every 28 treated and followed for six years) based on high certainty evidence. However, it may not reduce cardiovascular mortality (estimated six-year NNTB of 86) based on low certainty evidence, and may have little to no effect on thromboembolic complications such as stroke (estimated six-year NNTB of 588) and major cerebrovascular bleeding events (estimated six-year NNTB of 556) based on low certainty evidence. None of the studies reported minor cerebrovascular events.

With AF as a leading cause of cardiovascular morbidity, mortality, and healthcare utilisation globally, this review underscores the potential impact that co-ordination of care has on some outcomes for patients and the healthcare system. However, given the limited number of included studies and their methodological limitations as well as the heterogeneous nature of the interventions included in the analysis (i.e. integrated models of care versus eHealth models of care), further research is needed to determine the utility of organised clinical services for AF.

Implications for research

Further research is needed in this area. Future trials should:

1. compare different models of care organisation: nurse-led versus non-nurse-led multidisciplinary approach versus utilisation of mHealth;
2. collect information about race/ethnicity of participants to determine whether this has any influence on attendance or adherence to the individual components within organised care services for AF, and therefore its effectiveness;
3. include cost-effective analysis to assess the cost and the potential cost-benefit of the different models of care organisation;
4. be appropriately powered to robustly examine the effect on inconclusive outcomes;
5. examine health-related quality of life and AF quality of life to understand how outcomes for patients with care co-ordination could be further strengthened beyond positive impacts on mortality and hospitalisation;
6. evaluate the effectiveness of different components such as education, optimising pharmacotherapy, adherence to guideline recommendations, promoting self-care, and assessing the needs, values, and preferences of the patient and specific interventions like alcohol cessation strategies/programmes, obstructive sleep apnoea screening and treatment, obesity/weight management and blood pressure management to ascertain which should be included in AF organised clinical services;
7. assess the feasibility of implementing this care co-ordination.

As health care evolves with the widespread adoption of eHealth and mHealth technology, future research will look to advance AF care co-ordination through technologies that further strengthen communication between patients, clinicians, and the multidisciplinary team.

Ensuring equity of access to care co-ordination for AF is essential to implementation, and research to address and overcome challenges to equity of access may be warranted.

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Editorial and peer-reviewer contributions

Cochrane Heart supported the authors in the development of this intervention review.

The following people conducted the editorial process for this article:

- Sign-off Editor (final editorial decision): Rui Providencia, Barts Heart Centre, St Bartholomew's Hospital, Barts Health NHS Trust, London;
- Managing Editor (selected peer reviewers, provided editorial guidance to authors, edited the article): Joanne Duffield, Cochrane Central Editorial Service;
- Editorial Assistant (conducted editorial policy checks, collated peer-reviewer comments, and supported the editorial team): Lisa Wydrzynski, Cochrane Central Editorial Service;
- Copy Editor (copy editing and production): Lisa Winer, Cochrane Central Production Service;
- Peer reviewers (provided comments and recommended an editorial decision): Gregory YH Lip, Liverpool Centre for Cardiovascular Science, University of Liverpool, Liverpool John

Moores University and Liverpool Heart & Chest Hospital, Liverpool, UK (clinical/content review); Annabelle Santos Volgman, MD, Rush University Medical Center (clinical/content review); M Dulce Estêvão School of Health - University of Algarve, Faro, Portugal (consumer review); Nuala Livingstone, Cochrane Evidence Production and Methods Directorate (methods review); Jo Platt, Central Editorial Information Specialist (search review).

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Stewart S, Ball J, Horowitz JD, Marwick TH, Mahadevan G, Wong C, et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. *Lancet* 2015;**382**(9970):775-84. [DOI: 10.1016/S0140-6736(14)61992-9]

References to other published versions of this review

Ferguson 2019b

Ferguson C, Hendriks J, Gallagher C, Bajorek B, Inglis SC. Clinical service organisation for adults with atrial fibrillation. *Cochrane Database of Systematic Reviews* 2019, Issue 8. Art. No: CD013408. [DOI: 10.1002/14651858.CD013408]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Guo 2017

Study characteristics	
Methods	**Design:** cluster-randomised trial **Date of study:** 1 January 2017 and 1 May 2017 **Total duration of study:** 4 months **Country:** China **Setting:** Chinese PLA General Hospital and Meishan City People's Hospital
Participants	209 people diagnosed with AF **Number of clusters**: 2 **Intervention group** • Number randomised: 113 participants received a user-friendly mAF application developed for smart-phones based on the Android operating system • Mean age: 67.4 ± 10.6 years • Sex: 65 (57.5%) male • Type of AF: non-valvular • History of heart failure: 14 (12.4%) • CHA_2DS_2-VASc score: 2.6 **Control group** • Number randomised: 96 • Mean age: 70.9 ± 17.4 years • Sex: 53 (55.2%) male

Guo 2017 *(Continued)*

- Type of AF: non-valvular
- History of heart failure: 18 (18.8%)
- CHA_2DS_2-VASc score: 2.7

Inclusion criteria

- adult patients aged > 18 years with AF diagnosed with electrocardiogram and 24-hour Holter

Exclusion criteria

- individuals aged < 18 years, those with valvular atrial fibrillation (e.g. prosthetic), and those unable to provide written informed consent

Interventions	**Organised model of care**
	• **Type:** mHealth - a user-friendly mAF app
	• **Components**
	  ○ The mAF app was designed with versions for patients and doctors.
	  ○ The mAF app incorporates details such as the personal health record, stroke and bleeding risk assessment (CHA_2DS_2-VASc and HAS-BLED scores, respectively), and a clinical score to aid warfarin control prediction (SAMe-TT_2R_2), patient educational programmes, patient involvement self-care items, and structured follow-up components.

Outcomes	**Primary outcome:** usability, feasibility, acceptability of the mAF app assessed at 1 and 3 months **Secondary outcome:** participant knowledge of AF, quality of life improvement in participants with the mAF app, drug adherence to therapy, anticoagulation satisfaction assessed at 1 and 3 months
Notes	**Conflicts of interest:** GYHL: consultant for Bayer/Janssen, Bristol Myers Squibb/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife, and Daiichi-Sankyo. Speaker for Bayer, Bristol Myers Squibb/Pfizer, Medtronic, Boehringer Ingelheim, Microlife, Roche, and Daiichi-Sankyo. No fees are received personally. **Funding:** Chinese PLA Healthcare Foundation (13BJZ40), Beijing Natural Science Foundation (7142149), Beijing Natural Science Foundation (Z141100002114050), and National Natural Science Foundation of China (H2501). **Author's contact details** **Name:** Professor Gregory YH Lip OR Professor Yundai Chen **Institution:** University of Birmingham; Chinese PLA General Hospital **Email:** g.y.h.lip@bham.ac.uk; Yundai_Chen301@163.com **Address:** • **GYHL**: University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, UK • **YC**: Chinese PLA General Hospital, Department of Cardiology, Beijing 100853, China **Correspondence with author:** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients with atrial fibrillation were randomized to 2 groups (mAF App vs usual care) in a cluster randomized design based in 2 hospitals, Chinese PLA General Hospital and Meishan City People's Hospital, between January 1, 2017, and May 1, 2017"

Guo 2017 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: Method for concealment of allocation not detailed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Data input into analysis was performed by 2 individuals, who were blinded for the intervention groups"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Data were double checked independently by a third investigator"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Of the original cohort, 113 patients with the mAF App had a 1-month follow-up and 71 patients finished the 3-month follow-up" Comment: There is no statement asserting that analyses were performed on the intention to treat principle.
Selective reporting (reporting bias)	Low risk	Comment: The protocol is available and the results for all the pre-specified outcomes have been reported in the final publication.
Other bias	Unclear risk	Comment: Lack of clarity with regards to clusters and simlarity of participants between the two clusters.

Guo 2020a

Study characteristics	
Methods	**Design:** cluster-randomised trial **Date of study:** 1 June 2018 and 16 August 2019 **Total duration of study:** 1 year **Country:** China **Setting:** 40 participating cluster hospitals
Participants	3628 people diagnosed with AF **Number of clusters:** 20 sites per group **Intervention group:** • Number randomised: 1786 • Number lost to follow-up: 140 • Number of participants analysed: 1646 • Mean age: 67.0 ± 15.0 years • Sex: 625 (38.0%) females • Type of AF: new-onset AF: 195 (11.9%), paroxysmal AF: 673 (40.9%), persistent AF: 380 (23.1%), long-standing AF: 56 (3.4%), permanent AF: 48 (2.9%), unknown AF type: 281 (17.1%) • History of heart failure: 360 (21.9%) • CHA_2DS_2-VASc score: 3 (2 to 4) **Control group** • Number randomised: 1842

Guo 2020a *(Continued)*

- Number lost to follow-up: 164
- Number of participants analysed: 1678
- Mean age: 70.0 ± 12.0 years
- Sex: 637 (38.0%) females
- Type of AF: new-onset AF: 232 (13.8%), paroxysmal AF: 660 (39.3%), persistent AF: 448 (26.7%), long-standing AF: 101 (6.0%), permanent AF: 123 (7.3%), unknown AF type: 113 (6.7%)
- History of heart failure: 354 (21.1%)
- CHA_2DS_2-VASc score: 3 (2 to 4)

Inclusion criteria

- Patients ≥ 18 years of age
- Diagnosed with new-onset, paroxysmal, persistent, or permanent AF confirmed with electrocardiogram or 24-hour Holter monitors
- Congestive heart failure, hypertension, ≥ 75 years of age, diabetes, stroke, vascular disease, age 65 to 74, and sex category (female) (CHA_2DS_2-VASc) score ≥ 2

Exclusion criteria

- < 18 years of age
- Those with mechanical prosthetic valve or moderate/severe mitral stenosis
- Unable to provide informed consent
- Unable to be followed up for 1 year for any reason

Interventions

Organised model of care

- **Type:** mHealth - mobile AF application
- **Components of intervention**
  - In the mAFA intervention group, the doctors used the mAFA platform to manage participants with AF.
  - The mAFA platform provided clinical decision support tools (CHA_2DS_2-VASc, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly (HAS-BLED), sex, age, medical history, treatment, tobacco use, race (SAMeT-T_2R_2) scores) to facilitate guideline-based treatment recommendations, educational materials and patient involvement strategies with self-care protocols, and structured follow-up to support implementation of the ABC (Atrial Fibrillation Better Care) Pathway: A, Avoid stroke; B, Better symptom management; and C, Cardiovascular and other comorbidity risk reduction.

Control: participants in the usual care group received treatment and management by local doctors according to local clinical practice

Outcomes

Primary: composite of stroke/thromboembolism, all-cause death, and rehospitalisation assessed at 6 and 12 months

Secondary: rehospitalisation assessed at 6 and 12 months

Notes

Conflicts of interest: Dr Lip is a consultant for Bayer/Janssen, Bristol Myers Squibb/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon, and Daiichi-Sankyo; and is a speaker for Bayer, Bristol Myers Squibb/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo (no fees are directly received personally). Dr Lane has received grants from Bristol Myers Squibb and Boehringer Ingelheim (paid to the institution); and has received personal fees from Boehringer Ingelheim, Bristol Myers Squibb/Pfizer, Bayer, and Daiichii-Sankyo, outside the submitted work. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Guo 2020a *(Continued)*

research and educational grants. The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

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Correspondence with author: we contacted Professor Yutao Guo on 17 April 2023 to clarify whether major cerebrovascular bleeding events were reported as the number of participants who experienced at least 1 bleeding event in the paper. We received a reply from Professor Guo on 18 April 2023 confirming this was the case.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote**: "Randomization was done using a computer- generated randomisation list" **Comment**: The investigators describe a random component in the sequence generation process such as: Using a computer random number generator;
Allocation concealment (selection bias)	Unclear risk	**Comment**: Method of concealment is not described or not described in sufficient detail to allow a definite judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	**Quote**: "Investigators and site personnel were not masked to the intervention." **Comment**: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding;
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Comment**: Insufficient information to permit judgement of 'Low risk' or 'High risk';
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment**: Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
Selective reporting (reporting bias)	Low risk	**Quote 1:** "The design and rationale of the mAFA II trial has been described previously" **Comment**: The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way;
Other bias	Low risk	**Comment**: The study appears to be free of other sources of bias.

Hendriks 2012

Study characteristics	
Methods	**Design:** individual parallel-arm randomised clinical trial **Date of study:** January 2007 and December 2008. Follow-up was at least 1 year, with a mean follow-up of 22 months **Total duration of study:** 2 years **Country:** the Netherlands **Setting:** Maastricht University Medical Centre
Participants	712 people diagnosed with AF **Intervention group** • Number randomised: 356 participants received nurse-led care • Number lost to follow-up: 0 • Number of participants analysed: 356 • Mean age: 66 ± 13 years • Sex: 197 (55.3%) male • Type of AF: paroxysmal: 190 (53.4%), persistent: 68 (19.1%), permanent: 75 (21.1%), symptomatic: 294 (82.6%) • History of heart failure: 25 (7.0%) • CHA_2DS_2-VASc score: score of 0: 107 (30.0%), score of 1: 122 (34.3%), score of > 1: 127 (35.7%) **Control group** • Number randomised: 356 participants received usual care • Number lost to follow-up: 0 • Number of participants analysed: 356 • Mean age: 67 ± 12 years • Sex: 221 (62.1%) male • Type of AF: paroxysmal: 203 (57.0%), persistent: 44 (12.4%), permanent: 84 (23.6%), symptomatic: 296 (83.1%) • History of heart failure: 25 (7.0%) • CHA_2DS_2-VASc score: score of 0: 95 (26.7%), score of 1: 135 (37.9%), score of > 1: 126 (35.4%) **Inclusion criteria** • All patients ≥ 18 years referred for AF (documented on an electrocardiogram) by GPs or non-cardiology specialists to outpatient department **Exclusion criteria** • Patients were excluded in case of any comorbidity that is unsatisfactorily treated, e.g. unstable and uncontrolled hypertension, unstable heart failure defined as NYHA IV or necessitating hospital admission, 3 months before inclusion, untreated hyperthyroidism, current or foreseen pacemaker, internal cardioverter defibrillator or cardio resynchronisation therapy, or cardiac surgery, 3 months before inclusion.
Interventions	**Organised model of care** • **Type:** integrated model of care with collaborative multidisciplinary nurse-led intervention and help of decision support software under the supervision of a cardiologist • **Components of interventions** ◦ **Nurse-led care:**

Hendriks 2012 *(Continued)*

- The AF clinic was based on the chronic care model consisting of nurse-led outpatient care steered by decision support software based on the guidelines and supervised by a cardiologist.
- At the first visit, a nurse specialist took the participant's history and informed them about the pathophysiology of AF, its symptoms and possible complications, the results of the diagnostic tests, and treatment options.
- The dedicated software CardioConsult AF (Curit BV; Groningen, the Netherlands) was used to guide comprehensive management of AF and associated cardiovascular conditions.
- To further empower patients, they were instructed about rate, rhythm control and prophylactic vascular therapy and about when to report to the hospital. Participants could contact the nurse in person or by telephone between planned visits as needed.

Usual care

- Participants in the control group received usual care by a cardiologist in the outpatient clinic during visits scheduled to last 20 min for the first visit and 10 min for follow-up visits.
- During follow-up visits, participants were questioned for major adverse cardiovascular events and hospitalisations.
- All medical records were reviewed for such events after 1 and 2 years, and at the end of follow-up.

Outcomes

Primary outcome: composite of death from cardiovascular causes, and cardiovascular hospitalisation for heart failure, ischaemic stroke, acute myocardial infarction, systemic embolism, major bleeding, severe arrhythmic events, and life-threatening adverse effects of drugs assessed at 3, 6, and 12 months, and every 6 months thereafter

Secondary outcome: cardiovascular death, all-cause mortality, and all-cause hospitalisations assessed at 3, 6, and 12 months, and every 6 months thereafter

Notes

Conflicts of interest: none declared

Funding: University Hospital Maastricht as well as by unrestricted educational grants from Boehringer Ingelheim and Medtronic Bakken Research Centre. The sponsors were not involved in the study in any way.

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Correspondence with author: we contacted Professor Jeroen Hendriks on 17 April 2023 to clarify whether major cerebrovascular bleeding events were reported as the number of participants who experienced at least 1 bleeding event in the paper. We received a reply from Professor Hendriks on 28 April 2023 confirming this was the case.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were asked permission for use of their personal clinical data to be collected during their future visits. At the same time, we informed them about the AF clinic and nurse-led care, as well as the possibility of participation in a clinical trial. Patients were then randomly assigned to nurse-led care or usual care"

Hendriks 2012 *(Continued)*

		Comment: Method of random sequence generation not reported.
Allocation concealment (selection bias)	Unclear risk	Quote: "...a computerized one to one randomisation" Comment: Method of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: Method for blinding participants and personnel not detailed
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All primary outcome events were adjudicated on the basis of pre-specified criteria by an independent clinical endpoint committee that was not aware of the randomised treatment assignments"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "None of the patients were lost to follow-up"
Selective reporting (reporting bias)	Low risk	Quote: "The study was registered at Clinicaltrials.gov (identifier: NCT00753259)". Comment: The protocol is available and the results for all the pre-specified outcomes have been reported in the final publication. Economic outcomes data have been reported in other articles.
Other bias	Low risk	Comment: The study is free of other sources of bias

Li 2023

Study characteristics	
Methods	**Design:** individual parallel-arm randomised clinical trial **Date of study:** May 2019 to December 2020 **Total duration of study:** 12 months **Country:** Hong Kong **Setting:** The Chinese University of Hong Kong
Participants	40 people diagnosed with AF **Intervention group** • Number randomised: 20 participants received N-MBA • Number lost to follow-up: 2 • Number of participants analysed: 20 • Mean age: 72 ± 4 years • Sex: 13 (65%) male • Type of AF: paroxysmal: not reported • History of heart failure: not reported • CHA_2DS_2-VASc score: mean score 3.37, SD 2.19 **Control group** • Number randomised: 20 participants received usual care

Li 2023 *(Continued)*

- Number lost to follow-up: 3
- Number of participants analysed: 20
- Mean age: 73 ± 6 years
- Sex: 13 (65%) male
- Type of AF: paroxysmal: not reported
- History of heart failure: not reported
- CHA_2DS_2-VASc score: mean score 3.5, SD 1.69

Inclusion criteria

- People with documented AF who were not receiving oral anticoagulants
- Lived in the community
- Had CHA_2DS_2-VASc score ≥ 1 (men) or ≥ 2 (women)

Exclusion criteria: individuals with impaired communication or cognitive abilities or severe comorbidities

Interventions	**Organised model of care**
	• **Type:** collaborative multidisciplinary nurse-led, multicomponent behavioural activation programme
	• **Components of interventions**
	  ○ Risk profile assessment and shared decision-making regarding oral anticoagulant use
	  ■ "The nurse first conducted individualized risk assessments before their next medical appointment to make patients aware of their stroke risks with and without OACs and bleeding risks with OACs, using numeric and graphical pictograms as decision aids. The decision aids organized treatment options as option grids to facilitate comparison and clarification of the options."
	  ○ Empowerment-based educational module on AF self-care
	  ■ "5 weekly group-based educational module that covered all of the major topics related to AF self-care: medication management, symptom monitoring, crisis management, activities and exercise, and risk factor management to reduce the risks of stroke and bleeding. The educational content of each session complied with the major practice guidelines for AF management. To enhance effective learning, the nurse delivered each session using an empowerment model."
	  ○ Nurse-initiated telephone support
	  ■ "The nurse monitored patients' adherence to suggested self-care actions, symptom profiles, treatment efficacies, adverse effects, and goal attainment progress; identified barriers to self-care; and provided resolutions and continued support via regular telephone calls (four calls over 6 weeks). The participants were provided telephone access to the nurse for inquiries regarding disease management. The nurse provided health advice and counselling accordingly."
	  ○ Patient-initiated contact for professional advice
	  ■ "The nurse then encouraged the patients to discuss the use of OACs with their physicians. Assertive communication skills in asking questions, expressing concerns, and stating preferences regarding OACs for stroke prevention were highlighted. Scenario-based videos and role play rehearsals were used to enhance skill acquisition."
	Usual care
	• "Participants in the control group received standard care provided by the healthcare team of the study hospital. Standard care did not include any structured education regarding AF, but only unstructured information provided by the healthcare team."

Outcomes	**Primary outcome:** health-related quality of life measured using AFEQT **Secondary outcomes** • AF knowledge measured using AFKS • Medication adherence measured using MGLS • Anxiety and depression measured using HADS • Intention to use oral anticoagulant • Actual use of oral anticoagulant

Li 2023 *(Continued)*

	Timing of outcome assessment: postintervention and 6-month follow-up
Notes	**Conflicts of interest:** none declared **Funding**: this study was funded by the Research Grants Committee of Hong Kong through the General Research Fund (grant number: 14604418). **Author's contact details** **Name:** Assistant Professor Polly Li **Institution:** University of Hong Kong **Email:** pwcli@hku.hk **Address:** School of Nursing, LKS Faculty of Medicine, 5/F, HKUMed Academic Building, 3 Sassoon Road, The University of Hong Kong, Pokfulam, Hong Kong **Correspondence with author:** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The random list was generated by a computer programme with random block sizes (6, 8, and 10) and sequences within a block"
Allocation concealment (selection bias)	Low risk	Quote: "Sealed envelopes were used to ensure allocation concealment"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: single-blinded randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "An independent trained research assistant who was blinded to the study group allocation collected post-intervention data through EHR review and telephone interviews"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Of these, 48 fulfilled the eligibility criteria and 8 declined to participate, mainly due to reduced physical mobility that made them difficult to attend the intervention sessions. Finally, 40 participants were recruited for the pilot trial between May 2019 and December 2020, yielding a participation rate of 83.3%. The participants were randomized to receive either the N-MBA programme (n=20) or standard care (n= 20). The lost to follow-up rates at T1 and T2 were 7.5 and 12.5%, respectively. The overall adherence rate of the N-MBA group was 82.5%; one patient withdrew from the study after randomization due to an elective orthopaedic surgery. Six participants missed two sessions and three missed one session"
Selective reporting (reporting bias)	Low risk	Comment: All pre-specified outcomes in the protocol has been reported.
Other bias	Low risk	Quote: "The sociodemographic and clinical data were comparable between the two study groups at baseline"

Stewart 2015

Study characteristics	
Methods	**Design:** pragmatic, multicentre randomised controlled trial **Date of study:** 2 June 2010 to 29 March 2012; minimum of 24 months of follow-up completed on 31 March 2014 **Total duration of study:** 21 months **Country:** Australia **Setting:** 3 tertiary referral hospitals in Adelaide, Melbourne, and Canberra, Australia
Participants	335 people diagnosed with AF **Intervention group** • Number randomised: 168 participants received proactive management with respect to optimisation of gold-standard drug treatment and non-pharmacological management • Mean age: 72 ± 11 years • Sex: 84 (50%) male • Type of AF: newly diagnosed: 44 (26%), asymptomatic: 31 (19%), persistent: 149 (89%) • History of heart failure: 54 • CHA_2DS_2-VASc score: 3.7 **Control group** • Number randomised: 167 participants received standard management • Mean age: 71 ± 12 years • Sex: 90 (54%) male • Type of AF: newly diagnosed: 34 (20%), asymptomatic: 26 (16%), persistent: 153 (92%) • History of heart failure: 60 • CHA_2DS_2-VASc score: 3.6 **Inclusion criteria** • Had a diagnosis of chronic AF (defined as recurrent paroxysmal, persistent, or permanent AF) • Living independently in the community after the index admission (within a 40-kilometre radius) and provided informed consent **Exclusion criteria** • Primary diagnosis of valvular heart disease • Scheduled catheter ablation procedure • Pre-existing diagnosis of heart failure (including the index admission) • Alcohol-induced AF • Terminal disorder or malignant disease needing palliative care

Interventions	**Organised model of care**
	
	• **Type:** case management involving a collaborative multidisciplinary approach (specialised clinicians, i.e. cardiologist, family doctor, cardiac nurse, allied health)
	• **Components of intervention**
	  ◦ Proactive management with gold-standard drug treatment and non-pharmacological management
	  ◦ Provide in-hospital assessment to establish potential barriers to postdischarge management and initial contact to develop a therapeutic relationship with the patient and their family or carer
	  ◦ Structured postdischarge care, consisting of a home visit 7 to 14 days after discharge followed by a combination of repeat home visits, scheduled clinic reviews, and telephone follow-up

Stewart 2015 *(Continued)*

	Control group: no restrictions to standard postdischarge management at any stage. Ad hoc management as per usual standards of clinical care in Australia (subsidised access to routine medical care, hospital care, and pharmacotherapy)
Outcomes	**Primary outcome** • Event-free survival from unplanned admission assessed at 12 and 24 months • Death (all-cause) and associated days alive and out of hospital assessed at 12 and 24 months **Secondary outcomes** Unplanned, cardiovascular-specific, and all-cause readmission and length of hospital stay. Thrombotic events (including ischaemic stroke and acute coronary syndrome), bleeding events, and de novo heart failure-related admissions assessed at 12 and 24 months Treatment success in maintaining nominated rate or rhythm control; clinical stability, health-related quality of life assessed with SF-12 and EQ-5D-5L. Exercise levels, depressive symptoms, the Center for Epidemiologic Studies Depression Scale, and cognitive function assessed at 12 and 24 months Incremental cost utility ratio, incremental net monetary benefit, and value of perfect information
Notes	**Conflicts of interest:** authors declare no competing interests **Funding**: National Health and Medical Research Council of Australia (519823) with additional fellowship funding provided to SS (1041796), JB (1017804), and MJC (1032934) **Author's contact details** **Name:** Professor Simon Stewart **Institution:** Australian Catholic University **Email:** stewart@acu.edu.au **Address:** Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Victoria 3000, Australia **Correspondence with author:** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An independent data management team randomly allocated participants via telephone, using a computer-generated protocol. We used a predetermined randomisation sequence with block groups for every study site. We stratified randomisation according to clinician nominated post-discharge management".
Allocation concealment (selection bias)	Unclear risk	Comment: Method of allocation concealment not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients, but not the monitoring study team, were aware of the random allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "SAFETY is a multicentre randomised trial with masked endpoint acquisition and adjudication"

Stewart 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The same proportion of participants in both groups withdrew consent to be followed up and were censored for study outcomes earlier than planned (19 [11%] of 168 allocated to the SAFETY intervention and 18 [11%] of 167 assigned standard management" Quote: "We did all efficacy analyses on an intention-to-treat basis while unaware of random allocations"
Selective reporting (reporting bias)	Low risk	Comment: The protocol is available and the results for all the pre-specified outcomes have been reported in the final publication.
Other bias	Low risk	Comment: The study is free of other sources of bias

van den Dries 2020

Study characteristics	
Methods	**Design:** cluster randomised, pragmatic, non-inferiority trial **Date of study:** not reported **Total duration of study:** not reported **Country:** the Netherlands **Setting:** primary care practices located in the region of 3 affiliated secondary care hospitals (Zwolle, Deventer, and Hardenberg)
Participants	1657 people diagnosed with AF **Number of clusters:** 15 practices in intervention group and 11 practices in control group **Intervention group** • Number randomised: 941 • Number lost to follow-up: 3 all outcomes; 12 secondary outcomes; 411 no consent • Number of participants analysed: 527 (primary outcome); 522 (secondary outcomes) • Mean age: 76 (71 to 81) years • Sex: 239 (45.4%) female • History of heart failure: 72 (13.7%) **Control group** • Number randomised: 716 • Number lost to follow-up: 3 all outcomes; 9 secondary outcomes • Number of participants analysed: 713 (primary outcome); 704 (secondary outcomes) • Mean age: 78 (73 to 84) years • Sex: 374 (52.5%) female • History of heart failure: 136 (19.1%) **Inclusion criteria** • All patients within the participating practices with documented AF • Aged 65 years or older were assessed at the practices for eligibility using their electronic medical records **Exclusion criteria**

van den Dries 2020 *(Continued)*

- Presence of an internal cardioverter-defibrillator or a cardiac resynchronisation therapy device
- Cardioversion, cardiac ablation, or cardiac surgery < 3 months prior to inclusion or being planned
- Heart valve surgery in the past
- Rheumatic mitral valve stenosis
- Pulmonary vein isolation in the past or being planned
- Being legally incapable of providing informed consent
- Life expectancy shorter than 3 months
- Participation in another randomised trial on AF

Interventions	**Organised model of care**
	• **Type:** integrated model of care involving case management and incorporating a collaborative multidisciplinary approach (nurse, GP, cardiologist)
	• **Components of intervention**
	  ○ The intervention consisted of 3 pivotal items.
	  ■ Quarterly AF check-ups by the practice nurse on symptoms and comorbidities, notably assessment of early signs and symptoms of heart failure and also patient education
	  ■ Case management of anticoagulant treatment, including INR measurements performed by the intervention practice in those treated with a VKA, special attention to drug compliance, and monitoring of kidney function in participants using a NOAC
	  ■ Easy-access consultation of anticoagulation clinics and/or cardiologists, thus truly enabling 'shared care and responsibility' between primary care, anticoagulation clinics, and cardiology care
	  ○ When participants needed referral to secondary care or additional check-ups by a cardiologist (in case of other cardiac conditions or pacemaker), they continued their participation in the intervention arm.
	  ○ Practice nurses in the intervention practices received a 3-hour training at the start of the intervention with education on signs and symptoms of AF and heart failure, rate and rhythm control, anticoagulant treatment, and an explanation of the most important recommendations of the guidelines on AF.
	  ○ In addition, 3 meetings were organised throughout the 2-year follow-up period for both practice nurses and GPs to:
	  ■ share experiences and 'best practices';
	  ■ discuss complex patients; and
	  ■ provide additional education on topics based on existing questions of the practice nurses.
	  ○ Decisions regarding pharmacotherapy and referral to cardiology care were left to the GPs, guided by the Dutch College of General Practitioners' guidelines on AF.
	
	Control: usual care could vary per patient, but for most participants it involved a once-yearly consultation of a cardiologist or AF nurse at the outpatient cardiology department of the affiliated hospital. Some participants may already have been discharged from treatment by their cardiologist, and for those participants, the GP was the first person to contact in case of signs or symptoms related to AF or other conditions. However, this occurs on an 'ad hoc basis', initiated by the participant. For participants using a VKA, anticoagulation clinics affiliated to the local hospital performed the INR measurements and created the dosage calendar, without involvement of the GP. For participants using a NOAC, no structured control was in place in the control group.

Outcomes	**Primary:** all-cause mortality assessed at 24 months **Secondary** • Cardiovascular and non-cardiovascular mortality assessed at 24 months • Cardiovascular and non-cardiovascular hospitalisation assessed at 24 months • MACE assessed at 24 months • Stroke assessed at 24 months • Major bleeding assessed at 24 months • Clinically relevant non-major bleeding assessed at 24 months

van den Dries 2020 *(Continued)*

- Health-related quality of life assessed at 24 months
- Cost-effectiveness

Notes	**Conflicts of interest:** Ms Orchard reports investigator-initiated grants from Pfizer/Bristol Myers Squibb. Dr Sanders reports having served on the advisory board of Medtronic, Abbott Medical, Boston Scientific, CathRx, and PaceMate. Dr Sanders reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Medtronic, Abbott Medical, and Boston Scientific. Dr Sanders reports that the University of Adelaide has received on his behalf research funding from Medtronic, Abbott Medical, Boston Scientific, and Microport. Dr Neubeck reports investigator-initiated grants from Pfizer Bristol Myers Squibb and honorarium from Daiichi Sakyo outside the submitted work. Dr Hendriks reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Medtronic and Pfizer/Bristol Myers Squibb outside the submitted work. **Funding**: The ALL-IN trial was funded with an unrestricted grant from theStichting Achmea Gezondheidszorg (SAG number Z646), the HeinHogerzeil Stichting, and Roche Diagnostics Nederland B.V. There were no restrictions to the execution of the study or the publication process by any of the subsiding parties of this study. **Author's contact details** **Name:** Carline J van den Dries **Institution:** University Medical Center Utrecht/Utrecht University **Email:** c.j.vandendries@umcutrecht.nl **Address:** Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht/Utrecht University, Str. 6.131, PO Box 85500, 3508 GA Utrecht, the Netherlands **Correspondence with author:** we contacted Dr Carline van den Dries on 17 April 2023 to clarify whether major cerebrovascular bleeding events were reported as the number of participants who experienced at least 1 bleeding event in the paper. We received a reply from Dr van den dries on 4 May 2023 providing us the data to include in our meta-analysis for major cerebrovascular bleeding events.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Quote:** " Randomization occurred at the level of primary care practices (clusters), performed by an independent researcher through off-site computerised block randomization stratified by practice size. Because of cluster randomization, one practice (including all eligible patients within this practice) was allocated to either the intervention arm or the control arm. Randomization at this practice level was necessary to prevent contamination of the intervention and thus dilution of any true effect, as it is practically impossible for a GP and his/her practice nurse to provide integrated care to one AF patient while refraining from doing so to the next."
Allocation concealment (selection bias)	High risk	**Quote 1:** "As all patients participating in the intervention needed to have this clearly noted in their files, researchers could not be blinded for treatment allocation during data collection". **Quote 2:** " Randomization occurred at the level of primary care practices (clusters), performed by an independent researcher through off-site computerised block randomization stratified by practice size. Because of cluster randomization, one practice (including all eligible patients within this practice) was allocated to either the intervention arm or the control arm. Randomization at this practice level was necessary to prevent contamination of the intervention and thus dilution of any true effect, as it is practically impossible for a GP and his/her practice nurse to provide integrated care to one AF patient while refraining from doing so to the next."

van den Dries 2020 *(Continued)*

		Comment: Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Quote:** "The Medical Ethics Committee provided a waiver of informed consent for the collection of anonymized baseline and outcome data for all eligible patients in both arms, yet all strictly under the auspices of the treating GP. It was decided that to ensure the scientific validity of the trial such a waiver of informed consent for anonymized data collection was necessary, for three reasons: (i) to enable the assessment of otherwise undetectable possible selection bias caused by providing informed consent for participation after randomization, inherent to cluster randomized trials, (ii) to enhance the generalizability of our findings, especially to frail elderly AF patients, and (iii) informing all eligible patients in the control practices would involve providing information and education on AF and its risks, thus inducing a risk of contamination. Moreover, no additional examinations for anonymized data collection were needed and thus no additional risk was imposed to patients. This approach is increasingly applied in cluster randomized trials to ensure its merits to science and society" **Comment:** Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "An independent adjudication committee, blinded for treatment allocation, adjudicated all causes of death." **Comment:** Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Comment:** Reasons for missing outcome data unlikely to be related to true outcome; Missing outcome data balanced in numbers across intervention groups
Selective reporting (reporting bias)	Low risk	**Quote:** "Full details on the study design and protocol have been previously reported." **Comment:** The protocol is available and the results for all the pre-specified outcomes have been reported in the final publication.
Other bias	Low risk	**Comment:** The study appears to be free of other sources of bias.

Wijtvliet 2020

Study characteristics	
Methods	**Design:** multicentre randomised controlled trial **Date of study:** December 2012 through November 2017 **Total duration of study:** 5 years **Country:** the Netherlands **Setting:** 2 academic hospitals, 5 non-academic teaching hospitals, and 1 non-teaching hospital
Participants	1375 people diagnosed with AF **Intervention group** • Number randomised: 686

Wijtvliet 2020 *(Continued)*

- Number lost to follow-up: 15
- Number of participants analysed: 671
- Mean age: 64 ± 10 years
- Sex: 450 (67%) male
- Type of AF: paroxysmal: 410 (61%), non-paroxysmal: 166 (25%)
- History of heart failure: 93 (14%)
- CHA_2DS_2-VASc score: 0: 162 (24%), 1: 122 (18%), ≥ 2: 387 (58%)

Control group

- Number randomised: 689
- Number lost to follow-up: 6
- Number of participants analysed: 683
- Mean age: 64 ± 11 years
- Sex: 441 (65%) male
- Type of AF: paroxysmal: 429 (63%), non-paroxysmal: 140 (20%)
- History of heart failure: 66 (10%)
- CHA_2DS_2-VASc score: 0: 173 (25%), 1: 131 (19%), ≥ 2: 379 (56%)

Inclusion criteria

- Patients with newly diagnosed AF detected on ECG, Holter recordings or event recorder with a duration > 30 seconds, in the 3 months before inclusion
- Patients with a history of diagnosed AF, with no regular control at a cardiologist for AF in the last 2 years and referred by a (non-) cardiologic medical specialist for new diagnostics or therapeutic issue
- Age ≥ 18 years

Exclusion criteria

- No electrocardiographic objectified AF
- Unstable heart failure defined as NYHA IV or heart failure necessitating hospital admission < 3 months before inclusion
- Acute coronary syndrome (acute myocardial infarction or unstable angina pectoris, with 2 of the following characteristics: chest pain and/or ischaemic electrocardiographic changes and/or cardiac enzyme rise) < 3 months before inclusion
- Untreated hyperthyroidism or < 3 months euthyroidism before inclusion
- Foreseen pacemaker, internal cardioverter defibrillator, and/or cardiac resynchronisation therapy
- Cardiac surgery ≤ 3 months before inclusion
- Planned cardiac surgery
- Regular control and treatment, also for AF, at another specialised outpatient cardiac clinic
- Patient is not able to fill in the questionnaires
- Participation in other clinical study

Interventions	**Organised model of care**
	• **Type:** collaborative multidisciplinary intervention involving a specialised nurse using a decision-support tool, in consultation with the cardiologist
	• **Components of intervention**
	  ○ Nurse-led care included treatment of participants by a specialised nurse using guidelines-based decision-support software (Cardio Consult AFVR Curit Software; Groningen, the Netherlands) ensuring comprehensive treatment of AF and associated conditions, covering cardiovascular risk factor management, antithrombotic treatment, rate control, and rhythm control.
	  ○ Complete cardiological diagnostic tests and treatments were installed during the first outpatient visit.
	  ○ To enhance patient adherence, the nurse provided psychosocial support as well as personalised education on pathophysiology, symptoms, and complications of AF.

Wijtvliet 2020 *(Continued)*

Control: usual care consisted of routine outpatient management by a cardiologist without a specified clinical pathway

Outcomes

Primary outcome: a composite of cardiovascular death and hospital admission for arrhythmias, heart failure, thromboembolic events, major bleeding, acute coronary syndrome, or life-threatening effects of drugs assessed at 3, 6, and 12 months, and yearly thereafter

Secondary outcomes

- All components of the primary endpoint assessed at 3, 6, and 12 months, and yearly thereafter
- All-cause mortality assessed at 3, 6, and 12 months, and yearly thereafter
- Total number and duration of unplanned all-cause hospitalisations assessed at 3, 6, and 12 months, and yearly thereafter
- Total number and duration of unplanned cardiovascular hospitalisations assessed at 3, 6, and 12 months, and yearly thereafter
- Total number and duration of unplanned hospitalisations related to AF assessed at 3, 6, and 12 months, and yearly thereafter
- Recurrent unplanned cardiovascular hospitalisations assessed at 3, 6, and 12 months, and yearly thereafter
- Costs and cost-effectiveness (ICER, QALYs based on EQ-5D-5L)
- Implementation of care (the extent to which the comprehensive cardiovascular treatment is in accordance with the most recent ESC guidelines management of AF, the HF guidelines of acute and chronic heart failure, and the CVD prevention guidelines)
- Quality of life (SF-36, EQ-5D, and AFSS) assessed at 3, 6, and 12 months, and yearly thereafter
- Anxiety and/or depression (HADS) assessed at 3, 6, and 12 months, and yearly thereafter
- Knowledge of AF (Netherlands Knowledge Scale on AF) assessed at 3, 6, and 12 months, and yearly thereafter
- Compliance to medication (MMAS and PAM) assessed at 3, 6, and 12 months, and yearly thereafter
- PAM self-management score assessed at 3, 6, and 12 months, and yearly thereafter

Notes

Conflicts of interest

- EPJW, ICVG, RJF, PB, AE, JE, RT, ADIA, SMJK, and JGPT declare no competing interests.
- RGT reports grants and personal fees from Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, and Daiichi-Sankyo and grants from Bayer during the conduct of the study.
- NAHAP reports grants from Boehringer Ingelheim, Medtronic, Bayer, Pfizer, Bristol Myers Squibb, Daiichi-Sankyo, and grants from the Netherlands health insurance companies DSW, Achmea, and CZ, during the conduct of the study, all to the institution.
- MR reports grants from Netherlands Cardiovascular Research Initiative funded by Dutch Heart Foundation, outside the submitted work.
- JGLML reports grants from the Netherlands Cardiovascular Research Initiative funded by the Dutch Heart Foundation, grants from Boehringer Ingelheim, Medtronic, Abbott, Bayer, Pfizer, Bristol Myers Squibb, Daiichi-Sankyo, and Biotronik, and grants from the Netherlands health insurance companies DSW, Achmea, and VGZ, all to the institution, and personal fees from Medtronic, outside the submitted work.
- HJGMC reports grants from the Netherlands Cardiovascular Research Initiative: an initiative with support of the Dutch Heart Foundation, CVON 2014-9: Reappraisal of atrial fibrillation: interaction between hyper coagulability, electrical remodelling, and vascular destabilization in the progression of atrial fibrillation (RACE V) outside the submitted work; and grants from Boehringer Ingelheim, Medtronic, Abbott, Bayer, Pfizer, Bristol Myers Squibb, and Daiichi-Sankyo, and from the Netherlands health insurance companies DSW, Achmea, and VGZ, during conduct of the study, all to the institution.

Funding: the trial was supported by Netherlands healthcare insurance companies (DSW, Achmea, and CZ), Boehringer Ingelheim, Bayer, Pfizer, Bristol Myers Squibb, and Daiichi-Sankyo, but all had no role in the design or execution of the trial; company representatives did not review the protocol or the manuscript.

Author's contact details

Wijtvliet 2020 *(Continued)*

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Correspondence with author: we contacted Dr Petra Wijtvliet on 15 April 2021 requesting data on cardiovascular hospitalisation and AF-related ED visits. We received a reply from Dr Wijtvliet on 6 May 2021 providing us the data to include in our meta-analysis for cardiovascular hospitalisation and AF-related ED visits.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed with the use of a centralized web-based system"
Allocation concealment (selection bias)	Low risk	Quote: "After providing written informed consent, all patients were randomly assigned in a 1:1 ratio stratified by centre to nurse-led care or usual-care provided by a cardiologist. Randomization was performed with the use of a centralized web-based system"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: Method for blinding participants and personnel not detailed
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote 1:** "An independent data and safety monitoring board reviewed independently and in a blinded fashion the accumulating safety and efficacy data at regular intervals during the trial" **Quote 2:** "All primary endpoint events were adjudicated by an independent clinical endpoint committee (not aware of the randomised treatment assignments) that used the above-mentioned definitions of the components of the primary endpoint"
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Quote 1:** "Numbers do not always add up to 100% for characteristics not listed or missing variables at baseline" **Quote 2:** Analyses were performed according to the intention-to-treat principle"
Selective reporting (reporting bias)	Low risk	**Comment:** The protocol is available and the results for all the pre-specified outcomes have been reported in the final publication.
Other bias	Low risk	**Comment:** The study is free of other sources of bias

Yan 2022

Study characteristics

Methods	**Design:** multicentre randomised controlled trial **Date of study:** October 2018 through September 2020

Yan 2022 *(Continued)*

	Total duration of study: 2 years **Country:** China **Setting:** a tertiary referral hospital in Beijing, China, at the Cardiology Department which consists of 3 units with a 50-bed capacity per unit and an average of 800 patient admissions annually. 2 of the 3 units, Cardiology Unit 1 and Cardiology Unit 2, were selected.
Participants	249 people diagnosed with AF **Intervention group** • Number randomised: 120 • Number lost to follow-up: 4 • Number of participants analysed: 116 • Mean age: 65 ± 11.5 years • Sex: 75 (65%) male • Type of AF: not reported • History of heart failure: 23 (20%) • CHA_2DS_2-VASc score: 0: 15 (13%), 1: 14 (12%), ≥ 2: 87 (75%) **Control group** • Number randomised: 129 • Number lost to follow-up: 10 • Number of participants analysed: 119 • Mean age: 65 ± 10 years • Sex: 69 (58%) male • Type of AF: not reported • History of heart failure: 22 (18.5%) • CHA_2DS_2-VASc score: 0: 8 (7%), 1: 18 (15%), ≥ 2: 93 (78%) **Inclusion criteria** • Stable patients referred to either Cardiology Unit 1 or Unit 2 • Aged ≥ 18 years • Diagnosed with AF by a 12-lead ECG recording and confirmed by a cardiologist at admission **Exclusion criteria** • Have comorbid pulmonary embolism, congenital heart disease, or valvular heart disease • Have severe heart failure (i.e. NYHA Class IV) • Current or foreseen internal cardiac defibrillator (except for atrioventricular node ablation plus His-bundle pacemaker) • Cardiac surgery (including percutaneous coronary intervention) within 3 months before inclusion or planned • Terminal malignancy, or life expectancy < 6 months • Unable to obtain informed consent
Interventions	**Organised model of care** • **Type:** collaborative multidisciplinary intervention involving a specialised nurse in consultation with a multidisciplinary team including a cardiologist, an electrophysiologist, a psychologist, and a physiotherapist • **Components of intervention at pre-discharge phase** ○ "The specialist cardiac nurse determined patients' health requirements in a face-to-face interview and worked together with the members of the multidisciplinary team, to assess the condition of

Yan 2022 *(Continued)*

	patients, treatment methods, medication therapy, exercise tolerability, and to discuss and formulate a personalized follow-up scheme." ○ "The specialist nurse played a pivotal role in developing and conducting a patient-specific management plan." • **Components of intervention at postdischarge phase** ○ Educational and psychological support. ○ Social media tools were adopted to achieve better management. ○ The specialist cardiac nurse became a liaison between participants and members of the multidisciplinary team. **Control:** guideline-based treatment and care as usual
Outcomes	**Primary outcome:** a composite of cardiovascular hospitalisation for heart failure, stroke, acute myocardial infarction, systematic embolism, major bleeding and severe arrhythmia, and cardiovascular death **Secondary outcome:** quality of life (SF-36) assessed at 6 and 12 months
Notes	**Conflicts of interest:** Yan H, Du Y-X, Wu F-Q, Lu X-Y, Chen R-M, Zhang Y declare no competing interests. **Funding**: the trial was supported by a grant from the Capital Nursing Research Project, Beijing, China (No. 17HL02). **Author's contact details** **Name:** Professor Harry JGM Crijns **Institution:** Capital Medical University **Email:** wufangqin@ccmu.edu.cn **Address:** College of Nursing, Capital Medical University No. 10 You-an-men Wai Xi-tou-tiao, Feng-tai District, Beijing 10 0 069, China **Correspondence with author:** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomly assigned into either Cardiology Unit 1 or Cardiology Unit 2, using a computer-generated random sequence upon admission by personnel who were neither aware of the allocation nor took part in the study"
Allocation concealment (selection bias)	Unclear risk	Comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Participants and the specialist cardiac nurse were not blinded to the group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Two independent researchers who were unaware of the allocation, accumulated and analyzed previously mentioned data"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Fourteen (5.6%) patients were lost to follow-up (4 and 10 in the multidisciplinary team and usual- care groups, respectively)"

Yan 2022 *(Continued)*

Selective reporting (reporting bias)	Low risk	Comment: All pre-specified outcomes in the trial registry were reported.
Other bias	Low risk	Quote: "The characteristics of the patients at inclusion in the study are presented in Table 1 ; there were no significant differ- ences in demographic features including age, sex, level of educa- tion, and clinical status (history of associated diseases, CHA 2 DS 2 - VASc score, and HAS-BLED score) between the two groups; how- ever, the control group had a higher percentage of patients with hypertension (p = 0.007)"

AF: atrial fibrillation
AFEQT: Atrial Fibrillation Effect on Quality of life questionnaire
AFKS: Atrial Fibrillation Knowledge Scale
AFSS: Atrial Fibrillation Severity Scale
CHA_2DS_2-VASc: Congestive heart failure, Hypertension, Age ≥ 75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65 to 74 and Sex category (female) score
CVD: cardiovascular disease
ECG: electrocardiogram
ED: emergency department
ESC: European Society of Cardiology
GP: general practitioner
HADS: Hospital Anxiety and Depression Scale
HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly score
HF: heart failure
ICER: incremental cost-effectiveness ratio
INR: international normalised ratio
mAF: mobile atrial fibrillation
mAFA: mobile atrial fibrillation application
MACE: major adverse cardiac events
mHealth: mobile health
MGLS: Morisky-Green-Levine Adherence Scale
MMAS: Morisky Medication Adherence Scale
NOAC: non-vitamin K antagonist oral anticoagulant
N-MBA: nurse-led behavioural activation programme
NYHA: New York Heart Association
OACs: oral anticoagulants
PAM: Patient Activation Measure
PLA: People's Liberation Army
QALYs: quality-adjusted life-years
SD: standard deviation
SAMe-TT_2R_2: Sex, Age < 60 years, Medical history, Treatment, Tobacco use, Race score
SF-12: 12-item Short Form Health Survey
SF-36: 36-item Short Form Health Survey
VKA: vitamin K antagonist

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

Study	Reason for exclusion
ACTRN12608000074392	Ineligible intervention: purely an educational intervention
Bowyer 2017	Ineligible intervention: purely an educational intervention
Chen 2017	Ineligible intervention: purely an educational intervention

Study	Reason for exclusion
ChiCTR-ICR-15007036	Ineligible intervention: focused on the management of antithrombotic therapy
Cohen 1996	Ineligible intervention: focused on anticoagulation management
Costa 2019	Ineligible intervention: purely an educational intervention for people with AF treated with warfarin
Davy 2017	Ineligible intervention: education and behavioural intervention
Gagne 2019	Ineligible intervention: primarily educational intervention
Gallagher 2020	Ineligible intervention: not multidisciplinary, solely nurse focused
Hendriks 2006	Ineligible intervention: focused on medication adherence
Hershey 2019	Ineligible intervention: intervention focused on dietary behaviour change
IRCT2015012120744N1	Ineligible intervention: telenursing
ISRCTN10135302	Ineligible intervention: focused on medication adherence
Kellen 2006	Ineligible intervention: education and behavioural intervention
Khalifehzadeh-Esfahani 2018	Ineligible intervention: not multidisciplinary, and medication focused
Khan 2004	Ineligible intervention: focused mainly on education and self-monitoring to manage warfarin therapy
Maikranz 2017	Ineligible intervention: purely educational intervention to increase patient knowledge about oral anticoagulation
Manotti 2001	Ineligible intervention: computer-aided management on the quality of treatment in anticoagulated patients
Matchar 2002	Ineligible intervention: anticoagulation clinic with frequency of patient self-testing of prothrombin
Matchar 2003	Ineligible intervention: anticoagulation clinic
Matchar 2015	Ineligible intervention: focused on prescription of anticoagulation and INR self-testing
McIntyre 2021	Ineligible intervention: education and behaviour focused
Najafi 2018	Ineligible intervention: education and behavioural intervention
NCT00829478	Ineligible intervention: single-contact education session
NCT01928121	Ineligible intervention: primary care management
NCT02064114	Ineligible intervention: intervention focused on weight reduction
NCT02734875	Ineligible intervention: only focused on anticoagulation management
NCT02745236	Ineligible intervention: nurse practitioner led, not multidisciplinary
NCT02941978	Ineligible intervention: motivational interviewing to support oral anticoagulation adherence

Study	Reason for exclusion
NCT02996435	Ineligible intervention: smartphone to improve adherence to rivaroxaban
NCT03126214	Ineligible intervention: pharmacist led, not multidisciplinary
NCT03174093	Ineligible intervention: mHealth app focused on anticoagulation care
NCT03512483	Ineligible intervention: telehealth appointments
NCT03645564	Ineligible intervention: focused on adherence to DOACs
NCT04076020	Ineligible intervention: health literacy and information technology
NCT05145634	Ineligible intervention: education and behaviour focused
NCT05333445	Ineligible intervention: education and behaviour focused
Phibbs 2016	Ineligible intervention: INR self-testing
Pogosova 2018	Ineligible intervention: counselling programme on quality of life
Rakhshan 2019	Ineligible intervention: education and behavioural intervention
Ricci 2009	Ineligible intervention: implantable home monitoring devices
Siebenhofer 2019	Ineligible intervention: primary care management
Talboom-Kamp 2017	Ineligible intervention: eHealth anticoagulation management
Tang 2017a	Ineligible intervention: education and behavioural intervention
Turchioe 2019	Ineligible intervention: education and behavioural intervention
Ulrich 2019	Ineligible intervention: primary care management of antithrombotic treatment
Valencia 2019	Ineligible intervention: sole focus on medication prescription
Vinereanu 2017	Ineligible intervention: focused on treatment with oral anticoagulants and educational intervention
Voller 2005	Ineligible intervention: focused on self-management of oral anticoagulation
Wang 2019	Ineligible intervention: focused on assessing the appropriateness of initiating an anticoagulant
Watzke 2000	Ineligible intervention: focused on self-testing and self-dosing in anticoagulation clinic
You 2008	Ineligible intervention: focused on pharmacist-managed anticoagulation service
Zadeh 2019	Ineligible intervention: education and behavioural intervention

AF: atrial fibrillation
DOACs: direct oral anticoagulants
ECG: electrocardiogram
eHealth: healthcare services delivered electronically via the internet
FDA: US Food and Drug Administration
INR: international normalised ratio

mHealth: mobile health
RCT: randomised controlled trial
SMS: short message service

Characteristics of studies awaiting classification *[ordered by study ID]*

Hsieh 2021

Methods	**Design:** individual parallel randomised controlled trial **Date of study:** October 2018 to January 2021 **Total duration of study:** 2 years **Country:** Taiwan **Setting:** cardiovascular outpatient department at a medical centre in northern Taiwan
Participants	232 people diagnosed with AF **Intervention group** • Number randomised: 116 • Number lost to follow-up: 1 • Number of participants analysed: 115 • Mean age: 72 ± 13 years • Sex: 63 (50%) male • Type of AF: paroxysmal: 85 (74%), persistent: 14 (12%), permanent: 16 (14%) • History of heart failure: 39 (34%) • CHA_2DS_2-VASc score: not reported **Control group** • Number randomised: 116 • Number lost to follow-up: 0 • Number of participants analysed: 116 • Mean age: 75 ± 10 years • Sex: 53 (46%) male • Type of AF: paroxysmal: 86 (74%), persistent: 7 (6%), permanent: 23 (20%) • History of heart failure: 39 (33.6%) • CHA_2DS_2-VASc score: not reported **Inclusion criteria** • Diagnosed with AF by cardiologists • Receiving anticoagulant treatment • Aged above 20 years • Able to speak and read Taiwanese or Mandarin to understand and follow instructions • Able to use a mobile phone or computer correctly **Exclusion criteria** • Diagnosed with mental disorders • Involved in other clinical trials
Interventions	**Intervention:** the programme included 5 domains: patient information collection, instructions on AF knowledge, instructions on anticoagulation medicine, self-monitoring of symptoms, and professional consultation.

Hsieh 2021 *(Continued)*

	Control: standard instructions. The AF management manual was provided to participants with explanations. In addition, 3 sessions of telephone coaching taught participants how to manage their disease at 1 month, 3 months, and 6 months after random assignment.
Outcomes	**Outcomes** • Brief Coping Orientation to Problems Experienced (COPE) scale at 1, 3, and 6 months • Medication Adherence Rating Scale (MARS) at 1, 3, and 6 months • Quality of life measured using EQ-5D-3L at 1, 3, and 6 months • Readmission events 2 years after initiating the intervention
Notes	**Conflicts of interest:** none declared **Funding**: this study was supported by a grant from the Ministry of Science and Technology, Taiwan (MOST grant 107-2314-B016-013-MY3). The funding agency had no influence on the study design, data collection or analysis, decision to publish, or preparation of the manuscript. **Author's contact details** **Name:** Professor Chi-Wen Kao **Institution:** National Defense Medical Center, Taipei, Taiwan **Email:** chiwenkao@ndmctsgh.ed.tw **Address:** School of Nursing, National Defense Medical Center, No 161, Sec 6, Minchuan E Rd, Neihu District, Taipei, 11490, Taiwan **Reason:** unclear if intervention meets the criteria for organised clinical services for AF

AF: atrial fibrillation
CHA_2DS_2-VASc: Congestive heart failure, Hypertension, Age ≥ 75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65 to 74 and Sex category (female) score

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

ACTRN12616001109493

Study name	Effectiveness of integrated care management for atrial fibrillation on all-cause hospitalisation and mortality: a randomised controlled trial
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Primary diagnosis of AF • ECG or rhythm strip • Confirmation of AF emergency department or outpatient presentation **Exclusion criteria:** • Age < 18 years • History of myocardial infarction or coronary surgery within 3 months prior to enrolment • Valvular heart disease needing intervention • Left ventricular ejection fraction < 35% • Active malignancy • Autoimmune or systemic inflammatory disease • Severe liver or renal dysfunction • Unstable INRs

ACTRN12616001109493 *(Continued)*

- Malabsorption disorders
- Untreated hyperthyroidism
- Recent participation in a weight management programme (< 3 months prior to enrolment)
- Pregnancy
- Inability to provide informed consent

Interventions

Intervention: participants in the active (intervention) group all undergo protocolised clinical investigation, including an echocardiogram, 24-hour Holter monitoring or treadmill (to assess rate control), laboratory testing (thyroid function and cardiovascular profile) and ECG, before visiting the specialised AF outpatient clinic (iCARE-AF clinic). The treatment team includes e.g. cardiologists, electrophysiologists, GPs, specialised nurses, and pharmacists, providing an integrated, comprehensive approach to AF management. The specialised nurse is the case manager and care coordinator. The intervention period for each participant is 2 years. During 3-monthly consultations (30 to 45 minutes) in the first year, participants will visit the nurse who will take their medical history and screen for cardiovascular (CV) risk factors. The nurse provides structured education, tailored to the patient's abilities and needs, incorporating the cardiac condition, possible complications, diagnostic test results, treatment options, and risk factor management. The care provider uses a decision-support software for comprehensive AF and CV risk management. The software serves as an electronic checklist to prevent incomplete diagnostic and therapeutic guideline-adherent AF and CV risk management and can be used for patient educational goals. The software is designed as a tool to assist both care provider and patient (e.g. in order to provide tailored care and education, which requires active patient input and participation during consultations). In fact, this system is considered to navigate and support decision-making in the treatment team throughout the entire care process. CV risk factor management will be performed using an approach that has been successfully used in a prior study from the group and was assessed and approved by the Royal Adelaide Hospital Human Research Ethics Committee. This includes the following elements.

- **Weight loss.** This will be addressed by using structured multidisciplinary motivational and goal-directed face-to-face visits every 3 months in the first year, and every 6 months thereafter. Participants will be encouraged to utilise support counselling in scheduled reviews, nutritional behaviour reflection, barriers to goal achievement and nutritional decision coaching will be addressed in the 20- to 40-minute counselling sessions. Verbal and written tailored educational material will be provided. The participant will be able to schedule additional intervening visits in the event of an impending relapse. If additional support is required, 24-hour email and telephone contact will be available. Initial weight reduction will be attempted by a meal plan and behaviour modification programme, with an emphasis on education for permanent lifestyle changes and behaviour modification programme. The initial goal will be to reduce body weight by 10% from baseline.
  - Lifestyle journal. Participants in the intervention group will be instructed to maintain a self-monitoring lifestyle journal, covering dietary intake and exercise.
  - Exercise. Physical activity is initially prescribed at 20 minutes of low intensity based on participant's choice (e.g. walking, aqua-aerobics) thrice weekly, increasing to 200 min of moderate-intensity physical activity weekly. Type of activity and duration are logged into the lifestyle journal. Exercise is planned for total follow-up.
- **Cardio-metabolic risk assessment and management**. Coexistent CV risk factors as indicated below will be identified through historical patient records and fasting plasma testing. Following identification, optimal management according to current evidence-based practice guidelines will be addressed by the nurse/cardiologist in 30- to 45-minute consultations and referral to dedicated specialists (e.g. diabetes and sleep disordered breathing) if indicated.
- **Hypertension.** Participants will be asked to measure their blood pressure (BP) twice daily using a home-automated monitor. In addition, exercise stress testing will be performed to determine the presence of exercise-induced hypertension. Increase in BP to over 200/100 with exercise will be considered further evidence to optimise control. Initial therapeutic advice will include dietary salt restriction and weight loss with an increase in aerobic physical activity. Pharmacotherapy will be initiated using angiotensin-aldosterone axis active agents by preference, and other agents where necessary to achieve a target BP of < 130/80 mmHg in rest on at least 80% of random patient acquired BP readings as listed above. In addition, echocardiography will be used to monitor any objective evidence of end-organ injury (e.g. left ventricular hypertrophy). Changes in the dose and number of antihypertensive agents will be recorded at each 3-monthly visit.

ACTRN12616001109493 *(Continued)*

- **Glucose tolerance and hyperinsulinaemia.** If fasting glucose is between 100 and 125 mg/dL, a 2-hour oral glucose tolerance test will be performed. Impaired glucose tolerance (IGT) will be initially managed with lifestyle measures such as diet and aerobic exercise. If participants are unable to maintain glycosylated haemoglobin values below 6.5 percent after 3 months, metformin will be started. Participants with poor glycaemic control (glycosylated haemoglobin > 7%) will be referred to diabetes clinic.
- **Hyperlipidaemia.** Management of dyslipidaemia will be in accordance with the evidence-based practice guidelines. Initially lifestyle measures will be used. If participants are unable to achieve LDL cholesterol of less than 100 mg/dL after 3 months, then statin will be initiated. Fibrates will be used for isolated cases of hypertriglyceridaemia (TG > 500 mg/dL) or added to statin therapy if TG > 200 mg/dL and non-HDL cholesterol is > 130 mg/dL after 3 months of therapeutic lifestyle measures.
- **Sleep apnoea.** Participants will be referred to a dedicated sleep disorder unit for overnight polysomnography. Continuous positive airway pressure (CPAP) will be prescribed in the presence of a clinically compatible history of sleep apnoea and sleep study results (Respiratory Disturbance Index (RDI) and desaturation levels). Generally, continued lifestyle measures with periodic evaluation may be pursued if RDI = 15 to 30, CPAP will be prescribed if RDI > 30.
- **Smoking.** The "5A" (Ask, Assess, Advice, Assist, and Arrange follow up) structured smoking cessation framework will be adapted. Smokers will be offered behavioural support and follow-up within the specialised clinic. Pharmacotherapy may be added.
- **Alcohol.** Written and verbal counselling will be provided aiming to reduce alcohol intake (3 standard drinks per week) with abstinence as the ultimate goal.

Control: clinical investigation, treatment of AF, risk factor management as well as the follow-up schedule will be left up to the treating physician.

Outcomes	**Primary outcome:** a composite of all-cause mortality and hospitalisation at 3, 6, 9, 12, 18, 24 months **Secondary outcomes** • Cardiovascular hospitalisation at 3, 6, 9, 12, 18, 24 months • Cardiovascular mortality at 3, 6, 9, 12, 18, 24 months • AF symptom burden and severity (AFSS) at 3, 6, 9, 12, 18, 24 months • Sleep apnoea (Berlin questionnaire) at 3, 6, 9, 12, 18, 24 months • AF-related knowledge (AFKS) at 3, 6, 9, 12, 18, 24 months • Quality of life (SF-36) at 3, 6, 9, 12, 18, 24 months • Anxiety and depression (HADS) at 3, 6, 9, 12, 18, 24 months
Starting date	1 May 2018
Contact information	**Name:** Prof Prashanthan Sanders **Institution:** Centre for Heart Rhythm Disorders, Royal Adelaide Hospital **Email:** prash.sanders@adelaide.edu.au **Address:** Centre for Heart Rhythm Disorders, The Royal Adelaide Hospital-4G751, Port Road Adelaide SA 5000, Australia
Notes	**Conflicts of interest:** none declared. **Funding**: this study is supported by the University of Adelaide. **Reason:** still recruiting (anticipated date of last data collection is 2 June 2025).

Laranjo 2022

Study name	Coordinating health care with artificial intelligence-supported technology for patients with atrial fibrillation: protocol for a randomised controlled trial
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Aged ≥ 18 years • Have a documented diagnosis of AF (including recently diagnosed AF, chronic AF, or paroxysmal or persistent AF) • Have a mobile phone that is able to receive calls • Are able to receive SMS text messages or emails and open weblinks embedded in them • Are competent in the English language as ascertained by the study researchers **Exclusion criteria:** • Are participating in another AF clinical trial • Are pregnant • Have a medical illness with anticipated life expectancy of < 3 years • Are unable to provide written consent • Have a concomitant illness, physical impairment (e.g. hearing impairment), or mental condition that in the opinion of the study team or the primary physician could interfere with the conduct of the study, including outcome assessment
Interventions	**Intervention:** the AF-Support programme comprises 7 patient outreaches (digital visits) over 6 months through automated voice calls (IVR with voice recognition) and SMS text messages or emails, supplemented by an educational website. The automated telephone system uses AI to interact with patients and simulate human conversation. The AI underpinning the automated telephone system (i.e. conversational AI) includes 2 main components: automatic speech recognition, which is able to recognise patient voice responses and translate them into text, and natural language processing and understanding, which identifies the semantic and syntactic elements from the user utterance. The system was culturally adapted to Australia and trained to recognise the Australian accent in uttered speech. In addition, the system has a back-end feature called 'Pardon Me'; if the patient's verbal response is not understood, it will repeat the complete question and ask the patient to press a button corresponding to their response (e.g. "please press 1 for always, 2 for often, and 3 for sometimes"), ensuring that the user hears the question more than once and has a chance to respond either verbally or with a number option. **Control:** usual care, which consists of postdischarge instructions from the cardiologist regarding medications, lifestyle modification recommendations, encouragement of follow-up with a GP to be organised by the participant, and additional cardiologist appointments, as needed.
Outcomes	**Primary outcome:** AF-related quality of life at 6 months in the intervention group compared with the control group, measured using the AFEQT questionnaire (total score) **Secondary outcomes** • AFEQT domain scores (symptoms, daily activities, treatment concerns, and treatment satisfaction), medication adherence, lifestyle behavioural outcomes at 6 months • AF knowledge at 6 months • Patient activation at 6 months • Patient care experience at 6 months • Health outcomes, and healthcare service use at 6 months Feasibility of the intervention, focusing on acceptability and engagement with different intervention components will also be assessed.
Starting date	1 December 2020

Laranjo 2022 *(Continued)*

Contact information	**Name:** Ms Ritu Trivedi, Dr Liliana Laranjo **Institution:** Westmead Applied Research Centre and University of Sydney **Email:** liliana.laranjo@sydney.edu.au **Address:** Westmead Applied Research Centre, Faculty of Medicine and Health, University of Sydney, Level 6, Block K, Entrance 10, Westmead Hospital, Hawkesbury Road, Westmead, NSW, 2145, Australia
Notes	**Conflicts of interest:** none declared. **Funding**: this work is funded by the Digital Health Cooperative Research Centre as part of a collaborative partnership with HMS, which provided in-kind support for the development and tailoring of the intervention to the Australian context. The Westmead Applied Research Centre, University of Sydney, and the Western Sydney Local Health District provide in-kind professional support. Study funders do not have authority over the study design; collection, management, analysis, and interpretation of data; writing of the report; and decision to submit the report for publication. The authors would like to thank the technology partner (HMS) and team members from the Westmead Applied Research Centre, HMS, and the Digital Health Cooperative Research Centre for their efforts in the development of the Atrial Fibrillation-Support intervention. **Reason:** completed (date of last data collection was 3 June 2022, recruited 103 out of the planned 385 participants). No results published.

NCT03834844

Study name	Meditation and Education That is Nurse Delivered for Symptom Management in Paroxysmal Atrial Fibrillation (MEND-AF2)
Methods	Factorial randomised controlled trial
Participants	**Inclusion criteria:** • Individuals with symptomatic PAF • A symptomatic episode of PAF within the last 6 months • 18 years of age or older • Able to read and understand English • Able to participate in weekly phone calls • Able to attend 2 sessions in clinic that are 6 weeks apart **Exclusion criteria:** • Diagnosed with low cardiac function (NYHA Class IV) • Life expectancy of less than 6 months • Hospitalised in prior 3 months for illness other than PAF • Previously practised mindfulness • Cognitive impairment
Interventions	**Experimental 1:** AF Education. Participant receives 6 modules of AF education topics that are intended to be completed consecutively, 1 each week. **Experimental 2:** Mindfulness Meditation Practice. Each participant watches a mindfulness meditation introductory video in the initial session and then is asked to practice for 10 minutes each day using guided audio, which includes a different topic each week. The time duration of the guided meditations increases to 15 minutes each day during Weeks 3 to 6.

NCT03834844 *(Continued)*

	Experimental 3: Weekly Phone Calls. Each week for the 6-week intervention, the researcher will contact the participant by phone at an agreed-upon time and will discuss any questions, issues, or concerns that are voiced by the participant within 5 to 15 minutes. **Experimental 4:** AF Education and Mindfulness Meditation. Participant receives 6 modules of AF education topics that are intended to be completed consecutively, 1 each week. Each participant watches a mindfulness meditation introductory video in the initial session and then is asked to practice for 10 minutes each day using guided audio, which includes a different topic each week. The time duration of the guided meditations increases to 15 minutes each day during Weeks 3 to 6. **Experimental 5:** AF Education and Weekly Phone Calls. Participant receives 6 modules of AF education topics that are intended to be completed consecutively, 1 each week. Each week for the 6-week intervention, the researcher will contact the participant by phone at an agreed-upon time and will discuss any questions, issues, or concerns that are voiced by the participant within 5 to 15 minutes. **Experimental 6:** Mindfulness Meditation and Phone Calls. Each participant watches a mindfulness meditation introductory video in the initial session and then is asked to practice for 10 minutes each day using guided audio, which includes a different topic each week. The time duration of the guided meditations increases to 15 minutes each day during Weeks 3 to 6. Each week for the 6-week intervention, the researcher will contact the participant by phone at an agreed-upon time and will discuss any questions, issues, or concerns that are voiced by the participant within 5 to 15 minutes. **Experimental 7:** Meditation and Education and Phone Calls. Each participant watches a mindfulness meditation introductory video in the initial session and then is asked to practice for 10 minutes each day using guided audio, which includes a different topic each week. Participant receives 6 modules of AF education topics that are intended to be completed consecutively, 1 each week. The time duration of the guided meditations increases to 15 minutes each day during Weeks 3 to 6. Each week for the 6-week intervention, the researcher will contact the participant by phone at an agreed-upon time and will discuss any questions, issues, or concerns that are voiced by the participant within 5 to 15 minutes. **Control:** Usual Care. Participant receives same care as patients not enrolled in study intervention.
Outcomes	**Primary outcomes** • Change from baseline Atrial Fibrillation Symptom Burden and Symptom Severity Scores at 6 weeks, 6 and 12 months • Change from baseline in AF Quality of Life Score at 6 weeks, 6 and 12 months **Secondary outcome:** change from baseline in anxiety at 6 weeks, 6 and 12 months
Starting date	1 May 2018
Contact information	**Name:** Dr Linda Ottoboni **Institution:** Stanford University **Email:** lottoboni@stanfordhealthcare.org **Address:** Stanford University, Stanford, California, 94305, USA
Notes	**Conflicts of interest:** none declared. **Funding**: not reported. **Reason:** still recruiting (estimated study completion is 31 December 2023).

NCT04609202

Study name	Person centered nurse led atrial fibrillation care
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Patients aged > 18 years with diagnosis of AF • Referred for follow-up after AF • Able to provide informed consent • Able and willing to fill in questionnaires **Exclusion criteria:** • Atrial flutter diagnosis • Severe heart failure (corresponding to NYHA IIIB and NYHA IV) • Cardiac surgery < 3 months prior to hospitalisation for AF • Planned surgical procedures (catheter ablation, cardiac surgery) • AF in connection with acute coronary syndrome or infection • Not able to fill in questionnaires
Interventions	**Intervention:** person-centred care includes patient narratives, partnership and documentation of a health plan **Control:** usual care, which is follow-up by doctors after hospitalisation for AF
Outcomes	**Primary outcomes** • HRQoL measured by EQ-5D questionnaire at 6 and 12 months • Arrhythmia-related quality of life (ASTA) at 6 and 12 months **Secondary outcomes** • Anxiety (HADS) at 6 and 12 months • Depression (HADS) at 6 and 12 months • Symptom burden (ASTA) at 6 and 12 months • Lifestyle habits: smoking, diet, physical activity, and alcohol use measured by a questionnaire developed by The Swedish National Board of Health and Welfare at 6 and 12 months • Illness perception (B-IPQ) at 6 and 12 months • QALYs (EQ-5D) at 12 months
Starting date	19 October 2020
Contact information	**Name:** Karin H Ängerud **Institution:** Umeå University **Email:** karin.hellstrom.angerud@umu.se **Address:** Universitetstorget 4, 901 87 Umeå, Sweden
Notes	**Conflicts of interest:** none declared. **Funding:** not reported. **Reason:** still recruiting (estimated study completion is 20 May 2024).

NCT04622514

Study name	New model of integrated care of older patients with atrial fibrillation in rural China (MIRACLE-AF)
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • The village clinics need to be willing and able to provide integrated care to their patients with AF • The village doctor from 1 village clinic serves all AF patients from 2 to 3 nearby villages • The village doctors are trained to adequately use the telemedicine system • Patients aged 65 years or above • Patients diagnosed AF by an ECG, AF specialist, or hospital discharge letter • Patient is receiving the medical care provided by village clinics • Able to provide written informed consent **Exclusion criteria:** • Moderate to severe rheumatic mitral stenosis or heart valve replacement history • Presence of implantable cardiac defibrillator or CRT device • Cardiac ablation or surgery < 3 months prior to inclusion or being planned • Pulmonary vein isolation or left atrial appendage occlusion history or plan to perform any of the above operations • Life expectancy < 3 months • Participation in other clinical trials related to AF • Unable to understand and sign the informed consent form
Interventions	**Intervention:** people-centred integrated care, which involves reorienting the model of care: using of telemedicine platform and online consulting clinic; co-ordinating services: contract service by village doctor and online AF specialist; and empowering and engaging people: provide village doctor ABC pathway training course; regular visit and drug delivery by village doctor (community support); patients and their family members education **Control:** routine outpatient clinic by AF specialist
Outcomes	**Primary outcome:** composite of cardiovascular death and all stroke (all stroke include ischaemic or hemorrhagic stroke and TIA) at 3 years **Secondary outcomes** • All-cause mortality at 3 years • Cardiovascular death at 3 years • Cardiovascular hospitalisation at 3 years • Ischaemic or hemorrhagic stroke at 3 years • Major bleeding at 3 years • Clinically relevant non-major bleeding at 3 years • Quality of life measured by EQ-5D at 3 years
Starting date	10 November 2020
Contact information	**Name:** Ming Chu, Zidun Wang **Institution:** The First Affiliated Hospital of Nanjing Medical University **Email:** chuming@njmu.edu.cn / wangzidun@qq.com **Address:** The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China, 201129
Notes	**Conflicts of interest:** none declared.

NCT04622514 *(Continued)*

	Funding: not reported. **Reason:** active, not recruiting (estimated study completion is 30 May 2024).

NCT05773768

Study name	EHRA-PATHS: Clinical and Health Economic Evaluation of New Care Pathways (EHRA-PATHS)
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Newly diagnosed AF (paroxysmal, persistent, or permanent) • ≥ 65 years of age • Willing and able to participate and to attend the scheduled follow-up visits **Exclusion criteria:** • AF episode was due to a trigger (i.e. postoperative, infection, hyperthyroidism, etc.) • Life expectancy < 1 year • Participation in another clinical study (registry studies not included) • Severe cognitive impairment/dementia (defined based on MMSE and CDR scoring systems)
Interventions	**Intervention:** New Care Program. The healthcare provider will use the EHRA-PATHS' newly developed care pathways to assess whether there is an indication for presence of risk factors and comorbidities. If this is the case, the care pathways will show possible next steps for confirming the presence of these risk factors and comorbidities. If confirmed, treatment according to the current guidelines should be initiated. Since this leads to an individualised management plan, procedures can differ between patients and will also depend on local processes. **Control:** the healthcare provider follows current clinical practice with regard to history taking, physical examination, etc.
Outcomes	**Primary outcome:** identification and management of risk factors and comorbidities - number of risk factors and comorbidities that are identified and for which treatment is initiated during base mapping and at 6 months **Secondary outcomes** • AF symptom burden. Measured with the AFSS at 6 months • Quality of life. Measured with the EQ-5D-5L at 6 months • Referrals to other disciplines. The referrals to other disciplines will consist of the number of referrals and the percentage of patients referred at 6 months • Patient and healthcare provider satisfaction. Measured with a patient and healthcare provider satisfaction questionnaire at 6 months • Healthcare resource use/costs. Measured with the iMCQ at 6 months • HRQoL/utility. Measured with the EQ-5D-5L and iMCQ at 6 months
Starting date	1 September 2023
Contact information	No contacts provided.
Notes	**Conflicts of interest:** none declared. **Funding:** not reported. **Reason:** not yet recruiting (estimated study completion is 1 January 2025).

Schmidt 2018

Study name	Investigation of a novel integrated care concept (NICC) for patients suffering from chronic cardiovascular disease (CardioCare MV)
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Heart failure (ICD code I50, NYHA II-IV) or AF (I48, EHRA II-IV) or therapy-resistant hypertension (I10 to 15 mmHg, ≥ 3 antihypertensives from different drug classes, SBP > 140/90 mmHg or ≥ 4 antihypertensives irrespective of the blood pressure, with at least 1 drug being a diuretic) • Member of health insurance company Allgemeine Ortskrankenkasse Nordost or Techniker Krankenkasse. This is required because patients of the NICC group need to sign an integrated care contract with their health insurance company to allow for legitimate roll-out of intersectoral care delivery model NICC according to German social law. • Residence in Mecklenburg-Vorpommern • Age ≥ 18 years • Written informed consent **Exclusion criteria:** • Pregnancy, suspected pregnancy, or breastfeeding period • Participation in another clinical trial up to 30 days before inclusion in this trial • Cognitive deficits: patients need to be able to read and understand the German language as presented on a tablet • Chronic kidney disease requiring dialysis or creatinine clearance < 15 mL/min
Interventions	**Intervention:** novel integrated care concept (NICC), which combines telemedicine with intensive support by a care centre, including a call centre, an integrated care network including inpatient and outpatient care providers and guideline therapy for patients **Control:** treatment according to current practice as described in the guidelines of the ESC
Outcomes	**Primary outcomes** • Composite endpoint consisting of mortality, stroke, and myocardial infarction at 12 months • Number of days spent in hospital during the study period at 12 months • Composite endpoint of mortality, stroke, myocardial infarction, and cardiac decompensation at 12 months **Secondary outcomes** • Costs, such as stationary medical costs, ambulant medical costs at 12 months • Quality of life as measured with the EQ-5D-5L and the HeartQoL at 12 months • Depression (PHQ-9) at 12 months • Anxiety (GAD-7) at 12 months • Well-being (WHO-5) at 12 months • Illness-specific social support (SSUK-8) and patient activation (PAM13-D) at 12 months Safety will be assessed by focusing on serious adverse events.
Starting date	1 December 2017
Contact information	**Name:** Prof Christian Schmidt **Institution:** University of Rostock **Email:** christian.schmidt@med.uni-rostock.de

Schmidt 2018 *(Continued)*

	Address: University of Rostock, Ernst-Heydemann-Str. 8, 18057 Rostock, Germany
Notes	**Conflicts of interest:** Armin Brüge is an employee of Philips Medizin Systeme Böblingen GmbH. Drs Henriette Neumeyer and Gisela Hostenkamp are employees of Philips GmbH Market DACH. Dr Katja Krockenberger is an employee of AMEDON GmbH, and Bernard Brandewiede is CEO of AMEDON GmbH. All other authors declare no conflicts of interest. **Funding:** this trial will be financed by the Gemeinsamer Bundesausschuss (Federal Joint Committee) within the project HerzEffekt MV (funding code: 01NVF16003). Diagnostic procedures and treatment using both NICC and standard care will be partly covered by the health insurance companies AOK Nordost and TK. **Reason:** status unknown, last update of trial registry was 29 November 2019 (estimated study completion is 30 September 2020). No results published.

Smigorowsky 2017

Study name	The effect of nurse practitioner led-care on quality of life in patients with atrial fibrillation
Methods	Individual parallel randomised controlled trial
Participants	**Inclusion criteria:** • Patients aged 18 years or older • With documented AF • Able to provide informed consent, and able and willing to complete the study questionnaires on their own or with assistance **Exclusion criteria:** • Patients referred for atrioventricular node ablation or pulmonary vein isolation • Patients who have failed rate control or antiarrhythmic medications, or patients who have moderate to severe mitral or aortic valvular heart disease • Patients with unstable AF or who cannot or are unwilling to attend follow-up appointments
Interventions	**Intervention:** includes a nurse practitioner consult, including medical history, physical examination, patient teaching, treatment plan, and follow-up at 3 and 6 months **Control:** usual cardiologist consultation with follow-up determined by the cardiologist's practice pattern
Outcomes	**Primary outcome:** the difference in change in AFEQT scores from baseline to 3 and 6 months **Secondary outcomes** • Difference in change in EQ-5D from baseline to 6 months • Difference in composite outcomes of death from cardiovascular causes, cardiovascular hospitalisation, and emergency room visits between the intervention and control groups (for ischaemic stroke, heart failure, acute myocardial infarction, systemic embolism, major bleeding, severe arrhythmic events, and life-threatening adverse effects of drugs) at 6 months • Satisfaction with healthcare provider care will be assessed as measured by the overall mean score of the CSQ completed at 6 months
Starting date	31 July 2016
Contact information	**Name:** Marcie Smigorowsky **Institution:** University of Alberta

Smigorowsky 2017 *(Continued)*	**Email:** rtsuyuki@ualberta.ca **Address:** Mazankowski Alberta Heart Institution, Edmonton, Alberta, Canada, T6G 2B7
Notes	**Conflicts of interest:** RTT has received investigator-initiated grants from Merck Canada, Sanofi, and AstraZeneca, and as president of SmHeart Consulting Inc, has received consulting and speaking fees from Merck. All other authors declare that they have no competing interests. **Funding:** funding has been granted by the University Hospital Foundation: TD Fellowship Fund. The funding body was not involved in the design of the study, nor will they be involved in the collection, analysis, or interpretation of data. They also will not be involved with writing any manuscripts for publication related to this study (RES0031590). **Reason:** completed, last update in trial registry was 27 April 2021. No results published.

ABC: Atrial fibrillation Better Care
AF: atrial fibrillation
AFEQT: Atrial Fibrillation Effect on QualiTy-of-life questionnaire
AFKS: Atrial Fibrillation Knowledge Scale
AFSS: Atrial Fibrillation Severity Scale
AI: artificial intelligence
ASTA: Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia
B-IPQ: Brief Illness Perception Questionnaire
CDR: Clinical Dementia Rating
CRT: cardiac resynchronisation therapy
CSQ: Consultation Satisfaction Questionnaire
ECG: electrocardiogram
EHRA: European Heart Rhythm Association
ESC: European Society of Cardiology
GAD-7: General Anxiety Disorder-7
GP: general practitioner
HADS: Hospital Anxiety and Depression Scale
HDL: high-density lipoprotein
HRQoL: health-related quality of life
ICD: International Classification of Diseases
iMCQ: iMedical Consumption Questionnaire
INR: international normalised ratio
IVR: interactive voice response
LDL: low-density lipoprotein
MGLS: Morisky, Green and Levine Adherence Scale
MMSE: Mini-Mental State Examination
NICC: novel integrated care concept
NYHA: New York Heart Association
OAC: oral anticoagulants
PAF: paroxysmal AF
PAM13-D: German language Patient Activation Measure
PHQ-9: Patient Health Questionnaire-9
QALYs: quality-adjusted life-years
SBP: systolic blood pressure
SF-36: 36-item Short Form Health Survey
SMS: short message service
SSUK-8: illness-specific social support scale modified German short version
TG: triglycerides
TIA: transient ischaemic attack
WHO-5: World Health Organization-5 Well-Being Index

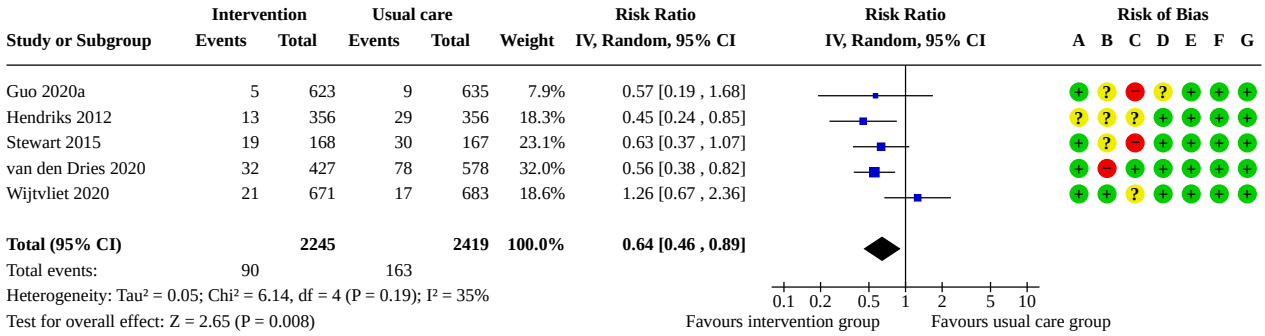
DATA AND ANALYSES

Comparison 1. Clinical service organisation for adults with atrial fibrillation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 All-cause mortality	5	4664	Risk Ratio (IV, Random, 95% CI)	0.64 [0.46, 0.89]
1.2 All-cause mortality - sensitivity analysis	3	2401	Risk Ratio (IV, Random, 95% CI)	0.71 [0.40, 1.24]
1.3 All-cause hospitalisation	2	1340	Risk Ratio (IV, Random, 95% CI)	0.94 [0.88, 1.02]
1.4 All-cause hospitalisation - sensitivity analysis	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.5 Cardiovascular mortality	5	4564	Risk Ratio (IV, Random, 95% CI)	0.64 [0.35, 1.19]
1.6 Cardiovascular mortality - sensitivity analysis	3	2301	Risk Ratio (IV, Random, 95% CI)	0.82 [0.18, 3.88]
1.7 Cardiovascular hospitalisation	5	3641	Risk Ratio (IV, Random, 95% CI)	0.83 [0.71, 0.96]
1.8 Cardiovascular hospitalisation - sensitivity analysis	4	2636	Risk Ratio (IV, Random, 95% CI)	0.79 [0.67, 0.94]
1.9 AF-related emergency department visits	2	2612	Risk Ratio (IV, Random, 95% CI)	0.54 [0.18, 1.63]
1.10 AF-related emergency department visits - sensitivity analysis	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.11 Thromboembolic complications	5	4653	Risk Ratio (IV, Random, 95% CI)	1.14 [0.74, 1.77]
1.12 Thromboembolic complications - sensitivity analysis	3	2401	Risk Ratio (IV, Random, 95% CI)	1.15 [0.66, 2.01]
1.13 Major cerebrovascular bleeding events	3	2964	Risk Ratio (IV, Random, 95% CI)	1.25 [0.79, 1.97]
1.14 Major cerebrovascular bleeding events - sensitivity analysis	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.15 All bleeding events	4	3299	Risk Ratio (IV, Random, 95% CI)	1.13 [0.82, 1.55]
1.16 All bleeding events - sensitivity analysis	2	1047	Risk Ratio (IV, Random, 95% CI)	1.07 [0.66, 1.71]
1.17 AF symptom burden	1		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.17.1 Fatigue	1	246	Risk Ratio (IV, Random, 95% CI)	1.19 [0.85, 1.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.17.2 Dyspnoea	1	246	Risk Ratio (IV, Random, 95% CI)	0.95 [0.68, 1.32]
1.17.3 Palpitations	1	246	Risk Ratio (IV, Random, 95% CI)	1.50 [1.15, 1.96]
1.17.4 Dizziness/Syncope	1	246	Risk Ratio (IV, Random, 95% CI)	1.42 [0.85, 2.39]
1.17.6 Chest pain	1	246	Risk Ratio (IV, Random, 95% CI)	1.24 [0.83, 1.84]

Analysis 1.1. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 1: All-cause mortality



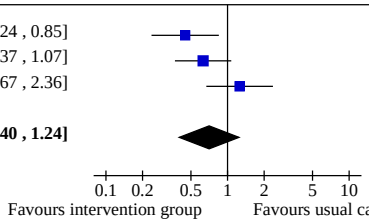
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.2. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 2: All-cause mortality - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	13	356	29	356	31.8%	0.45 [0.24 , 0.85]
Stewart 2015	19	168	30	167	36.2%	0.63 [0.37 , 1.07]
Wijtvliet 2020	21	671	17	683	32.1%	1.26 [0.67 , 2.36]
Total (95% CI)		**1195**		**1206**	**100.0%**	**0.71 [0.40 , 1.24]**
Total events:	53		76			

Heterogeneity: Tau² = 0.16; Chi² = 5.34, df = 2 (P = 0.07); I² = 63%
Test for overall effect: Z = 1.21 (P = 0.23)
Test for subgroup differences: Not applicable

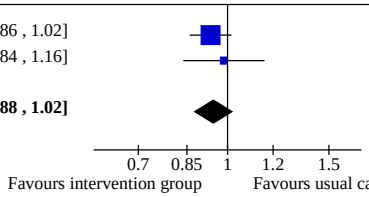


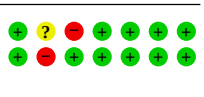
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.3. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 3: All-cause hospitalisation

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Stewart 2015	141	168	150	167	79.1%	0.93 [0.86 , 1.02]
van den Dries 2020	158	427	217	578	20.9%	0.99 [0.84 , 1.16]
Total (95% CI)		**595**		**745**	**100.0%**	**0.94 [0.88 , 1.02]**
Total events:	299		367			

Heterogeneity: Tau² = 0.00; Chi² = 0.33, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.13)
Test for subgroup differences: Not applicable

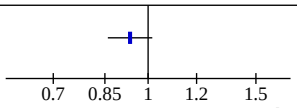


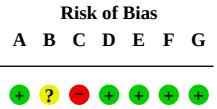


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.4. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 4: All-cause hospitalisation - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Risk Ratio IV, Random, 95% CI
Stewart 2015	141	168	150	167	0.93 [0.86 , 1.02]



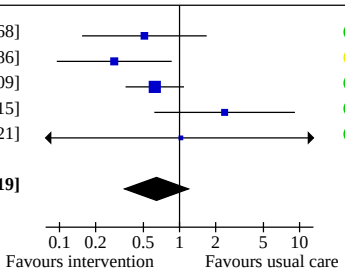


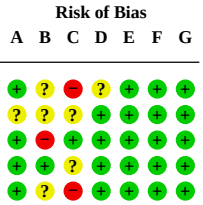
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.5. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 5: Cardiovascular mortality

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Guo 2020a	4	623	8	635	18.4%	0.51 [0.15 , 1.68]
Hendriks 2012	4	356	14	356	20.6%	0.29 [0.09 , 0.86]
van den Dries 2020	17	427	37	578	40.9%	0.62 [0.36 , 1.09]
Wijtvliet 2020	7	671	3	683	15.5%	2.38 [0.62 , 9.15]
Yan 2022	1	116	1	119	4.6%	1.03 [0.06 , 16.21]
Total (95% CI)		**2193**		**2371**	**100.0%**	**0.64 [0.35 , 1.19]**
Total events:	33		63			

Heterogeneity: Tau² = 0.16; Chi² = 5.94, df = 4 (P = 0.20); I² = 33%
Test for overall effect: Z = 1.42 (P = 0.16)
Test for subgroup differences: Not applicable



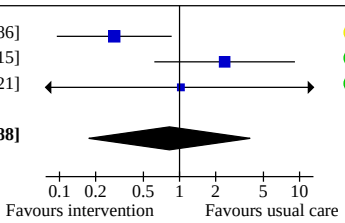


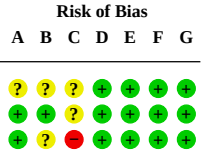
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.6. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 6: Cardiovascular mortality - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	4	356	14	356	42.1%	0.29 [0.09 , 0.86]
Wijtvliet 2020	7	671	3	683	38.1%	2.38 [0.62 , 9.15]
Yan 2022	1	116	1	119	19.8%	1.03 [0.06 , 16.21]
Total (95% CI)		**1143**		**1158**	**100.0%**	**0.82 [0.18 , 3.88]**
Total events:	12		18			

Heterogeneity: Tau² = 1.17; Chi² = 5.77, df = 2 (P = 0.06); I² = 65%
Test for overall effect: Z = 0.24 (P = 0.81)
Test for subgroup differences: Not applicable



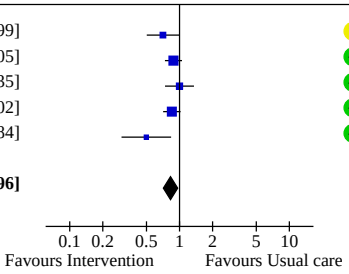


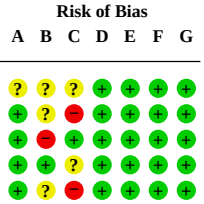
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.7. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 7: Cardiovascular hospitalisation

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	48	356	68	356	14.4%	0.71 [0.50 , 0.99]
Stewart 2015	93	168	105	167	31.0%	0.88 [0.74 , 1.05]
van den Dries 2020	62	427	84	578	16.9%	1.00 [0.74 , 1.35]
Wijtvliet 2020	158	671	189	683	30.4%	0.85 [0.71 , 1.02]
Yan 2022	17	116	35	119	7.2%	0.50 [0.30 , 0.84]
Total (95% CI)		**1738**		**1903**	**100.0%**	**0.83 [0.71 , 0.96]**
Total events:	378		481			

Heterogeneity: Tau² = 0.01; Chi² = 6.42, df = 4 (P = 0.17); I² = 38%
Test for overall effect: Z = 2.48 (P = 0.01)
Test for subgroup differences: Not applicable



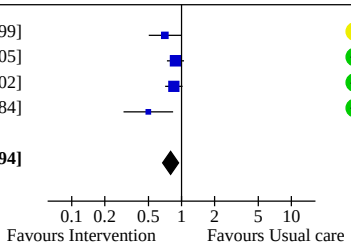


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.8. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 8: Cardiovascular hospitalisation - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	48	356	68	356	17.6%	0.71 [0.50 , 0.99]
Stewart 2015	93	168	105	167	37.0%	0.88 [0.74 , 1.05]
Wijtvliet 2020	158	671	189	683	36.4%	0.85 [0.71 , 1.02]
Yan 2022	17	116	35	119	8.9%	0.50 [0.30 , 0.84]
Total (95% CI)		**1311**		**1325**	**100.0%**	**0.79 [0.67 , 0.94]**
Total events:	316		397			

Heterogeneity: Tau² = 0.01; Chi² = 5.04, df = 3 (P = 0.17); I² = 40%
Test for overall effect: Z = 2.69 (P = 0.007)
Test for subgroup differences: Not applicable

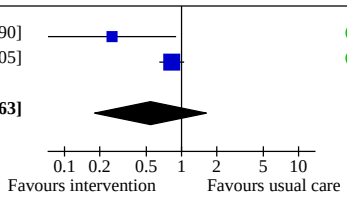


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.9. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 9: AF-related emergency department visits

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Guo 2020a	3	623	12	635	35.6%	0.25 [0.07 , 0.90]
Wijtvliet 2020	98	671	121	683	64.4%	0.82 [0.65 , 1.05]
Total (95% CI)		**1294**		**1318**	**100.0%**	**0.54 [0.18 , 1.63]**
Total events:	101		133			

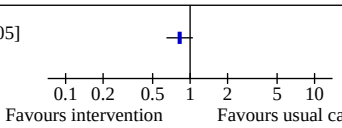
Heterogeneity: Tau² = 0.47; Chi² = 3.21, df = 1 (P = 0.07); I² = 69%
Test for overall effect: Z = 1.09 (P = 0.28)
Test for subgroup differences: Not applicable

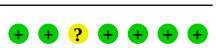


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.10. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 10: AF-related emergency department visits - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Risk Ratio IV, Random, 95% CI
Wijtvliet 2020	98	671	121	683	0.82 [0.65 , 1.05]



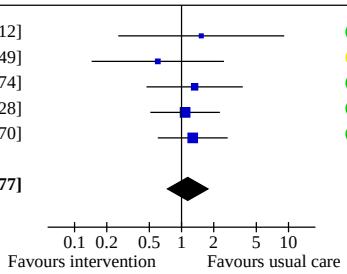


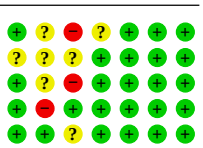
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.11. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 11: Thromboembolic complications

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Guo 2020a	3	623	2	635	5.9%	1.53 [0.26 , 9.12]
Hendriks 2012	3	356	5	356	9.3%	0.60 [0.14 , 2.49]
Stewart 2015	8	168	6	167	17.6%	1.33 [0.47 , 3.74]
van den Dries 2020	12	423	15	571	33.7%	1.08 [0.51 , 2.28]
Wijtvliet 2020	15	671	12	683	33.5%	1.27 [0.60 , 2.70]
Total (95% CI)		**2241**		**2412**	**100.0%**	**1.14 [0.74 , 1.77]**
Total events:	41		40			

Heterogeneity: Tau² = 0.00; Chi² = 1.07, df = 4 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



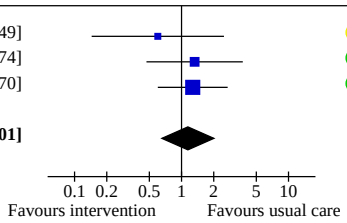


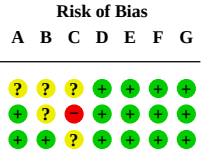
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.12. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 12: Thromboembolic complications - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	3	356	5	356	15.4%	0.60 [0.14 , 2.49]
Stewart 2015	8	168	6	167	29.1%	1.33 [0.47 , 3.74]
Wijtvliet 2020	15	671	12	683	55.4%	1.27 [0.60 , 2.70]
Total (95% CI)		**1195**		**1206**	**100.0%**	**1.15 [0.66 , 2.01]**
Total events:	26		23			

Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.48 (P = 0.63)
Test for subgroup differences: Not applicable



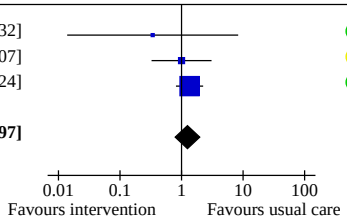


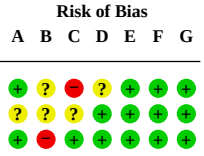
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.13. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 13: Major cerebrovascular bleeding events

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Guo 2020a	0	623	1	635	2.1%	0.34 [0.01 , 8.32]
Hendriks 2012	6	356	6	356	16.7%	1.00 [0.33 , 3.07]
van den Dries 2020	28	423	28	571	81.3%	1.35 [0.81 , 2.24]
Total (95% CI)		**1402**		**1562**	**100.0%**	**1.25 [0.79 , 1.97]**
Total events:	34		35			

Heterogeneity: Tau² = 0.00; Chi² = 0.88, df = 2 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)
Test for subgroup differences: Not applicable

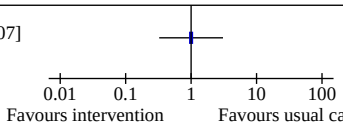




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.14. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 14: Major cerebrovascular bleeding events - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Risk Ratio IV, Random, 95% CI
Hendriks 2012	6	356	6	356	1.00 [0.33 , 3.07]

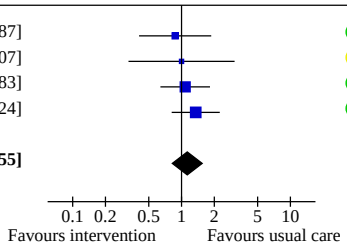


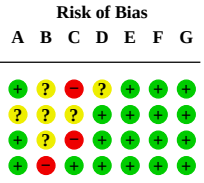
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.15. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 15: All bleeding events

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Guo 2020a	12	623	14	635	17.1%	0.87 [0.41 , 1.87]
Hendriks 2012	6	356	6	356	7.9%	1.00 [0.33 , 3.07]
Stewart 2015	25	168	23	167	36.3%	1.08 [0.64 , 1.83]
van den Dries 2020	28	423	28	571	38.6%	1.35 [0.81 , 2.24]
Total (95% CI)		**1570**		**1729**	**100.0%**	**1.13 [0.82 , 1.55]**
Total events:	71		71			

Heterogeneity: Tau² = 0.00; Chi² = 0.98, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.75 (P = 0.45)
Test for subgroup differences: Not applicable

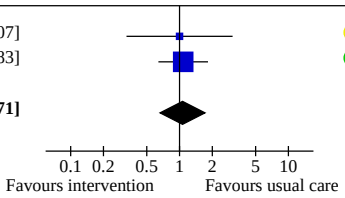




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.16. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 16: All bleeding events - sensitivity analysis

Study or Subgroup	Intervention Events	Intervention Total	Usual care Events	Usual care Total	Weight	Risk Ratio IV, Random, 95% CI
Hendriks 2012	6	356	6	356	17.9%	1.00 [0.33 , 3.07]
Stewart 2015	25	168	23	167	82.1%	1.08 [0.64 , 1.83]
Total (95% CI)		**524**		**523**	**100.0%**	**1.07 [0.66 , 1.71]**
Total events:	31		29			

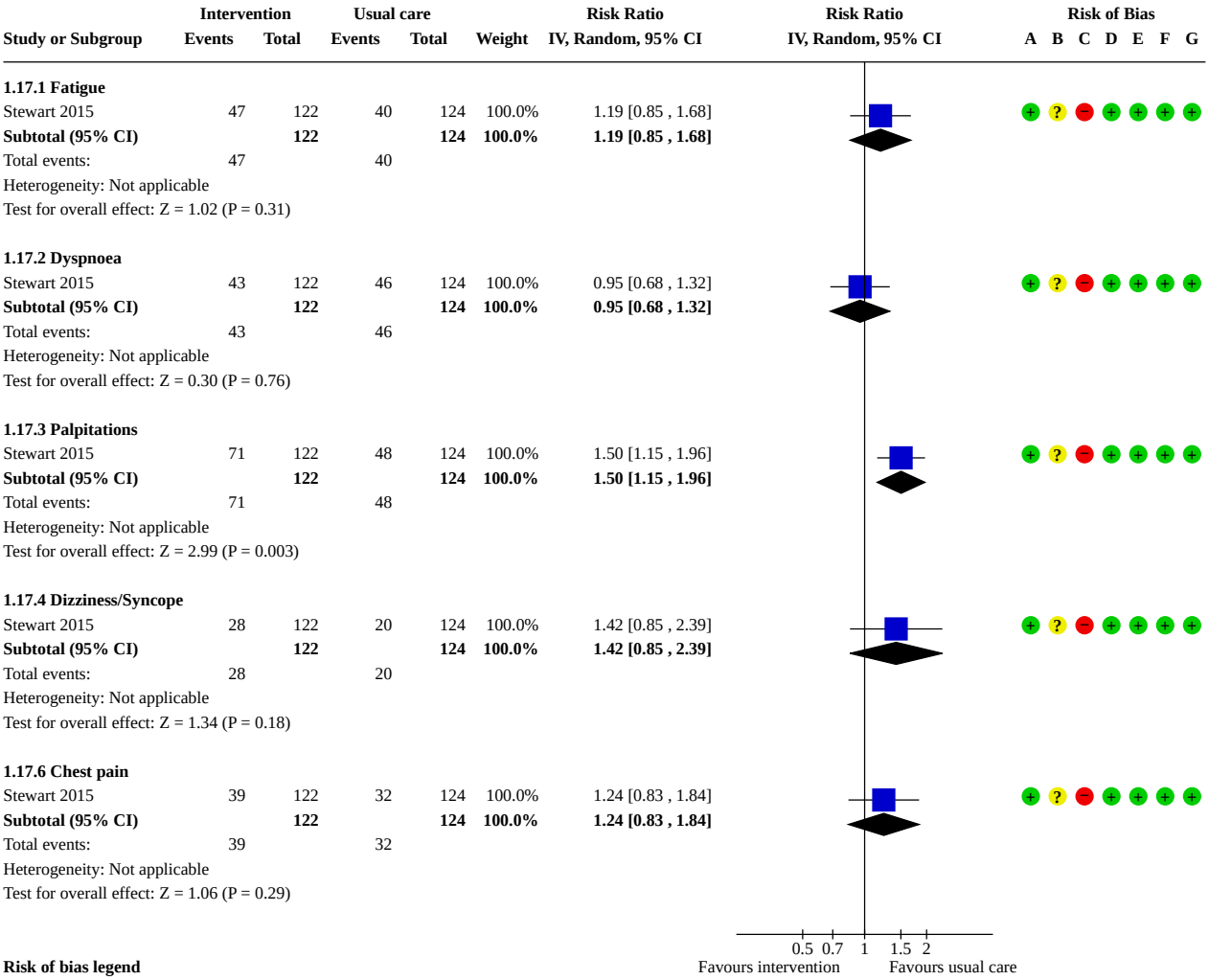
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0% 

Test for overall effect: Z = 0.26 (P = 0.79)
Test for subgroup differences: Not applicable

Risk of Bias: A B C D E F G
Hendriks 2012: ? ? ? + + + +
Stewart 2015: + ? − + + + +

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.17. Comparison 1: Clinical service organisation for adults with atrial fibrillation, Outcome 17: AF symptom burden



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

APPENDICES

Appendix 1. Search strategies

CENTRAL

#1 MeSH descriptor: [Disease Management] this term only
#2 (disease* NEAR/5 manag*)
#3 MeSH descriptor: [Patient Care Management] this term only
#4 MeSH descriptor: [Medication Therapy Management] this term only
#5 MeSH descriptor: [Patient Care Team] explode all trees
#6 MeSH descriptor: [Patient-Centered Care] this term only
#7 (patient* NEAR/3 manag*)
#8 (patient* NEAR/4 (care or caring))

#9 (deliver* NEAR/2 care)
#10 (manag* NEAR/5 care)
#11 ((management or care) NEAR/5 program*)
#12 (case NEAR/5 manag*)
#13 MeSH descriptor: [Home Care Services] this term only
#14 MeSH descriptor: [Home Care Services, Hospital-Based] this term only
#15 (home NEAR/5 (intervention* or care))
#16 (home NEXT visit*)
#17 homecare
#18 MeSH descriptor: [Ambulatory Care] this term only
#19 (ambulatory NEAR/2 (care or caring))
#20 MeSH descriptor: [Patient Discharge] this term only
#21 (discharg* NEAR/5 program*)
#22 (practice NEXT guideline*)
#23 MeSH descriptor: [Practice Guidelines as Topic] this term only
#24 (comprehensive* NEAR/5 (care or caring))
#25 multidisciplinary
#26 (treatment* NEAR/5 plan*)
#27 (nurse* NEAR/5 led)
#28 (discharg* NEAR/5 plan*)
#29 MeSH descriptor: [Outpatient Clinics, Hospital] this term only
#30 (outpatient* NEAR/2 (clinic* or hospital*))
#31 ((Outpatient* or out-patient*) NEAR/3 (care or service*))
#32 (Clinic* NEAR/3 (visit* or special* or outpatient* or out-patient* or service*))
#33 Clinic-based care
#34 (Inpatient NEAR/3 (care or service))
#35 (Care NEAR/3 (primary or communit* or home or integrated or nurse-led or collaborative or multidisciplin* or comprehensive or co-ordinated))
#36 MeSH descriptor: [Ambulatory Care Facilities] this term only
#37 (interdisciplinary or inter-disciplinary or multidisciplinary or multi-disciplinary)
#38 (service* NEAR/3 home)
#39 (team* NEAR/3 (health or patient or medical or care or healthcare))
#40 MeSH descriptor: [Delivery of Health Care, Integrated] this term only
#41 (post-discharge NEAR/3 follow-up)
#42 ((Nurse* or pharmacist* or physio* or dietician*) NEAR/5 (outpatient* or out-patient*))
#43 (integrat* NEAR/3 (health* or deliver*))
#44 MeSH descriptor: [Comprehensive Health Care] this term only
#45 (comprehensive NEAR/2 health*)
#46 MeSH descriptor: [Patient Care Planning] explode all trees
#47 MeSH descriptor: [Health Services Research] this term only
#48 MeSH descriptor: [Community Health Services] explode all trees
#49 (commun* NEAR/2 (healthcare or health* or service*))
#50 MeSH descriptor: [Community Health Centers] this term only
#51 MeSH descriptor: [Cell Phone] explode all trees
#52 (phone* or telephon*)
#53 (cellphone* or mobiles or smartphone*)
#54 ((mobile or handheld or hand held or cell* or phone*) NEAR/2 (device* or technolog* or app* or health*))
#55 MeSH descriptor: [Text Messaging] this term only
#56 sms
#57 ((text or short or multimedia or multi media or mms) NEAR/1 messag*)
#58 (texting* or texted or texter*)
#59 MeSH descriptor: [Telemedicine] this term only
#60 (mhealth or m health or ehealth or e health or telemedicine* or telehealth or telemonitor*)
#61 MeSH descriptor: [Reminder Systems] this term only
#62 (reminder* NEXT (text* or system* or messag*))
#63 (digital NEAR/3 (care or health* or model*))
#64 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #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 or #57 or #58 or #59 or #60 or #61 or #62 or #63
#65 MeSH descriptor: [Atrial Fibrillation] this term only
#66 ((atrial or auricular or atrium) NEAR/2 fibrillation*)
#67 (A-fib or Afib)

#68 #65 or #66 or #67
#69 #64 and #68

MEDLINE Ovid

1 Disease Management/
2 (disease* adj5 manag*).tw.
3 Patient Care Management/
4 Medication Therapy Management/
5 exp Patient Care Team/
6 Patient-Centered Care/
7 (patient* adj3 manag*).tw.
8 (patient* adj4 (care or caring)).tw.
9 (deliver* adj2 care).tw.
10 (manag* adj5 care).tw.
11 ((management or care) adj5 program*).tw.
12 Case Management/
13 (case adj5 manag*).tw.
14 Home Care Services/
15 Home Care Services, Hospital-Based/
16 (home adj5 (intervention* or care)).tw.
17 (home adj visit*).tw.
18 homecare.tw.
19 Ambulatory Care/
20 (ambulatory adj2 (care or caring)).tw.
21 Patient Discharge/
22 (discharg* adj5 program*).tw.
23 (practice adj guideline*).tw.
24 Practice Guidelines as Topic/
25 (comprehensive* adj5 (care or caring)).tw.
26 multidisciplinary.tw.
27 (treatment* adj5 plan*).tw.
28 (nurse* adj5 led).tw.
29 (discharg* adj5 plan*).tw.
30 Outpatient Clinics, Hospital/
31 (outpatient* adj2 (clinic* or hospital*)).tw.
32 ((Outpatient* or out-patient*) adj3 (care or service*)).tw.
33 (Clinic* adj3 (visit* or special* or outpatient* or out-patient* or service*)).tw.
34 Clinic-based care.tw.
35 (Inpatient adj3 (care or service)).tw.
36 (Care adj3 (primary or communit* or home or integrated or nurse-led or collaborative or multidisciplin* or comprehensive or co-ordinated)).tw.
37 Ambulatory Care Facilities/
38 (interdisciplinary or inter-disciplinary or multidisciplinary or multi-disciplinary).tw.
39 (service* adj3 home).tw.
40 (team* adj3 (health or patient or medical or care or healthcare)).tw.
41 "Delivery of Health Care, Integrated"/
42 (post-discharge adj3 follow-up).tw.
43 ((Nurse* or pharmacist* or physio* or dietician*) adj5 (outpatient* or out-patient*)).tw.
44 (integrat* adj3 (health* or deliver*)).tw.
45 Comprehensive Health Care/
46 (comprehensive adj2 health*).tw.
47 exp Patient Care Planning/
48 Health Services Research/
49 exp Community Health Services/
50 (commun* adj2 (healthcare or health* or service*)).tw.
51 Community Health Centers/
52 exp Cell Phones/
53 (phone* or telephon*).tw.
54 (cellphone* or mobiles or smartphone*).tw.
55 ((mobile or handheld or hand held or cell* or phone*) adj2 (device* or technolog* or app* or health*)).tw.
56 Text Messaging/

57 sms.tw.
58 ((text or short or multimedia or multi media or mms) adj1 messag*).tw.
59 (texting* or texted or texter*).tw.
60 Telemedicine/
61 (mhealth or m health or ehealth or e health or telemedicine* or telehealth or telemonitor*).tw.
62 Reminder Systems/
63 (reminder* adj (text* or system* or messag*)).tw.
64 (digital adj3 (care or health* or model*)).tw.
65 or/1-64
66 Atrial Fibrillation/
67 ((atrial or auricular or atrium) adj2 fibrillation*).tw.
68 (A-fib or Afib).tw.
69 or/66-68
70 randomized controlled trial.pt.
71 controlled clinical trial.pt.
72 randomized.ab.
73 placebo.ab.
74 clinical trials as topic.sh.
75 randomly.ab.
76 trial.ti.
77 70 or 71 or 72 or 73 or 74 or 75 or 76
78 exp animals/ not humans.sh.
79 77 not 78
80 65 and 69 and 79

Embase Ovid

1 disease management/
2 (disease* adj5 manag*).tw.
3 exp patient care/
4 medication therapy management/
5 (patient* adj3 manag*).tw.
6 (patient* adj4 (care or caring)).tw.
7 (deliver* adj2 care).tw.
8 (manag* adj5 care).tw.
9 ((management or care) adj5 program*).tw.
10 case management/
11 (case adj5 manag*).tw.
12 exp home care/
13 (home adj5 (intervention* or care)).tw.
14 (home adj visit*).tw.
15 homecare.tw.
16 ambulatory care/
17 (ambulatory adj2 (care or caring)).tw.
18 hospital discharge/
19 (discharg* adj5 program*).tw.
20 (practice adj guideline*).tw.
21 practice guideline/
22 (comprehensive* adj5 (care or caring)).tw.
23 multidisciplinary.tw.
24 (treatment* adj5 plan*).tw.
25 (nurse* adj5 led).tw.
26 (discharg* adj5 plan*).tw.
27 outpatient department/
28 (outpatient* adj2 (clinic* or hospital*)).tw.
29 ((Outpatient* or out-patient*) adj3 (care or service*)).tw.
30 (Clinic* adj3 (visit* or special* or outpatient* or out-patient* or service*)).tw.
31 Clinic-based care.tw.
32 (Inpatient adj3 (care or service)).tw.
33 (Care adj3 (primary or communit* or home or integrated or nurse-led or collaborative or multidisciplin* or comprehensive or co-ordinated)).tw.
34 (interdisciplinary or inter-disciplinary or multidisciplinary or multi-disciplinary).tw.

35 (service* adj3 home).tw.
36 (team* adj3 (health or patient or medical or care or healthcare)).tw.
37 integrated health care system/
38 (post-discharge adj3 follow-up).tw.
39 ((Nurse* or pharmacist* or physio* or dietician*) adj5 (outpatient* or out-patient*)).tw.
40 (integrat* adj3 (health* or deliver*)).tw.
41 health care/
42 (comprehensive adj2 health*).tw.
43 exp patient care planning/
44 health services research/
45 community care/
46 (commun* adj2 (healthcare or health* or service*)).tw.
47 health center/
48 exp mobile phone/
49 (phone* or telephon*).tw.
50 (cellphone* or mobiles or smartphone*).tw.
51 ((mobile or handheld or hand held or cell* or phone*) adj2 (device* or technolog* or app* or health*)).tw.
52 text messaging/
53 sms.tw.
54 ((text or short or multimedia or multi media or mms) adj1 messag*).tw.
55 (texting* or texted or texter*).tw.
56 telemedicine/
57 (mhealth or m health or ehealth or e health or telemedicine* or telehealth or telemonitor*).tw.
58 reminder system/
59 (reminder* adj (text* or system* or messag*)).tw.
60 (digital adj3 (care or health* or model*)).tw.
61 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 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 or 57 or 58 or 59 or 60
62 atrial fibrillation/
63 ((atrial or auricular or atrium) adj2 fibrillation*).tw.
64 (A-fib or Afib).tw.
65 62 or 63 or 64
66 random$.tw.
67 factorial$.tw.
68 crossover$.tw.
69 cross over$.tw.
70 cross-over$.tw.
71 placebo$.tw.
72 (doubl$ adj blind$).tw.
73 (singl$ adj blind$).tw.
74 assign$.tw.
75 allocat$.tw.
76 volunteer$.tw.
77 crossover procedure/
78 double blind procedure/
79 randomized controlled trial/
80 single blind procedure/
81 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80
82 (animal/ or nonhuman/) not human/
83 81 not 82
84 61 and 65 and 83
85 limit 84 to embase

CINAHL

S91 S63 AND S67 AND S90
S90 S89 NOT S88
S89 S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82
S88 S86 NOT S87
S87 MH (human)
S86 S83 OR S84 OR S85

S85 TI (animal model*)
S84 MH (animal studies)
S83 MH animals+
S82 AB (cluster W3 RCT)
S81 MH (crossover design) OR MH (comparative studies)
S80 AB (control W5 group)
S79 PT (randomized controlled trial)
S78 MH (placebos)
S77 MH (sample size) AND AB (assigned OR allocated OR control)
S76 TI (trial)
S75 AB (random*)
S74 TI (randomised OR randomized)
S73 MH cluster sample
S72 MH pretest-posttest design
S71 MH random assignment
S70 MH single-blind studies
S69 MH double-blind studies
S68 MH randomized controlled trials
S67 S64 OR S65 OR S66
S66 TX (A-fib or Afib)
S65 TX ((atrial or auricular or atrium) n2 fibrillation*)
S64 (MH "Atrial Fibrillation")
S63 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 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 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62
S62 TX (digital n3 (care or health* or model*))
S61 TX (reminder* n1 (text* or system* or messag*))
S60 (MH "Reminder Systems")
S59 TX (mhealth or m-health or ehealth or e-health or telemedicine* or telehealth or telemonitor*)
S58 (MH "Telemedicine")
S57 TX (texting* or texted or texter*)
S56 TX ((text or short or multimedia or multi media or mms) n1 messag*)
S55 TX sms
S54 (MH "Text Messaging")
S53 TX ((mobile or handheld or hand held or cell* or phone*) n2 (device* or technolog* or app* or health*))
S52 TX (cellphone* or mobiles or smartphone*)
S51 TX (phone* or telephon*)
S50 (MH "Cellular Phone+")
S49 (MH "Community Health Centers")
S48 TX (commun* n2 (healthcare or health* or service*))
S47 (MH "Community Health Services+")
S46 (MH "Health Services Research")
S45 (MH "Patient Care Plans")
S44 TX (comprehensive n2 health*)
S43 TX (integrat* n3 (health* or deliver*))
S42 TX ((Nurse* or pharmacist* or physio* or dietician*) n5 (outpatient* or out-patient*))
S41 TX (post-discharge n3 follow-up)
S40 (MH "Health Care Delivery, Integrated")
S39 TX (team* n3 (health or patient or medical or care or healthcare))
S38 TX (service* n3 home)
S37 TX (interdisciplinary or inter-disciplinary or multidisciplinary or multi-disciplinary)
S36 (MH "Ambulatory Care Facilities")
S35 TX (Care n3 (primary or communit* or home or integrated or nurse-led or collaborative or multidisciplin* or comprehensive or co-ordinated))
S34 TX (Inpatient n3 (care or service))
S33 TX Clinic-based care
S32 TX (Clinic* n3 (visit* or special* or outpatient* or out-patient* or service*))
S31 TX ((Outpatient* or out-patient*) n3 (care or service*))
S30 TX (outpatient* n2 (clinic* or hospital*))
S29 (MH "Outpatient Service")
S28 TX (discharg* n5 plan*)

S27 TX (nurse* n5 led)
S26 TX (treatment* n5 plan*)
S25 TX multidisciplinary
S24 TX (comprehensive* n5 (care or caring))
S23 (MH "Practice Guidelines")
S22 TX (practice n1 guideline*)
S21 TX (discharg* n5 program*)
S20 (MH "Patient Discharge")
S19 TX (ambulatory n2 (care or caring))
S18 TX (ambulatory n2 (care or caring))
S17 (MH "Ambulatory Care")
S16 TX homecare
S15 TX (home n1 visit*)
S14 TX (home n5 (intervention* or care))
S13 (MH "Home Health Care")
S12 TX (case n5 manag*)
S11 (MH "Case Management")
S10 TX ((management or care) n5 program*)
S9 TX (manag* n5 care)
S8 TX (deliver* n2 care)
S7 TX (patient* n4 (care or caring))
S6 TX (patient* n3 manag*)
S5 (MH "Patient Centered Care")
S4 (MH "Multidisciplinary Care Team+")
S3 (MH "Medication Management")
S2 TX (disease* n5 manag*)
S1 (MH "Disease Management")

ClinicalTrials.gov

atrial fibrillation AND disease management

WHO ICTRP

atrial fibrillation AND disease management

HISTORY

Protocol first published: Issue 8, 2019

CONTRIBUTIONS OF AUTHORS

CF: responsible for the conception and design of the protocol, and for co-co-ordinating and completing the protocol, including writing the protocol. Acted as adjudicator in study selection. Completed data extraction, assessment of risk of bias in the included studies, checked data entry, and performed data analysis, GRADE assessment, and interpretation of data. Wrote the review document. Read and reviewed the final review document prior to submission. CF is the guarantor for the review.

SA: screened studies for inclusions and exclusion. Completed assessment of risk of bias in the included studies, performed data analysis, GRADE assessment, and interpretation of data. Addressed all editorial and peer-review comments. Read and reviewed the final review document prior to submission.

JH: contributed to the conception, design, and writing of the protocol. Contributed to the writing of the final review. Read and reviewed the final review prior to submission.

CG: contributed to the conception, design, and writing of the protocol. Contributed to the writing of the final review. Read and reviewed the final review prior to submission.

BB: contributed to the conception, design, and writing of the protocol. Read and reviewed the final review prior to submission.

AD: screened studies for inclusion and exclusion. Supported data extraction and data entry.

SCI: contributed to the conception, design, and writing of the protocol. Acted as an adjudicator in data extraction, assessment of risk of bias in the included studies, and GRADE assessment and contributed to the writing of the final review. Read and reviewed the final review prior to submission.

FS: screened studies for inclusion and exclusion. Completed data extraction, assessment of risk of bias in the included studies, data entry and performed data analysis, GRADE assessment, and interpretation of data. Wrote the review document. Read and reviewed the final review document prior to submission.

DECLARATIONS OF INTEREST

CF declares receiving a Post-doctoral fellowship grant from the Heart Foundation of Australia and an Investigator grant from the Australian National Health and Medical Research Council (NHMRC) (APP1196262) and a grant from the National Stroke Foundation (all paid to institution, but CF benefitted from the payments). CF works as a Professor at the University of Wollongong and Western Sydney Local Health District. CF is the Chair of the Cardiovascular Nursing Council of the Cardiac Society of Australia and New Zealand (voluntary role). CF was also a member of the Guideline Working Group for the management of atrial fibrillation by the Heart Foundation, Australia and Cardiac Society of Australia and New Zealand. CF declares that he has published opinions on the topic via social media outlets. CF is affiliated with the Stroke Foundation (Australia) and the Heart Foundation (Australia), who have declared an opinion or position on the topic.

SA declares having no conflicts of interest.

JH works as Professor of Cardiovascular Nursing at the Flinders University. JH declares a Future Leader Fellowship from the National Heart Foundation of Australia (paid to institution) and speakers fee from Biotronik for a presentation (paid to institution; funds may have been used to support projects in which JH was involved, but JH did not have access to the funds). JH was a member of the Task Force Writing Committee to develop the 2016 European Society of Cardiology Guidelines for the management of atrial fibrillation; and the Australian clinical guidelines for the diagnosis and management of atrial fibrillation 2018, in collaboration with the National Heart Foundation and the Cardiac Society of Australia and NZ (unpaid positions). JH also declares that he is the lead author and investigator of an unfunded trial included in the analysis of this review (Hendriks 2012); he was not involved in assessing the eligibility of that study, extracting or analysing data, assessing risk of bias, or grading the certainty of the evidence.

CG declares having published an opinion piece on integrated care (PMID: 33624053) and being a contributing author of a post hoc analysis of the original trial by JH and colleagues (Hendriks 2012); unfunded study. CG was not involved in assessing the eligibility of that study, extracting or analysing data, assessing risk of bias, or grading the certainty of the evidence.

BB declares working as a Clinical Academic Pharmacist at the Royal North Shore and Hunter New England Local Health District as well as membership of the Guideline Working Group for the management of atrial fibrillation by the National Heart Foundation, Australia (unpaid position).

AD declares having no conflicts of interest.

SCI declares a Fellowship grant from the Heart Foundation Australia via their institution and being the chair of the Cardiovascular Nursing Council 2016-2022 and Professional and Ethical Standards Committee 2022-2024 (voluntary roles) with the Cardiac Society of Australia and New Zealand (CSANZ). SCI was an Editor with Cochrane Heart. She was not involved in the editorial process for this review.

FS declares having no conflicts of interest. FS is supported by an Australian Government Research Training Program (RTP) Scholarship and by a PhD Scholarship from Western Sydney University.

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Internal sources

- -, Other

  N/A

External sources

- National Institute for Health Research (NIHR), UK

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- National Health and Medical Research Council, Australia

  A/Prof Caleb Ferguson is supported by a 2020 NHMRC Investigator Grant (APP1196262).
- Heart Foundation (Australia), Australia

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  A/Prof Sally C Inglis and Professor Jeroen Hendriks are supported by a Heart Foundation Future Leader Fellowship.

- Australian Government Research Training Program, Australia

  Fahad Shaikh is supported by an Australian Government Research Training Program (RTP) Scholarship and by a PhD Scholarship from Western Sydney University.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The following amendments were made after the publication of the study protocol (Ferguson 2019a).

1. We rephrased our objectives to a single sentence that follows the recommended guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* and avoids pre-empting the findings of the review.
2. We amended the exclusion criteria to exclude cardiac rehabilitation, as it has a particular focus on exercise with some education support.
3. We amended the inclusion criteria to state that clinical service interventions must be multicomponent and involve a multidisciplinary approach to be eligible. Multicomponent and multidisciplinary approach means patients are provided with comprehensive care which meets the definition of clinical service organisations for AF.
4. For the outcome thromboembolic complications, we refined the definition to include stroke and/or TIA instead of stroke and TIA to ensure we captured and included all relevant thromboembolic complications.
5. We changed the definition of all-cause hospitalisation to include only hospital admissions (i.e. not AF-related emergency department visits), as an emergency department visit may not necessarily lead to an admission.
6. We did not include Scopus as a bibliographic database, as PubMed and MEDLINE content are a subset of Scopus and should have captured all the relevant articles, in addition to Embase.
7. We calculated and reported the number needed to treat for all-cause mortality, all-cause hospitalisation, cardiovascular mortality, thromboembolic complications, and major cerebrovascular bleeding events to ensure the results are interpretable by governmental agencies and stakeholders.
8. We planned to use summary information (log hazard ratio and variance) from the included studies to calculate time-to-event data for all-cause or cardiovascular mortality (Higgins 2023a). However, these were not reported in the included studies.
9. For cross-over RCTs, we planned to take all measurements from intervention E periods and all measurements from intervention C periods and analyse these as if the trial were a parallel-group trial of E versus C. Whilst this approach generates a unit of analysis issue, it is conservative and less serious than other types of unit of analysis issues, as it underweights rather than overweights studies. However, no cross-over RCTs were included in the review.
10. We planned to assess for potential publication bias using funnel plots. However, this was precluded by an insufficient number of studies (< 10).
11. We deleted the following planned subgroup analyses to reduce the risk of type I error:
    a. people who underwent AF catheter ablation versus people on medical treatment alone; and
    b. people with paroxysmal AF versus non-paroxysmal AF.
12. Had we found definitive evidence of heterogeneity ($I^2 > 50\%$), we planned to explore potential reasons for differences by conducting the subgroup analyses listed below and meta-regression (Normand 1999). However, this was precluded by insufficient studies.
    a. Age (more than 65 years versus under 65 years).
    b. Sex (women versus men).
    c. History of heart failure.
    d. People with a CHA_2DS_2-VASc score of 2 or greater versus people with a score of 0 to 1.
    e. Comparison of type of intervention (case management versus multidisciplinary versus integrated care versus eHealth models).

INDEX TERMS

Medical Subject Headings (MeSH)

*Atrial Fibrillation [mortality] [therapy]; Bias; Cause of Death; Hospitalization; Quality of Life; *Randomized Controlled Trials as Topic; Stroke [mortality]; Telemedicine

MeSH check words

Adult; Aged; Humans