# **BMJ Open** A systematic review protocol for examining 30-day readmission costs for atrial fibrillation patients

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### ABSTRACT

Introduction Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and readmissions of AF patients place a huge burden on the healthcare system, including economically. With an increasing prevalence, the burden of AF will continue evolving. To illuminate the readmission-specific economic burden, we aim to provide quality evidence on the cost of readmissions within 30 days where AF has been the primary diagnosis at the index admission.

Methods and analysis We will conduct a systematic review of all peer-reviewed articles examining readmission costs for AF patients. We will search MedLine, Cumulative Index to Nursing and Allied Health Literature. Scopus and Cochrane Library for articles written in English. published in peer-reviewed journals from inception to 2019. Reporting of this protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols checklist. Studies will be included if patients were aged 18 years and over. AF was the primary diagnosis of index admission and costs of readmission within 30 days were reported. Quality assessment of studies will be done using a modified Evers checklist. Study results will be summarised in a Forest plot and heterogeneity tested for using the Cochran's Q and I<sup>2</sup> statistic. A random-effects model will be applied for metaanalysis if studies are sufficiently homogeneous. The cost of readmission to hospital within 30 days for AF patients is the main outcome of interest while additional outcomes are 30-day readmission rate, predictors of readmission and predictors of readmission costs.

Ethics and dissemination Formal ethical approval is not required as no patients will be involved. Dissemination of results will be through a peer-reviewed publication. PROSPERO registration number CRD42019132017

### **INTRODUCTION**

Atrial fibrillation (AF) is a cardiac arrhythmia<sup>1</sup> sustained by irregular electrical activity in the heart.<sup>2</sup> Asynchronous atrial contraction and ventricular excitation affect the ejection of blood into circulation.<sup>3</sup> Without pharmacological or surgical intervention, or direct-current cardioversion to terminate the dysrhythmia, AF progresses and episodes of electrical disturbance become regular and eventually permanent.<sup>2</sup> In cases of permanent AF, restoration of sinus rhythm is either

### Strengths and limitations of this study

- Systematic review protocol of published peer-reviewed articles following Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols quidelines.
- Provides highest level of evidence to decision makers.
- Informs on the economic impact of readmission in atrial fibrillation (AF) patients.
- Availability of high-quality studies examining the costs and readmission rates of AF patients may be limited.
- Varving cost inclusions and methods of cost com-parisons limit opportunity for subgroup analyses.

Protected by copyright, including for uses related to text difficult or inadvisable.<sup>2</sup> The progressive evolution of AF is underscored by electrical, structural and anatomical remodelling of the atria which causes functional impairment atria which causes functional impairment of the heart.<sup>2 4</sup> Electrical remodelling alters ion channel expression and/or function and  $\blacksquare$ contributes to drug resistance, recurrence following cardioversion and progression to persistent AF.<sup>2</sup> Structural remodelling prestraining, ents as fibrotic separation of muscle fascicles and slowing of electrical conductance with replacement of dead cardiomyocytes and headways permanent AF.<sup>2</sup> Anatomic remodelling affects the discharge of ions and action potentials in autonomic nervous signalling, establishing a positive-feedback loop.

The absolute prevalence of AF has increased over time, showing an age-related gradient in which patients aged 85 years and over are most at risk and comprise 9%–10% **g**. of all cases.<sup>4</sup> Alongside a rise in prevalence, the number of hospitalisations of AF patients has increased and readmission accounts for a large proportion of these.<sup>5</sup> Unplanned readmissions are recognised as a safety and quality indicator in healthcare,<sup>6</sup> because they often result from failure to provide adequate care during the prior admission.<sup>7</sup> International literature consistently reports a high number of 30-day readmissions for AF patients,<sup>8-10</sup>

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including after surgical intervention.<sup>11-13</sup> Iñiguez Vázquez et al<sup>8</sup> compared readmission between non-AF and AF patients in Lugo, Spain and found AF patients were readmitted more frequently than non-AF patients. A retrospective cohort study in the USA found that 22.7% of newly diagnosed AF and 17.6% of chronic AF patients were readmitted in 30 days postdischarge,<sup>10</sup> suggesting that AF patients have been poorly managed during the index admission. Hence, identifying predictors of readmission becomes important to identify patients are high risk of readmission.

To understand resource use dedicated to managing AF patients during readmission, it is important to examine the economic impact on the healthcare system. Coyne et al examined three federally funded USA databases for costs of hospital treatment of non-valvular AF.<sup>14</sup> The results showed the overall national cost of treatment was US\$6.65 billion, and 44% (US\$2.93 billion) was specifically dedicated to hospitalisations where AF was the primary diagnosis.<sup>14</sup> Based on prospective data collection from the Euro Heart Survey enrolling 5333 patients, inpatient care and interventional procedures consumed >70% of total annual costs and were main drivers of increase costs.<sup>15</sup> At a patient level, annual direct costs were estimated at approximately US\$10100 to US\$14200 in the USA and €450 to €3000 in Western Europe per patient per year.<sup>16</sup> Therefore, the economic burden of AF-related readmissions is significant at the national and patient level, and when taken into consideration alongside the number of readmissions, AF patients are clearly in need of improved management.

Readmissions have become a growing focus of decision and policy makers with various funding models developed around the world to provide incentive to reduce readmission. In the UK, a non-payment policy introduced in 2011 ensures readmission above hospital-specific readmission rates are not funded.<sup>6</sup> The Hospital Readmission Risk Reduction Program for US Medicare patients penalises hospitals at a fixed percentage if their readmission rate is higher than the risk-adjusted benchmark.<sup>6</sup> In Australia, a series of three funding options designed to financially penalise readmissions will be trialled for 2 years from July 2019 while providing incentive to improve care during the index or prior admission.<sup>6</sup>

The evolving burden AF places on healthcare systems currently requires significant hospital and economic resources and the rising prevalence of AF indicates this will continue. Readmissions in particular consume a large portion of healthcare resources while being central to policy reform. Accordingly, this systematic review protocol will aim to examine the costs of readmissions following an index admission where AF has been the primary diagnosis.

#### **METHODS AND ANALYSIS**

This systematic review protocol is registered with PROS-PERO and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols checklist<sup>17</sup> presented as online supplementary file 1. The systematic review will be conducted based on a modification of the Cochrane Handbook for Systematic Reviews of Interventions,<sup>18</sup> given the topic of review is costs, rather than intervention. The completed review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>19</sup>

### **Population**

The systematic review will focus on the costs of readmis-sions to hospital 30 days following discharge at index admis-sion where AF has been the primary diagnosis. Reporting of a primary diagnosis of AF at index admission should be in the section identifying the population of eligible texts. 8 Primary diagnoses are commonly defined using the International Statistical Classification of Diseases and Related Health Problems 9th or 10th revision codes. The population will be limited to patients aged 18 years and over. If including patient age has not been reported or the primary diagnosis for the index admission was not specified or could not be discerned, the study will be excluded.

not be discerned, the study will be excluded.

Study design
Studies will be included if costs associated with hospital se re readmission within 30 days of discharge where AF was the primary diagnosis at index admission have been reported. Peer-reviewed articles will be included unless the full text cannot be obtained. Any letters, conference papers, abstracts, editorials, reviews, theory papers, theses or dissertations will be excluded.

The search strategy has been developed by the authors with assistance from a research search search search search strategies for all databases are included in online supplementary file 2. A second independent librarian will review the final search strategy against the Peer Review of Electronic Search Strategy checklist.<sup>20</sup> The search strategy aims to retrieve published cost analyses written in English (figure 1) from all countries reporting readmission costs associated with AF patients. We will search MedLine (via Ovid), Cumulative Index to Nursing and S Allied Health Literature, Cochrane Library and Scopus databases with no limit on publication date to capture all cost analyses published from inception to 2019. In addition to synonymous textwords, 'readmission', 'atrial fibrillation' and 'cost' will be key Medical Subject Headings used to capture the study population and key outcomes of interest. To identify additional papers, Google Scholar and hand searches of reference lists will be used. Further, the Australia and New Zealand Clinical Trials Register and ClinicalTrials.gov websites will be searched for clinical trials examining readmission costs in parallel with published results in peer-reviewed journals.

### Study selection

Citations retrieved from the search will be managed in EndNote and duplicates removed. Two independent

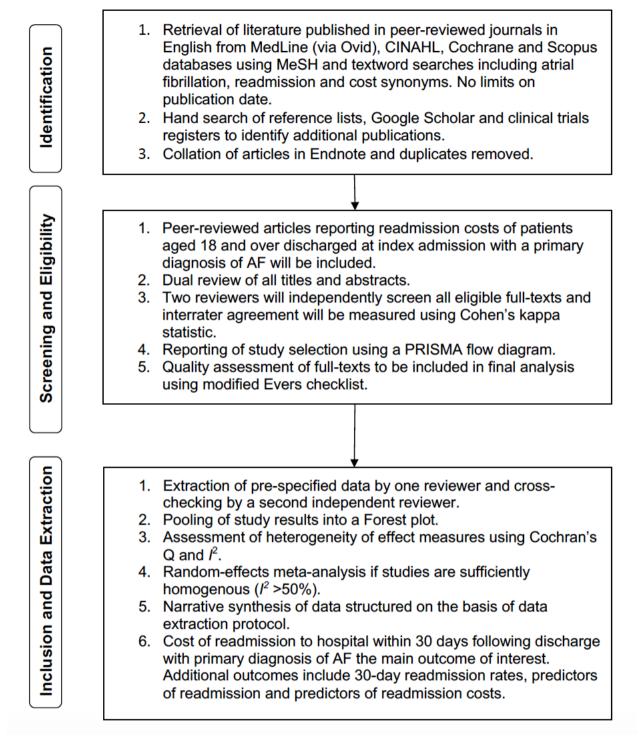


Figure 1 Schematic of the key systematic review processes. AF, atrial fibrillation; CINAHL, Cumulative Index to Nursing and Allied Health Literature; MeSH, Medical Subject Heading; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

reviewers will screen all titles and abstracts for eligibility against the inclusion/exclusion criteria. Two reviewers will independently screen all eligible full texts. Interrater agreement will be calculated using Cohen's kappa statistic.<sup>21</sup> Agreement of >80% (strong level of agreement) is desirable.<sup>21 22</sup> Selection discrepancies will be resolved through discussion and independent assessment by a

third reviewer, if needed. This process will be reported using a PRISMA flow diagram.

### Quality assessment

A modified Evers checklist<sup>23</sup> will be used to assess methodological validity of full-text studies selected for inclusion. Because no standardised or validated checklist specifically for cost studies exists, modification of the Evers checklist<sup>23</sup> is required to reflect that the studies retrieved are not full economic evaluations. The modified Evers checklist is presented in online supplementary file 3.

#### **Data extraction**

Data will be extracted by one reviewer and cross-checked independently by a second reviewer. Disagreements will be resolved by discussion and consultation with a third reviewer, if required. Data items to extract will be relevant to the review question to facilitate a narrative synthesis. These items include time period of study, study setting (eg, country, primary care) or source of data (eg, database used); study design; number of eligible patients; causes of readmission captured (eg, all-cause, AF-relayed) and how they were identified (eg. International Statistical Classification of Diseases and Related Health Problems, 10th Revision code); subgroups compared (eg, all-cause vs AF-related readmission, primary vs secondary diagnosis of AF); reporting of costs (eg, currency and year, conversion rates); cost components/costs included; statistical analysis; number of readmissions within 30 days; predictors of readmission identified; predictors of costs; overall cost results. Cost results will be inflated to a common currency and currency year using national or international Consumer Price Index inflation indices where appropriate.

#### **Outcomes**

The main outcome of interest is the cost of readmission to hospital within 30 days following discharge where AF was the primary diagnosis at index admission. This will include relevant monetary values. Cost comparisons may be different between papers, for example, measured between the index admission versus readmission or between consecutive readmissions. Additional outcomes include 30-day readmission rate, predictors of readmission and predictors of readmission costs if reported.

#### **Data analysis**

If possible, data will be pooled and reported in a Forest plot to visually summarise the results of each study. Heterogeneity of effect measures will be assessed using Cochran's Q test and quantified using the  $I^2$  statistic. An  $I^2$  value of >50% will be considered to show substantial heterogeneity as differences between study results are beyond those attributable to chance alone.<sup>24</sup> If studies are sufficiently homogenous, we will apply a random-effects model to better deal with different effect sizes between studies. Cost data collected from specific jurisdictions is considered the best resource to assist in decision-making regarding resource allocation in the local context.<sup>25</sup> Therefore, grouping studies based on income level, for example, will maintain comparability. However, we anticipate meta-analysis may not be possible due to a small number of eligible studies and the sensitivity of cost data to specific settings which limits transferability of cost estimates.<sup>26</sup>

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