Impact of health literacy and its interventions on health outcomes in those with atrial fibrillation: a systematic review protocol

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ABSTRACT
Introduction Atrial fibrillation (AF) is associated with increased risk of stroke, heart failure and death. Health literacy, an aspect that falls within precision health, has been recognised as an important factor. We will be focusing on the impact of these interventions specifically to AF and its health outcomes.

Methods and analysis This protocol is informed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocols. The results will be reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses to determine the impacts of health literacy interventions on AF outcomes. Searches will be carried out on databases including MEDLINE, EMBASE, Web of Science, CINAHL, Embcare, Cochran Library and Google Scholar. Citations will be collected via Endnote 20, then into Covidence for duplicate removal, and article screening. Extraction will occur using a standardised extraction tool and studies will be synthesised using best evidence synthesis. Downs and Black’s checklist will be used for risk of bias and assessment of overall quality of evidence will use the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Ethics and dissemination Approval from human research ethics committee is not required. Dissemination will occur in peer-reviewed journals and conference presentations.

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STRENGTHS AND LIMITATIONS OF THIS STUDY
⇒ This will be the first review to operationalise health literacy interventions in people with atrial fibrillation.
⇒ The protocol for this systematic review and meta-analysis follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.
⇒ This systematic review will use the Downs and Black checklist for quality appraisal and the Grading of Recommendations, Assessment, Development and Evaluation recommendations for certainty of evidence.
⇒ The meta-analysis will provide a synthesis of the evidence of health literacy interventions consistent with (a) knowledge, (b) action and (c) health outcomes.
⇒ Different study designs and definitions of health literacy interventions as well as varied outcomes may limit the ability the extent of comparative analysis.

INTRODUCTION
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and represents significant morbidity and mortality worldwide.1 The worldwide prevalence of AF is estimated at 0.51% of population and projected to increase further.2 In addition to an increased risk of stroke, heart failure and all-cause death, AF continues to contribute to the growing burden on the healthcare system and its resources.1

Health literacy plays a critical role within a patient’s healthcare and quality of life, and improving it has been a recognised goal by the WHO.3,4 Health literacy has been defined according to three types: functional health literacy, interactive health literacy and critical health literacy.5 It involves people’s knowledge and interactions with health information via four dimensions: accessing, understanding, appraising and applying.6 Health literacy can be considered as an aspect of ‘precision health’, which involves the processes of lifetime monitoring and collection of health data, analysis of collected data and subsequent informed, personalised decision-making and interventions.7–10 A recent scoping review9 identified nine categories of data that can be collected: sociodemographic, anthropometric, clinical, genomic, perspective, behavioural, psychological, nutritional and socioenvironmental data.

Currently, a range of definitions and terms have been used in the health literacy literature, with different aims and contexts, which has created uncertainty and a lack of clarity as
to what these constitute. This is particularly pronounced when considering health literacy interventions as a core component of precision health initiatives. Our systematic review and meta-analysis aims to evaluate the effectiveness of health literacy interventions for people with AF. In doing so, we aim to synthesise the current literature to identify the impacts of health literacy interventions on (a) health literacy and knowledge; (b) patient action and behaviour change arising from health literacy and knowledge and (c) health outcomes (eg, quality of life, hospitalisations and/or morbidity/mortality) as a consequence to action taken arising from improvements in health literacy.

**Objectives**
This systematic review will explore precision health, in particular, the impact of health literacy and its interventions, on AF outcomes. Thus, the systematic review will endeavour to answer the following:
1. How do health literacy interventions generate additional benefits for precision health initiatives?
2. What questionnaires and tools are currently available and have been used to assess health literacy interventions generally and in AF?
3. How effective are health literacy interventions in improving both knowledge and subsequent beneficial actions for AF?
4. How effective are health literacy interventions that improve knowledge and subsequent beneficial actions in resulting in improved health outcomes such as quality of life, hospitalisations and reduced morbidity/mortality?

**METHODS**

**Guidelines and registration**
This protocol for our systematic review was done with guidance and adherence to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 guidelines, Cochrane guidelines and other reviews already conducted in this area. Registration was submitted to the International Prospective Register of Systematic Reviews, an international database for systematic reviews prospectively registered by the Centre for Reviews and Dissemination of the University of York (https://www.crd.york.ac.uk/prospero). This occurred on 29 April 2022 and was last updated on 10 May 2022.

**Patient and public involvement**
None

**Eligibility criteria**
Selection of studies will consider the following.

**Study designs**
Randomised control trials and observational studies will be included. Conference presentations, thesis, secondary research (review articles) will be excluded.

**Population**
Included studies that have enrolled individuals with a primary diagnosis of non-valvular AF. Any age, baseline physical activity or different backgrounds will be considered, as well as those in various settings, such as hospital-based, hospital outpatient clinics, private clinics, primary care, research-based specialist university clinics. No restrictions will be placed on duration of symptoms or time since diagnosis. Studies in which participants are diagnosed with valvular AF will be excluded.

**Interventions**
This review will consider studies that evaluate interventions and initiatives focused on health literacy that are aimed at improving any of the following (a) knowledge and/or literacy, (b) patient action and behaviour change and (c) health outcomes, including quality of life, hospitalisations, morbidity/mortality.

Interventions may endeavour to improve any dimension, or similar aspect of health literacy, such as a patient’s ability to read, write, approach numeracy, communicate and/or use electronic technology. Interventions considered can address health literacy in any domain or setting, and may be in the form of different medium. This can involve face-to-face mediums, such as verbal communication, written communication, visual aids and supportive systems. We also acknowledge the growing usage of remote mediums and digital initiatives, such as online resources, web-based resources, social media, and mobile applications.

Such intervention fits within Gambhir *et al*’s model of precision health within the ‘Integrated health portal’, allowing for learning and adaptation that feeds back into the rest of the model.

**Comparator**
In addition to usual clinical care, we will be considering behavioural data, sociodemographic data and clinical data as part of our comparators. Viana *et al*’s scoping review on precision health research showed that these were the top three types of data used for precision health (behavioural (48%), sociodemographic (44%), clinical (43.6%)).

**Outcomes**
Three categories of outcomes will be collected: outcomes concerned with the knowledge and understanding of AF following intervention; outcomes measuring any resulting patient action following intervention; and finally, outcomes measuring health, wellness and quality of life. Due to the broad nature of measures for outcomes, the following is not an exhaustive list. Any additional outcomes suitable for the three categories listed above will be considered and agreed on by all researchers involved.

Examples of outcomes include:
- Those related to knowledge and understanding.
  - Test of Functional Health Literacy in Adults (TOFHLA) and short-TOFHLA (s-TOFHLA).
- Rapid Estimate of Adult Literacy in Medicine (REALM)\textsuperscript{20}/REALM-Short Form (REALM-SF).\textsuperscript{21}
- Medical achievement reading test.\textsuperscript{22}
- Those related to action.
- Self-reported measures.
- Those related to health, wellness, and quality of life.
- All-cause mortality.
- Hospitalisations and rehospitalisation rates.
- Heart function.
- Quality of life.\textsuperscript{23}
-Generic instruments: Medical Outcome Study Short-Form 36,\textsuperscript{24} 12-Item Short-Form Health Survey,\textsuperscript{25} EuroQol 5-Dimensional.\textsuperscript{26,27}
- AF-specific instruments: Atrial Fibrillation Effect on Quality-of-Life,\textsuperscript{28} AF-QOL-18,\textsuperscript{29} QLAF questionnaire,\textsuperscript{30} Atrial Fibrillation Quality of Life Questionnaire.\textsuperscript{31}
- Symptom scales.\textsuperscript{23}
- Physical activity: Internal Physical Activity Questionnaire,\textsuperscript{32} Lawton-Brody iADL scale,\textsuperscript{33} Katz-ADL scale.\textsuperscript{34}
- Self-reported measures.
- Ability to perform activities of daily life (ADLs).
- Work and productivity.

**Information sources**

Searches will be carried out on MEDLINE (via PubMed platform), EMBASE (via OVID platform), Web of Science (via Clarivate platform), CINAHL (via EBSCOhost platform), Emcare (via OVID platform), Cochrane Library and Google Scholar.\textsuperscript{35}

Additionally, to ensure completeness, grey literature\textsuperscript{36} will be included and citation searching of included articles will be undertaken. Grey literature, or evidence not published in commercial publications can include academic papers, such as theses/dissertations, research and/or governmental reports, conference papers. We intend to search for such literature through resources such as OpenGrey, Scopus and Proquest Digital Dissertations and Digital Dissertations and Conference Papers Index. We also aim to hand-search through relevant conference proceedings and abstracts such as the Cardiac Society of Australia and New Zealand, Asia Pacific Heart Rhythm Society and Heart Rhythm Society conferences.

**Search strategy**

The draft search strategy was developed initially using the PubMed platform, Medical Subject Headings and key phrases identified during preliminary searches. These were initially performed in January 2022 and then updated in April 2022 and assisted in refining search terms within the (Population, Intervention, Comparator and Outcomes) PICO structure. Phrases specific to the intervention, comparator and outcome components were developed by first identifying core key phrases relevant to our questions, then searching PubMed using these phrases and expanding on synonyms using existing articles and search strategies. We based our search on previous literature including Viana et al.'s\textsuperscript{9} review of precision health. The search will be limited to 2012 onwards as well as English language to minimise risk to including studies published before the research field was mature.

The draft search strategy was reviewed by a librarian specialising in medicine and was also reviewed by the research team. A complete search strategy, which has been adapted to syntax and subject headings of other databases, is included in online supplemental appendix 1.

Citations from databases will be imported to EndNote 20 (Clarivate Analytics) for article collection, then to Covidence for the remaining processes. Duplicates will be removed electronically via Covidence and checked manually. Eligibility for inclusion will involve two independent reviewers, and first will be done based on title and abstract screening, followed by full-text review. At both stages, reviewers will be blinded to each other’s decisions until discussions occur.

Disagreements between reviewers where one reviewer has recommended a study for inclusion based on full-text review whereas the other has not will automatically be escalated in Covidence. Instances where the third adjudicating reviewer decides yes will be included, whereas those stated no will be excluded. In cases where the third reviewer is uncertain these will be discussed as a group.

**Data extraction**

Data will be extracted from studies by two independent reviewers using piloting forms and a standardised extraction tool. Extraction will be structured by the following domains:

1. Article characteristics, which include title, name of first author, publication year, country of study, study type.
2. Participant details, which include number of participants, demographics, characteristics, study location, recruitment procedures, inclusion and exclusion criteria.
3. Methods, which include identification of AF, definition and application of precision health initiatives, exposure measurement.
4. Outcomes, which include measurement tool, timing of measurements, method of aggregation, summary data.

Authors of papers will be contacted to request missing or additional data, where required.

**Data synthesis**

Best evidence synthesis will be used. Meta-analysis of intervention (effectiveness) can be carried out; however, we will need to account for substantial heterogeneity between and within included studies. Specifically for our review, outcomes will need to be compared according to the specific health literacy intervention carried out. The process for meta-analysis will be informed following data extraction, based on the assumptions of homogeneity.

If homogeneity is sufficient between groups within these categories, a consensus will be reached between all authors regarding the inclusion within the meta-analysis either as a large group or several subgroups. If eligible studies are clearly homogenous, studies will be allocated to appropriate categories, a consensus will be reached between all authors regarding the inclusion within the meta-analysis either as a large group or several subgroups. If eligible studies are clearly homogenous, studies will be allocated to appropriate categories, a consensus will be reached between all authors regarding the inclusion within the meta-analysis either as a large group or several subgroups. If eligible studies are clearly homogenous, studies will be allocated to appropriate
subgroups for analysis. This process will be done by each reviewer independently, determining the factors that would allow for the most accurate comparisons to be made.

In the case of substantial heterogeneity between methods and outcomes and/or instances where there are not sufficient number of outcomes that can be analysed (eg, according to the three questions of (a) knowledge and/or literacy, (b) patient action and behaviour change and (c) health outcomes, including quality of life, hospitalisations, morbidity/mortality) we will carry out the best evidence synthesis in the place of meta-analysis.

To assess the impact of heterogeneity across studies, a statistic test of inconsistency will be carried out, returning $I^2$ which will be reported as a percentage. The Cochrane Handbook for Systematic Reviews of Interventions provides a suggested guide for interpretation of $I^2$, group percentages into 0%–40%, 30%–60%, 50%–90%, 75%–100% to potentially mean no importance, moderate, substantial and considerable heterogeneity, respectively. If present, heterogeneity will be explored, and potential options, such as excluding studies with obvious outlying results, will be explored.

Strategies to combat potential publication data will include searches of unpublished studies, contact authors in their respective field and including grey literature. Further statistical tests, such as the Begg and Mazumbar’s rank correlation test and Egger’s linear regression model, may be applied to each category and overall analyses. On publication bias being detected, Duval and Tweedie’s trim and fill correction may be applied and the resultant effect sizes and 95% CIs examined in further detail.

The Downs and Black’s 27-item checklist can be used to assess methodological quality of randomised and non-randomised trials. It provides: an overall score for study quality, and a profile of scores for the quality of reporting internal validity, power and external validity.

The data generated from this SR/MA such as Downs and Black’s rating of quality and/or risk of bias as well as data extraction will be available as supplementary material along with the final report/publication.

A Summary of Findings (SoF) will be created using GRADEpro GDT. The SoF will present the following information where appropriate: absolute risks for the treatment and control, estimates of relative risk and a ranking of the quality of the evidence based on the risk of bias, directness, heterogeneity, precision and risk of publication bias of the review results. The Grading of Recommendations, Assessment, Development and Evaluation approach will be used to assess quality of evidence.

Clinical implications

This research aims to comprehensively synthesise through systematic review and meta-analysis the existing published and grey literature of health literacy interventions as a component of precision health to improve (a) knowledge and literacy, (b) patient action and behaviour change and (c) health outcomes. We anticipate this information being used to inform the assessment and future implementation of health literacy interventions not only improving the use of such terms in research and practice but having impact on patient outcomes, cost-effectiveness and accessibility.

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Contributors All authors (TL, DK, KBF, NO, MAB, RM) have contributed to the focus of this systematic review topic and revisions associated with this protocol manuscript. Specifically, DK, TL and RM were responsible for the initial conceptualisation of this work. TL, DK, RM led the planning and design, and all authors were involved in the conduct and reporting of this manuscript. All authors (TL, DK, KBF, NO, MAB, RM) made substantial contributions to the drafting and critical revision of the work and all authors (TL, DK, KBF, NO, MAB, RM) approved the final manuscript.

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