Topic Brief: Atrial Fibrillation Ablation

Date: 9/19/2022
Nomination Number: 981

Purpose: This document summarizes the information addressing a nomination submitted on May 9, 2022, through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: The nominator of this topic represents a healthcare delivery organization and is interested in the harms and benefits of catheter ablation for atrial fibrillation (AF), particularly potential overuse in selected groups (those with ejection fraction greater than 35%). They plan to generate a clinical algorithm for optimal use of AF ablation with the findings of the proposed evidence review.

Program Decision: While the nomination met selection criteria, the EPC Program did not select this topic for a new systematic review.

Key Findings

- We found multiple systematic reviews that address the topic, but they did not assess some subgroups of interest
- We identified 39 publications that address the nomination questions, and also focus on important subgroups. However many of these publications on subgroups are related to a single study, the CABANA trial.

Background

Atrial fibrillation is the most common type of treated heart arrhythmia. With this condition, the normal beating in the upper chambers of the heart is irregular, and blood doesn't flow as well as it should through the heart. It may happen in brief episodes (paroxysmal atrial fibrillation) or it may be permanent (persistent atrial fibrillation). Atrial fibrillation can lead to increased risk of stroke, heart failure, and chronic fatigue. It is estimated that 12.1 million people in the United States will have atrial fibrillation in 2030.[1]

Atrial fibrillation can be treated with medication to control the heart rhythm or rate; or a procedure called catheter ablation to control the heart's rhythm and rate. Catheter ablation is a non-surgical procedure that can be used when medication is not effective. The goal is to reduce the frequency and duration of AF episodes as well as to reduce AF symptoms.

Factors that might affect the effectiveness treatment include type of atrial fibrillation, heart failure, age, hypertension, valvular heart disease, and chronic obstructive pulmonary disease.

[1] https://www.cdc.gov/heartdisease/atrial_fibrillation.htm

Understanding differences in effectiveness for subgroups would inform decision-making around treatment.

A 2019 joint guideline from the American Heart Association, American College of Cardiology, and Heart Rhythm Society on atrial fibrillation states that AF catheter ablation may be reasonable in selected patients with symptomatic atrial fibrillation and heart failure with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for heart failure. It does not provide guidance for other subgroups.[1]

The nominator represents a healthcare delivery organization of 30 physician groups in the US. He voiced concerns about the potential for overuse of catheter ablation for those who may not have failed medical therapy and those with heart failure and preserved ejection fraction. He would like a review of the evidence to understand the most appropriate candidates who are likely to benefit from the catheter ablation. His organization is building a clinical algorithm, and they plan to incorporate findings from an AHRQ review into the algorithm, when available.

AHRQ has reached out to the American Heart Association and confirmed that they are interested in using the proposed review to inform the update of their 2019 guideline on management of atrial fibrillation.

Scope

1. What are the effectiveness and harms of catheter ablation for the treatment of atrial fibrillation (AF) in different patient subpopulations (e.g., variation in effectiveness based on age, sex, and comorbidities, such as obesity, sleep apnea, heart failure with reduced ejection fraction, hypertension, alcohol use disorder, etc.)?
2. What is the durability of therapeutic effect of catheter ablation for the treatment of AF?
3. What are the AF-related healthcare utilization and costs (from pre-ablation to post-ablation) among patients receiving ablation treatment?

Contextual question: What is the frequency of overutilization of catheter ablation for the treatment of AF (e.g., what the frequency of catheter ablation for the treatment of AF that is discordant with the existing AHA/ACC guideline recommendations[1]?

PICOs	KQs 1-2	KQ 3
Population	Adults (aged 18 years and older) with a diagnosis of AF, including paroxysmal, persistent, and long-standing AF with and without concomitant heart failure (stratified by age, sex, and comorbidities)	Adults (aged 18 years and older) with a diagnosis of AF, including paroxysmal, persistent, and long-standing AF, with and without concomitant heart failure (stratified by age, sex, and comorbidities)
Intervention	Catheter ablation	Catheter ablation
Comparator	Medical treatment with either rate control medications (e.g., beta blockers) or antiarrhythmic drugs (e.g., amiodarone)	Medical treatment with either rate control medications (e.g., beta blockers) or antiarrhythmic drugs (e.g., amiodarone)
Outcomes	• All-cause mortality • All-cause hospitalization • Heart failure related hospitalization • AF recurrence	Healthcare costs associated with performing a catheter ablation procedure vs costs associated with pharmacologic treatment

	• Incidence of thromboembolic events (DVT or PE) • Incidence of thromboembolic stroke • Frequency of anticoagulant use • Bleeding frequency secondary to anticoagulant use • Patient quality of life • Harms related to the ablation procedure (e.g., cardiac tamponade, TIA, atrio-esophageal fistula etc)	

Abbreviations: AF= Atrial Fibrillation; DVT= Deep Venous Thrombosis; KQ= Key Question; PE = Pulmonary Embolism; TIA= Transient Ischemic Attack

Assessment Methods

See Appendix A.

Summary of Literature Findings

We identified multiple systematic reviews for all questions. Of these, we identified three systematic reviews in support of the NICE guidelines[2], that addressed all three questions. However the reviews did not address all subgroups of interest, it included CHADSVASC score and presence/absence of heart failure; and the review and economic modeling focused on paroxysmal atrial fibrillation. We identified other reviews that focused on older adults[3], people with heart failure[4-8], those with preserved ejection fraction[9-12], and catheter ablation for first-line therapy[13-21] (4 of nine reviews focused on paroxysmal atrial fibrillation, and none on people with heart failure and preserved ejection fraction). However these reviews did not address the full range of subgroups of interest. Most systematic reviews focused solely on RCTs.

We identified 38 publications in our targeted search for KQ 1-2, with some focusing on subgroups of interest. Some were multiple publications from a single study, the CABANA trial[22-28].

Four studies addressed KQ 3, with three including cost-effectiveness analysis.

While we found publications that would address subgroups of interest of the nomination, we note that most come from a single study, the CABANA trial, which may decrease enthusiasm for a new systematic review.

Key question	Systematic reviews	Study publications (July 2017-July 2022)
KQ 1 and 2: effectiveness and durability of effect	Total-19 • AHRQ, Cochrane, VA ESP-0 • SR-19[2, 5, 13, 14, 16, 18, 21, 29-40] Subgroup • Older adults-1[41] • Heart failure-5[4-8] • Heart failure with preserved ejection fraction-4[9-12] • Paroxysmal a fib-4[15, 17, 19, 20] • Ablation as first-line-9[13-21]	Total • RCT-23 publications o General[22-25, 42-47] o Atrial fibrillation type[26] o First-line[48-52] o Race[27] o Sex[28] o Heart failure[23, 46, 53-55] • Non-RCT-15 publications o General[56-62] o CAD[63] o Heart failure[54] o Older adults[64]

		○ Heart failure with preserved ejection fraction[65, 66] ○ Sex[67, 68] ○ Valvular disease[69] • Clinicaltrials ○ NCT04037397 (recruiting). Persistent AF, LVEF>40% ○ NCT04942171 (not yet recruiting). Outcome cognition, depression, anxiety ○ NCT04282850 (recruiting). Paroxysmal or persistent AF, HF with LVEF>50% ○ NCT04160000 (recruiting) HFpEF & paroxysmal or persistent AF ○ NCT04342832 (recruiting) LVEF<40% ○ NCT05364866 (recruiting). Various EF
KQ 3: Cost, resource utilization	Total AHRQ, Cochrane, VA ESP-0 SR-2[2, 70]	Total-4[60, 71-73] Clinicaltrials.gov • NCT04342832 (recruiting) LVEF<40%

KQ=key question; HFpEF=heart failure with preserved ejection fraction; LVEF=left ventricular ejection fraction

Summary of Selection Criteria Assessment

Atrial fibrillation is a common condition and there is uncertainty about patient subgroups that would benefit most. While we found publications that would address subgroups of interest of the nomination that could be included in a new systematic review, we note that most come from a single study, the CABANA trial. Potential partners include a health delivery organization and clinical professional group.

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We conducted a search for existing systematic reviews. We searched for high-quality, completed or in-process evidence reviews published in the last three years June 2019 to June 2022 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
    - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
    - EHC Program https://effectivehealthcare.ahrq.gov/
- US Department of Veterans Affairs Products publications
    - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
    - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited Medline search of primary literature published within the last five years from July 2017 through July 2022. We reviewed the entire search yield for relevance to the three nomination questions.

Ovid MEDLINE ALL <1946 to July 05, 2022>
Date searched: July 6, 2022
1 *Atrial Fibrillation/ (55737)
2 (AFib or "atrial fibrillation" or ((long-standing or paroxysmal or persistent) adj3 fibrillation)).ti,ab,kf. (85233)
3 or/1-2 (92210)
4 Catheter Ablation/ (37100)
5 ("catheter ablation" or preablation or postablation).ti,ab,kf. (17050)
6 or/4-5 (42392)

7 Adrenergic beta-Antagonists/ or Adrenergic beta-Antagonists.rn. or Anti-Arrhythmia Agents/ or Anti-Arrhythmia Agents.rn. (68116)
8 Acebutolol/ or Acecainide/ or Acetyldigitoxins/ or Acetyldigoxins/ or Adenosine/ or Ajmaline/ or Alprenolol/ or Amiodarone/ or Aprindine/ or Atenolol/ or Atropine/ or Bepridil/ or Bretylium Tosylate/ or Bunaftine/ or Bupranolol/ or Cardiac Glycosides/ or Carteolol/ or Celiprolol/ or Cymarine/ or Deslanoside/ or Digitalis Glycosides/ or Digitoxin/ or Digoxin/ or Dihydroalprenolol/ or Disopyramide/ or Dronedarone/ or Encainide/ or "Enkephalin, Ala(2)-MePhe(4)-Gly(5)"/ or Felodipine/ or Flecainide/ or Hyoscyamine/ or Lidocaine/ or Lorajmine/ or Losartan/ or Magnesium Sulfate/ or Medigoxin/ or Metipranolol/ or Metoprolol/ or Mexiletine/ or Moricizine/ or Nadolol/ or Nicorandil/ or Oxprenolol/ or Practolol/ or Prajmaline/ or Procainamide/ or Propafenone/ or Propranolol/ or Quinidine/ or Sotalol/ or Sparteine/ or Timolol/ or Tocainide/ or Verapamil/ (205043)
9 (Acebutolol or Acecainide or Acetyldigitoxins or Acetyldigoxins or Adenosine or Ajmaline or Alprenolol or Amiodarone or Aprindine or Atenolol or Atropine or Bepridil or Bretylium Tosylate or Bunaftine or Bupranolol or "Cardiac Glycosides" or Carteolol or Celiprolol or Cymarine or Deslanoside or Digitalis Glycosides or Digitoxin or Digoxin or Dihydroalprenolol or Disopyramide or Dronedarone or Encainide or "Enkephalin, Ala(2)-MePhe(4)-Gly(5)" or Felodipine or Flecainide or Hyoscyamine or Lidocaine or Lorajmine or Losartan or "Magnesium Sulfate" or Medigoxin or Metipranolol or Metoprolol or Mexiletine or Moricizine or Nadolol or Nicorandil or Oxprenolol or Practolol or Prajmaline or Procainamide or Propafenone or Propranolol or Quinidine or Sotalol or Sparteine or Timolol or Tocainide or Verapamil).ti,ab,kf,rn. (363410)
10 ("2-(2-(4-(4-nitrobenzyloxy)phenyl)ethyl)isothiourea methanesulfonate" or "3,4-dihydroxyacetophenone" or "3-methoxy-O-demethylencainide" or "4-hydroxyphenylethanol" or "5-hydroxydecanoic acid" or "5-hydroxypropafenone" or "6-methyl-2-ethyl-3-hydroxypyridine" or "AH 23848" or alinidine or allapinin or almokalant or anisodamine or azimilide or benzobarbital or berbamine or bidisomide or "BN 50739" or bretylium or bumecain or butobendin or canadine or cariporide or changrolin or cicletanine or cifenline or clofilium or "cyclopiazonic acid" or "diethylamino-ethmozine" or "digoxin-like factors" or diprafenone or dofetilide or "DuP 734" or "E 4031" or enadoline or enkephalin or ethacizine or ethylisopropylamiloride or falipamil or fenozan or fosinoprilat or "fructose-1,6-diphosphate" or gidazepam or glimepiride or heptacaine or honokiol or "HU 211" or ibutilide or indenolol or "KT 362" or landiolol or lappaconitine or lorcainide or losartan carboxylic acid or magnolol or nifekalant or nizofenone or "O-demethylencainide" or otenzepad or "PD 117302" or phenazepam or pilsicainide or pirmenol or pranolium or propisomide or recainam or rilmakalim or scoparone or sematilide or sesamodil or spiradoline or sulotroban or talinolol or tedisamil or terikalant or tertatolol or tetrahydropalmatine or thiazolidine or thymogen or tilisolol or tiracizine or "tyrosyl-arginyl-phenylalanyl-lysinamide").ti,ab,kf,rn. (37079)
11 (antiarrhythm* or anti-arrhythm* or beta- antagonist$1 or betaantagonist$1 or betablocker$1 or beta-blocker$1 or ((drug$1 or medical or medicine or pharma*) adj2 (therapy or therapies treatment$1))).ti,kf. or (rhythm* and rate and control).ti. (49797)
12 or/7-11 (459520)
13 and/3,6,12 (1996)
14 limit 13 to english language (1774)
15 limit 14 to yr="2019 -Current" (391)
16 (meta-analysis or "systematic review").pt. or (meta-analysis or metaanalysis or ((evidence or scoping or systematic or umbrella) adj3 (review or synthesis))).ti. (355088)
17 and/15-16 (34)
18 limit 14 to yr="2017 -Current" (586)
19 18 not 17 (552)

20 ("controlled clinical trial" or "randomized controlled trial").pt. or (control* or comparative or placebo or random* or trial).ti,kf. (1583933)
21 and/19-20 (138)
22 18 not (17 or 21) (414)
23 exp cohort studies/ or exp epidemiologic studies/ or exp evaluation studies as topic/ or "observational study".pt. (4003641)
24 (before-after or cohort$1 or evaluation studies or follow-up* or "interrupted time" or longitudinal or (pre adj2 post) or propensity-score or prospective$2 or retrospective$2).ti,ab,kf. (3072119)
25 or/23-24 (5272855)
26 and/22,25 (206)

EBM Reviews - Cochrane Central Register of Controlled Trials June 2022
Date searched: July 6, 2022
1 Atrial Fibrillation/ (5237)
2 (AFib or "atrial fibrillation" or ((long-standing or paroxysmal or persistent) adj3 fibrillation)).ti,ab. (13659)
3 or/1-2 (14067)
4 Catheter Ablation/ (1638)
5 ("catheter ablation" or preablation or postablation).ti,ab. (1875)
6 or/4-5 (2943)
7 Adrenergic beta-Antagonists/ or Anti-Arrhythmia Agents/ (6175)
8 Acebutolol/ or Acecainide/ or Acetyldigitoxins/ or Acetyldigoxins/ or Adenosine/ or Ajmaline/ or Alprenolol/ or Amiodarone/ or Aprindine/ or Atenolol/ or Atropine/ or Bepridil/ or Bretylium Tosylate/ or Bunaftine/ or Bupranolol/ or Cardiac Glycosides/ or Carteolol/ or Celiprolol/ or Cymarine/ or Deslanoside/ or Digitalis Glycosides/ or Digitoxin/ or Digoxin/ or Dihydroalprenolol/ or Disopyramide/ or Dronedarone/ or Encainide/ or "Enkephalin, Ala(2)-MePhe(4)-Gly(5)"/ or Felodipine/ or Flecainide/ or Hyoscyamine/ or Lidocaine/ or Lorajmine/ or Losartan/ or Magnesium Sulfate/ or Medigoxin/ or Metipranolol/ or Metoprolol/ or Mexiletine/ or Moricizine/ or Nadolol/ or Nicorandil/ or Oxprenolol/ or Practolol/ or Prajmaline/ or Procainamide/ or Propafenone/ or Propranolol/ or Quinidine/ or Sotalol/ or Sparteine/ or Timolol/ or Tocainide/ or Verapamil/ (21985)
9 (Acebutolol or Acecainide or Acetyldigitoxins or Acetyldigoxins or Adenosine or Ajmaline or Alprenolol or Amiodarone or Aprindine or Atenolol or Atropine or Bepridil or Bretylium Tosylate or Bunaftine or Bupranolol or "Cardiac Glycosides" or Carteolol or Celiprolol or Cymarine or Deslanoside or Digitalis Glycosides or Digitoxin or Digoxin or Dihydroalprenolol or Disopyramide or Dronedarone or Encainide or "Enkephalin, Ala(2)-MePhe(4)-Gly(5)" or Felodipine or Flecainide or Hyoscyamine or Lidocaine or Lorajmine or Losartan or "Magnesium Sulfate" or Medigoxin or Metipranolol or Metoprolol or Mexiletine or Moricizine or Nadolol or Nicorandil or Oxprenolol or Practolol or Prajmaline or Procainamide or Propafenone or Propranolol or Quinidine or Sotalol or Sparteine or Timolol or Tocainide or Verapamil).ti,ab. (41908)
10 ("2-(2-(4-(4-nitrobenzyloxy)phenyl)ethyl)isothiourea methanesulfonate" or "3,4-dihydroxyacetophenone" or "3-methoxy-O-demethylencainide" or "4-hydroxyphenylethanol" or "5-hydroxydecanoic acid" or "5-hydroxypropafenone" or "6-methyl-2-ethyl-3-hydroxypyridine" or "AH 23848" or alinidine or allapinin or almokalant or anisodamine or azimilide or benzobarbital or berbamine or bidisomide or "BN 50739" or bretylium or bumecain or butobendin or canadine or cariporide or changrolin or cicletanine or cifenline or clofilium or "cyclopiazonic acid" or "diethylamino-ethmozine" or "digoxin-like factors" or diprafenone or dofetilide or "DuP 734" or "E 4031" or enadoline or enkephalin or ethacizine or

ethylisopropylamiloride or falipamil or fenozan or fosinoprilat or "fructose-1,6-diphosphate" or gidazepam or glimepiride or heptacaine or honokiol or "HU 211" or ibutilide or indenolol or "KT 362" or landiolol or lappaconitine or lorcainide or losartan carboxylic acid or magnolol or nifekalant or nizofenone or "O-demethylencainide" or otenzepad or "PD 117302" or phenazepam or pilsicainide or pirmenol or pranolium or propisomide or recainam or rilmakalim or scoparone or sematilide or sesamodil or spiradoline or sulotroban or talinolol or tedisamil or terikalant or tertatolol or tetrahydropalmatine or thiazolidine or thymogen or tilisolol or tiracizine or "tyrosyl-arginyl-phenylalanyl-lysinamide").ti,ab. (2395)
11 (antiarrhythm* or anti-arrhythm* or beta- antagonist$1 or betaantagonist$1 or betablocker$1 or beta-blocker$1 or ((drug$1 or medical or medicine or pharma*) adj2 (therapy or therapies treatment$1))).ti,kf. or (rhythm* and rate and control).ti. (5675)
12 or/7-11 (53741)
13 and/3,6,12 (333)
14 limit 13 to yr="2017 -Current" (133)

Epistemonikos
Date searched: July 6, 2022
(title:((title:(AFib OR "atrial fibrillation") OR abstract:(AFib OR "atrial fibrillation")) AND (title:("catheter ablation" OR preablation OR postablation) OR abstract:("catheter ablation" OR preablation OR postablation)) AND (title:(antiarrhythm* OR anti-arrhythm* OR beta-antagonist$1 OR betaantagonist$1 OR betablocker$1 OR beta-blocker$1 OR drug$1 OR medical OR medicine OR pharma* OR (rhythm* AND rate AND control)) OR abstract:(antiarrhythm* OR anti-arrhythm* OR beta-antagonist$1 OR betaantagonist$1 OR betablocker$1 OR beta-blocker$1 OR drug$1 OR medical OR medicine OR pharma* OR (rhythm* AND rate AND control)))) OR abstract:((title:(AFib OR "atrial fibrillation") OR abstract:(AFib OR "atrial fibrillation")) AND (title:("catheter ablation" OR preablation OR postablation) OR abstract:("catheter ablation" OR preablation OR postablation)) AND (title:(antiarrhythm* OR anti-arrhythm* OR beta-antagonist$1 OR betaantagonist$1 OR betablocker$1 OR beta-blocker$1 OR drug$1 OR medical OR medicine OR pharma* OR (rhythm* AND rate AND control)) OR abstract:(antiarrhythm* OR anti-arrhythm* OR beta-antagonist$1 OR betaantagonist$1 OR betablocker$1 OR beta-blocker$1 OR drug$1 OR medical OR medicine OR pharma* OR (rhythm* AND rate AND control))))) (79)

PROSPERO
Date searched: July 6, 2022
(AFib OR "atrial fibrillation") AND ("catheter ablation" OR preablation OR postablation)AND (antiarrhythm* OR anti-arrhythm* OR beta-antagonist* OR betaantagonist* OR betablocker* OR beta-blocker* OR drug* OR medical OR medicine OR pharma* OR (rhythm* AND rate AND control)) AND (Intervention OR Systematic Review OR Meta-Analysis OR IPD OR PMA OR Network meta-analysis OR Review of reviews OR Cost effectiveness):RT WHERE CD FROM 06/07/2019 TO 06/07/2022 (106)

ClinicalTrials.gov
Date searched: July 6, 2022
AREA[ConditionSearch] Atrial Fibrillation AND AREA[InterventionSearch] ((ablation OR preablation OR postablation) AND (antiarrhythmia OR betaantagonist OR betablocker OR drug OR medical OR medicine OR pharmacotherapy or pharmacological)) AND AREA[StudyFirstPostDate] EXPAND[Term] RANGE[07/06/2017, 07/06/2022] (92)

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes. Treatment for atrial fibrillation is available in the US.
1b. Is the nomination a request for an evidence report?	The nominator is interested in guidance to assist in healthcare decision-making. Such guidance would ideally be supported by an evidence review.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes. The nominator is interested in effectiveness and harms of treatment.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	It is estimated that 12.1 million people in the United States will have AFib in 2030. In 2019, AFib was mentioned on 183,321 death certificates and was the underlying cause of death in 26,535 of those deaths.[2]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	More than 454,000 hospitalizations with AFib as the primary diagnosis happen each year in the United States.[2]
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes. The nominator is interested in both benefits and harms, especially for important subgroups
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes. National AF cost is estimated to range from $6.0 to $26.0 billion[74].
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	We identified multiple systematic reviews addressing all three questions, included high-quality reviews developed to inform NICE guidance. These reviews however did not address the range of subgroups of interest to the nominator including race/ethnicity, sex, and other comorbidities. In addition the most recent systematic reviews do not include the latest findings from the CABANA study. The most recent search dates for reviews published in 2022 was January 2022. Publications about the CABANA trial have been published since.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	The 2019 ACC/AHA/HRS joint guideline recommends: AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF[1]. It does not provide guidance for other subgroups.

[2] https://www.cdc.gov/heartdisease/atrial_fibrillation.htm

4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	We identified 43 publications in our targeted scan. 39 address KQ 1 and 2; 4 address KQ 3. Subgroups include: older age, race, sex, heart failure, heart failure with preserved ejection fraction, and type of atrial fibrillation. The size of the review is estimated medium.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes. Stakeholders, including the American Heart Association, are interested in optimizing treatments for patient subgroups.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	The nominator is interested in incorporating the evidence into a clinical algorithm, which would lead to implementation of the evidence.