Effective Health Care

Interventional Management of Atrial Fibrillation

Results of Topic Selection Process & Next Steps

This nomination was submitted by the American Heart Association (AHA) and the American College of Cardiology (ACC). The nominators are interested in an update to the 2013 AHRQ evidence review on treatments for atrial fibrillation. This includes benefits and harms of procedural, pharmacologic, and nonpharmacological interventions for rate control and rhythm control. The AHA and ACC plan to use an AHRQ evidence review to update relevant portions of the 2014 AHA/ACC/HRS guidelines for managing patients with atrial fibrillation.

Due to limited program resources, the program will not develop a review at this time. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Interventional Management of Atrial Fibrillation

Topic #: 0699

Nomination Date: 07/26/2016

Topic Brief Date: 02/17/2017

Authors:
Mark Helfand
Robin Paynter

Conflict of Interest: After starting the topic, we identified a potential conflict of interest with the initial investigator for this report. At that point, we reassigned the topic to Dr. Helfand and Robin Paynter, who have no conflict of interests pertinent to the topic.

Summary of Key Findings:

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review on this topic would not be duplicative of an existing product.
    - Although we identified 30 evidence reviews published between 2012 and 2016, no review, or combination of a few reviews, offered a comprehensive examination of procedures to treat atrial fibrillation. A 2015 AHRQ technology assessment report reviewed studies of catheter ablation for atrial fibrillation. While its main topic was medical therapy vs. ablation, one question addressed cryoablation versus radiofrequency catheter ablation.
- Impact: The nomination has high impact potential. The standard of care may become unclear. The American Academy of Family Physicians (AAFP) is creating evidence-based guidelines on pharmacologic treatments for AF, but not updating the procedural treatments for AF. This means there will be up-to-date guidelines for one course of treatment, but not another, leaving the standard of care on uneven ground. Once the AAFP published updated guidelines on pharmacologic treatments, there

may be practice variation due to the up-to-date guidelines on one course of treatment, and outdated guidelines on procedural treatment.

- Feasibility: An AHRQ evidence review is feasible at this time.
    - *Size/scope of review:* We found nine studies about atrioventrical node ablation and pacemakers for rate control (KQ1) and 22 studies that examine electrical cardioversion as a treatment for atrial fibrillation (KQ 2). In Medline and other searches, we identified 28 studies concerning procedures for rhythm control including AF ablation by pulmonary vein isolation, open surgical procedures, minimally invasive procedures, transcatheter procedures, surgical Maze procedure, and cardiac resynchronization therapy. Several of these studies include subgroup analyses, such as stratification by gender, comorbidities, age, etc.
    - *Clinicaltrials.gov:* We identified 18 clinical trials across all three key questions.
- Value: This topic has high value potential. The American College of Cardiology and the American Heart Association have partnered to create joint guidelines for the procedural treatment of atrial fibrillation.

Table of Contents

Introduction ..... 1 "
Methods ..... 4 "
Appropriateness and Importance ..... 4 "
Desirability of New Review/Duplication ..... 4 "
Impact of a New Evidence Review ..... 4 "
Feasibility of New Evidence Review ..... 4 "
Value ..... 4 "
Compilation of Findings ..... 4 "
Results ..... 4 "
Appropriateness and Importance ..... 5 "
Desirability of New Review/Duplication ..... 5 "
Impact of a New Evidence Review ..... 5 "
Feasibility of a New Evidence Review ..... 5 "
Value ..... 6 "
Summary of Findings ..... 7 "
References ..... 8 "
Appendices ..... 15 "
Appendix A. Selection Criteria Summary ..... A-1 "
Appendix B. Search Strategy & Results (Feasibility) ..... B-1 "

Introduction

Atrial Fibrillation (A-Fib or AF) is the most common cardiac arrhythmia. In 2010, it was estimated that approximately 33.5 million people around the world suffered from A-Fib.[1] A-Fib occurs when the heart's upper chambers (atria) beat out of coordination with the lower chambers (ventricles).[2] The goal of treating this irregularity is to control how many times per minute the ventricles contract (rate control) and to restore a normal heart rhythm (rhythm control).

Topic nomination 0699 was received on July 26, 2016. It was nominated by the American Heart Association (AHA) and American College of Cardiology (ACC). While the nominator initially requested a full update of the 2013 AHRQ review examining treatments (pharmacologic and nonpharmacological) for atrial fibrillation, we narrowed the scope to focus on procedural interventions, which were of greatest relevance to cardiologists and were areas of uncertainty in the prior AHRQ review. The questions for this nomination are:

Key Question 1. What are the comparative safety and effectiveness of procedural rate-control therapies in patients with AF who have failed initial pharmacotherapy? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?

Key Question 2. What are the comparative safety and effectiveness of electrical cardioversion compared to antiarrhythmic agents for conversion of AF to sinus rhythm? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?

Key Question 3. What are the comparative safety and effectiveness of newer procedural rhythm-control therapies (either separately or in combination with each other)?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, and outcomes (PICOs) of interest. See Table 1.

Table 1. Key Questions and PICOs

Key Question	1. What are the comparative safety and effectiveness of procedural rate control therapies in patients with AF who have failed initial pharmacotherapy? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?	2. What are the comparative safety and effectiveness of **electrical cardioversion** compared to antiarrhythmic agents for conversion of AF to sinus rhythm? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?	3. What are the comparative safety and effectiveness of newer **procedural rhythm-control therapies** (either separately or in combination with each other)?
Population	• Adults (age > 18 years) with AF (includes atrial flutter): ○ Including paroxysmal AF (recurrent episodes that self-terminate in less than 7 days), persistent AF (recurrent episodes that last more than 7 days), and permanent AF (an ongoing long-term episode) ○ Excluding patients with known reversible causes of AF (including but not limited to postoperative, post-myocardial infarction, hyperthyroidism) • Specific populations of interest include: ○ Patients stratified by age (≤40, 41–64, 65–74, 75–84, 85+) ○ Patients with different types of AF (paroxysmal, persistent, or permanent) ○ Patients with specific comorbidities (heart failure, coronary artery disease, kidney disease, hypertrophic cardiomyopathy, thyroid disease, or pulmonary disease) ○ Patients who have previously failed a previous rate-control or rhythm-control pharmacological therapeutic strategy ○ Women ○ Patients with an enlarged left atrium ○ Patients at high risk for stroke and bleeding events (e.g., patients with diabetes, heart failure, and hypertension) ○ Patients stratified by race/ethnicity	• Adults (age > 18 years) with AF (includes atrial flutter): ○ Including paroxysmal AF (recurrent episodes that self-terminate in less than 7 days), persistent AF (recurrent episodes that last more than 7 days), and permanent AF (an ongoing long-term episode) ○ Excluding patients with known reversible causes of AF (including but not limited to postoperative, post-myocardial infarction, hyperthyroidism) • Specific populations of interest include: ○ Patients stratified by age (≤40, 41–64, 65–74, 75–84, 85+) ○ Patients with different types of AF (paroxysmal, persistent, or permanent) ○ Patients with specific comorbidities (heart failure, coronary artery disease, kidney disease, hypertrophic cardiomyopathy, thyroid disease, or pulmonary disease) ○ Patients who have previously failed a previous rate-control or rhythm-control pharmacological therapeutic strategy ○ Women ○ Patients with an enlarged left atrium ○ Patients at high risk for stroke and bleeding events (e.g., patients with diabetes, heart failure, and hypertension) ○ Patients stratified by race/ethnicity	• Adults (age > 18 years) with AF (includes atrial flutter): ○ Including paroxysmal AF (recurrent episodes that self-terminate in less than 7 days), persistent AF (recurrent episodes that last more than 7 days), and permanent AF (an ongoing long-term episode) ○ Excluding patients with known reversible causes of AF (including but not limited to postoperative, post-myocardial infarction, hyperthyroidism) • Specific populations of interest include: ○ Patients stratified by age (≤40, 41–64, 65–74, 75–84, 85+) ○ Patients with different types of AF (paroxysmal, persistent, or permanent) ○ Patients with specific comorbidities (heart failure, coronary artery disease, kidney disease, hypertrophic cardiomyopathy, thyroid disease, or pulmonary disease) ○ Patients who have previously failed a previous rate-control or rhythm-control pharmacological therapeutic strategy ○ Women ○ Patients with an enlarged left atrium ○ Patients at high risk for stroke and bleeding events (e.g., patients with diabetes, heart failure, and hypertension) ○ Patients stratified by race/ethnicity
Intervention	• Procedures for rate control ○ AVN ablation and permanent pacemaker implantation ○ deflectable cryoablation balloon catheter (Arctic Front®, Cryocath, Montréal, Quebec, Canada) ○ high-intensity focused ultrasound balloon catheter (ProRhythm, Ronkonkoma, NY,	Electrical Cardioversion	• Procedures for rhythm control ○ AF ablation by pulmonary vein isolation ○ Open surgical procedures ○ Minimally invasive procedures ○ Transcatheter procedures ○ Surgical Maze procedure ○ Cardiac resynchronization therapy ○ Hybrid ablation

	USA		○ Cryoballoon 2nd generation ○ PV ostial isolation ○ wide area circumferential ablation (WACA)
Comparators	Other procedural, nonpharmacological, and other specific individual pharmacological rate-control therapies, including: • Non-pharmacological rate-control therapies • Beta-blockers (e.g., acebutolol, atenolol, bisoprolol, carvedilol, esmolol [acute rate lowering only], metoprolol, nadalol, nebivolol, timolol) • Calcium channel blockers (verapamil, diltiazem) • Other (digoxin, amiodarone, dronedarone)	• Pharmacological agents for rhythm control: ○ Amiodarone ○ Disopyramide ○ Dofetilide ○ Dronedarone ○ Flecainide ○ Ibutilide (acute conversion only) ○ Propafenone ○ Sotalol	Other procedural, nonpharmacological, and other specific pharmacological rhythm-control therapies
Outcomes	• Intermediate outcomes: ○ Restoration of sinus rhythm (conversion) ○ Maintenance of sinus rhythm ○ Recurrence of AF at 12 months ○ Development of cardiomyopathy • Final outcomes: ○ Mortality (all-cause, cardiac) ○ Myocardial infarction ○ Cardiovascular hospitalizations ○ Heart failure symptoms ○ Control of AF symptoms (e.g., palpitations, exercise capacity) ○ Quality of life ○ Functional status ○ Stroke and other embolic events ○ Bleeding events • Adverse effects of intervention(s): ○ Adverse effects from drug therapies (e.g., hypotension, hypothyroidism and hyperthyroidism, arrhythmias (bradyarrhythmias, tachyarrhythmias, or proarrhythmias), allergic reactions, hepatotoxicity, neurotoxicity, pulmonary toxicity, ophthalmologic toxicity, dermatologic toxicity) ○ Procedural complications (e.g., pulmonary vein stenosis, left atrial esophageal fistula, and phrenic nerve palsy)	• Intermediate outcomes: ○ Restoration of sinus rhythm (conversion) ○ Maintenance of sinus rhythm ○ Recurrence of AF at 12 months ○ Development of cardiomyopathy • Final outcomes: ○ Mortality (all-cause, cardiac) ○ Myocardial infarction ○ Cardiovascular hospitalizations ○ Heart failure symptoms ○ Control of AF symptoms (e.g., palpitations, exercise capacity) ○ Quality of life ○ Functional status ○ Stroke and other embolic events ○ Bleeding events • Adverse effects of intervention(s): ○ Adverse effects from drug therapies (e.g., hypotension, hypothyroidism and hyperthyroidism, arrhythmias (bradyarrhythmias, tachyarrhythmias, or proarrhythmias), allergic reactions, hepatotoxicity, neurotoxicity, pulmonary toxicity, ophthalmologic toxicity, dermatologic toxicity) ○ Procedural complications (e.g., pulmonary vein stenosis, left atrial esophageal fistula, and phrenic nerve palsy)	• Intermediate outcomes: ○ Restoration of sinus rhythm (conversion) ○ Maintenance of sinus rhythm ○ Recurrence of AF at 12 months ○ Development of cardiomyopathy • Final outcomes: ○ Mortality (all-cause, cardiac) ○ Myocardial infarction ○ Cardiovascular hospitalizations ○ Heart failure symptoms ○ Control of AF symptoms (e.g., palpitations, exercise capacity) ○ Quality of life ○ Functional status ○ Stroke and other embolic events ○ Bleeding events • Adverse effects of intervention(s): ○ Adverse effects from drug therapies (e.g., hypotension, hypothyroidism and hyperthyroidism, arrhythmias (bradyarrhythmias, tachyarrhythmias, or proarrhythmias), allergic reactions, hepatotoxicity, neurotoxicity, pulmonary toxicity, ophthalmologic toxicity, dermatologic toxicity) ○ Procedural complications (e.g., pulmonary vein stenosis, left atrial esophageal fistula, and phrenic nerve palsy)

Abbreviations: AF=Atrial Fibrillation; AVN=Atrioventricular Node

Methods

To assess topic nomination 0699, *Interventional Management of Atrial Fibrillation,* for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. " Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. " Establish the overall *importance* of a potential topic as representing a health or " healthcare issue in the United States. "
3. " Determine the *desirability of new evidence review* by examining whether a new " systematic review or other AHRQ product would be duplicative. "
4. " Assess the *potential impact* a new systematic review or other AHRQ product.
5. " Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. " Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance (see Appendix A).

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews pertaining to the key questions of the nomination. Table 2 includes the citations for the reviews that were determined to address the key questions.

Impact of a New Evidence Review

The impact of a new evidence review was assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether a new review could influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.). See Appendix A.

Feasibility of New Evidence Review

We conducted a literature search in Ovid/Medline from December 2011 to December 2016.

We reviewed all identified titles and abstracts for inclusion and classified identified studies by study design, to assess the size and scope of a potential evidence review. See *Table 2, Feasibility Column, Size/Scope of Review* for the citations of included studies.

We also searched Clinicaltrials.gov for recently completed or in-process unpublished studies. See Appendix B for the Ovid/Medline search strategy and links to the ClinicalTrials.gov search.

Value

We assessed the nomination for value (see Appendix A). We considered whether a partner organization could use the information from the proposed evidence review to facilitate evidence-based change; or the presence of clinical, consumer, or policymaking context that is amenable to evidence-based change.

Compilation of Findings

We constructed a table outlining the selection criteria as they pertain to this nomination (see Appendix A).

Results

Appropriateness and Importance

This is an appropriate and important topic. According to UpToDate, approximately 33.5 million people worldwide suffered from AF in 2010.[1]

Desirability of New Review/Duplication

A new evidence review examining interventional management of atrial fibrillation would not be duplicative of an existing product. A new evidence review examining procedural treatments for atrial fibrillation would not be duplicative. Although we identified 30 evidence reviews published between 2012 and 2016, no review, or combination of a few reviews, offered a comprehensive examination of procedures to treat atrial fibrillation. Most of the evidence reviews were very narrow in scope, offering almost no comparisons of treatments. See *Table 2, Duplication* for the systematic review citations that were determined to address the key questions.

Impact of a New Evidence Review

The standard of care may become unclear. The American Academy of Family Physicians is creating evidence-based guidelines on pharmacologic treatments for AF. To inform this guideline they are doing a bridge for key questions related to pharmacologic treatments in the 2013 AHRQ systematic review. They are not updating the portion on procedural treatments for AF. This means there will potentially be up-to-date guidelines for one course of treatment, but not another, leaving the standard of care on uneven ground. Once the AAFP publishes updated guidelines on pharmacologic treatments, there may be practice variation due to the up-to-date guidelines on one course of treatment, and outdated guidelines on procedural treatment. It is also the general consensus of the cardiology community that the 2014 guidelines need to be updated. Thus an updated evidence review would have potential impact and inform clinical care.

Feasibility of a New Evidence Review

A new evidence review examining interventional management of atrial fibrillation is feasible. All key questions are well covered. We identified 52 published studies (12 RCTs[3-17]) published since 2012. Nine studies were identified for KQ 1,[18-26] 22 studies for KQ 2,[3,4,27-46] and 28 studies for KQ 3.[5-17,19,20,36,46-58] We infer there are likely many more studies than the ones identified due to the large number of evidence reviews identified.

We identified 18 Clinical Trials across the three key questions from ClinicalTrials.gov. See *Table 2, Feasibility* for the citations that were determined to address the key questions.

Table 2. Key questions with the identified corresponding evidence reviews and original research

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Original Research)
1: Procedures for Rate Control	Total number of completed or in-process evidence reviews: 3 AVN Ablation • Other: 2[59,60] Pacemaker • Other (Meta-Analysis): 1[61]	<u>Size/scope of review</u> Relevant Studies: 9 AVN Ablation • Prospective: 1[18] • Prospective Cohort: 2[19,20] • Observational: 2[21,22] Pacemaker • Prospective: 3[23-25] • Longitudinal: 1[26] <u>ClinicalTrials.Gov</u> Relevant studies: 5 • Recruiting: 2[62,63] • Not yet recruiting: 2[64,65] • Complete: 1[66]

Key Question	Duplication (Completed or In-Process Evidence Reviews)	Feasibility (Published and Ongoing Original Research)
2: Electrical Cardioversion	Total number of completed or in-process evidence reviews: 5 • Cochrane: 1[67] • Other: 3[68-70] • Other (Meta-Analysis): 1[71]	Size/scope of review Relevant Studies: 22 • RCT: 2[3,4] • nRCT: 1[27] • Prospective: 4[28-31] • Prospective Cohort: 2[32,33] • Prospective Observational: 3[34-36] • Observational: 2[37,38] • Survey: 1[39] • Retrospective: 7[40-46] ClinicalTrials.Gov Relevant studies: 4 • Not yet recruiting: 1[64] • Recruiting: 3[72-74]
3: Procedures for Rhythm Control	Total number of completed or in-process evidence reviews: 22 PVI • AHRQ: 1[75] • Other: 2[76,77] Surgical Procedures • Cochrane: 1[78] • Other: 2[76,79] • Other (Protocol): 1[80] Minimally Invasive Surgery • Other: 2[81,82] • Other (Protocol): [83,84] Transcatheter Procedure • AHRQ Technology Assessment: 1[85] • Cochrane: 2[86,87] • Other: 8[76,88-94] Surgical Maze Procedure • AHRQ: 1[75] Cardiac Resynchronization • AHRQ Technology Assessment: 1[95] • Other: 2[70,96]	Size/scope of review Relevant Studies: 28 PVI • RCT: 1[5] • Prospective Cohort: 2[47,48] • Retrospective: 1[49] Surgical Procedures • RCT: 3[6-8] • Prospective Cohort: 1[36] • Retrospective: 1[46] Minimally Invasive Surgery • RCT: 2[9,10] • nRCT: 1[50] • Retrospective: 1[51] Transcatheter Procedure • RCT: 6[11-16] • Prospective: 4[52-55] • Observational: 2[56,57] Surgical Maze Procedure • Prospective Cohort: 1[58] Cardiac Resynchronization • RCT: 1[17] • Prospective Cohort: 2[19,20] ClinicalTrials.Gov Relevant studies: 11 • Not yet recruiting: 3[64,97,98] • Recruiting: 4[99-102] • Active, not recruiting:2[103,104] • Complete: 2[105,106]

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; AVN=Atrioventricular Node; nRCT=Non-Randomized Controlled Trial; PVI= Pulmonary Vein Isolation; RCT=Randomized Controlled Trial

Value

The potential for value is high given the ACC/AHA has partnered and will create an evidence-based guideline based on the results of an AHRQ evidence review.

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review on this topic would not be duplicative of an existing product.
    - Although we identified 30 evidence reviews published between 2012 and 2016, no review, or combination of a few reviews, offered a comprehensive examination of procedures to treat atrial fibrillation. A 2015 AHRQ technology assessment report reviewed studies of catheter ablation for atrial fibrillation. While its main topic was medical therapy vs. ablation, one question addressed cryoablation versus radiofrequency catheter ablation.
- Impact: The nomination has high impact potential. Within the cardiology community, it is widely agreed that the 2014 guidelines need to be updated. The standard of care may become unclear. The American Academy of Family Physicians (AAFP) is creating evidence-based guidelines on pharmacologic treatments for AF, but not updating the procedural treatments for AF. This means there will be up-to-date guidelines for one course of treatment, but not another, leaving the standard of care on uneven ground. Once the AAFP published updated guidelines on pharmacologic treatments, there may be practice variation due to the up-to-date guidelines on one course of treatment, and outdated guidelines on procedural treatment.
- Feasibility: An AHRQ evidence review is feasible at this time.
    - *Size/scope of review:* We found 9 studies about atrioventrical node ablation and pacemakers for rate control (KQ1) and 22 studies that examine electrical cardioversion as a treatment for atrial fibrillation (KQ 2). In Medline and other searches, we identified 28 studies concerning procedures for rhythm control including AF ablation by pulmonary vein isolation, open surgical procedures, minimally invasive procedures, transcatheter procedures, surgical Maze procedure, and cardiac resynchronization therapy. Several of these studies include subgroup analyses, such as stratification by gender, comorbidities, age, etc.
    - *Clinicaltrials.gov:* We identified 18 clinical trials across all three key questions.
- Value: nomination has high value potential. The American College of Cardiology and the American Heart Association have partnered to create joint guidelines for the procedural treatment of atrial fibrillation.

References (

1. " Leonard Ganz DS. Epidemiology of and risk factors for atrial fibrillation. *UpToDate.* 2016;INTERNET: https://www.uptodate.com/contents/epidemiology-of-and-risk-factors-for-atrial-fibrillation.
2. " Mayo Foundation for Medical Education and Research. Atrial fibrillation. *INTERNET: http://www.mayoclinic.org/diseases-conditions/atrial-fibrillation/home/ovc-20164923?utm_source=Google&utm_medium=abstract&utm_content=Atrial-fibrillation&utm_campaign=Knowledge-panel.* 2016.
3. " Bellone A, Etteri M, Vettorello M, et al. Cardioversion of acute atrial fibrillation in the emergency department: a prospective randomised trial. *Emerg Med J.* Mar 2012;29(3):188-191.
4. " Chen WS, Gao BR, Chen WQ, et al. Comparison of pharmacological and electrical cardioversion in permanent atrial fibrillation after prosthetic cardiac valve replacement: a prospective randomized trial. *J Int Med Res.* Aug 2013;41(4):1067-1073.
5. " Atienza F, Almendral J, Ormaetxe JM, et al. Comparison of radiofrequency catheter ablation of drivers and circumferential pulmonary vein isolation in atrial fibrillation: a noninferiority randomized multicenter RADAR-AF trial. *J Am Coll Cardiol.* Dec 16 2014;64(23):2455-2467.
6. " Budera P, Straka Z, Osmancik P, et al. Comparison of cardiac surgery with left atrial surgical ablation vs. cardiac surgery without atrial ablation in patients with coronary and/or valvular heart disease plus atrial fibrillation: final results of the PRAGUE-12 randomized multicentre study. *Eur Heart J.* Nov 2012;33(21):2644-2652.
7. " Chernyavskiy A, Kareva Y, Pak I, Rakhmonov S, Pokushalov E, Romanov A. Quality of Life after Surgical Ablation of Persistent Atrial Fibrillation: A Prospective Evaluation. *Heart Lung Circ.* Apr 2016;25(4):378-383.
8. " Gillinov AM, Gelijns AC, Parides MK, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med.* Apr 09 2015;372(15):1399-1409.
9. " Wang X, Wang X, Song Y, Hu S, Wang W. Efficiency of radiofrequency ablation for surgical treatment of chronic atrial fibrillation in rheumatic valvular disease. *Int J Cardiol.* Jul 1 2014;174(3):497-502.
10. " Kuck K-H HBAESWKTAMAELLTBGWS. Impact of complete versus incomplete circumferential lines around the pulmonary veins during catheter ablation of paroxysmal atrial fibrillation: Results from the gap-atrial fibrillation-German atrial fibrillation competence network 1 trial. 2016; 1) (no pagination:http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=cctr&NEWS=N&AN=CN-01133181, 9.
11. " Mont L, Bisbal F, Hernandez-Madrid A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). *Eur Heart J.* Feb 2014;35(8):501-507.
12. " Verma A, Jiang CY, Betts TR, et al. Approaches to catheter ablation for persistent atrial fibrillation. *N Engl J Med.* May 07 2015;372(19):1812-1822.
13. " Zhang XD, Gu J, Jiang WF, et al. Optimal rhythm-control strategy for recurrent atrial tachycardia after catheter ablation of persistent atrial fibrillation: a randomized clinical trial. *Eur Heart J.* May 21 2014;35(20):1327-1334.
14. " Jones DG, Haldar SK, Hussain W, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. *J Am Coll Cardiol.* May 07 2013;61(18):1894-1903.
15. " Hunter RJ, Berriman TJ, Diab I, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). *Circ Arrhythm Electrophysiol.* Feb 2014;7(1):31-38.
16. " Di Biase L, Mohanty P, Mohanty S, et al. Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted

Device: Results From the AATAC Multicenter Randomized Trial. *Circulation.* Apr 26 2016;133(17):1637-1644.
17. " Ciszewski J, Maciag A, Kowalik I, et al. Comparison of the rhythm control treatment strategy versus the rate control strategy in patients with permanent or long-standing persistent atrial fibrillation and heart failure treated with cardiac resynchronization therapy - a pilot study of Cardiac Resynchronization in Atrial Fibrillation Trial (Pilot-CRAfT): study protocol for a randomized controlled trial. *Trials.* Oct 04 2014;15:386.
18. " Issa ZF, Amr BS, Laham H. Long-term follow-up in AV junction ablation via the SVC in patients undergoing concurrent device implantation: a single center experience. *Pacing Clin Electrophysiol.* Feb 2015;38(2):254-258.
19. " Eisen A, Nevzorov R, Goldenberg G, et al. Cardiac resynchronization therapy in patients with atrial fibrillation: a 2-year follow-up study. *Pacing Clin Electrophysiol.* Jul 2013;36(7):872-877.
20. " Jedrzejczyk-Patej E, Lenarczyk R, Pruszkowska P, et al. Long-term outcomes of cardiac resynchronization therapy are worse in patients who require atrioventricular junction ablation for atrial fibrillation than in those with sinus rhythm. *Cardiol J.* 2014;21(3):309-315.
21. " Reddy YM, Gunda S, Vallakati A, et al. Impact of Tricuspid Regurgitation on the Success of Atrioventricular Node Ablation for Rate Control in Patients With Atrial Fibrillation: The Node Blast Study. *Am J Cardiol.* Sep 15 2015;116(6):900-903.
22. " Himmel F, Reppel M, Mortensen K, Schunkert H, Bode F. A strategy to achieve CRT response in permanent atrial fibrillation without obligatory atrioventricular node ablation. *Pacing Clin Electrophysiol.* Aug 2012;35(8):943-947.
23. " Yedlapati N, Fisher JD. Pacemaker diagnostics in atrial fibrillation: limited usefulness for therapy initiation in a pacemaker practice. *Pacing Clin Electrophysiol.* Sep 2014;37(9):1189-1197.
24. " Witkowski M, Bissinger A, Grycewicz T, Lubinski A. Asymptomatic atrial fibrillation in patients with atrial fibrillation and implanted pacemaker. *Int J Cardiol.* Jan 15 2017;227:583-588.
25. " Wang RX, Lee HC, Li JP, et al. Sudden death and its risk factors after atrioventricular junction ablation and pacemaker implantation in patients with atrial fibrillation. *Clin Cardiol.* Oct 17 2016.
26. " Debski M, Ulman M, Zabek A, Haberka K, Lelakowski J, Malecka B. Gender differences in dual-chamber pacemaker implantation indications and long-term outcomes. *Acta Cardiol.* Feb 2016;71(1):41-45.
27. " Turco P, D'Onofrio A, Stabile G, et al. Feasibility and efficacy of electrical cardioversion after cardiac resynchronization implantation in patients with permanent atrial fibrillation. *J Interv Card Electrophysiol.* Dec 2012;35(3):331-336; discussion 336.
28. " Ari H, Gurdogan M, Erdogan E, et al. Short-term outcome of early electrical cardioversion for atrial fibrillation in hyperthyroid versus euthyroid patients. *Cardiol J.* 2012;19(1):53-60.
29. " Bernard-Brunet A, Saint Etienne C, Piver E, et al. Incomplete recovery of mechanical and endocrine left atrial functions one month after electrical cardioversion for persistent atrial fibrillation: a pilot study. *J.* 2014;12:51.
30. " De Vos CB, Limantoro I, Pisters R, et al. The mechanical fibrillation pattern of the atrial myocardium is associated with acute and long-term success of electrical cardioversion in patients with persistent atrial fibrillation. *Heart Rhythm.* Sep 2014;11(9):1514-1521.
31. " Zimmermann AJ, Bossard M, Aeschbacher S, et al. Effects of sinus rhythm maintenance on left heart function after electrical cardioversion of atrial fibrillation: implications for tachycardia-induced cardiomyopathy. *Can J Cardiol.* Jan 2015;31(1):36-43.
32. " Akdemir B, Altekin RE, Kucuk M, et al. The significance of the left atrial volume index in cardioversion success and its relationship with recurrence in patients with non-valvular atrial fibrillation subjected to electrical cardioversion: a study on diagnostic accuracy. *Anadolu Kardiyol Derg.* Feb 2013;13(1):18-25.

33. " Toso E, Blandino A, Sardi D, et al. Electrical cardioversion of persistent atrial fibrillation: acute and long-term results stratified according to arrhythmia duration. *Pacing Clin Electrophysiol.* Sep 2012;35(9):1126-1134.
34. " Elbers PW, Prins WB, Plokker HW, van Dongen EP, van Iterson M, Ince C. Electrical cardioversion for atrial fibrillation improves microvascular flow independent of blood pressure changes. *J Cardiothorac Vasc Anesth.* Oct 2012;26(5):799-803.
35. " Kiliszek M, Opolski G, Wlodarczyk P, Dabrowski R, Ponikowski P. Cardioversion of Atrial Fibrillation (RHYTHM-AF) International Registry in Poland. *Cardiol J.* 2014;21(5):484-491.
36. " Sponga S, Leoni L, Buja G, Nalli C, Voisine P, Gerosa G. Role of an aggressive rhythm control strategy on sinus rhythm maintenance following intra-operative radiofrequency ablation of atrial fibrillation in patients undergoing surgical correction of valvular disease. *J Cardiol.* Oct 2012;60(4):316-320.
37. " Alegret JM, Vinolas X, Martinez-Rubio A, et al. Gender Differences in Patients with Atrial Fibrillation Undergoing Electrical Cardioversion. *J Womens Health (Larchmt).* Jun 2015;24(6):466-470.
38. " Vazquez M, Santos E, Rodriguez I, et al. Assessment of silent microembolism by magnetic resonance imaging after cardioversion in atrial fibrillation. *Rev Esp Cardiol (Engl).* Feb 2012;65(2):139-142.
39. " Hernandez-Madrid A, Svendsen JH, Lip GY, et al. Cardioversion for atrial fibrillation in current European practice: results of the European Heart Rhythm Association survey. *Europace.* Jun 2013;15(6):915-918.
40. " Arrigo M, Jaeger N, Seifert B, Spahn DR, Bettex D, Rudiger A. Disappointing Success of Electrical Cardioversion for New-Onset Atrial Fibrillation in Cardiosurgical ICU Patients. *Crit Care Med.* Nov 2015;43(11):2354-2359.
41. " Crijns HJ, Weijs B, Fairley AM, et al. Contemporary real life cardioversion of atrial fibrillation: Results from the multinational RHYTHM-AF study. *Int J Cardiol.* Apr 1 2014;172(3):588-594.
42. " Gronberg T, Hartikainen JE, Nuotio I, et al. Can we predict the failure of electrical cardioversion of acute atrial fibrillation? The FinCV study. *Pacing Clin Electrophysiol.* Mar 2015;38(3):368-375.
43. " Gronberg T, Nuotio I, Nikkinen M, et al. Arrhythmic complications after electrical cardioversion of acute atrial fibrillation: the FinCV study. *Europace.* Oct 2013;15(10):1432-1435.
44. " Kim H, Lee JP, Yoon HJ, et al. Association between Doppler flow of atrial fibrillatory contraction and recurrence of atrial fibrillation after electrical cardioversion. *J Am Soc Echocardiogr.* Oct 2014;27(10):1107-1112.
45. " Steinberg BA, Schulte PJ, Hofmann P, et al. Outcomes after nonemergent electrical cardioversion for atrial arrhythmias. *Am J Cardiol.* May 15 2015;115(10):1407-1414.
46. " van Breugel HN, Gelsomino S, de Vos CB, et al. Maintenance of sinus rhythm after electrical cardioversion for recurrent atrial fibrillation following mitral valve surgery with or without associated radiofrequency ablation. *Int J Cardiol.* Aug 1 2014;175(2):290-296.
47. " Dukkipati SR, Woollett I, Mc EH, et al. Pulmonary Vein Isolation Using the Visually Guided Laser Balloon: Results of the U.S. Feasibility Study. *J Cardiovasc Electrophysiol.* Jun 15 2015.
48. " Teunissen C, Kassenberg W, van der Heijden JF, et al. Five-year efficacy of pulmonary vein antrum isolation as a primary ablation strategy for atrial fibrillation: a single-centre cohort study. *Europace.* Sep 2016;18(9):1335-1342.
49. " Adlbrecht C GMRBSJKAGH. Prognostic value of induction of atrial fibrillation before and after pulmonary vein isolation. 2013; 2:212. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=cctr&NEWS=N&AN=CN-00917126, 164.

50. " Zembala M, Filipiak K, Kowalski O, et al. Minimally invasive hybrid ablation procedure for the treatment of persistent atrial fibrillation: one year results. *Kardiol Pol.* 2012;70(8):819-828.
51. " Wang P, Dong JZ, Long DY, et al. Impact of different termination modes on atrial fibrillation termination in catheter ablation of persistent atrial fibrillation. *Chin Med J.* Jun 2012;125(11):1877-1883.
52. " Blandino A, Toso E, Scaglione M, et al. Long-term efficacy and safety of two different rhythm control strategies in elderly patients with symptomatic persistent atrial fibrillation. *J Cardiovasc Electrophysiol.* Jul 2013;24(7):731-738.
53. " Ling LH, Taylor AJ, Ellims AH, et al. Sinus rhythm restores ventricular function in patients with cardiomyopathy and no late gadolinium enhancement on cardiac magnetic resonance imaging who undergo catheter ablation for atrial fibrillation. *Heart Rhythm.* Sep 2013;10(9):1334-1339.
54. " Wu L, Yao Y, Zheng L, Zhang K, Zhang S. Long-term follow-up of pure linear ablation for persistent atrial fibrillation without circumferential pulmonary vein isolation. *J Cardiovasc Electrophysiol.* May 2014;25(5):471-476.
55. " Bunch TJ, May HT, Bair TL, et al. Five-year outcomes of catheter ablation in patients with atrial fibrillation and left ventricular systolic dysfunction. *J Cardiovasc Electrophysiol.* Apr 2015;26(4):363-370.
56. " Gaita F, Sardi D, Battaglia A, et al. Incidence of cerebral thromboembolic events during long-term follow-up in patients treated with transcatheter ablation for atrial fibrillation. *Europace.* Jul 2014;16(7):980-986.
57. " Gallo C, Battaglia A, Anselmino M, et al. Long-term events following atrial fibrillation rate control or transcatheter ablation: a multicenter observational study. *J Cardiovasc Med (Hagerstown).* Mar 2016;17(3):187-193.
58. " Ad N HLFTWMHSD. Minimally invasive stand-alone cox-maze procedure for patients with nonparoxysmal atrial fibrillation. 2013; 3:792. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=cctr&NEWS=N&AN=CN-01006947, 96.
59. " Ganesan AN, Brooks AG, Roberts-Thomson KC, Lau DH, Kalman JM, Sanders P. Role of AV nodal ablation in cardiac resynchronization in patients with coexistent atrial fibrillation and heart failure a systematic review. *Journal of the American College of Cardiology.* Feb 21 2012;59(8):719-726.
60. " Yin J, Hu H, Wang Y, et al. Effects of atrioventricular nodal ablation on permanent atrial fibrillation patients with cardiac resynchronization therapy: a systematic review and meta-analysis. *Clinical cardiology.* Nov 2014;37(11):707-715.
61. " Shali S, Su Y, Ge J. Interatrial septal pacing to suppress atrial fibrillation in patients with dual chamber pacemakers: A meta-analysis of randomized, controlled trials. *International journal of cardiology.* Sep 15 2016;219:421-427.
62. " First Affiliated Hospital of Wenzhou Medical Univeristy. Comparison of His Bundle Pacing and Bi-Ventricular Pacing in Heart Failure With Atrial Fibrillation. *ClinicalTrials.gov.* 2016;NCT02805465.
63. " Federal State Budgetary Institution, V. A. Almazov Federal North-West Medical Research Centre, of the Ministry of Health. Atrioventricular Node Ablation in Patients With Atrial Fibrillation and Moderate Chronic Heart Failure (VISTA). *ClinicalTrials.gov.* 2016;NCT01512381.
64. " Eastbourne General Hospital. Electrical Cardioversion, Ablation or Pace and Ablate for Persistent Atrial Fibrillation (CAPAPAF-65). *ClinicalTrials.gov.* 2015;NCT02528604.
65. " University of Rochester. Junctional AV Ablation in CRT-D: JAVA-CRT. *ClinicalTrials.gov.* 2016;NCT02946853.
66. " Azienda Ospedaliera Cardinale G. Panico. Rate RESPONSIVe Pacing in Patients With Permanent AF Underwent AV Node ABLation and bivEntricular Pacing (RESPONSIBLE) (RESPONSIBLE). *ClinicalTrials.gov.* 2015;NCT02354989.

67. " Lewis SR, Nicholson A, Reed SS, Kenth JJ, Alderson P, Smith AF. Anaesthetic and sedative agents used for electrical cardioversion. 3:http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=coch&NEWS=N&AN=00075320-100000000-09161.
68. " Kirkland S, Stiell I, AlShawabkeh T, Campbell S, Dickinson G, Rowe BH. The efficacy of pad placement for electrical cardioversion of atrial fibrillation/flutter: a systematic review. *Academic Emergency Medicine.* Jul 2014;21(7):717-726.
69. " Klein HH, Trappe HJ. Cardioversion in Non-Valvular Atrial Fibrillation. *Deutsches Arzteblatt International.* Dec 11 2015;112(50):856-862.
70. " Barra S, Providencia R, Tang A, Heck P, Virdee M, Agarwal S. Importance of Implantable Cardioverter-Defibrillator Back-Up in Cardiac Resynchronization Therapy Recipients: A Systematic Review and Meta-Analysis. *Journal of the American Heart Association.* Nov 06 2015;4(11).
71. " Shurrab M, Elitzur Y, Healey JS, et al. VDD vs DDD pacemakers: a meta-analysis. *The Canadian journal of cardiology.* Nov 2014;30(11):1385-1391.
72. " Maastricht University Medical Center. Acute Cardioversion Versus Wait And See-approach for Symptomatic Atrial Fibrillation in the Emergency Department (ACWAS). *ClinicalTrials.gov.* 2016;NCT02248753.
73. " Uppsala University Hospital. Electrical Cardioversion of Recent Onset Atrial Fibrillation - Silent Thromboembolic Events, Reverse Atrial Remodeling (ECAF-STAR). *ClinicalTrials.gov.* 2016;NCT02955004.
74. " University of Aarhus. Comparison of High Versus Escalating Shocks in Cardioverting Atrial Fibrillation. *ClinicalTrials.gov.* 2016;NCT02923414.
75. " Al-Khatib SM, Allen LaPointe NM, Chatterjee R, et al. Rate- and rhythm-control therapies in patients with atrial fibrillation: a systematic review. *Annals of Internal Medicine.* Jun 3 2014;160(11):760-773.
76. " Schleifer JW, Ramakrishna H. Perioperative atrial fibrillation: a systematic review of evolving therapeutic options in pharmacologic and procedural management. *Annals of cardiac anaesthesia.* Oct-Dec 2015;18(4):565-570.
77. " Vaidya K, Arnott C, Russell A, Masson P, Sy RW, Patel S. Pulmonary Vein Isolation Compared to Rate Control in Patients with Atrial Fibrillation: A Systematic Review and Meta-analysis. *Heart, lung & circulation.* Aug 2015;24(8):744-752.
78. " Huffman MD, Karmali KN, Berendsen MA, et al. Concomitant atrial fibrillation surgery for people undergoing cardiac surgery. 8:http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=coch&NEWS=N&AN=00075320-100000000-10219.
79. " Kearney K, Stephenson R, Phan K, Chan WY, Huang MY, Yan TD. A systematic review of surgical ablation versus catheter ablation for atrial fibrillation. *Annals of cardiothoracic surgery.* Jan 2014;3(1):15-29.
80. " McClure GR, Belley-Cote EP, Singal RK, et al. Surgical ablation of atrial fibrillation: a protocol for a systematic review and meta-analysis of randomised controlled trials. *BMJ open.* Nov 02 2016;6(11):e013273.
81. " Je HG, Shuman DJ, Ad N. A systematic review of minimally invasive surgical treatment for atrial fibrillation: a comparison of the Cox-Maze procedure, beating-heart epicardial ablation, and the hybrid procedure on safety and efficacy. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* Oct 2015;48(4):531-540; discussion 540-531.
82. " Phan K, Phan S, Thiagalingam A, Medi C, Yan TD. Thoracoscopic surgical ablation versus catheter ablation for atrial fibrillation. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery.* Apr 2016;49(4):1044-1051.
83. " Charles Pearman DG, Shi Sum Poon, Laura Bonnett, Neeraj Mediratta Surgical ablation for atrial fibrillation: a comparison of hybrid ablation vs. epicardial ablation alone. *PROSPERO.* 2016;CRD42016043389

84. " Marwan Saad RN, Islam Elguindy, Ahmed Mahmoud, Akram Elguindy, Amr Barakat, Amgad Mentias, Ahmed Abuzaid, Waddah Maskoun, Asif Sewani, Hakan Paydak, Sanjeev Saksena Efficacy and safety of cryoballoon versus radiofrequency ablation for atrial fibrillation: a meta-analysis of randomized clinical trials. *PROSPERO.* 2016;CRD42016041772.
85. " Skelly A, Hashimoto R, Al-Khatib S, et al. AHRQ Technology Assessments. *Catheter Ablation for Treatment of Atrial Fibrillation*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015.
86. " Nyong J, Amit G, Adler AJ, et al. Efficacy and safety of ablation for people with non-paroxysmal atrial fibrillation. 11:http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=coch&NEWS=N&AN=00075320-100000000-10496.
87. " Tuohy S MDODMGJ. Catheter ablation versus medical therapy for patients with symptomatic atrial fibrillation: Systematic review and meta-analysis of randomized controlled trials. 2014; 8 SUPPL. 1:S400. Available at: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=cctr&NEWS=N&AN=CN-01050048, 183.
88. " Anselmino M, Matta M, D'Ascenzo F, et al. Catheter ablation of atrial fibrillation in patients with left ventricular systolic dysfunction: a systematic review and meta-analysis. *Circulation. Arrhythmia and electrophysiology.* Dec 2014;7(6):1011-1018.
89. " Anselmino M, Matta M, D'Ascenzo F, et al. Catheter ablation of atrial fibrillation in patients with diabetes mellitus: a systematic review and meta-analysis. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology.* Oct 2015;17(10):1518-1525.
90. " Fadahunsi O, Talabi T, Olowoyeye A, Iluyomade A, Shogbesan O, Donato A. Ablation of Complex Fractionated Atrial Electrograms for Atrial Fibrillation Rhythm Control: A Systematic Review and Meta-analysis. *The Canadian journal of cardiology.* Jun 2016;32(6):791-802.
91. " Ganesan AN, Nandal S, Luker J, et al. Catheter ablation of atrial fibrillation in patients with concomitant left ventricular impairment: a systematic review of efficacy and effect on ejection fraction. *Heart, lung & circulation.* Mar 2015;24(3):270-280.
92. " Zhu M, Zhou X, Cai H, et al. Catheter ablation versus medical rate control for persistent atrial fibrillation in patients with heart failure: A PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. *Medicine.* Jul 2016;95(30):e4377.
93. " Anselmino M, Battaglia A, Gallo C, et al. Atrial fibrillation and female sex. *Journal of Cardiovascular Medicine.* Dec 2015;16(12):795-801.
94. " Al Halabi S, Qintar M, Hussein A, et al. Catheter Ablation for Atrial Fibrillation in Heart Failure Patients: A Meta-Analysis of Randomized Controlled Trials. *JACC. Clinical electrophysiology.* Jun 01 2015;1(3):200-209.
95. " Rickard J, Michtalik H, Sharma R, et al. AHRQ Technology Assessments. *Use of Cardiac Resynchronization Therapy in the Medicare Population*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015.
96. " Lopes C, Pereira T, Barra S. Cardiac resynchronization therapy in patients with atrial fibrillation: a meta-analysis. *Revista portuguesa de cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of cardiology : an official journal of the Portuguese Society of Cardiology.* Nov 2014;33(11):717-725.
97. " Andrade J. Early Aggressive Invasive Intervention for Atrial Fibrillation (EARLY-AF). *ClinicalTrials.gov.* 2016;NCT02825979.
98. " University of Turin, Italy. Atrial Fibrillation Ablation Compared to Rate Control Strategy in Patients With Impaired Left Ventricular Function (AFARC-LVF). *ClinicalTrials.gov.* 2015;NCT02509754.
99. " Amit G. AMIOdarone vs. Catheter Ablation for Prevention of Recurrent Symptomatic Atrial Fibrillation (AmioCAAF). *ClinicalTrials.gov.* 2016;NCT02341105.

100. " Imperial College London. Ablation Verses Anti-arrhythmic Therapy for Reducing All Hospital Episodes From Recurrent Atrial Fibrillation (AVATAR-AF). *ClinicalTrials.gov.* 2016;NCT02459574.
101. " Meshalkin Research Institute of Pathology of Circulation. Ablation and Left Atrium Reduction During Mitral Valve Surgery for Atrial Fibrillation (ALARM-vs-AF). *ClinicalTrials.gov.* 2016;NCT02047279.
102. " Biosense Webster, Inc. Atrial Fibrillation Progression Trial (ATTEST). *ClinicalTrials.gov.* 2016;NCT01570361.
103. " Uppsala University Hospital.Catheter Ablation Compared With Pharmacological Therapy for Atrial Fibrillation (CAPTAF Trial) (CAPTAF). *ClinicalTrials.gov.* 2014;NCT02294955.
104. " VZW Cardiovascular Research Center Aalst. Pulmonary Vein Isolation With Versus Without Continued Antiarrhythmic Drug Treatment in Subjects With Recurrent Atrial Fibrillation (POWDER-AF). *ClinicalTrials.gov.* 2016;NCT02475642.
105. " Samsung Medical Center. The Concomitant Cryomaze Procedure Using Nitreous Oxide Cryoprobe: Comparison With Argon Based Cryoprobe. *ClinicalTrials.gov.* 2016;NCT01812356.
106. " Deutsches Herzzentrum Muenchen. Ablation of Complex Fractionated Electrograms With or Without Additional Linear Lesions for Persistent Atrial Fibrillation (ADLINE). *ClinicalTrials.gov.* 2016;NCT02059369.

Appendices

Appendix A: Selection Criteria Summary (

Appendix B: Search Strategy & Results (Feasibility)

Appendix A. Selection Criteria Summary (

Selection Criteria	Supporting Data
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, interventions are available in the US.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review on procedural interventions for atrial fibrillation.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on comparative effectiveness.
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, it is biologically plausible. Yes, it is consistent with what is known about the topic.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. According to UpToDate, approximately 33.5 million people worldwide suffered from AF in 2010.[1]
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	Yes, this topic affects heath care decisions for a large, vulnerable, often elderly population. The procedures for treating AF all require some sort of hospitalization.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers. There are several options for treating AF, and guidelines are based on low strength of evidence, and are 3 years old.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes, this nomination addresses both benefits and potential harms of procedures aimed at treating AF.
2e. 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, this nomination represents a condition that may results in high costs due for consumers and payers.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A new evidence review examining procedural treatments for atrial fibrillation would not be duplicative. Although we identified 30 evidence reviews published between 2012 and 2016, no review, or combination of a few reviews, offered a comprehensive examination of procedures to treat atrial fibrillation.
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 standard of care may become unclear. The AAFP is creating evidence-based guidelines on pharmacologic treatments for AF, but not updating the procedural treatments for AF. This means there will be up-to-date guidelines for one course of treatment, but not another, leaving the standard of care on uneven ground.

4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Once the AAFP published updated guidelines on pharmacologic treatments, there may be practice variation due to the up-to-date guidelines on one course of treatment, and outdated guidelines on procedural treatment.
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)	An AHRQ evidence review on procedural interventions to treat AF is feasible. We identified 52 published studies (12 RCTs) published since 2012. We infer there are likely many more studies than the ones identified due to the large number of evidence reviews identified. We identified 18 Clinical Trials across the three key questions from ClinicalTrials.gov.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, this nomination exists within a clinical, consumer, and policy-making context. A review on this topic would inform the creation of an ACC/AHA joint clinical practice guideline as well as impact clinical decision-making to optimize benefits of treatment while reducing potential harms. Parents and doctors will be able to use the results of an AHRQ systematic review to aid in AF treatment decision-making.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, the ACC/AHA has partnered and will create an evidence-based guideline based on the results of an AHRQ evidence review.

Abbreviations: AAFP=American Academy of Family Physicians; ACC=American College of Cardiology; AF=Atrial Fibrillation; AHA=American Heart Association; AHRQ=Agency for Healthcare Research and Quality; RCT=Randomized Controlled Trial

Appendix B. Search Strategy & Results (Feasibility)

Topic: Procedural Interventions for the Treatment of Atrial Fibrillation **Date:** December 23, 2016 **Database Searched:** Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present – (contains all PubMed content up to 24 hours ago or most recent PubMed file update)	KQ1: What are the comparative safety and effectiveness of **newer procedural and other nonpharmacological rate-control therapies** compared with pharmacological agents in patients with AF who have failed initial pharmacotherapy? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?
Concept	Search String
Atrial Fibrillation	1. atrial fibrillation/ or atrial flutter/ 2. (atrial* or auricular*) adj fibrillat*).tw,kf. 3. or/1-2
Procedures for rate control non-pharmacological rate-control therapies	4. Cardiac Pacing, Artificial/ or Pacemaker, Artificial/ 5. pacemaker*.tw,kf. 6. ((AVN* node or AV or A-V or Atrioventricular* or Atrio-ventricular*) adj2 (ablate* or ablation* or ablating)).tw,kf. 7. (nonpharmacolog* or non-pharmacolog* or nondrug or non-drug).tw,kf. 8. or/4-7 9 rate-control*.tw,kf. 10 and/3,8-9
Limits	11 limit 10 to yr="2011 -Current" 12 limit 11 to english language 13 limit 12 to humans 14 limit 13 to animals 15 13 not 14 16 limit 15 to (comment or editorial or letter or news) 17 15 not 16 18 remove duplicates from 17
N=43	
Systematic Review N=4	
Randomized Controlled Trials N=0	
Other N=39	
Topic: Procedural Interventions for the Treatment of Atrial Fibrillation **Date:** December 23, 2016 **Database Searched:** Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present – (contains all PubMed content up to 24 hours ago or most recent PubMed	KQ2: What are the comparative safety and effectiveness of **electrical cardioversion** compared to antiarrhythmic agents for conversion of AF to sinus rhythm? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?

file update)	
Concept	Search String
Atrial Fibrillation	1 atrial fibrillation/ or atrial flutter/ 2 ((atrial* or auricular*) adj fibrillat*).tw,kf. 3 or/1-2
Electrical Cardioversion	4 electrical cardioversion*.tw,kf. $ 5 and/3-4 6 "sinus rhythm*".tw,kf. $ 7 and/5-6 $
Limits	8 limit 7 to yr="2011 -Current" 9 limit 8 to english language 10 limit 9 to humans 11 limit 10 to animals 12 10 not 11 13 limit 12 to (comment or editorial or letter or news) 14 12 not 13 15 remove duplicates from 14 16 limit 15 to systematic reviews 17 15 not 16 18 limit 17 to (clinical trial, all or clinical trial or controlled clinical trial or pragmatic clinical trial or randomized controlled trial) 19 17 not 18
N = 114	
Systematic Review = 7	
Randomized Controlled Trials = 43	
Other N=64	
Topic: Procedural Interventions for the Treatment of Atrial Fibrillation **Date:** December 23, 2016 **Database Searched:** Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present – (contains all PubMed content up to 24 hours ago or most recent PubMed file update)	KQ3. What are the comparative safety and effectiveness of newer **procedural rhythm-control therapies, other nonpharmacological rhythm-control therapies, and pharmacological agents** (either separately or in combination with each other) for maintenance of sinus rhythm in patients with AF? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?
Atrial Fibrillation	1 atrial fibrillation/ or atrial flutter/ 2 ((atrial* or auricular*) adj fibrillat*).tw,kf. 3 or/1-2
procedural rhythm-control therapies, other nonpharmacological rhythm-control therapies, and pharmacological agents	4 (rhythm* adj3 control*).tw,kf. 5 (electrical cardioversion* or (pulmonary adj4 (ablate* or ablating or ablation*)) or (open adj surger*) or (minimal* adj invasive) or transcatheter* or trans-catheter* or (surgical* adj maze*) or (cardiac* adj resynchron*)).tw,kf. 6 Anti-Arrhythmia Agents/ or (Amiodarone or Disopyramide or Dofetilide or Dronedarone or Flecainide or Ibutilide or Propafenone or Sotalol).tw,kf. 7 (nonpharmacolog* or non-pharmacolog* or nondrug or non-drug).tw,kf.

	8 or/5-7 9 and/3-4,8
Limits	10 limit 9 to yr="2011 -Current" 11 limit 10 to english language 12 limit 11 to humans 13 limit 12 to animals 14 12 not 13 15 limit 14 to (comment or editorial or letter or news) 16 14 not 15 17 remove duplicates from 16 18 limit 17 to systematic reviews 19 17 not 18 20 limit 19 to (clinical trial, all or clinical trial or controlled clinical trial or pragmatic clinical trial or randomized controlled trial) 21 19 not 20
N = 228	
Systematic Review = 27	
Randomized Controlled Trials = 57	
Other N= 144	