

Updating Systematic Reviews: Stroke Prevention in Atrial Fibrillation

A PCORI Virtual Multi-Stakeholder Workshop

January 5, 2017



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Agenda

- Welcome and Housekeeping
- Introductions (AHRQ, then Jennifer Croswell)
- Background and goals for the day:
 - History of the Topic to Date
 - Relevant Comments from the Previous Workshop
 - Prior Stroke Prevention in Atrial Fibrillation Review Key Questions
 - Proposed Update: Key Questions, Outcomes, and Study Designs
 - Questions to Guide the Discussion
- Discussion
- Summary and closing remarks



Welcome

Housekeeping

- Participants' lines are live
 - Please mute your line when you are not speaking to reduce background noise
- Today's conversation is being recorded and will be posted to the PCORI web site
- We will take comments in the order indicated on the agenda
- Comments and questions from the public may be submitted via the chat window
 - We will attempt to include these submissions in the discussion when feasible
 - We cannot guarantee a question will be addressed



History of the Topic to Date



Atrial Fibrillation: Scope of Review

- PCORI held a previous multi-stakeholder workshop on December 7, 2016 to discuss a 2013 Agency for Healthcare Research and Quality (AHRQ) systematic review on the treatment of atrial fibrillation (i.e., a focus on *rate and rhythm control*)
- During that meeting, multiple stakeholder expressed a strong preference for reviewing the evidence related to ***stroke prevention*** in atrial fibrillation (particularly newer anticoagulation agents, or NOACs)
- Participants also indicated that many questions in the rate and rhythm control review did not have much new evidence in the intervening time period
- PCORI is responding to the feedback by partnering with AHRQ to update its 2013 systematic review on stroke prevention in atrial fibrillation instead



Relevant Comments from the Previous Workshop



Relevant Comments from Prior Workshop

- Clear interest in focusing on how the benefits and harms of various anticoagulants may be different for specific subpopulations (e.g., older adults and specifically older women)
 - Within this, need to understand falls risk as well as need for/impact of variable dosing
- Interest in understanding how adherence (or lack thereof) to newer anticoagulants (NOACs) may influence ultimate benefit (given lack of monitoring compared to warfarin)
- Need to consider additional outcomes not covered in the last review—particularly quality of life and cognitive function
- Need to include new interventions not available at time of last review, e.g., edoxaban, left atrial occlusion devices



Relevant Comments from Prior Workshop

- Note that the bleeding risk tool has inadequacies that should be considered and addressed with the new review
- Note need to consider more types of evidence than just RCTs
- Does the risk of falls/bleeding impact treatment decisions in stroke prevention? That is, is it being used as a justification not to anticoagulate in atrial fibrillation?
- Contextual interest in litigation ads related to NOACs and how this may affect care



Prior Stroke Prevention in Atrial Fibrillation Review Questions



Prior Review Questions

1. In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of available clinical and imaging tools for predicting thromboembolic risk?
2. In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of clinical tools and associated risk factors for predicting bleeding events?
3. What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events:
 - a. In patients with nonvalvular atrial fibrillation?
 - b. In specific subpopulations of patients with nonvalvular atrial fibrillation?



Prior Review Questions

4. What are the comparative safety and effectiveness of available strategies for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?
5. What are the comparative safety and effectiveness of available strategies for switching between warfarin and other, novel oral anticoagulants in patients with nonvalvular atrial fibrillation?
6. What are the comparative safety and effectiveness of available strategies for resuming anticoagulation therapy or performing a procedural intervention as a stroke prevention strategy following a hemorrhagic event (stroke, major bleed, or minor bleed) in patients with nonvalvular atrial fibrillation?



Proposed Update: Key Questions, Outcomes, and Study Designs



Key Question 1

1. In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of available clinical and imaging tools for predicting thromboembolic risk?

Clinical tools	Individual risk factors	Imaging tools
CHADS2 score	INR level	Transthoracic echo
CHADS2-VASc score	Duration and frequency of atrial fibrillation	Transesophageal echo
Framingham risk score		CT scans
ABC stroke risk score		Cardiac MRIs



Key Question 2

2. In patients with nonvalvular atrial fibrillation, what are the comparative diagnostic accuracy and impact on clinical decisionmaking (diagnostic thinking, therapeutic, and patient outcome efficacy) of clinical tools and associated risk factors for predicting bleeding events?

Clinical tools	Individual risk factors
CHADS2 score	INR level
CHADS2-VASc score	Duration and frequency of atrial fibrillation
Framingham risk score	Age
ABC stroke risk score	Prior stroke
HAS-BLED score	Type of atrial fibrillation
HEMORR2HAGES score	Cognitive impairment
ATRIA score	Falls risk
Bleeding Risk Index	Presence of heart disease



Key Question 3

3. What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events in patients with nonvalvular atrial fibrillation?

In specific subpopulations of patients with nonvalvular atrial fibrillation, to include (but are not limited to):

Age	Previous bleed
Presence of heart disease	Recent acute coronary syndrome with or without PCI/stenting
Type of atrial fibrillation	Recent PCI/stenting outside of an acute coronary syndrome
Comorbid conditions (such as end-stage renal disease)	Recent stenting for peripheral vascular disease
When in therapeutic range	Pregnant
When non-adherent to medication	Previous thromboembolic event



Key Question 3

3. What are the comparative safety and effectiveness of specific anticoagulation therapies, antiplatelet therapies, and procedural interventions for preventing thromboembolic events in patients with nonvalvular atrial fibrillation?

Interventions to be studied will include (but are not limited to):

Anticoagulation therapy:	Antiplatelet therapy:	Procedures:
Warfarin	Clopidogrel	Surgeries (e.g., left atrial appendage occlusion, resection/removal)
Vitamin K antagonists	Aspirin	Minimally invasive (e.g., Atriclip, LARIAT)
Dabigatran	Dipyridamole	Transcatheter (WATCHMAN, AMPLATZER, PLAATO)
Rivaroxaban	Combinations of antiplatelets	
Apixaban		
Edoxaban		



Outcomes for Key Question 3

Thromboembolic outcomes:	Bleeding outcomes:	Other clinical outcomes:	
Cerebrovascular infarction	Hemorrhagic stroke	Mortality	Dyspepsia
Transient ischemic attack	Intracranial hemorrhage	Myocardial infarction	Health-related QOL
Systemic embolism (excludes PE and DVT)	Extracranial hemorrhage	Cognitive function	Long-term adherence to therapy
	Major bleed (stratified by type and location)	Infection	Health services utilization
	Minor bleed (stratified by type and location)	Heart block	Functional capacity
		Esophageal fistula	Tamponade



Study Designs, All Questions

- RCTS, prospective and retrospective observational studies, or registries



Questions to Guide the Scoping Discussion



Scoping Question 1

- **PCORI is proposing to focus the update on the first three key questions, based on the comments we heard during the first stakeholder workshop.**
- This would allow the Evidence-based Practice Center to dig deep into the evidence on clinical risk prediction tools and for studies of multiple designs that have emerged on newer interventions for stroke prevention.
- It would also allow for a greater focus on subpopulations of interest (such as older women, or those who are less adherent with treatment).
- **We are interested in your feedback on this proposed approach to the update.**



Scoping Question 2

- We have provided specifics regarding the clinical tools, risk factors, patient subpopulations, treatment interventions, outcomes, and study designs we propose the Evidence-based Practice Center focus on (note that these lists are not exhaustive).
- We want to acknowledge and thank **AHRQ's EPC Program Scientific Resource Center at the Portland VA Research Foundation** for doing the lion's share of this background work on this list.
- **Is anything critical missing?**



Scoping Question 3

- **Do you have any other comments for us on behalf of your organization?**



Discussion



Order of Comments

- Patients and Patient Representatives
- Clinicians
- Industry
- Research
- Patients and Patient Representatives

**Comments are not required of participants. Any participant may pass on the opportunity to comment.*



Order of Comments

Patients and Patient Representatives

- Alliance for Aging Research
 - Sue Peschin
- American Heart Association
 - Mark Estes
- WomenHeart
 - Susan Campbell

Clinicians

- American Geriatrics Society
 - Michael Rich
- American Academy of Family Physicians
 - Melanie Bird
- American College of Cardiology
 - Paul Varosy

Industry

- AdvaMed
 - Chan Branham
- Boehringer Ingelheim
 - Pranav Gandhi
- Boston Scientific
 - Ken Stein
- Bristol-Myers Squibb
 - Priti Jhingran

Research

- CDC
 - Mary George
- FDA/CDER
 - Stephen Grant



Summary and Closing Remarks



THANK YOU!

