

### **Prior Key Questions from the 2013 Systematic Review on the Treatment of Atrial Fibrillation**

1. What are the comparative safety and effectiveness of pharmacological agents used for ventricular rate control in patients with atrial fibrillation? 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 a strict rate-control strategy versus a more lenient rate-control strategy in patients with atrial fibrillation? (HR <80 or <110) 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 and other nonpharmacological rate-control therapies compared with pharmacological agents in patients with atrial fibrillation for whom initial pharmacotherapy was ineffective? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?
4. What are the comparative safety and effectiveness of available antiarrhythmic agents and electrical cardioversion for conversion of atrial fibrillation to sinus rhythm? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?
5. 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 atrial fibrillation patients? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?
6. What are the comparative safety and effectiveness of rate-control therapies versus rhythm-control therapies in patients with atrial fibrillation? Do the comparative safety and effectiveness of these therapies differ among specific patient subgroups of interest?

**(The Analytic Framework can be found on page ES-5.)**

## Questions to Guide the Scoping Discussion

PCORI will be conducting a targeted update of the prior systematic review. One emphasis for PCORI's new Evidence Synthesis Program is on achieving the relatively rapid deployment of rigorous, relevant, and actionable comparative effectiveness research, placed in context, for a wide variety of stakeholders. For this reason we are seeking your assistance in identifying the current highest priority areas from the prior comprehensive review to refine and focus the scope for this update.

1. The prior review provided a comprehensive summary of available pharmacological and interventional approaches to both rate and rhythm control strategies. Is there a rationale to prioritize updating the review of the evidence to one strategy or the other at this time (i.e., reviewing just rate control strategies, or just rhythm control strategies)? If so, why? Similarly, is there a case to be made for limiting the review to only pharmacological interventions or non-pharmacological interventions for either strategy?
2. The prior review directly compared the effectiveness of rate control strategies versus rhythm control strategies in improving a number of outcomes among patients with atrial fibrillation (key question 6). Unlike many of the other key questions associated with this review, which had low to insufficient strength of evidence to support the findings, the investigators found moderate strength of evidence that the two strategies (with pharmacologic interventions) are equivalent in terms of stroke and cardiovascular and all-cause mortality. Rate control strategies were shown to be superior in terms of reducing cardiovascular hospitalizations (high strength of evidence), whereas there was a suggestion that rhythm control might better control heart failure symptoms (low strength of evidence). To your knowledge, are there new studies addressing this question of the direct comparison of the two control strategies that would be important to include in an update of the evidence? Are there remaining uncertainties associated with this question (e.g., specific subpopulations that might benefit more or less from the two strategies) which would make it important to retain in this updated review?
3. The prior review found moderate to high strength of evidence for a fair number of treatment comparisons of various electrical or pharmacologic methods of cardioversion to restore normal sinus rhythm (key question 4), although the evidence was less certain regarding maintenance of sinus rhythm and recurrence of atrial fibrillation. Would you retain this question as being of high priority in the updated review, and if so, would you refocus it in any way given the prior findings?
4. Is the issue of strict versus lenient rate-control (i.e., heart rate <80 versus <110 BPM) still strongly debated? Is there new evidence that you are aware of since the prior review that would definitively add to our knowledge on this issue?
5. Is there anything that is emerging in the area of atrial fibrillation treatment since the prior review that you feel needs to be addressed by this update? Is something critical missing?
6. Do you have any other comments for us on behalf of your organization?

Thank you again on behalf of PCORI for your time and your assistance!