Prioritizing Comparative Effectiveness Research Questions for New Oral Anticoagulants : A Stakeholder Workshop

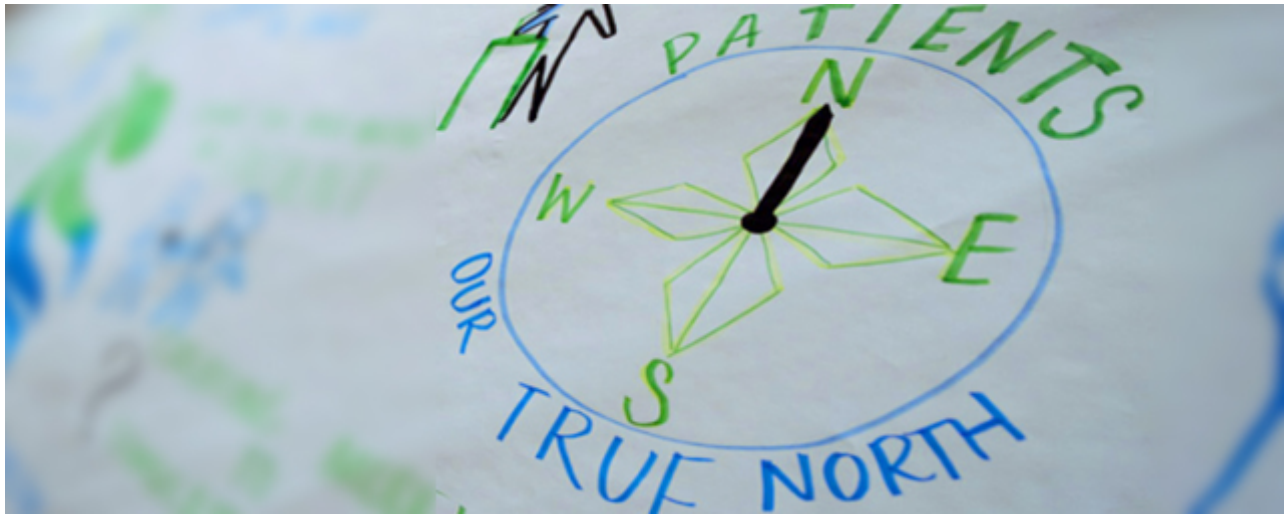
June 9, 2015

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Welcome

- Please introduce yourself
- State your name and primary stakeholder affiliation



Housekeeping

Today's webinar is open to the public and is being recorded.

- Members of the public are invited to listen to this webinar.
- Topic briefs and other materials are available on the PCORI site.
- Comments may be submitted via chat. No public comment period is scheduled today.

Reminders for the group

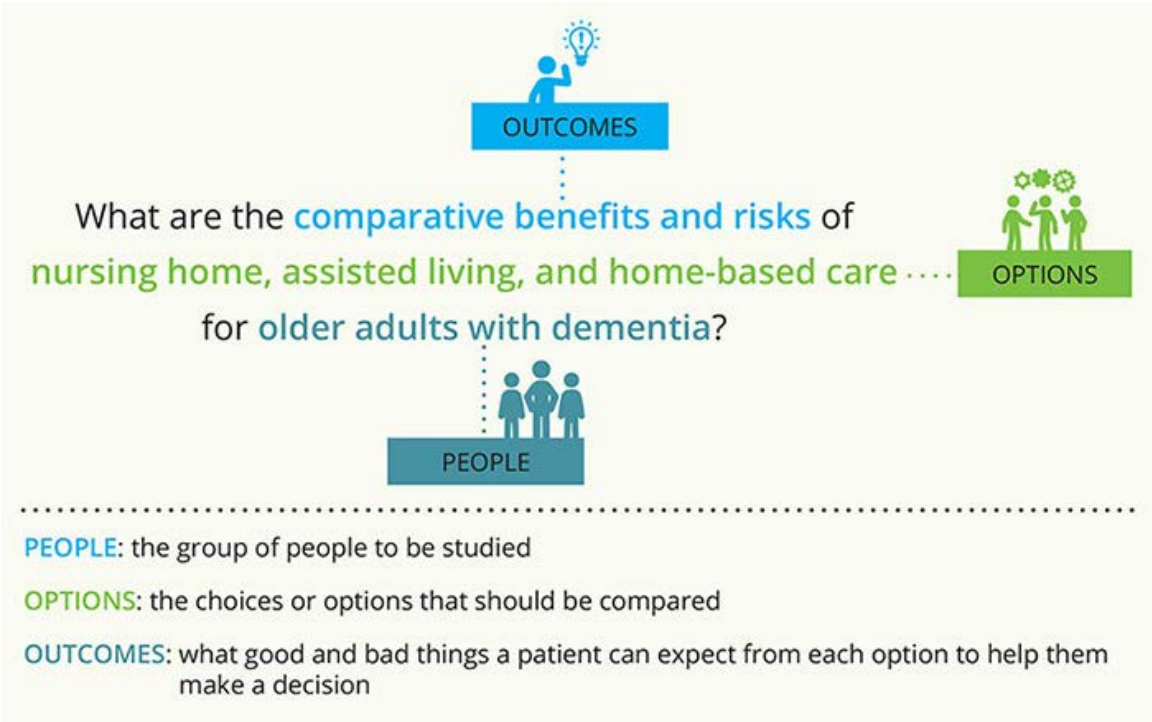
- Please signify your intent to speak by standing your name placard on end.
- Where possible, we encourage you to avoid acronyms in your discussion of these topics.

For those on the phone

- If you experience any technical difficulties, please alert us via chat or email support@meetingbridge.com.

Purpose of the Workshop

- Identify, refine, and prioritize 2-3 clinical comparative effectiveness research questions on the use of **New Oral Anticoagulants** whose findings could improve patient-centered outcomes.



Question refinement process

- **Step 1: Discuss the questions submitted by the group**
  - Tier 3 Criteria
- **Step 2: Rank the questions in order of priority**
- **Step 3: Refine the top 2-3 research questions**
  - Identification of populations, interventions, comparators, outcomes, duration and settings
  - Expanded discussion of specific populations of interest, health decisions, and treatments
  - Consideration of study design, challenges to conducting research on specific question, and ongoing work in the field

PCORI Tier 3 Criteria

Tier 3	• **Patient-Centeredness**: is the comparison relevant to patients, their caregivers, clinicians or other key stakeholders and are the outcomes relevant to patients? • **Impact of the Condition on the Health of Individuals and Populations**: Is the condition or disease associated with a significant burden in the US population, in terms of disease prevalence, costs to society, loss of productivity or individual suffering? • **Assessment of Current Options**: Does the topic reflect an important evidence gap related to current options that is not being addressed by ongoing research. • **Likelihood of Implementation in Practice**: Would new information generated by research be likely to have an impact in practice? (E.g. do one or more major stakeholder groups endorse the question?) • **Durability of Information**: Would new information on this topic remain current for several years, or would it be rendered obsolete quickly by new technologies or subsequent studies?

Step 1: Questions submitted by participants

- Approximately 50 questions, 4 Buckets
  1. Comparative benefits and harms among the NOACs
  2. Comparative benefits and harms of NOACs versus Warfarin.
  3. Special clinical settings
  4. Not CER or out of scope

Within Group Comparisons

1. What are the comparative benefits and harms among the NOACs:
   - In patients with AF and other cardiac issues such as Intra-Cardiac Thrombus, Hypertrophic Cardiomyopathy, Heart Failure and Left Ventricular Dysfunction as defined by ejection fraction ≤40% and no current indication for anticoagulation
   - In patients with AF having procedures such as AF Ablation, Device Implantation, Hemofiltration and Dialysis
   - In patients with suspected or conformed Heparin-induced thrombocytopenia
   - In special population patients (geriatric, renal dysfunction) with atrial fibrillation?
   - In patients with atrial fibrillation, VTE and knee and hip replacement
   - In special population patients (geriatric, obese) who have undergone surgery for hip and knee replacement
   - In patients with For stroke prevention in atrial fibrillation differ when
     - (a) Stratified and reported in aggregate across a priori subgroups; and
     - (b) When data are analyzed at a patient level to create profiles of individuals with better (or worse) response to treatment
   - In women on oral contraceptives or hormone replacement therapy with a DVT
   - For stroke prevention in non-valvular atrial fibrillation in women over the age 75 and no prior history of stroke or TIA as represented by residual stroke risk?
   - For incident stroke prevention in non-valvular atrial fibrillation in males and females with no prior history of history of stroke or TIA and with 100kg body weight?

Within Group Comparisons

2. What is the clinical impact of sex-related differences in safety using the new oral anticoagulants in patients treated for VTE using the new oral anticoagulants?

NOACs versus Warfarin

3. What are the differences in thrombosis and bleeding rates between new oral anticoagulants (as a group or a specific agent) versus self monitored/telemedicine-adjusted warfarin?

- In patients with atrial fibrillation, VTE and knee and hip replacement
- In African-American, Asian American, Hispanic, and Native American patients with atrial fibrillation
- In patients with atrial fibrillation depending on their age bracket (roughly 35-54, 55-64, 65-74, 75-79, 80+)
- In patients with atrial fibrillation and end stage renal disease +/- dialysis (Warfarin vs. Apixaban 5 or 2.5)
- In patients with AF or history of venous thromboembolism on anticoagulation who are well controlled on a vitamin K antagonist defined as having a time in therapeutic range >65% for the past year.
- In patients with AF
    - Stratified by CHA2DS2-VASc score (0 = low, 1 = intermediate, 2 or higher = high)
    - Stratified by the quality of anticoagulation in patients currently on warfarin (% TTR, <55 = low, 55 - 65 = intermediate, and >65 = high)
- In Whites vs. non Whites (Blacks/Hispanic, and Asians)
- Warfarin in AF vs the NOAC in patients with CYP2C9 polymorphism (wild type vs. CYP2C9*2/CYP2C9*3)

NOACs versus Warfarin

4. What are the differences in thrombosis and bleeding rates in low body weight (i.e., < 60 kg) and high body weight (i.e., > 120 kg) patients with venous thromboembolism? Atrial fibrillation?

5. What are the risks of bleeding between new oral anticoagulants (as a group or a specific agent) versus each other and/or versus warfarin when added to aspirin and a P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) in patients with acute coronary syndromes requiring stent placement and an indication for therapeutic anticoagulation?

6. What are the comparative adherence rates amongst patients with AF, DVT, VTE on warfarin versus NOACs in a real world setting and what is the impact of adherence on harms and benefits such as stroke, systemic embolisms, bleeding events?

7. What patient characteristics or factors are associated with benefits or harms for a population with AF, DVT, or VTE that switch from warfarin to a NOACs?

Special Settings

8. What are the comparative safety and effectiveness of standardized perioperative strategies (stopping warfarin and bridging with enoxaparin OR switching to NOAC temporarily OR stopping NOAC and restarting) for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

9. What are the most effective patient engagement strategies to encourage adherence/persistence to OAC therapy?

Special Settings

10. What is the impact of patient out-of-pocket costs for OACs on adherence/persistence?

11. What are the comparative benefits and harms of the NOACs compared to LMWHs for extended treatment in patients with venous thromboembolism and active cancer?

Step 2: Prioritization

- Please check your email. You will receive a link to a prioritization exercise.
- You will see the newly revised questions discussed this morning. Please rank the questions in order of priority, with 1 being highest.
- Once you have completed the prioritization exercise, you may leave for lunch.
- We will resume our discussion by 1pm.

LUNCH

12:15pm – 1:00pm

Results from Step 2 Prioritization

What are the most effective patient engagement strategies to encourage adherence/persistence to long-term OAC therapy

Results

- Does dose adjustment (using blood levels and/or measures of renal function) improve bleeding rates for patients prescribed NOACs?

- How do 3 strategies (continuing treatment at same dose, reducing dose, or stopping treatment) compare for patients who have been on an anticoagulant for at least 6 months after an episode of DVT or PE?

- What are the comparative safety and effectiveness of standardized perioperative strategies (stopping warfarin and bridging with enoxaparin OR switching to NOAC temporarily OR stopping NOAC and restarting) for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

- What are the comparative benefits and harms of the NOACs compared to LMWHs for extended treatment in patients with venous thromboembolism and active cancer?

- Is the initial use of a NOAC as effective as initial treatment with a heparin for the acute treatment of DVT or PE?

- Other: important topic not included in this list.

Step 3: Question Refinement

- What are the challenges raised in conducting research on these questions, and how might those challenges be addressed?
- What is the most appropriate study design? What are the advantages and disadvantages of particular designs?
- Is there ongoing work in this area that PCORI should consider? If so, how could PCORI best fund research to complement this work?

PCORI Methodology Standards for PCOR: Standards for Formulating Research Questions

- **RQ-3 Identify specific populations and health decision(s) affected by the research.** Describe: 1) the specific health decision the research is intended to inform; 2) the specific population for whom the health decision is pertinent; and 3) how study results will inform the health decision.
- **RQ-4 Identify and assess participant subgroups.** Identify participant subgroups of interest and, where feasible, design the study with adequate precision and power to reach conclusions specific to these subgroups.
- **RQ-5 Select appropriate interventions and comparators.** Comparator treatment(s) must be chosen to enable accurate evaluation of effectiveness or safety compared to other viable options for similar patients. Describe how the chosen comparator(s) define the causal question, reduce the potential for biases, and allow direct comparisons.
- **RQ-6 Measure outcomes that people representing the population of interest notice and care about.** Identify and include outcomes the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform an identified health decision.

Closing remarks

- Meeting summary will be distributed in a few weeks
- Prioritized questions and deliberations from workshop will be shared with PCORI leadership
- PCORI governance will determine next steps

Thank You

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