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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Stroke Prevention in Atrial Fibrillation
Patients: A Systematic Review Update

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking
scientific information submissions from the public. Scientific information is being
solicited to inform our review of *Stroke Prevention in Atrial Fibrillation Patients: A
Systematic Review Update,* which is currently being conducted by the AHRQ's
Evidence-based Practice Centers (EPC) Program. Access to published and
unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE
OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: SEADS@epc-src.org.
Print submissions:
Mailing Address:
Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator

PO Box 69539

Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):

Portland VA Research Foundation

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3710 SW U.S. Veterans Hospital Road

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FOR FURTHER INFORMATION CONTACT:

Ryan McKenna, Telephone: 503-220-8262 ext. 51723 or Email: SEADS@epc-src.org.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for *Stroke Prevention in Atrial Fibrillation Patients: A Systematic Review Update*. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Stroke Prevention in Atrial Fibrillation Patients: A Systematic Review Update*, including those that describe adverse events. The entire research protocol, including the key questions, is also

available online at: https://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=2481

This is to notify the public that the EPC Program would find the following information on *Stroke Prevention in Atrial Fibrillation Patients: A Systematic Review Update* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
  - *For completed studies that do not have results on ClinicalTrials.gov*, please provide a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
- *A list of ongoing studies that your organization has sponsored for this indication.* In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute ALL Phase II and above clinical trials sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution will be very beneficial to the EPC Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at:
https://www.effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

The Key Questions

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

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

III. 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

Contextual Question

What are currently available shared decision-making tools for patient and provider use for stroke prophylaxis in atrial fibrillation, and what are their relative strengths and weaknesses?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings)

Populations:

Inclusion

I. Humans

II. Adults (age ≥18 years of age)

III. Patients with nonvalvular AF (including atrial flutter):

    A. Paroxysmal AF (recurrent episodes that self-terminate in less than 7 days)

    B. Persistent AF (recurrent episodes that last more than 7 days until stopped)

    C. Permanent AF (continuous)

    D. Patients with AF who experience acute coronary syndrome

IV. Subgroups of interest for KQ3 include (but are not limited to):

    A. Age

    B. Sex

    C. Race/ethnicity

    D. Presence of heart disease

    E. Type of AF

    F. Comorbid conditions (such as moderate to severe chronic kidney disease (eGFR<60), dementia)

    G. When in therapeutic range

    H. When non-adherent to medication

    I. Previous thromboembolic event

    J. Previous bleed

    K. Pregnant

Exclusion

Patients who have known reversible causes of AF (including but not limited to postoperative, hyperthyroidism)

All subjects are <18 years of age, or some subjects are under <18 years of age but results are not broken down by age

Intervention:

Inclusion

KQ 1: Clinical and imaging tools and associated risk factors for assessment/evaluation of thromboembolic risk:

    I. Clinical tools include:

        A.   CHADS2 score

        B.   CHADS2-VASc score

        C.   Framingham risk score

        D.   ABC stroke risk score

   II. Individual risk factors include:

        A.   INR level

        B.   Duration and frequency of AF

        C.   Age

        D.   Prior stroke

        E.   Type of AF

        F.   Cognitive impairment

        G.   Falls risk

        H.   Presence of heart disease

        I.   Presence and severity of CKD

        J.   DM

        K.   Sex

        L.   Race/ethnicity

        M.   Cancer

        N.   HIV

  III. Imaging tools include:

        A.   Transthoracic echo (TTE)

        B.   Transesophageal echo (TEE)

C. CT scans

D. Cardiac MRIs

KQ 2: Clinical tools and individual risk factors for assessment/evaluation of intracranial hemorrhage bleeding risk:

I. Clinical tools include:
   A. HAS-BLED score
   B. HEMORR2HAGES score
   C. ATRIA score
   D. Bleeding Risk Index
   E. ABC Bleeding Risk score

II. Individual risk factors include:
   A. INR level
   B. Duration and frequency of AF
   C. Age
   D. Prior stroke
   E. Type of AF
   F. Cognitive impairment
   G. Falls risk
   H. Presence of heart disease
   I. Presence and severity of CKD
   J. DM
   K. Sex
   L. Race/ethnicity
   M. Cancer
   N. HIV

KQ 3: Anticoagulation, antiplatelet, and procedural interventions:

I. Anticoagulation therapies:
   A. VKAs: Warfarin
   B. Newer anticoagulants (direct oral anticoagulants [DOACs])

    i. Direct thrombin Inh-DTI: Dabigatran

    ii. Factor Xa inhibitors:

      a. Rivaroxaban

      b. Apixaban

      c. Edoxaban

II. Antiplatelet therapies:

 A. Clopidogrel

 B. Aspirin

 C. Dipyridamole

 D. Combinations of antiplatelets

    i. Aspirin+dipyridamole

III. Procedures:

 A. Surgeries (e.g., left atrial appendage occlusion, resection/removal)

 B. Minimally invasive (e.g., Atriclip, LARIAT)

 C. Transcatheter (WATCHMAN, AMPLATZER, PLAATO)

Exclusion

None

Comparator:

Inclusion

KQ 1: Other clinical or imaging tools listed for assessing thromboembolic risk

KQ 2: Other clinical tools listed for assessing bleeding risk

KQ 3: Other anticoagulation therapies, antiplatelet therapies, or procedural interventions for preventing thromboembolic events

Exclusion

For KQ 3, studies that did not include an active comparator

Outcomes:

Inclusion

    I. Assessment of clinical and imaging tool efficacy for predicting thromboembolic risk and bleeding events (KQ1 and 2):

        A.   Diagnostic accuracy efficacy

        B.   Diagnostic thinking efficacy (defined as how using diagnostic technologies help or confirm the diagnosis of the referring provider)

        C.   Therapeutic efficacy (defined as how the intended treatment plan compares with the actual treatment pursued before and after the diagnostic examination)

        D.   Patient outcome efficacy (defined as the change in patient outcomes as a result of the diagnostic examination)

Patient-centered outcomes for KQ3 (and for KQ1 [thromboembolic outcomes] and KQ2 [bleeding outcomes] under "Patient outcome efficacy"):

    II. Thromboembolic outcomes:

        A.   Cerebrovascular infarction

        B.   TIA

        C.   Systemic embolism (excludes PE and DVT)

    III. Bleeding outcomes:

        A.   Hemorrhagic stroke

        B.   Intracerebral hemorrhage

        C.   Extracranial hemorrhage

        D.   Major bleed (stratified by type and location)

        E.   Minor bleed stratified by type and location)

    IV. Other clinical outcomes:

        A.   Mortality

            i.   All-cause mortality

            ii.   Cardiovascular mortality

        B.   Myocardial infarction

        C.   Infection

D.   Heart block

E.   Esophageal fistula

F.   Cardiac tamponade

G.   Dyspepsia

H.   Health-related quality of life

I.   Functional capacity

J.   Health services utilization (e.g., hospital admissions, outpatient office visits, ER visits, prescription drug use)

K.   Long-term adherence to therapy

L.   Cognitive function

Exclusion

Study does not include any outcomes of interest

Timing:

Inclusion

Timing of follow-up not limited

Exclusion

None

Settings:

Inclusion

Impatient and outpatient

Exclusion

None

Study design:

Inclusion
    I. Original peer-reviewed data
    II. N ≥ 20 patients
    III. RCTs, prospective and retrospective observational studies

Exclusion

Not a clinical study (e.g., editorial, nonsystematic review, letter to the editor, case series, case reports)

Abstract-only or poster publications; articles that have been retracted or withdrawn

Because studies with fewer than 20 subjects are often pilot studies or studies of lower quality, we will exclude them from our review.

Systematic reviews, meta-analyses, or methods articles (used for background and component references only)

Language:

Inclusion
    I. English-language publications
    II. Published on or after August 1, 2011

Exclusion
Non-English-language publications

Relevant systematic reviews, meta-analyses, or methods articles (will be used for background only)

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