Results of Topic Selection Process & Next Steps

The nominator, ACOG is interested in a new evidence review on Evaluation and management of headaches in pregnancy to develop a new clinical practice guideline.

This topic will go forward for refinement as a new systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase. When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to https://effectivehealthcare.ahrq.gov/email-updates.

Topic Brief

Topic Number and Name: #0817, Evaluation and management of headaches in pregnancy

Nomination Date: 9/5/2018

Topic Brief Date: 2/7/2019

Authors
Jill Huppert
Robin Paynter

Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.
Background

When a pregnant patient presents with a headache, the clinician must first distinguish between a primary headache (when pain is the disease) from a secondary headache (when pain is a symptom of another disease). The primary decisional dilemma is how to make this diagnosis so to begin correct therapy. Primary headache disorders are classified as migraines (acute, chronic), tension headaches or cluster headaches. In pregnant women, secondary headaches may arise from pre-eclampsia/eclampsia or during the postpartum period from anesthesia (post-dural puncture headache) or changes in hormones, hydration, and sleep patterns. In any woman, serious secondary causes can include neurologic emergencies such as intracranial hemorrhage, cerebral venous thrombosis, and pituitary apoplexy.

Headaches are common in pregnancy. In US and international studies, 12-29% of pregnant women met migraine diagnostic criteria, and another 10-16% reported non-migraine headaches. While these headaches are benign, they take a toll on quality of life. Migraine headaches have been associated with some poor outcomes in pregnancy. Post-dural puncture headaches (PDPH) are also common: one third of women in the US have a cesarean section, and most of these are receive spinal anesthesia. Up to 30% of these develop PDPH, which is the third most common reason for obstetric claims against anesthesiologists. Even without cesarean section, most women have some type of epidural anesthesia during labor. Although the incidence of accidental dural puncture is less than 1% after epidural anesthesia, more than half of those women develop PDPH. PDPH is notoriously unresponsive to pain medications, and can interfere with maternal-newborn bonding and increase the length of hospitalization. The standard treatment has been a second procedure (epidural blood patch).

Although most headaches during pregnancy are benign, they can also be an indication that a woman is suffering from a dangerous etiology that requires emergent intervention. For example, 2-10% of pregnant women develop preeclampsia, which requires careful management to avoid harm to the mother and child. Headaches can be a symptom that predicts preeclampsia. Cerebral venous thrombosis is another rare but serious outcome that can cause headaches.

There are two significant clinical decisional dilemmas: first, clinicians need guidance on how to quickly and accurately diagnose whether a headache is due to a serious etiology, while weighing the risks and benefits of available imaging and diagnostic tests in pregnancy and guidance is lacking. Secondly, clinicians need guidance on the relative benefits and harms of treatment options for primary headaches to improve the quality of life for pregnant women, but guidance is lacking.

ACOG has not written any guidelines, committee opinions or practice bulletins for any headache topics. The AAP/ACOG “Guidelines for perinatal Care. 2017” mentions headache as a complication of infection, pre-eclampsia, and neuroaxial anesthesia, but does not mention diagnosis, prevention or treatment. The American Headache Society has not published any guidance for pregnant women. Their three recent guidelines based on their own reviews do not mention pregnant women: migraine prophylaxis in 2015, pharmacologic treatment of acute migraine in the emergency department in 2016, and treatment of cluster headache.

Nominator and Stakeholder Engagement
The nominator (ACOG) is responsive and engaged, and has agreed to the proposed scope.

Key Questions and PICOTs
The key questions for this nomination are:
1. In pregnant women, what is the diagnostic accuracy of instruments or imaging used to identify [rule out] serious underlying secondary causes of headache?

2. What are the harms, effectiveness, and comparative effectiveness and harms of treatments for headache in pregnancy?
   a. By headache type:
      i. migraines (acute, chronic)
      ii. tension headaches
      iii. cluster headaches
      iv. postpartum headaches
      v. pre-eclampsia headaches
      vi. suspected medication overuse or withdrawal (analgesics)
   b. Within each subtype, does effectiveness differ for new onset vs. pre-existing headaches?

3. What are the harms, effectiveness, and comparative effectiveness of interventions to prevent headache in pregnancy?
   a. By headache type:
      i. migraines (acute, chronic)
      ii. tension headaches
      iii. cluster headaches
      iv. postpartum headaches
   b. Within each subtype, does effectiveness differ for new onset vs. pre-existing headaches?

The contextual question is: how should diagnostic tests or treatment algorithms be modified in the pregnant woman?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, outcomes, timing, and setting (PICOTS) of interest (Table 1).
<table>
<thead>
<tr>
<th>Key Questions</th>
<th>KQ1: diagnosis of serious etiology</th>
<th>KQ2: treatment</th>
<th>KQ3: prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Pregnant and postpartum women with new and existing headaches</td>
<td>Pregnant and postpartum women with:</td>
<td>Pregnant and postpartum women with:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Migraine</td>
<td>- Migraine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Tension</td>
<td>- Tension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cluster</td>
<td>- Cluster</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Postpartum</td>
<td>- Postpartum</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- With preeclampsia and headache</td>
<td>- With preeclampsia and headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Analgesic medication overuse or withdrawal</td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>Diagnostic tests/instruments, Assessment plus imaging (CT, MRI, MRV, MRA)</td>
<td>Pharmacologic</td>
<td>Pharmacologic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- acetaminophen, anti-emetics, antihistamines, caffeine, magnesium, NSAIDs, OTC analgesic,</td>
<td>- verapamil, prednisolone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- triptans, narcotics, butalbital</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-pharmacologic (hydration, physiotherapy, others)</td>
<td>Non-pharmacologic (hydration, physiotherapy, others)</td>
</tr>
<tr>
<td>Comparators</td>
<td>Other test, no test, Assessment without imaging, usual care?</td>
<td>Other treatment, Placebo, No intervention</td>
<td>Other treatment, Placebo, No intervention</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Urgent etiology</td>
<td>Symptom severity, Resolution</td>
<td>Occurrence rate/frequency, Symptom severity</td>
</tr>
<tr>
<td></td>
<td>- Intracranial hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Increased intracerebral pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Cerebral venous thrombosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Pituitary apoplexy (Sheehan’s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Pre-rupture, expanding cerebral aneurysm</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Seizure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Setting</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
</tbody>
</table>
Methods

We assessed nomination #0817, Evaluation and management of headaches in pregnancy, for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criterion determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

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.

Desirability of New Review/Duplication
We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

Impact of a New Evidence Review
The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review
We conducted a literature search in PubMed from December 2013 to December 2018. Because of the low return, the librarian validated the search strategy, using a list of the citations from two of the most recent reviews. The search found all of them so for a feasibility search strategy it is robust. We then supplemented the librarian search strategy by with the simplified search strategy recommended by Rice et al. We searched PubMed for “similar articles” using the four SR and five trials identified by the librarian search. We reviewed all identified titles and abstracts for inclusion and classified identified studies by key question and study design to assess the size and scope of a potential evidence review. See Appendix C for the PubMed search strategy, validation citations, and simplified search strategy strings, as well as the ClinicalTrials.gov search.

Value
We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.
Results

See Appendix A for detailed assessments of all EPC selection criteria.

Appropriateness and Importance
This is an appropriate and important topic. Headaches in pregnancy are common. Women need safe and effective treatment of primary headaches to improve quality of life. Women need prompt diagnosis of rare but serious etiologies to avoid serious consequences.

Desirability of New Review/Duplication
A new evidence review would not be duplicative of an existing evidence review. We found no up-to-date systematic reviews for the key questions. We found several non-systematic reviews as background. See Table 2, Duplication column.

For KQ1 (diagnosis) we found only one SR on the diagnosis of cerebral venous thrombosis during pregnancy. This review is of uncertain quality, as it included case series and case reports, with a total of only 66 patients for metaanalysis. The literature search date ended September 2016.

For KQ2 (treatment), we found four SRs, each with limitations and outdated literature searches:

- Carstairs et al (2016) addressed effects of ondansetron (an anti-emetic) on birth defects. However, the search end date was November 2015, and HA indication was not mentioned. Ondansetron is used in non-pregnant women for nausea associated with migraine.
- Basurto et al (2015) published a good quality Cochrane review of pharmacotherapy to treat PDPH, and included a subset of pregnant women. However, the search ended July 2014.
- Alavero et al (2016) was a good quality Cochrane review of posture and fluids for PDPH, however, the review included only one study with obstetric participants (n=80), and the search ended February 2015.
- Marchenko et al (2015) reviewed the reproductive safety of triptans for migraine, and included a meta-analysis. However, the search ended in “2014.”

For KQ3 (prevention), we found 2 reviews, both on post-dural puncture headache (PDPH).

- Park et al (2018) compared the effect of bedrest to early ambulation on incidence of PDPH, but it was unclear if they included pregnant women in their strategy. Despite the recent publication, the literature search ended in “2014.”
- Lee et al (2018) compared the type of spinal needle used in women undergoing cesarean section with no initial limitation on dates; however, the end of the search date was not specified. The authors were contacted.

We found no review protocols in the PROSPERO database.

Impact of a New Evidence Review
A new systematic review may have moderate level of impact. There is a lack of current guidance. Practice patterns are difficult to determine.

ACOG has not written any guidelines, committee opinions or practice bulletins for any headache topics. The AAP/ACOG “Guidelines for perinatal Care. 2017” mentions headache as a complication of infection, pre-eclampsia, and neuroaxial anesthesia, but does not mention diagnosis, prevention or treatment. The American Headache Society has not published any guidance for pregnant women. Their three recent guidelines based on their own reviews do not
mention pregnant women: migraine prophylaxis in 2015, pharmacologic treatment of acute migraine in the emergency department in 2016, and treatment of cluster headache.

Feasibility of a New Evidence Review
A new evidence review may be feasible for KQ2 if the outcome of interest focuses on harms, especially for migraine treatment, and for KQ3 if the intervention of interest is prevention of PDPH.

KQ1: not feasible
We found no observational or randomized studies on KQ1 (diagnosis) in the last 5 years. The yield might be higher if dates were expanded, however, it is unlikely that any diagnostic studies that focus on pregnant women will be discovered. Several non-systematic reviews suggest that this evidence is limited and expert opinion will continue. We found no protocols in progress in PROSPERO, and no trials registered at clinicaltrials.gov.

KQ2: harms may be feasible for migraine only; effectiveness is not feasible
For KQ2, the librarian search limited to randomized or pragmatic trial designs identified 121 citations, of which 2 (2%) were relevant. The “similar articles” search in PubMed produced an additional 69 citations with relevant titles, from which we identified 18 citations. All of these were observational treatment studies that focused on three medication classes: triptans (9), NSAIDS (6), and a single anti-emetic (ondansetron (2)). None of these reported on effectiveness, all outcomes were maternal and fetal safety and harms. We found no protocols in progress in PROSPERO, and a single completed registry (for triptans) in clinicaltrials.gov.

The yield will be higher for KQ2 if the dates are expanded, if each drug name is included in the search string, if observational trial designs are included, and if additional databases are used. We found no mention of cluster, tension, postpartum, or medication use headaches in these results, which suggests that this topic could be further restricted to migraine therapy.

KQ3: prevention is only feasible for post-dural puncture headache.
The librarian search yielded three citations (one observational and two RTC) The simplified search strategy identified an additional four RCTs and two more observational studies. All of these focused on prevention of PDPH. We found no studies on prevention of migraine, no protocols in progress in PROSPERO, and no trials registered at clinicaltrials.gov.

Not surprisingly, there was a similar low yield for clinical trials. The search of clinicaltrials.gov yielded 102 citations, but after title and abstract review, only six pertained to pregnancy and headache. Four are reported as complete, with no results listed on the website.

See Table 2, Feasibility column.

Table 2. Key Questions and Results for Duplication and Feasibility

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 1: Diagnosis</td>
<td>Total number of identified systematic reviews: 1 Diagnosis of CVT</td>
<td>Size/scope of review Relevant Studies Identified: 0 Clinicaltrials.gov • Recruiting: 0 • Active: 0 • Complete: 0</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------------------</td>
<td>--------------------------------</td>
</tr>
</tbody>
</table>
| KQ 2: Treatment | Total number of identified systematic reviews: 4 (outdated)  
Medication (PDPH) 17  
Posture/fluid (PDPH) 19  
Triptans (migraine) 18  
Ondansetron (antiemetic) 16 | Size/scope of review  
Relevant Studies Identified:  
• RCT: 0  
• Observational: 20 25-40, 49-52 |
| KQ 3: Prevention | Total number of identified systematic reviews: 2 (unsure dates)  
Prevention of PDPH 20, 21 | Size/scope of review  
Relevant Studies Identified:  
• RCT (PDPH): 6 3, 42-46  
• Observational: 3 41, 47, 48 |

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question, PDPH=postdural puncture headache, RCT=randomized controlled trial; CVT=cerebral venous thrombosis

**Value**
The potential for value is moderate as the nominator (ACOG) is planning to write a guideline. The organization is well respected with high potential to influence practice. However, current practice patterns are unknown.

**Summary of Findings**

- **Appropriateness and importance:** The topic is both appropriate and important, as headaches are common, and medication side effects are worrisome to patients and providers.
- **Duplication:** A new review would not be duplicative of an existing product. We found no recent existing systematic reviews for any key question.
- **Impact:** A new systematic review has moderate impact potential.
- **Feasibility:** A new review may be feasible if the KQs were modified. KQ1 is not feasible. KQ2 (Harms of migraine therapy) is feasible; effectiveness is not feasible. For KQ3, prevention of PDPH is feasible. The evidence base is likely small to medium.
- **Value:** The potential for value is moderate as the nominator is planning to write a guideline that could influence practice.
References
### Appendix A. Selection Criteria Assessment

<table>
<thead>
<tr>
<th>Selection Criteria</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Appropriateness</strong></td>
<td></td>
</tr>
<tr>
<td>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.?</td>
<td>Yes</td>
</tr>
<tr>
<td>1b. Is the nomination a request for a systematic review?</td>
<td>Yes</td>
</tr>
<tr>
<td>1c. Is the focus on effectiveness or comparative effectiveness?</td>
<td>Yes</td>
</tr>
<tr>
<td>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?</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>2. Importance</strong></td>
<td></td>
</tr>
<tr>
<td>2a. Represents a significant disease burden; large proportion of the population</td>
<td>12-29% of pregnant women have migraine, and another 10-16% reported non-migraine headaches; up to one third of women develop PDPH after obstetric anesthesia. These headaches impact quality of life. Medications in pregnancy may cause fetal and infant harms.</td>
</tr>
<tr>
<td>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</td>
<td>Yes</td>
</tr>
<tr>
<td>2c. Represents important uncertainty for decision makers</td>
<td>Yes</td>
</tr>
<tr>
<td>2d. Incorporates issues around both clinical benefits and potential clinical harms</td>
<td>Yes</td>
</tr>
<tr>
<td>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</td>
<td>No/ Not assessed</td>
</tr>
<tr>
<td><strong>3. Desirability of a New Evidence Review/Duplication</strong></td>
<td>No recent published systematic reviews cover any of the KQ</td>
</tr>
<tr>
<td>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)</td>
<td></td>
</tr>
<tr>
<td><strong>4. Impact of a New Evidence Review</strong></td>
<td>Current guidelines are based on expert opinion.</td>
</tr>
<tr>
<td>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)?</td>
<td>Unknown</td>
</tr>
<tr>
<td>4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>5. Primary Research</strong></td>
<td>The literature base is likely to be small, and based on observational study designs. The exception is that some RCTs exist for prevention and treatment of PDPH.</td>
</tr>
<tr>
<td>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)</td>
<td></td>
</tr>
<tr>
<td><strong>6. Value</strong></td>
<td>Yes</td>
</tr>
<tr>
<td>6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change</td>
<td>Yes</td>
</tr>
<tr>
<td>6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)</td>
<td>Yes. The nominator (ACOG) intends to use the SR to develop a guideline, with high potential to influence practice.</td>
</tr>
</tbody>
</table>

**Abbreviations:** AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question


49. Wood ME, Frazier JA, Nordeng HM, et al. Longitudinal changes in neurodevelopmental outcomes between 18 and 36 months in children with prenatal triptan exposure: findings from


Appendix B. Search for Evidence Reviews (Duplication)

Listed below are the sources searched, hierarchically

<table>
<thead>
<tr>
<th>Primary Search</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHRQ: Evidence reports and technology assessments</td>
<td>0</td>
</tr>
<tr>
<td><a href="https://effectivehealthcare.ahrq.gov/">https://effectivehealthcare.ahrq.gov/</a>;</td>
<td></td>
</tr>
<tr>
<td><a href="https://www.ahrq.gov/research/findings/ta/index.html">https://www.ahrq.gov/research/findings/ta/index.html</a>;</td>
<td></td>
</tr>
<tr>
<td><a href="https://www.ahrq.gov/research/findings/evidence-based-reports/search.html">https://www.ahrq.gov/research/findings/evidence-based-reports/search.html</a></td>
<td></td>
</tr>
<tr>
<td>VA Products: PBM, and HSR&amp;D (ESP) publications, and VA/DoD EBCPG Program</td>
<td>0</td>
</tr>
<tr>
<td><a href="https://www.hsrd.research.va.gov/publications/.esp/">https://www.hsrd.research.va.gov/publications/.esp/</a></td>
<td></td>
</tr>
<tr>
<td>Cochrane Systematic Reviews</td>
<td>2</td>
</tr>
<tr>
<td><a href="http://www.cochranelibrary.com/">http://www.cochranelibrary.com/</a></td>
<td>17, 19</td>
</tr>
<tr>
<td>HTA (CRD database): Health Technology Assessments</td>
<td>0</td>
</tr>
<tr>
<td><a href="http://www.crd.york.ac.uk/crdweb/">http://www.crd.york.ac.uk/crdweb/</a></td>
<td></td>
</tr>
</tbody>
</table>

Secondary Search

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochrane Protocols</td>
<td>0</td>
</tr>
<tr>
<td><a href="http://www.cochranelibrary.com/">http://www.cochranelibrary.com/</a></td>
<td></td>
</tr>
<tr>
<td>PROSPERO Database (international prospective register of systematic reviews and protocols)</td>
<td>0</td>
</tr>
<tr>
<td><a href="http://www.crd.york.ac.uk/prospero/">http://www.crd.york.ac.uk/prospero/</a></td>
<td></td>
</tr>
</tbody>
</table>

Tertiary Search

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed</td>
<td>5</td>
</tr>
<tr>
<td><a href="https://www.ncbi.nlm.nih.gov/pubmed/">https://www.ncbi.nlm.nih.gov/pubmed/</a></td>
<td>6, 16, 18, 20, 21</td>
</tr>
</tbody>
</table>


Appendix C. Search Strategy & Results (Feasibility)

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to December 14, 2018
Date Searched: December 17, 2018
Searched by: Robin Paynter, MLIS

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pregnancy/ or Pregnancy Complications/ or Pregnancy Complications, Cardiovascular/ or Hypertension, Pregnancy-Induced/ or Pregnancy, High-Risk/ or Pregnant Women/ or Postpartum Period/ or Pregnancy Trimesters/ or Pregnancy Trimester, First/ or Pregnancy Trimester, Second/ or Pregnancy Trimester, Third/ or Pre-Eclampsia/</td>
<td>838652</td>
</tr>
<tr>
<td>2</td>
<td>(pregnancy or pregnancies or pregnant or eclamps* or gestation* or postpartum or postpartum or preeclamps* or pre-eclamps* or puerper* or ((gestat* or pregnan* or postpartum or post-partum or puerper*)) adj10 hypertens*).ti,ab,hw,kf.</td>
<td>1021452</td>
</tr>
<tr>
<td>3</td>
<td>or/1-2</td>
<td>1021452</td>
</tr>
<tr>
<td>4</td>
<td>headache/ or headache disorders/ or headache disorders, primary/ or migraine disorders/ or migraine with aura/ or migraine without aura/ or tension-type headache/ or cluster headache/ or *headache disorders, secondary/</td>
<td>53489</td>
</tr>
<tr>
<td>5</td>
<td>(headache* or migraine*).ti,ab,hw,kf.</td>
<td>105294</td>
</tr>
<tr>
<td>6</td>
<td>or/4-5</td>
<td>105294</td>
</tr>
<tr>
<td>7</td>
<td>and/3,6</td>
<td>4418</td>
</tr>
<tr>
<td>8</td>
<td>limit 7 to english language</td>
<td>3691</td>
</tr>
<tr>
<td>9</td>
<td>Diagnosis/ or early diagnosis/ or delayed diagnosis/ or (di or dg).fs. or (assess* or CT or diagnos* or imaging or instrument* or MRI or MRIs or MRV or MRVs or MRA or MRAs or test or tests or testing).ti,ab,kf.</td>
<td>8072726</td>
</tr>
<tr>
<td>10</td>
<td>and/8-9</td>
<td>1955</td>
</tr>
<tr>
<td>11</td>
<td>limit 10 to (adaptive clinical trial or clinical trial, all or clinical trial or controlled clinical trial or equivalence trial or pragmatic clinical trial or randomized controlled trial)</td>
<td>150</td>
</tr>
<tr>
<td>12</td>
<td>limit 11 to yr=&quot;2013 -Current&quot;</td>
<td>35</td>
</tr>
<tr>
<td>13</td>
<td>limit 10 to (meta analysis or systematic reviews)</td>
<td>87</td>
</tr>
<tr>
<td>14</td>
<td>limit 13 to yr=&quot;2015 -Current&quot;</td>
<td>29</td>
</tr>
<tr>
<td>15</td>
<td>Primary Prevention/ or Secondary Prevention/ or pc.fs. or (prevent* or verapamil or prednisolone or hydrat* or physiotherap*).ti,ab,kf.</td>
<td>2268250</td>
</tr>
<tr>
<td>16</td>
<td>and/7,15</td>
<td>787</td>
</tr>
</tbody>
</table>
### ClinicalTrials.gov
Date searched: December 17, 2018

( pregnant OR pregnancy OR pregnancies OR gestation OR post-partum OR postpartum OR pre-eclampsia OR puerper* OR perinatal OR peri-natal ) AND ( headache OR headaches OR migraine OR migraines ) AND INFLECT EXACT ( "Active, not recruiting" OR "Completed" ) [OVERALL-STATUS] = 102 studies

### Citations used to test/validate the search strategy (citations culled from the included studies lists in the Negro review (#1 below) and Wabnitz review (#3 below)):

**Similar article search strategy:**

Limit results to English language, pregnant and published after 2013

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
</tr>
</thead>
<tbody>
<tr>
<td>#28</td>
<td>Similar articles for PubMed (Select 25812804)</td>
</tr>
<tr>
<td>#26</td>
<td>Similar articles for PubMed (Select 23903901)</td>
</tr>
<tr>
<td>#25</td>
<td>Similar articles for PubMed (Select 23489333)</td>
</tr>
<tr>
<td>#23</td>
<td>Search (#22) AND pregnan* Filters: English</td>
</tr>
<tr>
<td>#22</td>
<td>Similar articles for PubMed (Select 24805878)</td>
</tr>
<tr>
<td></td>
<td>Search (#20) AND pregnan* Filters: English Sort by: PublicationDate</td>
</tr>
<tr>
<td>#21</td>
<td>PublicationDate</td>
</tr>
<tr>
<td>#20</td>
<td>Similar articles for PubMed (Select 26176166)</td>
</tr>
<tr>
<td>#19</td>
<td>Similar articles for PubMed (Select 25644494)</td>
</tr>
<tr>
<td>#18</td>
<td>Search (#17) AND pregnan* Filters: English Sort by: PublicationDate</td>
</tr>
<tr>
<td>#17</td>
<td>Similar articles for PubMed (Select 26939384)</td>
</tr>
<tr>
<td>#15</td>
<td>Search (#14) AND pregnan* Filters: English</td>
</tr>
<tr>
<td>#14</td>
<td>Similar articles for PubMed (Select 28274514)</td>
</tr>
<tr>
<td>#13</td>
<td>Search #10 Filters: English Sort by: PublicationDate</td>
</tr>
<tr>
<td>#10</td>
<td>Similar articles for PubMed (Select 28678882)</td>
</tr>
</tbody>
</table>

**Original nomination**
A topic nomination was submitted on the EHC website:

Submitted on Wednesday, September 5, 2018 - 09:52

==Topic Suggestion==
1. Describe your topic: Our topic nomination is Headaches in Pregnancy. The following is a list of clinical questions practitioners consider when managing such cases:
   a. Which headache symptoms require prompt/urgent evaluation?
   b. When is imaging indicated for headaches during pregnancy?
   c. What are the treatment options for migraine during pregnancy (include both acute and preventative treatment)?
   d. What are the treatment options for tension or cluster headaches during pregnancy?
   e. How is medication overuse headache diagnosed and treated?
   f. How should headache associated with preeclampsia be evaluated and treated?
   g. How should postpartum headache be evaluated and treated?
   h. When is screening for depression warranted in the workup of headaches?

The population of interest includes pregnant patients with headaches (general, tension, cluster) or migraines. The interventions we would like to know more about include prophylactic drug intervention (verapamil, prednisolone) for cluster headaches, physiotherapy or OTC analgesics for tension headaches, MRI or CT imaging for general headaches, and preventive measures (hydration, avoidance of precipitants) or acute treatment options (paracetamol, anti-emetics, NSAIDs) for migraines. The outcomes include recurrence, rate or severity of headaches or migraines.

==Importance of Suggested Topic==
2. Describe why this topic is important: This is an important topic for review because although headaches during pregnancy can be benign, they can also be an indication that a woman is suffering from a more dangerous condition such as a stroke, hemorrhage, eclampsia, or cerebral venous thrombosis. Clinicians need guidance on how to quickly, accurately identify whether a woman is suffering from one of these more serious issues. Additionally, pregnant women more commonly suffer from migraines and tension headaches which can be unpleasant to manage while pregnant. Guidance on treatment options for these conditions is needed to improve the quality of life for pregnant women.

3. Tell us why you are suggesting this topic: We are nominating the topic of headaches in pregnancy because evidence based guidance on diagnosis and treatment options for migraines, tension headaches, and cluster headaches are needed to ensure clinicians are appropriately prepared to care for pregnant women with these conditions.

Target date:

==Impact of a New Evidence Report==
4. Describe what you are doing currently and what you are hoping will change because of a new evidence report.: ACOG is currently working on new clinical guidance in the form of a Practice Bulletin on Headaches in Pregnancy. We hope that a new evidence report will provide more definitive information on treatment options for the different types of headaches pregnant women may experience, to improve their overall health and wellbeing.

5. How will you or your group use the information from a new evidence report? A new evidence report on headaches in pregnancy will be used to develop future clinical guidance in the form of Practice

C-1
Bulletins or Committee Opinions on this topic. Clinicians will then be better qualified to identify, make appropriate treatment decisions, and improve health outcomes for pregnant women with headaches.

6. How would you or your group plan to disseminate information from the report? Who would you plan to disseminate it to? ACOG will share the information in this report with its 57,000 members through our website, and will update our clinical guidance to be reflective of the findings from this report.

==Other Stakeholders Who Could Use a New Evidence Report==
7. Do you know of organizations that could use an evidence report to change clinical practice? Are you a part of, or have you been in contact with, any organizations that might implement the research findings of an evidence report? International Headache Society, American Headache Society, American College of Physicians, Society for Maternal-Fetal Medicine, Society for Academic Specialists in General Obstetrics and Gynecology

8. Would you be willing to partner with another organization to develop policy, program, guidelines, or dissemination and implementation materials? This information is for internal discussion only and will not be displayed on the EHC Program Web site.: Yes

==Supporting Document==
Upload Document:
Title or short description:
Comments or notes about this file:

==Information About You==
Provide a description of your role or perspective: Professional society
If you are you making a suggestion on behalf of an organization, please state the name of the organization: The American College of Obstetricians and Gynecologists
Please tell us how you heard about the Effective Health Care Program: AHRQ Alert/Correspondence
First name: Virginia
Last name: Andrews
Title: Program Assistant
Email address: vandrews@acog.org
May we contact you if we have questions about your nomination? Yes

The results of this submission may be viewed at:
https://effectivehealthcare.ahrq.gov/node/16119/submission/5979