Effective Health Care

Maternal Risk Assessment Tools for Venous Thromboembolism

Results of Topic Selection Process & Next Steps

The nominator, Association of Women's Health Obstetrical and Neonatal Nurses (AWHONN), is interested in a new evidence review on maternal risk assessment tools for venous thromboembolism in order to develop a new guideline.

We found few research articles addressing risk assessment tools in pregnant women. Because of this limited evidence base, a new review is not feasible at this time. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Name: Maternal risk assessment tools for venous thromboembolism, #0771

Nomination Date: 03/01/2018

Topic Brief Date: 04/23/2018

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

Summary

- This nomination meets the selection criteria of appropriateness and importance, duplication, and value.
- Feasibility is limited due to the small number of primary research articles. A variety of assessment tools are presented, and few of these are validated, which would limit comparability.

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Background

Venous thromboembolism (VTE) in pregnancy is one of the most significant causes of maternal morbidity and mortality in the United States; the pooled overall incidence of pregnancy-related VTE was 1.2 per 1000 deliveries. **(Kourlaba et al. 2016)** With about 4 million births/year in the USA[1], this correspond to 4800 cases of VTE and 32 maternal deaths per year. Mortality is a rare but serious outcome; other more common outcomes are morbidity and resource use.

VTE in pregnancy is preventable with early risk identification. Once high-risk women are identified, appropriate prophylaxis can be started. Clinicians rely on existing clinical practice guidelines from the American College of OBGYN (ACOG) and the American College of Chest Physicians (ACCP).**(Bates et al. 2012)** However, these guidelines are based on expert opinion and differ greatly. For example, a recent paper showed that under ACOG guidelines, 1.0% of patients would receive post-caesarean pharmacologic prophylaxis [95% confidence interval (CI) 0.3-3.0%) compared with 34.8% of patients under ACCP guidelines (95% CI 29.6-40.4%) **(Palmerola et al. 2016)**. Another showed that even when a site accepts the ACCP guidance, compliance is low: of 32% identified with a risk factor, only 1% were given prophylactic anticoagulation. **(Alsayegh et al. 2016)**

Because of this uncertainty, clinicians need a review of existing VTE risk assessment tools (also called "scores") to improve timely identification of pregnant and postpartum women at risk for VTE.

Nominator and Stakeholder Engagement: AWHONN representatives confirmed that they wanted a systematic review, and endorsed the suggested PICOTs. At this time, they are not interested in working with other partners.

The **key questions** for this nomination are:

1. What is the effectiveness of VTE risk assessment tools to identify pregnant and postpartum women at increased risk of VTE?
    a. Does effectiveness differ with pregnancy period (preconception, antenatal, intrapartum, postpartum)

2. What are the harms of VTE risk assessment tools when used in pregnant and postpartum women at increased risk of VTE?

3. What is the comparative effectiveness of VTE risk assessment tools to identify pregnant and postpartum women at increased risk of VTE?

4. What are the comparative harms of VTE risk assessment tools when used in pregnant and postpartum at increased risk of VTE?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, outcomes, timing, and setting (PICOTS) of interest (Table 1).

[1] https://www.statista.com/statistics/195908/number-of-births-in-the-united-states-since-1990/

Table 1. Key Questions (KQ) and PICOTS

PICOTS	KQ	
Population:	KQ 1-4	Women of childbearing age (preconception appointment), pregnant women, and those up to 6 weeks postpartum
Intervention(s):	KQ 1-4	VTE risk assessment tool (or score)
Comparator(s):	KQ 1-2	• No VTE risk assessment tool, usual care
	KQ 3-4	• Other VTE risk assessment tool
Outcome(s):	KQ 1, KQ 3	• Sensitivity • Specificity • Positive predictive value • Number needed to treat
	KQ 2, KQ 4	• Unnecessary treatment • Medication side effects • Resource use • Number needed to harm
Timing:	KQ 1-4	• From preconception appointment through 6 weeks postpartum
Setting	KQ 1-4	• Any

Abbreviations: VTE: venous thromboembolism

Methods

We assessed nomination, maternal risk assessment tools for venous thromboembolism, # 0771, for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria (Appendix A). Assessment of each criterion determined the need for evaluation of the next one.

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 initially conducted a literature search in PubMed from March 2013 to March 2018. Due to the limited yield we also used a simplified search strategy to extend the search **(Rice et al. 2017)**. We entered four citations into PubMed and used the "similar article feature" to identify additional articles with no date restrictions. We reviewed all identified titles and abstracts for inclusion and classified them by study design, to assess the size and scope of a potential evidence review.

See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search.

Compilation of Findings
We constructed a table with the selection criteria and our assessments (Appendix A).

Results

Appropriateness and Importance
This is an appropriate and important topic. In one recent study, the pooled overall incidence of pregnancy-related VTE was 1.2 per 1000 deliveries. The pooled VTE case fatality rate was 0.68% and the recurrence rate was 4.27%. The pooled risk of major bleeding was 1.05%. Post-thrombotic syndrome seemed to have a negative effect on quality of life. **(Kourlaba et al. 2016)**

With about 4 million births/year in the USA[2], this corresponds to 4800 cases of VTE and 32 maternal deaths per year. The CDC estimates that about 9% of maternal deaths are attributable to complications from VTE. Mortality is a rare but serious outcome; other more common outcomes are morbidity and resource use. These serious outcomes are preventable if women are identified and given prophylactic anticoagulation therapy.

Desirability of New Review/Duplication
A new evidence review on maternal risk assessment tools for venous thromboembolism would not be duplicative of an existing product. We found only one systematic review that addressed prevention of in venous thromboembolism pregnancy, but this review is likely outdated (2014) and did not describe risk assessment tools.**(Bain et al. 2014)** We found no systematic reviews of VTE risk assessment tools for any population. See Table 2, Duplication column.

Impact of a New Evidence Review
A new systematic review on Maternal risk assessment tools for venous thromboembolism may have a moderate level of impact. Current guidance is inconsistent and based on limited, observational data. **(James and Committee on Practice 2011 (2017)) (Bates et al. 2012)** An expert consensus recommends that all hospitals use a risk assessment tool. **(D'Alton et al. 2016)**These authors propose using modifications of the Caprini and Padua scores which are validated in non-pregnant medical and surgical populations. However, these modified scores have not been validated. This guidance is difficult to follow in clinical practice.

Feasibility of a New Evidence Review
A new evidence review examining Maternal risk assessment tools for venous thromboembolism may not be feasible. The initial Pubmed search identified two potential original research articles, plus two recent guidance papers. Despite expanding the search dates for the search, we found

[2] https://www.statista.com/statistics/195908/number-of-births-in-the-united-states-since-1990/

only seven studies that could potentially be used to assess KQ1 (sensitivity, specificity) or KQ 2 (harms: missed diagnosis, bleeding events). **(Cavazza et al. 2012; Chauleur et al. 2008; Dargaud et al. 2017; Lindqvist, Kublikas, and Dahlback 2002; Sultan et al. 2016; Testa et al. 2015; Weiss and Bernstein 2000)**

Studies varied in size (sample sizes range from 233 to 433,000). Five included all pregnant women, however one was limited to women undergoing cesarean section; and another was limited to women with a prior VTE or thrombophilia. Each study proposed a unique scoring system. Some were named (Lyons, Thrombocalc) and the rest used a variety of clinical factors (e.g., age 35, BMI, prior VTE) to derive a score. This heterogeneity could limit our ability to synthesize the evidence for KQ 1-2. We found no studies relevant to KQ 3-4, comparing more than one VTE assessment tool or scoring system in the same population. See Table 2, Feasibility column.

Table 2. Key questions and Results for Duplication and Feasibility

Key Question	Duplication (01/2015-03/2018)	Feasibility (2000-03/2018)
KQ 1: Effectiveness of VTE risk assessment tools	Total number of identified systematic reviews: 0	Size/scope of review Relevant Studies Identified: 7 o Population based: 1 birth registry o Cohort: 5 o Retrospective case control: 1 Clinicaltrials.gov: 0
KQ 2: Harms of VTE risk assessment tools	Total number of identified systematic reviews: 0	Size/scope of review Relevant Studies Identified: 7 (same as above) Clinicaltrials.gov: 0
KQ 3: Comparative effectiveness of VTE risk assessment tools	Total number of identified systematic reviews: 0	Size/scope of review Relevant Studies Identified: none Clinicaltrials.gov: 0
KQ 4: Comparative harms of VTE risk assessment tools	Total number of identified systematic reviews: 0	Size/scope of review Relevant Studies Identified: None Clinicaltrials.gov: 0

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

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would not be duplicative of an existing product. No systematic reviews were found.
- Impact: A new systematic review has high potential. Existing guidance is inconsistent and based on limited data/expert opinion.
- Feasibility: A new review is not feasible. The evidence base is likely too small and heterogeneous for a meaningful evidence synthesis.

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Appendix A. Selection Criteria Summary

Selection Criteria	Assessment
1. Appropriateness	
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.?	Yes
1b. Is the nomination a request for a systematic review?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
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?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	The pooled overall incidence of pregnancy-related VTE was 1.2 per 1000 deliveries. The pooled VTE case fatality rate was 0.68% and the recurrence rate was 4.27%. The pooled risk of major bleeding was 1.05%. Post-thrombotic syndrome seemed to have a negative effect on quality of life. **(Kourlaba et al. 2016)** With about 4 million births/year, this correspond to 4800 cases of VTE and 32 maternal deaths per year.
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	Yes. This is a preventable cause of maternal death.
2c. Represents important uncertainty for decision makers	Yes.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes. Prevention of VTE reduces maternal morbidity and mortality, but increased risk of maternal bleeding.
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	Yes. Cost of treatment, increased resource use with monitoring, hospitalization with either prevention methods or VTE incidence.
3. Desirability of a New Evidence Review/Duplication	
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)	Yes, would not be redundant. We could find no reviews on risk assessment tools for VTE in pregnancy. We found only one Cochrane review (from 2014) of VTE prevention in pregnancy/postpartum likely needs updating; this review does not assess VTE risk assessment tools. **(Bain et al. 2014)**
4. Impact of a New Evidence Review	
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)?	Yes, rationale. Guidelines are inconsistent and based on limited data. **(Bates et al. 2012; D'Alton et al. 2016; James and Committee on Practice 2011 (2017))**

Selection Criteria	Assessment
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes, but not easy to assess given varied guidance.
5. Primary Research	
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)	Size/scope of review: we found 7 studies that might address KQ 1-2. None for KQ 3-4. We found no planned studies on ClinicalTrials.gov.

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

Appendix B. Search for Evidence Reviews (Duplication)

Listed are the sources searched.

Search date: January 1, 2015 to March 30, 2018
AHRQ: Evidence reports and technology assessments, USPSTF recommendations
VA Products: HSR&D **(ESP)** publications, and VA/DoD EBCPG Program
Cochrane Systematic Reviews and Protocols http://www.cochranelibrary.com/
PubMed
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/

Appendix C. Search Strategy & Results (Feasibility)

PubMed Search Strategy (Dates: 3/28/2013 to 3/28/2018)
Search (risk assessment tool) AND ((venous[Title/Abstract]) AND thromboembolism[Title/Abstract])
Search (((risk assessment tool) AND ((venous[Title/Abstract]) AND thromboembolism[Title/Abstract]))) AND maternal
Search (((risk assessment tool) AND ((venous[Title/Abstract]) AND thromboembolism[Title/Abstract]))) AND prenatal Schema: all
Search (((risk assessment tool) AND ((venous[Title/Abstract]) AND thromboembolism[Title/Abstract]))) AND preg*
Search (((preg*) OR prenatal) OR postpartum) OR maternal
Search (((venous[Title/Abstract]) AND thromboembolism[Title/Abstract])) AND ((((preg*) OR prenatal) OR postpartum) OR maternal)
Search (((venous[Title/Abstract]) AND thromboembolism[Title/Abstract])) AND ((((preg*) OR prenatal) OR postpartum) OR maternal) Filters: published in the last 5 years
Search ((((((venous[Title/Abstract]) AND thromboembolism[Title/Abstract])) AND ((((preg*) OR prenatal) OR postpartum) OR maternal)) AND "last 5 years"[PDat])) AND "risk assessment"[Title/Abstract] Filters: published in the last 5 years
Search ((((((venous[Title/Abstract]) AND thromboembolism[Title/Abstract])) AND ((((preg*) OR prenatal) OR postpartum) OR maternal)) AND "last 5 years"[PDat])) AND risk assessment tool Filters: published in the last 5 years

Simplified Search Strategy- all dates to 3/28/2018
Similar articles for PubMed (Select 28832906) **(O'Shaughnessy et al. 2017)**
Similar articles for PubMed (Select 27400171) **(Berkin et al. 2016)**
Similar articles for PubMed (Select 24519568) **(Bain et al. 2014)**
Similar articles for PubMed (Select 27607857) **(D'Alton et al. 2016)**

Clinicaltrials.gov link for this search:

https://clinicaltrials.gov/ct2/results?pg=1&load=cart&id=NCT01176305+OR+NCT01357941+OR+NCT00745212+OR+NCT00878826