TITLE: Thrombophilia Testing for Early Pregnancy Loss: Clinical Effectiveness and Guidelines

DATE: 24 March 2015

RESEARCH QUESTIONS

1. What is the clinical effectiveness of thrombophilia testing in women with early pregnancy loss?
2. What are the evidence-based guidelines for thrombophilia testing in women with early pregnancy loss?

KEY FINDINGS

One systematic review, one non-randomized study, and five evidence-based guidelines were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and August 7, 2014. Internet links were provided, where available.

The list of articles for this report was selected by one author and summarized by a second author.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

Disclaimer: The Rapid Response Service is an information service for those involved in planning and providing health care in Canada. Rapid responses are based on a limited literature search and are not comprehensive, systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that CADTH could identify using all reasonable efforts within the time allowed. Rapid responses should be considered along with other types of information and health care considerations. The information included in this response is not intended to replace professional medical advice, nor should it be construed as a recommendation for or against the use of a particular health technology. Readers are also cautioned that a lack of good quality evidence does not necessarily mean a lack of effectiveness particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up to date, CADTH does not make any guarantee to that effect. CADTH is not liable for any loss or damages resulting from use of the information in the report.

Copyright: This report contains CADTH copyright material and may contain material in which a third party owns copyright. This report may be used for the purposes of research or private study only. It may not be copied, posted on a web site, redistributed by email or stored on an electronic system without the prior written permission of CADTH or applicable copyright owner.

Links: This report may contain links to other information available on the websites of third parties on the Internet. CADTH does not have control over the content of such sites. Use of third party sites is governed by the owners’ own terms and conditions.
SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Selection Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
</tr>
<tr>
<td><strong>Study Designs</strong></td>
</tr>
</tbody>
</table>

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

One systematic review, one non-randomized study, and five evidence-based guidelines were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss were identified. No relevant health technology assessments.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

One systematic review, one non-randomized study, and five evidence-based guidelines were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss.

A systematic review on Factor V Leiden and prothrombin G20210A testing in women with recurrent pregnancy loss examined their test performance, effect sizes, and treatment effectiveness. The authors reported statistically significant increased odds for the association of recurrent pregnancy loss with F5 in case-control and in cohort studies and noted that results for F2 testing were similar. The evidence for clinical utility indicated that anticoagulation treatments were not effective and could lead to net harms.

The non-randomized study evaluated testing for hereditary thrombophilia alone or in combination with uterine artery Doppler (UAD) for predicting recurrent complications in patients with previous preeclampsia, placental abruption, or stillbirth. The authors did not find thrombophilia testing to be useful in improving the accuracy of UAD alone in predicting complications.
Five evidence-based guidelines\(^3-7\) were identified regarding the clinical effectiveness of thrombophilia testing for women who have had early pregnancy loss. Detailed recommendations are provided in Table 2.

### Table 2: Summary of Guidelines and Recommendations\(^a\)

<table>
<thead>
<tr>
<th>Author</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACOG (2013)(^3)</td>
<td>“There is insufficient evidence to either screen for or treat women with inherited thrombophilias and obstetric histories that include complications such as fetal growth restriction or preeclampsia.” Major Recommendations</td>
</tr>
<tr>
<td>ACMG (2013)(^4)</td>
<td>“5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss.” Major Recommendations</td>
</tr>
<tr>
<td>RCOG (2011)(^5)</td>
<td>“Women with second-trimester miscarriage should be screened for inherited thrombophilias including factor V Leiden, factor II (prothrombin) genemutation and protein S” page 8.</td>
</tr>
<tr>
<td>Baglin et al. (2010)(^6)</td>
<td>“Testing for heritable thrombophilias in selected patients, such as those with a strong family history of unprovoked recurrent thrombosis, may influence decisions regarding duration of anticoagulation (C). It is not possible to give a validated recommendation as to how such patients should be selected.” page 210</td>
</tr>
<tr>
<td>SISET (2009)</td>
<td>Specific guidance not reported.</td>
</tr>
</tbody>
</table>

\(^a\) Verbatim recommendations.

ACMG = American College of Genetics and Genomics; ACOG = American College of Obstetricians and Gynecologists; RCOG = Royal College of Obstetricians and Gynecologists; SISET = Italian Society for Haemostasis and Thrombosis.
Thrombophilia Testing for Early Pregnancy Loss

REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses

Randomized Controlled Trials
No literature identified.

Non-Randomized Studies

Guidelines and Recommendations
   See: Major Recommendations

   PubMed: PM23288205

   See: Section 5.4 Thrombophilias, page 8

   See: Guideline, page 210

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies

Statistical Model


Decision Analysis


Guidelines and Recommendations

Methodology Unclear


See: Pregnant Patients, pages 9-13

See: Page 2

Review Articles


