



TITLE: Thrombophilia Testing for Women Who Have Had Pregnancy Loss: Clinical Evidence, Cost-effectiveness, and Guidelines

DATE: 13 August 2014

RESEARCH QUESTIONS

1. What is the clinical evidence regarding thrombophilia testing for women who have had early pregnancy loss?
2. What is the cost effectiveness of thrombophilia testing for women who have had early pregnancy loss?
3. What are the evidence-based guidelines regarding thrombophilia testing for women who have had early pregnancy loss?

KEY FINDINGS

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

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.

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SELECTION CRITERIA

Table 1: Selection Criteria	
Population	Women who have had early pregnancy loss
Intervention	Thrombophilia testing (any, including testing for Factor V Leiden, prothrombin mutations, protein C, protein S or antithrombin deficiencies, antiphospholipid syndrome)
Comparator	None
Outcomes	Clinical effectiveness (benefits – e.g., prevention of future pregnancy loss, prevention of other thromboses; harms – e.g., clots, harms associated with use of anticoagulants), cost-effectiveness, guidelines
Study Designs	HTAs, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, guidelines

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, economic evaluations, and evidence-based guidelines.

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

Additional references of potential interest are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

- Bradley LA, Palomaki GE, Bienstock J, Varga E, Scott JA. Can Factor V Leiden and prothrombin G20210A testing in women with recurrent pregnancy loss result in improved pregnancy outcomes?: Results from a targeted evidence-based review. *Genet Med*. 2012 Jan;14(1):39-50.
[PubMed: PM22237430](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

- Verspyck E, Borg JY, Roman H, Thobois B, Pia P, Marpeau L. Hereditary thrombophilia and recurrence of ischemic placental disease. *Am J Obstet Gynecol*. 2010 Jan;202(1):54-5.
[PubMed: PM19782960](#)

Economic Evaluations

No literature identified.

Guidelines and Recommendations

3. Lussana F, Dentali F, Abbate R, d'Aloja E, D'Angelo A, De Stefano V, et al. Screening for thrombophilia and antithrombotic prophylaxis in pregnancy: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISST). *Thromb Res.* 2009 Nov;124(5):e19-e25.
[PubMed: PM19671474](#)
4. Hickey SE, Curry CJ, Toriello HV. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. *Genet Med.* 2013 Feb;15(2):153-6.
[PubMed: PM23288205](#)
Summary available:
<http://www.guideline.gov/content.aspx?id=47146&search=thrombophilia>
5. American College of Obstetricians and Gynecologists (ACOG). Inherited thrombophilias in pregnancy. Washington (DC): The College; 2013 Sep. (ACOG practice bulletin; no. 138). Summary available: <http://www.guideline.gov/content.aspx?id=47061>
See: Major Recommendations
6. Royal College of Obstetricians and Gynaecologists. The investigation and treatment of couples with recurrent first-trimester and second-trimester miscarriage [Internet]. London: The College; 2011. [cited 2014 Aug 12]. (RCOG Green-top guideline no.17). Available from: <http://www.rcog.org.uk/files/rcog-corp/GTG17recurrentmiscarriage.pdf>
See: Section 5.4 Thrombophilias, page 8
7. Baglin T, Gray E, Greaves M, Hunt BJ, Keeling D, Machin S, et al. Clinical guidelines for testing for heritable thrombophilia. *British Journal of Haematology* [Internet]. 2010 [cited 2014 Aug 12];149(2):209–220. Available from:
<http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.08022.x/pdf>
See: Guideline, page 2

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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies

Statistical Model

8. Bajaj PS, Veenstra DL. A risk-benefit analysis of factor V Leiden testing to improve pregnancy outcomes: a case study of the capabilities of decision modeling in genomics. *Genet Med.* 2013 May;15(5):374-81.
[PubMed: PM23138100](#)

Decision Analysis

9. Woodham PC, Boggess KA, Gardner MO, Doyle NM. Routine antenatal thrombophilia screening in high-risk pregnancies: a decision analysis. *Am J Perinatol.* 2011 Jun;28(6):495-500.
[PubMed: PM21380983](#)

Guidelines and Recommendations

Methodology Unclear

10. Davenport WB, Kutteh WH. Inherited thrombophilias and adverse pregnancy outcomes: a review of screening patterns and recommendations. *Obstet Gynecol Clin North Am.* 2014 Mar;41(1):133-44.
[PubMed: PM24491988](#)
11. Genetic testing for inherited thrombophilia [Internet]. [Portland (OR)]: Regence Blue Cross Blue Shield; 2014. [cited 2014 Aug 12]. (Policy no.47). Available from:
<http://blue.regence.com/trgmedpol/geneticTesting/qt47.pdf>
See: Pregnant Patients, pages 9-13
12. Thrombophilia: Factor V Leiden and prothrombin gene mutation [Internet]. Hamilton (ON): Thrombosis Canada; 2013. [cited 2014 Aug 12]. Available from:
<http://thrombosiscanada.ca/guides/pdfs/FactorVL-PGM.pdf>
See: Page 2

Review Articles

13. Lopes L, Jacob GP. Thrombophilia testing in pregnancy: should we agree to disagree? *J Perinat Med.* 2014 Jun 19.
[PubMed: PM24945420](#)
14. American College of Obstetricians and Gynecologists Women's Health Care Physicians. ACOG Practice Bulletin No. 138: Inherited thrombophilias in pregnancy. *Obstet Gynecol.* 2013 Sep;122(3):706-17.
[PubMed: PM23963422](#)

15. Dudding TE, Attia J. Maternal factor V Leiden and adverse pregnancy outcome: deciding whether or not to test. *J Matern Fetal Neonatal Med.* 2012 Jul;25(7):889-94.
[PubMed: PM21854123](#)
16. de Jong PG, Goddijn M, Middeldorp S. Testing for inherited thrombophilia in recurrent miscarriage. *Semin Reprod Med.* 2011 Nov;29(6):540-7.
[PubMed: PM22161466](#)
17. Galioto NJ, Danley DL, Van Maanen RJ. Recurrent venous thromboembolism. *Am Fam Physician [Internet].* 2011 Feb 1 [cited 2014 Aug 12];83(3):293-300. Available from:
<http://www.aafp.org/afp/2011/0201/p293.html>
[PubMed: PM21302870](#)
18. Lockwood C, Wendel G, Committee on Practice Bulletins- Obstetrics. Practice bulletin no. 124: inherited thrombophilias in pregnancy. *Obstet Gynecol.* 2011 Sep;118(3):730-40.
[PubMed: PM21860314](#)
19. Middeldorp S. Is thrombophilia testing useful? *Hematology Am Soc Hematol Educ Program [Internet].* 2011 [cited 2014 Aug 12];2011:150-5. Available from:
<http://asheducationbook.hematologylibrary.org/content/2011/1/150.long>
[PubMed: PM22160027](#)
20. Carbone JF, Rampersad R. Prenatal screening for thrombophilias: indications and controversies. *Clin Lab Med.* 2010 Sep;30(3):747-60.
[PubMed: PM20638586](#)
21. Davis SM, Branch DW. Thromboprophylaxis in pregnancy: who and how? *Obstet Gynecol Clin North Am.* 2010 Jun;37(2):333-43.
[PubMed: PM20685557](#)
22. Soare AM, Popa C. Deficiencies of proteins C, S and antithrombin and activated protein C resistance--their involvement in the occurrence of Arterial thromboses. *J Med Life [Internet].* 2010 Oct [cited 2014 Aug 12];3(4):412-5. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3019073>
[PubMed: PM21254740](#)
23. Pabinger I. Thrombophilia and its impact on pregnancy. *Thromb Res.* 2009;123 Suppl 3:S16-S21.
[PubMed: PM19203641](#)