CRD summary
This review concluded that transvaginal sonography was the single best diagnostic tool for identifying ectopic pregnancy; abdominal pain or vaginal bleeding should prompt a transvaginal sonogram and serum human chorionic gonadotropin testing. Despite the limitations of the review and available evidence, the conclusion about the relative accuracy of transvaginal sonography with components of physical examination is likely to be reliable.

Authors' objectives
To assess the accuracy and precision of the patient history, clinical examination, readily-available laboratory tests, and sonography in the diagnosis of ectopic pregnancy in women with abdominal pain or vaginal bleeding during early pregnancy.

Searching
MEDLINE and EMBASE were searched from 1965 up to December 2012 for studies in English; search terms were reported.

Study selection
Prospective studies that evaluated patient history, clinical examination, and/or readily available laboratory tests, in at least 100 women of reproductive-age who were experiencing abdominal pain or vaginal bleeding during proven early pregnancy were eligible for inclusion. Studies had to use a reference standard of surgical visualization and/or clinical follow-up for all pregnancies, and provide sufficient data to produce 2x2 tables of test performance. Studies limited to women with ruptured ectopic pregnancies, and studies involving assisted reproduction and in vitro fertilisation were excluded.

All included studies had an assessment of symptoms for recruiting women, and excluded women with evidence of hypovolemic shock. No further study or participant details were reported.

Two reviewers scanned titles and abstracts; it seems full papers were examined in the same way (although this was not explicitly stated). Disagreements were resolved by discussion or referral to a third reviewer.

Assessment of study quality
Two independent reviewers assessed study quality for blinding, incorporation bias, sample size, and patient recruitment; studies where incorporation bias was detected were excluded. Disagreements were resolved by discussion or referral to a third reviewer.

Data extraction
Two reviewers independently extracted data to produce 2x2 tables of test performance. Sensitivity, specificity, and positive and negative likelihood ratios were calculated with corresponding 95% confidence intervals. A correction of 0.5 was added to each cell if one or more were zero.

Methods of synthesis
Where at least three studies were available, pooled estimates of sensitivity, specificity and positive/negative likelihood ratios, with 95% confidence intervals, were calculated using a random-effects model; otherwise a narrative synthesis was presented. Heterogeneity was investigated using $I^2$.

Results of the review
Fourteen studies (12,101 patients, range 141 to 6,621) were included in the review; seven studies were included in the meta-analysis. Ten studies had blinded test interpretation and consecutive recruitment of at least 300 patients (level 1 quality; six studies) or 100 to 299 patients (level 2 quality; four studies); four studies did not recruit patients.
consecutively (level 3 quality). In the level 1 and 2 quality studies, the prevalence of ectopic pregnancy among women with abdominal pain or vaginal bleeding was 15% (95% CI 10 to 22; I²=96%; 10 studies).

Transvaginal sonography had a positive likelihood ratio of 111 (95% CI 12 to 1028; I²=88%). During physical examination, the highest positive likelihood ratios were for cervical motion tenderness during a digital vaginal examination (4.9, 95% CI 1.7 to 14; I²=93%; three studies) and abdominal pain with cough or tenderness during light palpation (range 4.2 to 4.5). All aspects of patient history and symptoms had positive likelihoods of over 1.5; the presence of an adnexal mass on bimanual examination had a positive likelihood of 2.4 (95% CI 1.6 to 3.7; I²=0%; three studies). Normal findings did not decrease the likelihood of an ectopic pregnancy, as negative likelihood ratios were over 0.5.

Sensitivity, specificity, and further results were reported where only individual studies were available.

**Authors’ conclusions**

Transvaginal sonography was the single best diagnostic modality for evaluating women with suspected ectopic pregnancy; patient history and clinical examination alone were insufficient to indicate or eliminate the possibility of ectopic pregnancy. The presence of abdominal pain or vaginal bleeding during early pregnancy should prompt a transvaginal sonogram and quantitative serum human chorionic gonadotropin testing.

**CRD commentary**

The review addressed a clear question supported by appropriate inclusion criteria. Relevant sources were searched, but the search was limited and relevant studies could have been missed. Diagnostic and statistical filters were used during the search, which could have resulted in further studies being missed. Each stage of the review process was conducted in duplicate, which reduced the risk of error and bias.

Study quality was assessed using appropriate criteria, but some relevant criteria (such as the handling of uninterpretable results) were not assessed. There were limitations with the methods of synthesis. Firstly, the model used to derive pooled estimates did not maintain the intra-study link between sensitivity and specificity, which could result in the overestimation of accuracy; more robust models were available that could produce summary estimates whilst maintaining the link between related measures. Secondly, the meta-analyses were conducted using a random-effects model with only three studies per analysis; this was an insufficient number of studies to inform the distribution of accuracy across the studies within the model.

Despite the limitations of the review and available evidence, and the uncertainty regarding the reliability of the results for the individual tests being evaluated, the authors’ conclusion about the relative accuracy of transvaginal sonography with components of physical examination is likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that, in haemodynamically stable patients, the appropriate evaluation included transvaginal sonography and serial serum human chorionic gonadotropin testing, and that patients with signs and symptoms of excessive blood loss or haemodynamic collapse should have gynaecological evaluation immediately.

**Research:** The authors did not state implications for research.

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**Bibliographic details**

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