Table 4: Clinical evidence tables for diagnostic accuracy for ultrasound features for tubal ectopic pregnancy

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Full citation

Ahmed, Ahmed A., Tom, Brian D. M., Calabrese, Peter, Ectopic pregnancy diagnosis and the pseudo-sac, Fertility and Sterility, 81, 1225-8, 2004

Ref Id

875655

Country/ies where the study was carried out

UK

Study type

Retrospective cohort study</td>
<td>Sample size

n=77 who had diagnostic laparoscopy for suspected ectopic pregnancy

Characteristics

Not reported

Inclusion Criteria

• Patients with suspected ectopic pregnancy who had diagnostic laparoscopy for confirmation.
• hCG>2000iu/L with no intrauterine or extrauterine pregnancy
• presence of heterogeneous adnexal mass or</td>
<td>Tests

Data recorded: patient history, examination, hCG level, transvaginal ultrasound (TVUS) findings, laparoscopy findings, final diagnosis. Histopathological examination was performed to confirm the diagnosis of ectopic pregnancy</td>
<td>Methods

Retrospective review of a series of cases. Review of theatre records.</td>
<td>Results

UTERUS: PSEUDOSAC
Pseudosac: any reported sac within the uterine cavity in the absence of a double decidual sac or a yolk sac
<table>
<tr><td></td><td>US pseudosac</td><td>US no pseudosac</td><td>total</td></tr>
<tr><td>ectopic pregnancy +</td><td>3</td><td>50</td><td>53</td></tr>
<tr><td>ectopic pregnancy -</td><td>14</td><td>10</td><td>24</td></tr>
<tr><td>total</td><td>17</td><td>60</td><td>77</td></tr>
</table>
TUBE & OVARY: COMPLEX ADNEXAL MASS
Heterogeneous adnexal mass
<table>
<tr><td></td><td>US adnexal mass</td><td>US no adnexal mass</td><td>total</td></tr>
<tr><td>ectopic pregnancy +</td><td>34</td><td>19</td><td>53</td></tr>
<tr><td>ectopic pregnancy -</td><td>3</td><td>21</td><td>24</td></tr>
</table>
</td>
<td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? No – 13/90 women who underwent laparoscopy for possible ectopic pregnancy were excluded.
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate exclusions? Unclear – the authors specify inclusion criteria, including an hCG level of >2000IU/L, adnexal mass or suboptimal</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Aim of the study Impact of ultrasound finding of pseudosac (uterine sac without double decidual ring or yolk sac) on management of possible ectopic pregnancy **Study dates** Jan 1997 - Jan 2000 **Source of funding** Not reported	an adnexal ring by TVUS • suboptimal rise (<50%) of hCG over 48 hours in the absence of an intrauterine sac if absolute level <2000iu/L **Exclusion Criteria** • patients who had diagnostic laparoscopy for exclusion of heterotopic pregnancy, or based on clinical suspicion alone (not US or hCG assessment for ectopic pregnancy) • haemodynamically unstable			total 37 40 77	rise in hCG. 13/90 women undergoing laparoscopy for suspected ectopic pregnancy were excluded, but the specific reasons are not stated. **Could the selection of patients have introduced bias? RISK: HIGH** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? unclear

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? Yes - Histopathological examination was performed to confirm the diagnosis.

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. Were the reference standard results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **DOMAIN 4: FLOW AND TIMING** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? unclear 2. Did all patients receive a reference standard? yes

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>3. Did patients receive the same reference standard? yes
4. Were all patients included in the analysis? yes

Could the patient flow have introduced bias? RISK: LOW

Other information</td></tr>
<tr><td>Full citation

Barnhart, Kurt T., Fay, Courtney A., Suescum, Maria, Sammel, Mary D., Appleby, Dina, Shaunik, Alka, Dean, Anthony J., Clinical factors affecting the accuracy of ultrasonography in symptomatic first-trimester pregnancy, Obstetrics and Gynecology,</td><td>Sample size

n=2058 (178 lost to follow up) --> n=1880
n=739 women identified as having an ultrasound diagnosis in any one of the five categories other than indeterminate

Characteristics

mean age: 26 years (range 13–48 years)
mean parity: 1.3 (range 0–9)

Inclusion Criteria</td><td>Tests

Index test: transvaginal ultrasound (TVUS)
Reference standard: patient followed by the gynaecology service until a definitive diagnosis was made or the patient was lost to follow-up</td><td>Methods

All patients received a transvaginal ultrasonography (TV US) that was reviewed and interpreted by a board-certified radiologist.
US diagnoses were classified:

1. definite intrauterine pregnancy (visualization of a gestational sac with a yolk sac, embryo, or both);</td><td>Results

TUBE & OVARY: ADNEXAL MASS
<u>definite ectopic pregnancy:</u> extrauterine gestational sac with yolk sac, embryo or both Sensitivity 13.2 (9.9–17) Specificity 99.9 (99.6–100)
<table><tr><td></td><td>US "definite ectopic"</td><td>US no "definite ectopic"</td><td>total</td></tr><tr><td>ectopic pregnancy +</td><td>50</td><td>330</td><td>380</td></tr><tr><td>ectopic pregnancy -</td><td>1</td><td>1499</td><td>1500</td></tr><tr><td>total</td><td>51</td><td>1829</td><td>1880</td></tr></table>
TUBE & OVARY: COMPLEX ADNEXAL MASS</td><td>Limitations

Risk of bias assessed using QUADAS-II
DOMAIN 1: PATIENT SELECTION
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? Yes - all women presenting to the emergency department with first-trimester pain, bleeding, or both
2. Was a case-control design avoided? yes</td></tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>117, 299-306, 2011

Ref Id

875697

Country/ies where the study was carried out

USA

Study type

Retrospective cohort study

Aim of the study

Evaluate factors associated with accuracy of initial ultrasonography in patients with symptomatic first-trimester pregnancy (for diagnosis of EP)</td>
<td>Need for acute gynaecological consultation after TVUS
all women presenting to the emergency department with first-trimester pain, bleeding, or both and one or more of:

• an indeterminate ultrasonography (no definite intrauterine pregnancy or ectopic pregnancy);
• an abnormal intrauterine pregnancy;
• an ectopic pregnancy that was not immediately admitted for operative management;
• an intrauterine pregnancy requiring gynaecologic evaluation</td>
<td></td>
<td>2. probable intrauterine pregnancy (intrauterine echogenic sac-like structure without visualization of a yolk sac or embryo);
3. definite ectopic pregnancy (extrauterine gestational sac with yolk sac, embryo or both);
4. probable ectopic pregnancy (inhomogeneous adnexal mass or extrauterine sac-like structure without identification of a yolk sac or embryo);
5. nondiagnostic or pregnancy of unknown location (no evidence of either ectopic pregnancy or intrauterine pregnancy);</td>
<td><u>probable ectopic pregnancy:</u>
inhomogeneous adnexal mass or extrauterine sac-like structure without identification of a yolk sac or embryo:
Sensitivity 42.1 (36.7–47.7) Specificity 98.1 (97.2–98.7)
<table>
<tr><th></th><th>US "probable ectopic pregnancy"</th><th>US no "probable ectopic pregnancy"</th><th>total</th></tr>
<tr><td>ectopic pregnancy+</td><td>139</td><td>241</td><td>380</td></tr>
<tr><td>ectopic pregnancy-</td><td>29</td><td>1471</td><td>1500</td></tr>
<tr><td>total</td><td>168</td><td>1711</td><td>1880</td></tr>
</table>
</td>
<td>3. Did the study avoid inappropriate exclusions? yes

Could the selection of patients have introduced bias?
RISK: LOW
B. CONCERNS REGARDING APPLICABILITY
Is there concern that the included patients do not match the review question? CONCERN: LOW

DOMAIN 2: INDEX TESTS
A. RISK OF BIAS

1. Were the index test results interpreted without knowledge of the results of the reference standard? yes
2. If a threshold was used, was it pre-specified? yes

Could the conduct or interpretation of the index test have</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates August 1999 - Sept 2007 **Source of funding** Not reported	**Exclusion Criteria** None reported		6. nonviable intrauterine pregnancy (ultrasound evidence of a fetal death, anembryonic gestation, or retained products of conception) Final diagnosis defined as: 1. visualised intrauterine pregnancy: intrauterine gestational sac with yolk sac or embryo; 2. ectopic pregnancy: visualised extrauterine gestational sac with yolk sac or embryo or nonvisualised ectopic pregnancy: no products of conception on uterine evacuation or		**introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes - follow up until definitive diagnosis 2. Were the reference standard results interpreted without knowledge of the results of the index test? no - ultrasound findings were communicated to the emergency department attending before

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
			confirmed with surgical pathologic specimens and a rise in postoperative quantitative hCG concentration); 3. spontaneous miscarriage: identification of products of conception on uterine evacuation or complete resolution of hCG from the serum		gynaecology consultation **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **DOMAIN 4: FLOW AND TIMING** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? unclear 2. Did all patients receive a reference standard? unclear - reportedly followed up until definitive diagnosis of IUP, EP, or miscarriage,

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>not clear what was used for diagnosis
3. Did patients receive the same reference standard? unclear - not clear what was used for diagnosis
4. Were all patients included in the analysis? No, 178 women were lost to follow up.

Could the patient flow have introduced bias? RISK: UNCLEAR

Other information</td></tr>
<tr><td>Full citation

Dart,R., Howard,K., Subclassification of indeterminate pelvic ultrasonograms: stratifying the risk of ectopic pregnancy, Academic Emergency</td><td>Sample size

n=248 patients were identified. n=20 patients were excluded because a final diagnosis could not be determined n=228 used in analysis

Characteristics

Not reported</td><td>Tests

Index test: transvaginal ultrasound
Reference test: An extrauterine pregnancy visualised at laparoscopy or laparotomy and confirmed at pathology.</td><td>Methods

Ultrasonography was performed using either an Acuson 128 (Acuson, Mountain View, CA) or an ATL Ultramark 9 HDI (Advanced Technologies Laboratories, Bothell, WA) scanner. All transvaginal probes used a 5-MHz transducer</td><td>Results

Total confirmed ectopic pregnancy=32/228

UTERUS: EMPTY UTERUS
<u>Empty uterus:</u> Empty endometrial cavity with or without a thickened endometrium
ectopic pregnancy n=25/94; LR= 2.2 (95%CI 1.1-5.0)<table><tr><td></td><td>US empty uterus</td><td>US no empty uterus</td><td>total</td></tr><tr><td>ectopic pregnancy +</td><td>25</td><td>7</td><td>32</td></tr></table></td><td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? Yes - retrospective review was made of consecutive ED patients presenting</td></tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Medicine, 5, 313-319, 1998

Ref Id

91148

Country/ies where the study was carried out

USA

Study type

Retrospective cohort study

Aim of the study

To determine whether the subclassification of indeterminate ultrasound readings can identify patients who are at differing risk for ectopic pregnancy</td>
<td>Inclusion Criteria

first-trimester pregnant women who presented with abdominal pain and/or bleeding who received pelvic ultrasonography:

• positive serum hCG
• a transvaginal ultrasound examination performed during the ED visit that was read as indeterminate (i.e., it was neither diagnostic for an IUP nor suggestive of an ectopic pregnancy)

Exclusion Criteria

• post dilatation and evacuation procedure,
• recently delivered a baby,</td>
<td></td>
<td></td>
<td>
<table>
<tr><td>ectopic pregnancy -</td><td>69</td><td>127</td><td>196</td></tr>
<tr><td>total</td><td>94</td><td>134</td><td>228</td></tr>
</table>

UTERUS: FLUID INSIDE UTERUS
<u>Nonspecific fluid</u>: Anechoic intrauterine fluid collection <10 mm mean diameter without an echogenic border
ectopic pregnancy=4/30; LR=1.0 (95%CI 0.32-3.1)
<table>
<tr><td></td><td>US nonspecific fluid</td><td>US no nonspecific fluid</td><td>total</td></tr>
<tr><td>ectopic pregnancy+</td><td>4</td><td>28</td><td>32</td></tr>
<tr><td>ectopic pregnancy-</td><td>26</td><td>170</td><td>196</td></tr>
<tr><td>total</td><td>30</td><td>198</td><td>228</td></tr>
</table>
</td>
<td>with abdominal pain/bleeding and positive B-hCG
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias?
RISK: LOW

B. CONCERNS REGARDING APPLICABILITY
Is there concern that the included patients do not match the review question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpreted without knowledge of the results of the reference standard? yes</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates August 1991 - December 1994 **Source of funding** Not reported	• final diagnosis that could not be definitively determined. TVUS showing definite IUP or suggestive of ectopic pregnancy: • diagnostic for an IUP: presence of an intrauterine gestational sac with a clearly visible yolk sac or fetal pole with or without a fetal heart beat. • suggestive of ectopic pregnancy: an extrauterine sac with or without a fetal pole or yolk sac, a complex mass discrete from the ovary, and the presence of a moderate to large amount of anechoic fluid or any amount of fluid with echogenic components (the				2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	presence of echogenic components is suggestive of clotted blood) in the cul-de-sac or abdomen.				results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? yes 4. Were all patients included in the final

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>analysis? No - 20 patients (8%) were excluded because a final diagnosis could not be determined

Could the patient flow have introduced bias? RISK: HIGH

Other information</td></tr>
<tr><td>Full citation

Dart, Robert Gerard, Burke, Garett, Dart, Linda, Subclassification of indeterminate pelvic ultrasonography: prospective evaluation of the risk of ectopic pregnancy, Annals of Emergency Medicine, 39, 382-8, 2002

Ref Id</td><td>Sample size

n=780, n=145 lost to follow up
n=635 for analysis

Characteristics

Not reported

Inclusion Criteria

• first trimester pregnant women with abdominal pain or vaginal bleeding
• positive hCG test result,
• a transvaginal ultrasonographic</td><td>Tests

Index: TVUS
Reference test: EP diagnosed by (1) Extrauterine pregnancy visualized at laparoscopy; (2) in patients managed with methotrexate, either identification of an ectopic pregnancy at follow-up ultrasonographic examination or hCG values that increase or plateau in patients after curettage and without evidence of chorionic villi at pathology</td><td>Methods

Ultrasonographic examinations were performed with an Acuson 128 (Acuson, Mountain View, CA) or an ATL Ultramark 9 HDI (Advanced Technologies Laboratories, Bothell, WA) scanner. The Acuson machine used a 5-MHz transvaginal transducer. The Ultramark machine allowed the operator to adjust the frequency of the transvaginal</td><td>Results

UTERUS: EMPTY UTERUS
<u>Empty uterus:</u> Empty endometrial cavity with or without a thickened endometrium.
<table><tr><td></td><td>US empty uterus</td><td>US no empty uterus</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>36</td><td>10</td><td>46</td></tr><tr><td>ectopic pregnancy-</td><td>223</td><td>366</td><td>589</td></tr><tr><td>total</td><td>259</td><td>376</td><td>635</td></tr></table>UTERUS: FLUID INSIDE UTERUS
<u>Nonspecific fluid:</u> Anechoic intrauterine fluid collection of <10mm in mean sac diameter without an echogenic border</td><td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? Yes – consecutive emergency department patients in the first trimester of pregnancy with a chief complaint of abdominal pain or vaginal bleeding and who had an indeterminate transvaginal</td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
875765 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study **Aim of the study** Determine the frequency of ectopic pregnancy among subclasses of indeterminate ultrasonographic examinations **Study dates** 1 January 1995 - 31 August 2000	examination performed during the ED visit that was classified as indeterminate (ie, it was neither diagnostic of an IUP nor suggestive or diagnostic of an ectopic pregnancy) **Exclusion Criteria** • patient recently delivered or passed definite products of conception at home or in the ED; • patient was after a dilatation and evacuation (D&E) procedure; • patient was lost to follow-up TVUS that was diagnostic of IUP or suspected/diagnosed ectopic pregnancy:		transducer from 5 to 10 MHz	<table><tr><td></td><td>US nonspecific fluid</td><td>US no nonspecific fluid</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>6</td><td>40</td><td>46</td></tr><tr><td>ectopic pregnancy-</td><td>121</td><td>468</td><td>589</td></tr><tr><td>total</td><td>127</td><td>508</td><td>635</td></tr></table>	ultrasonographic examination at the time of the ED visit 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? Yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding Supported by an institutional seed grant from Boston Medical Center	• TVUS diagnostic of an IUP: presence of an intrauterine gestational sac containing a clearly defined yolk sac or fetal pole. • TVUS suggestive or diagnostic of an ectopic pregnancy: visualisation of a complex adnexal mass separate from the ovary, identification of an extrauterine sac-like structure with or without a yolk sac or fetal pole, or identification of a moderate to large amount of anechoic fluid or any echogenic fluid in the cul de sac.				2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **DOMAIN 4: FLOW AND TIMING** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? yes

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>4. Were all patients included in the analysis? No 145/780 (18.6%) women were lost to follow up and therefore excluded from the analysis.

Could the patient flow have introduced bias? RISK: HIGH

Other information</td></tr>
<tr><td>Full citation

Hammoud, Ahmad O., Hammoud, Ihab, Bujold, Emmanuel, Gonik, Bernard, Diamond, Michael P., Johnson, Samuel C., The role of sonographic endometrial patterns and endometrial thickness in the differential</td><td>Sample size

n=441; 38/441 lost to follow up; final n=403

Characteristics

mean age: 27.9 ± 6.7 years

Inclusion Criteria

abdominal pain and/or vaginal bleeding in the first trimester and a positive pregnancy test</td><td>Tests

Index tests: TVUS and TAS
Reference test: pathologic diagnosis when surgery was performed; when m edical treatment was used, final ectopic pregnancy diagnosis was based on a combination of clinical evaluation, hormone studies, and established sonographic criteria for ectopic pregnancy that included the presence of a complex extra ovarian adnexal mass</td><td>Methods

All ultrasound examinations were performed with both TAS and TVUS technique</td><td>Results

UTERUS: PSEUDO-GESTATIONAL SAC<table><tr><td></td><td>US pseudosac</td><td>US no pseudosac</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>8</td><td>249</td><td>257</td></tr><tr><td>ectopic pregnancy-</td><td>2</td><td>144</td><td>146</td></tr><tr><td>total</td><td>10</td><td>393</td><td>403</td></tr></table>This is a combined value for TAS + TVUS</td><td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? Yes - retrospective study included all patients who were referred to the Radiology Department for pelvic ultrasonography who had abdominal</td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
diagnosis of ectopic pregnancy, American Journal of Obstetrics and Gynecology, 192, 1370-5, 2005 **Ref Id** 875852 **Country/ies where the study was carried out** USA **Study type** Retrospective cohort study **Aim of the study** examine the usefulness of the endometrial trilaminar patter n and thickness in the diagnosis of ectopic pregnancy	**Exclusion Criteria** • unstable condition • required urgent surgical intervention that precluded an ultrasound study • visible IUP on emergency department scan				pain and/or vaginal bleeding in the first trimester and a positive pregnancy test 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? Yes – excluded patients whose condition was unstable and who needed urgent surgical intervention that precluded an ultrasound study **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **DOMAIN 2: INDEX TESTS** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates July 1999 - July 2003 **Source of funding** Not reported					1. Were the index test results interpreted without knowledge of the results of the reference standard? yes 2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW (combined use of TAS and TVUS considered) **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Is the reference standard likely to correctly classify the target condition? Yes – pathologic confirmation or combination of clinical evaluation, hormone studies, and established sonographic criteria 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					<u>DOMAIN 4: FLOW AND TIMING</u> **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? no - surgery or clinical follow up after treatment 4. Were all patients included in the analysis? No, 38 women were lost to follow up and excluded from the analysis. **Could the patient flow have introduced bias? RISK: HIGH** **Other information**
Full citation	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Malek-Mellouli, Monia, Oumara, Maina, Ben Amara, Fethi, Zouch, Ons, Neji, Khaled, Reziga, Hedi, Prediction of ectopic pregnancy in early pregnancy of unknown location, La Tunisie medicale, 91, 27-32, 2013 **Ref Id** 875961 **Country/ies where the study was carried out** Tunisia **Study type** Prospective cohort study	n=2675, of which n=94 were PUL (used in analysis) Normal intrauterine pregnancy was diagnosed in 1990 women (74%), miscarriage in 513 (19%) and ectopic pregnancy in 78 women **Characteristics** • previous history of ectopic pregnancy n=5 • previous history of miscarriage n=27 • previous history of caesarean section n=19 **Inclusion Criteria** • suspected early pregnancy complications, who had been referred for an ultrasound scan by their general practitioners or the	Index tests: TVS Reference test: confirmed with laparoscopy and histological examination of the biopsy specimens	All women underwent a transvaginal ultrasound examination with a 7.5 MHz probe (logic 400 pro series, GE ultrasound Europe; beethovenstrasse 239, 42665 solingin, Germany). Ectopic pregnancy: heterogeneous mass seen in the adnexal region adjacent to the ovary, a mass with a hyper echogenic ring around the gestational sac in the adnexal region, or the presence of an embryo with or without a heart beat in the adnexal region accompanied by raised serum levels of hCG	ectopic pregnancy=40/94; IUP=18/94; miscarriage of IUP=17/94; spontaneous resolution=19/94 **PERITONEAL CAVITY: FREE FLUID** **Free fluid in pouch of Douglas** AUC: 0.60 Sensitivity: 0.26 95%CI (0.14-0.42) Specificity: 0.94 95%CI (0.84-0.99)	**Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias?** **RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW - women with PUL only **DOMAIN 2: INDEX TESTS** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Aim of the study identify diagnostic parameters which are predictive of ectopic pregnancies in women with early pregnancies of unknown location (PUL) **Study dates** August 2007 - February 2009 **Source of funding** Not reported	hospital consultant in the emergency department • pregnancy of unknown location (PUL) **Exclusion Criteria** • visualisation of any evidence of an intrauterine pregnancy, • identification of an adnexal mass thought to be an ectopic pregnancy, or blood in the pouch of Douglas on the initial scan, • visualisation of products of conception through the speculum • clinically unstable patients • women with an acute abdomen				1. Were the index test results interpreted without knowledge of the results of the reference standard? yes 2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias?** **RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>standard? yes - those included in 2x2 (PUL only)
3. Did patients receive the same reference standard? yes
4. Were all patients included in the analysis? yes

Could the patient flow have introduced bias? RISK: LOW

Other information</td></tr>
<tr><td>Full citation

Mehta,T.S., Levine,D., McArdle,C.R., Lack of sensitivity of endometrial thickness in predicting the presence of an ectopic pregnancy, Journal of Ultrasound in Medicine, 18, 117-122, 1999</td><td>Sample size

n=676 referred with clinical suspicion of ectopic pregnancy; n=548 excluded with IUP or abnormal IUP; n=128 analysed

Characteristics

mean age: 31.0 years (range 19 to 44 years)

Inclusion Criteria</td><td>Tests

Index test: TVUS
Reference test: medical records, clinical and sonographic follow up</td><td>Methods

Static sonographic images were reviewed for endometrial thickness, presence or absence of fluid within the endometrial cavity, presence of an adnexal mass, and presence of a moderate or large amount of free fluid</td><td>Results

TUBE & OVARY: COMPLEX ADNEXAL MASS (adnexal mass with sac/fetal pole/fetal heart beat may have been included too)
<u>Extraovarian adnexal mass</u>
<table><tr><td></td><td>US mass</td><td>US no mass</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>25</td><td>17</td><td>42</td></tr><tr><td>ectopic pregnancy-</td><td>1</td><td>85</td><td>86</td></tr><tr><td>total</td><td>26</td><td>102</td><td>128</td></tr></table>
PERITONEAL CAVITY: FREE FLUID</td><td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? Yes – sonographic images from all women attending with suspicion of EP (positive pregnancy test with symptoms of pain or bleeding,</td></tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Ref Id

91697

Country/ies where the study was carried out

USA

Study type

Retrospective cohort study

Aim of the study

evaluate endometrial thickness measurements of all patients who were examined with clinical suspicion of ectopic pregnancy

Study dates

1 January 1993 - 31 December 1995</td>
<td>clinical suspicion of ectopic pregnancy (positive pregnancy test with symptoms of pain or bleeding, or both)

Exclusion Criteria

normal IUP or abnormal IUP on TVUS</td>
<td></td>
<td></td>
<td><u>Moderate or large amount of free fluid</u>
<table>
<tr><th></th><th>US free fluid</th><th>US no free fluid</th><th>total</th></tr>
<tr><td>ectopic pregnancy+</td><td>25</td><td>17</td><td>42</td></tr>
<tr><td>ectopic pregnancy-</td><td>0</td><td>86</td><td>86</td></tr>
<tr><td>total</td><td>25</td><td>103</td><td>128</td></tr>
</table>
UTERUS: FLUID INSIDE THE UTERUS
<u>Endometrial fluid</u>
<table>
<tr><th></th><th>US endometrial fluid</th><th>US no endometrial fluid</th><th>total</th></tr>
<tr><td>ectopic pregnancy+</td><td>11</td><td>31</td><td>42</td></tr>
<tr><td>ectopic pregnancy-</td><td>41</td><td>45</td><td>86</td></tr>
<tr><td>total</td><td>52</td><td>76</td><td>128</td></tr>
</table>
</td>
<td>or both) were assessed without knowledge of pregnancy outcome
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate exclusions? Yes - patients with sonographic evidence of normal or abnormal IUP were excluded (n=548/676 excluded for IUP)

Could the selection of patients have introduced bias?
RISK: LOW

B. CONCERNS REGARDING APPLICABILITY
Is there concern that the included patients do not match the review question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding Not reported					1. Were the index test results interpreted without knowledge of the results of the reference standard? Yes – images assessed without knowledge of pregnancy outcome 2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Is the reference standard likely to correctly classify the target condition? Yes – by surgery, by negative findings on dilatation and curettage with abnormally rising hCG levels, by sonographic demonstration of an adnexal mass separate from the ovary without an IUP, or by a combination of these methods 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? unclear 2. Did all patients receive a reference standard? Yes 3. Did patients receive the same reference standard? No - by one or more of: surgery, negative findings on dilatation and curettage with abnormally rising hCG levels, sonographic demonstration of an adnexal mass separate from the ovary without an IUP

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					4. Were all patients included in the analysis? Unclear – only those with transvaginal sonograms, adequate clinical follow up and determination of serum hCG within 24 hours were included. It is not stated how many exclusions (if any) this led to. **Could the patient flow have introduced bias? RISK: UNCLEAR** **Other information**
Full citation Moore, Chris, Todd, William M., O'Brien, Elizabeth, Lin, Henry, Free fluid in Morison's pouch on bedside ultrasound predicts need	**Sample size** n=242; n=241 had TAS (n=90 IUP; n=150 no definite IUP, n=1 ectopic pregnancy) Subsequent TVS pelvic US was performed by the Department of Radiology during the initial patient visit on n=226 patients	**Tests** Index test: TAS and TVS in some cases. Pelvic US result was classified as intrauterine pregnancy (IUP) or no definitive IUP, and fluid in the cul-de-sac was classified as present or absent Reference test: radiology US and/or operative	**Methods** Bedside transabdominal US was performed using a B-K Medical Hawk XDI ultrasound scanner (B-K Medical, Herlev, Denmark). The US was recorded on S-VHS videotape	**Results** confirmed ectopic pregnancy: n=28/242 **PERITONEAL CAVITY: FREE FLUID** **<u>Free fluid in the pelvis</u>** • emergency room TAS: free fluid seen n=23/241: Sensitivity 39% 95%CI (29, 59); Specificity 94% 95%CI (90, 97); LR+ 7.0 95%CI (3.4, 14) • radiology-performed TVS: free fluid seen n=69/226: Sensitivity 53% (36, 69);	**Limitations** **Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
for operative intervention in suspected ectopic pregnancy, Academic emergency medicine : official journal of the Society for Academic Emergency Medicine, 14, 755-8, 2007 **Ref Id** 875992 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study **Aim of the study** prospectively determine if emergency	**Characteristics** Not reported **Inclusion Criteria** female patients with positive pregnancy test results who presented in the first trimester with abdominal pain and/or vaginal bleeding and for whom the emergency physician intended to obtain imaging or consultation **Exclusion Criteria** • declined enrolment • found not to be pregnant • data form was not filled out	findings - operative records, online medical records, and/or telephone conversations		Specificity 74% (67, 80); LR+ 2.0 (1.4, 3.0)	2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias?** **RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? yes 2. If a threshold was used, was it pre-specified? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
physician-performed transabdominal pelvic ultrasonography (TAS) with determination of free abdominal fluid in the hepatorenal space predicted the need for operative intervention **Study dates** February 2003 - January 2004 **Source of funding** Not reported					**Could the conduct or interpretation of the index test have introduced bias?** **RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					have introduced bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes - those included in 2x2 (PUL only) 3. Did patients receive the same reference standard? yes - operative/surgical 4. Were all patients included in the analysis? yes

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Could the patient flow have introduced bias?
RISK: LOW

Other information</td></tr>
<tr><td>Full citation

Nadim, B., Infante, F., Lu, C., Sathasivam, N., Condous, G., Morphological ultrasound types known as 'blob' and 'bagel' signs should be reclassified from suggesting probable to indicating definite tubal ectopic pregnancy, Ultrasound in obstetrics & gynecology : the official journal of the International Society of</td><td>Sample size

n=849 analysed

Characteristics

Age (ectopic pregnancy cohort) 30.6 ± 5.6 years
Gestational age (ectopic pregnancy cohort) 39.9 ± 11.7 days

Inclusion Criteria

probable ectopic pregnancy (inhomogeneous adnexal mass (‘blob’ sign) or extrauterine sac-like structure (‘bagel’ sign)) or a pregnancy of unknown location (PUL), i.e.</td><td>Tests

Index test: TVUS
Reference test: gold standard for the diagnosis of tubal ectopic pregnancy was histopathological confirmation of chorionic villi in the removed Fallopian tube. Women with a PUL were followed up by repeat TVUS and quantitative hCG analysis until a final diagnosis was reached.</td><td>Methods

TVS was performed by a clinical fellow using a Medison X8 or Medison Accuvix V20 Prestige (Samsung Medison, Seoul, South Korea) ultrasound system, equipped with a 4–9-MHz transvaginal probe.</td><td>Results

probable ectopic pregnancy: n=240/849 (n=174/240 blob sign; 66/240 bagel sign)
PUL: n=609/849 (EP=47/609; 24/47 blob sign, 19/47 bagel sign, 4/47 gestational sac with embryo/yolk sac)

TUBE & OVARY: COMPLEX ADNEXAL MASS
<u>blob sign:</u> Sensitivity 89.8% (82.2–94.4); Specificity 99.5% (98.5–99.8); LR+ 169.1 (54.6–523.8); LR- 0.103 (0.057–0.185)
<table><tr><td></td><td>US blob</td><td>US no blob</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>88</td><td>10</td><td>98</td></tr><tr><td>ectopic pregnancy-</td><td>3</td><td>562</td><td>565</td></tr><tr><td>total</td><td>91</td><td>572</td><td>663</td></tr></table>
TUBE & OVARY: ADNEXAL MASS
<u>bagel sign:</u> Sensitivity 83.3% (70.4–91.3); specificity 99.6% (98.7–99.9); LR+ 235.0 (58.6–942.8); LR- 0.167 (0.089–0.315)
<table><tr><td></td><td>US bagel</td><td>US no bagel</td><td>total</td></tr></table></td><td>Limitations

Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? yes
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate exclusions? unclear - 101 women with blob sign underwent surgery, and they present results for these, but not for the 97 other women with blobs, who were managed conservatively; bag</td></tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Ultrasound in Obstetrics and Gynecology, 51, 543-549, 2018

Ref Id

876001

Country/ies where the study was carried out

Australia

Study type

Retrospective cohort study

Aim of the study

determine whether specific ultrasound markers (inhomogeneous adnexal mass (‘blob’ sign) or extrauterine sac-like structure (‘bagel’ sign)) can be used to</td>
<td>with no signs of extra- or intrauterine pregnancy (IUP), at their first TVS

Exclusion Criteria

• definite tubal ectopic pregnancy
• IUP
• non-tubal ectopic pregnancy</td>
<td></td>
<td></td>
<td>
<table>
<tr><td>ectopic pregnancy+</td><td>40</td><td>8</td><td>48</td></tr>
<tr><td>ectopic pregnancy-</td><td>2</td><td>562</td><td>564</td></tr>
<tr><td>total</td><td>42</td><td>570</td><td>612</td></tr>
</table>
TUBE & OVARY: ADNEXAL MASS
<u>gestational sac with embryo "definite ectopic pregnancy":</u> Sensitivity 84.0% (64.3–92.7); Specificity 99.9% (99.2–100); LR+ 930.3 (57.9–14 937.7); LR- 0.173 (0.075–0.401)
<table>
<tr><td></td><td>US "definite ectopic pregnancy"</td><td>US no "definite ectopic pregnancy"</td><td>total</td></tr>
<tr><td>ectopic pregnancy+</td><td>21</td><td>4</td><td>25</td></tr>
<tr><td>ectopic pregnancy-</td><td>0</td><td>562</td><td>562</td></tr>
<tr><td>total</td><td>21</td><td>566</td><td>587</td></tr>
</table>
</td>
<td>el sign – only 50/85 had surgery

Could the selection of patients have introduced bias?
RISK: UNCLEAR
B. CONCERNS REGARDING APPLICABILITY
Is there concern that the included patients do not match the review question?
CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpreted without knowledge of the results of the reference standard? yes
2. If a threshold was used, was it pre-specified? yes

Could the conduct or interpretation of the index test have introduced bias?
RISK: LOW</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
predict a definite tubal ectopic pregnancy **Study dates** November 2006 - June 2016 **Source of funding** Not reported					**B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? no - operative/surgical or repeat US and clinical follow up. Those who did not have the same reference standard (ie treated conservatively) were excluded 4. Were all patients included in the analysis? Yes.

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the patient flow have introduced bias? **RISK: HIGH** **Other information**
Full citation Sadek,A.L., Schiotz,H.A., Transvaginal sonography in the management of ectopic pregnancy, Acta Obstetricia et Gynecologica Scandinavica, 74, 293-296, 1995 **Ref Id** 65458 **Country/ies where the study was carried out** Norway **Study type**	**Sample size** n=525 women referred with abdominal pain and/or vaginal bleeding in the first trimester of pregnancy were evaluated by TVUS **Characteristics** • mean age 31 years (range 23-43) • duration of amenorrhoea 6.5 weeks (range 4-12) **Inclusion Criteria** All patients referred with amenorrhoea, abdominal pain and/or vaginal bleeding with	**Tests** Index test: TVUS Reference test: If ectopic pregnancy was suspected, treated laparoscopically with linear salpingostomy or salpingectomy using diathermy technique; all tubal or uterine material and abdominal fluid was examined histologically.	**Methods** sonographic examination was performed by a gynaecologist as part of the initial evaluation with the patient in the lithotomy position using a 5 MHz vaginal transducer (General Electric 3200 or Aloka SSD-650)	**Results** ectopic pregnancy was suspected when the pregnancy test was positive and TVUS showed (a) empty uterus or pseudosac, and (b) free pelvic fluid and/or a tubal mass **suspected ectopic pregnancy n=57; confirmed ectopic pregnancy n=53** • empty uterus n=48/57 • pseudosac n=5/57 • tubal mass n=45/57 • free pelvic fluid n=54/57 **PERITONEAL CAVITY: FREE FLUID** **Free pelvic fluid:** Sensitivity 96.2%; Specificity 99.4%; PPV 94.4% (51/54); NPV 99.6% (469/471) | | US free fluid | US no free fluid | total | | --- | --- | --- | --- | | ectopic pregnancy+ | 51 | 2 | 53 | | ectopic pregnancy- | 3 | 469 | 472 | | total | 54 | 471 | 525 |	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias?** **RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td>Prospective cohort study

Aim of the study

evaluate the role of transvaginal sonography (TVUS) in the early diagnosis of symptomatic EP and its influence in facilitating laparoscopic management

Study dates

January 1990 - January 1993

Source of funding

Not reported</td><td>positive pregnancy test

Exclusion Criteria

Not reported</td><td></td><td></td><td>TUBE & OVARY: COMPLEX ADNEXAL MASS
<u>Tubal mass:</u> Sensitivity 81.1%; Specificity 99.6%; PPV 95.6% (43/45); NPV 97.9% (470/480)<table><tr><td></td><td>US tubal mass</td><td>US no tubal mass</td><td>total</td></tr><tr><td>ectopic pregnancy+</td><td>43</td><td>10</td><td>53</td></tr><tr><td>ectopic pregnancy-</td><td>2</td><td>470</td><td>472</td></tr><tr><td>total</td><td>45</td><td>480</td><td>525</td></tr></table></td><td>question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpreted without knowledge of the results of the reference standard? yes
2. If a threshold was used, was it pre-specified? yes

Could the conduct or interpretation of the index test have introduced bias?
RISK: LOW
B. CONCERNS REGARDING APPLICABILITY
Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW

<u>DOMAIN 3: REFERENCE STANDARD</u>
A. RISK OF BIAS</td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **DOMAIN 4: FLOW AND TIMING** **A. RISK OF BIAS** 1. Was there appropriate interval

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? yes - operative/surgical 4. Were all patients included in the analysis? Yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**