Check for updates

SYSTEMATIC REVIEW

Diagnosis of pelvic endometriosis: A systematic review and accuracy meta-analysis of non-invasive tests available in primary care [version 1; peer review: awaiting peer review]

Thomas Bainton[1,2], Sobanakumari Jeyapala[2], Javier Zamora[3-5], Khalid S Khan[5,6], Amer Raza[1,2]

[1]Metabolism Digestion and Reproduction, Imperial College London, London, UK
[2]Department of Obstetrics and Gynaecology, Chelsea and Westminster Hospital NHS Foundation Trust, London, SW10 9NH, UK
[3]Institute of Metabolism and Systems Research, University of Birmingham, UK, Birmingham, UK
[4]Clinical Biostatistics Unit, Hospital Ramon y Cajal (IRYCIS), Madrid, 28034, Spain
[5]Department of Preventative Medicine and Public Health, University of Granada, Grenada, Spain
[6]Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Madrid, Spain

v1 **First published:** 28 Apr 2023, **12**:453
https://doi.org/10.12688/f1000research.131729.1
Latest published: 28 Apr 2023, **12**:453
https://doi.org/10.12688/f1000research.131729.1

Abstract

Background: Endometriosis is a chronic, often debilitating condition with a current significant delay from symptom onset to diagnosis with much of this in primary care.
Methods: A systematic review and meta-analysis of the primary literature was conducted to investigate the accuracy of symptoms, clinical history and first-line non-invasive tests to predict pelvic endometriosis (PROSPERO: CRD42020187543). We searched Medline, Embase, Web of Science and Scopus from conception (1966; 1972; 1997; 2004 respectively) to September 2022 for primary test accuracy studies assessing non-invasive tests against reference standard diagnosis for endometriosis. Two authors independently conducted data extraction and quality assessment. Grading of evidence was performed using a novel visual pentagon model. Meta-analyses of test accuracy was estimated using bivariate random effects models.
Results: The 125 included studies (250,574 participants) showed mixed quality. Studies applying non-surgical (database/self-reporting) reference standard had a greater risk of bias. In 98 studies applying surgical reference standard, summary diagnostic odds ratios for endometriosis were: dysmenorrhoea 2.56 (95% confidence interval 1.99-3.29); pelvic pain 2.56 (1.73-3.74); dyschezia 2.05 (1.36-3.10); dyspareunia 2.45 (1.71-3.52); family history of endometriosis 6.79 (4.08-11.3); nulligravidity of 2.01 (1.62-2.50); body mass index (BMI) $\geq$30kg/m^2 0.37 (0.19-0.68); trans-vaginal ultrasound scan (TVUSS) endometrioma 91.2 (44.0-189); TVUSS invasive endometriosis 26.1 (9.28-73.5); and cancer antigen-125 (CA-125) >35U/mL 16.0 (8.09-31.7). Sensitivity analysis excluding all high-risk studies found concordant

Open Peer Review

Approval Status *AWAITING PEER REVIEW*

Any reports and responses or comments on the article can be found at the end of the article.

results.
Conclusions: This meta-analysis collated the performance of non-invasive tests for endometriosis across a comprehensive and geographically varied population. Study quality was mixed, however results were consistent with high-risk studies excluded. These findings will inform future prediction models for triage in primary care.

Keywords
Endometriosis, diagnosis, prediction, diagnostic laparoscopy, primary care, pelvic pain, dysmenorrhoea

This article is included in the Endometriosis collection.

Corresponding author: Thomas Bainton (t.bainton22@imperial.ac.uk)

Author roles: Bainton T: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Jeyapala S**: Investigation, Methodology, Writing – Review & Editing; **Zamora J**: Formal Analysis, Resources, Software, Writing – Review & Editing; **Khan KS**: Conceptualization, Methodology, Supervision, Writing – Review & Editing; **Raza A**: Conceptualization, Methodology, Project Administration, Supervision, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2023 Bainton T *et al*. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Bainton T, Jeyapala S, Zamora J *et al.* **Diagnosis of pelvic endometriosis: A systematic review and accuracy meta-analysis of non-invasive tests available in primary care [version 1; peer review: awaiting peer review]** F1000Research 2023, **12**:453 https://doi.org/10.12688/f1000research.131729.1

First published: 28 Apr 2023, **12**:453 https://doi.org/10.12688/f1000research.131729.1

Introduction

Endometriosis is a chronic condition affecting women of reproductive age characterised by extra-uterine deposits of endometrial tissue with a prevalence of up to 10%.[1–3] It can be found in peritoneal deposits, ovarian endometriomata, and invasive disease, with sufferers experiencing pain and sub-fertility.[2,4–6] There is currently a 7-12 years delay between symptom onset and definitive diagnosis, by laparoscopy and biopsy.[7–9] Reducing this has long a research priority.[10,11] Up to 58% of sufferers present to primary care 10 or more times before diagnosis, demonstrated across a variety of healthcare systems and geographies.[4,7,12–14] A better understanding of the accuracy with which symptoms, clinical history and non-invasive tests diagnose pelvic endometriosis would aid triage and referral.

Many studies have attempted to find replacement tests for diagnostic laparoscopy.[15–17] These are often invasive or otherwise not applicable to primary care.[16,18] Previous meta-analyses have been restricted by a narrow inclusion criteria yielding a small number of eligible studies, limiting findings.[19] Meta-analyses assessing imaging and biomarkers showed that no individual test met their criteria as a replacement or triage test alone, but findings on trans-vaginal ultrasound and serum CA-125 showed a high specificity for disease.[20,21] These studies did not include assessment of other clinical factors. A 2019 narrative review demonstrated the importance of clinical factors in prediction of disease, but primary studies were not assessed for quality and absence of meta-analysis limited quantitative assessment of test performance.[22]

A 2021 case-control study reporting on the accuracy of a simple patient-completed questionnaire identified those at high or low risk of disease with good accuracy reflecting the utility of assessment of patient reported symptoms at a primary care level.[23]

Research related to endometriosis is increasing in volume, with 75% of primary studies published in the last decade.[24,25] Given this, and due to the limitations of previous reviews a new comprehensive systematic review and meta-analysis is required. We performed such an evidence synthesis and determined the accuracy of symptoms, clinical history, a simple low-cost biomarker and first line ultrasound for the diagnosis of pelvic endometriosis by means of a comprehensive systematic review and accuracy meta-analysis.

Methods

The protocol was designed and registered with PROSPERO (Registration number: CRD42020187543).[26] Reporting followed the PRISMA guidelines.[27,59]

Patient and public involvement

A virtual patient and public involvement meeting involving endometriosis sufferers at Chelsea and Westminster Hospital, London was held following an open invitation on social media to inform them of plans for this study. The aim was to better understand non-invasive predictors of endometriosis and reduce the diagnostic delay, which was well supported and resonated with their personal experience. No specific ethical approval was required for the patient and public involvement, in accordance with Health Research Authority (HRA) guidelines. No specific ethical approval was required as this study retrieved and synthesised data from already published studies. No individual participant data was collected and no participant consent was required.

Literature search and study selection

Medline, Embase, Web of Science and Scopus were searched from conception (1966; 1972; 1997; 2004 respectively) to September 2022 Search strategies are shown in Table 1 (*see Extended data*).[53] Review article references were also screened.

Titles and abstracts were screened independently by two authors (TB; SJ) using EndNote-X9 and duplicate or irrelevant studies removed. Full texts were screened and justification for inclusion or exclusion recorded, differences were resolved by discussion with the senior author (AR).[28]

We included published peer reviewed studies reporting accuracy estimates to predict pelvic endometriosis (peritoneal; ovarian; disease >5mm retroperitoneal invasion) for one or more index tests in participants with reported presence/absence of endometriosis. Included tests were dysmenorrhoea; pelvic pain; dyschezia; dyspareunia; nulligravidity; BMI $\geq$30kg/m^2; family history of endometriosis; transvaginal ultrasound finding (TVUSS) of endometrioma; TVUSS finding of invasive disease; serum CA-125 >35U/mL.

Target population was reproductive age women excluding pregnancy or systemic co-morbidities. Studies with reporting non-reproductive age participants were included only where their data could be excluded from meta-analysis. Studies were included where a 2x2 contingency table for index test(s) could be constructed. We imposed no limits to language of

publication, setting, or number of participants. All non-English studies were translated by a medically trained native speaker.

Studies reporting laboratory and ultrasound tests were included only when performed prior to reference standard and using only standard 2D protocols. Definitions for each test for the purposes of study selection are shown in Table 2 (see *Extended data*).[54]

We excluded reviews; case reports; studies where information on recruitment or study population was unavailable; letters; and abstracts. Studies reporting non-pelvic endometriosis were included only where pelvic endometriosis was reported separately. Authors were contacted to obtain full texts only. Failing this, they were obtained through the British Library. Studies with incomplete data preventing determination of inclusion, exclusion or test accuracy were excluded.

Data extraction and quality assessment

For each included study, two authors (TB; SJ) independently recorded information on study characteristics and data was extracted to form 2x2 tables. Where there was unreliability in data extraction from some non-English language studies, these were excluded.

Risk of bias was assessed independently by two authors (TB; SJ) using the Quality Assessment of Diagnostic Test Accuracy Studies (QUADAS 2) tool.[29] For studies regarding serum CA-125 or TVUSS we included the additional questions: 'was the index test performed by a single operator?' to assess inter-observer bias; and 'was timing in the participants' menstrual cycle controlled for?'. We adjusted the original question 'if a threshold was used, was it pre-specified?' to 'was there a clear definition of what was considered a positive test?'.

Data synthesis

Due to differences in design, studies were divided into groups according to application of the reference standard: 'Complete verification', all participants received visual inspection of the pelvis at surgery; 'Partial verification', all cases received surgical confirmation but controls did not; and 'Database/self-reporting', cases confirmed by healthcare coding or self-reporting and controls from healthy populations not known to have endometriosis.

Statistical analysis was conducted using Stata software (version 15)[30] to allow exploration of heterogeneity and statistical pooling using a bivariate random effects model and produced summary accuracy measures and summary receiver operative characteristic curves for each index test. A bivariate random effects model was applied for index tests with ≥5 contributing studies, and a univariate fixed effects model for index test with ≤4.

Index tests were assessed for performance as a 'rule-in' or 'rule-out' tool with pre-specified threshold summary accuracy of 95% sensitivity/50% specificity or 95% specificity/50% sensitivity respectively.

Results

Study selection and characteristics

Of 22,016 studies identified 125 met the inclusion criteria involving 250,574 participants (Figure 1). Details of included studies by number of participants and index test(s) are shown Table 2 (see *Extended data*[54]). Characteristics of included and excluded studies are shown in Tables 3 and 4 (see *Extended data*).[55,56]

Mean number of index tests per study was 2 (range 1-6). A total of 241 were assessed across all studies. Included studies were geographically varied: 45 Europe, 34 North America, 19 Asia/Oceania, 13 the Middle East/Africa, 12 South America, and 2 transcontinental. Publication date ranged from 1986 and 2022 with 57% since 2010: 4 before 1989; 22, 1990-1999; 18, 2000-2009; and 71, 2010-2022.

Most studies (75) were 'single-gate' design with 50 of 'two-gate' design, including all studies in the partial verification and database/self-reporting groups. The mean prevalence of endometriosis in studies of a 'single-gate' design was 52% (range 9-93%), due to the selection of matched controls, prevalence in 'two-gate' studies was not relevant. There was heterogeneity in population selection, with participants having surgery for a broad range of indications such uterine fibroids or adnexal cysts as well as pelvic pain or sub-fertility.

In the 61 studies assessing symptom-based tests 20 did so by self-administered questionnaire; 14 by structured interview; 12 by clinical history taking, and 15 were undefined (Table 5 - see *Extended data*).[57]

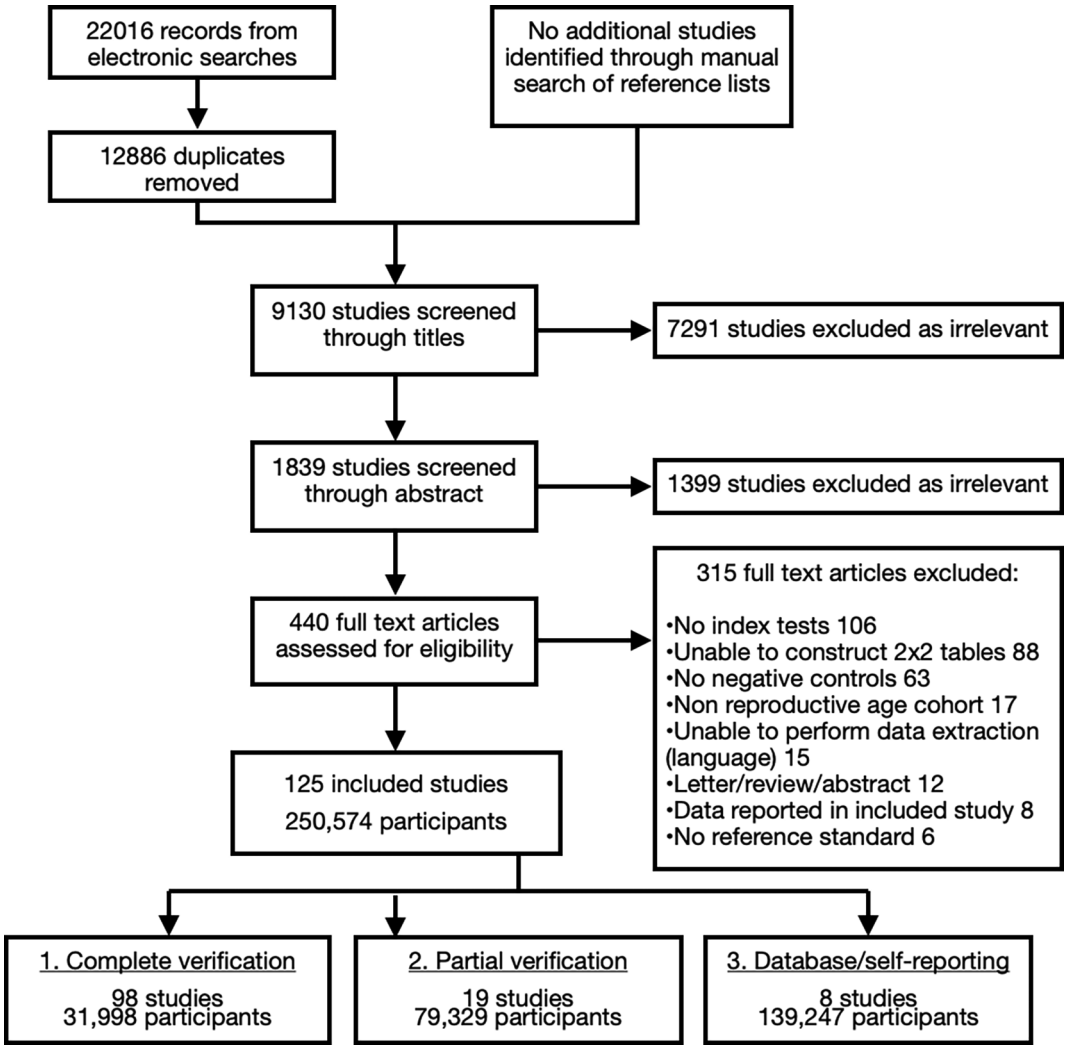


Figure 1. Flowchart of selection of studies included in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis and division into groups by means of application of the reference standard.

Quality of included studies

Risk of bias

The assessment of study quality by QUADAS-2 is presented in Figures 2-6. Overall methodological quality was mixed, with 5 studies presenting a low risk of bias across all domains[31–35] and 64 presenting a high risk of bias or applicability in at least one domain.

In patient selection, 22 studies presented a low risk of bias, with 73 and 30 presenting an unclear or high risk respectively. Non-consecutive or non-random selection, two-gate selection for cases and controls, and having a highly selected group of participants (infertility cohort, surgery for a narrow indication etc.) were the main reasons for a high risk of bias.

Symptom based index tests presented an unclear or high risk of bias due to a lack of definition of a positive test and of blinding. Just 9 studies presented a low risk in symptom-based tests across all groups. Index tests applicable to clinical history or investigations performed better, with 66 studies presenting a low risk. Reasons for an unclear or high risk of bias were a lack of pre-specified criteria for a positive test; no blinding to results of the reference standard; and inter-observer variability regarding imaging. Studies in the partial verification group assessed a proportionally higher number of index tests nulligravidity and BMI $\geq$30kg/m^2, which, less subjective to interpretation presented a lower risk of bias.

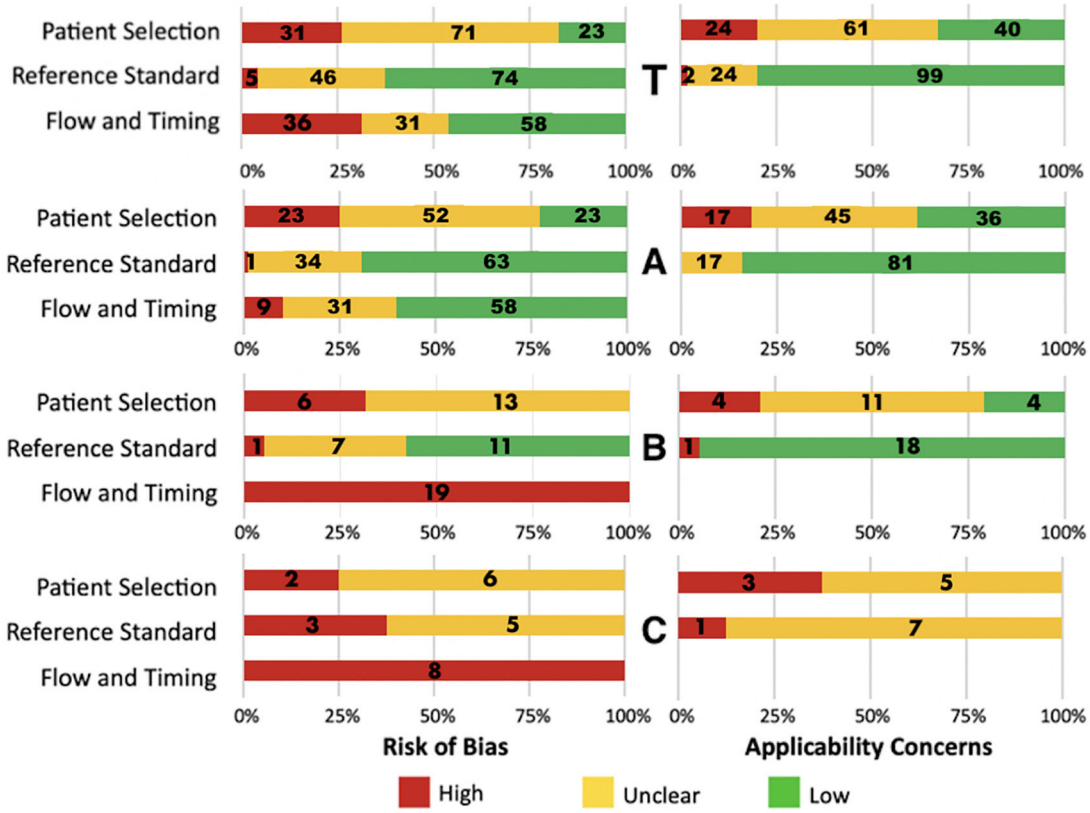


Figure 2. Risk of bias and applicability concerns among studies included in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis. Graph: review authors' judgements on each domain presented as percentages across included studies in: T all studies; A Complete verification; B Partial verification; and C Database/self-reporting groups.

The risk of bias regarding the reference standard performed best in the complete and partial verification groups where 74 studies were at low risk of bias. Those with an unclear or high risk lacked information on how likely the surgery was to correctly classify the target condition or operators not blinded to the result of index test(s). In the database/self-reporting group, 5 studies assessed for probable surgical confirmation by means of additional codes at the time of recording and therefore presented a lower risk, all other studies were high risk.

In flow and timing, the complete verification group presented the lowest risk. An unclear or high risk of bias was attributable to a long (>12 months) or unclear time interval, and a high or unclear withdrawal of participants from analysis. All other studies presented a high risk as not all participants received the same reference standard.

Applicability

In patient selection, 40 studies gave low concern, with 63 and 22 giving unclear or high risk respectively. An unclear or high risk was attributable to the two-gate selection of controls, or the study likely to only classify a limited spectrum of disease (tertiary centres or infertility clinics).

In regard the reference standard, 97 studies showed a low concern. Studies in the database/self-reporting group were deemed high/unclear depending on whether additional coding input for surgery was recorded.

Test accuracy

Due to heterogeneity in methodology and study quality, meta-analysis was performed on studies from each group separately.

The accuracy of index tests to predicting endometriosis was variable, although results across groups were consistent. Each index test gave a positive likelihood for the presence of pelvic endometriosis, apart from a BMI $\geq$30kg/m^2, which

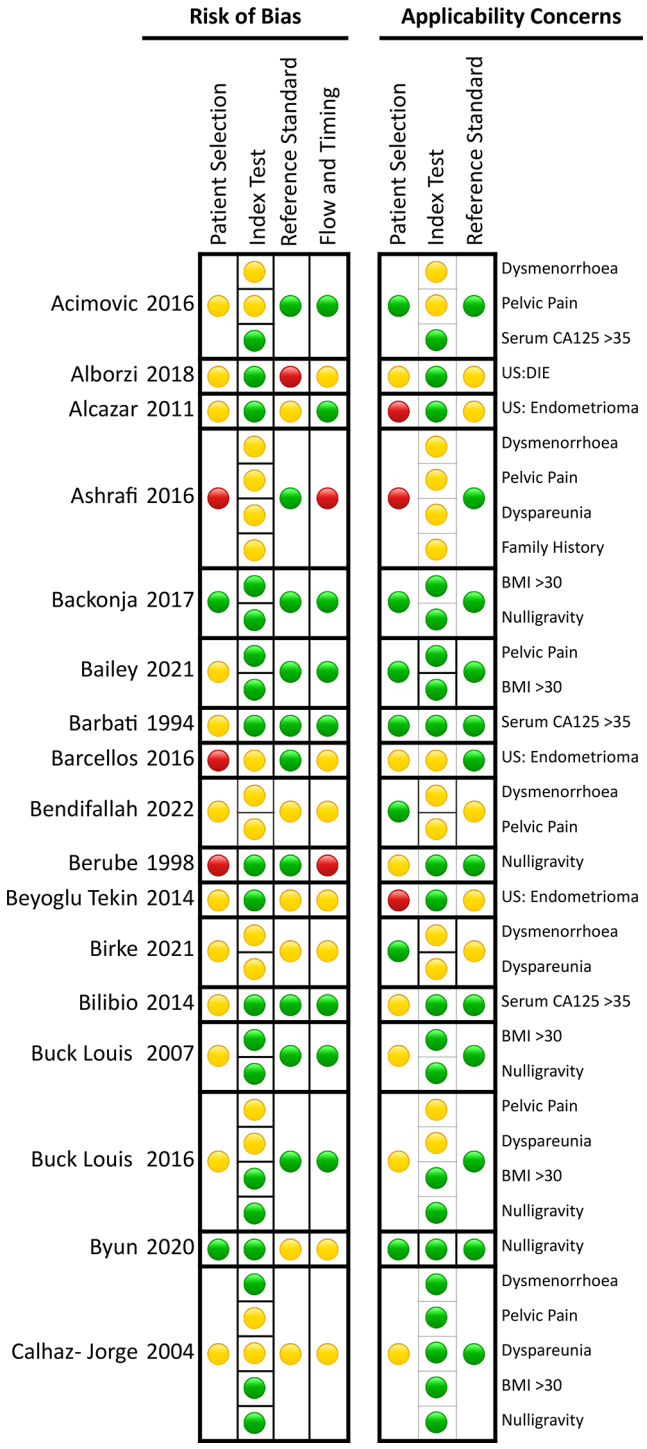


Figure 3. Reviewers assessment of risk of bias and applicability by application of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool for included studies in the diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests complete verification group. BMI, body mass index. CA-125, cancer antigen-125. US, ultrasound. DIE, deep invasive endometriosis.

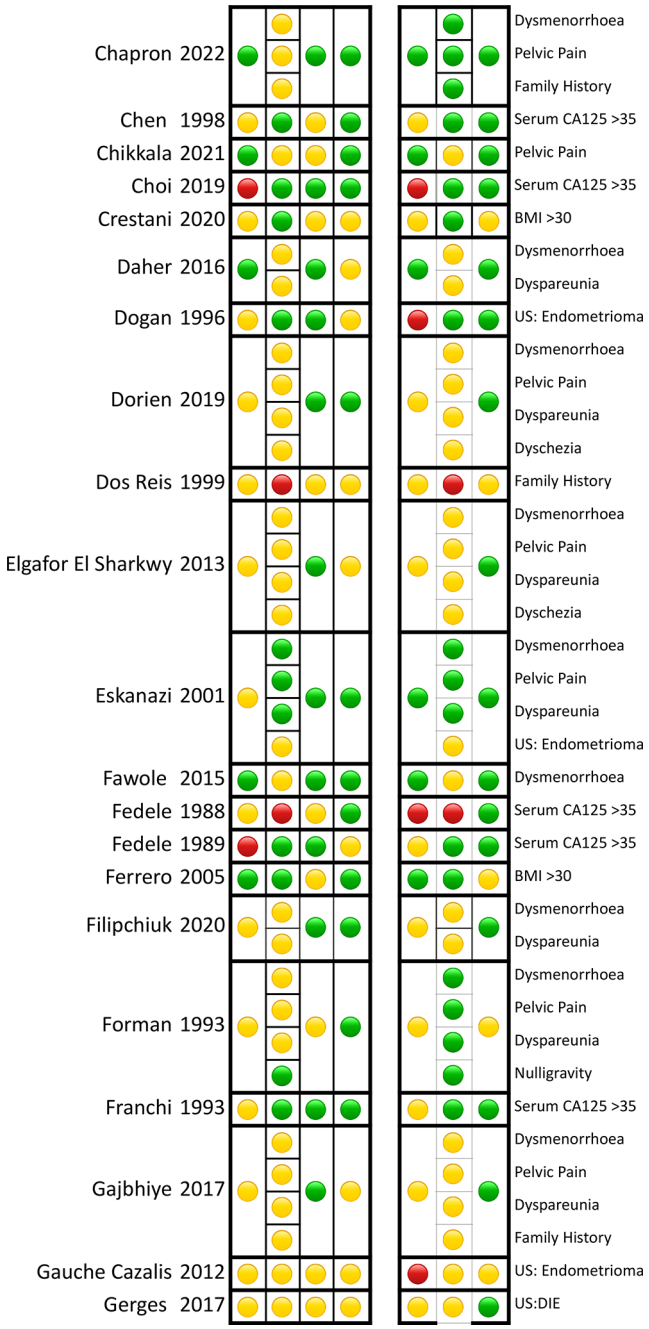


Figure 3. (continued)

decreased the likelihood of disease. The positive likelihood ratio (LR+) for disease was highest in investigation tests and there was a trend towards a greater specificity than sensitivity. The summary results of bi/univariate meta-analysis are shown in Figure 7. An assessment of confidence in individual sensitivity and specificity of each test is displayed by a visual pentagon model, the methodology for this assessment is described in the discussion and legend shown in Figure 8.

Investigation category tests were the best performing overall and TVUSS finding of endometrioma gave the highest summary LR+ at 21.6, at sensitivity and specificity of 77.2% and 96.4% respectively. Serum CA-125 >35U/mL showed sensitivity and specificity of 55.8% and 92.7% respectively, with LR+ of 7.63. TVUSS finding of DIE had showed sensitivity and specificity of 86.5% and 80.2% with LR+ of 4.39.

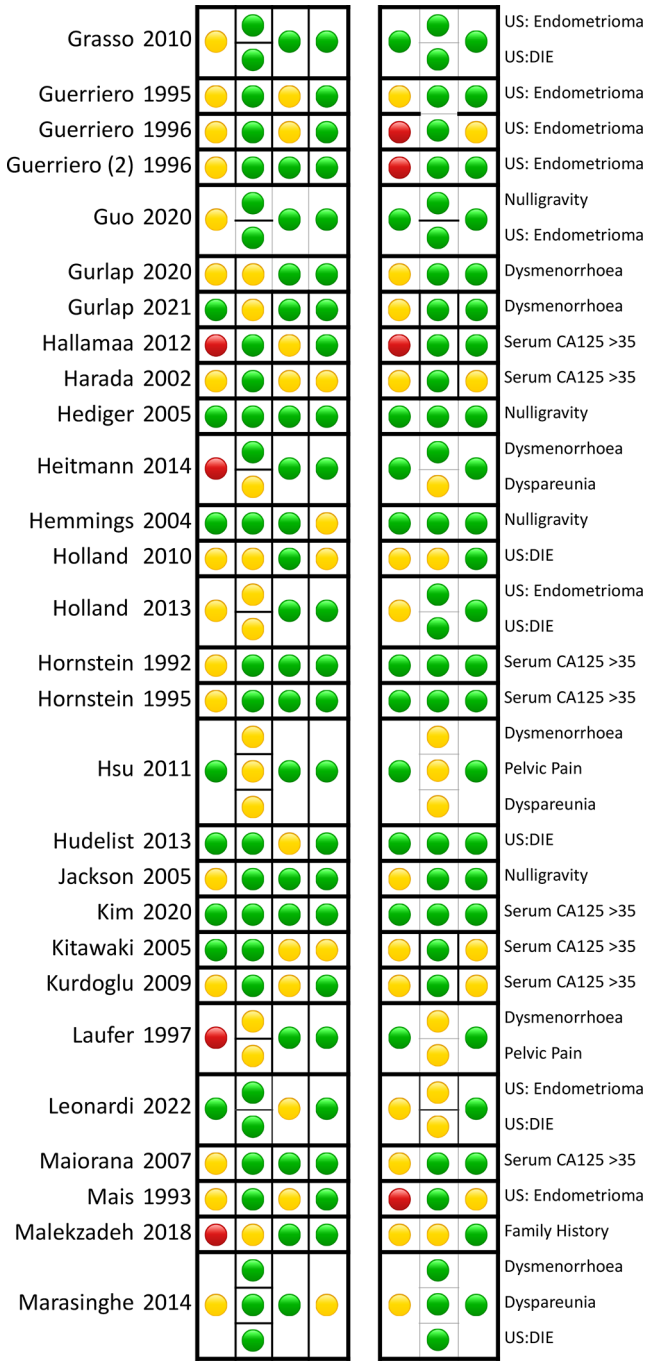


Figure 3. (continued)

Symptom based tests showed LR+ within a similar range: 1.47 (dysmenorrhoea) to 1.93 (dyspareunia). Symptoms showed a generally higher specificity than sensitivity. Dyspareunia showed the highest LR+ at 1.93 with a sensitivity and specificity of 36.3% and 81.1% respectively.

Family history of endometriosis showed a LR+ of 6.25 with a high specificity (98.5%) but low sensitivity (9.25%). The finding of BMI ≥30kg/m^2 showed a decreased likelihood of diagnosis of endometriosis (LR+ 0.44).

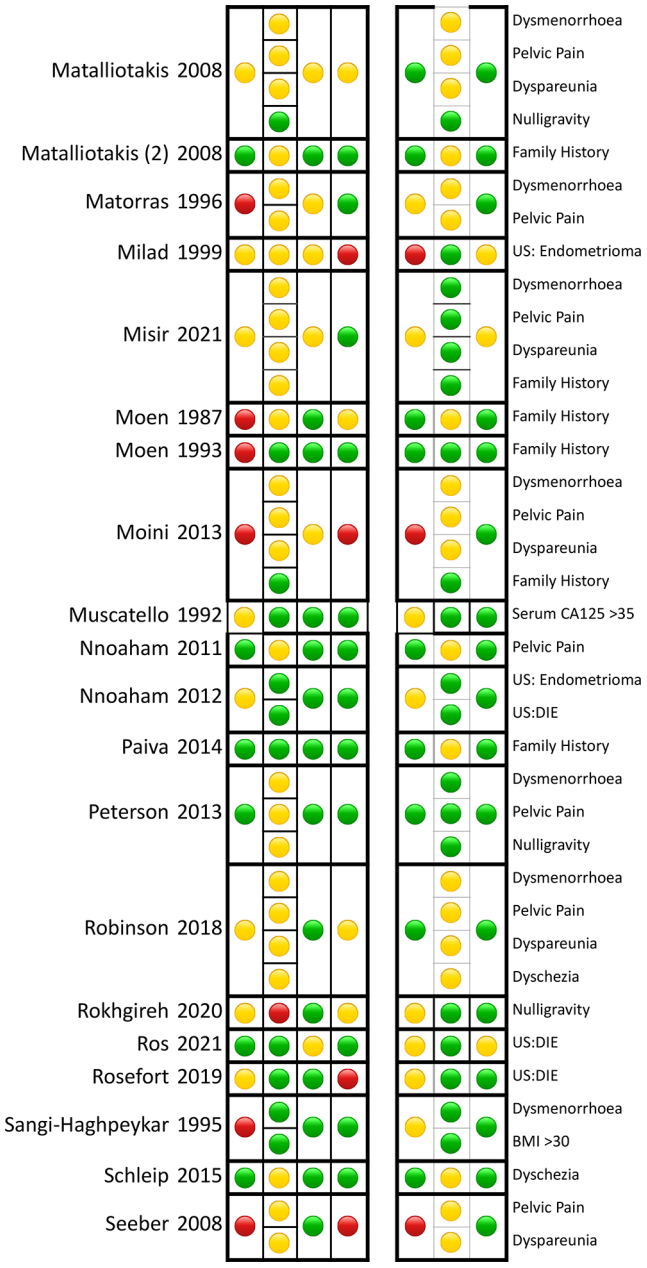


Figure 3. (continued)

Hierarchical Summary Receiver Operating Characteristics (HSROC) curves for index tests in each group are shown in Figures 9-11. The HSROC curves show the greatest area under the curve (AUC) for investigation category tests.

In the partial verification group, symptom index tests showed a greater LR+ than the complete verification group, range 2.47 (dysmenorrhoea) to 7.13 (dyschezia). Specificity was also higher, range 69% (dysmenorrhoea) to 92% (dyschezia).

In the database/self-reporting group symptom-based index tests performed similarly to other groups. In partial verification and database/self-reporting groups BMI ≥30 kg/m^2 showed no correlation with disease and had 95% CI crossing 1.0. In all other index tests across all groups the 95% CI was >1.0.

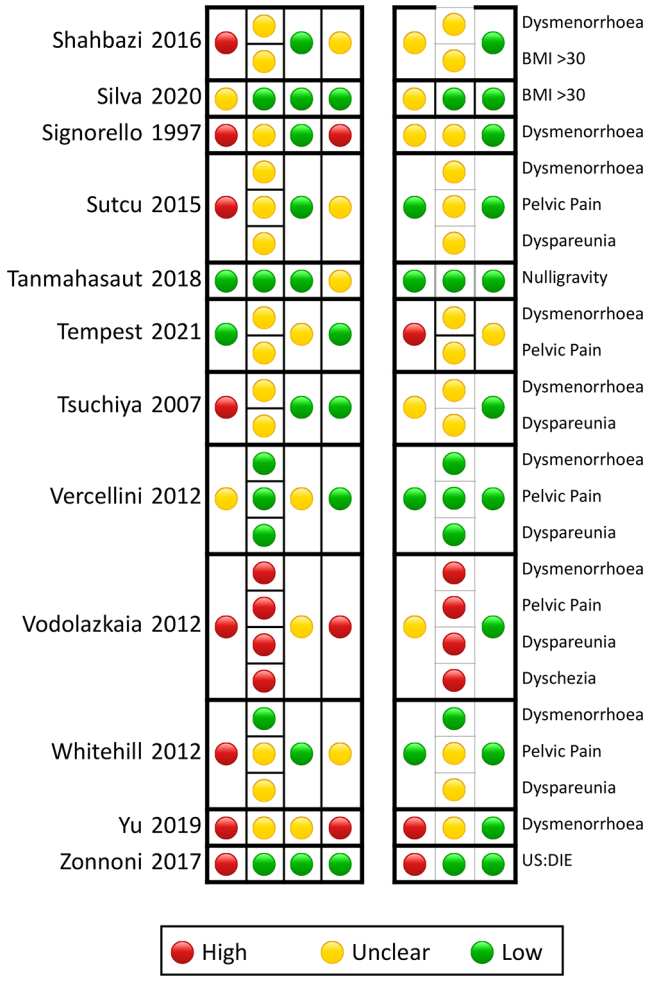


Figure 3. (continued)

The greatest inter-study variability in confidence intervals was shown in Forest plots for the symptom-based tests, notably pelvic pain. The inter study variance for specificity was generally lower than that for sensitivity, as was the overall width of confidence intervals. Forest plots for each index test in each group are shown in Figures 12-18.

Sensitivity analysis performed for studies without any high-risk features is shown in Table 6 (see *Extended data*[58]). All studies included are from the complete verification group. Summary accuracy measures are consistent with those in this group for the majority of index tests, although sensitivity for TVUSS finding of endometrioma and DIE reduced to 69.8% and 73.4% respectively.

Discussion

Main findings

This meta-analysis presents an up-to-date, large, and geographically varied data set identifying predictive factors for diagnosis of pelvic endometriosis with a high degree of confidence. Index tests showed a positive association with endometriosis and trended towards a greater specificity than sensitivity, excluding elevated BMI, which demonstrated an inverse correlation. TVUSS finding of endometrioma reached a desired threshold for use as a 'rule-in' test and none achieved a summary sensitivity of >95%. A family history of endometriosis, dyschezia and serum CA-125 >35U/mL showed summary specificity of >90% although low sensitivity. Sensitivity was poor for symptom and clinical history tests, where the best performing was dysmenorrhoea.

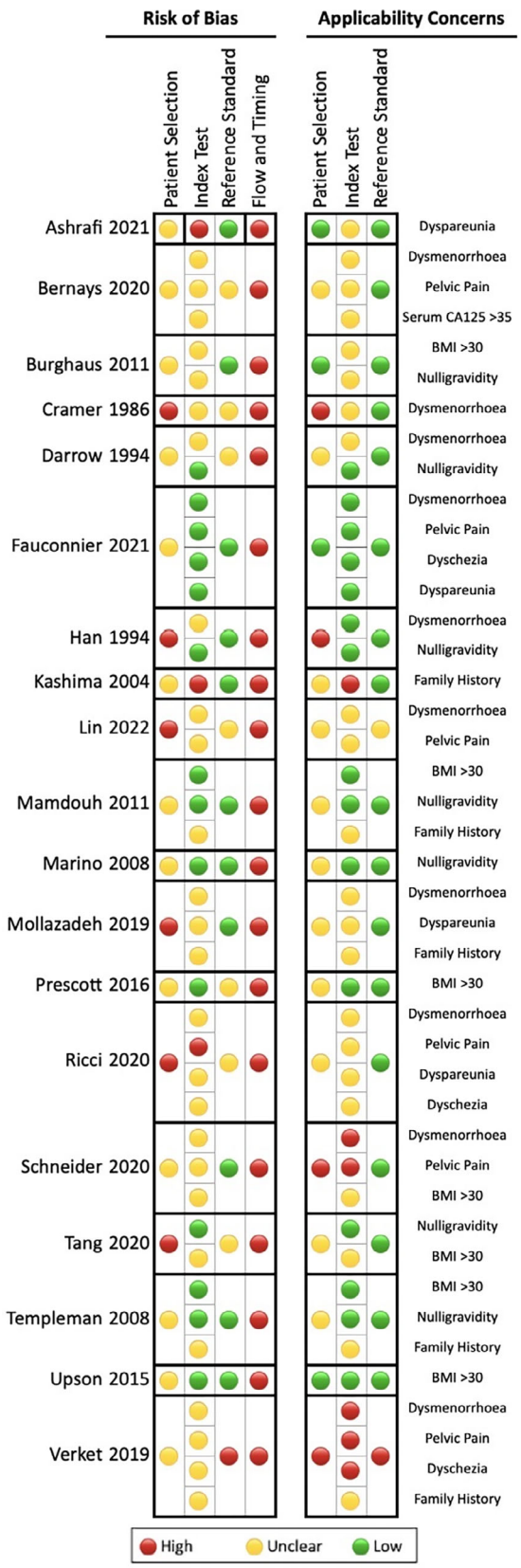


Figure 4. Reviewers assessment of risk of bias and applicability by application of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool for included studies in the diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests partial verification group. BMI, body mass index.

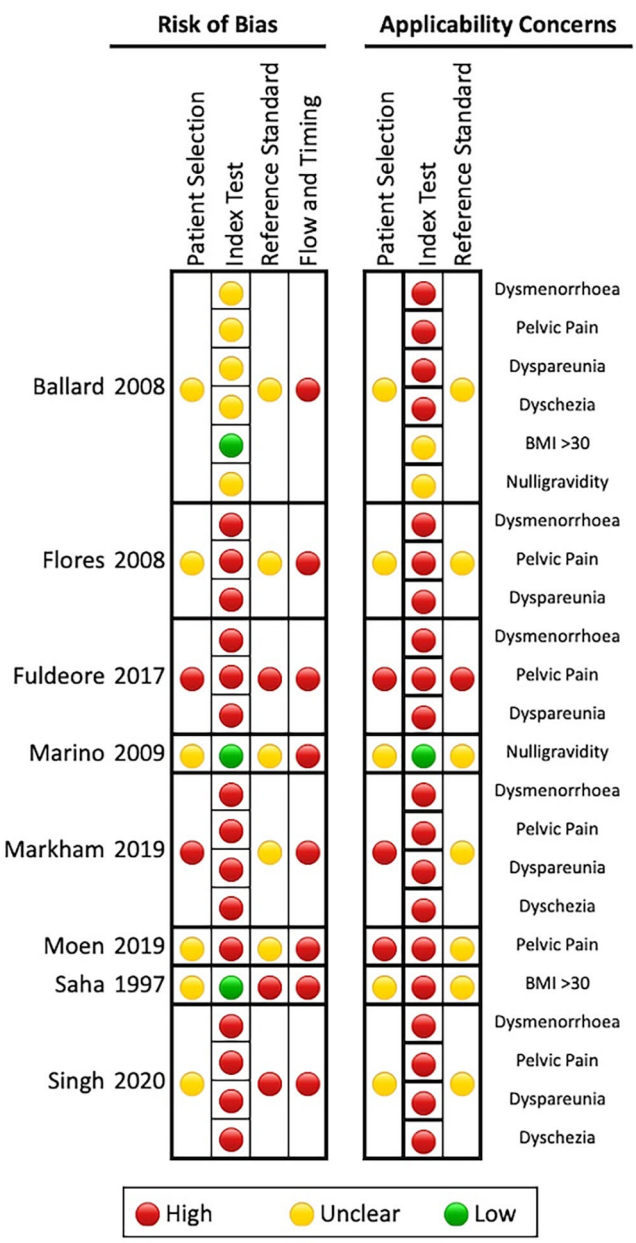


Figure 5. Reviewers assessment of risk of bias and applicability by application of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool for included studies in the diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests database/self-reporting group. BMI, body mass index.

Strengths and limitations

We undertook a thorough search of the current literature, undergoing analysis by two independent reviewers with strict quality assessment. Attempts were made to mitigate inter-study heterogeneity by division of studies into groups. All index tests are relevant to primary care, are immediately available without novel techniques or additional training and can assist in the triage of those with symptoms that could be attributable to endometriosis.

There were, however, limitations. Due to difficulties in data extraction from some non-English journals, 15 studies were excluded from the analysis. Some studies, such as Chapron *et al* 2005, which was seminal in providing a clinical prediction model for moderate/severe endometriosis, were not able to be included due to the inability for construct 2x2 tables.[36] We did not contact authors to obtain individual data that was not available in the published text.

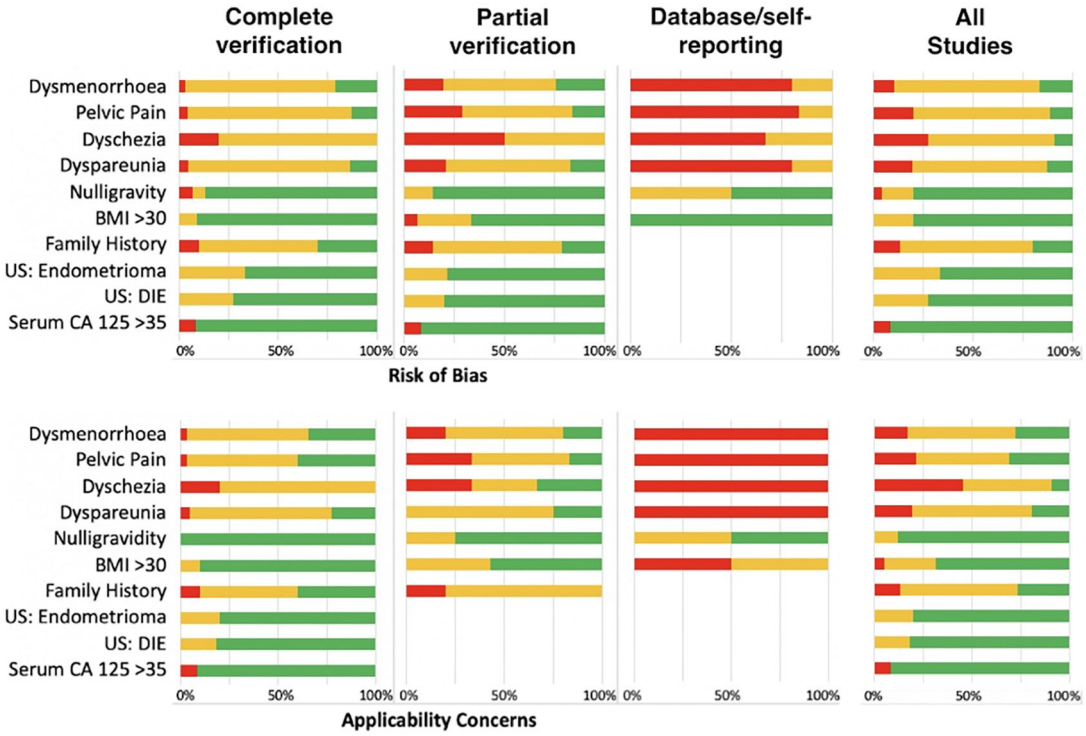


Figure 6. Risk of bias and applicability concerns graph: reviewers authors' judgements on each index test presented as percentages across included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests by application of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.

Overall, there was significant methodological variance and population heterogeneity in age; presentation; and stage of disease. Variation in selection of cases and controls may not reflect a clinically representative population. Prevalence of disease was higher than seen in the general female population, which may reflect a high degree of surgical accuracy, but also indicates the selective nature of study populations.

There is the possibility of inappropriate assignment of cases and controls, occurring in both directions due to uneven application of the reference standard, although we attempted to account for this by assigning groups. We included studies that diagnosed endometriosis by visual inspection and there is debate regarding this in the absence of histological confirmation.[37–39]

There was variation in the definition of positive symptom index tests. This is common across many reviews and although there is guidance on symptom reporting, it was not clearly followed in all studies.[40–42] Assessment of symptoms varied, with most studies using a self-administered questionnaire. Although the use of standardised validated tools would better allow for comparison across studies, the nuance and detail acquired through clinical history taking is likely to better grasp the nature and significance of a symptom and its implications.

It is likely that imaging and surgical techniques have developed over time. A trend towards recent studies may mitigate this. Imaging modalities such as MRI and advanced sonographic techniques were not assessed due to their lack of universal availability in a primary care setting.

Considering the balances of strengths and weaknesses, however, we believe that our data synthesis presents an objective summary of the current evidence.

Interpretation

An understanding of the degree of likelihood associated with various symptoms and features in the clinical history can help assessment of patients with possible endometriosis in primary care.

	Outcome	No. of Studies (Participants)	Summary Accuracy Measures					Assessment of Confidence	
			Sensitivity (95% CI)	Specificity (95% CI)	DOR (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)	Sensitivity Pentagon	Specificity Pentagon
A	Dysmenorrhoea	35 (10,405)	69.8% (60.7-77.6)	52.5% (41.7-63.1)	2.56 (1.99-3.29)	1.47 (1.27-1.70)	0.57 (0.49-0.68)		
	Pelvic Pain	29 (10,477)	46.9% (33.0-61.2)	74.3% (63.8-82.7)	2.56 (1.73-3.74)	1.83 (1.44-2.33)	0.71 (0.59-0.87)		
	Dyschezia	6 (1453)	19.2% (10.5-32.5)	89.1% (78.1-95.4)	2.05 (1.36-3.10)	1.85 (1.26-2.72)	0.90 (0.84-0.97)		
	Dyspareunia	25 (6832)	36.3% (29.4-43.8)	81.1% (72.2-87.7)	2.45 (1.71-3.52)	1.93 (1.42-2.61)	0.78 (0.72-0.85)		
	Nulligravidity	15 (8187)	55.3% (46.3-64.0)	61.8% (53.0-69.9)	2.01 (1.61-2.50)	1.45 (1.27-1.65)	0.72 (0.64-0.81)		
	BMI ≥30kg/m²	10 (3750)	10.9% (4.58-23.7)	75.1% (63.2-84.1)	0.37 (0.19-0.68)	0.44 (0.25-0.77)	1.23 (1.09-1.30)		
	Family History	11 (5346)	9.25% (7.12-11.9)	98.5% (97.1-99.2)	6.79 (4.08-11.3)	6.25 (3.75-10.4)	0.92 (0.90-0.94)		
	TVUSS: Endometrioma	16 (6819)	77.2% (61.0-87.9)	96.4% (93.0-98.2)	91.2 (44.0-189)	21.6 (11.7-39.8)	0.24 (0.13-0.42)		
	TVUSS: DIE	12 (3264)	86.5% (61.2-96.3)	80.2% (52.3-93.8)	26.1 (9.28-73.5)	4.39 (1.74-11.1)	0.17 (0.06-0.48)		
	Serum CA-125 > 35U/mL	17 (2091)	55.8% (37.5-72.7)	92.7% (82.5-97.1)	16.0 (8.09-31.7)	7.63 (3.73-15.6)	0.48 (0.33-0.69)		
B	Dysmenorrhoea	9 (7718)	76.1% (60.9-86.6)	69.2% (60.0-77.0)	7.13 (3.34-15.2)	2.47 (1.83-3.34)	0.35 (0.20-0.59)		
	Pelvic Pain	4 (1601)	62.2% (45.7-76.3)	88.6% (72.7-95.8)	12.8 (5.89-28.1)	5.46 (2.46-12.1)	0.43 (0.31-0.60)		
	Dyschezia	3* (766)	57% (48-65)	92% (85-99)	2.05 (xx-xx)	7.13 (3.2-65)	0.47 (0.35-0.84)		
	Dyspareunia	4 (2039)	51.3% (46.6-59.0)	90.1% (76.7-96.2)	9.65 (3.91-23.8)	5.21 (2.20-12.3)	0.54 (0.50-0.58)		
	Nulligravidity	8 (48,177)	43.1% (35.1-57.5)	74.9% (62.4-84.2)	2.55 (1.93-3.38)	1.84 (1.43-2.35)	0.72 (0.65-0.80)		
	BMI ≥30kg/m²	7 (69,266)	13.9% (9.70-19.7)	87.3% (82.3-90.9)	1.11 (0.95-1.29)	1.09 (0.96-1.25)	0.99 (0.97-1.01)		
	Family History	5 (44,442)	12.4% (7.98-18.9)	97.8% (93.1-99.3)	6.23 (2.08-18.7)	5.58 (1.91-16.3)	0.89 (0.85-0.95)		
C	Dysmenorrhoea	5 (133,883)	70.1% (41.0-88.8)	66.7% (38.1-86.7)	4.70 (1.85-11.9)	2.11 (1.16-3.82)	0.45 (0.24-0.85)		
	Pelvic Pain	6 (109,376)	44.4% (23.5-67.6)	90.3% (78.0-96.1)	7.47 (4.75-11.8)	4.59 (2.88-7.33)	0.61 (0.44-0.87)		
	Dyschezia	3* (56,042)	38% (0-80)	82% (53-100)	2.78 (xx-xx)	2.11 (0-xx)	0.76 (0.2-1.89)		
	Dyspareunia	5 (105,309)	44.4% (18.6-73.6)	84.2% (55.8-95.8)	4.26 (2.76-6.57)	2.81 (1.57-5.05)	0.66 (0.47-0.93)		
	Nulligravidity	2* (27,819)	61% (60-62)	43% (43-44)	1.18 (xx-xx)	1.07 (1.05-1.11)	0.91 (0.86-0.93)		
	BMI ≥30kg/m²	2* (47,791)	10% (10-11)	92% (91-92)	1.28 (xx-xx)	1.25 (0.99-1.11)	0.98 (0.97-0.99)		

Figure 7. Summary diagnostic results of bivariate meta-analysis of index tests for included studies in A: complete verification group; B: partial verification group; C: database/self-reporting group. BMI, body mass index. TVUSS, transvaginal ultrasound scan. DIE, deep invasive endometriosis. CA-125, cancer antigen-125. DOR, diagnostic odds ratio. LR, likelihood ratio. *univariate analysis where fewer than 4 studies included.

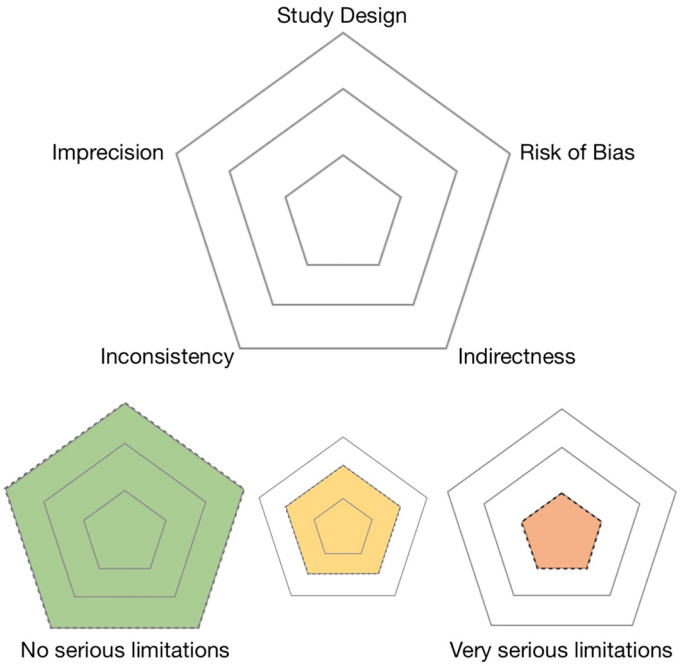


Figure 8. Graphic display of grading of accuracy measures by visual pentagon model applied to index test sensitivity and specificity from included studies in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis as displayed in Figure 7. Score of 0 to -2 in each of 5 domains: design (study design type); risk of bias (QUADAS 2 risk of bias); indirectness (QUADAS 2 applicability); inconsistency (visual assessment of inter-study variance in confidence intervals); and imprecision (width of confidence intervals)

The negative association between elevated BMI and endometriosis shown in the complete verification group is consistent with that demonstrated previously.[43] This was not replicated across other groups. This may reflect a greater negative correlation between elevated BMI in higher risk populations in all surgical cohorts who may have more severe disease. This possibility is consistent with previous studies, demonstrating a significantly lower BMI in those with severe compared to mild disease and a 12-14% decrease in the likelihood of endometriosis being diagnosed for each unit increase in BMI (kg/m2).[31,44] The interplay between BMI and endometriosis pathogenesis, however, remains poorly understood.

The trend of data from the partial verification and database/self-reporting groups to demonstrate better performing accuracy measures was likely a reflection of the selection of controls. This effect seems to outweigh the possibility of an undiagnosed disease burden in controls not exposed to a surgical reference standard. The accuracy of self-reported diagnosis of endometriosis has been assessed and performs well,[45] false attribution of disease in the self-reporting group may therefore only present a small source of bias.

A greater specificity than sensitivity of tests may be associated with their correlation to disease severity. Dyschezia and dyspareunia have been linked to severe disease due to the involvement of a precise anatomical location in cases of invasive disease.[46,47] Tests showing a greater sensitivity such as dysmenorrhea were also less specific.

Previous systematic reviews have similarly highlighted the heterogeneity and poor methodological quality of primary studies, limiting interpretation of findings.[17,48] As our methodology allowed a wide inclusion criteria, we applied a novel grading protocol in order to more quantitively assess limitations. Grading of evidence for index tests was performed for sensitivity and specificity by application of a visual pentagon model for grading of test accuracy studies described by Rogozinska and Khan.[49] This methodology is described in detail elsewhere but briefly, studies were given a score of 0 to -2 in each of 5 domains: design (study design type); risk of bias (QUADAS 2 risk of bias); indirectness (QUADAS 2 applicability); inconsistency (visual assessment of inter-study variance in confidence intervals); and imprecision (width of confidence intervals). The complete verification group shows the fewest limitations, whist the database/self-reporting studies showed very serious limitations. There was greater limitation in the investigation category tests due to more highly selective populations and a generally higher inter-study inconsistency and imprecision.

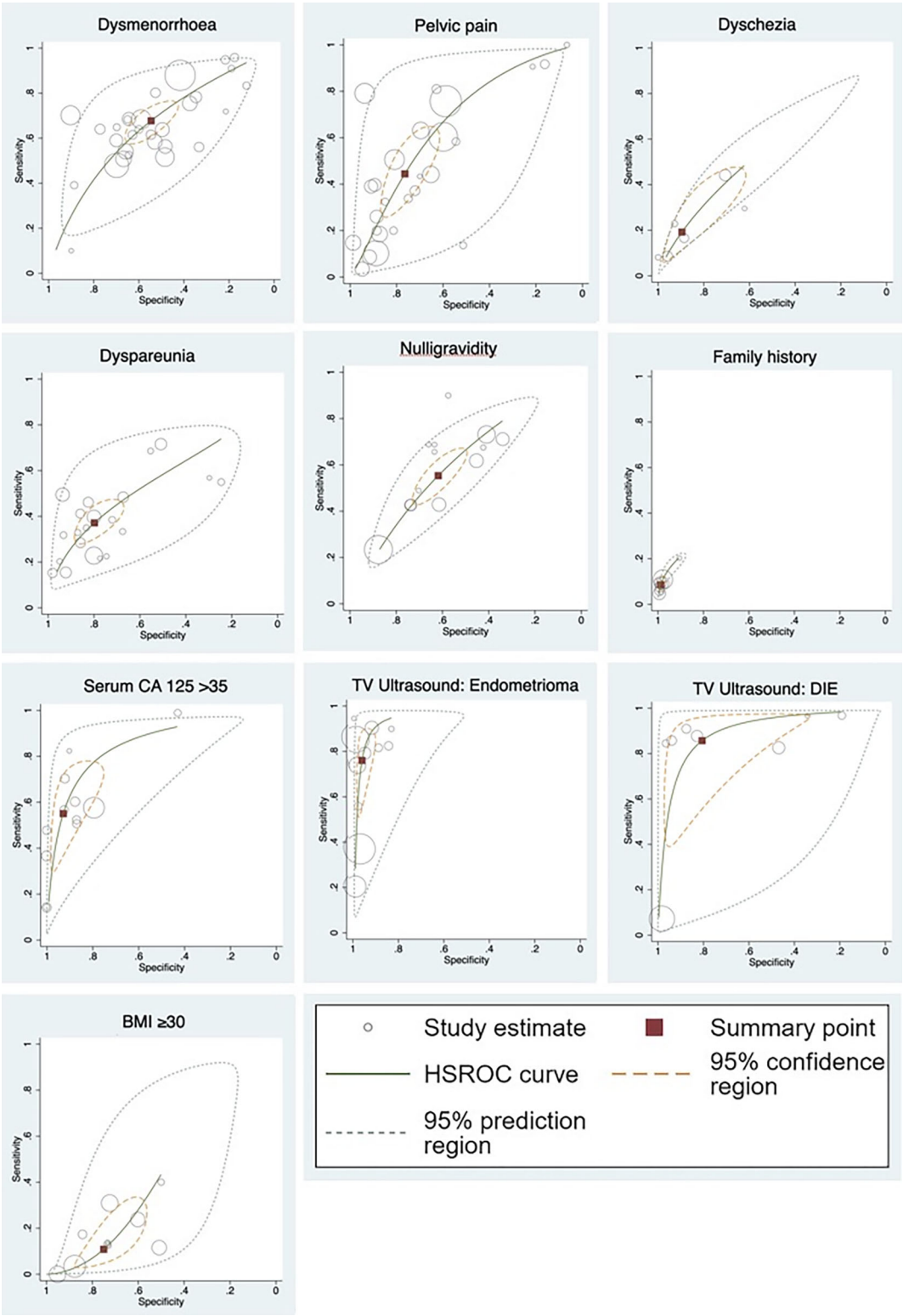


Figure 9. Bivariate analysis Hierarchical Summary Receiver Operating Characteristics (HSROC) curve for index tests from studies included in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis in the complete verification group for the diagnosis of endometriosis. BMI, body mass index. TV, transvaginal, DIE, deep invasive endometriosis. CA-125, cancer antigen-125.

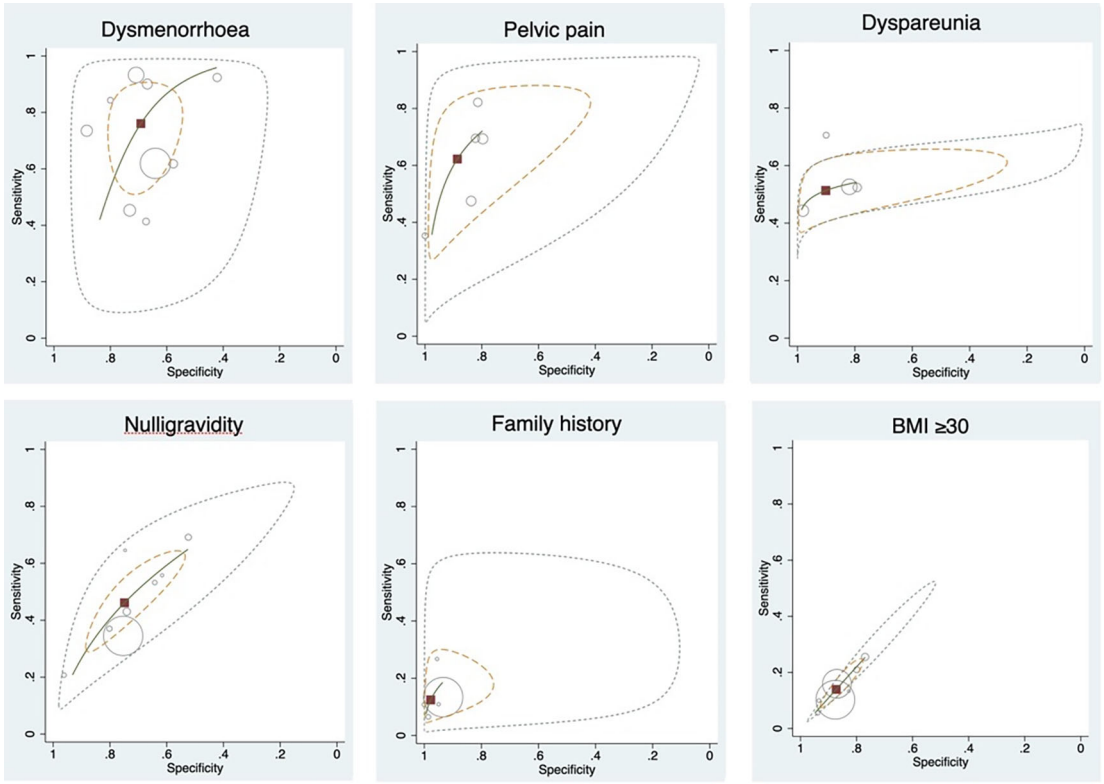


Figure 10. Bivariate analysis Hierarchical Summary Receiver Operating Characteristics (HSROC) curve for index tests from studies included in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis in the partial verification group for the diagnosis of endometriosis. (Index tests with fewer than 5 studies omitted). BMI, body mass index.

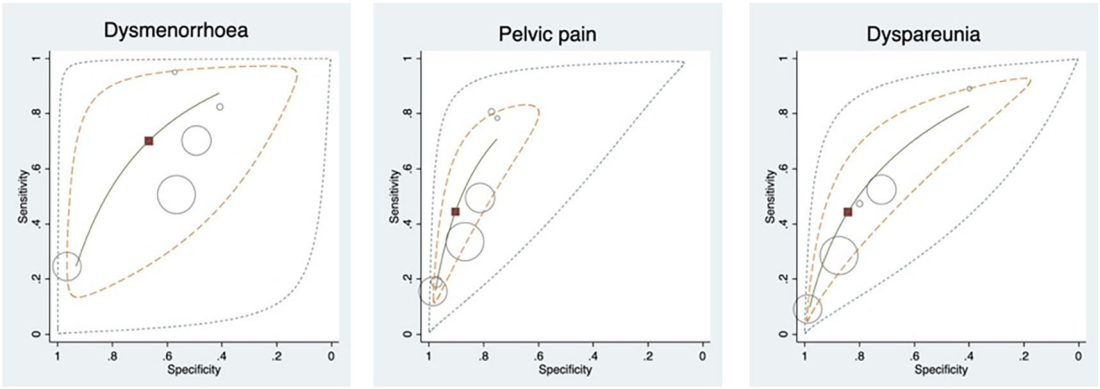
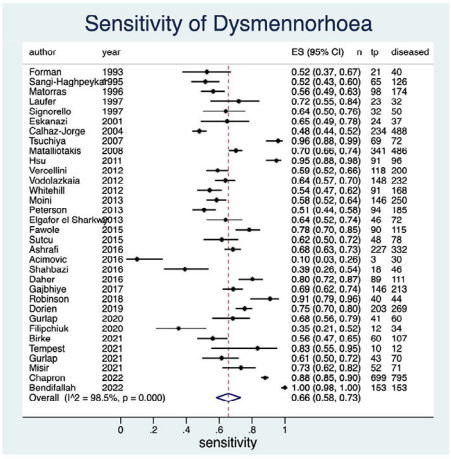
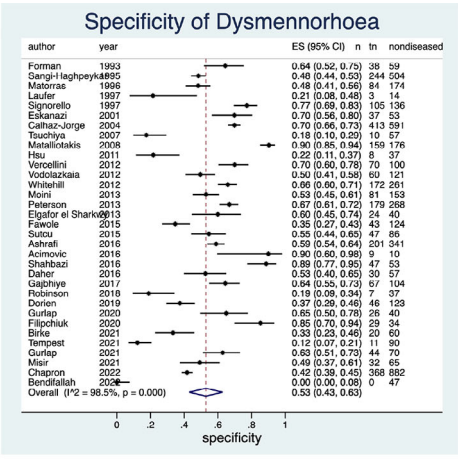
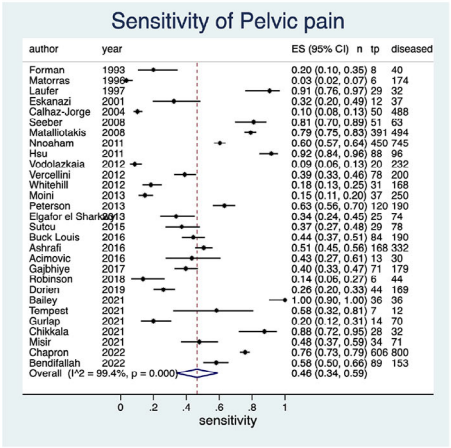
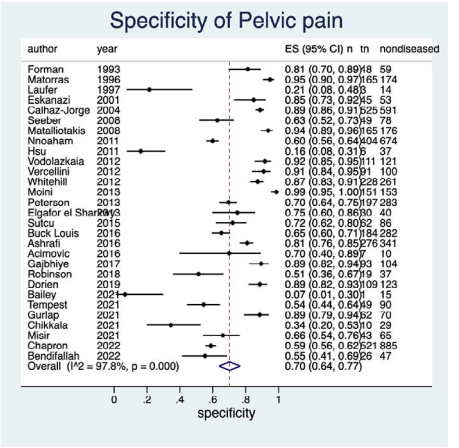


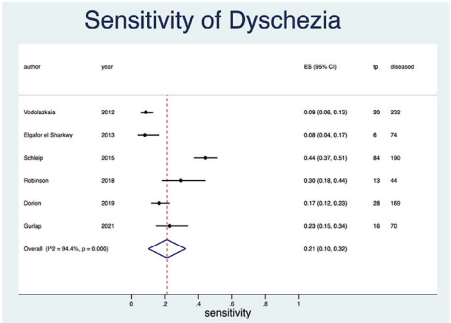
Figure 11. Bivariate analysis Hierarchical Summary Receiver Operating Characteristics (HSROC) curve for index tests from studies included in the systematic review and meta-analysis of non-invasive tests for the diagnosis of endometriosis in the database/self-reporting group for the diagnosis of endometriosis. (Index tests with fewer than 5 studies omitted).

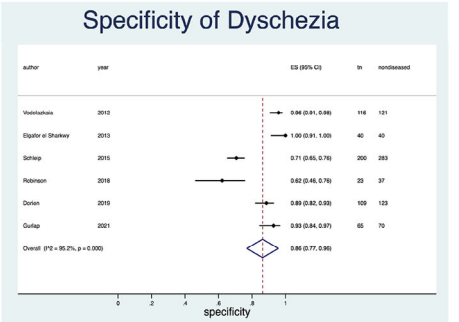


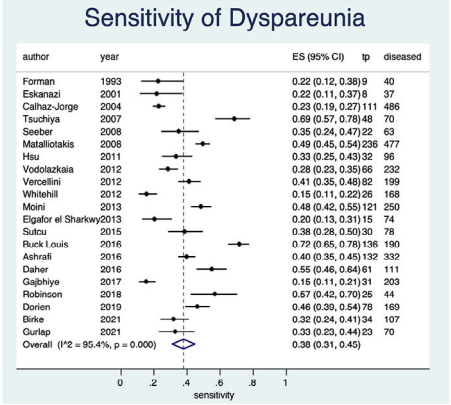












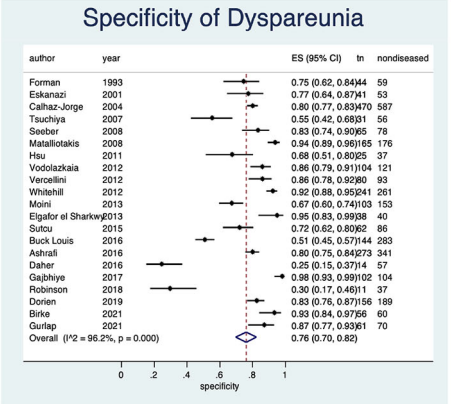
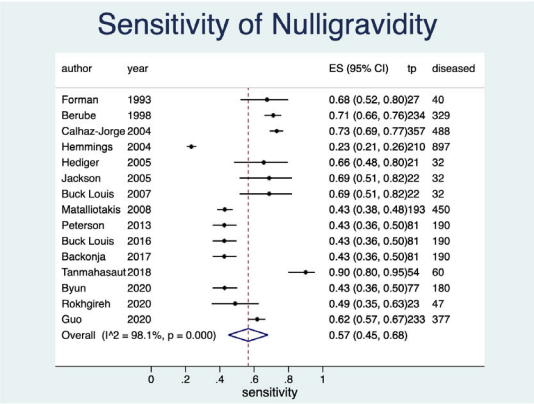
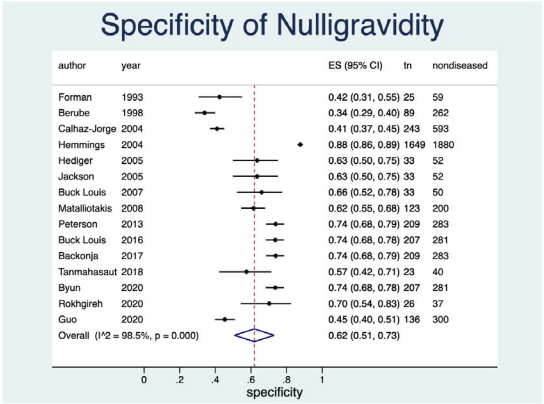
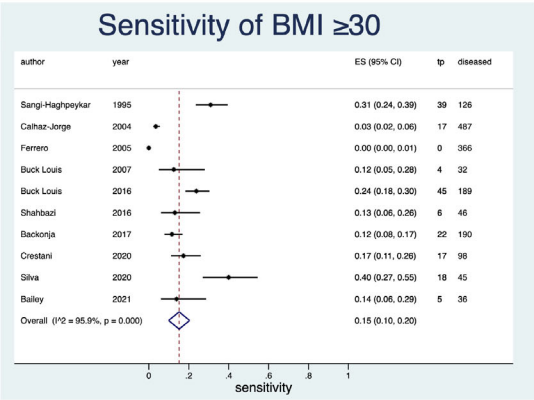
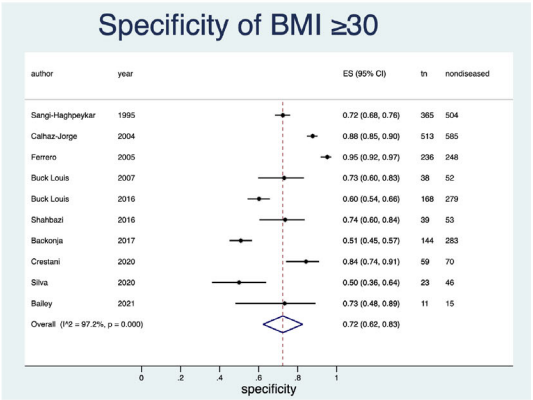


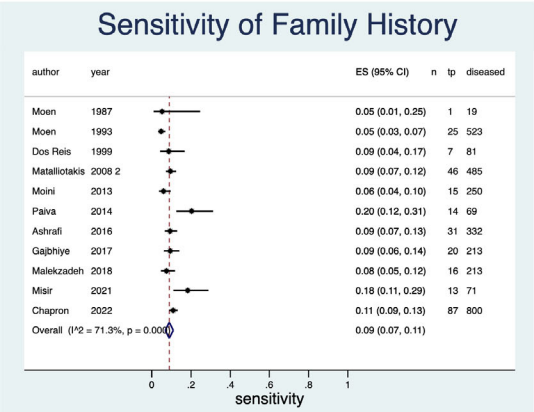
Figure 12. Forest Plots for sensitivity and specificity of symptom-based index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests complete verification group.











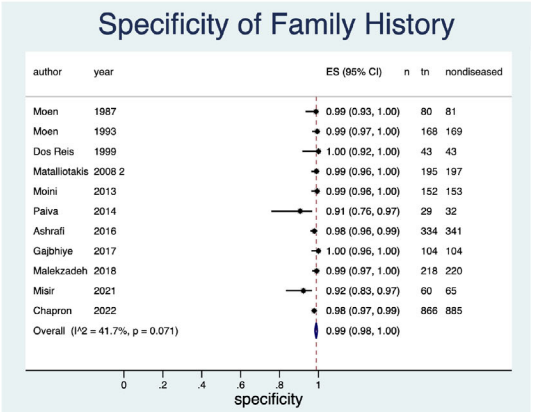


Figure 13. Forest Plots for sensitivity and specificity of clinical feature index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests complete verification group.

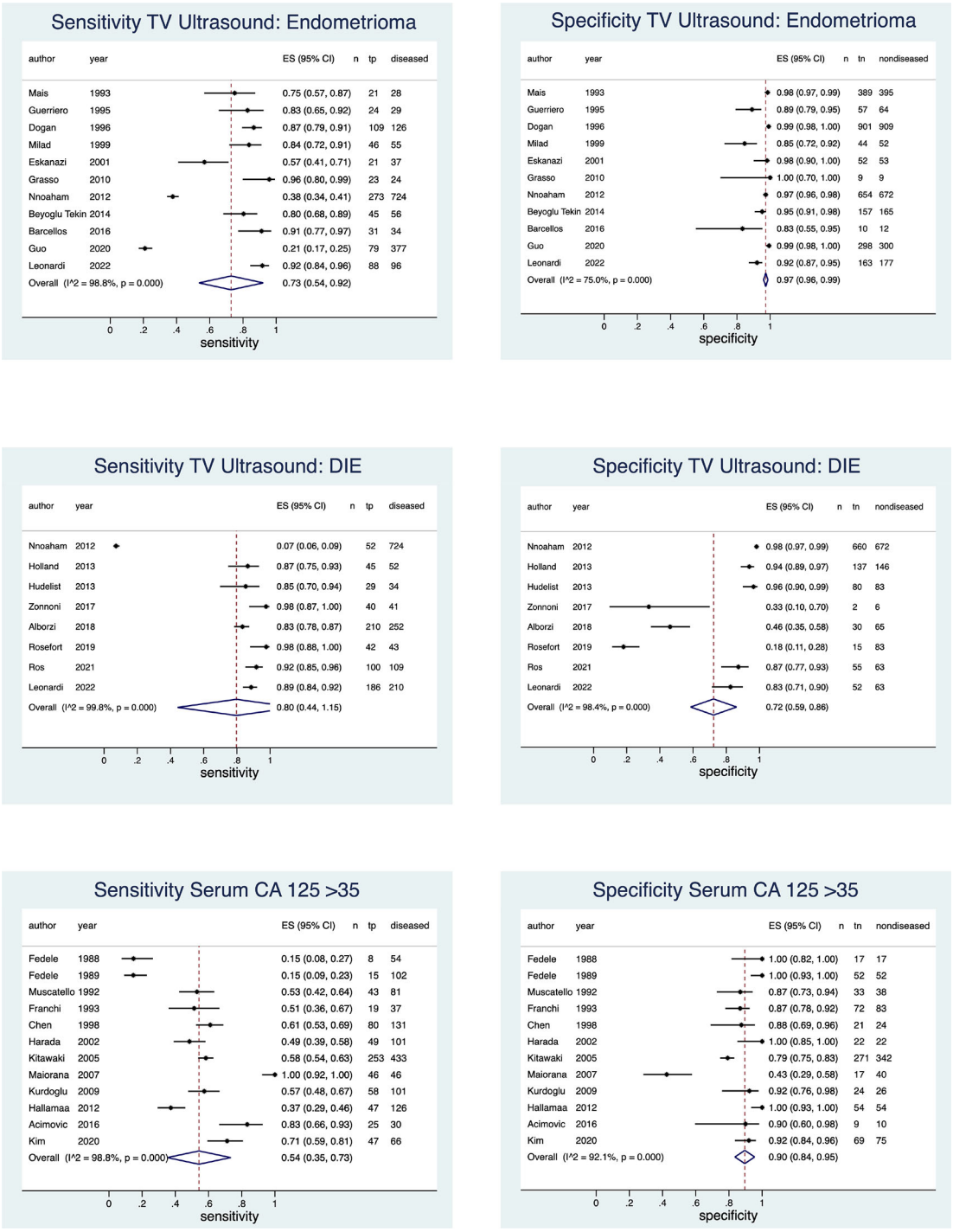


Figure 14. Forest Plots for sensitivity and specificity of investigation index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests complete verification group.

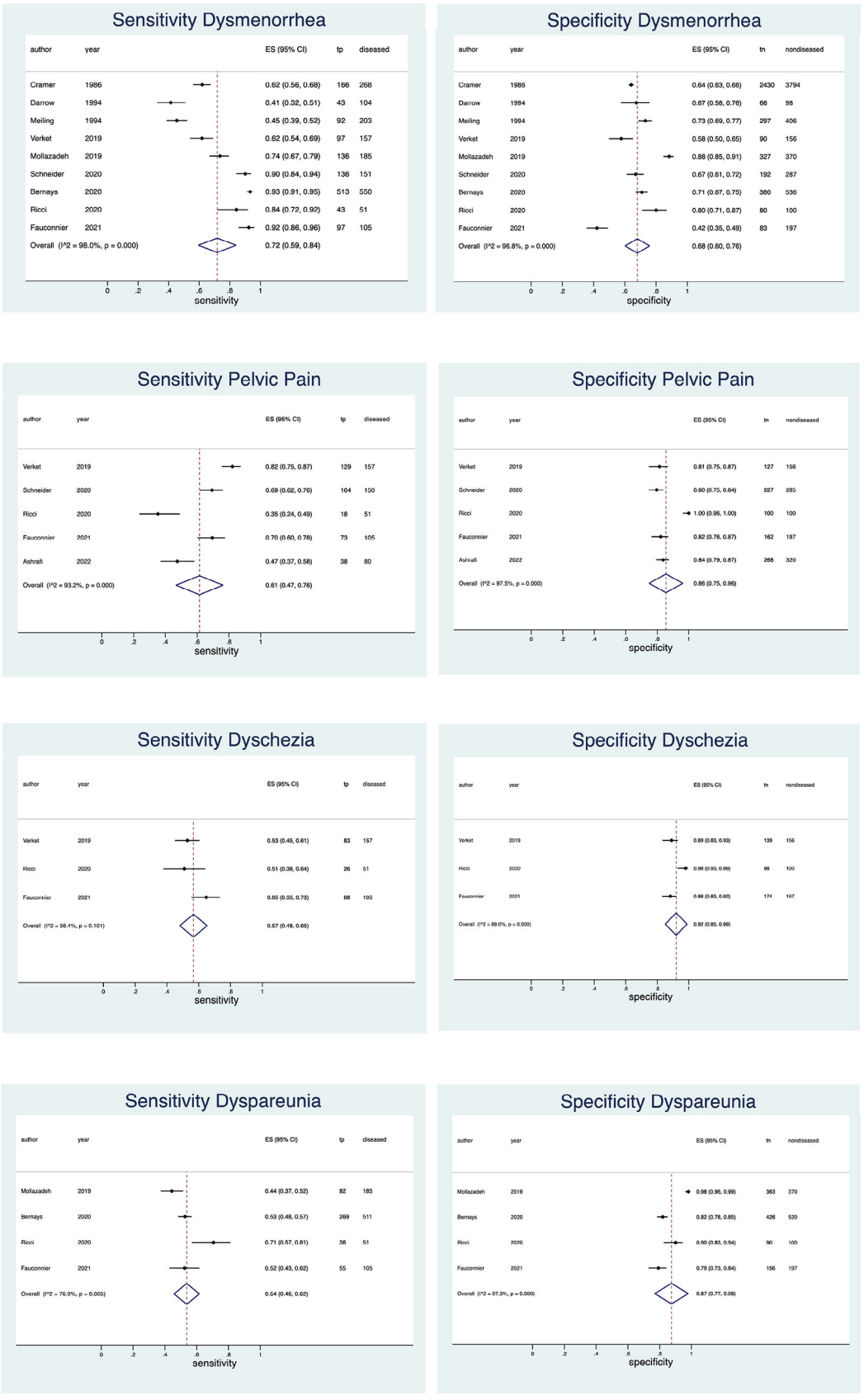
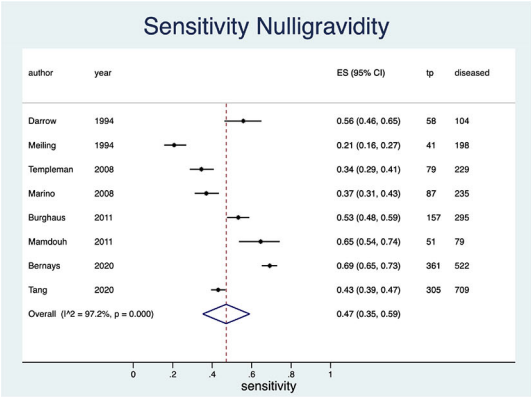
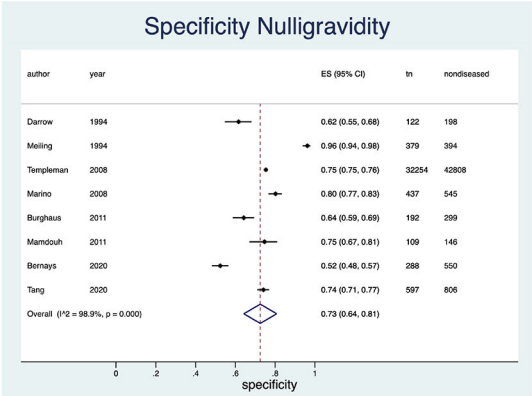
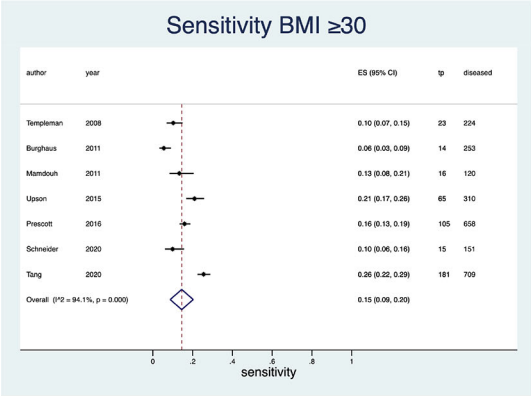
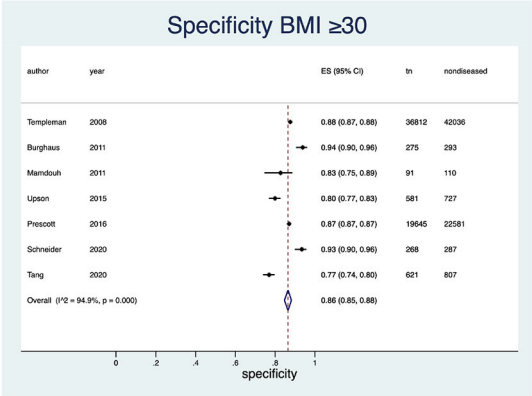


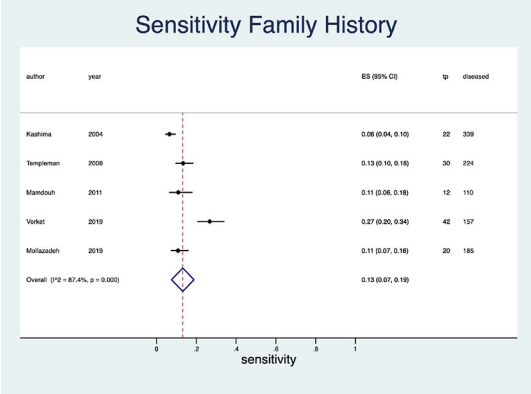
Figure 15. Forest Plots for sensitivity and specificity of symptom-based index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests partial verification group.











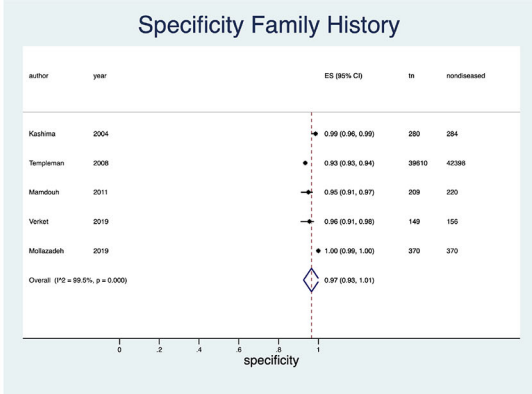


Figure 16. Forest Plots for sensitivity and specificity of clinical feature index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests partial verification group.

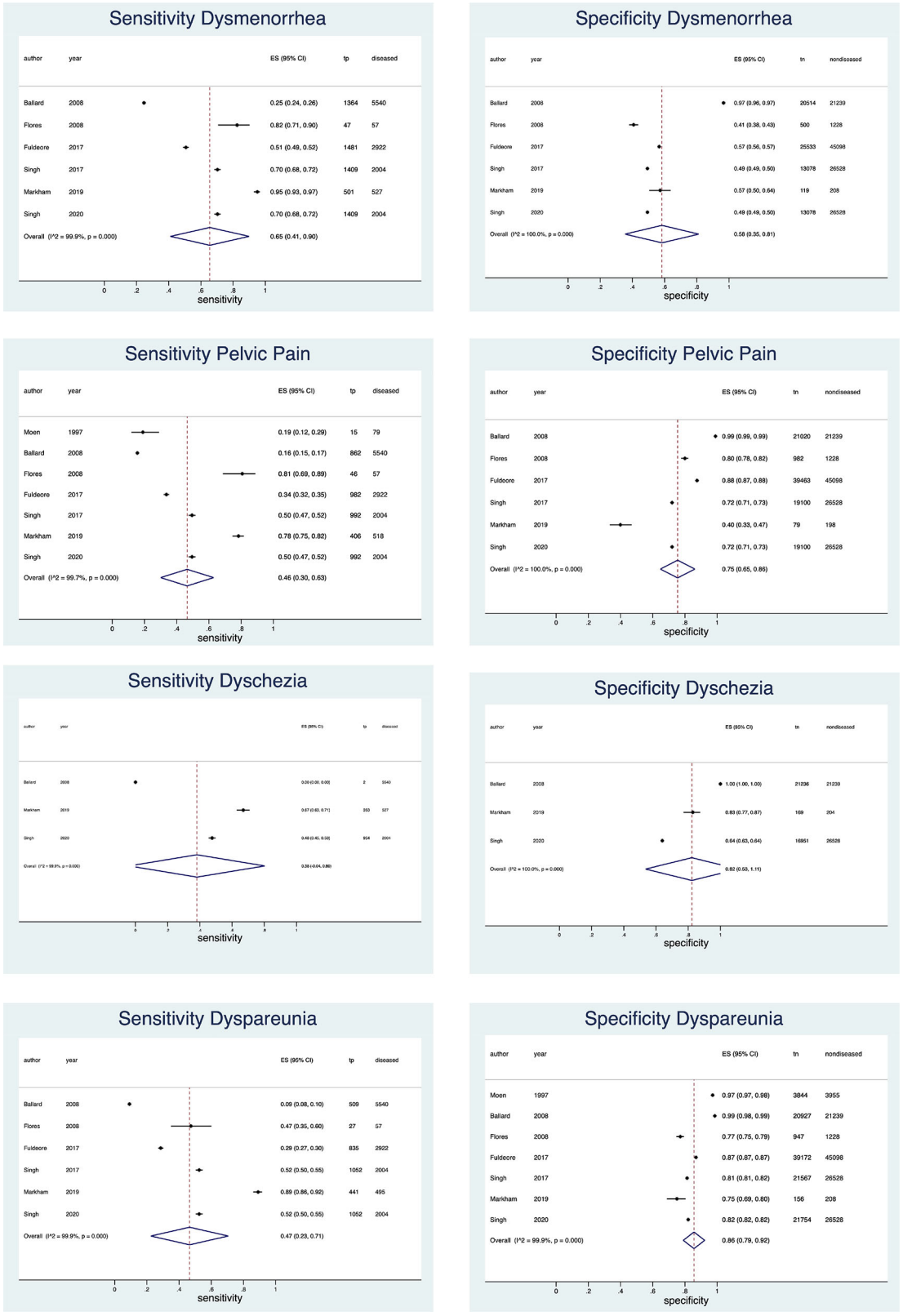


Figure 17. Forest Plots for sensitivity and specificity of symptom-based index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests database/self-reporting group.

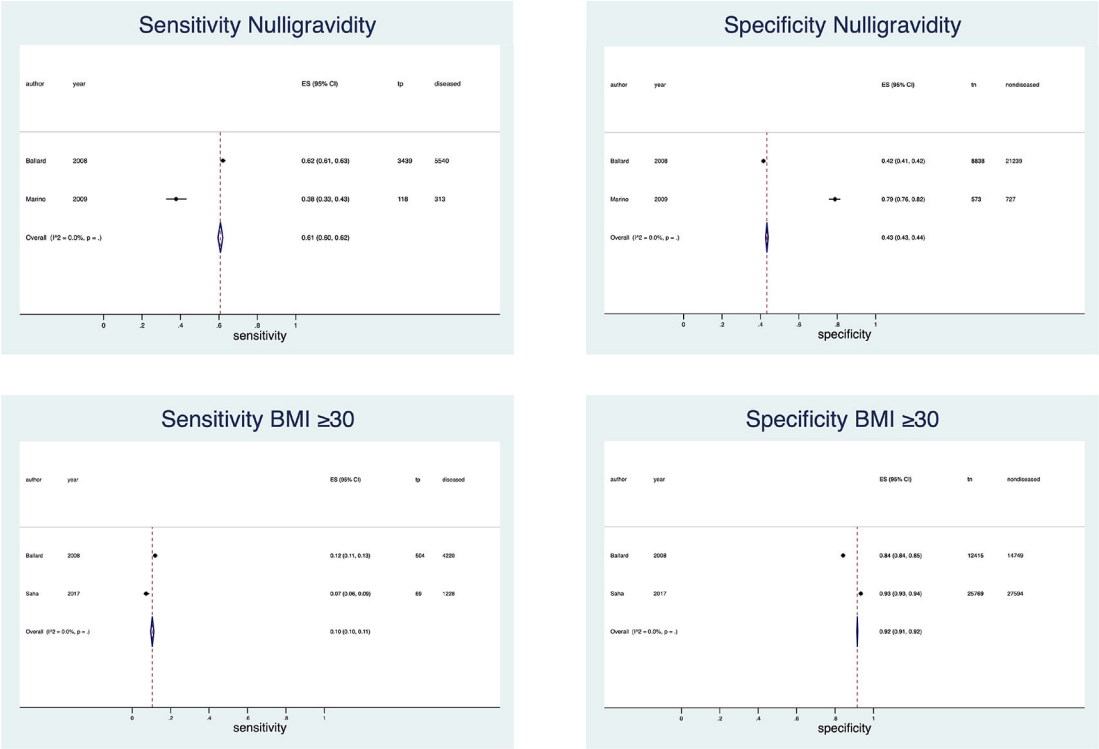


Figure 18. Forest Plots for sensitivity and specificity of clinical feature index tests for included studies in diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests database/self-reporting group.

Conclusions

Research recommendations

The need for high-quality studies of predictive factors for endometriosis remains, particularly assessing populations attending primary care. Further multivariate analysis in powerful primary observational studies assessing factors that can be immediately and readily assessed in primary care would be of great value, as we anticipate the index tests assessed in this study to provide a greater degree of accuracy when applied in combination.[4,36,50]

We examined serum CA-125 at a cut off >35 U/mL, considered the upper limit of normal range, meta-analysis from 2016 found a cut off of 30 U/mL gave a sensitivity and specificity of 52% and 93% respectively, but sensitivity dropped to just 24% for detection of minimal disease.[51] Further research assessing the accuracy of CA-125 at different thresholds and in combination with other tests could help improve accuracy.

Two recent studies (Fauconnier *et al* 2021 and Chapron *et al* 2022) assessed the accuracy of a patient-completed questionnaire and epidemiological data for the early identification of endometriosis and found it could do so with high diagnostic accuracy.[23,52] Although these studies were conducted in a high-risk population undergoing surgery, the model maintained accuracy in population with a lower endometriosis prevalence of 10%. We do not anticipate a clinical score replacing laparoscopy due to its added therapeutic advantages and requirement to exclude other pathologies. If, however, disease can be predicted with a high degree of accuracy early on, medical therapy may be instigated and referral made for definitive diagnosis and counselling regarding treatment, prognosis and fertility in a timely manner with the aim of reducing the current extraordinary delay.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Figshare: Table 1.xlsx. https://doi.org/10.6084/m9.figshare.22419178.v1.[53]

This project contains the following extended data:

- Table 1. xlsx (key word search strategy for all databases to identify primary studies for inclusion).

Figshare: Table 2.xlsx. https://doi.org/10.6084/m9.figshare.22419184.v1.[54]

This project contains the following extended data:

- Table 2. xlsx (index tests and definitions for the purposes of study selection and data extraction and number of included studies and participants reporting on each index test by group according to confirmation of diagnosis of endometriosis. BMI, body mass index; TVUSS, trans-vaginal ultrasound scan; DIE, deep invasive endometriosis; CA-125, cancer antigen-125).

Figshare: Table 3.xlsx. https://doi.org/10.6084/m9.figshare.22419187.v1.[55]

This project contains the following extended data:

- Table 3. xlsx (characteristics of all included studies in the systematic review and meta-analysis).

Figshare: Table 4.xlsx. https://doi.org/10.6084/m9.figshare.22419967.v1.[56]

This project contains the following extended data:

- Table 4. xlsx (excluded studies and reason for exclusion of all screened full texts in the systematic review and meta-analysis).

Figshare: Table 5.xlsx. https://doi.org/10.6084/m9.figshare.22419973.v1.[57]

This project contains the following extended data:

- Table 5. xlsx (method of assessment for all included studies assessing participants for a symptom-based index test (61) in the systematic review and meta-analysis Diagnosis of pelvic endometriosis: a systematic review and accuracy meta-analysis of non-invasive tests available in primary care).

Figshare: Table 6.xlsx. https://doi.org/10.6084/m9.figshare.22419976.v1.[58]

This project contains the following extended data:

- Table 6. xlsx (sensitivity analysis - summary diagnostic results of bivariate meta-analysis of index tests for included studies excluding those with any high-risk feature for bias or applicability. BMI, body mass index. TVUSS, transvaginal ultrasound scan. DIE, deep invasive endometriosis. CA-125, cancer antigen-125. DOR, diagnostic odds ratio. LR, likelihood ratio).

Reporting guidelines

Figshare: PRISMA checklist for 'Diagnosis of pelvic endometriosis: A systematic review and accuracy meta-analysis of non-invasive tests available in primary care'. https://doi.org/10.6084/m9.figshare.22420591.v1.[59]

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Acknowledgements

KSK is Distinguished Investigator at University of Granada funded by the Beatriz Galindo (senior modality) program of the Spanish Ministry of Education.

References

1. Eskenazi B, Warner ML: **Epidemiology of endometriosis.** *Obstet. Gynecol. Clin. N. Am.* 1997; **24**(2): 235–258.
Publisher Full Text

2. Farquhar C: **Endometriosis.** *BMJ.* 2007; **334**(7587): 249–253.
PubMed Abstract | Publisher Full Text | Free Full Text

3. Giudice LC: **Clinical practice. Endometriosis.** *N. Engl. J. Med.* 2010; **362**(25): 2389–2398.
Publisher Full Text

4. Ballard KD, Seaman HE, de Vries CS, *et al.*: **Can symptomatology help in the diagnosis of endometriosis? Findings from a national case-control study--Part 1.** *BJOG.* 2008; **115**(11): 1382–1391.
Publisher Full Text

5. Prescott J, Farland LV, Tobias DK, *et al.*: **A prospective cohort study of endometriosis and subsequent risk of infertility.** *Hum. Reprod.* 2016; **31**(7): 1475–1482.
Publisher Full Text

6. Fuldeore MJ, Soliman AM: **Prevalence and Symptomatic Burden of Diagnosed Endometriosis in the United States: National Estimates from a Cross-Sectional Survey of 59,411 Women.** *Gynecol. Obstet. Investig.* 2017; **82**(5): 453–461.
Publisher Full Text

7. Nnoaham KE, Hummelshoj L, Webster P, *et al.*: **Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries.** *Fertil. Steril.* 2011; **96**(2): 366–373.e8.
Publisher Full Text

8. Kuznetsov L, Dworzynski K, Davies M, *et al.*: **Diagnosis and management of endometriosis: summary of NICE guidance.** *BMJ.* 2017; **358**: j3935.
Publisher Full Text

9. Zondervan KT, Becker CM, Koga K, *et al.*: **Endometriosis.** *Nat. Rev. Dis. Primers.* 2018; **4**(1): 9.
Publisher Full Text

10. Rogers PAW, D'Hooghe TM, Fazleabas A, *et al.*: **Priorities for endometriosis research: Recommendations from an international consensus workshop.** *Reprod. Sci.* 2009; **16**(4): 335–346.
Publisher Full Text

11. Rogers PA, Adamson GD, Al-Jefout M, *et al.*: **Research Priorities for Endometriosis.** *Reprod. Sci.* 2017; **24**(2): 202–226.

12. Arruda MS, Petta CA, Abrão MS, *et al.*: **Time elapsed from onset of symptoms to diagnosis of endometriosis in a cohort study of Brazilian women.** *Hum. Reprod.* 2003; **18**(4): 756–759.
Publisher Full Text

13. Surrey E, Soliman AM, Trenz H, *et al.*: **Impact of Endometriosis Diagnostic Delays on Healthcare Resource Utilization and Costs.** *Adv. Ther.* 2020; **37**(3): 1087–1099.
PubMed Abstract | Publisher Full Text | Free Full Text

14. **UK All Party Parliamentary Group on Endometriosis Inquiry Report. *Endometriosis in the UK: time for change (October 2020).*** **UK All Party Parliamentary Group on Endometriosis.** 2020.

15. Liu E, Nisenblat V, Farquhar C, *et al.*: **Urinary biomarkers for the non-invasive diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2015; **2015**(12).
PubMed Abstract | Publisher Full Text | Free Full Text

16. Gupta D, Hull ML, Fraser I, *et al.*: **Endometrial biomarkers for the non-invasive diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2016; **2016**(4): Cd012165.
Publisher Full Text

17. Nisenblat V, Prentice L, Bossuyt PM, *et al.*: **Combination of the non-invasive tests for the diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2016; **2016**(7): Cd012281.
Publisher Full Text

18. May KE, Conduit-Hulbert SA, Villar J, *et al.*: **Peripheral biomarkers of endometriosis: A systematic review.** *Hum. Reprod. Update.* 2010; **16**(6): 651–674.
PubMed Abstract | Publisher Full Text | Free Full Text

19. Nisenblat V, Prentice L, Bossuyt PMM, *et al.*: **Combination of the non-invasive tests for the diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2016; **2016**(7).
Publisher Full Text

20. Nisenblat V, Bossuyt PMM, Shaikh R, *et al.*: **Blood biomarkers for the non-invasive diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2016; **2016**(5).

21. Nisenblat V, Bossuyt PM, Farquhar C, *et al.*: **Imaging modalities for the non-invasive diagnosis of endometriosis.** *Cochrane Database Syst. Rev.* 2016; **2**(2): Cd009591.
PubMed Abstract | Publisher Full Text

22. Agarwal SK, Chapron C, Giudice LC, *et al.*: **Clinical diagnosis of endometriosis: a call to action.** *Am. J. Obstet. Gynecol.* 2019; **220**(4): 354.e1–354.e12.
Publisher Full Text

23. Fauconnier A, Drioueche H, Huchon C, *et al.*: **Early identification of women with endometriosis by means of a simple patient-completed questionnaire screening tool: a diagnostic study.** *Fertil. Steril.* 2021; **116**(6): 1580–1589.
Publisher Full Text

24. Bruggmann D, Elizabeth-Martinez A, Klingelhofer D, *et al.*: **Endometriosis and its global research architecture: an in-depth density-equalizing mapping analysis.** *Bmc Womens Health.* 2016; **16**.
Publisher Full Text

25. Malvezzi H, Marengo EB, Podgaec S, *et al.*: **Endometriosis: current challenges in modeling a multifactorial disease of unknown etiology.** *J. Transl. Med.* 2020; **18**(1): 311.
Publisher Full Text

26. Bainton TJS, Raza A: **A systematic review of the literature to determine the accuracy measures of various predictors of endometriosis.** Published 2020. Accessed.
Reference Source

27. Page MJ, McKenzie JE, Bossuyt PM, *et al.*: **The PRISMA 2020 statement: an updated guideline for reporting systematic reviews.** *BMJ.* 2021; **372**: n71.
Publisher Full Text

28. ***EndNote* [computer program]. Version EndNote X9. Philadelphia, PA: Clarivate.** 2013.

29. Whiting PF, Rutjes AW, Westwood ME, *et al.*: **QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies.** *Ann. Intern. Med.* 2011; **155**(8): 529–536.
Publisher Full Text

30. StataCorp: **Stata Statistical Software: Release 15. College Station TSL.** 2017.

31. Hediger ML, Hartnett HJ, Louis GM: **Association of endometriosis with body size and figure.** *Fertil. Steril.* 2005; **84**(5): 1366–1374.
Publisher Full Text

32. Paiva P, Lappas M, Barker G, *et al.*: **Using symptom scores, lifestyle measures and biochemical markers to create a test for endometriosis.** *Journal of Endometriosis and Pelvic Pain Disorders.* 2014; **6**(3): 135–143.
Publisher Full Text

33. Backonja U, Hediger ML, Chen Z, *et al.*: **Beyond Body Mass Index: Using Anthropometric Measures and Body Composition Indicators to Assess Odds of an Endometriosis Diagnosis.** *J. Womens Health (Larchmt).* 2017; **26**(9): 941–950.
Publisher Full Text

34. Tanmahasamut P, Preukthanathorn R, Dangrat C: **Serum interleukin 6 and cancer antigen 125 in the non-invasive diagnosis of endometriosis.** *Journal of Endometriosis and Pelvic Pain Disorders.* 2018; **10**(2): 116–122.
Publisher Full Text

35. Kim H, Choi YS, Kim JS, *et al.*: **Identification of Serum Biomarkers for Diagnosis of Endometriosis Using Multiplex Immunoassays.** *Reprod. Sci.* 2020; **27**(5): 1139–1147.
Publisher Full Text

36. Chapron C, Barakat H, Fritel X, *et al.*: **Presurgical diagnosis of posterior deep infiltrating endometriosis based on a standardized questionnaire.** *Hum. Reprod.* 2005; **20**(2): 507–513.
Publisher Full Text

37. Kazanegra R, Zaritsky E, Lathi RB, *et al.*: **Diagnosis of stage I endometriosis: comparing visual inspection to histologic biopsy specimen.** *J. Minim. Invasive Gynecol.* 2008; **15**(2): 176–180.
Publisher Full Text

38. Dunselman GA, Vermeulen N, Becker C, *et al.*: **ESHRE guideline: management of women with endometriosis.** *Hum. Reprod.* 2014; **29**(3): 400–412.
Publisher Full Text

39. Lier MCI, Vlek SL, Ankersmit M, *et al.*: **Comparison of enhanced laparoscopic imaging techniques in endometriosis surgery: a diagnostic accuracy study.** *Surg. Endosc.* 2020; **34**(1): 96–104.
Publisher Full Text

40. Chen CX, Kwekkeboom KL, Ward SE: **Self-report pain and symptom measures for primary dysmenorrhoea: a critical review.** *Eur. J. Pain.* 2015; **19**(3): 377–391.
Publisher Full Text

41. Doggweiler R, Whitmore KE, Meijlink JM, *et al.*: **A standard for terminology in chronic pelvic pain syndromes: A report from the chronic pelvic pain working group of the international**

continence society. *Neurourol. Urodyn.* 2017; **36**(4): 984–1008.
Publisher Full Text

42. Steingrímsdóttir ÓA, Landmark T, Macfarlane GJ, *et al.*: **Defining chronic pain in epidemiological studies: a systematic review and meta-analysis.** *Pain.* 2017; **158**(11): 2092–2107.
Publisher Full Text

43. Liu Y, Zhang W: **Association between body mass index and endometriosis risk: a meta-analysis.** *Oncotarget.* 2017; **8**(29): 46928–46936.
Publisher Full Text

44. Yi KW, Shin JH, Park MS, *et al.*: **Association of body mass index with severity of endometriosis in Korean women.** *Int. J. Gynaecol. Obstet.* 2009; **105**(1): 39–42.
Publisher Full Text

45. Shafrir AL, Wise LA, Palmer JR, *et al.*: **Validity of self-reported endometriosis: a comparison across four cohorts.** *Hum. Reprod.* 2021; **36**(5): 1268–1278.
Publisher Full Text

46. Seracchioli R, Mabrouk M, Guerrini M, *et al.*: **Dyschezia and posterior deep infiltrating endometriosis: analysis of 360 cases.** *J. Minim. Invasive Gynecol.* 2008; **15**(6): 695–699.
Publisher Full Text

47. Fauconnier A, Chapron C: **Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications.** *Hum. Reprod. Update.* 2005; **11**(6): 595–606.
Publisher Full Text

48. May KE, Villar J, Kirtley S, *et al.*: **Endometrial alterations in endometriosis: a systematic review of putative biomarkers.** *Hum. Reprod. Update.* 2011; **17**(5): 637–653.
Publisher Full Text

49. Rogozińska E, Khan K: **Grading evidence from test accuracy studies: what makes it challenging compared with the grading of effectiveness studies?** *Evid. Based Med.* 2017; **22**(3): 81–84.
Publisher Full Text

50. Eskenazi B, Warner M, Bonsignore L, *et al.*: **Validation study of nonsurgical diagnosis of endometriosis.** *Fertil. Steril.* 2001; **76**(5): 929–935.
Publisher Full Text

51. Hirsch M, Duffy JMN, Davis CJ, *et al.*: **Diagnostic accuracy of cancer antigen 125 for endometriosis: a systematic review and meta-analysis.** *BJOG Int. J. Obstet. Gynaecol.* 2016; **123**(11): 1761–1768.
Publisher Full Text

52. Chapron C, Lafay-Pillet MC, Santulli P, *et al.*: **A new validated screening method for endometriosis diagnosis based on patient questionnaires.** *EClinicalMedicine.* 2022; **44**: 101263.
Publisher Full Text

53. Bainton T, Jeyapala S, Zamora J, *et al.*: **Table 1.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

54. Bainton T: **Table 2.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

55. Bainton T: **Table 3.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

56. Bainton T: **Table 4.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

57. Bainton T: **Table 5.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

58. Bainton T: **Table 6.xlsx. figshare.** *Figure.* 2023.
Publisher Full Text

59. Bainton T:PRISMA checklist. Diagnosis of pelvic endometriosis- A systematic review and accuracy meta-analysis of non-invasive tests available in primary care.docx. [Dataset]. *figshare.* 2023.
Publisher Full Text

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research