Assessment

	Judgement	Research evidence
Problem	**Is the problem a priority?** ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	There is currently no objective test for pelvic inflammatory disease, and symptoms can vary widely from severe to none. Clinical diagnosis involves bimanual examination of the cervix and uterus to detect tenderness among women presenting with acute lower pelvic pain, fever and vaginal or cervical discharge. The procedure is uncomfortable, invasive and subjective, thereby presenting a significant barrier to clinicians and women. Pelvic inflammatory disease cases could be missed and may increase women's risk of ectopic pregnancy and infertility. Laparoscopic examination is considered the gold standard for diagnosing pelvic inflammatory disease (or endometrial biopsy. transvaginal sonography, magnetic resonance imaging techniques or Doppler studies) but, because of their impracticality as a screening tool, until more accurate diagnostics are available, clinicians are advised to have a low threshold for syndromic management for suspected cases of pelvic inflammatory disease. **High cost of molecular STI testing** There is a need for cheaper platforms, near-patient or point-of-care tests for *C. trachomatis* and *N. gonorrhoeae* and potentially for *M. genitalium*. **Antimicrobial resistance** There is increasing concern about the treatment of people with *N. gonorrhoeae*, since high rates of resistance to penicillin, tetracycline and quinolone have been documented globally. Resistance to commonly used first-line medications (azithromycin) and reports of treatment failure or reduced susceptibility in *N. gonorrhoeae* to cephalosporin (a last-line treatment for *N. gonorrhoeae*) raise concern that *N. gonorrhoeae* could become untreatable.
Test accuracy	**How accurate is the test?** ○ Very inaccurate ● Inaccurate ○ Accurate ○ Very accurate ○ Varies ○ Don't know	We systematically reviewed the literature, searching up to September 2019. In summary, we identified five studies that assessed the diagnostic accuracy of lower abdominal pain syndromic management to detect any STI (Table A5.1), five studies for genital chlamydia (Table A5.2) and four studies for genital gonorrhoea (Table A5.3) and three studies for genital trichomoniasis (Table A5.4). For detection of any STI (chlamydia, gonorrhoea or trichomoniasis), five studies provided eight estimates for pooling. The pooled sensitivity for detecting chlamydia, gonorrhoea or trichomonas using a syndromic management approach (lower abdominal pain) is 30.0% (95% CI: 17.7–46.0%), and pooled specificity is 73.3% (95% CI: 56.3–85.4%).

	Judgement	Research evidence
Test accuracy		

Table A5.5. GRADE summary of findings table for abdominal pain and any STI

Test result	Number of results per 1000 people tested (95% confidence interval)	Number of participants (studies)	Certainty of the evidence (GRADE)
	Prevalence of 5% typically seen in:		
True positives	15 (9–23)	3908 (5)	⨁⨁⨁⨁ High
False negatives	35 (27–41)		
True negatives	696 (535–811)	3908 (5)	⨁⨁⨁◯ Moderate[a,b]
False positives	254 (139–415)		

a Most studies showed consistent results.

b The threshold for unnecessary treatment was high (about 75%), and the confidence intervals cross that threshold and there is therefore some imprecision for false positives.

Accuracy of criteria for pelvic inflammatory disease in the WHO syndromic management flow chart (also similar to the minimal criteria of the United States Centers for Disease Control and Prevention)

The value of various clinical characteristics to identify pelvic inflammatory disease has been studied among 651 women in the United States of America (PEACH Study) *(1)*.

Table A5.6. Diagnostic test characteristics of clinical signs of pelvic inflammatory disease

Clinical characteristic	Sensitivity in % (95% confidence interval)	Specificity in % (95% confidence interval)
Abdominal tenderness	93.9 (90.6–96.3)	7.4 (4.8–10.7)
Cervical motion tenderness	91.6 (88.0–94.5)	12.6 (9.1–16.7)
Uterine tenderness	94.2 (91.0–96.6)	5.3 (3.1–8.2)
Adnexal tenderness	95.5 (92.6–97.5)	3.8 (2.1–6.5)
Minimal criteria of the United States Centers for Disease Control and Prevention	83.3 (78.7–87.3)	21.8 (17.5–26.5)

Source: Peipert et al. *(1)*.

	Judgement	Research evidence
Test accuracy		

Table A5.7. Evaluation of supportive criteria for diagnosing endometritis

Clinical characteristic	Sensitivity in % (95% confidence interval)	Specificity in % (95% confidence interval)	Positive likelihood ratio	Negative likelihood ratio	Measure of separation (95% confidence interval)[a]
Abnormal cervical or vaginal discharge	79.7 (74.6–84.2)	29.8 (24.8–35.2)	1.14	0.681	1.67 (1.15–2.43)
Elevated body temperature (>38°C)	11.1 (7.8–15.2)	94.7 (91.7–96.9)	2.09	0.939	2.25 (1.23–4.13)
Elevated leukocyte count (≥10 000 cells)	41.1 (35.1–47.3)	76.1 (70.6–81.0)	1.72	0.774	2.22 (1.54–3.22)
Positive bacterial results[b]	56.0 (50.2–61.6)	81.6 (77.0–85.6)	3.04	0.539	5.64 (3.94–8.06)

a Positive likelihood ratio/negative likelihood ratio.
b Polymerase chain reaction testing for *N. gonorrhoeae* or *C. trachomatis*.

Table A5.8. GRADE summary of findings table for the minimal criteria of the United States Centers for Disease Control and Prevention (tenderness) and detection of pelvic inflammatory disease based on sensitivity 83.8% and specificity 21.8%

Test result	Number of results per 1000 people tested (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	Prevalence of 5% typically seen in:		
True positives	42 (39–44)	651 (1)	⨁⨁⨁◯ Moderate[a]
False negatives	8 (6–11)		
True negatives	207 (166–252)	651 (1)	⨁⨁⨁◯ Moderate[a]
False positives	743 (698–784)		

CI: confidence interval.
a Most studies showed consistent results.
Single study sensitivity: 0.84 (95% CI: 0.79–0.87)
Single study specificity: 0.22 (95% CI: 0.17–0.27)

	Judgement	Research evidence
Test accuracy		**Other criteria to identify pelvic inflammatory disease** A study of 189 women clinically diagnosed with pelvic inflammatory disease from a hospital outpatient setting in Sweden reported the sensitivity of various symptoms and signs – tenderness of pelvic organs on bimanual exam. Laparoscopic confirmation of pelvic inflammatory disease was not conducted for these women *(2)*.

Table A5.9. Prediction of laparoscopically diagnosed PID: sensitivity and specificity of signs and symptoms, likelihood ratios and port-test probabilities (pretest probability = 79%)

Signs and symptoms	Sensitivity (%)	Specificity (%)	Laparoscopically diagnosed PID		Likelihood ratio* (Positive)	Post-test probability
			Present (n=494)	Absent (n=129)		
	(95% CI)	(95% CI)	No (%)	No (%)		
Vaginal discharge	74 (69.99–77.90)	24 (16.95–32.34)	366 (74)	98 (76)	0.98	0.79
Fever	47 (42.49–51.47)	64 (55.43–72.58)	234 (47)	47 (36)	1.30	0.83
Vomiting	14 (11.03–17.34)	88 (81.55–93.34)	68 (14)	16 (12)	1.11	0.81
Menstrual irregularity	45 (40.49–49.45)	57 (48.36–66.03)	223 (45)	56 (43)	1.04	0.80
Ongoing bleeding	25 (21.24–29.17)	77 (68.49–83.73)	124 (25)	29 (22)	1.12	0.81
Urinary symptoms	35 (30.81–39.41)	64 (55.43–72.58)	173 (35)	46 (36)	0.98	0.79
Proctitis symptoms	10 (7.43–12.90)	92 (86.21–96.22)	50 (10)	10 (8)	1.31	0.83
Tenderness of pelvic organs on bimanual examination	99 (97.65–99.67)	0.007 (<0.001–2.84)	489 (99)	128 (99)	1.00	0.79
Palpable adnexal mass or swelling	52 (47.52–56.51)	70 (61.06–77.54)	258 (52)	39 (30)	1.73	0.84
Erythrocyte sedimentation rate ≥15mm in 1st hour	81 (77.23–84.34)	33 (25.28–42.17)	402 (81)	86 (66)	1.22	0.82

*Likelihood ratio interpretation: >10 and <0.1 (large difference between pretest and post-test probability), 5-10 and 0.1-0.2 (moderate), 2-5 and 0.5-0.2 (small), 1-2 and 0.05-1 (small and rarely important).

For detection of chlamydia only, four estimates for the accuracy of lower abdominal pain to detect chlamydia were available to pool. The pooled sensitivity for detecting chlamydia using a syndromic management approach (lower abdominal pain) is 48.0% (95% CI: 24.0–73.0), and pooled specificity is 61.7% (95% CI: 41.9–78.3).

For detection of trichomonas only, four estimates for the accuracy of lower abdominal pain to detect *Trichomonas* were available to pool. The pooled sensitivity for detecting *Trichomonas* using a syndromic management approach (lower abdominal pain) is 39.7% (95% CI: 19.6–63.9), and pooled specificity is 60.6% (95% CI: 41.0–77.4).

Other infections

About half of diagnosed pelvic inflammatory disease cases are caused by an STI such as chlamydia, gonorrhoea or *M. genitalium* infection *(3)*. In the remaining cases, a specific cause is unclear, although pelvic inflammatory disease is polymicrobial *(4)*. [Sharma 2014] There is evidence linking idiopathic pelvic inflammatory disease to vaginal microbiota dysbiosis, including recent bacterial vaginosis (a dysbiotic condition), and bacterial vaginosis organisms have been detected among women with pelvic inflammatory disease *(5–7)*.

	Judgement	Research evidence
Desirable effects	**How substantial are the desirable anticipated effects of syndromic approach?** ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	**Desirable effects** **Consequences of appropriate treatment (true positive)** Immediate treatment of an acute pelvic inflammatory disease may avert adverse consequences such as chronic pelvic pain, ectopic pregnancy and infertility. **Consequences of appropriate treatment (true negative)** Alternative diagnoses possible Psychological benefit
Undesirable effects	**How substantial are the undesirable anticipated effects?** ○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	**Undesirable effects** **Consequences of missed cases (false negative)** Onward transmission of STIs Cost of "wrong" treatment Vulnerability to HIV Pelvic inflammatory disease and its sequelae Loss of confidence in the health system if inappropriately managed Burden of STIs **Consequences of unnecessary treatment (false positive)** Cost of treatment (side-effects) Potential stigma or relationship strain Antimicrobial resistance (especially *N. gonorrhoeae*) Loss of confidence in the health system if inappropriately managed Delayed management of the true cause of disease When treatment is based on the syndromic approach, most women with pelvic inflammatory disease were identified with pelvic inflammatory disease, and there were few missed cases (8 of 1000 women with abdominal pain) compared with not assessing for pelvic inflammatory disease, although many women were overtreated.
Certainty of the evidence of test accuracy	**What is the overall certainty of the evidence of test accuracy?** ○ Very low ○ Low ● Moderate ○ High ○ No included studies	
Certainty of the evidence of the effects of management	**What is the overall certainty of the evidence of effects of the management that is guided by the test results?** ○ Very low ○ Low ● Moderate ○ High ○ No included studies	The evidence for management was based on current WHO recommendations for treating women with pelvic inflammatory disease.

	Judgement	Research evidence
Certainty of effects	**What is the overall certainty of the evidence of effects of the test?** ○ Very low ○ Low ● Moderate ○ High ○ No included studies	
Values	**Is there important uncertainty about or variability in how much people value the main outcomes?** ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Higher value was placed on missing women with pelvic inflammatory disease based on the consequences of missing treatment for pelvic inflammatory disease (including damage to the reproductive tract). Value (although less) was placed on reducing the risk of onward transmission of STIs. Pelvic inflammatory disease after three years of follow-up: 18% infertility, 0.6% ectopic pregnancy, 29% chronic pelvic inflammatory disease (PEACH study *(1)*)
Balance of effects	**Does the balance between desirable and undesirable effects favour the intervention or the comparison?** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	There were few missed cases with a syndromic approach to lower abdominal pain, which was heavily valued. Although many women were treated unnecessarily, little value was placed on the overtreatment due to minimal side-effects. Therefore, assessing for pelvic inflammatory disease and managing syndromically was favoured over no treatment.
Resources required	**How large are the resource requirements (costs)?** ○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	We did not identify any published cost analysis related to lower abdominal pain syndrome. The average cost of pelvic inflammatory disease = £163 (range £96–960) *(8)*. Average lifetime cost of pelvic inflammatory disease =US$ 2400 *(9)*. There was little difference in costs between treating all or not treating or assessing for pelvic inflammatory disease, although greater costs if molecular testing was used.

	Judgement	Research evidence
Certainty of evidence of required resources	**What is the certainty of the evidence of resource requirements (costs)?** ○ Very low ○ Low ○ Moderate ○ High ● No included studies	
Cost–effectiveness	**Does the cost–effectiveness of the intervention favour the intervention or the comparison?** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	A pharmacist-managed syndromic intervention in Lima, Peru resulted in an estimated cost savings of US$1.51 per case adequately managed using a societal perspective *(10)*. This was primarily driven by the assumption that pharmacists will prescribe medications that are more effective and less costly compared with pharmacies in the control districts. However, this study did not truly have a societal perspective, only considering the medication cost but no other societal costs (includes women with vaginal discharge, lower abdominal pain – data not disaggregated for pelvic inflammatory disease syndrome). The Guideline Development Group agreed that, based on cost–effectiveness, assessing for pelvic inflammatory disease and managing syndromically is favoured rather than no assessment, treating all or molecular testing.
Equity	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	We identified no studies.
Acceptability	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	**Clinicians** We found poor provider adherence to recommended guidelines for diagnosing pelvic inflammatory disease. For example, only 70% of women attending STI clinics in the United States of America (2010–2011) who were diagnosed as having pelvic inflammatory disease met the criteria for pelvic inflammatory disease in accordance with the guidelines of the United States Centers for Disease Control and Prevention *(11)*. **Patients** We did not find any studies discussing the acceptability of syndromic management of lower abdominal pain.

	Judgement	Research evidence
Feasibility	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A randomized controlled trial of the feasibility and acceptability for pharmacy workers to recognize and manage STI syndromes was conducted in Lima, Peru *(12)*. Standardized simulated patients visited the pharmacies in the control and intervention districts and found that pharmacy workers in the intervention districts were significantly better at recognizing and managing the STI syndromes (including pelvic inflammatory disease) – adequate for 61% of pharmacies in the intervention arm versus 19% in the control arm for pelvic inflammatory disease. However, the syndromic approach relies on the patient recognizing the symptoms (to seek consultation with a health-care provider) and the skill of the health-care provider in adequately managing a woman with lower abdominal pain. Pelvic inflammatory disease diagnosis such as laparoscopy, ultrasound and magnetic resonance imaging – not available in primary or secondary health care in resource -limited settings.