Assessment

	Judgement	Research evidence
Problem	**Is the problem a priority?** ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	**Anorectal infection** Anorectal STIs are possible for individuals practising anal sex. Among men who have sex with men, anorectal STIs are relatively common and frequently asymptomatic but can cause proctitis, presenting as anal discharge and/or pain. Possible causes include *N. gonorrhoeae* and *C. trachomatis* including lymphogranuloma venereum, herpes simplex viruses (HSV-1, HSV-2) and *Treponema pallidum* (true positive). Proctitis can also be caused by non-infectious reasons. An individual with anorectal infections may also have concomitant infection at other anatomical sites. There is concern that, if people with anorectal STIs are not treated, this could increase HIV acquisition through inflammation and increased viral shedding. **High cost of molecular STI testing** Cheaper platforms, near-patient or point-of-care tests are needed for *C. trachomatis* and *N. gonorrhoeae*. **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 and 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 conducted a systematic review, searching up to September 2019, of the sensitivity and specificity of a syndromic management approach to identify multiple STIs related to anorectal discharge. In summary, we identified four studies that assessed the diagnostic accuracy of anorectal syndromic management to detect any STI (Table A7.1), five studies for anorectal chlamydia (Table A7.2) and five studies for anorectal gonorrhoea (Table A7.3). **For detection of any STIs** (chlamydia or gonorrhoea), four studies provided five estimates for pooling. The pooled sensitivity for detecting anal chlamydia or gonorrhoea using a syndromic management approach (anorectal syndrome) is 32.4% (95% CI: 11.4–64.0%), and pooled specificity is 81.7% (95% CI: 43.1–96.43%). **For detection of specific STIs** For detection of anal chlamydia, five estimates were available to pool. The pooled sensitivity for detecting anal chlamydia using a syndromic management approach is 11.1% (95% CI: 2.2–40.3%), and pooled specificity is 94.8% (95% CI: 87.1–98.0%). For detection of anal gonorrhoea, five studies providing five estimates were available to pool; the pooled sensitivity for detecting anal gonorrhoea using a syndromic management approach is 14.2% (95% CI: 6.1–29.7%), and pooled specificity is 94.4% (95% CI: 84.8–98.1%). For detection of herpes or syphilis, no estimates were found for evaluating the accuracy of syndromic management. For detection of lymphogranuloma venereum, one study among men who have sex with men from sexual health clinics in the Netherlands provided an estimate for the sensitivity of syndromic management to detect lymphogranuloma venereum: 4.6% (95% CI: 1.3–11.4%) *(7)*. Prevalence can vary widely (anorectal *N. gonorrhoeae*: 0.2–24%, anorectal *C. trachomatis* 2.1–23%) *(8–14)*, and there are behavioural and network correlates of those with greater likelihood of an STI *(15)*. Men who have sex with men are not homogeneous.

<table>
<tr><th></th><th>Judgement</th><th>Research evidence</th></tr>
<tr><td>Test accuracy</td><td></td><td>
The evidence for the value of adding risk assessment to the history of symptoms is mixed.

A study from India to detect anorectal C. trachomatis and N. gonorrhoeae among 508 patients (in 2008–2009) reported the accuracy for detecting C. trachomatis and N. gonorrhoeae in algorithms that used: (1) anorectal symptoms only (sensitivity of 0.8%), (2) receptive anal sex and/or anorectal discharge (sensitivity 41.7%, specificity 66.3%, positive predictive value 17.5%) and (3) addition of risk assessment (sensitivity 81.9%, specificity 20.1%, positive predictive value 14.9%) (1).

A study of 698 men who have sex with men in Kenya (2) explored model-derived risk score based on correlates of anorectal C. trachomatis or N. gonorrhoeae. The risk score was based on three correlates (age 18–24 years versus ≥25 years (2 points), people living with HIV (2 points) and condomless sex with a male partner (1 point). They report a sensitivity of 81% and specificity of 66%, with a number needed to treat of 12 for anorectal C. trachomatis or N. gonorrhoeae that might be possible in their context for asymptomatic men who have sex with men (see the table below). The correlates of anorectal C. trachomatis and N. gonorrhoeae among symptomatic men were people living with HIV (adjusted odds ratio (aOR) 17.1 [95% confidence interval (CI) 3.5–84]), receptive anal sex (aOR 53.5 [95% CI 6.4–444.9]) and versatile sex position (aOR 24.2 [95% CI 2.0–294.8]).

<table>
<tr><th colspan="7">Sensitivity, Specificity, NNT and Predictive Values of Risk Score at Different Cut Points</th></tr>
<tr><th>Risk Score Cut Point</th><th>Sensitivity</th><th>Specificity</th><th>Proportion Offered PT</th><th>NNT</th><th>PPV</th><th>NPV</th></tr>
<tr><td>1</td><td>95.2%</td><td>12.3%</td><td>88.0%</td><td>36</td><td>4.3%</td><td>98.4%</td></tr>
<tr><td>2</td><td>85.7%</td><td>39.5%</td><td>61.4%</td><td>24</td><td>5.5%</td><td>98.5%</td></tr>
<tr><td>3</td><td>81.0%</td><td>66.1%</td><td>35.7%</td><td>12</td><td>8.9%</td><td>98.8%</td></tr>
<tr><td>4</td><td>28.6%</td><td>97.5%</td><td>3.6%</td><td>3</td><td>31.6%</td><td>97.1%</td></tr>
<tr><td>5</td><td>19.1%</td><td>98.8%</td><td>1.9%</td><td>2</td><td>40.0%</td><td>96.7%</td></tr>
</table>
Abbreviations: NNT = number needed to treat; NPV = negative predictive value; PPV = positive predictive value

However, a study of 787 men who have sex with men from Peru (in 2012–2014) reported that most anorectal C. trachomatis or N. gonorrhoeae were detected in men with no relevant risk behaviour with their three most recent sex partners (6). Other studies (8) also suggest that adding risk factors may not increase the accuracy of syndromic management, and its value should be assessed in specific contexts.
</td></tr>
<tr><td>Desirable effects</td><td>How substantial are the desirable anticipated effects of syndromic approach?
○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know</td><td>
Desirable effects and undesirable effects

The potential consequences of true positive could include appropriate treatment, cure, side-effects, partner notification, reduced transmission of STI and HIV, resistance, couple difficulties and costs.

The potential consequences of true negative could include alternative diagnoses possible and psychological benefit.

The potential consequences of false negative could include cure still possible, persistent symptoms, complications, STI and/or HIV transmission, no counselling and no partner notification.

The potential consequences of false positive could include inappropriate treatment, side-effects, antimicrobial resistance, couple difficulties and costs.

Based on the sensitivity and specificity of anorectal syndrome to detect STIs, we calculated the number of people appropriately treated (true positive), the number of missed cases (false negative) and the number of people treated unnecessarily or overtreated (false positive)
</td></tr>
</table>

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<tr><th></th><th>Judgement</th><th>Research evidence</th></tr>
<tr><td>Undesirable effects</td><td>How substantial are the undesirable anticipated effects?
○ Large
● Moderate
○ Small
○ Trivial
○ Varies
○ Don't know</td><td rowspan="2">GRADE summary of findings tables: detection of any chlamydia or gonorrhoea using anorectal discharge
Pooled sensitivity: 0.32 (95% CI: 0.11 to 0.64) | Pooled specificity: 0.82 (95% CI: 0.43 to 0.96)
<table><tr><th rowspan="2">Test result</th><th colspan="2">Number of results per 100 patients tested (95% CI)</th><th rowspan="2">Number of participants (studies)</th><th rowspan="2">Certainty of the Evidence (GRADE)</th></tr><tr><th>Prevalence 20%
Typically seen in</th><th>Prevalence 50%
Typically seen in</th></tr><tr><td>True positives</td><td>6 (2 to 13)</td><td>16 (6 to 32)</td><td rowspan="2">2010
(4)</td><td rowspan="2">⨁⨁⨁◯
Moderate[a]</td></tr><tr><td>False negatives</td><td>14 (7 to 18)</td><td>34 (18 to 44)</td></tr><tr><td>True negatives</td><td>65 (34 to 77)</td><td>41 (22 to 48)</td><td rowspan="2">2010
(4)</td><td rowspan="2">⨁⨁⨁◯
Moderate[a]</td></tr><tr><td>False positives</td><td>15 (3 to 46)</td><td>9 (2 to 28)</td></tr></table>CI: Confidence interval
Explanations
[a] There was high heterogeneity across studies resulting in wide confidence.

A false positive diagnosis could cause STI-related stigma for the patient and their sexual partner(s), and they might take unnecessary antibiotics, with potential risks of adverse side-effects and contributing to the development of antimicrobial resistance.
Overtreatment is a key consideration. Antibiotic use can exert selection pressure, giving resistant strains advantage over susceptible strains, increasing the development of resistance. Resource-limited settings are an incubator of antimicrobial-resistant STIs since they have large STI burdens (16).
Increasing consumption of antibiotics (both humans and animals) (17), reliance on syndromic STI management, weaker health systems and limited regulations for governing the access, use and quality of antibiotics.
Considerations for certainty of test accuracy
Evidence is derived largely from men who have sex with men; heterosexual women also practise receptive anal sex, but there are no data on syndromic management of anorectal syndrome for women.</td></tr>
<tr><td>Certainty of the evidence of test accuracy</td><td>What is the overall certainty of the evidence of test accuracy?
○ Very low
○ Low
● Moderate
○ High
○ No included studies</td></tr>
<tr><td>Certainty of the evidence of the effects of management</td><td>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</td><td>We have evidence for treatment of the STIs related to anorectal discharge.</td></tr>
<tr><td>Certainty of effects</td><td>What is the overall certainty of the evidence of effects of the test?
○ Very low
○ Low
● Moderate
○ High
○ No included studies</td><td></td></tr>
</table>

<table>
<tr><th></th><th>Judgement</th><th>Research evidence</th></tr>
<tr><td>Values</td><td>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</td><td>The Guideline Development Group placed greater value on the false negatives (missed cases) than on the false positives (people unnecessarily treated).</td></tr>
<tr><td>Balance of effects</td><td>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</td><td>Although fewer people would be treated unnecessarily if the previous WHO syndromic management approach were used, there would be more missed cases compared with treating all, and greater value was placed on avoiding missed cases. In addition, there would be no missed cases or unnecessary treatment if molecular testing is used.
The Guideline Development Group therefore agreed that the balance of benefits and harm favours treating all or molecular testing.</td></tr>
<tr><td>Resources required</td><td>How large are the resource requirements (costs)?
○ Large costs
○ Moderate costs
● Negligible costs and savings
○ Moderate savings
○ Large savings
○ Varies
○ Don't know</td><td>We did not identify studies that evaluated the cost of anorectal syndrome management.
Korenromp (18) reported the unit costs of diagnostic and treatment commodities:
<table>
<tr><th>STI</th><th>Treatment</th><th>Dose per day</th><th>Treatment duration</th><th>Drugs, per dose</th><th>Drugs + service delivery</th></tr>
<tr><td>Gonorrhoea</td><td>Ceftriaxone 250 mg</td><td>1</td><td>1 day</td><td>US$ 0.57</td><td>US$ 10.71</td></tr>
<tr><td>Chlamydia</td><td>Azithromycin 500 mg</td><td>2</td><td>1 day</td><td>US$ 0.38</td><td>US$ 10.95</td></tr>
<tr><td>Trichomoniasis</td><td>Metronidazole 500 mg</td><td>4</td><td>1 day</td><td>US$ 0.01</td><td>US$ 10.05</td></tr>
<tr><td></td><td colspan="4">Diagnostic test</td><td></td></tr>
<tr><td>Gonorrhoea and chlamydia</td><td colspan="4">NAAT: assuming a price reduction starting 2016, from US$ 20 as of 2016 (specimen collection in primary care; testing in secondary and tertiary care facilities)</td><td>US$ 12.00[a]</td></tr>
<tr><td>Trichomoniasis</td><td colspan="4">Wet mount (point of care)</td><td>US$ 4.00</td></tr>
</table>
[a] Current cost of NAAT US$ 16.
There are negligible differences in costs when treating all or when using the previous WHO syndromic approach, but the greatest cost with molecular testing.</td></tr>
</table>

	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	No studies identified.
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	No studies identified. The Guideline Development Group agreed that, based on cost–effectiveness, treating all (the comparison) is favoured rather than the previous WHO syndromic approach.
Equity	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Most studies (seven of eight) involved men who have sex with men. We only identified one study that examined the accuracy of anorectal syndromic management among 345 trans-women in Brazil for detecting *C. trachomatis* and *N. gonorrhoeae* (in 2015–2016) *(5)*. In this study population, 48% were reported to be current sex workers. Those who reported more than five sexual partners in the preceding six months had higher odds for anorectal *C. trachomatis* (aOR 2.5 [0.9–6.9]. One study evaluated the value of presumptive treatment of anorectal *C. trachomatis* or *N. gonorrhoeae* (diagnosed using NAAT) among 277 men who have sex with men who were sex workers in Kenya *(19)*. Among this high-risk group of men, one of 10 would have asymptomatic *C. trachomatis* or *N. gonorrhoeae*. A study of 698 men who have sex with men in Kenya reported that those with higher risk of anorectal *C. trachomatis* or *N. gonorrhoeae* were asymptomatic men aged 18–24 years (aOR 7.6 [1.7–33.2]), people living with HIV (aOR 6.9 [2.2–21.6]) and men who had condomless anal sex in the preceding three months (aOR 3.8 [1.2–11.9]) *(2)*.

	Judgement	Research evidence
Acceptability	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No studies were identified.
Feasibility	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No studies were identified.