

Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1627 – Point-of-care testing for sexually transmitted infections provided by Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote areas

Applicant: The Kirby Institute, UNSW

Date of MSAC consideration: 24-25 November 2022

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of point of care (POC) testing for detection of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV) was received from the Kirby Institute, UNSW, by the Department of Health and Aged Care.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC did not support public funding of POC testing for sexually transmitted infections (STIs) provided by Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural and remote areas.

MSAC recognised that there is a clinical need for the proposed testing due to a high prevalence of STIs and the serious consequences of untreated infections representing a significant public health issue for the proposed population. MSAC considered the evidence provided demonstrated that POC testing for STIs reduced the time from testing to treatment and that the clinical benefits associated with this were clinically plausible. However, based on the evidence provided, the magnitude of the benefit and impact on health outcomes was highly uncertain. As a result of this, and also due to the economic model being overly complex and unreliable, MSAC considered the cost-effectiveness of POC testing for STIs compared to standard laboratory testing to be highly uncertain. MSAC considered the proposed MBS fee was very high and the costings should be re-examined. MSAC considered that the fee was not sufficiently justified given the lack of objective data demonstrating improved health outcomes for patients. MSAC also considered the financial estimates to be uncertain and likely underestimated.

MSAC suggested a revised application could consider targeting POC testing for STIs to people living in remote and very remote areas and alternative funding models to the MBS for services provided by Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote areas.

Consumer summary

The Kirby Institute applied for Medicare Benefits Schedule (MBS) funding of point of care (POC) testing for sexually transmitted infections (STIs) for people presenting to Aboriginal Medical Services or Aboriginal Community Controlled Health Organisations in rural and remote Australia.

STIs such as chlamydia, gonorrhoea and trichomonas are infections that are spread through sexual contact and individuals with these infections may or may not show any signs or symptoms of infection. STIs are treated with antibiotics. The long-term effects of untreated STIs can be serious and can include premature birth and problems with fertility. People aged 16 to 29 years old are most at risk and the rates of STIs in Aboriginal and Torres Strait Islander communities in rural and remote Australia are high.

Currently, people are tested for STIs, such as chlamydia, gonorrhoea and trichomonas, by collecting a sample usually a urine sample or swab. The sample is then sent to central laboratories where the test is performed. The results from these tests can take up to 14 days depending on where in Australia the patient is based. Patients can be given general antibiotics before the test results are known, however because the bacteria causing the infection won't be known, the antibiotics may not be targeting the right bacteria. Only when the results from the lab come back, will it be known whether the patient is on the right antibiotics. If they aren't, then the patient will be contacted to change to a different antibiotic, but there may be a delay of up to 14 days to receive the laboratory results. During this time there is a risk that patients may pass on infections if they are not treated or are on the wrong antibiotic. The application also reported that it can be hard to contact patients once the test results are received to make sure that they get appropriate care. Delays in the right treatment while waiting for test results may mean that there are more serious consequences as a result of the ongoing infection.

POC testing uses the same kind of samples as standard laboratory testing, but the samples are put through a machine at the clinic. This kind of POC testing takes 60 to 90 minutes to deliver a result. This shorter time from test to result may lead to quicker treatment for patients, meaning their infection will clear up quicker which can reduce spread of infection and can help avoid serious long-term effects of untreated STIs.

After considering the evidence, MSAC considered that POC testing was likely as accurate as standard laboratory testing and that for many patients, they would be able to receive their results and the correct antibiotic, on the same day. However, there was no difference in overall longer-term infection rates based on type of testing (with most patients having no infection detected during a repeat test, regardless of the type of test they had originally), and there was no evidence as to whether the quicker treatment led to better health outcomes in the longer-term.

MSAC considered that the cost of POC testing is much higher than for laboratory testing and the actual benefit to patients of this was very uncertain. The overall costs to the health system were also very high and likely to have been under-estimated. MSAC was not convinced that POC testing for STIs improved patient outcomes enough to justify the very high costs compared to standard laboratory testing.

MSAC's advice to the Commonwealth Minister for Health and Aged Care

MSAC did not support listing POC testing for STIs on the MBS. MSAC considered that POC testing was as accurate as the current standard laboratory testing but that it did not offer any additional safety or other health benefits and so did not justify the proposed high cost. MSAC considered that for people in remote and very remote parts of Australia there may be additional benefits in providing them faster access to test results but further evidence on this was needed.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that the application was for MBS listing of POC testing for STIs provided by Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote areas. MSAC noted the application presented two POC nucleic acid amplification tests (NAATs) tests, a dual test for chlamydia and gonorrhoea and a single test for trichomonas.

MSAC noted that these POC tests were previously considered by the MSAC Executive. The evidence presented to the MSAC Executive indicated that the sensitivity and specificity of the POC tests was comparable to standard laboratory testing and provided sufficient evidence to confirm the validity of using POC testing as a diagnostic test for chlamydia, gonorrhoea and trichomonas. The MSAC Executive considered that if the applicant wished to pursue an MBS fee that is higher than the existing MBS standard laboratory testing fees, the applicant would need to provide evidence that POC testing results in better health outcomes than standard laboratory testing, and this evidence would need to be supported with an appropriate economic analysis.

MSAC noted that the sexually transmitted infections (chlamydia, gonorrhoea and trichomonas) represent a significant public health issue, particularly in rural and remote Australia, affecting predominantly Aboriginal and Torres Strait Island populations. MSAC considered that the downstream sequelae of untreated STIs were significant and that reducing onward transmission of infection is of great importance to public health. MSAC noted the consultation feedback was supportive of POC testing as proposed in the application, although some feedback expressed concern that the 90-minute wait time for test results is long. However, MSAC considered that the wait time would provide an opportunity for additional sexual health education and being able to offer the proposed patient population test results on the same day was important.

MSAC noted that the Applicant Developed Assessment Report (ADAR) presented consultation with Australian patients (n=80), staff members and leadership of Aboriginal health organisations. International communities were also consulted. MSAC noted that whilst the research and consultation outcomes presented spoke to the feasibility, safety and acceptability of POC testing in Aboriginal and Torres Strait Islander communities, cultural perspectives or additional benefits of cultural importance of POC testing over standard laboratory testing were not specifically presented. MSAC noted that patients with direct lived experience of the POC testing, communities, community organisations and the Indigenous POCT Leaders Group referenced in the applicant's pre-MSAC response may be able to provide this lived experience expertise or community knowledge about important non-health benefits. MSAC agreed with ESC that presenting such additional qualitative evidence, including from community members who chose not have the POC testing and those outside of the health sector, would have been informative.

MSAC noted that the proposed item descriptor was age agnostic and considered that this was appropriate given the public health benefits of population level testing. MSAC agreed with ESC that the proposed item YYYY for testing of CT/NG following previous infection was redundant as there was no need to distinguish between testing for diagnosis (item XXXX) and repeat testing (item YYYY).

MSAC considered that the proposed fee for POC testing (\$150 for CT/NG and \$115 for TV) was significantly higher than the MBS fee for standard laboratory testing. MSAC considered that the components of the fee were not appropriately costed and that there was significant uncertainty around the ongoing costs in practice. MSAC noted that the capital costs for the GenExpert machine had not been included. MSAC noted that while GeneXperts had been provided as part of the TTANGO project, additional machines and replacements would need to be purchased as required, which may lead to significant costs (particularly in remote and very remote regions of

Australia where replacements may be needed more frequently due to harsh environmental conditions) and these costs were not included. Further, MSAC noted that the full infrastructure costs associated with delivering the test in these regions had not been included and therefore the cost for consumables (i.e. test cartridges) as proposed may be under-estimated. MSAC noted that the majority of the proposed fee was attributed to operator and training time and these figures (calculated on a per test basis) amounted to a significant amount per year. MSAC noted the stated ease of POC testing and considered that the training and quality control costs were likely to have been overestimated. MSAC also noted that one fee would be claimed, irrespective of the number or types of swabs taken (as is the case for the current standard laboratory testing items).

Regarding comparative safety, MSAC considered that POC testing had noninferior safety compared with standard laboratory testing for CT/NG and TV.

Regarding comparative effectiveness, MSAC noted that the evidence on the accuracy and performance of the POC tests was deemed to be at a low risk of bias and relatively robust with up to 9 sample datasets. MSAC considered the MSAC Executive minutes and noted that evidence demonstrated the reliability and validity (i.e., sensitivity and specificity) of the POC testing was non-inferior to standard laboratory testing.

Regarding the health outcomes associated with POC testing compared to standard laboratory testing, MSAC noted that the main clinical benefit, as presented in the ADAR, was that POC test results would be available in 60-90 minutes, as opposed to up to 2 weeks with standard laboratory testing. The ADAR claimed that improved change in clinical management (i.e. reduced test to treatment time) would result in more timely curative treatment; less clinic visits; more timely treatment of contacts and prevention of infection sequelae (such as mild to moderate Pelvic Inflammatory Disease [PID] and pregnancy-related complications).

MSAC noted that the key evidence for improved health outcomes was based on two studies (total n=1,095), both with moderate risks of bias. One study (Keizur, 2020¹) was a diagnostic before/after study conducted in two American cities. The other was the Australian Test, Treat and Go (TTANGO²) cluster-randomised controlled crossover trial led by the applicant which had a highly relevant population. MSAC noted that in the TTANGO study, while there were substantial reductions in the time to test results and time to appropriate treatment (change in patient management), there were no significant differences reported for health outcomes in terms of rates of infection at re-testing, and most patients were uninfected at re-testing, regardless of testing type. Data on any longer-term outcomes were not available.

MSAC deliberated on whether the evidence demonstrated that POC testing provided better health outcomes as requested by the MSAC Executive, and therefore whether POC testing was superior compared to standard laboratory testing as claimed in the ADAR. MSAC considered that it was clinically plausible that the reduced time from test to treatment with POC testing could lead to quicker resolution of infection which could reduce the chances of onward transmission and could reduce serious downstream sequelae. However, the evidence presented did not demonstrate that POC testing actually improved health outcomes compared to standard

¹ Keizur EM, Goldbeck C, Vavala G, et al. Safety and Effectiveness of Same-Day Chlamydia trachomatis and Neisseria gonorrhoeae Screening and Treatment Among Gay, Bisexual, Transgender, and Homeless Youth in Los Angeles, California, and New Orleans, Louisiana. *Sex Transm Dis* 2020; **47**(1): 19-23.

² Guy RJ, Ward J, Causer LM, et al. Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial. *Lancet Infect Dis* 2018; **18**(10): 1117-26

laboratory testing. Therefore, MSAC concluded that POC testing had noninferior clinical effectiveness compared to standard laboratory testing for chlamydia, gonorrhoea and trichomonas.

MSAC noted that the ADAR presented a cost-utility analysis that modelled a reduction in infection sequelae based on reduced time to treatment with POC testing. However, MSAC noted that a reduction in infection sequelae was not supported by the clinical evidence. MSAC considered that while this benefit may be clinically plausible, the magnitude of this effect was highly uncertain and therefore the ICER based on this modelled benefit was highly uncertain.

MSAC noted that the model represented a cross section of people eligible for testing who present repeatedly over the 10-year time horizon, resulting in accrual of costs and consequences that are not reflective of a single test, but rather a series of testing episodes over ten years. MSAC noted this was achieved using complex microsimulation modelling that required large numbers of simulations to generate stability in the results. MSAC noted a strength of microsimulation models was the ability to incorporate 'history' in the model however, the microsimulation model did not incorporate changes to reflect how population behaviour would change over time (e.g., the model did not incorporate changes over time in the probabilities of reinfections, uptake of testing, proportion of symptomatic patients, etc). As the microsimulation did not include this 'history', MSAC agreed with ESC that the model was unnecessarily overly complex. MSAC also considered that the 10-year time horizon in the model was too long based on the short-term clinical data that had been presented.

MSAC noted the population included in the model were patients aged between 16 and 29 years old. MSAC acknowledged that this was consistent with the pivotal TTANGO trial and with current national and jurisdictional guidelines but that this was not consistent with the proposed population for MBS funding (i.e., the proposed item descriptors are age agnostic). MSAC considered that an age agnostic approach should also be reflected in the economic model as it is likely that the ICER for POC testing would increase if people over the age of 29 years were included in the model. This would primarily be due to changes in the underlying prevalence of infections and a reduction in the probability of downstream sequelae such as maternal and pregnancy related adverse outcomes.

MSAC noted the commentary had identified a number of errors and inconsistencies in the ADAR model and sensitivity analyses presented in the commentary demonstrated the ICER was highly sensitive to a number of key drivers (see Table 14 and Table 15 for further information)). MSAC noted that the applicant's pre-ESC and pre-MSAC responses presented updated base-case ICERs of \$37,185 per QALY gained and \$38,398 per QALY gained respectively. MSAC also noted that, as requested by ESC, the applicant had presented a number of sensitivity analyses in the pre-MSAC response. However, the analyses were not undertaken exactly as requested by ESC and due to the lack of transparency in the model and applicant's pre-MSAC response, the revised ICER and sensitivity analyses could not be verified. Overall, MSAC considered the cost-effectiveness of POC testing compared with standard laboratory testing was highly uncertain due to the uncertainty in the magnitude of benefit modelled, use of an overly complex microsimulation model without incorporating changes to reflect population behaviour changes over time, errors in the model along with the lack of transparency and inability to verify updates prior to MSAC.

MSAC noted the financial estimates and agreed with ESC that the estimated number of people tested per year using POC testing and subsequent financial implications were not well described in the ADAR and still lacked clarity after the applicant's pre-ESC and pre-MSAC responses were considered. MSAC noted that the estimated number of people tested per year using POC testing

were based on post-COVID testing data from existing sites that offer the POC testing. While MSAC acknowledged the involvement of ACCHOs in developing these estimates, MSAC considered that the estimates were likely to be underestimated. That is, the estimated number of people tested per year using POC testing would be higher if the estimates had been based on pre-COVID testing data.

MSAC also queried whether the assumption of a maximum 300 tests/site per year also underestimates the likely utilisations of POC testing. MSAC noted the ADAR assumed that POC testing would substitute standard laboratory testing one-to-one (i.e., assumed that the overall number of people tested would not increase with POC testing) which MSAC considered is unlikely to be appropriate. MSAC considered it plausible that more people would be willing to undertake a test with same-day results than a test where results might not be available for up to 14 days. MSAC also noted the financial estimates had costed the POC test using 100% of the proposed MBS fee rather than applying the 85% rebate. MSAC also highlighted that the estimates did not include the cost of re-testing 3 months post treatment (per the clinical guidelines) and cost offsets for the downstream sequelae were based on 2016-17 costs, creating further uncertainty (potentially underestimating) the financial impact of MBS listing POC testing.

Overall, MSAC did not support public funding of PoC testing for STIs. MSAC recognised that there is a clinical need for the proposed testing due to a high prevalence of STIs and the serious consequences of untreated infections representing a significant public health issue for the proposed population. However, the clinical evidence did not demonstrate that POC testing actually improved health outcomes compared to standard laboratory testing and the economic and financial analysis were highly uncertain. As such, MSAC considered the evidence provided did not justify the high fee for POC testing for STIs.

MSAC deliberated on whether there was a subpopulation for whom POC testing would represent a particular benefit in terms of improving equity of access. MSAC noted that the applicant's pre-MSAC response proposed the population be restricted to government funded primary health care services providing care to predominantly Aboriginal and/or Torres Strait Islander peoples. MSAC noted that this would encompass both Aboriginal community-controlled services and government funded primary health care services in the modified Monash Model (MM) categories 2 to 7. MSAC considered the likely access to standard laboratory testing for these proposed areas and noted that MM 2 to 5 includes regional centres, large through to small rural towns and questioned whether access would be severely limited in these centres. MSAC considered that the categories MM6 (remote) and MM7 (very remote) represented the areas of Australia that would have the greatest clinical need and who would currently face restricted timely access and significant delays to test results from standard laboratory testing. MSAC therefore considered that people based in MM categories 6 and 7 could have the greatest potential to benefit from POC testing for STIs.

MSAC considered that a resubmission could target POC testing for those most at need (i.e. people in MM categories 6 to 7) who have very restricted access to standard laboratory testing. MSAC also noted that current block-funding arrangements are in place to provide access to the POC testing and that consideration could be given as to whether an alternative funding mechanism (other than the MBS) is more appropriate; particularly if the POC testing is focused on remote and very remote Australia. MSAC recommended that the fee for the POC testing needed to be revised and include all relevant costs with clear justification for their inclusion and source.

Alternatively, MSAC considered that should a resubmission continue to pursue the proposed population considered in this application (i.e. MM categories 2 to 7) then the errors and

significant concerns highlighted with the economic model would have to be fully addressed and the model would need to be re-specified. The resubmitted model should be based on the trial data and present a stepped analysis with the incremental cost per person tested. Any reduction in time to treatment and sequelae avoided and how these transform into QALYs should be clearly presented in accordance with the Technical Guidelines. MSAC further considered that the proposed fee would have to be reconciled to reflect the benefit of POC testing as based on the very limited data on longer-term patient outcomes available.

For either option, MSAC advised that the estimates around uptake of the testing and financial impact would need to be revised and clearly described in accordance with the approach taken in the resubmission with uptake based on extrapolation of pre-COVID testing rates. If any qualitative evidence (including a summary of previous or additional consultation with people with direct community and lived experience) on the likely uptake and implementation of POC testing in practice, possible impacts on equity and access and cultural sensitivities or impacts around the provision of testing for STIs in these communities is available, this should also be included.

4. Background

The MSAC has not previously assessed POC testing for CT, NG and TV, although these POC tests were previously considered by the MSAC Executive. The evidence presented to the MSAC Executive indicated that the sensitivity and specificity of the POC tests was comparable to standard laboratory testing and provided sufficient evidence to confirm the validity of using POC testing as a diagnostic test for CT, NG and TV. The MSAC Executive considered that if the applicant wished to pursue an MBS fee that is higher than the existing MBS standard laboratory testing fees, the applicant would need to provide evidence that POC testing results in better health outcomes than standard laboratory testing, and this evidence would need to be supported with an appropriate economic analysis.

5. Prerequisites to implementation of any funding advice

Both the combined Xpert CT/NG test and the Xpert TV POC test are included on the Australian Register of Therapeutic Goods (ARTG; ARTG ID 207540 Cepheid GeneXpert (CT/NG) effective from 28/3/2013 and ARTG ID 290014 Cepheid GeneXpert (TV) from 9/6/2017).

A quality assurance program to support pathology testing is required. It is envisaged that the management of quality assurance for POC testing could be co-ordinated under a quality assurance program such as the Quality Assurance for Aboriginal and Torres Strait Islander Medical Services (QAAMS) Program implemented by the Flinders University International Centre for Point of Care Testing (ICPOCT), which follows Australian guideline recommendations for POC testing.

6. Proposal for public funding

The ADAR proposed items for POC testing are shown in Table 1. For CT and/or NG, separate items were suggested for initial screening/diagnosis (item XXX) and follow-up testing (item YYY).

Table 1 ADAR Proposed item descriptor for point of care tests

Category 6 – PATHOLOGY SERVICE	Group PXX – Point of Care Tests
<p>MBS [Item number XXX]</p> <p>Detection of CT (<i>Chlamydia trachomatis</i>) and/or NG (<i>Neisseria gonorrhoeae</i>) via point-of-care testing performed at Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote settings for the diagnosis of CT or NG infection.</p> <p>Fee: \$150 Benefit: 75% = \$112.50 85% = \$127.50</p>	
Category 6 – PATHOLOGY SERVICE	Group PXX – Point of Care Tests
<p>MBS [Item number YYY]</p> <p>Detection of CT (<i>Chlamydia trachomatis</i>) and/or NG (<i>Neisseria gonorrhoeae</i>) via point-of-care testing performed at Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote settings, following previous CT or NG infection.</p> <p>Fee: \$150 Benefit: 75% = \$112.50 85% = \$127.50</p>	
Category 6 – PATHOLOGY SERVICE	Group PXX – Point of Care Tests
<p>MBS [Item number ZZZ]</p> <p>Detection of TV (<i>Trichomonas vaginalis</i>) via point of care testing performed at Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote settings for the diagnosis of TV infection.</p> <p>Fee: \$115 Benefit: \$86.25 75% = \$85% = \$97.75</p>	

Source: Table 4, pg 33 of MSAC 1627 ADAR

* Testing is conducted on demand, one test at a time, by a remote area nurse or Aboriginal health practitioner at or soon after the time of consultation.

The MBS item fees for the proposed POC tests for CT, NG and TV using the Cepheid GeneXpert system are higher than for the current standard of care (SOC) tests carried out in a hospital or pathology laboratory. Both the POC and SOC tests use equivalent technology i.e. they are both NAATs (see Table 1 and Table 2 for further details). The ADAR provided justification for the proposed fees, which includes both operator time and consumables costs, but excludes practitioner time, as the proposed items would be claimed in combination with a consultation item (which is already subsidised).

7. Population

The proposed population includes symptomatic individuals, or asymptomatic individuals (including those who do not disclose symptoms), at risk of sexually transmitted infection, attending Aboriginal Medical Services or Aboriginal Community Controlled Health Services in regional and remote areas as defined by the Australian Bureau of Statistics (ABS).

The National Aboriginal Community Controlled Health Organisation (NACCHO) and The Royal Australian College of General Practitioners (RACGP) “*National guide to a preventive health assessment for Aboriginal and Torres Strait Islander people (2018)*” recommends that all sexually active Aboriginal and Torres Strait Islander people aged ≤30 years or people with risk factors for STIs should be offered annual screening for CT, NG and TV. Anyone attending a regional or remote Aboriginal Medical Service or Aboriginal Community Controlled Health Service with the proposed POC testing capability would be eligible for POC test. The proposed MBS item descriptors do not limit the population to those aged ≤30 years, leaving the broader testing to clinician discretion.

8. Comparator

The comparator for POC testing is standard laboratory testing, which is the current standard of care (SOC). MBS items relevant to the comparator are shown in Table 2. Items 69316, 69317, 69319, and 69494 were added to the MBS on the 01 May 2007.

The patient sample would be sent to a laboratory for NAAT testing. This would involve a delay between sample collection and diagnosis.

Due to this delay, patients who are symptomatic or considered highly likely to have a CT and/or NG infection (i.e. a positive partner), would be offered treatment at the time of the initial consultation as per the appropriate jurisdictional guidelines for the management of symptomatic individuals. It has been reported that this leads to overtreatment of symptomatic patients by as much as 50%. Treatment initiation for TV is not recommended until receipt of test results unless abnormal vaginal discharge and a pH test is indicative of infection. Patients who are asymptomatic must wait for receipt of their results for treatment.

While SOC STI testing results may be delivered within a shorter timescale (~48 hours) to a health clinic in an urban setting, the additional time required for sample transportation to a central pathology laboratory from a regional or remote health clinic means that test results may not be available until around 14 days after the sample has been obtained during consultation at the health clinic. The mean interval between sample collection and treatment at remote clinics is 22 days (SD 24 days), with a median time to treatment of 13 days (IQR = 7–27). Contact tracing is not initiated until the patient returns to clinic for treatment.

Table 2 MBS items claimed for the comparator service

Category 6 – PATHOLOGY SERVICE
<p>69316 Detection of <i>Chlamydia trachomatis</i> by any method - 1 test (Item is subject to rule 26) (Item is subject to restrictions in rule PR.9.1 of explanatory notes to this category) Fee: \$28.65 Benefit: 75% = \$21.50 85% = \$24.40</p>
<p>69317 1 test described in item 69494 and a test described in 69316. (Item is subject to rule 26) Fee: \$35.85 Benefit: 75% = \$26.90 85% = \$30.50</p>
<p>69319 2 tests described in item 69494 and a test described in 69316. (Item is subject to rule 26) Fee: \$42.95 Benefit: 75% = \$32.25 85% = \$36.55</p>
<p>69494 Detection of a virus or microbial antigen or microbial nucleic acid (not elsewhere specified) 1 test (Item is subject to rule 6 and 26) Fee: \$28.65 Benefit: 75% = \$21.50 85% = \$24.40</p>
<p>73939 Initiation of a patient episode by collection of a specimen for 1 or more services (other than those services described in items 73922, 73924 or 73926), if the specimen is collected by or on behalf of the treating practitioner and if: () the service is performed in a prescribed laboratory or () the person is a private patient in a recognised hospital Fee: \$2.40 Benefit: 75% = \$1.80 85% = \$2.05</p>

Source: Commentary Table 1, pg 35 of MSAC 1627 ADAR+in-line commentary

9. Summary of public consultation input

The Department received responses to the consultation survey from nine individuals (four GPs, four registered nurses, one regional sexual health facilitator) and the following twelve organisations:

- Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM)
- Australian Pathology (AP)
- DiaSorin Australia Pty Ltd
- Mawarnkarra Health Service
- National Pathology Accreditation Advisory Council (NPAAC)
- Ngaanyatjarra Health Service
- Public Pathology Australia (PPA)
- The Australian Indigenous Doctors' Association (AIDA)
- The National Rural Health Alliance (NRHA)
- The Royal Australian College of General Practitioners (RACGP)
- The Royal Australian College of Physicians (RACP)
- Aboriginal Health Council of SA Ltd's Sexual Health and BBV Program

All feedback was supportive and noted that the STIs considered in the application are a significant public health issue in predominantly Aboriginal and Torres Strait Islander communities in rural and remote Australia. The statements highlighted that increased access to testing will help to close the gap and reduce health inequalities for Aboriginal and Torres Strait Islander people.

The feedback suggested the following advantages of the POC tests:

- Decreased turn-around time for the test result will lead to timelier diagnosis, resulting in quicker treatment initiation, improving patient management, reduce unnecessary use of antibiotics and improve patient prognosis with reduction in conditions linked to STIs.
- POC testing provides a clinical decision-making tool that can provide an accurate diagnosis for patients presenting with unexplained symptoms (e.g. abdominal pain) within 90 minutes.
- Potentially improved patient tolerability and awareness around STI testing, with increased agency and reduction in cultural and social stigma surrounding STIs.
- Decreased number of patients lost to follow up, and expedited contact tracing (which may reduce further transmission).
- Reduced financial and environmental impacts of flying samples to laboratories and tracing patients who return a positive result from laboratory-based testing.

Disadvantages stated in the feedback received were:

- 90 minutes is a long time for patients to wait for results. However, responses also noted:
 - the ability to find the patient after 90 minutes is greater than multiple days
 - the wait can provide an opportunity for sexual health education.
- Training is required to deliver this test which can be challenging with high staff turnover.

Other information provided in the consultation feedback included:

- Having an overly restrictive item descriptor (for example restricting by Aboriginal or Torres Strait Islander origin or having thresholds for when the POC test should be used) could result in challenges in determining patient eligibility for the POC test.
- POC tests may also benefit patients in both inner and outer regional areas where access to specialised health services are limited and all populations with high rates of STIs (irrespective of location), including men who have sex with men.
- There must be adequate quality control and training of providers to ensure effective provision of this service and service providers should have support from a supporting pathology laboratory or clinical microbiologist in case of technical/clinical difficulty.
 - The National Pathology Accreditation Advisory Council Standard on Requirements for POC testing in community settings is in final draft and awaiting release and this will replace existing guidelines.
 - The Royal College of Pathologists Australia - Quality Assurance Programs will develop a program for STI POC testing in 2022.

10. Characteristics of the evidence base

Overall, there was relatively limited evidence for every component of the assessment report, except for test accuracy in detection of CT, NG and TV via POC testing in remote communities. A summary of the key features of the evidence is shown in Table 3.

Table 3 Key features of the included evidence

Criterion	Type of evidence supplied	Extent of evidence supplied	Overall risk of bias in evidence base
Accuracy and performance of the test (cross-sectional accuracy)	Cross-sectional studies on the accuracy of POC NAAT compared with LAB NAAT for detection of CT	☒ k=8 datasets n=3,985	Low risk of bias
	Cross-sectional studies on the accuracy of POC NAAT compared with LAB NAAT for detection of NG	☒ k=9 datasets n=4,431	Low risk of bias
	Cross-sectional studies on the accuracy of POC NAAT compared with LAB NAAT for detection of TV	☒ k=4 datasets n=5,433	Low risk of bias
	Cross-sectional studies on the Test failure rate for the Xpert CT/NG assay	☒ k=9 datasets n=12,423	Low risk of bias
	Cross-sectional studies on the Test failure rate for the Xpert TV assay	☒ k=3 datasets n=2,601	Low risk of bias
Change in patient management	Studies assessing time to test results for Xpert CT/NG POC versus SOC testing	☒ k=8 datasets n=83791	Moderate risk of bias
	Studies assessing time to treatment for Xpert CT/NG POC versus SOC testing	☒ k=5 datasets n=2898	Moderate risk of bias
	Studies assessing time to treatment for Xpert CT/NG POC versus SOC testing	☒ k=3 datasets n=83791	Moderate risk of bias
	Studies assessing the proportion of infected patients receiving treatment within a specified period for Xpert CT/NG POC versus SOC testing	☒ k=3 datasets n=2107	Moderate risk of bias
	Studies assessing overtreatment of CT and/or NG negative patients for Xpert CT/NG POC versus SOC testing	☒ k=3 datasets n=824	Moderate risk of bias
	Studies assessing undertreatment of CT and/or NG positive patients for Xpert CT/NG POC versus SOC testing	☒ k=2 datasets n=1114	Moderate risk of bias
Health outcomes	Direct evidence comparing infection rates at retesting after POC vs SOC testing NAAT	☒ k=2 datasets n=1095	Moderate risk of bias

Source: Table 3, pg 7 of MSAC 1627 Commentary Executive Summary

CT = *Chlamydia trachomatis*; k = number of studies; LAB = laboratory-based; n = number of patients; NAAT = nucleic acid amplification test; NG = *Neisseria gonorrhoeae*; POC = point of care; SOC = standard of care; TV = *Trichomonas vaginalis*

11. Comparative safety

As the same samples need to be taken for all NAAT tests, there are no additional safety concerns with POC NAAT testing compared with standard laboratory NAAT testing.

12. Comparative effectiveness

As the evidence base for diagnostic accuracy and safety of the Xpert POC test was considered as established, the ADAR did not include analysis of the statistical precision of the evidence or size of the effect related to diagnostic testing. The following analysis has been undertaken to present a complete assessment to inform/support MSAC's deliberations on the effectiveness of the Xpert POC test.

The clinical effectiveness of POC testing (compared to SOC testing), depends on the accuracy of the test, whether it changes the way the infections are treated (in the individuals being tested, or their sexual partners), and the effectiveness of the treatment.

Analytical validity

Meta-analysis of the sample sets presented in the studies reporting on the diagnostic accuracy of POC Xpert CT/NG and/or TV testing compared with laboratory NAAT testing was performed using the midas command in STATA 15.1. The pooled sensitivity and specificity values are presented in Table 4.

Subgroup meta-analysis for different genitourinary or pharyngeal sample types was not possible as less than four datasets were available for analysis. Thus, median sensitivity and specificity values were calculated. The median sensitivity and specificity for all sample datasets were similar to the pooled values (Table 4).

The median sensitivity and specificity values of POC testing compared with standard laboratory testing for specific sample types were similar to the overall pooled and/or median values, varying between 88% and 100%, for all sample types except pharyngeal samples. The sensitivity of detecting CT in pharyngeal samples could not be determined accurately due to the lack of evidence.

When the pooled and/or median sensitivity and specificity of the POC Xpert CT/NG testing compared to laboratory NAAT testing was compared to the pooled values obtained in two systematic reviews (SRs) comparing the Xpert CT/NG assay to other NAATs, the results were very similar. The SRs reported that the pooled sensitivity for various specimen types varied between 90% and 96% and the specificity varied little (99–100%).

The majority of the studies included in the SRs did not use the Xpert CT/NG assay in a POC setting. As the diagnostic accuracy of the test was similar whether or not studies using the test under laboratory conditions were included, it suggests that the accuracy of the assay is little affected when performed by either laboratory or non-laboratory staff. Thus, the test appears to be sufficiently robust for use as a POC test in remote communities.

Table 4 The pooled (95% CI) or median (range) sensitivity and specificity of POC NAAT compared with standard laboratory NAAT testing for specific sample types

Sample type	Median sensitivity (range)	Median specificity (range)
Detection of Chlamydia trachomatis		
All (pooled, k=8 datasets)	94% (95% CI 87, 97)	100% (95% CI 99, 100)
All (median, k=8 datasets)	95% (50–100)	100% (96–100)
Rectal swabs (k=3)	88% (86–97)	99% (96–100)
Vaginal swabs (k=2)	96% (92–100)	99% (98–100)
Urine sample (k=1)	100%	100%
Pharyngeal swab (k=1)	50%	100%
Detection of Neisseria gonorrhoeae		
All (pooled, k=9 datasets)	96% (95% CI 88, 99)	100% (95% CI 99, 100)
All (median, k=9 datasets)	93% (78–100)	100% (99–100)
Rectal swabs (k=3)	93% (88–100)	100% (99–100)
Vaginal swabs (k=2)	93% (86–100)	100% (100–100)
Urine sample (k=1)	100%	100%
Pharyngeal swab (k=2)	85% (78–91)	100% (99–100)
Detection of Trichomonas vaginalis		
All (pooled, k=4 datasets)	99% (95% CI 92, 100)	100% (95% CI 99, 100)
All (median, k=4 datasets)	98% (89–100)	100% (99–100)
Vaginal swabs (k=2)	93% (89–97)	100% (100–100)
Urine sample (k=2)	98% (97–99)	100% (100–100)
Endocervical swabs (k=1)	100%	99%

Source: Commentary Table 8, pg 52 of MSAC 1627 ADAR+in-line commentary
k = number of studies; CI = confidence interval; NAAT = nucleic acid amplification test, POC = point of care

Test failure rate

The failure rate of the Xpert CT/NG assay was based on failure after repeat testing of samples with initial inconclusive/invalid results. The Australian study by Causer et al (2018)³ reported that 3.3% of tests failed at initial testing and the failure rate decreased to 0.9% after retesting.

The median failure rates on repeat testing are summarised in Table 5. The failure rate of the Xpert CT/NG assay was similar whether conducted in a POC setting or a laboratory setting. However, other laboratory CT/NG NAAT tests had a lower failure rate. The median failure rate after repeat testing of the Xpert TV assay was similar to the reference test.

Thus, POC testing using the Xpert CT/NG and TV assays is reliable if initial inconclusive/invalid tests are repeated, with no more than 1 in 100 patients not receiving a same-day result.

³ Causer, L. M., Guy, R. J., Tabrizi, S. N., Whiley, D. M., Speers, D. J., Ward, J., & Kaldor, J. M. (2018). Molecular test for chlamydia and gonorrhoea used at point of care in remote primary healthcare settings: a diagnostic test evaluation. *Sexually transmitted infections*, 94(5), 340-345.

Table 5 Median failure rate of the Xpert CT/NG and TV assays used in a POC or standard laboratory setting, compared to other laboratory-based NAATs

Setting	Xpert assay	Other laboratory NAAT test
	CT/NG assay	
POC setting	0.9% (range 0.7–1.8%), k=3 datasets	0% (range 0–0%), k=2 datasets
LAB setting	1.1% (range 0.3–2.9%), k= 6 datasets	0.3% (range 0–0.5%), k=7 datasets
Overall		0.2% (range 0–0.5%), k=9 datasets
	TV assay	
POC/LAB setting	0.3% (range 0.1–0.3%), k=3 datasets	0.2% (range 0.1–0.5%), k=3 datasets

Source: Table 5, pg 10 of MSAC 1627 Commentary Executive Summary
 CT= *Chlamydia trachomatis*; k = number of sample sets; LAB = laboratory-based; NAAT = nucleic acid amplification test; NG = *Neisseria gonorrhoea*; POC = point of care; TV = *Trichomonas vaginalis*

The predictive value of POC Xpert CT/NG or TV testing

The estimated prevalence rates of CT, NG and TV among 13,480 predominantly Indigenous Australian patients seen at the remote health services in central and northern Australia, which aligns with the proposed population in the PICO, were used to determine the predictive value of POC Xpert testing (Guy et al, 2015)⁴.

A summary of the results per 1,000 patients is presented in Table 6. For every 1000 people tested with POC rather than SOC, it is estimated that up to 26 people may receive a false positive result, and subsequently receive unnecessary antibiotic treatment. Conversely, approximately 13 patients would receive a false negative result (especially those who are asymptomatic), and would miss out on treatment. Additionally, contact tracing will not be initiated enabling the further spread of disease.

Table 6 Summary of the PPV, NPV and the number per 1,000 patients tested for CT, NG or TV who will receive a false positive or false negative result

Per 1,000 patients tested:	CT	NG	TV
Prevalence reported by Guy et al (2015)	11.5%	10.1%	17.6%
PPV	92.4%	91.5%	95.5%
NPV	99.2%	99.5%	99.8%
Total number of patients with positive test result (TP + FP)	117	106	182
Number with a false positive test result (FP)	9	9	8
Total number with a negative test result (TN + FN)	878	894	818
Number with a false negative test result (FN)	7	4	2

Source: Table 6, pg 10 of MSAC 1627 Commentary Executive Summary
 The pooled sensitivity and specificity values used to calculate PPV and NPV are taken from Table 4.
 CT = *Chlamydia trachomatis*; FN = false negative; FP = false positive; NG = *Neisseria gonorrhoea*; NPV = negative predictive value; PPV = positive predictive value; TN = true negative; TP = true positive; TV = *Trichomonas vaginalis*

⁴ Guy, R., Ward, J., Wand, H., Rumbold, A., Garton, L., Hengel, B., & Kaldor, J. (2015). Coinfection with *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*: a cross-sectional analysis of positivity and risk factors in remote Australian Aboriginal communities. *Sexually transmitted infections*, 91(3), 201-206.

Antimicrobial resistance

NG has been designated as a “high priority antibiotic resistant pathogen” by the World Health Organization (WHO). Conversely, clinically significant resistance to macrolides and tetracycline is rare for CT. Similarly, resistance to metronidazole is thought to be uncommon for TV.

Of strains tested from remote regions, where disease is spread predominantly through heterosexual transmission among Indigenous Australians, 2.5% of strains from the Northern Territory (NT) and 6.7% of strains from Western Australia (WA) were penicillin resistant (AGSP Annual Report 2017)⁵. No resistance to ceftriaxone in remote NT and WA regions was observed. Resistance to azithromycin and ciprofloxacin was also low in remote areas of the NT (0.6% and 1.3%, respectively) and WA (3.4% and 5.0%, respectively).

Current treatment recommendations for NG for the majority of Australia, is a dual therapeutic strategy of ceftriaxone and azithromycin. With this treatment, between 4% and 6% of patients with a NG infection would initially receive at least partially ineffective treatment based on the POC test, prior to the AMR test results being known. For symptomatic patients with an NG infection, it is assumed that the empiric treatment given in the SOC arm would be the same as the test-directed treatment given in the POC arm. Although no comparative evidence was identified, it is hypothesised that asymptomatic patients with infections which are resistant to the standard treatments would be more likely to receive inappropriate antibiotics in the POC arm than SOC arm, when the resistance profile of the NG infection would be provided at the same time as the test results.

Change in management outcomes

In total, 14 studies (9 studies included in the ADAR and 5 additional studies identified during scoping searches for the Commentary) provided evidence to inform change in management and health outcomes following Xpert CT/NG or TV POC testing in comparison to SOC. The TTANGO⁶ randomised controlled trial (RCT)⁷ provided comparative evidence directly relevant to the proposed PICO. There is currently limited evidence available for assessment from the expanded study TTANGO2.

An important clinical management outcome of POC testing for STIs is that they should provide a more rapid test result for the patient and healthcare provider (clinician or nurse). This should allow rapid identification of infections in asymptomatic patients and reduce the need for empiric treatment of symptomatic patients as patients can receive treatment with appropriate antibiotics based on their POC test result and on the same day as their test.

Time to test result

The mean or median time to obtaining a test result with Xpert CT/NG or Xpert TV POC testing was consistently shorter than SOC testing. Based on evidence from 8 studies, the median time to test results ranged from 90 minutes to 1 day for Xpert POC testing and 1 to 12 days for SOC NAAT testing. The shorter turnaround time means that patients are able to receive their results on the

⁵ Lahra, M.M., Enriquez, R.P., & George, C.R. (2019) Australian Gonococcal Surveillance Programme Annual Report, 2017. *Commun Dis Intell.* (2018) Apr 15;43. doi: 10.33321/cdi.2019.43.13.

⁶ Test Treat And GO (TTANGO)

⁷ Guy, RJ, Ward, J, Causer, LM, Natoli, L, Badman, SG, Tangey, A, Hengel, B, Wand, H, Whiley, D, Tabrizi, SN, Shephard, M, Fairley, CK, Donovan, B, Anderson, DA, Regan, DG, Maher, L & Kaldor, JM 2018, 'Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial', *Lancet Infect Dis*, vol. 18, no. 10, Oct, pp. 1117-1126.

same day as their clinic consultation. If patients are unwilling or unable to wait for 90 minutes to receive treatment based on their tests results, symptomatic patients may receive empiric treatment at the clinician’s discretion. Alternatively, patients with an infection identified by the POC testing will be required to return to the clinic or arrange another consultation to obtain appropriate test-directed antibiotic treatment.

Time to treatment

A reduction in the time to treatment with Xpert CT/NG POC testing was reported by 5 studies. The median time to treatment ranged from 0 to 3 days for POC testing and 6 to 18.5 days for SOC testing (Table 7). The reduction in the time to treatment reflected the reduction in time to receiving the Xpert CT/NG POC test results.

In the TTANGO study, the time to treatment was lower in the Xpert CT/NG POC test group than the SOC test group (median (interquartile range, IQR), 0 (0–6) vs 7 (0–15) days; mean±SD, 8.7±28 vs. 18.1±40 days).

Table 7 Time to treatment

Author Country	Outcome	POC testing	SOC
Cohen (2019) ⁸ USA	Median time to treatment, days,	1.7	6
	Mean time to treatment, days	0	4
Guy et al, 2018 (TTANGO) Australia	Median time to treatment, days (IQR)	0 (0–6)	7 (0–15)
	Mean time to treatment, days±SD	8.7±28	18.1±40
Keizur, 2020 ⁹ USA	Median time to treatment, days	3	18.5
Rivard (2017) ¹⁰ USA	Time to appropriate treatment for test positive patients, mean±SD hours	4.9±21.3	23.0±56.3
Wingrove, 2014 ¹¹ UK	Median time from test to treatment, days (IQR)	2 (1–6)	10 (7–11)

Source: Commentary Table 15, pg 79 of MSAC 1627 ADAR+in-line commentary
IQR = interquartile range; POC = point of care; SD = standard deviation; SOC = standard of care (in this case, testing within a laboratory setting); UK = United Kingdom; USA = United States of America

Three studies provided evidence for the proportion of patients treated on the same day following Xpert CT/NG POC testing (Table 8). In the TTANGO study intention to treat (ITT) population, significantly more patients in the Xpert CT/NG POC testing group received treatment on the same day as the test than in the SOC group (49% vs. 27%; RR 1.77 (95%CI 1.41, 2.23); p<0.0001). As empiric treatment was also available for the POC testing group, it is not possible to determine

⁸ Cohen S, Kohn R, Bacon O, et al. Implementation of point of care gonorrhoea and chlamydia testing in an STD clinic PrEP program, San Francisco, 2017–2018. *Sexually Transmitted Infections* 2019; 95(Suppl 1): A71-A2.

⁹ Keizur, EM, Goldbeck, C, Vavala, G, Romero-Espinoza, A, Ocasio, M, Fournier, J, Lee, SJ, Abdalian, SE, Rotheram, MJ & Klausner, JD 2020, 'Safety and Effectiveness of Same-Day Chlamydia trachomatis and Neisseria gonorrhoeae Screening and Treatment Among Gay, Bisexual, Transgender, and Homeless Youth in Los Angeles, California, and New Orleans, Louisiana', *Sex Transm Dis*, vol. 47, no. 1, Jan, pp. 19-23.

¹⁰ Rivard, KR, Dumkow, LE, Draper, HM, Brandt, KL, Whalen, DW & Ekwuatu, NE 2017, 'Impact of rapid diagnostic testing for chlamydia and gonorrhoea on appropriate antimicrobial utilization in the emergency department', *Diagn Microbiol Infect Dis*, vol. 87, no. 2, Feb, pp. 175-179.

¹¹ Wingrove I, McOwan A, Nwokolo N, Whitlock G. Diagnostics within the clinic to test for gonorrhoea and chlamydia reduces the time to treatment: a service evaluation. *Sex Transm Infect* 2014; 90(6): 474.

what proportion of patients in this group received empiric treatment or treatment guided by the POC testing.

An improvement in the proportion of patients treated on the same day as the test was maintained in the per protocol (PP) analysis of the TTANGO data (57% vs. 27%; RR 2.10 (95%CI 1.63, 2.62) $p < 0.0001$). This significant difference in the proportion of positive patients treated was maintained for the POC testing group versus the SOC group for the ITT and PP analyses at all the time points (≤ 2 days, ≤ 7 days, ≤ 4 months).

In addition to published data from the TTANGO study, unpublished data from the TTANGO2 study was included with the ADAR (as supplementary data) for the proportion of pregnant women with a positive STI test who received treatment, by test type and treatment interval. These results do not include the numbers of pregnant patients in each group but the percentages were comparable with the data for patients in the TTANGO study.

Table 8 Proportion of patients treated within specific periods

Author Country	Outcome	POC testing n/N (%)	SOC n/N (%)	RR (95%CI) Difference, %
Guy et al, 2018 (TTANGO) Australia	Treated same day, (ITT)	221/455 (49%)	111/405 (27%)	1.77 (1.41, 2.23); $p < 0.0001$
	Treated in ≤ 2 days, (ITT)	274/455 (60%)	122/405 (30%)	2.11 (1.64, 2.72); $p < 0.0001$
	Treated in ≤ 7 days, (ITT)	347 (76%)	191 (47%)	1.66, 1.41, 1.93; $p < 0.0001$
	Treated in ≤ 4 months, (ITT)	427/455 (94%)	347/405 (86%)	1.08 (1.02, 1.15); $p = 0.019$
	Treated same day, (PP)	180/318 (57%)	111/405 (27%)	2.10 (1.63, 2.62) $p < 0.0001$
	Treated in ≤ 2 days, (PP)	249/318 (78%)	122/405 (30%)	2.47 (1.84, 3.31) $p < 0.0001$
	Treated in ≤ 7 days, (PP)	278/318 (87%)	191/405 (47%)	1.88 (1.56, 2.26) $p < 0.0001$
	Treated in ≤ 4 months, (PP)	308/318 (97%)	347/405 (86%)	1.11 (1.04, 1.18) $p = 0.002$
Martin (2022) ¹² Zimbabwe	Proportion of positive results treated	39/61 (63.9%)	66/110 (60.0%)	3.9%
	Positive patients receiving syndromic treatment	5/61 (8.2%)	0/110 (0.0%)	8.2%
	Positive patients treated on same day based on Xpert diagnosis	1/61 (1.6%)	0/110 (0.0%)	1.6%
	Positive patients treated on subsequent day based on Xpert diagnosis	33/61 (54.1%)	66/110 (60.0%)	5.9%
Wynn et al (2018) Botswana	Patients treated the same day	42/54 (77)	NA	NA

Source: Commentary Table 17, pg 81 of MSAC 1627 ADAR+in-line commentary

CI = confidence interval; ITT = intention to treat; N = number of patients; NA = not applicable; POC = point of care; PP = per protocol; RR = relative risk; SOC = standard of care (in this case, testing within a laboratory setting)

¹² Martin, K, Dziva Chikwari, C, Mackworth-Young, CRS, Chisenga, M, Bandason, T, Dauya, E, Oлару, ID, Francis, SC, Mavodza, C, Nzombe, P, Nyamwanza, R, Hove, F, Tshuma, M, Machiha, A, Kranzer, K & Ferrand, RA 2022, "It was difficult to offer same day results": evaluation of community-based point-of-care testing for sexually transmitted infections among youth using the GeneXpert platform in Zimbabwe', *BMC Health Serv Res*, vol. 22, no. 1, Feb 10, p. 171.

Overtreatment of CT and/or NG negative patients

Evidence from the Australian TTANGO2 study (an expansion of the TTANGO study) and two international RCTs indicated that POC testing reduces “overtreatment” of patients without a CT and/or NG infection with antibiotics (Table 9). The TTANGO2 study suggested that 62% of those treated empirically in a SOC setting were uninfected. The introduction of POC testing made empiric treatment more selective (49% CT and NG negative). The two international RCTs reported a reduction in overtreatment of test-negative patients for POC testing versus SOC testing that ranged from 21% to 33%. As the two international RCTs were conducted in a different setting (urban emergency departments in the US) and in symptomatic populations, the applicability and generalisability of these data to the proposed use in Australia (asymptomatic and symptomatic patients in regional or remote health clinics) is uncertain.

Undertreatment of CT and/or NG positive patients

Evidence for “undertreatment” was available from the Australian TTANGO study based on the number of positive patients who did not receive antibiotic treatment at pre-specified time points, as discussed above. Empiric treatment was permitted in the TTANGO study for patients receiving POC testing or SOC testing based on the clinician’s discretion. For the per-protocol (PP) population, undertreatment was reduced for CT and/or NG positive patients receiving POC testing instead of the SOC test (PP population: same day, 43% vs 73%; up to 2 days, 22% vs, 70%; up to 7 days, 13% vs. 53%; up to 4 months, 3% vs. 14%).

In the RCT by Gaydos et al (2019)¹³, the overall undertreatment rate for both CT and NG (same day treatment) was 0% (0/13) for the POC test group and 43.8% (7/16) for the SOC group (difference of -43.8%; 95% CI -68.1%, -19.4%).

¹³ Gaydos CA, Ako MC, Lewis M, Hsieh YH, Rothman RE, Dugas AF. Use of a Rapid Diagnostic for Chlamydia trachomatis and Neisseria gonorrhoeae for Women in the Emergency Department Can Improve Clinical Management: Report of a Randomized Clinical Trial. *Ann Emerg Med* 2019; **74**(1): 36-44.

Table 9 Overtreatment and undertreatment of patients

Author Country	Outcome	POC testing n/N (%)	SOC n/N (%)	Difference RD or RR
Gaydos et al, 2019 USA	Overtreatment	CT 27/117 (23.1%) NG 31/122 (25.4%)	CT 53/114 (46.5%) NG 56/120 (46.7%)	CT -23.4% (95% CI -35.3%, -11.5%) NG -21.3% (95% CI -33.1%, -9.5%)
	Undertreatment	CT 0/10 (0%) NG 0/5 (0%)	CT 6/13 (46.2%) NG 4/7 (57.1%)	CT -46.2% (95% CI -73.3%, -19.2%) NG -57.1% (95% CI -93.8%, -20.5%)
Guy et al (2018) (TTANGO) Australia	Positive patients not treated on same day, (PP)	138/318 (43%)	294/405 (73%)	p<0.0001
	Positive patients not treated in ≤2 days, (PP)	69/318 (22%)	283/405 (70%)	p<0.0001
	Positive patients not treated in ≤7 days, (PP)	40/318 (13%)	214/405 (53%)	p<0.0001
May et al (2016) ¹⁴ USA	Overtreatment	8/37 (21.6%)	11/20 (55.0%)	RD, -33.4; (95% CI, -58.9, -7.9); RR, 0.39; (95% CI, 0.19, 0.82)
Smith et al. (2019) ¹⁵ Australia (TTANGO2) Conference presentation	Overtreatment (of those empirically treated on the same day)	49% CT & NG negative 10% CT & NG positive 13% CT positive 28% NG positive	62% CT & NG negative 10% CT & NG positive 6% CT positive 22% NG positive	Pre and post POC proportions p<0.01

Source: Commentary Table 18, pg 83 of the MSAC 1627 ADAR+in-line commentary

CT = *Chlamydia trachomatis*; N = number of patients; NA = not available; NG = *Neisseria gonorrhoea*; POC = point of care; PP = per protocol population; RD = risk difference; RR = relative risk; SOC = standard of care (in this case, testing within a laboratory setting); USA = United States of America

Retesting patients for reinfection or cure

It is uncertain whether Xpert CT/NG POC testing in comparison to SOC testing has a positive impact on the rate of retesting to determine reinfection or treatment resolution. Only the TTANGO study reported data for the number of positive patients retested at 3 weeks to 3 months after treatment following an Xpert NG/CT and SOC test to diagnose the initial STI. Retesting rates reported for the TTANGO study were low and comparable between the Xpert NG/CT POC test and SOC test groups (14% vs 17%).

¹⁴ May L, Ware CE, Jordan JA, et al. A Randomized Controlled Trial Comparing the Treatment of Patients Tested for Chlamydia and Gonorrhoea After a Rapid Polymerase Chain Reaction Test Versus Standard of Care Testing. *Sex Transm Dis* 2016; 43(5): 290-5.

¹⁵ Smith KS, Causer LM, Watchirs Smith L, Saha A, Andrewartha K, Walley B, Shephard M, Wand H, Richards JN, Badman SG, Tangey A, Marshall-Lang R, and Guy R, on behalf of the TTANGO2 collaboration. Presumptive treatment for Chlamydia and Gonorrhoea in remote aboriginal health services. Presented at the Australasian Sexual Health Conference 16-18 September 2019.

Health outcomes

STI reinfection after treatment

Direct comparative test to health outcomes evidence was available from the TTANGO study and another international RCT (Keizur et al, 2020)¹⁶. The health outcome was the rate of patient reinfection or failure to resolve the STI infection after antibiotic treatment.

Retesting of patients is recommended in the Australian STI management guidelines to confirm that patients have not been reinfected or that the infection has resolved following treatment.

Data from the TTANGO study suggested that the majority of patients were uninfected at retesting (i.e. cured, and not reinfected) (81% for Xpert CT/NG POC testing; 87% for SOC testing). However, there was no significant difference in the proportion of patients who were infected (and therefore the proportion reinfected) between the Xpert CT/NG POC test and SOC test groups (RR 1.42, 95% CI 0.64, 3.13; p=0.40). The proportion of patients presenting for a retest was low in both groups, and the lack of statistical significance may be due to the small sample size. There was no significant difference in participant reinfection or failure to resolve the initial infection between the POC and SOC testing groups in the international RCT (12% vs 20%; RR 0.60, 95% CI 0.33, 1.09).

Two noncomparative studies (Garrett et al, 2018¹⁷; Wynn et al, 2018¹⁸) reported a reduction in reinfection on retesting (59% at baseline vs 4% on retesting at 12 weeks after treatment; ~10% of infected patients positive on retesting at ≥4 weeks after treatment). In both studies, a higher proportion of patients were retested than in the TTANGO study.

Reductions in adverse reproductive health outcomes

Evidence supporting the impact of Xpert CT/NG and Xpert TV POC testing on the prevalence of PID and antenatal care was not included in the ADAR. However, the ADAR claimed it was reasonable to conclude that appropriately treating CT and NG infections in a timely manner is likely to reduce the risk of PID developing and other negative reproductive outcomes.

Clinical claim

The ADAR was inconsistent regarding whether the clinical claim was that use of Cepheid GeneXpert CT/NG and TV assays in a POC setting results in noninferior effectiveness compared with laboratory NAAT testing, or superior effectiveness compared with laboratory NAAT testing.

The analysis of the data during evaluation supported the claim of non-inferior effectiveness. Although the use of POC testing is *likely* to be superior to SOC testing (due to faster treatment of

¹⁶ Keizur, EM, Goldbeck, C, Vavala, G, Romero-Espinoza, A, Ocasio, M, Fournier, J, Lee, SJ, Abdalian, SE, Rotheram, MJ & Klausner, JD 2020, 'Safety and Effectiveness of Same-Day Chlamydia trachomatis and Neisseria gonorrhoeae Screening and Treatment Among Gay, Bisexual, Transgender, and Homeless Youth in Los Angeles, California, and New Orleans, Louisiana', *Sex Transm Dis*, vol. 47, no. 1, Jan, pp. 19-23.

¹⁷ Garrett, NJ, Osman, F, Maharaj, B, Naicker, N, Gibbs, A, Norman, E, Samsunder, N, Ngobese, H, Mitchev, N, Singh, R, Abdool Karim, SS, Kharsany, ABM, Mlisana, K, Rompalo, A & Mindel, A 2018, 'Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries', *PLoS One*, vol. 13, no. 4, p. e0196209.

¹⁸ Wynn, A, Ramogola-Masire, D, Gaolebale, P, Moshashane, N, Sickboy, O, Duque, S, Williams, E, Doherty, K, Klausner, JD & Morroni, C 2018, 'Prevalence and treatment outcomes of routine Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis testing during antenatal care, Gaborone, Botswana', *Sex Transm Infect*, vol. 94, no. 3, May, pp. 230-235.

asymptomatic patients with infections, and the fact that treatment of STIs should reduce the rate of longer-term sequelae), the evidence that POC reduces the infection rate at follow-up was highly uncertain (limited retesting data with non-statistically significant differences).

The ADAR claimed that the use of the Cepheid GeneXpert CT/NG and TV assays in a POC setting results in noninferior safety compared with laboratory NAAT testing. This claim was appropriate.

13. Economic evaluation

The ADAR presented a cost-utility analysis based on the reduced time to treatment observed in the TTANGO trial, and on this basis, a reduction in infection sequelae was modelled. The Commentary noted that while data from TTANGO may support a reduced time to treatment with POC testing, when a sample of patients were retested three weeks to three months after treatment, no difference in infection rates was observed between trial arms. The ADAR did not address how this observation appeared inconsistent with the reduction in infection sequelae modelled.

The population modelled appeared to represent a cross section of people eligible for testing who present repeatedly over the 10 year time horizon. This resulted in an accrual of costs and consequences that are not reflective of a single test, but reflect a series of testing episodes within a ten-year block of time. While the probability of long-term infection-related consequences increase over the cycles with repeated infection exposure, the nature of the ‘recycling’ population (i.e. inputs such as the proportion with infections, uptake of testing, proportion who are symptomatic, etc.) does not change over time despite the fact that behaviours within the population change over time due to ageing (such as a reduction in the number of partners and reproductive planning) or infection history (such as increased preventative measures or seeking prompt treatment).

MSAC may be more interested in an assessment question that addresses the cost-effectiveness of the proposed intervention relative to standard of care for the average eligible person at the time of model entry. Given that testing in subsequent years is for the identification of new infections only, a reasonable simplification of the model may be to exclude new infections (and re-testing for these new infections) in subsequent years. This approach may also avoid the need for more complex microsimulation modelling that requires large numbers of simulations to generate stability in the results.

A summary of the key components of the economic evaluation is presented in Table 10.

Table 10 Summary of the economic evaluation

Component	Description
Perspective	Health care system perspective. The Commentary considered that costs not typically presented in MSAC analyses were included (air evacuation, staff costs to locate and retrieve patients for follow-up appointments). MSAC may wish to consider whether these cost inclusions are reasonable in the circumstances of providing care in remote communities.
Population	Population consisted of women and men, aged 16–29, at high risk of STI infection attending Aboriginal medical services and Aboriginal Community Controlled Health Services. Pathways for men and women were separate due to different outcomes of infection. The pathways included patients presenting with symptomatic or asymptomatic infection and for women symptoms suspicious of PID. The Commentary noted that the proposed MBS item descriptors do not restrict by age. Use in less disease-prevalent persons will likely reduce the cost-effectiveness of POC testing.

Component	Description
Comparator	Laboratory testing
Type(s) of analysis	Cost-utility analysis.
Outcomes	Quality-adjusted life years. The Commentary noted that MSAC may also be interested in other outcomes, such as the incremental cost per additionally treated person within 7 days of sampling (as per the TTANGO trial) and incremental cost per infection sequelae avoided.
Time horizon	10 years. The Commentary noted that while this may be similar to a previously published economic evaluation, given the uncertainty in the extent of the reduction in infection-related sequelae resulting from the use of POC testing in the proposed population, extended time horizons may not be appropriate.
Computational method	Markov model using both microsimulation and probabilistic sampling simultaneously. The Commentary noted that it was unclear whether probabilistic sampling was applied in the base case, as results could not be verified, due to the use of random seeding.
Generation of the base case	Modelled evaluation based on trial data from the TTANGO trial which compared time to treatment using POC with laboratory testing and TTANGO2 data related to health service attendance and testing uptake. Other variables beyond the time of the trial related to health outcomes were obtained from published data. The Commentary noted that MSAC may be interested in a stepped presentation of the results where extrapolations of the trial data are incorporated separately in a transparent manner to allow the effects of these on the results to be distinguished.
Health states	<p>Health states for women</p> <ol style="list-style-type: none"> 1. Women attending a clinic who may have a STI. It is expected that a STI test will be conducted if a patient discloses symptoms and opportunistic testing may be conducted 2. Infection may clear and sequelae related to non-treatment and risk of PID 3. Sequelae related to non-treatment such as chronic pain, infertility and ectopic pregnancy 4. Sequelae related to longer term consequences of untreated CT/NG. <p>Health states for men</p> <ol style="list-style-type: none"> 1. Male attending a clinic who may have an STI. It is expected that and STI test will be conducted if a patient discloses symptoms and opportunistic testing may be conducted 2. Infection may clear and sequelae related to non-treatment and risk of epididymitis <p>Events related to infection sequelae are modelled within health states. The Commentary noted that a number of assumptions were made regarding the types of events experienced, durations in health states following events and subsequent transitions.</p>
Cycle length	One year. The Commentary noted that this was relatively long and not necessarily aligned with health state durations or events; within a cycle, patients may experience events which resolve. In addition, utility values were accrued in month units which may not reflect the duration of events experienced.
Transition probabilities	Expert advice and published literature. Time from sampling to treatment data were derived from TTANGO ^a and TTANGO2 ^b
Discount rate	5% for both costs and outcomes
Software	TreeAge Pro

Source: Compiled from Table 11, p64 of the MSAC 1627 ADAR with commentary added during the evaluation.

CT = Chlamydia trachomatis; PID = pelvic inflammatory disease; NG = Neisseria gonorrhoea; POC = point of care; STI = sexually transmitted infection; TV = Trichomonas vaginalis.

^a Guy, RJ, Ward, J, Causer, LM, Natoli, L, Badman, SG, Tangey, A, Hengel, B, Wand, H, Wwhiley, D, Tabrizi, SN, Shephard, M, Fairley, CK, Donovan, B, Anderson, DA, Regan, DG, Maher, L & Kaldor, JM 2018, 'Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial', *Lancet Infect Dis*, vol. 18, no. 10, Oct, pp. 1117-1126.

^b 'ADAR_Supplementary documents.pdf file included in the ADAR.

The Commentary noted that results presented in the ADAR could not be verified during the evaluation, due to the use of random seeding. A nominal base case was applied during the evaluation using a microsimulation of 10,000 trials with a fixed seed (seed 1) (Table 11). However, a number of errors were also identified, particularly with regard to how QALYs were

accrued over a model cycle, and so the ADAR analyses were revised during the evaluation to correct for these. The analysis was then restricted to reflect a single episode of testing. This was noted to be substantially higher than the expected value for a cohort passing through the model. When the microsimulation was performed repeatedly, wide variation in the results was observed, which suggested that the number of trials run was insufficient – which may be unsurprising given the small incremental benefit observed. Given that adjustments to the model no longer necessitated individual-based modelling, the revised base case presented in the Commentary adopted the cohort expected value approach. The revised base case ICER was observed to be \$20,453 per additional QALY gained.

Table 11 Stepped changes to generate the base case in the Commentary

	POC	SOC	Increment
ADAR base case [10,000 trials; seed 1]			
Cost	\$3,763.55	\$3,516.70	\$246.85
QALYs	8.4654	8.4581	0.0073
ICER			\$34,010
ADAR base case with corrections [10,000 trials; seed 1]^a			
Cost	\$4,256.06	\$4,068.06	\$188.00
QALYs	7.9595	7.9496	0.0100
ICER			\$18,876
Adjusted for single episode of testing [10,000 trials; seed 1]^b			
Cost	\$514.83	\$460.21	\$54.62
QALYs	8.0445	8.0435	0.0010
ICER			\$55,084
Expected cohort value (Commentary revised base case)			
Cost	\$569.08	\$541.23	\$27.86
QALYs	8.0454	8.0440	0.0014
ICER			\$20,453

Source: Commentary Table 31, pg 149 of MSAC 1627 ADAR+in-line commentary ICER = incremental cost-effectiveness ratio; POC = point of care; QALY = quality-adjusted life year; SOC = standard of care.

^a Corrected during the evaluation to account for errors identified through a model validation exercise that applied no discounting set with no utility decrements applied which observed >10 LYs being accrued. Other changes were made to correct for other inconsistencies identified during the evaluation (erroneous jump states or probabilities applied).

^b No infections or testing in subsequent years. The probability of infertility and ectopic pregnancies was also increased to reflect the average incidence, rather than incidences by number of prior PID episodes.

An alternate scenario was conducted during the evaluation which excluded costs not consistent with the perspective usually presented to MSAC (i.e. air evacuation, staff costs to locate and retrieve patients for follow-up appointments) (Table 12). The ICER was sensitive to the exclusion of these costs. MSAC may wish to consider whether these cost inclusions are reasonable in the circumstances of providing care in remote communities.

Table 12 Alternate scenario, excluding indirect health care costs

	POC	SOC	Increment
Cost	\$396.29	\$324.04	\$72.26
QALYs	8.0454	8.0440	0.0014
ICER			\$53,049

Source: Commentary Table 34, pg 151 of MSAC 1627 ADAR+in-line commentary.

ICER = incremental cost-effectiveness ratio; POC = point of care; QALY = quality-adjusted life year; SOC = standard of care.

Disaggregated costs are presented in Table 13. The incremental cost was driven by the cost of testing. Offsets were predominantly due to a reduction in infection sequelae (in particular preterm births) however were also driven by a reduction in the cost of staff time to locate and retrieve patients for treatment.

Table 13 Disaggregated costs (Commentary base case)

	POC	SOC	Increment
Test-related costs	\$224.40	\$122.43	\$101.98
Infection treatment costs	\$16.13	\$39.39	-\$23.26
Treatment	\$6.82	\$6.96	-\$0.14
Contact	\$6.28	\$22.74	-\$16.46
Clinic	\$1.61	\$7.12	-\$5.50
Antenatal	\$1.43	\$2.58	-\$1.15
Infection-sequelae costs	\$328.55	\$379.41	-\$50.86
PID	\$42.23	\$48.66	-\$6.43
DGI	\$1.51	\$1.65	-\$0.13
Pregnancy outcome all	\$202.31	\$235.84	-\$33.53
• Preterm births	\$177.43	\$206.84	-\$29.40
• Premature rupture of membranes	\$24.88	\$29.00	-\$4.12
Epididymitis	\$7.00	\$8.70	-\$1.70
Infertility	\$3.70	\$4.14	-\$0.44
Ectopic Pregnancy	\$39.26	\$43.97	-\$4.71
Chronic Pain	\$24.12	\$27.01	-\$2.90
Long-term sequelae	\$8.43	\$9.45	-\$1.02
Total cost	\$569.08	\$541.23	\$27.86

Source: Commentary Table 32, pg 150 of MSAC 1627 ADAR+in-line commentary.

DGI = disseminated gonococcal infection; PID = pelvic inflammatory disease; POC = point of care; SOC = standard of care.

The key drivers of the model are presented in Table 14.

Table 14 Key drivers of the model

Description	Method/Value	Impact Commentary revised base case: \$20,453/QALY gained
Inclusion of indirect health care costs	Cost of air evacuation and staff time to locate and retrieve patients for treatment were included.	High, favours POC testing Excluding these costs increased the ICER to \$53,049/QALY gained
Retesting following treatment	Not included within 3 weeks – 3 months following treatment. This is not consistent with recommendations in guidelines, or the clinical management algorithms presented in the ADAR.	High, favours POC testing Including the cost of retesting with the cost of treatment increased the ICER to \$50,065/QALY gained
Incidence of preterm births in untreated pregnant females	28% based on calculations of the population attributable fractions of events due to STIs (i.e. for every 100 preterm births, 28 were due to STIs). However the ADAR has applied this estimate to all births in pregnant untreated females (e.g. 28 preterm births for every 100 pregnancies in pregnant untreated females).	High, favours POC testing Reducing the incidence of preterm births in untreated pregnant females to 3.9% ^a increased the ICER to \$39,278/QALY gained
Duration of utility decrement	The utility decrement for events was applied in months, though this was not consistent with the source cited for most of the utility weights which also reported the expected duration of each of the event. Most events were reported in terms of days rather than weeks or months, as modelled in the ADAR.	High, favours POC testing Use of utility decrements for events adjusted for the duration of the event increased the ICER to \$33,624/QALY gained.
Proportion of population presenting to clinics who are female	67% based on TTANGO2 data. The data referred to persons aged <30 years who received an STI test, (65% female). The proportion of unique patients aged <30 years who were female and who attended a clinic at least once may be more appropriate (56.5%) as uptake of testing was applied subsequently to clinic attendees.	High, favours POC testing. Reducing this proportion to 56.5% increased the ICER to \$29,856/QALY gained.

Source: Table 14, pg 21 of MSAC 1627 Commentary Executive Summary

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year.

^a Assuming 14% of pregnancies result in preterm birth (preterm births observed in the Aboriginal population in the Northern Territory, reported in Morris, J, Brown, K & Newnham, J 2020, 'The Australian Preterm Birth Prevention Alliance', Aust N Z J Obstet Gynaecol, vol. 60, no. 3, Jun, pp. 321-323.), and if 28% of these are due to STIs, 3.9% of pregnancies with untreated STIs would result in pre-term births (due to STIs).

The results of key sensitivity analyses are summarised in Table 15 below. These were conducted during the evaluation around particular areas of concern identified. The analysis was sensitive to many of these changes, and as some were considered to be more appropriate to use in the analysis, multivariate analyses were performed. The ICER was observed to substantially increase with these multiple changes.

Table 15 Sensitivity analyses conducted during the evaluation

	Inc. cost	Inc. QALYs	ICER	% change
Base case	\$27.86	0.0014	\$20,453	
Distribution of persons attending (base case: 66.7% female)				
0% female	\$71.36	0.0001	\$871,779	4162%
56.5% female (distribution of attendees <30 years in TTANGO2) (#1)	\$34.68	0.0012	\$29,856	46%
100% female	\$6.43	0.0020	\$3,228	-84%
Females with infections (revised base case: 35.8%)				
30% (default in model file)	\$37.76	0.0011	\$32,956	61%
40.6% (any infections in <30 years reported in Guy et al. (2015) ^a)	\$19.66	0.0015	\$12,760	-38%
Females with infections, 30%, and males with infections, 25% (default in model file) (revised base case: 35.8% and 29%, respectively)	\$37.84	0.0011	\$33,137	62%
Proportion of males who are symptomatic at time of testing, 27% (as per Table 12 of the ADAR) (base case: 37%) (#2)	\$25.58	0.0014	\$18,719	-8%
Uptake of testing in asymptomatic females, 24.6% (average female <30 years testing rate in TTANGO2) (base case: 45%)	\$15.23	0.0008	\$17,967	-12%
Uptake of testing in asymptomatic males, 17.1% (average male <30 years testing rate in TTANGO2) (base case: 35%)	\$19.17	0.0013	\$14,220	-30%
Incidence of pre-term birth in untreated pregnant females, 3.9% (see Table 14) (base case: 28%) (#3)	\$53.17	0.0014	\$39,278	92%
Incidence of PROM in untreated pregnant females, 0.3% ^c (base case: 10%) (#3)	\$31.85	0.0014	\$23,366	14%
Proportion preterm births classed as moderately preterm, 9.6% (Newnham et al. 2022) ^b (base case: 41%)	\$34.83	0.0014	\$25,570	25%
Exclude indirect health care air evacuation costs	\$55.79	0.0014	\$40,963	100%
Exclude indirect health care staff costs for patient contact and retrieval	\$44.32	0.0014	\$32,539	59%
Exclude all indirect health care costs (#6)	\$72.26	0.0014	\$53,049	159%
Adjusting utility months for duration of events (see Table 14) (#4)	\$27.86	0.0008	\$33,624	64%
Retesting cost with treatment (see Table 14) (#5)	\$68.19	0.0014	\$50,065	145%
Multivariate analyses				
#1 AND #2	\$31.67	0.0012	\$27,134	33%
#1, #2 AND #3	\$47.64	0.0012	\$39,184	92%
#1, #2, #3 AND #4	\$47.64	0.0007	\$64,634	216%
#1, #2, #3, #4 AND #5	\$85.19	0.0007	\$115,581	465%
#1, #2, #3, #4, #5 AND #6	\$118.73	0.0007	\$161,085	688%

Source: Commentary Table 35, pg 151 of MSAC 1627 ADAR+in-line commentary.

^a Guy R, Ward J, Wand H, et al. Coinfection with Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis: a cross-sectional analysis of positivity and risk factors in remote Australian Aboriginal communities. Sex Transm Infect 2015; 91(3): 201-6

^b Newnham, JP, Schilling, C, Petrou, S, Morris, JM, Wallace, EM, Brown, K, Edwards, L, Skubisz, MM, White, SW, Rynne, B, Arrese, CA & Doherty, DA 2022, 'The health and educational costs of preterm birth to 18 years of age in Australia', Aust N Z J Obstet Gynaecol, vol. 62, no. 1, Feb, pp. 55-61.

^c Assuming 2% of pregnancies are affected by PROMs (South Australian Perinatal Practice Guidelines preterm prelabour rupture of the membranes) where 16% due to STIs (Table 12 of the ADAR).

DGI = disseminated gonococcal infection; ICER = incremental cost-effectiveness ratio; PID = pelvic inflammatory disease; POC = point of care; PROM = premature rupture of membranes; QALY = quality-adjusted life year; SOC = standard of care; STI = sexually transmitted infection.

In the applicant's pre-ESC response, the applicant presented a revised ICER of \$37,185 per QALY gained. No sensitivity analyses were presented alongside this updated ICER. The pre-ESC ICER was derived from changes made to the original ADAR ICER that included:

- amending the preterm birth rate 16.6 % in the treated arm (the pre-ESC response noted that 0% was incorrectly used in the treated arm in the original model)
- acceptance and incorporation of the Commentary proportion of women of 56.5% (67% in the original ADAR) who attended a clinic at least once in the TTANGO study
- correction of the rounding errors in the utilities associated with epididymitis
- reduction of the days of disutility in PID state from 12 to 10 days (reflecting that some patients with acute PID will be treated as outpatients rather than as inpatients)

In the applicant's pre-MSAC response, the applicant updated the base-case to \$33,387 per QALY gained with 10,000 microsimulations and noted that the base-case ICER was \$38,398 per QALY gained using probabilistic sensitivity analysis. When the time horizon was changed from 10 years to 5 years in the probabilistic sensitivity analysis, this resulted in an ICER of \$42,615 per QALY gained. Other sensitivity analyses were conducted on the base-case ICER and indicated that the ICER was most sensitive to the cost of the POC test and the probability of a positive test result. Additional analyses investigating the impact of other indirect out-of-pocket costs such as loss of productivity were explored. MSAC noted that due to the lack of transparency in the model and pre-MSAC response, the revised ICER and sensitivity analyses could not be verified prior to MSAC.14.

14. Financial/budgetary impacts

The ADAR adopted a market-based approach to estimate the use and cost of POC testing to the MBS, however rather than estimating the size of the market eligible for testing, current estimates of POC use were projected to account for use with MBS listing. It was unclear from the ADAR whether the current estimates reflected use across all age groups or whether this reflected use only in persons aged 16–29. The ADAR has assumed that each patient estimated to receive POC testing would have received standard laboratory testing in the absence of POC.

The financial implications to the MBS (i.e. calculated during the evaluation based on the MBS benefit) resulting from the proposed listing of POC testing for CT/NG and TV testing are summarised in Table 16.

Table 16 Net financial implications of POC testing for CT/NG and TV to the MBS

	2023	2024	2025	2026	2027	2028
No. persons tested per year using POC test	18,360	20,196	26,136	35,937	47,437	52,181
Cost to the MBS for POC CT/NG testing (\$127.50 per service) ^a	\$2,340,900	\$2,574,990	\$3,332,340	\$4,581,968	\$6,048,197	\$6,653,017
Cost to the MBS for POC TV testing (\$97.75 per service) ^a	\$1,794,690	\$1,974,159	\$2,554,794	\$3,512,842	\$4,636,951	\$5,100,646
Cost to the MBS for proposed POC testing	\$4,135,590	\$4,549,149	\$5,887,134	\$8,094,809	\$10,685,148	\$11,753,663
Reduction in use of standard CT/NG/TV tests	18,360	20,196	26,136	35,937	47,437	52,181
Reduction in cost to the MBS for standard CT/NG/TV testing (\$36.55 per service) ^a	\$671,058	\$738,164	\$955,271	\$1,313,497	\$1,733,817	\$1,907,198
Reduction in the cost of episode fees to the MBS (\$2.05 per service) ^a	\$37,638	\$41,402	\$53,579	\$73,671	\$97,246	\$106,970
Total reduction in costs to the MBS related to standard testing	\$708,696	\$779,566	\$1,008,850	\$1,387,168	\$1,831,062	\$2,014,168
Net cost to the MBS	\$3,426,894	\$3,769,583	\$4,878,284	\$6,707,641	\$8,854,086	\$9,739,495
Sensitivity analyses						
Increase to 300 patients tested per site per year	\$6,047,460	\$6,652,206	\$7,317,427	\$8,049,169	\$8,854,086	\$9,739,495
Incorporate re-testing						
4% re-testing rate (14% of those with infections identified, as per TTANGO ^b)	\$3,570,824	\$3,927,906	\$5,083,172	\$6,989,362	\$9,225,958	\$10,148,554
15% re-testing rate (50% of those with infections identified)	\$3,940,928	\$4,335,021	\$5,610,027	\$7,713,787	\$10,182,199	\$11,200,419
30% re-testing rate (100% of those with infections identified)	\$4,454,962	\$4,900,458	\$6,341,770	\$8,719,933	\$11,510,312	\$12,661,343

Source: Commentary Table 38 and 39, pg 158 of MSAC 1627 ADAR+in-line commentary.

^a Assuming the 85% level of rebate applies

^b Guy, RJ, Ward, J, Causer, LM, Natoli, L, Badman, SG, Tangey, A, Hengel, B, Wand, H, Whiley, D, Tabrizi, SN, Shephard, M, Fairley, CK, Donovan, B, Anderson, DA, Regan, DG, Maher, L & Kaldor, JM 2018, 'Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial', *Lancet Infect Dis*, vol. 18, no. 10, Oct, pp. 1117-1126.

CT = *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; POC = point of care; TV = *Trichomonas vaginalis*.

The average number of people tested per year at each site was assumed to increase from 170 in 2023 to 300 by 2028. The Commentary noted that the basis for the average number of tests performed was not described. While this appeared similar to the average number of tests per site

2020–2022 (178)¹⁹, this was lower than average test numbers in 2018 (300 tests per site per year)²⁰. The number of POC tests performed may be underestimated if use of testing returns to pre-COVID19 pandemic levels.

The ADAR did not consider the cost of retesting three months after treatment initiation as recommended in the guidelines and as per the clinical management algorithms presented in the ADAR. Given the additional cost associated with POC testing, and that as more patients are expected to receive treatment (as per the TTANGO trial), these costs may be substantial. Based on the estimations presented in the ADAR, up to 30% of patients each year tested may require retesting.

The ADAR included a reduction in cost due to fewer sequelae related to CT, NG or TV infections (Table 17). The Commentary noted that estimates used to derive the reduction in cases of PID, infertility, ectopic pregnancy, pre-term births and acute epididymitis were difficult to verify, and where able to, were likely overestimated (e.g. preterm births). Further it was noted that these costs were not separated by funding source and were higher than those applied for the treatment of the relevant sequelae applied in the economic analysis.

Table 17 Estimated reduction in costs

	2023	2024	2025	2026	2027	2028
Total reduction in costs related to cases avoided	\$2,882,166	\$3,170,383	\$4,383,917	\$5,641,417	\$7,446,670	\$8,143,838
<i>Revised</i>	\$2,172,309	\$2,389,540	\$3,092,346	\$4,251,976	\$5,612,609	\$6,173,870

Source: Commentary Table 47, pg 169 of MSAC 1627 ADAR+in-line commentary.

CT = *Chlamydia trachomatis*; NG = *Neisseria gonorrhoeae*; POC = point of care; TV = *Trichomonas vaginalis*.

15. Other relevant information

Influences on the feasibility and acceptability of POC Xpert CT/NG and TV testing in health care clinics in remote Aboriginal and Torres Strait Islander communities.

Six qualitative studies included in Table 8 of the ADAR provided information on the experiences of either healthcare workers and/or laboratory staff (n=5) or patients (n=1) with POC Xpert testing in remote communities. The additional articles included in Table 8 either provided opinions without any data or reported on the POC test used in settings that are not analogous to a remote community, and have not been discussed further.

The three Australian studies (Lafferty et al 2021, Natoli et al 2015, Natoli et al 2015b) reported on the experiences and/or public health implications for POC Xpert CT/NG testing from the TTANGO trial. These studies all reported common themes around the feasibility and acceptability of POC Xpert testing from the healthcare workers' perspective. These themes are summarised below:

Three studies were conducted in countries where routine diagnostic testing is not readily available due to lack of laboratory capacity. In these countries, syndromic management of STIs is the SOC. As many patients are asymptomatic, they are not treated. Identification and treatment

¹⁹ 8,000 tests performed annually across 45 decentralised health services (Section 1.4 of the ADAR).

²⁰ Section 3A.2.6 of the ADAR.

of these patients would potentially decrease both the prevalence and the morbidity from untreated STIs within these communities. These studies reported on the patient uptake of POC testing. One study also reported on the patients' attitude towards POC testing.

It should be noted that there was no explicit comparison to SOC in any of these studies, but it could be hypothesised that

- An effective POC Xpert CT/NG and TV testing program requires education and training programs to ensure healthcare workers and communities are well informed about STIs and available treatments, and the advantages of POC testing
 - Effective training programs on the use of the GeneXpert device and on conducting routine quality assurance are required
- A successful POC Xpert CT/NG and TV testing program results in most individuals who participate receiving same-day test results and treatment initiation, and also results in more effective contact tracing.
 - The major limitation of the test was that it does not determine antimicrobial resistance
- Overall, the advantages of POC Xpert CT/NG and TV testing identified by healthcare workers seemed to outweigh the perceived drawbacks or limitations associated with the test.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Proposed MBS fee and item descriptor:

- ESC supported the MBS item descriptor not being restricted by age or by Aboriginal or Torres Strait Islander origin, though considered that it should specify that it is for point-of-care testing at Aboriginal Medical Services and Aboriginal Community Controlled Health Organisations in rural and remote locations.
- The MBS item descriptor (YYYY) for testing following a previous infection appears redundant.
- The proposed fees of \$150 (*Chlamydia trachomatis* and *Neisseria gonorrhoeae*) and \$115 (*Trichomonas vaginalis*) for the point-of-care tests are high relative to MBS fees for standard laboratory testing and other point-of-care tests.

Clinical issues:

- The specificity and sensitivity of the point-of-care tests compared with standard laboratory testing had been previously accepted by the MSAC Executive and ESC considered that this was appropriate. ESC noted that the claim of non-inferior effectiveness was supported, and that point-of-care tests are likely to be superior to standard laboratory testing.
- The clinical data suggested that there was a reduced time to test results with point-of-care tests compared with standard laboratory tests.
- There was limited evidence regarding improvements in health outcomes; the main trials were not powered or of long enough duration to detect changes in longer term outcomes (such as maternal outcomes and downstream sequelae).

Safety:

- ESC considered that the point-of-care tests had non-inferior safety compared to standard laboratory testing and no safety concerns were identified.

Economic issues:

- The economic model developed by the applicant was overly complex and had errors that made interpretation of the results challenging. The model was based on the reduced times

to treatment observed in the clinical data and these were then extrapolated to longer-term health outcomes.

- The commentary conducted one-way and multivariate sensitivity analyses that showed that the ICER was highly sensitive to variations in a number of assumptions underlying the model. The commentary base case ICER of \$20,453 increased to \$161,085 per QALY gained in a multivariate sensitivity analysis (see Table 15). The applicant's pre-ESC response presented an updated ICER of \$37,185 per QALY gained that corrected for some of the errors identified in the commentary evaluation. No updated sensitivity analyses were provided by the applicant.
- Given the significant impact of input changes on the ICER in the commentary evaluation sensitivity analyses, ESC requested the applicant conduct updated sensitivity analyses to demonstrate how robust the new ICER is to changes in the model inputs. Alongside updating the sensitivity analyses around key parameters as identified in the commentary, ESC considered that additional sensitivity analyses to explore the impact of changes to the range of utility values and a reduced time horizon (10 years to 5 years) would also be informative. ESC considered it would still be beneficial to show MSAC two scenario analyses that demonstrated the impact of including indirect costs on the economic estimates.

Financial issues:

- The assumptions underpinning the financial estimates were unclear and ESC requested improved transparency to understand the assumptions informing the financial estimates.
- ESC requested that the financial estimates be updated to account for the corrected parameter inputs provided with the applicant's pre-ESC response. Updated sensitivity analyses of the financial estimates should also be presented in line with the relevant input changes in the updated economic sensitivity analyses.

Other relevant information:

- ESC considered that there could be additional benefits of cultural importance associated with point-of-care testing (such as greater ownership of samples and the testing process, which in turn could lead to increased self-management). However, these aspects were not fully explored **redacted**. ESC considered that more information regarding these aspects would be useful.
- ESC noted that more than 95% of health services who were involved in the key Australian study stated that they would continue their involvement.

ESC discussion

ESC noted that the application was for Medicare Benefits Schedule (MBS) listing of point-of-care (POC) testing for sexually transmitted infections provided by Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural or remote areas.

ESC noted that there were two POC tests under consideration. One was a dual cartridge test for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) and the other was a single cartridge test for *Trichomonas vaginalis* (TV). Both tests have been included on the Australian Register of Therapeutic Goods.

ESC noted that these POC tests had been previously considered by the MSAC Executive. The MSAC Executive noted that the evidence provided indicated that the sensitivity and specificity are comparable to standard laboratory testing. The MSAC Executive considered that the evidence provided was sufficient to confirm the validity of using POC testing as a diagnostic test for NG/CT and TV. The MSAC Executive considered that if the applicant wished to pursue an MBS fee that is higher than the existing MBS laboratory testing fees, the applicant would need to provide

evidence that POC testing results in better health outcomes than standard laboratory testing, and this evidence would need to be supported with an appropriate economic analysis.

ESC noted the consultation responses received. ESC considered that all feedback was generally very supportive of POC testing and that the sexually transmitted infections considered in the application are a significant public health issue in predominantly Aboriginal and Torres Strait Islander communities in rural and remote Australia. ESC noted that the statements highlighted that increased access to testing could help to close the gap and reduce health inequalities for Aboriginal and Torres Strait Islander people. ESC noted that the main disadvantage with the POC test was that the current timeframe of up to 90 minutes to wait for a result is potentially a long time for patients to wait for a result. However, ESC noted that the ability to trace patients after 90 minutes is greater than up to 14 days and that the waiting time would present an opportunity for sexual health education. ESC also noted that adequate quality control and training and support for providers was important. However, ESC raised concern about the very limited consultation with individual communities (particularly with patients and community members) undertaken during the pivotal Australian study. ESC considered that additional qualitative evidence from consultation would have been informative, particularly in regards to addressing potential implementation factors (such as culturally sensitive issues around education on STI issues) and the impact of POC testing on the local workforce and community. ESC noted that such issues could influence the uptake of POC testing in rural and remote Australia.

ESC noted that the rates of sexually transmitted infections have been increasing in Aboriginal and Torres Strait Islander people in Australia and represent a significant public health issue in regional and remote communities with potentially serious downstream sequelae. ESC noted that current guidelines recommend opportunistic testing of all people aged 16-29 years old²¹, or 15-35 years old (depending on jurisdiction) annually, as well as testing of all symptomatic patients on presentation to a health service. ESC noted that the MBS item descriptor in the application was not restricted by age. ESC considered that this was appropriate as there would be increased public health benefits in being age agnostic and not limiting the testing by age. ESC discussed whether the item descriptor should reference the guidelines but noted that the guidelines could change in the future, however ESC considered it could be useful to reference the guidelines in the explanatory note.

ESC noted that the proposed MBS item descriptor was specific to people presenting to Aboriginal Medical Services or Aboriginal Community Controlled Health Services in rural and remote areas, irrespective of Aboriginal and Torres Strait Islander origin. ESC noted that the policy paper questioned whether the MBS item descriptor should be restricted to Aboriginal and Torres Strait Islander people. ESC considered that including Indigenous Status within the MBS item descriptor could be potentially discriminatory and that some people may not wish to disclose whether they are of Aboriginal and Torres Strait Islander origin. ESC noted that there is a high prevalence of sexually transmitted infections throughout rural and remote locations and that people living in these regions are underserved by current testing modalities irrespective of Aboriginal and Torres Strait Islander origin. ESC further considered that any expansion of POC testing beyond the rural and remote setting (i.e. to metropolitan or urban settings) and/or removal of this restriction in the MBS item descriptor would necessitate the development of a new economic model as the benefits of POC testing would be different in urban compared with rural and remote settings.

ESC noted that the applicant proposed separate fees for a POC test to detect CT/NG (item XXXX) and TV (item ZZZZ) and considered that this was appropriate. ESC also noted the proposed item descriptors (item YYYY) for testing of CT/NG following previous infection. ESC considered that this item descriptor appeared redundant as the aim of retesting appears to be to identify any new

²¹ [RACGP - National guide to a preventive health assessment for Aboriginal and Torres Strait Islander people](#)

infection (not resolution of previous infection) and therefore it is not clinically relevant whether a test is a screening diagnostic test or a follow-up test.

ESC noted that the proposed fee for the POC testing (\$150 for CT/NG and \$115 for TV) was significantly higher than the MBS fee for standard laboratory testing. The proposed fee for POC testing was also significantly higher than the current MBS fee for other POC tests (for example items 73812 and 73826 [\$11.80] or 73839 [\$16.80] for quantification of glycated haemoglobin, the latter fee reflecting a Quality Assurance in Aboriginal Medical Services [QAAMS] Program item).

ESC noted the proposed fee was comprised primarily of operator time, consumables and training but excluded practitioner time and capital costs. ESC noted that the proposed item would be claimed in combination with a consultation item which is already subsidised. In addition, ESC noted that the capital equipment (the GeneXpert platform) has already been purchased at the majority of centres through other Commonwealth-funded programs. ESC also noted that the fee would likely be the same irrespective of number or types of swabs taken (as is the case for the current standard laboratory testing items).

ESC noted the policy paper queried whether the proposed MBS item descriptor should contain restrictions around the frequency of testing. ESC noted the public health benefits of regular and repeated testing and considered that frequency restrictions would likely be a barrier to this.

Regarding comparative safety, ESC noted the studies attributed no specific harms to POC testing for CT/NG and TV. ESC noted concerns that there could be a potential for increase in inappropriate treatment for patients with a positive POC test from asymptomatic NG (because they are treated before the antibiotic resistance profile of the NG strain is known), however considered that this outcome was not demonstrated in any dataset and the risk would be low. ESC therefore considered that the claim of non-inferior safety of POC testing compared to standard laboratory testing to be reasonable.

ESC noted the evidence on the accuracy and performance of the POC tests was deemed to be at a low risk of bias and relatively robust with up to 9 datasets. ESC noted the reliability and validity (i.e. sensitivity and specificity) of the POC testing had been previously accepted by the MSAC Executive.

ESC noted the applicant's claim that POC testing for CT/NG and TV will mean that test results are available in 60-90 minutes (as opposed to up to 2 weeks with standard laboratory testing). The applicant claimed that this would change clinical management with more timely curative treatment; less clinic visits; more timely treatment of contacts and increased treatment of infection sequelae (such as mild to moderate Pelvic Inflammatory Disease [PID]).

ESC noted that the evidence for change in patient management and processes was more limited; based on 4 to 8 studies (depending on test type) and all studies had a moderate risk of bias. ESC noted the evidence came from small studies with relatively narrow populations.

ESC noted that the evidence supporting change in patient outcomes was based on two studies (total n=1,095), both with moderate risks of bias. One study (Keizur, 2020)²² was a diagnostic before/after study conducted in two American cities. The other was the Australian Test, Treat and

²² Keizur EM, Goldbeck C, Vavala G, et al. Safety and Effectiveness of Same-Day Chlamydia trachomatis and Neisseria gonorrhoeae Screening and Treatment Among Gay, Bisexual, Transgender, and Homeless Youth in Los Angeles, California, and New Orleans, Louisiana. *Sex Transm Dis* 2020; **47**(1): 19-23.

Go (TTANGO) cluster-randomised controlled crossover trial²³ led by the applicant which had a highly relevant population. ESC noted that in the TTANGO study, there were substantial reductions in the time to test results and time to appropriate treatment, fewer clinic visits and more timely treatment of contacts with POC testing compared with standard laboratory testing. There were no significant differences reported in rates of infection at re-testing, and the majority of patients from both arms were uninfected at re-testing. ESC noted that the TTANGO study was not adequately powered or of long enough duration to determine longer-term outcomes such as maternal outcomes and there was an absence of preference-sensitive measures. ESC noted that further evidence from the expanded TTANGO trial (TTANGO 2, recently scaled up to TTANGO3) is expected but it is unclear when this might be available.

ESC noted that there were additional factors that were not presented in the applicant developed assessment report (ADAR) that could have been relevant. For example, the potential for POC testing increasing trust between patient and healthcare providers and possible motivation for healthcare workers in being able to provide a diagnostic service that results in immediate treatment. The cultural acceptability and individual preference for POCT testing compared with laboratory testing (i.e. through a sense of ownership of the process and results which may be motivational for self-management), ethical considerations and the potential to decrease the disparity of health outcomes related to sexually transmitted infections in Aboriginal and/or Torres Strait Islander Peoples (as per the ratified PICO) were not included as quantified outcomes. ESC noted that 95% of the services that were included in the TTANGO study stated that they wished to continue to offer POC testing and that there was considerable support from the healthcare workers in the study for POC testing.

ESC considered that POC testing had noninferior clinical effectiveness compared to standard laboratory testing for CT/NG and TV. ESC considered that POC testing had the potential to have superior clinical effectiveness but that the evidence was highly uncertain.

ESC noted the ADAR presented a cost-utility analysis that was based on reduced time to treatment with POC testing leading to a reduction in infection sequelae. ESC noted that the available evidence from the trials and the data underlying the health impacts in the economic model was limited. ESC noted that the model inputs were based on the TTANGO trial data that included only 16–29-year-old participants and that the model inputs were based on infection and sequelae rates pertaining to Aboriginal and Torres Strait Island people. ESC recalled the discussion around the MBS item descriptor and noted that if the prevalence of sexually transmitted infections in the eligible MBS population differs to the prevalence in the 16-29 year old population in the TTANGO trial and if this was applied in the economic model then the ICER may change.

ESC noted that the structure of the model was overly complex and a number of errors were identified during evaluation. The model assumed a 10-year time horizon with annual cycles. ESC noted that this further increased the complexity and challenges for interpreting model inputs as relatively short health events were transitioned to occur within annual cycles. While ESC considered shorter cycles would have been more straightforward, it did not consider that reducing the cycle length would change the economic estimates.

ESC noted the population modelled represented a cross section of people eligible for testing who present repeatedly over the 10-year time horizon, resulting in accrual of costs and consequences that are not reflective of a single test, but rather a series of testing episodes over ten years. This approach resulted in a complex microsimulation modelling that required large numbers of

²³ Guy RJ, Ward J, Causer LM, et al. Molecular point-of-care testing for chlamydia and gonorrhoea in Indigenous Australians attending remote primary health services (TTANGO): a cluster-randomised, controlled, crossover trial. *Lancet Infect Dis* 2018; **18**(10): 1117-26.

simulations to generate stability in the results. This was adjusted in the commentary, with a single episode of testing and cohort approach adopted. However, ESC noted the applicant's pre-ESC response that this was not appropriate as it excludes the probability of repeat testing and repeat infection which would be contrary to the guidelines.

ESC noted that the commentary sensitivity analyses demonstrated that the ICER was highly sensitive to a number of key drivers (with the Commentary base case ICER of \$20,453 per QALY gained increasing to \$161,085 per QALY gained in a multivariate sensitivity analysis, see Table 15). ESC noted from the pre-ESC response, the applicant had revised the ADAR model to correct some of the errors (but not all) that had been identified in the commentary and made some adjustments to variables based on the commentary sensitivity analyses. The pre-ESC response presented a revised ICER of \$37,185 per QALY gained. These changes included:

- amending the preterm birth rate 16.6 % in the treated arm (the pre-ESC response noted that 0% was incorrectly used in the treated arm in the original model)
- acceptance and incorporation of the Commentary proportion of women of 56.5% (67% in the original ADAR) who attended a clinic at least once in the TTANGO study
- correction of the rounding errors in the utilities associated with epididymitis
- reduction of the days of disutility in PID state from 12 to 10 days (reflecting that some patients with acute PID will be treated as outpatients rather than as inpatients)

However, ESC noted that no new sensitivity analyses were provided in the pre-ESC response and the updated ICER could not be validated by the Department²⁴.

ESC considered that it would be informative to have the commentary sensitivity analyses (as per Executive Summary table 15; ADAR plus in-line commentary table 35) re-conducted using the applicant's updated pre-ESC ICER to demonstrate how robust the updated results are to variations in key assumptions. ESC noted that the commentary sensitivity analysis regarding proportion of people who attend the clinic who are female (56.5%) had been accepted in the pre-ESC ICER. ESC considered that further exploration of this variable in the updated sensitivity analyses would still be informative to determine how sensitive the ICER is to changes in this proportion.

ESC considered that additional sensitivity analyses would also be informative. ESC noted that there was uncertainty regarding downstream utility values (particularly as up 50% of sexually transmitted infections are asymptomatic). ESC considered that exploration of the impact of changes to the range utility values (potentially testing the lower and upper bounds of any confidence intervals) used in the economic model (as opposed to a sensitivity analysis that accounts for rounding errors in utility values only) would be useful. ESC also noted that given the short-term follow-up of the key trial informing the model (3 months) that the 10-year time horizon of the model may be too long and that an additional sensitivity analysis using a 5-year time horizon would be informative.

ESC noted that one of the key drivers of the economic estimates was the inclusion of indirect costs (such as air evacuation costs and costs for locating and following up patients). ESC noted the applicant's pre-ESC response that stated that these costs are significant and borne by the services and so should be included. ESC considered it would still be beneficial to show MSAC the impact of including these costs. ESC considered that two scenario analyses should be conducted to explore the effect of these costs. One scenario (and set of sensitivity analyses) should be run with all indirect costs included and the second scenario (and set of sensitivity analyses) should be run with all indirect costs excluded.

²⁴ Note: sensitivity analyses were subsequently provided in the applicant's pre-MSAC response. See page 6 for further information.

ESC noted that the approach to estimating the uptake of POC testing and financials was not well described in the ADAR. ESC noted that the financial estimates assumed that all those who receive a POC test in the future would have received a standard laboratory test. ESC noted that it was assumed that the number of sites would grow from 45 to 108 (a 140% increase) and then a further 10% each year and the average number of people tested at each site was assumed to increase from 170 to 300 people per year. The source for these assumptions was not clear. ESC noted further concerns with the financial estimates that the follow-up costs were assumed to be 70% less with POC testing and that the scheduled fees were used (as opposed to the 85% rebate amount). ESC considered that providing MSAC with greater clarity around the assumptions used in the financial estimated would be informative for decision-making.

ESC noted that amendments made in the revised model presented in the pre-ESC response would potentially impact the financial estimates and these had not been updated. ESC considered that updated estimates accounting for the changes made to the ICER would be informative. The updated financial analyses should also include sensitivity analyses where key parameters (as per the economic model sensitivity analyses) are also varied to assess how robust the estimates are to various parameters (such as the proportion of women presenting to clinic and rates of preterm birth).

17. Applicant comments on MSAC's Public Summary Document

This rebate would contribute to reducing the substantial inequity of access to timely diagnostic results and treatment, and the subsequent reduction in poor health outcomes. The suggestion by MSAC to consider other funding models is not a sustainable solution and entrenches disempowerment. Aboriginal Health Organisations are largely reimbursed through Medicare and a rebate would ensure a sustainable funding model for the provision of STI POC testing to achieve the anticipated improvements in clinical and public health outcomes for First Nations people. Limitation of the rebate to only health services located in MM6-7 would continue to leave a large proportion of the target population without access to timely STI diagnosis and treatment as non-geographic barriers would remain unaddressed. Our analysis accurately reflects the health system costs including higher staff costs in regional and remote Australia, use of staff time to locate patients and evacuations to regional centres when additional care is required as standard practice. We reiterate the measurement of all short and long term clinically plausible outcomes (including pelvic inflammatory disease, premature rupture of membranes, pre-term births, and low birth weight babies) is not feasible in one trial. We used the best available evidence (1 locally relevant RCT; 36 observational studies) to inform the cost-effectiveness analysis presented in the application. Extensive community consultation has underpinned the successful implementation of STI POC testing in rural and remote primary health services for the past 7 years to ensure the cultural acceptability of this intervention. This includes peak Aboriginal Health organisations, their member health services, POC testing Leaders group (includes clinical staff responsible for POCT such as Aboriginal Health Workers and Practitioners), and patients. The advice to not recommend the rebate for STI POC testing in rural and remote primary health services is highly disappointing.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)