Chapter

A Practical Guide to Establishing a Molecular-Based Point-of-Care Testing Network for Chlamydia

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Abstract

This chapter provides a 'how to guide' to set up and manage a molecular-based point-of-care (POC) testing network to detect *Chlamydia trachomatis* (Chlamydia) in populations experiencing high burden of infection and sequelae as well as barriers to accessing routine laboratory services. The chapter outlines the experience of the Australian-based *Test, Treat and Go* (TTANGO) program which, to the authors' knowledge, represents the largest decentralised POC testing network for chlamydia (as well as gonorrhoea and trichomoniasis) in the primary care sector globally. The chapter provides an overview of the program's evolution from a randomised controlled trial through implementation, translation, and scale-up phases to a now national routine program with associated testing rebates. The chapter will examine the governance, training and quality management, and connectivity processes that underpin the TTANGO network and describe the clinical, cultural, operational and economic effectiveness of the network. Collectively, these elements provide a template for translation to low- and middle-income countries (LMIC) where *Chlamydia trachomatis* remains a significant contemporary health problem.

Keywords: point-of-care testing, primary care, chlamydia, sexually transmitted infections, decentralised

1. Introduction

1.1 Defining the clinical problem

Chlamydia is a very common sexually transmitted infection (STI) that is caused by the bacterium *Chlamydia trachomatis* (CT) and transmitted by unprotected sexual activity. Chlamydia remains a major contemporary health problem globally, with more than 128.5 million new cases of this infection being reported in adults aged between 15 and 49 years during 2020 [1, 2]. Collectively, chlamydia, as well as other related pathogens *Neisseria gonorrhoeae* (gonorrhoea, NG), *Trichomonas vaginalis*

(trichomoniasis, TV), and *Treponema pallidum* (syphilis, TP), accounted for more than one million new infections every day during 2020 [3]. Left untreated or undetected, chlamydia can have serious consequences, mainly in women, with pelvic inflammatory disease (PID) as well as tubal infertility and ectopic pregnancy being critical examples of onward sequelae [4, 5].

In Australia, young First Nations people experience among the highest rates of chlamydia (as well as gonorrhoea and trichomoniasis) in the world, with one third of all First Nations adults aged between 16 and 29 years testing positive for one or more of these infections during the period 2009–2011 [6]. The magnitude of the problem is exacerbated by a range of complex and interwoven social, cultural, and economic determinants of health and geographic factors including high mobility of remote populations; as well as lack of access to culturally appropriate health services, including pathology testing.

Fortunately, confirmed cases of chlamydia are readily treatable and curable, with azithromycin or doxycycline being the drugs of choice most widely used for the treatment of uncomplicated genital chlamydia infections [7].

1.2 Diagnostic capacity and the role of POC testing

In many LMIC, syndromic management is the first line of treatment for chlamydia and related infections, but this approach can lead to missed diagnoses if patients are asymptomatic or overtreatment (potentially with the wrong antibiotic) when the causative agent is not identified.

Clearly, the need for the early detection of chlamydia through regular pathology testing is the key to accurately identifying both asymptomatic and symptomatic infections and assisting in breaking the cycle of onward (or vertical) transmission. While access to pathology laboratories in urban settings is generally readily available, the use of laboratory testing for diagnosis in rural and remote regions is more problematic, and (from the Australian experience) uptake of testing has been relatively low [8]. Also, the turnaround time for laboratory results on samples collected from rural and remote communities can often be between 1 and 2 weeks, but importantly, the time for patient follow-up and treatment can be even longer, up to several weeks [9].

Molecular-based point-of-care (POC) pathology testing for STIs such as chlamydia has the potential to be a 'game changer', particularly in the rural and remote context, as the test can be conducted during the patient consultation with the result available within a significantly shorter time frame (i.e., within hours) and facilitate more rapid initiation of curative treatment and partner notification.

Chronologically, POC testing was seeded in the global primary care setting during the late 1990s/early 2000s through chronic disease applications (notably diabetes and renal and heart disease) and then in acute care settings (for tests such as electrolytes, blood gases, and cardiac troponin) [10]. Historically, the uptake of POC testing for infectious disease up to the early-2010s was limited to immunochromatographic lateral flow technologies which suffered from poor analytical performance, notably poor sensitivity [7]. However, the advent of molecular-based technologies (namely, nucleic acid amplification tests which detect DNA or RNA from infectious agents) has completely transformed this field through substantial improvements in simplified test process, closed cartridge systems and diagnostic accuracy, with development and application of a wide test menu for POC testing for infectious disease now outstripping those of chronic and acute modalities.

However, while the market for POC testing for infectious disease has grown exponentially in combination with an increased demand for public health research impact, there is a critical need to consider how to systematically and sustainably integrate POC testing in this field. Importantly, foundational medical science implementation and scale-up strategies that prioritise patient safety and optimise diagnostic accuracy are essential in enabling the desired clinical and public health benefits from such disruptive technology [10, 11].

This chapter draws on the Australian experience and lessons learned from field application of POC testing across chronic, acute, and infectious diseases over the past 25 years to provide a 'how to guide' to set up and manage a molecular-based point-of-care (POC) testing network to detect *Chlamydia trachomatis* (Chlamydia) infection in at-risk rural, remote, and/or disadvantaged communities [10–12].

2. An optimised program logic framework for the implementation and management of a POC testing network: From concept to public health impact

The key to the development of sustainable and impactful POC testing is a systematic and stepwise program logic model to its integration in primary care. The steps involved in this process are outlined in **Figure 1**.

Firstly, there must be an identified and defined clinical need to justify the introduction and establishment of a POC testing service. A clinical needs assessment should be undertaken in consultation with appropriate multidisciplinary clinical teams and tailored to meet local, jurisdictional, or national needs. The proposed POC testing solution will be dependent on factors such as population size, age structure, ethnicity and culture, geographic location and accessibility or otherwise to a pathology laboratory service, and availability and expertise of local health service staff [13].

There must be universal acceptance and recognition from stakeholders in their decision to adopt this technology that POC testing is a medical science discipline. The successful translation of POC testing from the laboratory to the field is dependent on adherence to and adaptation of core laboratory principles and standard good

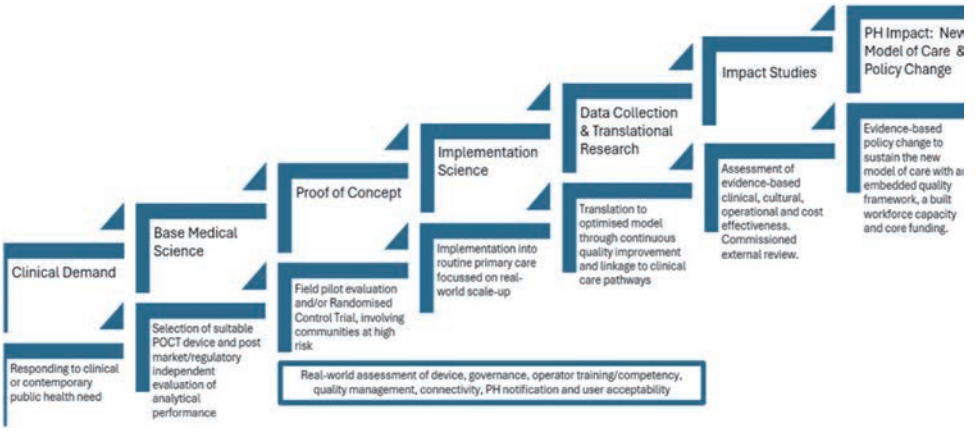

Figure 1.
The systematic and stepwise building of a sustainable and impactful POC testing model © Matthews S and Shephard M, 2024.

laboratory practices (notably relating to device selection, training of non-laboratory health professionals, analytical method and surveillance of analytical quality, and minimisation of preanalytical and postanalytical sources of error) which mitigate patient harm.

In today's global market, there are often multiple devices available that can potentially perform the required POC tests. It is important to critically review the manufacturer's claims, existing regulatory approvals, independent published literature available on these devices or, as a minimum, consult with professional colleagues, notably pathologists and medical scientists, who have had experience with result interpretation and safe practice with the device(s) concerned. As a guiding principle, a POC testing device should be able to achieve at least equivalent analytical performance for the required tests compared to the corresponding laboratory device when used for the same clinical purpose.

Critically, the performance of devices must be verified independently in a 'proof of concept' phase; this applies not only to an assessment of the analytical quality of the device but also to non-analytical factors such as ease of specimen collection; user friendliness/stakeholder acceptability; complexity of use, including the number of manual steps involved; physical footprint within the health service (including ancillary needs for storage of testing reagents and requirements for AC or battery power); environmental friendliness and real-time connectivity (particularly in the face of poor or non-existent internet availability); and a cost-benefit analysis of introducing the device (investigating the balance between affordability, accessibility, and diagnostic accuracy, as well as covering both fixed and variable costs) [14].

Independent evaluation of the device should be undertaken either at/with the support of the local pathology laboratory and then, ideally, at the intended site of field use by the (trained) operators who would be conducting tests in routine practice at their service. Field evaluation can occur, for example, as a pilot study or as part of a randomised controlled trial (across a small number of targeted sites that are known to service communities with a high burden of disease) to allow comparison to the usual standard of care.

The next stepwise phases involve broader implementation of the program to reach more targeted sites with high disease prevalence and to systematically scale up the program to reach the point where POC testing becomes part of routine practice.

In these implementation/translational phases, the following core regulatory elements should be embedded into the system:

- Establishing appropriate governance of the network, including both clinical, scientific, and cultural governance
- Training of POC testing operators including initial and ongoing assessment of their competency
- Continuous surveillance of analytical quality, through application of standard laboratory practices such as quality control (QC) and external quality assurance (EQA) testing
- Intensive scientific and technical support for trained operators (including device troubleshooting and corrective actions, as well as logistic support for delivery of consumables and quality testing materials)

- Connectivity (the electronic capture of patient results and their transference to a patient medical record, to public health authorities for surveillance and to the program for monitoring implementation).

All these elements should be subjected to stakeholder evaluation, internal quality auditing processes, and actioning of opportunities for process improvement to ensure continuous quality improvement (CQI) practices and optimisation of the routine model.

Ideally, at this point, POC testing should also be integrated into relevant clinical pathways for patient care and management. Adherence to jurisdictional or national guidelines, requirements, or standards for POC testing should also be followed.

It should be noted that there are opportunities for stakeholder engagement, co-design and both quantitative and qualitative research to be conducted along the spectrum of activities described thus far, with research findings relating to the analytical performance in the field and laboratory, as well as stakeholder acceptability being examples of key questions to be answered at this point.

However, once the primary care model is fully operational and scaled, then it is possible to develop specific research activities to assess the clinical, cultural, operational, and economic impacts of introducing this POC testing service for its intended purpose [15]. For infectious diseases, clinical benefits usually focus on measures such as increased testing uptake, earlier detection of disease, reduction in time to initiate treatment, and days of infections averted. Cultural benefits are important when the work supports rural and remote indigenous health services and communities; here, patient satisfaction with the process of POC testing and reduction in loss to follow-up are key outcome measures. Operational benefits focusing on POC testing operator and medical practitioner satisfaction are important to assess, with the increased sense of responsibility and empowerment for operators and immediacy of clinical decision making for doctors being important considerations. Until the past decade, cost effectiveness had not been researched well in POC testing studies, but now, this measure has become increasingly important as governments seek an evidence-base of measurable cost benefits in determining whether to fund POC testing activities and their associated return on investment [16, 17].

Finally, when all steps have been scientifically and robustly implemented, the larger-scale public health impacts of the POC testing model may be realised; these may relate to the new model of care bringing about evidence-based policy change; building a large and resilient workforce capacity; or, in the specific case of infectious diseases, averting significant numbers of infectious days for a jurisdiction or nation, complementing national diagnostic testing frameworks (as seen in COVID-19) and providing an evidence-base for inclusion within pathology testing rebating schemes (such as described below).

Timewise, the evolution of a POC testing model from a medical science concept to broad impact may take a decade or more, but with all elements systematically implemented, the model is most likely to be well accepted, deliver high analytical quality, and minimise patient risk and thus be sustainable.

3. Application of this stepwise template to POC testing for chlamydia: The Australian experience

In Australia, the Flinders University International Centre for Point-of-Care Testing (ICPOCT) and the Kirby Institute, University of New South Wales, jointly manage

several POC testing networks for infectious diseases on behalf of the Australian Government's Department of Health and Aged Care [11]. The longest standing network, now of more than a decade's duration, is the *Test, Treat ANd GO* (TTANGO) program which, to our knowledge, represents the largest decentralised molecular-based POC testing network for chlamydia (as well as gonorrhoea and trichomoniasis) in the primary care sector globally.

Following the stepwise template outlined above, we will now describe the evolution of the TTANGO network from concept to public health impact.

3.1 Responding to clinical need

The clinical need for a POC testing program to detect chlamydia (and gonorrhoea) resulted from a disproportionately high burden of these STIs in young adults living in remote First Nations communities and a call to action from clinicians. The aim of introducing POC testing was to detect new cases of these infections, thereby enabling faster initiation of curative treatment, reducing the risk of sequelae and onward transmission to partners, and decreasing overall disease prevalence in the community.

3.2 Evaluation of new molecular-based POC testing technology

The GeneXpert® testing system (Cepheid, USA) was first introduced into Australia in 2013. The GeneXpert measures chlamydia and gonorrhoea on a single test cartridge using molecular based, nucleic acid amplification [NAAT] technology – detecting a single DNA target for chlamydia and dual DNA targets (NG2 and NG4) for gonorrhoea, and with a result turnaround time of 90 minutes. The GeneXpert system comprises a laptop required to drive the testing process, a modular GeneXpert device (four-module being the preferred configuration for TTANGO services), and closed testing cartridges for the simultaneous dual measurement of CT and NG.

The device underwent two initial evaluations—one in the laboratory setting and one in the primary care environment [18, 19].

The laboratory evaluation conducted GeneXpert POC tests on 372 characterised CT (or NG) bacterial strains and concluded the Xpert CT/NG testing cartridge was highly sensitive and specific for these infectious agents [18].

Just under 2500 (2486) self-collected urine or lower vaginal swabs were tested by both the GeneXpert POC test on-site in the field and parallel NAAT-based laboratory tests. The overall concordance for chlamydia was 99.4% (95% confidence intervals [CI] 99.1–99.7%) with a positive concordance of 98.6% (CI 95.9–99.7%) and negative concordance of 99.5% (CI 99.1–99.8%) (POC testing for NG demonstrated similar overall concordance of 99.9% compared to parallel laboratory testing) [19].

3.3 Proof of concept: The TTANGO trial (2013–2015)

The field evaluation of the CT/NG POC test was conducted as part of a cluster-randomised crossover trial called the TTANGO Trial. The TTANGO Trial, undertaken from 2013 to 2015, represented the first phase in the evolution of the (now national) TTANGO Program and the world-first use of molecular-based POC technology for STI in a primary care setting (outside the laboratory environment). The three-year TTANGO Trial was undertaken in 12 remote Aboriginal health services, which were spread across three Australian states (Western Australia, South Australia and

Queensland) and encompassed outer regional, remote or very remote locations. These services all met the following inclusion criteria: their health service conducted more than 150 CT/NG tests annually on young adults aged between 16 and 29 years and had a positivity rate for either CT or NG of 10% of higher. Services were randomised equally to either standard care with laboratory testing for 12 months (control group) followed by the additional availability of POC testing for the next 12 months (intervention group) or the reverse modality [19].

In addition to the excellent analytical performance observed during the trial (as described above), clinical effectiveness (time-to-treat) studies identified that 60% of the 455 patients who tested positive for CT/NG in the intervention group were treated in ≤2 days compared to 30% of the 405 patients who were diagnosed as positive using laboratory testing; while 76% of those patients in the intervention group were treated in ≤7 days compared to 47% when laboratory testing was used for diagnosis [20].

POC testing operators trained during the trial participated in in-depth interviews and questionnaires to assess their level of acceptability with the new technology. Overall, they reported the GeneXpert was user-friendly and useful in the primary care setting, while POC testing had improved STI management through more timely and targeted treatment, earlier commencement of partner notification and reduced time and effort associated with patient recall [7, 21]. From the patient perspective, the perceived usefulness of the POC technology centred on the following aspects: POC testing almost entirely eliminated the need for patient recall associated with previous laboratory-based testing; POC testing reduced the time between sample collection and delivery of treatment, an important consideration when acknowledging the significant population mobility in remote communities; and POC testing heightened awareness of STIs among community members as well as creating an opportunity for broader health education (particularly while the patient was waiting in the clinic for their test result) [21].

3.4 Implementation and scale-up phase (TTANGO2 and TTANGO3) (2016–2024)

Following the success of the randomised controlled trial, the Australian Government funded the scale-up of molecular-based STI POC testing through (i) a translational research program (called TTANGO2) which operated from 2016 to 2019 and then (ii) the routine implementation of the program (TTANGO3) from 2020 to 2024. As part of the scale-up process, molecular-based POC testing for TV on the GeneXpert was added to the TTANGO2 STI panel in April 2018, following regulatory approval of this test by the Australian Therapeutic Goods Administration (TGA) and independent evaluation of the test performance by the TTANGO study organisers [22].

Scale-up has continued to the present day, with the number of enrolled health services increasing to 31 by 2019, 58 by 2022, and 76, as of August 2024, with the TTANGO program now having a reach across all mainland Australian states and the Northern Territory (**Figures 2** and **3**). The jurisdictional breakdown of enrolled services is as follows: Western Australia 25, Northern Territory 17, Queensland 15, South Australia 10, New South Wales 6, and Victoria 3.

The guidelines for inclusion as a participating health service in the current program include being in a community classified as regional, remote or very remote, where the community prevalence of two STIs (CT, NG, or TV) in 15–29-year-olds is 10% or higher, and where the health service must service predominantly Aboriginal or Torres Strait Islander people (>50%).

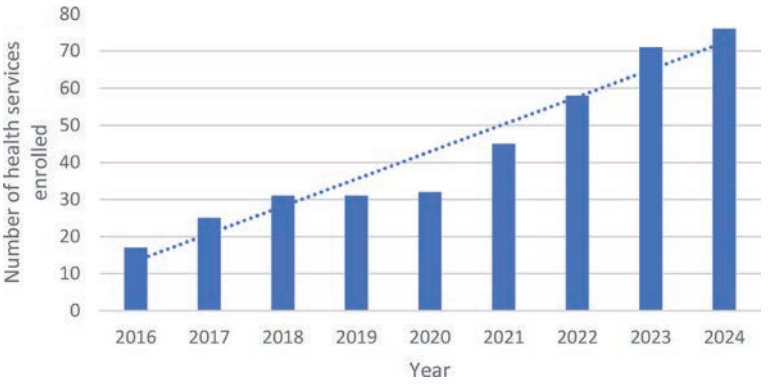

Figure 2.
Cumulative increase in total enrolments within TTANGO (2016–2024).

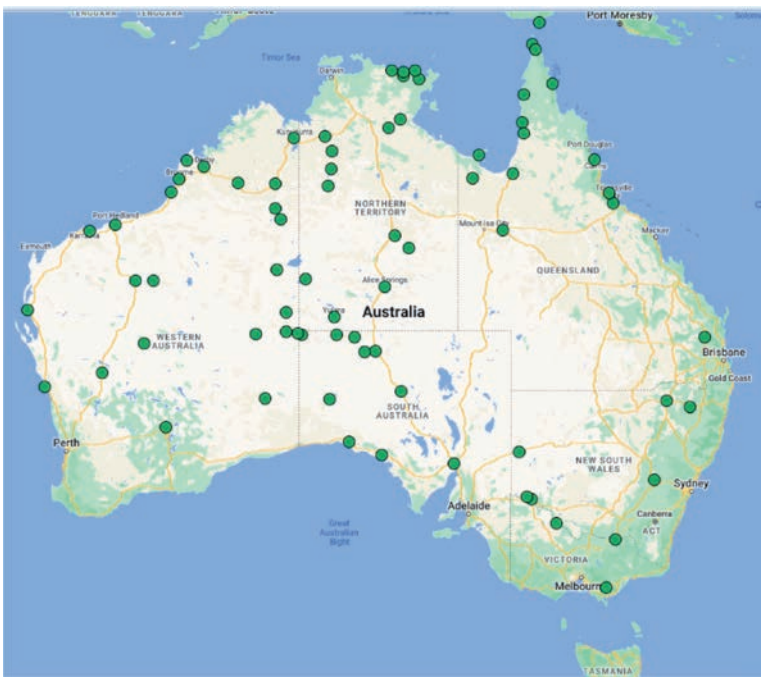

Figure 3.
Location of services enrolled in TTANGO Program, August 2024.

Core elements embedded in the routine operational model include the following:

3.4.1 Governance

During TTANGO2, the governance structure included an investigator group, an executive (management) committee, and an operational group. The executive (management) committee comprised senior TTANGO researchers from the lead academic institutions as well as a representative from the state/territory governments and the jurisdictional First Nations health bodies involved. The management committee oversaw the TTANGO operational team who were responsible for the day-to-day

management, delivery and logistics of the program and who collaborated with a range of partners including those from industry and suppliers of quality materials. As a complementary CQI measure, a TTANGO Aboriginal and Torres Strait Islander Reference Group (comprising at least one Aboriginal and/or Torres Strait Islander Health Worker/Practitioner from each State/Territory who was also an active POC testing operator in the program) was established in 2018. The Reference Group advised on cultural safety (notably in relation to training resource development and promotional resources) and acted as cultural ambassadors for the program; this latter group was suspended during the COVID-19 pandemic but has resumed operation in 2024 known as the First Nations POC Testing Leaders Group (**Figure 4**).

3.4.2 Training and competency assessment of POC testing operators

A series of flexible training resources were developed for the program including a hard copy manual, laminated poster sets comprising step-by-step guides for the conduct of patient and quality testing practices, instructional videos, and access to an on-line version of these resources via a password-protected area on the program's website (www.ttango.com.au).

In terms of training delivery, options include on-site face-to-face training (at both individual services and regional training sessions) as well as web-based tele- or video-conference platforms (including GoToMeeting, TEAMS, and Webex—desktop sharing programs that allow users to interact with trainers online in real-time via the internet). Since early 2024, a new Learning Management System (LMS) has been introduced as an alternative to in-person or videoconference training which continue to be available to health services. The LMS is an online (Moodle-based) platform where operators can undertake self-guided theoretical training and competency for the TTANGO program, as well as for other POC testing networks for infectious diseases managed by ICPOCT/Kirby (see later); LMS training is facilitated by a series of self-guided modules which include disease-specific modules applicable to individual programs such as TTANGO as well as generic POC testing modules which apply to the broader Flinders ICPOCT/Kirby suite of infectious disease POC testing networks and quality systems.

No matter which mode of training delivery is used, all GeneXpert operators are required to undertake both theoretical and practical competency assessments; the

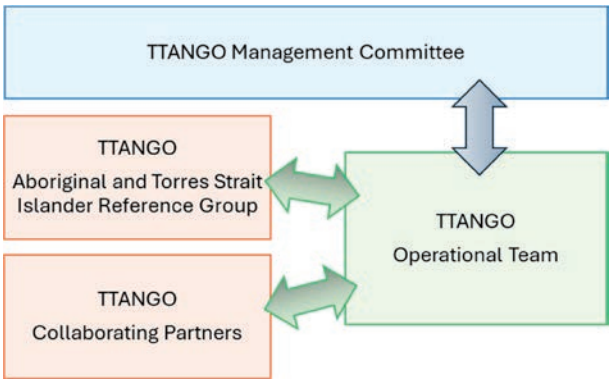

Figure 4.
Governance structure for the TTANGO routine operational program.

former involves completing a multiple-choice written assessment while the latter is assessed by performing practical tests on the GeneXpert using samples with a known infection load (previously specifically manufactured training samples, now QC samples). Unique operator logins used for GeneXpert testing and quality test result submission, and certificates of competency are issued for a period of 1 year to operators who successfully complete both the theoretical and practical components. Following expiry, operators must undergo a competency renewal process to be able to continue patient testing.

3.4.3 Quality management

To monitor the analytical quality of the GeneXpert devices in TTANGO, each health service is required to perform regular testing of quality control (QC) and external quality assurance (EQA) samples.

From 2016 to 2022, services tested one CT/NG positive QC swab sample (and one TV positive QC swab sample post 2018) each month on their GeneXpert. These samples were made in-house for the program [23]. Since March 2023, a commercial supplier (Microbix Biosystems Inc) has been contracted to provide both a positive and negative quality control swab material for the program. Operators enter their QC testing results online through the participant only area on the TTANGO website; here, immediate feedback on the accuracy of the result is available using a colour-coded action system which directs operators to appropriate QC actioning strategies (for discordant QC or test errors).

Health services are required to complete External Quality Assurance (EQA) testing using dry swab samples of varying infectious loads prepared specifically for the TTANGO program by the National Serology Reference Laboratory (NRL). From 2016 to 2020, there were two testing events comprising four swabs per event. From 2021 onwards, there were three testing events with five swabs to be tested per event. Each EQA swab has an expected result, which is unknown to the operator at the time of testing. Results are entered online via the TTANGO website and the TTANGO scientific team then prepare site-specific EQA reports which are issued to the operators who conducted the testing as well as health service managers/supervisors. Each report demonstrates how the services' GeneXpert results compare to the expected results and to other participating health services in a de-identified manner.

It should be noted that parallel laboratory testing has continued to be performed on each patient sample tested at the POC on the GeneXpert which has provided a further means of monitoring analytical quality and patient safety while also maintaining mandatory public health notifications for chlamydia (and gonorrhoea). Parallel laboratory testing will be phased out in November 2024 with the establishment of alternative notification pathways and changes to public health policy to recognise POC testing in the case definition for mandatory notifications of chlamydia (and gonorrhoea) cases.

3.4.4 Scientific and technical support

The TTANGO operational team provides a scientific help desk which operates during business hours (9 am to 5 pm) during the working week. The help desk offers support for issues relating to troubleshooting, technical issues, maintenance and logistics, as well as interpretation of QC results and EQA reports.

3.4.5 Connectivity

A tailored connectivity system was built for the TTANGO program to capture digital POC test results for CT/NG and TV electronically and deliver them to a range of end users for the purposes of clinical management; surveillance of analytical quality; program implementation; and public health surveillance through the mandatory notification of positive CT (and NG) results which are notifiable diseases within Australia. The notification process also extends to TV, which is a notifiable disease in the Northern Territory [24]. The connectivity system represented the first of its type in Australia that was established independent of laboratory pathology providers to support POC testing for infectious disease in remote primary health services.

3.5 Key findings and assessment of evidence-based outcomes

3.5.1 Uptake of POC testing (2016-present)

During the 7-year period between 2016 and 2022, 30,160 CT/NG (and 15,993 TV) POC tests were performed in the TTANGO Program (total 46,153 tests) [25]. The statistically significant upward trend in testing numbers observed during the first 4 years of the program was dampened during the subsequent period of April 2020 to December 2022 due to the influence of the COVID-19 pandemic when health professional resources were diverted away from mainstream care activities. As of August 2024, the total number of STI POC tests performed has now exceeded 55,000. Positivity rates for CT (and NG and TV) during the 2022–2024 period were approximately 10% (and 9 and 8.5%) respectively.

3.5.2 Training and competency assessment

From January 2016 to June 2024, 1243 health professionals attended a TTANGO GeneXpert training session; a total of 803 (56%) received face-to-face training and 402 (32%) attended training remotely via web-based online platforms. Face-to-face training was the main form of training delivery prior to the COVID-19 pandemic, while travel restrictions during the pandemic saw a shift towards online platforms post 2022 (**Figure 5**). Since the recent introduction of the LMS training option in 2024, 38 new operators have been trained using this modality.

Of the 1243 who undertook training, 1002 (81%) successfully completed the new operator competency assessment process.

From January 2016 to June 2024, a total of 1294 operator competencies were completed, comprising new operators (n = 1002 [77%]) and operators renewing their competency (n = 292 [23%]).

Nurses continue to be the main health professional group trained in TTANGO, representing 72% (719/1002) of new operators trained, while Aboriginal Health Workers/Practitioners made up 21% (206/1002) of the new operator pool. A breakdown of new operator competencies by profession and year is shown in **Figure 6**.

3.5.3 Analytical quality

From 2016 to 2022, the concordance between GeneXpert POC patient testing and parallel laboratory NAAT testing was 99.0% (4071/4111) for CT (and 99.3% for NG and 98.9% for TV) [25]. Among the very low number of discordant results, there was

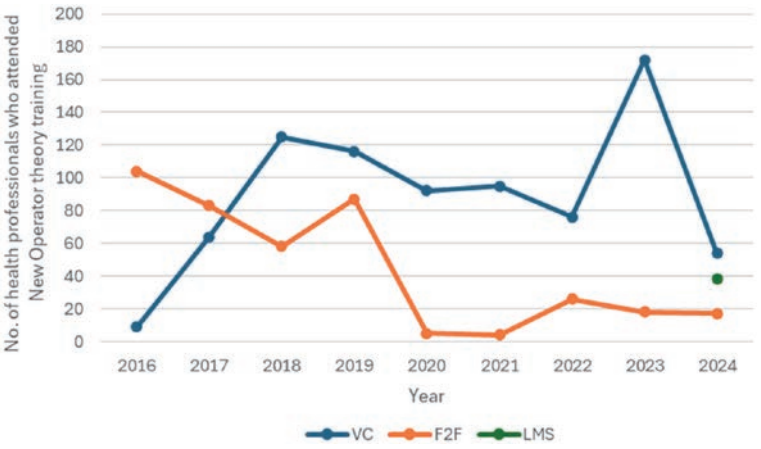

Figure 5.
New operator training attendance, by modality (Jan 2016–June 2024).

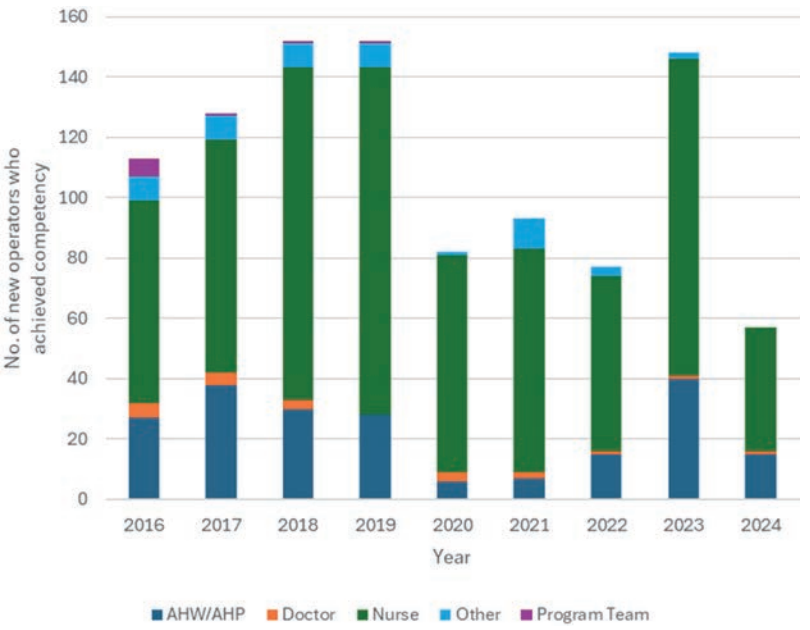

Figure 6.
New operator competency certifications, split by profession and year.

no specific pattern associated with either program sites or year of testing. The number of unsuccessful CT/NG tests (subcategorised as 'invalid', 'error', or 'no result') on the GeneXpert was 3.1% (which fell to 1.8% when samples were available for retesting).

Figure 7 summarises the results of QC testing conducted since the introduction of the commercial Microbix QC product in April 2023. In total, just over 1700 QC tests for CT were performed in the 12-month period from April 2023 to April 2024. Overall concordance with the expected result on just over 1600 valid QC tests was 97.0% (1558/1606), with concordance for the positive QC being 97.4% (795/816) and concordance for the negative QC 96.6% (763/790). The majority of the discordant

results were attributed to transcription errors in reporting of results, which triggered retraining of operators. Rates of unsuccessful QC tests for CT were less than 6% (102/1708), most of which were due to an 'invalid' test result being reported (see footnote to **Figure 7**).

Table 1 summarises the results of EQA testing across the most recent three testing cycles conducted during 2023. There were 15 EQA samples tested, six that were positive for CT with varying infectious loads and nine negative samples for CT. In total, 571 (560 + 11) tests were performed during this one-year period. The overall concordance with the expected EQA result on the 560 valid tests was 97.3% (553/560), with concordance for the positive EQA samples being 96.9% (222/229) and concordance for the negative EQA 97.2% (322/331). Rates of unsuccessful QC tests for CT were less than 3% (11/571).

3.5.4 Clinical effectiveness

Consistent with the findings of the original TTANGO Trial, clinical effectiveness studies conducted during TTANGO from 2016 to 2019 showed that patients testing positive for CT and/or NG by POC testing were treated more rapidly than those undergoing laboratory testing [25]. The median time to treat following a positive CT and/or NG POC test was 1 day (interquartile range [IQR] 0–3) compared to 11 days for a positive laboratory test (IQR 0–65). A greater proportion of patients testing positive in the intervention period were treated compared to the control period across all time periods (≤2 days 37 versus 22%; and ≤ 7 days 48 versus 30%, respectively). Based on this difference in median time to treat, study researchers estimated that POC testing for CT (and NG and TV) averted 4930 (and 5620 and 7075) infectious days, during this four-year period [25].

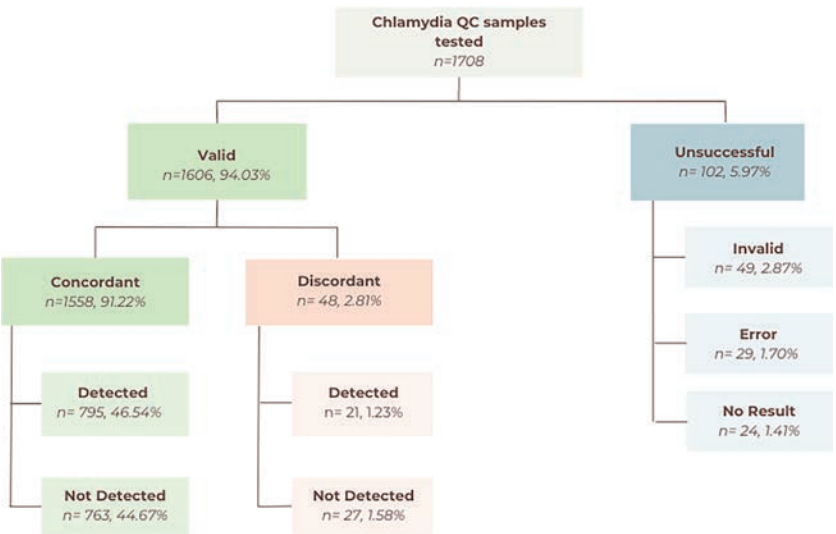

Figure 7.
QC testing performed in TTANGO post the introduction of dual testing samples since April 2023. Note: 'Invalid' tests can occur due to a multitude of operator, cartridge, and device-related issues, while 'error' and 'no result' usually reflect device-related or power-related issues.

Survey ID	Sample ID	Expected result	Submitted results		
			Not detected *%(n)*	**Detected** *%(n)*	**Unsuccessful** *%(n)*
Survey 1 2023-04-21	Sample A	Detected	*2.56% (1)*	*92.31% (36)*	*5.13% (2) [no result]*
	Sample B	Not detected	*94.87% (37)*	*5.13% (2)*	*0.0% (0)*
	Sample C	Not detected	*94.87% (37)*	*2.56% (1)*	*2.56% (1) [no result]*
	Sample D	Detected	*12.63% (1)*	*60.66% (37)*	*0.0% (0)*
	Sample E	Not detected	*89.47% (34)*	*5.26% (2)*	*5.26% (2) [no result]*
Survey 2 2023-07-19	Sample A	Detected	*0.0% (0)*	*100% (34)*	*0.0% (0)*
	Sample B	Not detected	*100% (35)*	*0.0% (0)*	*0.0% (0)*
	Sample C	Not detected	*100% (35)*	*0.0% (0)*	*0.0% (0)*
	Sample D	Not detected	*85.71% (30)*	*8.57% (3)*	*5.71% (2) [no result]*
	Sample E	Not detected	*100% (35)*	*0.0% (0)*	*0.0% (0)*
Survey 3 2023-10-18	Sample A	Not detected	*97.56% (40)*	*2.44% (1)*	*0.0% (0)*
	Sample B	Detected	*2.44% (1)*	*95.12% (39)*	*2.44% (1) [invalid]*
	Sample C	Detected	*4.88% (2)*	*92.68% (38)*	*2.44% (1) [invalid]*
	Sample D	Not detected	*97.56% (40)*	*0.0% (0)*	*2.44% (1) [invalid]*
	Sample E	Detected	*4.88% (2)*	*92.68% (38)*	*2.44% (1) [invalid]*

Boxes highlighted in green indicate the percentage (%) and number (n) of results which were concordant with the expected QA results; boxes in red indicate the percentage (%) and number (n) of results which were discordant with the expected QA result; boxes in yellow indicate the percentage (%) and number of results that were unsuccessful.

Table 1.
Summary of results from 3 EQA testing cycles during 2023.

3.5.5 Operational effectiveness

A follow-up acceptability study was conducted during the implementation phase of TTANGO2 to explore the facilitators and barriers to enable the optimised scale-up of STI POC testing in the remote First Nations sector [26]. In-depth interviews were conducted with 15 healthcare workers (nurses and Aboriginal Health Workers) and five managers from seven health services with a spread of geographic remoteness and varying STI POC testing rates. Acceptability of STI POC in TTANGO2 was high, due mainly to the self-efficacy (confidence and competence in the ability to perform the test and implement STI POC testing readily) and perceived effectiveness of the technology (the extent to which POC testing was perceived as likely to achieve its intended purpose/the effectiveness of the STI POC testing pathway versus laboratory testing and standard STI test-and-treat pathways). Patient reach (including strategies for patient engagement) was also considered an enabler of POC testing scale-up.

The main barrier to POC testing implementation was the high rate of turnover among staff working in the remote setting [26], which is an ongoing issue within remote health in Australia, in general. To try and increase the uptake of POC testing operator training, the TTANGO program has recently implemented an online learning platform to make the training more accessible to health service staff, particularly those on short-term contracts. The program team are also investigating alternative workforce models, including the possibility of training non-clinical staff to conduct

POC testing; this could include staff local to the community providing a more stable operator pool.

3.5.6 Cost effectiveness

A recent study evaluated the cost-effectiveness of using molecular POC testing for chlamydia, gonorrhoea and trichomoniasis compared to standard laboratory testing. Using a decision analytic model comparing the costs (mean cost per person tested) and outcomes (quality adjusted life year gain [QALY]) over a 10-year time horizon, the study found POC testing for these three infections was likely to be cost-effective in remote communities. The main drivers of reduced costs for molecular POC testing compared to laboratory testing were decreased staff time required for follow-up of patients for treatment and decreased incidence of hospitalisations for acute PID and other sequelae including ectopic pregnancy, as well as decreased incidence of preterm births and low birth weight babies. The one-way sensitivity analysis showed that the variables most likely to affect the incremental cost effectiveness ratio were the prevalence of STIs, the cost of the POC test, and health care attendance of women as a proportion of all attendees. In all sensitivity analyses POC testing remained either less costly or cost effective compared to laboratory testing and was under the threshold for public funding in Australia [27, 28].

4. Broad public health impact of the TTANGO STI POC testing program

The range of evidence-based outcome benefits demonstrated in TTANGO (reported above) has now led to broader public health impacts as well as policy change at the national government level.

During the recent global COVID-19 pandemic, the Australian Government invited the Kirby Institute and Flinders ICPOCT to develop a POC testing network to deliver molecular-based POC testing for SARS-CoV-2 using the GeneXpert in the most remote and vulnerable First Nations communities across the country; this so-named Aboriginal and Torres Strait Islander COVID-19 POC Testing network literally serviced those communities that were outside the reach of both urban and regional Australian laboratories. In setting up this emergency response network in early 2020, we were able to leverage the existing TTANGO program which already had established training, quality, and connectivity systems in place as well as a significant work-ready and skilled workforce who were competent in performing GeneXpert tests. The (then) 35 TTANGO services formed the first intake of sites in the COVID-19 network, which was supplemented by the addition of more than 60 further services that were provided with GeneXpert devices by the Australian Government. The Aboriginal and Torres Strait Islander COVID-19 POC Testing Program made a major contribution to Australia's public health response to the pandemic, averting between 23,000 and 122,000 SARS-Cov-2 infections and saving the Australian healthcare system between $337 Million and $1.8 Billion in health costs [11, 17, 29, 30].

In June 2022, the Aboriginal and Torres Strait Islander COVID-19 POC Testing Program transitioned to a new multiplex respiratory test panel which enabled SARS-CoV-2 as well as influenza A, influenza B, and respiratory syncytial virus (RSV) POC tests to be performed on a single cartridge. In early 2024, the TTANGO STI and Respiratory Infections networks merged to form the national First Nations Molecular POC Testing Program.

In its federal budget in May 2024, the Australian Government Department of Health and Aged Care announced a new Medicare rebate item for STI POC testing undertaken by remote and very remote health services (Modified Monash Model MM6 and MM7 [31]) in the First Nations Molecular POC Testing Program. The rebate, to commence in November 2024, includes funding to not only cover the cost of the consumables required for CT/NG and TV POC testing, but also a component to cover workforce capacity to perform the tests. Importantly, the rebate was contingent on eligible services continuing to participate in and demonstrate sound analytical performance for QC and EQA STI testing.

5. Discussion and concluding remarks

5.1 Comparison of TTANGO with other international POC testing programs for sexually transmitted infections

The TTANGO Program is unique in its scale (76 sites and 6 jurisdictions), geographic reach (rural and remote Australia), setting (primary health care, Aboriginal community controlled and government managed), strong Indigenous governance, networked connectivity (for program oversight, clinical management and notifiable disease reporting), operational implementation (in a non-laboratory environment), training and operational support (developed and delivered to cater to primary care clinician end-users), and, as of November 2024, sustained public funding.

In the United Kingdom, the Dean Street Express clinic has been offering molecular POC testing for STIs (chlamydia and gonorrhoea) as part of a rapid testing service for asymptomatic screening for several years [32]. While using the same GeneXpert technology as the TTANGO program and conducting high volumes of testing, this service is limited to one urban location in central London and is implemented through a specialist sexual health service catering to urban clientele. Testing at this service is performed by dedicated technicians at their in-house laboratory using a high-volume throughput platform (GeneXpert Infinity) rather than by clinical staff in a primary care clinic setting using a 4-module platform. Similar to the TTANGO program, test results are electronically returned to patient records through a bespoke, tailored connectivity system allowing seamless recording and distribution of results as required.

Molecular STI POC testing has recently been demonstrated to improve clinical outcomes in studies undertaken in Papua New Guinea, South Africa and Rwanda, but all these reported studies were of short-term duration (less than 1 year) [33–37].

From 2018 to 2023, the World Health Organisation also conducted a multi-country validation study which focused solely on the analytical performance of these POC tests on the same technology as that used in TTANGO [2, 3].

To our knowledge, there are no other examples globally of large, networked, decentralised molecular POC testing networks for STIs implemented and integrated in primary care settings, and with testing performed by clinical staff.

5.2 TTANGO provides a potential template for translation to low- and middle-income countries

The TTANGO STI POC Testing Program for chlamydia (as well as gonorrhoea and trichomoniasis) provides a perfect template on how to translate a POC testing model from a seed concept to an impactful national public health program embedded

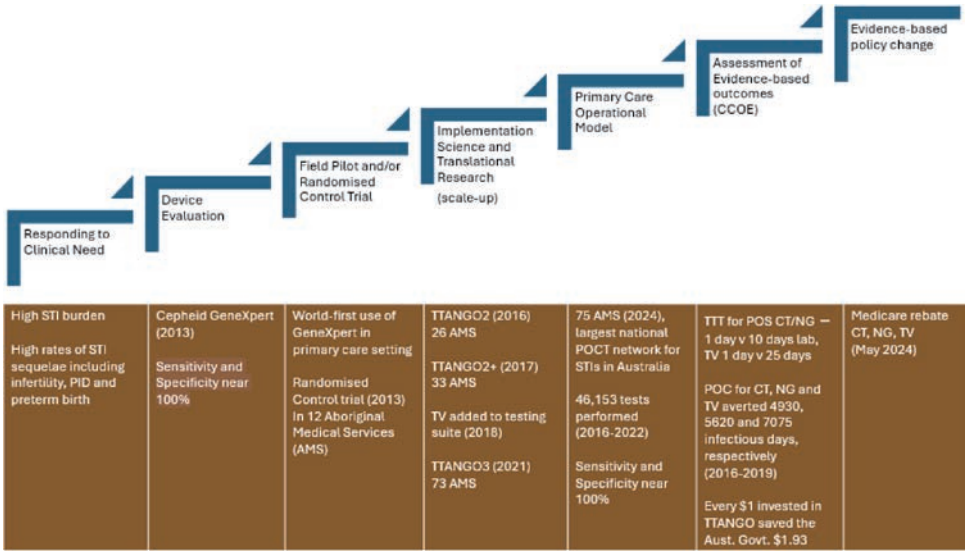

Figure 8.
From medical science to public health impact—the TTANGO Program.

in routine patient care (**Figure 8**). Using a systematic and stepwise research strategy over a decade in the making, the TTANGO network now represents a long-standing, sustainable and optimised network that could become a model for translation to low-and-middle income countries (LMIC) where *Chlamydia trachomatis* remains a significant contemporary health problem.

5.3 Challenges to translating this model to low- and middle-income countries

As mentioned previously, molecular STI POC testing has been trialled in several low-and middle-income health care settings including PNG, South Africa and Rwanda; however, this technology has not been widely scaled up in these settings [33–37]. While the affordability of the technology itself is often considered to be out of reach for low- and middle-income countries considering scale up of molecular technology, it is likely that the key infrastructure components will be the larger challenge to the translation of such a large, decentralised model in these settings. The need for a reliable power supply, dispersed connectivity, and secure supply chain for consumables, along with providing timely support for equipment maintenance and replacement to minimise disruption to use, are critical and rely on existing infrastructure. Ensuring a sufficient, competent cadre of POC test operators and the ability to offer ongoing support and troubleshooting to those as required needs to be tailored to the local setting. High turnover and limited workforce capacity is an issue often common to both high and low resource settings. A sustainable funding model to support the required infrastructure and operational implementation needs to be identified and confirmed in order to adequately scale up this model and ensure equitable access.

5.4 Challenges for the continuing evolution of the TTANGO program

While acknowledging the longevity and transferability of the TTANGO model, the TTANGO research team remains committed to investigate further means to

continually improve the quality and scope of the program. Sources of sustainable funding need to be continually explored. To ensure equitable access and benefits of POC testing are available to all young people living in remote Australia, more work needs to be done to enhance POC testing uptake through collaborative, co-designed approaches including patient and provider engagement, alternative workforce models and POC testing integration as additional assays become available and expanded.

Key to the success of the TTANGO program is the ongoing active involvement of First Nations peoples and ACCHOs in all aspects of the program from its inception. STIs remain a sensitive area of healthcare, particularly in remote communities, and ensuring cultural safety for patients is a key consideration. Reducing shame and stigma associated with STIs, normalising STI testing and maintaining confidentiality are critical components to any STI program, particularly in small communities where healthcare workers may be related to their patients. While rapid test results enable faster access to treatment and contact tracing, consideration of who can access results, and how results are managed, must be prioritised to ensure patient safety.

As it has been demonstrated that the implementation of a decentralised STI POC testing program in regional and remote settings in Australia is feasible, acceptable, clinically effective and cost effective, there is an ethical imperative to ensure the technology is widely available in these settings. Currently the Medicare rebate for STI POC testing is only available to services in remote and very remote areas and yet a far higher proportion of First Nations peoples live in regional Australia. Therefore, the rebate should be extended to include these areas also to ensure equitable and sustainable access to STI POCT.

5.5 Future directions and emerging technologies for molecular-based POC testing

The GeneXpert system is comparatively expensive, technically complex and requires a laptop to drive the testing process. Consistent with the well-accepted REASSURED diagnostic criteria [14], global manufacturers should be continually encouraged to improve the affordability, accessibility and accuracy of future molecular-based technologies, as well as to provide devices with smaller footprints and assay methods with reduced turnaround time for results [14].

There is some light on the horizon. mobiNAAT is a mobile phone–based NAAT that uses a small magnetofluidic cartridge to perform isothermal amplification and provides results in around 1 hour. A small pilot of this technology measuring *Chlamydia trachomatis* was recently conducted in the emergency department setting and demonstrated 100% concordance with a laboratory NAAT [38].

The combination of CRISPR (clustered regularly interspaced short palindromic repeats) technology with isothermal amplification provides a novel means by which higher amplification efficiency of molecular targets and reduced reaction times can be potentially achieved on a less expensive and more user-friendly platform [39, 40]; indeed, CRISPR-based methods could become the new reality in the field of molecular diagnostics for infectious diseases over the next decade [41].

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Conflict of interest

The authors have no conflict of interest to declare.

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