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REVIEW

Paving the way for quality assured, decentralised point-of-care testing for infectious disease in primary care - Real world lessons from remote Australia

Tanya L. Applegate[a], Louise M. Causer[a], Ineka Gow[a], Nina Alternetti[b], Lorraine Anderson[c], Bianca Borgnolo[a], Lauren Cooney[a], Philip Cunningham[d,e], Melanie Fernando[a], Belinda Hengel[a], Rae-Lin Huang[f], Kyana Kayago[a], Jonathan M. King[a], Hau Joe Lew[a], Marianne Martinello[a,g], Melisa Milic[b], Kelcie Miller[b], Sean O'Connor[h], Prital Patel[a,i], Emily Phillips[a], William Rawlinson[j,k], Akriti Sharma[a], Mark D.S. Shephard[b], Annie Tangey[a], Kirsty Smith[a], Ashton L. Williams[a], Kelly Andrewartha[b], Rebecca Guy[a] and Susan J. Matthews[b]On behalf of Molecular POC testing team and the National Aboriginal and Torres Strait Islander Health Protection AHPPP Subcommittee

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ABSTRACT

Introduction: Decentralized molecular testing for infectious disease diagnosis at the point-of-care (POC) is critical to address inequities in access to timely, informed health care. The COVID-19 pandemic accelerated the demand, development and adoption of POC tests for infectious diseases globally. This has provided opportunities to maximize the individual benefits and public health impact of POC testing, particularly in remote and resource-limited primary care settings. Despite this, there remains a lack of harmonized, regulatory compliance and quality management frameworks for the delivery of molecular POC testing networks outside the laboratory setting.

Areas Covered: This Perspective describes real-world lessons and experiences of delivering a fit-for-purpose, quality framework for one of the world's largest decentralized molecular POC testing programs for infectious disease across rural and remote Australian communities. Here we detail unique, key considerations to ensure the quality of POC testing in primary health settings with global application.

Expert Opinion: There is an ethical and public health imperative to provide sustained access to decentralized POC testing for infectious disease in primary care. Genuine partnerships across stakeholders and disciplines are essential to deliver well governed, fit-for-purpose quality management POC testing frameworks and increase equitable access to timely, high-quality person-centered care.

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KEYWORDS
Decentralized; diagnostics; fit-for-purpose; infectious disease; point-of-care; quality assurance; quality framework; primary care

1. Introduction

1.1. Integrated molecular point-of-care (POC) testing – an opportunity to improve equitable remote health care access and delivery

The COVID-19 pandemic enhanced global awareness of the need for molecular point-of-care (POC) testing for the rapid detection of infectious diseases of public health significance. Molecular POC testing can prompt interventions to reduce transmission and minimize public health impact, especially among people at risk with limited access to vaccines and treatments [1–7]. In many settings, high-quality, reliable, decentralized POC testing is critical to ensure equitable and timely diagnosis and management of infectious disease. This is particularly important among people who are vulnerable to infectious diseases due to socioeconomic or structural barriers to health care, who experience stigma or discrimination and/or other social determinants of health, have limited access to vaccines and treatments or live in resource-limited, rural, or remote communities. POC testing also stimulates the demand for testing among people who may not otherwise have access to, or engage in, care through conventional pathways [8–11]. The societal recognition of the value of POC testing during COVID-19 has generated public demand and a new market opportunity for health technology providers [12–15]. This increased awareness has occurred in parallel with an explosion in investment and technological advancement to accelerate product development [16,17]. This surge in novel POC testing technologies, including the capacity to test for several infections simultaneously, provides the opportunity to revolutionize healthcare. Documented impacts of POC testing for infectious diseases compared to laboratory-based testing include enhanced access to integrated testing [18–20] and reduced time to etiologic diagnosis and appropriate treatment

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Article highlights

- In many settings, high-quality,integrated, decentralized molecular POC testing is critical to ensure equitable, timely diagnosis and management of infectious diseases. Molecular POC testing is particularly important among people most vulnerable to infectious disease and/or living in resource-limited, rural or remote communities.
- Large-scale implementation of molecular POC testing programs delivered in primary care by non-laboratory professionals has unique considerations, requiring fit-for-purpose regulations, standards and testing accreditation schemes.
- Decentralized POC testing and networks must be underpinned by fit-for-purpose, adaptable, quality frameworks informed by complementary and transdisciplinary expertise to maximize clinical and public health impact.
- Unique quality assurance considerations for decentralized POC testing are discussed, drawing on the implementation of a globally unique, molecular POC testing for infectious disease network in rural and remote primary care in Australia.
- Multi-stakeholder and transdisciplinary partnership models, centered around person's needs and primary health practices, are essential for successful POC implementation, adoption and impact.

[11,21–23]. Demonstrated impacts also include increased treatment uptake reducing transmission and morbidity [24,25] and minimized inappropriate antimicrobial use associated with resistance and side-effects [26–32]. In rural and remote communities, POC testing can provide significant advantages in reducing major barriers, particularly unavoidable delays to obtain a laboratory result [11,33]. These delays can compound into major interruptions in care for people who move frequently between communities.

Our team previously shared an implementation model for decentralized POC testing for infectious disease with people and community at its center [34]. A critical element underpinning this model is fit-for-purpose quality frameworks (Figure 1). While there is increasing recognition of the value of POC testing for infectious disease [15,35], there are very few examples of large, integrated and decentralized high-quality POC testing programs delivered in primary care. The implementation of primary care POC testing programs delivered outside of the clinical laboratory by non-laboratory professionals, have unique considerations and solutions, requiring fit-for-purpose regulations, quality assurance programs and testing accreditation schemes [36–38].

2. Body

2.1. Global context and existing quality assurance frameworks

2.1.1. Achieving global excellence in quality frameworks for molecular POC testing

Many countries, including the United States (US), have demonstrated foresight and leadership in recognizing the need to adapt quality standards to serve a broad range of medical testing environments, assays, personnel, clinical and community needs. US regulatory authorities (i.e. Center for Disease Control and Prevention, Food and Drug Administration) have built flexibility into their frameworks through post-market 'Clinical Laboratory Improvement Amendments (CLIA) waivers' for diagnostic tests while maintaining processes that eliminate sources of errors and mitigate the risk of harm [39,40]. The 'CLIA-waived' framework recognizes the risk of pre-analytical, analytical, and post-analytical errors differ significantly across methods and device complexities and modifies the stringency of quality management requirements relative to the technical considerations and test environment. Certified 'CLIA-waived' tests, deemed to be simple and with a low risk of error, can be conducted in an accredited 'CLIA-waived' site. CLIA-waived sites have decreased regulatory and technical requirements such as education and training, quality control (QC), external

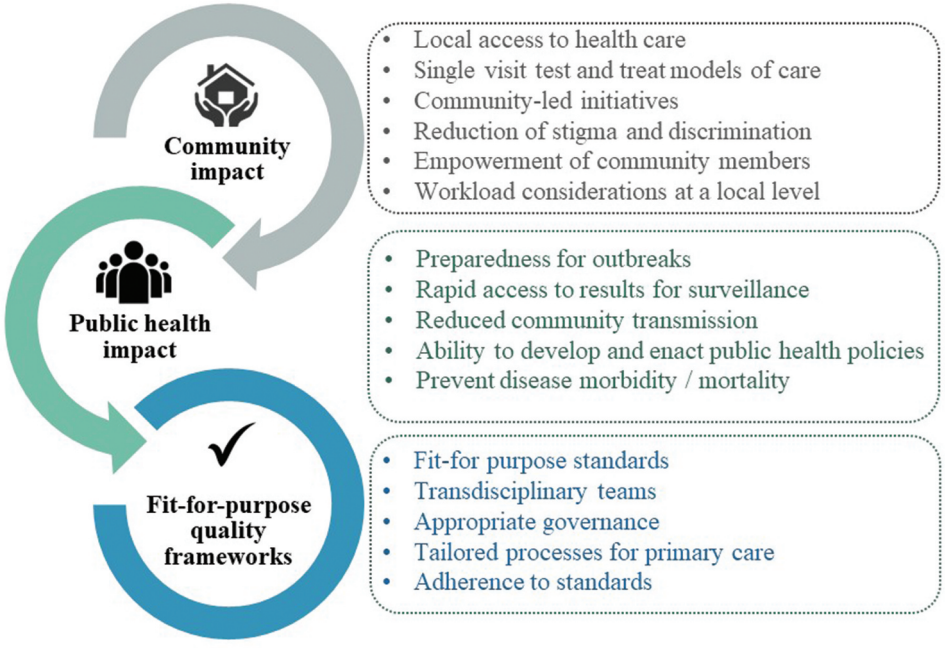

Figure 1. Decentralized POC testing must be underpinned by fit-for-purpose quality frameworks that maximize community and public health impacts and minimize harm.

quality assurance (EQA), and test management. Individualized Quality Control Plans (IQCP) are another regulatory adaption which allow laboratories to evolve their QC programs to meet their unique laboratory and clinical needs, as well as regulatory standards and policy requirements [41,42]. These adaptable frameworks enable clinical and scientific groups to ensure patient safety is maintained across the spectrum of POC test complexity while reducing barriers to access. Such a flexible diagnostic regulatory landscape is not currently available in Australia [43].

2.1.2. Keeping pace with a rapidly changing POC testing landscape – adapting quality standards

Australia is recognized as having one of the highest quality healthcare systems globally, including centralized medical testing market approval, medical testing standards and laboratory accreditation. The current system in Australia however is not equipped to keep pace with the extraordinary increase in the demand, commercialization, and adoption of new POC testing technologies outside of a clinical laboratory. Nor does Australia have a fit-for-purpose accreditation for decentralized POC testing outside the laboratory setting. The Australian Commission on Safety and Quality of Health Care (ACSQHC) supports the National Pathology Accreditation Scheme Advisory Council (NPAAC) to govern medical testing standards and minimum POC testing requirements in line with international standards [44–47]. The ACSQHC also provides oversight of the accreditation and evaluation of compliance to these quality standards, independently managed by the National Association of Testing Authority (NATA) [48,49]. Laboratory accreditation is directly linked to subsidized pathology service on the Medicare Benefits Schedule (MBS). Recognizing the need to adapt to community expectations and state-of-the-art technology, ACSQHC is currently leading a public health technology assessment review of the NPAAC requirements for POC testing, in anticipation of delivering its third edition. This provides a timely opportunity to incorporate post-pandemic learnings for future preparedness, expand testing access points and support adoption of quality POC testing for all [50]. Delivery of a quality assurance framework for decentralized POC testing that is appropriate for the service type, model of delivery, remoteness and population needs to be informed by transdisciplinary and complementary expertise, including medical testing and primary care expertise [51] (Figure 2).

2.1.3. Understanding the benefits and risks of quality molecular POC testing

As no diagnostic test is perfect [52], a public health risk-benefit analysis of any POC test within a clinical testing pathway is critical [51,53,54]. The main risks related to the quality of molecular POC testing results are the possibility of false-positive and negative results. These risks are inherent in all diagnostic tests, but with different implications when results are available in real-time to inform clinical management. False negatives may increase the potential for disease progression and community transmission, and can result from preanalytical/analytical factors. These can include non-detection of low pathogen load associated with early or delayed testing, misidentification of samples, poor sample collection technique, poor specimen quality and new pathogen strains that impact assay performance. False positives may lead to socio-economic and cultural disruption, unnecessary treatment and impact public health responses. False positives can be caused by misidentification of specimens, biological or amplicon contamination or persistent detection at low cycle thresholds for weeks post-infection [55–57].

To minimize the risk of harm associated with false-negatives or false-positives, the analytical test performance must be assessed through a quality management framework consistent with national and international regulatory requirements [58]. This is important when POC tests are conducted

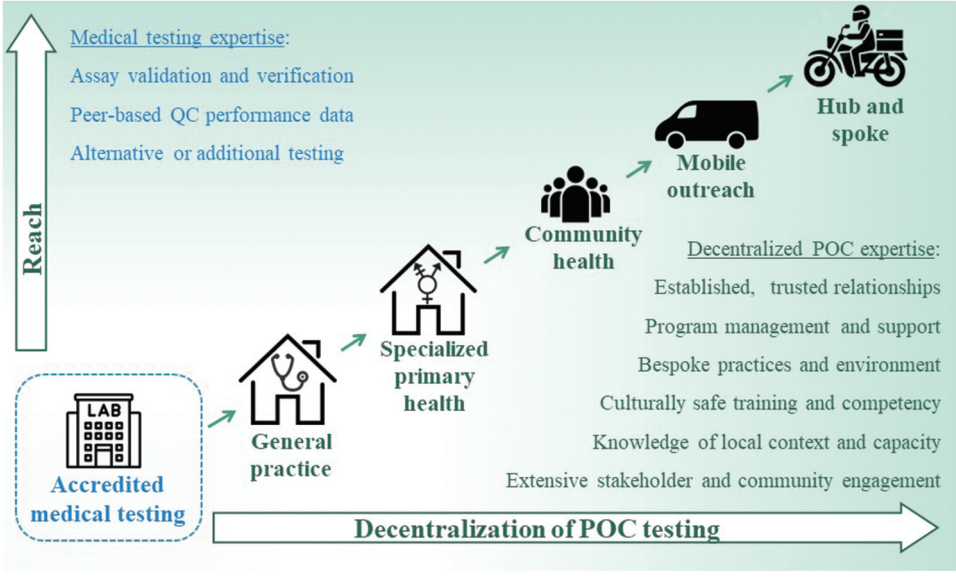

Figure 2. Specialist pathology testing expertise for quality assurance frameworks for decentralized POC testing models, outside an accredited medical testing facility: i.e. general practice, specialist primary health, community health, mobile and hub & spoke models.

by non-laboratory health workers in decentralized primary care services. For health workers, POC testing is often an additional responsibility in an already under-resourced and high-pressure environment relating to broader community responsibilities [43,59–63].

The operational performance of a molecular POC test is influenced by sensitivity and uptake. A highly sensitive test used in only 20% of the eligible population will detect a smaller proportion of infections in the community than a test used in 50% of the eligible population. Thus, the focus of decentralized should equally be on community-led models to optimize the uptake of the test, including health promotion and clinical education. Workforce support, reimbursement of operators, and flexible training and competency modalities are also critical as many operators may be task shifting and have competing demands [34].

2.1.4. Decentralized molecular POC testing in rural and remote primary care

A body of literature is emerging on considerations to deliver fit-for-purpose, high-quality, safe, sustainable, and adaptable decentralized POC testing [37,64–68]. These considerations are particularly relevant for rural and remote primary care services, which have additional and unique challenges, including large distances from urban centers, inequitable delays in return of standard-of-care pathology results and limited resources [36,38,69–71]. Reflecting this need in Australia, SARS-CoV-2 POC testing used to diagnose the first case in Aboriginal and Torres Strait Islander people living in rural or remote communities, was recommended within the Communicable Diseases Network Australia National Guidelines for Urban and Regional Aboriginal and Torres Strait Islander Communities for COVID-19 and the Public Health Laboratory Network's COVID-19 testing framework [50,72].

2.2. Our perspective

2.2.1. The first nations molecular POC testing program – the background

The First Nations Molecular POC Testing Program (referred to as the Program herein) offers molecular POC testing to over 100 Australian rural and remote Aboriginal and Torres Strait Islander communities [34,73]. This Program is overseen by the National Aboriginal and Torres Strait Islander Health Protection subcommittee of the Australian Health Protection Principal Committee, replacing the former Aboriginal and Torres Strait Islander Advisory Group on COVID-19 [74]. The Program is delivered by an operational team from the Kirby Institute (UNSW Sydney) and Flinders University International Centre for Point-of-Care Testing in partnership with many stakeholders (see Acknowledgments). In this Program, approximately two-thirds of services are in remote areas. Services range in population size from 80 to 9,000 people per community with a median aerial distance to the nearest laboratory of 569 kilometers (354 miles) [34,75]. At the beginning of the COVID-19 pandemic, the Program rapidly expanded by leveraging infrastructure from a molecular POC testing network for sexually transmitted infections (STI: *Chlamydia trachomatis [CT], Neisseria gonorrhoea [NG] and Trichomatis vaginalis [TV])* [11,21,76]. Evidence from the STI POC program recently supported the Australian Government's recent decision to approve reimbursement POC testing for CT/NG & TV for providers in remote and very remote Australia [77]. This is the first POC test for infectious disease to be listed as a subsidized pathology service on the MBS. The reimbursement covers the cost of purchasing the test, and a portion of the operator's time to conduct the test.

The Program now offers POC testing for seven infectious diseases using the GeneXpert System (Cepheid, Sunnyvale, CA, U.S.A.). This includes the three above-mentioned STIs and a respiratory cartridge allowing the simultaneous detection of SARS-CoV-2, Influenza A, Influenza B, and Respiratory Syncytial Virus. The Program adopted the GeneXpert® System as this was the only approved SARS-CoV-2 POC assay approved for emergency use in Australia at the Program's commencement in March 2020. SARS-CoV-2 lateral flow assays were subsequently approved and independently rolled-out in November 2022. The multiplex respiratory testing component (SARS-CoV-2, Flu A/B, RSV) of the Program has continued to support clinical care pathways that include respiratory lateral flow assays.

Molecular POC testing is delivered by local health service staff in rural and remote community- and government-led Aboriginal and Torres Strait Islander primary health care who have been trained and deemed competent in POC testing. The success of this delivery model is underpinned by the strong partnership and leadership by Aboriginal Community Controlled Health Organisations (ACCHOs), which are primary health care services initiated and governed by the local Aboriginal communities [34,78]. In infectious disease, the Program is globally unique in its strong community-led approach, cultural governance and operational oversight and multidisciplinary stakeholder partnership model, and its application of a novel POC testing framework with community at its center [34]. The Program's success and rapid scale-up were facilitated by an expert operational team (see section 2.1.4 Resources), consisting of medical laboratory scientists, public health epidemiologists, information technology specialists, logisticians, clinicians, POC testing experts, regional coordinators, training specialists and Aboriginal Health Workers. The multidisciplinary expertise, input from key stakeholders including health service and medical staff, local clinics, peak ACCHOs, pathology industry, public health physicians and the Australian Government has proved invaluable in ensuring a responsive and adaptable network.

2.2.2. Guidance on the implementation of a decentralized molecular POC testing network for infectious disease in primary care – a missing piece

During the roll out of the Program under an emergency response, the lack of guidance on the large-scale implementation of rapid, low- to moderate-complexity molecular POC tests for infectious disease in decentralized settings was highlighted [34]. In addition to the considerations prior to Program implementation, such as defining a clinical case and selecting fit-for-purpose technology [53], there were several factors to consider [34]. Here, we focus on key quality assurance elements that are unique to decentralized molecular POC testing in rural and

remote primary care, sharing collective learnings from one of the world's largest decentralized molecular POC testing networks in these settings (also summarized in Figure 3).

2.3. Consultative regulatory and governance models (**Figure 3(a)**)

Fit-for-purpose regulatory models and testing frameworks to encompass decentralized POC testing need to be developed in collaboration with a broad range of stakeholders. Stakeholder expertise must include an extensive understanding of primary and remote care, to enable POC testing options that provide equitable access to rapid disease diagnosis and appropriate linkage to care. Clinical and cultural governance, specific to community needs, are critical and need to be prioritized for remote community-based settings to ensure the safety of POC testing approaches, training and resources, and to maximize community acceptance, clinic integration, and adoption.

2.3.1. Tailored clinical governance

Clinical governance ensures safety, quality, and continuous improvement in the delivery of care through health technologies. Clinical governance uses a person-centered, all-of-systems approach to develop clinically safe, usable, and continually improving products and services. The provision of appropriate clinical governance, as defined in current regulatory documents, can be challenging to achieve in decentralized POC testing networks, where a broad range of analytical testing may be offered (i.e. non-communicable and infectious disease) and limitations in specialist pathologist workforce capacity may exist. Tailored clinical governance structures are most likely needed for remote communities, including linkage of senior remote medical staff to programmatic clinical governance through multidisciplinary quality committees. Bespoke accreditation pathways for primary care POC testing sites adaptable to setting-specific requirements are needed. Expanded, task sharing delivery models provided by community health practitioners, nurses or peers with lived experience may require custom-built risk management, POC testing and linkage to care strategies.

2.3.2. Cultural governance

Current regulatory frameworks do not recognize the need for cultural governance, however this is imperative and critical to ensure that any POC testing solution is locally relevant and meets community needs. To achieve this, appropriate POC testing solutions for the Program, are designed in partnership with health services; a process requiring extensive consultation with jurisdictional peak bodies, local community, and key stakeholder groups. All aspects of the POC testing model need ongoing cultural oversight and cultural safety embedded throughout to ensure the specific needs of each local community are met. Cultural governance ensures the POC testing Program is also continually responsive to community needs and feedback in all aspects. Specific examples include co-design processes for the interpretation and communication of a test result, engagement of Aboriginal and Torres Strait Islander staff and community to review and provide advice on training, information sheets and other resources to improve health literacy implemented by the Program.

2.4. Resource considerations, including personnel and facilities (**Figure 3(b)**)

2.4.1. Diverse, transdisciplinary operational and research team

An essential resource to successfully deliver a high-quality decentralized molecular POC testing program is a well-resourced multidisciplinary operational team (see also Figure 4). Genuine and ongoing engagement with stakeholders and organizations across the sector is essential for continuous quality improvement processes. The amount of time required to deliver activities across the program should not be underestimated (Table 1).

2.4.2. Health service facilities and environmental conditions

The provision of a safe and secure working environment in remote primary care, which is also suitable for POC testing, requires a combination of ongoing in-person and remote site assessments. Site suitability assessments need to account for the vastly different

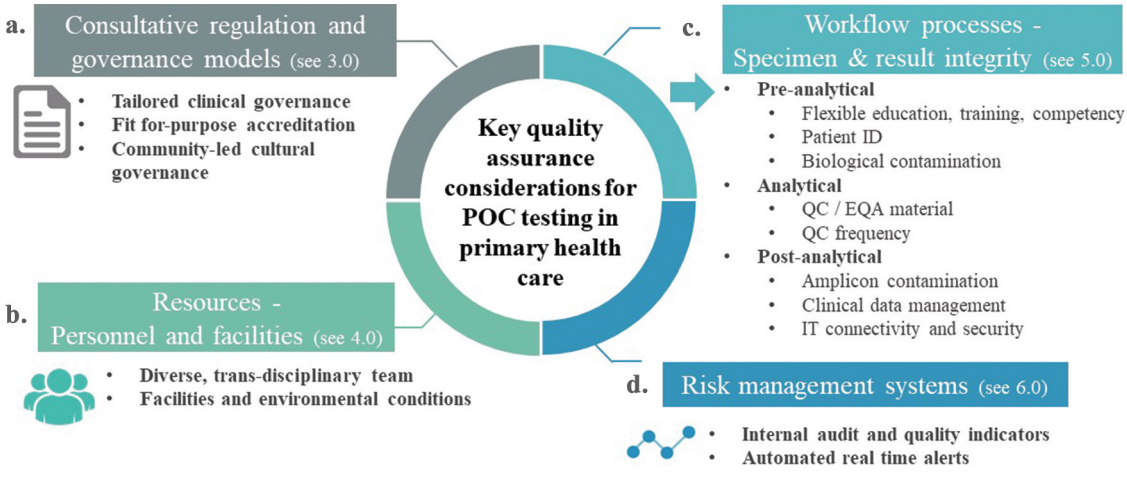

Figure 3. Key quality assurance elements to consider that encompass decentralized POC testing needs in remote primary health care: (a) Consultative regulatory and governance models (b) Resources – personnel and facilities, (c) Workflow processes – specimen and result integrity, (d) Risk management systems.

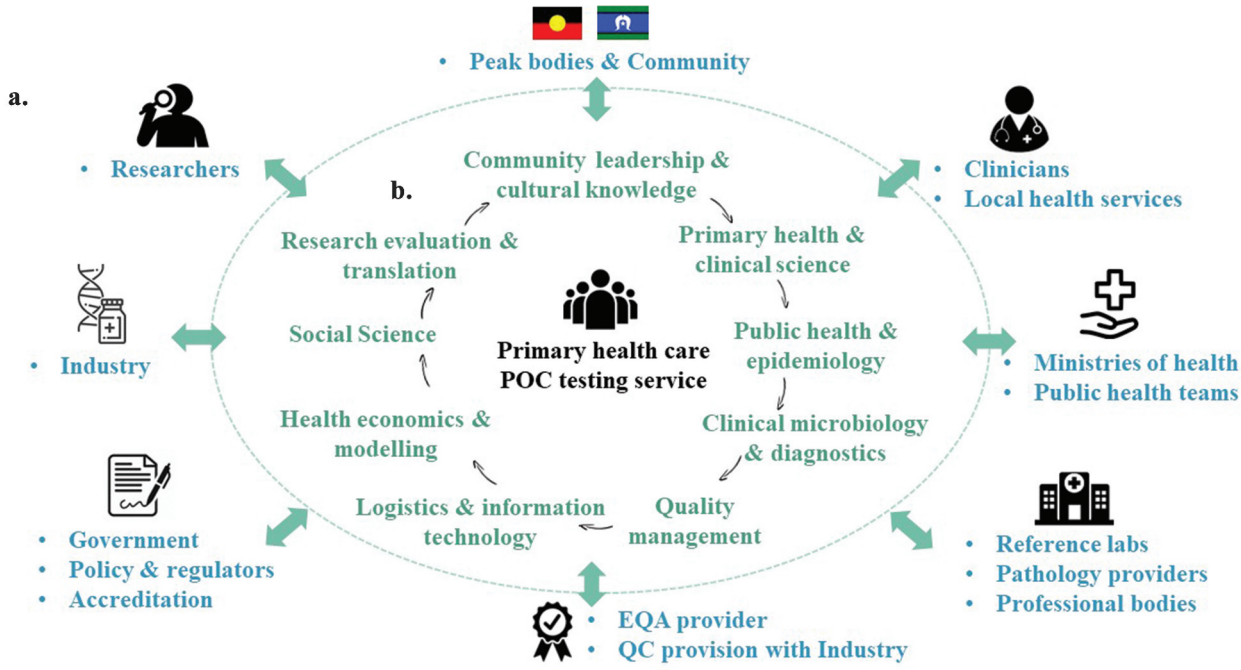

Figure 4. Wrap around quality program for decentralized POC testing services in remote primary health care: (a) Multistakeholder partnerships, supported by (b) A transdisciplinary operational and research team.

Table 1. Operational team services and activities to deliver a quality program for decentralized POC testing.

Service	Activity
Stakeholder management	• Relationship building, regular engagement and communication (community health services, physicians, reference laboratories, ministries of health).
Cultural leadership	• Ensuring cultural safety of all processes.
	• Development of bespoke easy to understand infographics and culturally appropriate education and POC training partnership with services.
Technical support	• Help desk support for operator training and competency assessment, device registers, operator registers, resolution of technical issues, support for routine device maintenance, quality testing and result submission and interpretation, movement of devices, connectivity
	• Device maintenance and ensuring optimal functioning. • Connectivity issues/investigate information systems. • Provide a specialist pathology testing service with expertise in decentralized POC testing, in partnership with vendors and laboratories as needed.
Logistics support	• Monitoring of supply deliveries, including surge supplies/stock expiry, cartridge rationing during epidemics/pandemics. • Buying and procuring services, equipment, and consumables; validating reagents; managing inventory and logistical supply; monitoring consumables usage and ensuring cartridge rationing during epidemics and pandemics.
QC/EQA Programs	• Identification and purchasing of suitable quality materials, QC and EQA test processes, QC and EQA portals for result submission, monitoring and corrective actions for QC and EQA, QC and EQA participation compliance.
Quality indicators	• Develop, maintain, monitoring, reporting, communicating results – including concordance with expected results, monitoring/corrective action for unusual results or escalating incidents.
Incident response	• Root cause analysis investigation. • Retraining and key messages. • Monitoring environmental test compliance and corrective action.
	• Reporting product defects to industry partners and/or TGA.
Regulatory framework	• Bespoke accreditation pathways.

clinical environments and local work-flow practices, which are often limited by space, staffing and resources. Key considerations in these environments include suitable sample, equipment, reagent and consumable storage locations. Changes to clinics require regular review to implement workflow solutions that ensure facilities remain fit-for-purpose. Compliance with operational checks after portable equipment is moved is central to ensure device performance. Long and complicated transport routes need to be mapped, managed and optimized to uphold cold-chain requirements and timely provision of equipment and consumables, accounting for seasonal or extreme weather events. The capacity to retain samples to meet regulatory requirements, retesting or referral in settings can be challenging with limited refrigerated and non-refrigerated space. Additionally, special consideration needs to be given regulating environmental factors within the operating specifications of the device/test that differ

from that of controlled laboratory test environments (e.g. temperature, power losses, accessibility of internet connection, flooding, fire).

2.5. Processes to ensure specimen and result integrity (Figure 3(c))

In addition to fundamental training and resource considerations, pragmatic risk/benefit assessments of all pre-analytical (before the POC test), analytical (during the test), post-analytical (after the test) processes are necessary to customize workflow and minimize risk of error [42].

2.5.1. Pre-analytical considerations

2.5.1.1. Flexible operator education, training, and competency models. Operator competency is defined as having the appropriate skills, knowledge and conduct to perform the POC test safely; critical to the success and efficacy of any POC testing network. Underpinning operator training and competency assessment is a rigorous risk assessment of specimen collection and testing, with locally appropriate risk mitigation strategies embedded in the standard operating procedures and training resources. The need for a variety of flexible training, retraining and competency assessment options for remote health service staff is essential. Comprehensive training includes prerequisite work health and safety training, on-site face-to-face training sessions, self-paced online learning modules and online guided training. Training must also suit the diverse professional backgrounds of staff who will be engaged to conduct POC testing. This training must build local capacity while at the same time support high staff turnover and shortages. During pandemic-imposed jurisdictional border closures, tropical monsoonal seasons or in very remote locations where in-person training is not practical or possible, culturally safe, and innovative POC operator training programs may need to incorporate remote learning modules (See Text Box 1).

2.5.1.2. Specimen collection and positive patient ID. Primary care workers should already be trained and competent in positive patient identification processes for routine pathology testing. However, POC training and competency assessment needs to reinforce the cross-checking of patient details when collecting and labeling specimens, patient confidentiality, specimen integrity and minimum sample acceptance criteria prior to POC testing.

2.5.1.3. Data entry and test selection. The implications of constrained and busy personnel at primary care services require that processes are in place to minimize risks of error when conducting a POC test. These processes are particularly focused on ensuring the entry of correct patient and test data or use of the correct test cartridge. There needs consideration as to how to best integrate POC testing with existing clinic digital health infrastructure and workflows to leverage systems, minimize additional administrative burden, and ensure data integrity. In close consultation with clinic staff, practical processes such as automated electronic request forms, barcodes containing key patient information, test lists, data-entry cross checking and enhanced operator access controls may need to be developed to address identified data entry or test selection risks.

2.5.1.4. Biological contamination. Any molecular amplification test is at risk of biological or amplicon contamination and this risk is best mitigated by a series of comprehensive pre-analytical, analytical and post-analytical controls. It is important to acknowledge that the risk of contamination can only be minimized, and never eliminated, even when conducted within a highly controlled laboratory facility [79]. If regulatory approval is granted for product use at the POC, then it is important that the manufacturer's product instructions for use and standard training resources also include specific processes to minimize contamination risk.

Although molecular closed-cartridge POC testing systems include engineering controls to minimize the risk of contamination, additional facility controls need to be considered in primary care settings. A thorough review and risk assessment of clinic and POC testing workflow, often in compact multi-purpose spaces, is needed to identify additional steps to minimize contamination risk [42,80]. To minimize the risk of biological contamination, considerations may include limiting foot-traffic, separating storage, consulting, testing and doffing areas, safe disposal of contaminated equipment (such as bagging), use of disposable bench-coat between each test and appropriate cleaning protocols.

POC testing for infectious disease in primary care may be performed infrequently, depending on local needs and priorities. Infrequent testing in primary care settings may require emphasis during POC operator training on compliance with standard operating procedures, such as appropriate use of gloves/masks and eye-protection as required. As POC tests are often used on demand, rather than high throughput, clear guidance on the need to generate one test order and conduct one test at a time is critical to minimize the risk of error. Providing operators with a benchmark for what might be considered a reasonable maximum number of tests that can be conducted on the specific device per day, further reduces the risk of cross-contamination (and risk of error – see below), while managing clinic expectations of test throughput. To minimize the risk of biological contamination, clear procedures are required to ensure operators are not conducting tests when infected with respiratory viruses and

Box 1. Culturally safe and innovative, remote learning POC operator training program modules.

a) online prerequisite training modules for work health and safety, hand hygiene and personal protective equipment, donning and doffing, and sample disposal according to universal precautions;
b) theory training for the molecular POC test, including common sources of pre- and post-analytical error, quality control and assurance and patient confidentiality;
c) Appropriate steps to mitigate biological/ amplicon contamination and correct disposal of materials used in testing;
d) remotely observed practical competency assessment by means of successful and concordant negative and positive quality control;
e) remote re-training when competency issues are identified or following significant protocol changes.

to restrict foot-traffic of clinic staff through the POC testing area. This is particularly important during local outbreaks, where demand for POC testing with rapid result time may exceed local device and/or staff capability.

2.5.2. Analytical considerations – quality control and external quality assurance

2.5.2.1. Fit-for-purpose quality control materials. Internal QC programs are critical to verify device and cartridge performance and thus confirm the validity of a diagnostic result before it is issued. Comprehensive POC QC programs consist of in-built cartridge controls to verify assay performance, device system self-checks to provide assurance on the equipment and testing process, plus regular testing of QC materials of known concentrations at clinically important cutoffs as required. Key considerations such as stability and format are important to identify optimal QC product criteria and processes for use by non-laboratory, health service staff in remote/regional primary health care services (Table 2). Ideally, QC testing (and EQA testing, below) should replicate the entire process of the patient sample testing pathway, from the sample type and preparatory steps, through to who conducts the test, interprets and reports the results. For this reason, POC testing operators are trained to perform QC (and EQA) at a regular frequency to maintain operator confidence [81]. Negative QC testing can support the detection of biological or amplicon contamination (see post-analytical considerations below) but may not detect intermittent false positives.

2.5.2.2. Flexible quality control testing frequency. In line with internal quality control programs [41], the frequency of quality control in remote primary care needs careful consideration. Although monthly QC is straightforward to communicate and monitor, sites may go through short periods (e.g. a few months) where no testing occurs due to lack of need or workforce constraints. QC testing on the same day as patient testing is an alternative for low test sites but requires systems to ensure QC tests are performed prior to release of patient results. If a POC technology is new to market, an emergency use only assay, or there are epidemiological changes and emerging variants of concern (as was the case for SARS-CoV-2), the QC frequency may also need to be adapted. Changing epidemiology needs to consider pretest probability, such as low prevalence settings with no known community transmissions to high prevalence and established community transmission (Table 3).

2.5.2.3. Bespoke external quality assurance. External quality assurance programs, which provide peer reviewed, blinded analysis of samples with negative or known infectious load are essential for assessing within-clinic analytical performance and result comparability across clinics. Bespoke EQA specimens may need to be considered for remote primary care (see Table 2). This includes recognizing the potential need to modify included strains as new knowledge on the pandemic or epidemic emerges. Previous data from the Program demonstrate high analytical performance by non-laboratory staff in remote primary health care services [82].

2.5.3. Post-analytical considerations

The majority of post-analytical considerations nuanced for remote POC testing services center around minimizing the risk of amplicon contamination, result management, interpretation, and communication.

Table 2. Optimized QC/EQA specifications and processes.

Specification checklist	Considerations
Material approved for use	• Only incorporate material recommended in POC test instructions for use, often provided by the POC test kit manufacturer.
Material format	• Ideally, the QC specimen format should mimic sample type and entire test process (e.g. swab or liquid).
Internal controls	• If required, ensure material contains stabilized human DNA to pass internal sample adequacy control.
Inactivation	• Deactivated material, e.g. by gamma irradiation, is required to allow safe product transportation and reduce infectivity risk to operator.
Format and handling	• Ideally there would be no requirement for reconstitution using specialized laboratory equipment (ie. calibrated pipettes). • Vial size should facilitate safe handling with the assay manufacturer's sampling pipette (avoided altogether where possible), ideally with no additional equipment required. • Handling processes should minimize risk of bubble formation or aerosol formation.
Stability	• Product shipped at ambient temperature, with defined stability data inclusive of a broad temperature range expected during transit. No cold chain required. • Homogeneity testing provided by the manufacturer for each batch produced.
Clinical relevance	• Material should be targeted at clinical decision points for the particular assay/test, such as circulating variants of concern or clinically important viral loads for quantitative assays. • Custom designed negative or positive controls of varying viral loads, genotypes are available as required.
Volume	• Sample volume should be adequate to allow for repeat testing, if required for corrective action.
Vial identification	• Ensure ease of specimen identification through clarity of product labels; e.g. unique product identifiers that are easily identified by non-laboratory staff.
Instructions for Use	• Is the commercial format suitable or are bespoke, customized versions of instructions for use required to support non-laboratory use.
Dispatch	• Customized QC dispatch lists to maximize successful and timely delivery to remote health services.
Results	• Automated recording into real-time data base available for operators and program monitoring, including flagging of unusual results (see section 2.6 below).

Table 3. Case study – individualized QC frequency to phases of SARS-CoV-2 epidemic among first nations people living in remote communities in Australia.

Phase of epidemic	QC frequency and discordant result response	Response on discordant QC result
Phase I: No known community transmission	Monthly negative and positive QC. Negative QC sample after each positive case.	Case discussions. Testing of sample at a laboratory on a different platform.
Phase 2: Established, local community transmission	Monthly negative and positive QC. Negative transport media (blank) sample after each positive sample run in the module of positive test.	As for Phase I, plus Testing of additional negative transport media (blank) samples on each active module. Re-training on 5 key steps (See above).
Phase 3: Established, national transmission	Monthly negative and positive QC. Negative transport media (blank) sample after each positive sample up to a maximum of 4 negative transport media samples per day per clinic with aim to cover all modules at least once where possible.	Testing of sample at a laboratory on a different platform. Environmental swabbing and alternative platform testing (pre-and post-clean). Extensive site cleaning.

2.5.3.1. Amplicon contamination. Although molecular POC testing devices are designed as closed-cartridge systems with minimal risk of amplified material contaminating the environment, used test cartridges contain large amounts of amplified (noninfectious) nucleic acid. Cartridges require careful handling and may require additional post-analytical preventative measures in primary care settings. Additional measures include a review of fit-for-purpose decontamination (products, frequency and processes) in line with the manufacturer's recommendations. There also needs to be robust disposal of used cartridges and inspection of leakage, routine environmental swabbing prompt cleaning and corrective action. Addressing this, additional precautionary measures in the Program include individually double bagging each used test cartridge with disposal into covered hazardous waste containers located 1.5 m from device. Environmental swab testing for evidence of potential contamination in remote primary care also has unique considerations. Due to remote locations, health-service staff themselves may need to be trained in collecting environmental swabs. Clinic layout, including the proximity of testing location to sample collection and storage areas, requires careful consideration and real-time monitoring of quality indicators with strong automated connectivity systems (see below). Depending on the in-built cartridge controls (e.g. sample adequacy control, sample probe check, internal quality checks) cycle threshold (Ct) and reaction curve analysis may also be important for verifying assay performance and result validity.

2.5.3.2. Clinical data management and communication. While electronic POC test results are subject to standard review and authorization procedures, the availability of a real-time result when the person being tested might be present at the service adds a layer of unique considerations [83]. While the presence of the person, knowledge of clinical history and local epidemiology can inform the interpretation and communication of this real-time result, programs may consider the co-development of clear and standardized messaging during result delivery. If customized data verification processes do identify any errors or incidents of concern, result amendment may be required, followed by measures to mitigate risk of harm. Robust processes must also be in place to ensure samples are retained for a defined period (e.g. 1 month) for repeat testing or laboratory testing, in line with test-specific regulatory guidelines. This can be a particular challenge for small clinics with limited refrigerated storage space and infrequent sample transport to centralized laboratory services.

Case study: During the COVID-19 pandemic, a positive results hotline was established to provide real-time support to the services during the peak of the pandemic period. The trusted relationship, local community knowledge and connection with public health team were critical when the first positive result could trigger a rapid, public health outbreak response (Figure 5). During the COVID-19 pandemic, the Australian Government Department of Health and Aged Care contracted an external evaluation of the Program, conducted by the Nous Group, concluding it was highly successful, saved lives and reduced the spread of COVID-19 [78]. The Nous evaluation interviews of health service staff in the Program gave positive reports of their experiences with the Program Hotline. Services reported that '*Hotline staff were always supportive, helped to alleviate the panic surrounding a positive test, and provided clear and detailed instructions. They were always responsive, providing 24/7 support. Services reported feeling that the Program "had their backs" and were never judgmental in the support they gave. They saw the support provided by the Program as a foundational element to its success*' [73].

2.5.3.3. IT connectivity and security – clinical, public health and programmatic considerations. Information management systems within primary health care can require bespoke solutions to accommodate clinical, jurisdictional, and programmatic needs for both computerized and non-computerized information [54,83]. Internet connectivity often requires various solutions (such as telecommunication services, modems, satellite links) to ensure real-time data delivery to the clinician and patient electronic health record, public health surveillance and program databases as required. Clinical, ethical and cybersecurity requirements to maintain confidentiality and integrity of patient information, results and management include careful consideration of data transit, storage, access, timeframes and back-up. Processes to withhold or amend results and communication of these events must be considered and carefully implemented. Mandatory public health notifications may be required depending on the infection (e.g. SARS-CoV-2, influenza,

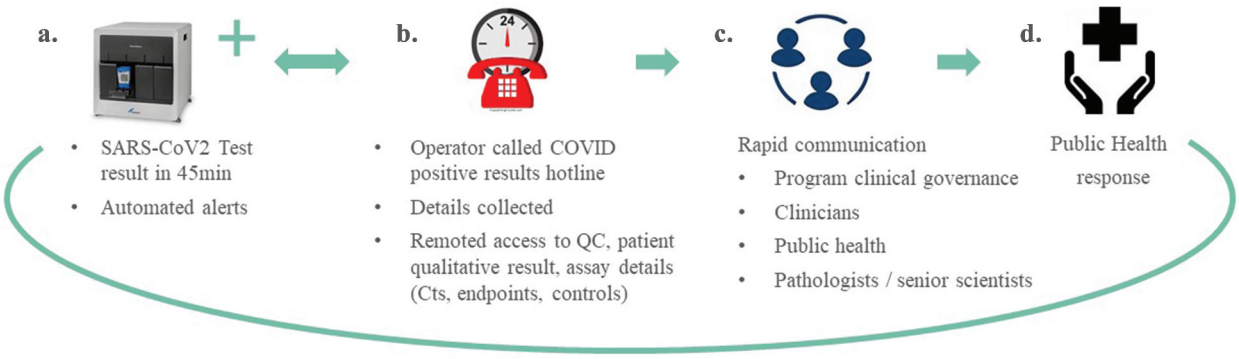

Figure 5. Automated alerts and positive results hotline during the peak of COVID-19 pandemic was critical to rapid communication and public health action. This included (a) Assay result and automated alerts, (b) POC operators called the positive results hotline, details were collected, (c) Information was relayed to program clinical governance, clinicians, public health pathologists/senior scientist in <2 hours, (d) Public health response initiated as required.

respiratory syncytial virus, chlamydia and gonorrhea). Programmatic requirements include real-time information on the test results (date/device/type/batch number, result/operator identity/patient identity), stock control, cartridge use, machine performance, and access to QC results. These data can be collated and visualized as graphs and tables using real-time, updated data as part of continual quality management processes to support responses to abnormal out-of-limit results. Details of a real-world functional connectivity system implemented to support the Program have been described elsewhere [83].

2.6. *Key risk management system components* (**Figure 3 (d)**)

A proactive, comprehensive risk management system is the cornerstone to the provision of safe, high-quality decentralized POC testing services and patient care. Continuous quality improvement processes that include transparent and holistic internal auditing, as well as incorporating feedback from operators, personnel, patients and other key stakeholders ensures systems meet the health services risk profile and minimize patient harm.

2.6.1. *Internal evaluation/audit program - preventative, investigative and corrective actions*

A risk management system must prioritize the minimization of risk to patient safety and ensure processes conform to identified standards. Our Program has developed key quality indicators (Table 4), supported by automated alerts specific to POC testing, which are continually monitored in real-time, with formal review by a quality committee monthly [84–86].

2.6.2. *Automated real time alerts – identifying first cases in community and flagging unusual results for monitoring*

During the COVID-19 pandemic, our Program developed real-time incident alerts to ensure immediate public health responses were implemented and able to support and protect people living in remote communities. Real-time alerts included any SARS-CoV-2 positive test, the first SARS-CoV-2 positive result within a community and for two or more weak positive results within 2 weeks at the same service. These were monitored by the Program and scientific staff. Further processes, such as additional quality controls or decision support tools to support the management of a potential contamination event were also developed.

As the Program moved out of an emergency response, additional alerts of unusual results, including discordant QCs (e.g. unexpected prevalence of weak results or co-detections when using the multiplex assay) were implemented to rapidly identify deviations and proportional corrective action. Regular monitoring of negative QCs and identification of an unusual result enabled the team to immediately review patient testing, inclusive of results prior to the discordant/unusual result, positive result trends, patient symptoms, epidemiological links and any relevant diagnostic algorithms used at the site. This allowed the team to make informed assessment of the clinical significance and impact on pending or released results. If contamination was considered probable, based on environmental swabbing positivity, additional actions were requested at the site on a case-by-case basis. This included temporary cessation of patient testing, environmental swab testing, deep-cleaning and replacement of equipment and consumables.

Continuous monitoring and evaluation of risks, mitigation strategies and effectiveness during the implementation of decentralized POC testing provides the opportunity to improve tests/activities, optimize interventions and enhance equity of access for vulnerable populations.

3. Conclusion

In recent years, the world has witnessed extraordinary increases in market demand and technological advances for decentralized POC testing for infectious disease. The First Nations Molecular POC testing Program across rural and remote Australia has demonstrated its critical role in providing rapid results, facilitating timely treatment and public health responses, and reducing associated morbidities. This experience has provided us with important insights into the unique quality considerations of decentralized POC testing in primary health care, shared in this Perspective. A broad range of complementary expertise is needed to meet the needs of a range of decentralized POC testing models, requiring specialists in both centralized medical testing and decentralized POC testing. A flexible, fit-for-purpose quality framework is needed to not only to adapt to different

Table 4. Quality indicators for automated tracking, reporting and review.

Quality indicator	Description
Device functionality	• Count and proportion of nonsuccessful[1] results. • Number of devices requiring repair. • Number of device checks overdue.
Results under investigation	• Number of co-detections. • Proportion of positive results that are co-detections.
Monitoring for contamination risk	• Proportion of positive results with cycle threshold (CT) >35. • Proportion of positive results triggering non-negative alerts[2]. • Discordant blank MTMs. • Positive results from environmental swabbing (either routine testing or targeted testing in response to indicators above)
Connectivity functioning and verification process	• Time-to-receipt of result to POC database. • Days to e-mail notification of positive result to relevant stakeholders.
Quality control review	• Proportion of eligible sites completing monthly QC. • Number and percentage of concordant QC results. • Number and percentage of discordant QC results. • Ct results for positive QC (with acceptability thresholds).
External Quality Assurance	• External provider report. • Eligible sites that performed EQA and submitted results. • Number and percentage of discordant EQA results. • Ct values for EQA (with acceptability thresholds).
Patient identification	• Number of resolved/unresolved results. • Number of retracted results. • Number of amended results
Training and education	• Number of operators who attended theory training. • Number of operators who achieved competency/renewed competency.
Program uptake	• Number of patients tests, including by key population. • Number of sites testing.

[1]. A nonsuccessful result is defined as a result where the sample provided to the device was inadequate, or the test failed due to human error, or a technical error in the device occurred during a test; [2]. Where three patient results >35Ct are detected at one testing site in a two-week period.

settings but also contexts such as the speed of implementation during existing epidemics versus emergency responses. Adaptable frameworks must consider clinical and cultural governance, real-world resources and operational capabilities, adaptation of workflow and processes to ensure specimen and result integrity. Although the experiences shared here are centered around rural and remote care, most of these principles can be applied to services in urban centers, perhaps serving people for whom conventional healthcare structures and pathways are not suitable. We hope that by sharing our lessons learned in this specialist field, together we can maintain this incredible momentum and inspire new opportunities that realize the full benefits of POC testing and achieve equitable access to all.

4. Expert opinion

4.1. Adaptable, inclusive, culturally responsive and fit-for-purpose frameworks across the POC testing pipeline – paving the way to equitable access

POC testing for infectious disease can help close the gap for numerous critical, unmet health care needs of vulnerable communities. The world is uniquely placed to leverage recent momentum in POC technology demand, development and access and maximize its clinical and public health benefits. However, to realize the full potential and global impact of POC testing will require a significant and collective shift in our approach to the frameworks, policies and practice under which this technology sits. While this paper shared our Perspective on unique elements underpinning quality POC testing in rural and remote communities in Australia, the need for adaptable, inclusive, and fit-for-purpose frameworks can equally be applied across the entire pipeline of POC testing – from clinical use case and design, development, registration, accreditation, financing, and implementation.

Underpinning the inception, development and implementation of any POC test for infectious disease should be meaningful collaboration with vulnerable populations. Structures that ensure vulnerable populations are engaged throughout builds strong, trusted relationships and advocacy champions, while providing the opportunity to maximize clinical relevance and adoption at the local level. Inclusive partnerships facilitate knowledge, protocol, sample and data sharing, needed to co-create POC tools best suited to community need. Community leadership and cultural governance within a human-centered approach supports the means for self-reliance and determination, and an opportunity to influence the very structures and determinants at the root cause of vulnerability.

Multistakeholder partnerships are essential to co-develop specifically designed, fit-for-purpose POC testing regulatory frameworks, including novel financing solutions such as public/private partnership models to incentivize and support investment. Multidisciplinary teams are required to develop flexible and streamlined POC testing regulation and approval pathways, such as recognition of low complexity devices to support scale up and adoption in remote or resource-limited settings. Bespoke

POC testing accreditation models must be tailored to effectively meet the real-world needs to support adoption in remote or resource limited settings. Broad and inclusive expertise in decentralized POC testing is required to successfully develop sustainable and adaptable financing models that recognize the need to fund workforce, connectivity and quality assurance as well as the POC testing equipment and consumables. Effective, inclusive multistakeholder partnerships are also required to co-create training and accreditation pathways for the POC testing workforce to support the sustainable implementation of POC testing for infectious disease in primary health care. Knowledge sharing across sectors with synergistic skills is critical to facilitate the identification of solutions to overcome perceived barriers, often created within discipline or expertise silos.

It is one year since the 76th World Health Assembly Inaugural Diagnostic Day recommended all countries adopt national diagnostic strategies, inclusive of POC testing. To meet this goal, our next challenge is to think creatively and together build adaptable, inclusive, culturally responsive and fit-for-purpose frameworks that ensure equitable access to POC testing for infectious disease for all.

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