Emerging technologies in point-of-care molecular diagnostics for resource-limited settings

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Emerging molecular technologies to diagnose infectious diseases at the point at which care is delivered have the potential to save many lives in developing countries where access to laboratories is poor. Molecular tests are needed to improve the specificity of syndromic management, monitor progress towards disease elimination and screen for asymptomatic infections with the goal of interrupting disease transmission and preventing long-term sequelae. In simplifying laboratory-based molecular assays for use at point-of-care, there are inevitable compromises between cost, ease of use and test performance. Despite significant technological advances, many challenges remain for the development of molecular diagnostics for resource-limited settings. There needs to be more advocacy for these technologies to be applied to infectious diseases, increased efforts to lower the barriers to market entry through streamlined and harmonized regulatory approaches, faster policy development for adoption of new technologies and novel financing mechanisms to enable countries to scale up implementation.

KEYWORDS: in vitro diagnostics • infectious diseases • molecular diagnosis • point-of-care • resource-limited settings

Diagnostic tests are critical for effective patient management and disease control, but they are undervalued compared with drugs and vaccines with far less being spent on research and development [1]. The problem has been most acute in resource-limited settings where overreliance on syndromic management and presumptive treatment has resulted in the neglect of laboratories [2]. In recent years, there has been a growing recognition that sub-standard laboratory services have become the ‘Achilles’ Heel of Global Health’ [3]. Whereas medicines might be available, patient access to appropriate therapy is often dependent on tests capable of delivering an accurate diagnosis in a timely manner. Although increased investment in diagnostic services in developing countries is now recognized as a priority by the international donor community, for patients outside of major urban centers the lack of access to a functioning laboratory is a serious barrier to care. Easy-to-use rapid tests are needed that can be performed at the point-of-care (POC) without referral to a centralized laboratory [4].

Whereas some simple rapid tests may not be as highly sensitive as their laboratory-based counterparts, the increased accessibility of POC tests provides considerable benefit for patient management and disease control [5].

The introduction of simple rapid diagnostic tests has dramatically improved disease control and patient care for infections such as HIV and malaria. The rapid POC HIV tests are lateral flow immunochromatographic devices that can be used to detect HIV antibodies in a finger-pricked blood sample and sensitivities and specificities of >99% can be achieved when compared with laboratory-based tests [4,6]. The rapid malaria tests detect malarial antigen in blood from patients with fever with high sensitivity and specificity [7,8]. These POC tests are inexpensive (US$0.5–1.00), easy to use and give a visual readout within 20 min.

Unfortunately, there are many infections for which satisfactory POC tests are not yet available in resource-poor settings. Successful immunochromatographic lateral flow technologies require diagnostic targets that are present
in high concentration in specimens, such as antigen or antibodies in blood. A limitation of antibody detection tests is that they cannot be used to distinguish active disease from past or previously treated infection. Hence, treatment cannot be given based on serologic test results alone [9]. Antigen detection offers an alternative approach, but, with the exception of malaria tests, these types of tests often suffer from low sensitivity as the antigen target is not present in sufficient quantity in specimens such as blood or urine.

Molecular technologies, either with amplification of nucleic acids or without, offer higher sensitivity and specificity than serological tests, but they are generally performed in a laboratory with sophisticated equipment and highly trained personnel. In recent years, novel rapid detection platforms and a range of isothermal amplification techniques have been developed that do not require thermocycling, making it easier to adapt for use in resource-limited settings. There are excellent review articles on the details of these technologies, which will not be repeated here [4,10-16].

In this article, we identify infectious diseases in developing countries that would benefit from a POC molecular test, the potential impact of such tests and highlight barriers that may hinder their development and entry to the market for widespread use. Mention or depiction of any specific product or commercial enterprise does not imply endorsement or recommendation by the authors.

Need for POC molecular diagnostic tests
Diagnostic tests are used to assist treatment decisions, to screen for infectious disease in asymptomatic persons and for surveillance, an application which has increased in importance for some previously neglected diseases due to renewed efforts by WHO and others to eliminate them. A further emerging need is detection of drug resistance where standard drug regimens are no longer effective, which for some diseases such as tuberculosis (TB) is threatening to destabilize efforts to control the disease [17]. Priorities for new molecular diagnostics for resource-limited settings are those which shall have the highest impact on individual and public health. POC molecular tests are needed to improve the specificity of syndromic management, to monitor progress toward disease elimination and to screen for asymptomatic infections with the goal of interrupting disease transmission and preventing long-term sequelae.

Table 1 presents a selection of diseases and syndromes for which POC molecular tests are needed, some of which are described in more detail below. Table 2 presents some examples of existing molecular tests.

HIV
WHO and UNAIDS have committed to putting 15 million people living with HIV on treatment and to eliminate new HIV infection in infants by 2015 [18]. Expanding access to HIV treatment and eliminating mother to child transmission of HIV in the developed world is possible where there are robust laboratory infrastructures able to utilize a wide range of molecular techniques to determine treatment eligibility through a CD4 count, to monitor HIV viral load and provide HIV diagnosis for infants less than 18 months of age. In the developing world, there are major barriers to scaling up such interventions. For adults, the use of rapid tests to detect antibodies to HIV allows the diagnosis of HIV to be made. However, infants born to HIV-positive mothers carry their maternal antibodies up to 18 months of age and a nucleic acid amplified test is required to detect virus in a blood sample for the definitive diagnosis of HIV. Studies have shown that mortality and clinical outcomes are worse in younger patients and those with advanced disease at the time of HIV treatment initiation, highlighting the importance of early diagnosis and treatment [19,20]. For HIV patients already on treatment, less than 30% in the developing world have access to a viral load assay. Whereas in developed countries monitoring viral load is considered routine, lack of access to such tests in developing countries prevents patients from knowing if their treatment is effective and when a change in drug regimen is needed to prevent deterioration of their condition and the emergence of drug resistance. Through donor funding, a robust pipeline of POC molecular technologies are now ready for market entry [16,21].

Tuberculosis
With an estimated global prevalence of 12 million and annual mortality of 1.3 million, TB is primarily a disease of developing countries and the most frequently recorded cause of adult death in some African countries [22,23]. It is an aerosol-borne disease and control depends on detection and treatment of infectious pulmonary cases. It is a difficult disease to detect, particularly in the early stages and of the estimated 8.6 million new cases reported in 2012, WHO estimates that 3 million were missed by national notification systems [24].

Diagnosis depends on detection of Mycobacterium tuberculosis bacilli in samples collected from suspected patients. For pulmonary TB, the sample of choice is expectorated sputum. Traditional methods of diagnosis such as smear microscopy and chest radiography have insufficient sensitivity and specificity and culture requires up to 6 weeks for a result. Molecular methods are now used in developed countries, but the cost and requirement for laboratory infrastructure and skilled technical staff have prevented their adoption in low-resource settings. It has been estimated that if a single-visit test that was 100% accurate was widely implemented 625,000 lives could be saved each year and a test with 85% sensitivity and 97% specificity might save 392,000 lives [25].

A major challenge to test development is the complex sample matrix, which is often very viscous and may contain compounds that inhibit enzymes used for nucleic acid amplification. Recently, a PCR test with integrated sample extraction was endorsed by WHO [26]. The GeneXpert assay for tuberculosis (Xpert TB/RIF test, Cepheid Inc., Sunnyvale, CA, USA) has been found to be sensitive and easy to use [27], but concerns about cost, the need for a steady electrical supply and, in some regions, air conditioning are likely to restrict its
### Table 1. Point-of-care molecular diagnostics needed in resource-limited settings and their potential impact.

<table>
<thead>
<tr>
<th>Diseases/syndromes</th>
<th>Rationale for NAATs</th>
<th>Impact of POC NAATs</th>
<th>Ref.</th>
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<tbody>
<tr>
<td><strong>Diagnostics for screening or early case detection</strong></td>
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<tr>
<td>Early infant diagnosis of HIV</td>
<td>Diagnosis of HIV in infants requires virus detection as infants carry their maternal HIV antibodies for 12–18 months. Delay in diagnosis leads to increased mortality</td>
<td>A test with 90% sensitivity, 90% specificity and minimal laboratory infrastructure requirements could save ~180,000 DALYs if 5% of the targeted population has access to treatment, and 2.5 million DALYs could be saved if 100% of the population has access to treatment</td>
<td>[4]</td>
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<tr>
<td>TB</td>
<td>Smear microscopy is insensitive. Culture facilities not commonly available and takes 4–6 weeks</td>
<td>A rapid diagnostic for TB requiring no laboratory infrastructure, with at least 85% sensitivity for smear-positive and smear-negative cases, and 97% specificity, could directly or indirectly save ~400,000 lives annually</td>
<td>[25]</td>
</tr>
<tr>
<td>** Syndromes **</td>
<td></td>
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<tr>
<td>Febrile illness in children</td>
<td>Multiple causes with low concentration of pathogens in blood</td>
<td>A multiplex molecular POC test for the detection of common causes of fever in blood samples</td>
<td></td>
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<tr>
<td>Acute lower respiratory infections</td>
<td>Culture and antigen detection are insensitive. Serology can only give a retrospective diagnosis</td>
<td>A new diagnostic test for bacterial ALRI with at least 95% sensitivity and 85% specificity accompanied by greater treatment access and minimal laboratory infrastructure requirements could save ≥405,000 adjusted lives. A new diagnostic for severe ALRI would also bring significant benefit provided access to effective hospital care is increased globally</td>
<td>[31]</td>
</tr>
<tr>
<td>Genital discharge due to chlamydial and gonococcal infections</td>
<td>Antigen detection insensitive and antibody-based tests cannot be used to distinguish between active and past infection</td>
<td>A new diagnostic with 85% sensitivity and 90% specificity for both gonorrhoea and chlamydia that requires minimal laboratory infrastructure could save ~3 million DALYs, avert &gt;12 million incident gonorrhoea and chlamydia infections. A test that requires no laboratory infrastructure could save ~4 million DALYs, avert &gt;16.5 million new gonorrhoea and chlamydia infections, and prevent &gt;212,000 HIV infections a year</td>
<td>[35]</td>
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<tr>
<td>Sepsis</td>
<td>Multiple causes in critically ill patients where rapid intervention is required</td>
<td>Not known</td>
<td></td>
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<tr>
<td><strong>Diagnostics for monitoring progress toward disease elimination</strong></td>
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<td>NTDs targeted for elimination</td>
<td>Lower pathogen load in specimens as disease prevalence deceases</td>
<td>POC molecular tests will allow mobile teams to assess progress toward elimination and impact of interventions. Multiplex POC tests will allow the detection of multiple targets from the same specimens saving time and effort</td>
<td>[41]</td>
</tr>
</tbody>
</table>

ALRI: Acute lower respiratory infection; DALY: Disability-adjusted life year; NAATs: Nucleic acid amplification tests; NTDs: Neglected tropical diseases; POC: Point-of-care; TB: Tuberculosis.
Several new POC molecular technologies for TB diagnosis are in development and clinical performance studies to assess their accuracy are awaited. In addition to diagnosis, molecular tests have the potential to identify polymorphisms in the TB genome that predict treatment failure due to drug resistance. Due to the complexity of TB treatment regimens and the large number of alleles that need screening, some clinics are looking to next-generation sequencing as a means of assessing drug susceptibility. For low-resource settings, sensitivity is sacrificed due to the requirement for more simple technology that is affordable and accessible. The Xpert TB/RIF test incorporates a test for resistance to a single drug (rifampicin), which in some settings is taken as a predictor of treatment failure but in others prompts referral of the patient for further testing.

Syndromes

Acute lower respiratory infection (pneumonia)

Acute lower respiratory infections are the leading cause of death in young children, each year killing an estimated 1.2 million children in the first 4 years of life [30]. There are many causes of acute lower respiratory infections, and clinical presentation is non-specific. A molecular assay targeting all the major causes of pneumonia would be useful. At lower levels of the healthcare system, it may be sufficient to have a simple POC molecular test that can distinguish between bacterial and viral pneumonia so that the health provider can prescribe antibiotics only when needed. It has been estimated that a new test to identify bacterial pneumonia that is 95% sensitive, 85% specific and requires only minimal infrastructure could save 152,000 lives each year, if accompanied by effective treatment [31]. A POC molecular test would allow for more rational use of antibiotics, lowering the risk of induction of antibiotic resistance.

Fever

Fever in children is a cause for concern, as it may indicate a condition where rapid intervention is required to prevent further complications or death. Major causes of fever in developing countries include dengue, typhoid, malaria, leptospirosis and scrub typhus [32]. The etiology of febrile illness in children...
is complex as causes may vary by geographical location and season, environmental factors such as rainfall and temperature or the presence or absence of vectors such as mosquitoes or mites are also influential. Implementation studies with the rapid malaria tests suggests that fever previously assumed to be due to the malaria parasite often has other causes [33,34]. To aid treatment decisions, there is a need for multiplex molecular tests for use at the POC that identify the major causes of fever.

Genital discharge caused by sexually transmitted infections
Sexually transmitted infections (STIs) are largely asymptomatic, but early detection and treatment is needed to prevent long-term reproductive complications and to interrupt the chain of transmission within a community [35]. Molecular tests are preferred as antigen detection is insensitive and serological antibody-based tests cannot be used to distinguish active from past infection. There are many laboratory-based molecular tests for the screening of genital chlamydial and gonococcal infections. However, the highest STI disease burden is in resource-limited settings that do not have access to these molecular assays [36]. In recent years, a number of isothermal amplification techniques have been developed and applied to the detection of STIs. Should these prove suitable for use at POC in resource-poor settings, they may provide increased access treatment and so play a role in reducing disease burden [37].

Sepsis
Sepsis is a serious medical condition resulting from a profound immune response to a severe infection. It is sometimes referred to as ‘blood poisoning’ and as with other syndromes there are multiple causes, including Gram-negative and Gram-positive bacteria [38,39]. A multiplex molecular test that could be used at the POC to distinguish between bacterial and viral causes would lead to evidence-based treatment. In addition to improving patient outcomes, the reduction in inappropriate prescribing of antibiotics would slow down the emergence of resistance.

Neglected tropical diseases targeted for elimination
Mass drug administration is the main control strategy for trachoma, lymphatic filariasis, onchocerciasis, schistosomiasis, ascariasis, trichuriasis and hookworm infection. These diseases are targeted for elimination by 2020 with support from WHO, World Bank and a consortium of donors and pharmaceutical companies [40]. After multiple rounds of mass drug administration, the prevalence of disease decreases with a concomitant decrease in the pathogen load with the result that detection by microscopy will no longer be sufficiently sensitive [40]. Antigen detection or molecular tests are needed to detect remaining cases and monitor progress toward elimination. These tropical diseases are often co-endemic, with multiple infections found within communities and even within the same individual. It is therefore more cost-effective to coordinate monitoring and post-elimination surveillance using multiplex nucleic acid amplification tests that combine detection of multiple pathogens from a single sample would be advantageous [41,42].

For other neglected disease such as Human African trypanosomiasis and visceral leishmaniasis, the problem is different as the treatment is toxic and there is currently no effective measure of cure [43]. A POC test to monitor treatment and indicate when treatment should stop would be most useful for patient management [44,45].

Malaria elimination
The introduction and rapid scale up of immunochromatographic tests for malaria diagnosis has shown how increased access to effective diagnostics permits evidence-based treatment decisions. Due to the availability of low cost rapid lateral flow devices nucleic acid-based tests, POC are not required for clinical decision-making in high burden settings. However, as progress is made toward elimination there will be a need for molecular tests to detect infection in low prevalence settings and to monitor progress toward elimination [46].

Resistance detection
Antibiotic resistance is a serious and growing threat to efforts to control infectious disease and resource-limited settings are highly vulnerable to the emergence and spread of disease that cannot be cured by standard drug regimens [47–49]. POC molecular tests that combine diagnosis of the infection with predicted susceptibility to antibiotics will allow early initiation of appropriate treatment. Molecular tests are well suited to this task as resistance is frequently due to genetic mutations, either polymorphisms within the genome or horizontal transfer of resistance conferring mobile elements such as plasmids. Currently, some array and bead-based molecular platforms are being applied to the detection of drug resistance, but few have been commercialized [50–52].

Technical considerations
Healthcare in resource-limited settings is often delivered in challenging environments and POC tests require a robustness that is not needed in industrialized countries [53,54]. Table 3 summarizes the various challenges in terms of environmental, facility and human resource requirements. Most of the molecular assays require a constant source of electricity and alternative solutions are required [55–57]. Heat stability is a major issue for molecular tests, in which a variety of enzymes central to the amplification process may be adversely affected by tropical climates where tests may be transported and stored in temperatures exceeding 40°C. Conversely, in some settings, temperatures can drop well below freezing and products may be subjected to repeated cycles of freezing and thawing. Air conditioning should not be a prerequisite for the storage and operation of the test and devices that incorporate enzymatic reactions sensitive to temperature should undergo exhaustive stability testing to determine their operating parameters. High humidity is also problematic for some technology and careful attention should be paid to construction of electrical...
Ease of use is a high priority in POC molecular tests in resource-limited settings. The ideal are ‘sample in-answer out’ platforms that require minimal training and no specialist skills. Results should be unequivocal with clear indicators of quality and, if for diagnosis, should be available in time to allow same day initiation of treatment. Labeling and instruction for use must be appropriate for the user of the test and in languages easily understood by the practitioner and others in the supply chain. Training needs should be ascertained for the test user and any health workers who shall need to interpret the result.

A further consideration is data transmission and recording of results. Many of the new devices incorporate wireless or mobile phone technology, but little attention has so far been paid to who will receive the data and how it will be received, stored and made available to the health worker and their patients for future consultations.

Safe disposal of waste from testing is also a challenge for POC tests. Devices and consumables should incorporate materials that can be discarded with minimum damage to the environment. Infected materials require safe disposal to protect the public and ‘used’ test devices may need transporting in a safe manner to a site with appropriate disposal facilities.

Testing at POC using simple to perform rapid tests that do not require referral to a laboratory can greatly increase access to appropriate healthcare for those diseases. They shall have most impact in setting where laboratory-based tests are difficult to access by the population. However, decentralized testing poses challenges where people using the tests may lack the experience or capacity to implement quality assurance measures. To assure quality, it shall be necessary to monitor both the quality of the devices through post-market surveillance and to monitor the performance of the end users, with appropriate training for those found lacking.

### Innovative technologies for use at POC

Molecular diagnosis of infectious diseases relies on the detection of characteristic genetic signals within a sample that identify the pathogen to a high degree of certainty. The ability to amplify specific fragments of nucleic acids allows very sensitive detection but access to molecular diagnostics in developing countries remains limited by the lack of laboratory facilities and technical personnel capable of supporting such technology. While progress has been made in target discovery facilitated by next-generation sequencing technologies, the development of robust and affordable detection platforms has lagged behind. In addition to detecting the amplified nucleic acids, the device may need to incorporate technology to concentrate and purify samples. Filtration has been shown to be an effective alternative to centrifugation, as is used in the Xpert TB/RIF test (Cepheid Inc.), where following chemical disruption samples are exposed to a membrane where the bacteria are captured but smaller particles and fluids pass through and are thus removed. Following this purification step, the remaining sample is transferred using automated plungers and valves to various chambers within an integrated cassette where they are first exposed to sonication to disrupt the cells and release the DNA before being mixed with the amplification and detection reagents. The system has been shown to be highly effective with complex samples such as sputum; however, the sophisticated manufacturing processes and materials required in construction of the cassettes are costly, reducing the affordability of the technology. The emergence of nanoparticle and microfluidic technologies offers alternative mechanisms for sample handling. There have been a number of promising studies using magnetized nanoparticles to purify...
samples, which offer efficient capture due to their high surface-to-volume ratio while being amenable to manipulation in microfluidic systems [10,59]. Nanoparticles have also been used to facilitate specific detection and differentiation of multiple nucleic acid targets [60-64]. An exciting development is the development of nanosensors that can detect nucleic acids without an amplification step [65]. Sample handling for tests to be used at the POC should be minimal and microfluidic devices offer ease of use in addition to reduced costs due to the small volumes employed [66-71].

While there are promising technologies in the pipeline that may contribute to the production of affordable easy-to-use diagnostic devices, such tests have yet to reach the market in developing countries.

**Expert commentary**

POC detection platforms that offer rapid detection without recourse to a laboratory are being developed but with little commercial incentive research on the neglected diseases is mainly undertaken in the not-for-profit and academic sectors. Many of the innovative molecular techniques have been published in peer-reviewed journals, but few have been applied to detection of infectious diseases and few have been commercialized and marketed [14,72]. Companies often felt that there is no real motivation to support the development of diagnostic products for infectious diseases due to the perceived low return on investment. The market for tests to detect infectious diseases at the POC is poorly understood, both in terms of volume and pricing and there is currently little information available to indicate potential sales of such tests in developing countries. Even when a company has an interest in developing diagnostics for infectious diseases, the path from product development to delivery for an in vitro diagnostic typically takes between 15 and 20 years. Following the development process, a product faces many hurdles before it becomes available in a laboratory or clinic in a resource-limited setting [73]. Many test developers are small companies that do not have capacity to market a device in the complex markets of Africa or Asia [74]. Distributors and training and support networks must be established, and products must be registered. Approval may be required from National Regulatory Authorities (NRA), which is a costly and lengthy process that can delay the product launch for years [75]. Regulatory processes are not harmonized and fresh applications may need to be prepared for each country where the device is to be sold. Tests considered a potential risk to individual or public health must provide evidence of their scientific validity and analytic and clinical performance. For tests designed for use at the POC, studies must be undertaken in settings representative of the site of use and not in a centralized reference laboratory. Companies may spend years finding sites in developing countries, negotiating clinical trial protocols, waiting for ethical approval and then doing the study. Duplication is common. The first company to launch a POC CD4 test has done more than 60 trials, causing delays in patient access and pushing up prices. This is a huge disincentive to innovation as, even if a diagnostic test is available today, it would take another 5–10 years for national policy to be made for adoption and for widespread implementation.

In recognition of these barriers to market entry, international efforts aimed at reducing the barriers and accelerating uptake of POC tests are being piloted. UNITAID, a not-for-profit organization hosted by WHO, is funding the London School of Hygiene and Tropical Medicine, the Clinton Health Access Initiative and Médecins Sans Frontières to develop consensus on target product profiles, including performance expectations, and to conduct field evaluations of new POC molecular tests for CD4 test, HIV viral load assays and early infant diagnostic tests for HIV using standardized protocols. A network of competent laboratory and POC sites has been selected to conduct these studies. Sites were selected not only for their competence in performing diagnostic evaluations, but also because they have access to appropriate target populations. Study design and protocols have been agreed by an international panel of experts and the sites will be subject to external monitoring to ensure trial quality. The sites are available to manufacturers for performance studies of new tests to gather data for regulatory submissions. Once studies are completed, the data shall be reviewed jointly by a panel of international experts, and representatives from NRA. Companies shall then be able to use the data for regulatory approval. By creating a body of data from high-quality, independently monitored studies with joint regulatory review of results, the necessity to duplicate studies in individual countries may be removed. The selected study sites and agreed protocols may be viewed on the International Diagnostics Centre website created by London School of Hygiene and Tropical Medicine [76].

Other efforts to streamline and harmonize regulatory approval processes include the work of the International Medical Devices Regulatory Forum. A pilot program is underway for a single audit program for assessing the manufacturers’ quality management systems [77]. By having agreed standards of inspection, a single audit can be undertaken by a recognized competent organization rather than individual NRAs auditing the site themselves and duplicating work done by others, a costly process that delays market entry. Regional Working Parties are also working toward reducing the delays and costs of regulating diagnostic devices in resource-limited settings, including an Asian Harmonization Working Party [78], the Pan African Harmonization Working Party [79] and the Latin American Alliance for the Development of *In Vitro* Diagnostics [80].

A number of donors have worked with WHO and other partners to substantially reduce the price of the XpertMTB/RIF assay to detect TB and rifampicin resistance for countries in the developing world [81]. More innovative financing for POC molecular tests are needed to enable countries to have greater access to diagnostics and treatments for HIV/AIDS and TB in low-income countries.

**Five-year view**

Technological advances are creating new opportunities for the delivery of healthcare in developing countries through
decentralized diagnosis at the point at which care is provided. To exploit these opportunities and create diagnostic services that are affordable and accessible to populations in resource-limited setting, robust POC devices are needed that can be used by unskilled personnel to give unequivocal results in a short time. The priority for product development should be based on clinical need and the opportunity to interrupt transmission and eventually eliminate the disease as a public health problem.

Once developed, access to the market should be accelerated by streamlining clinical evaluation and harmonizing regulatory approval processes to remove unnecessary duplication and delay. An urgent priority is to resolve how regulatory science can keep pace with rapid technological advances, as novel detection platforms are created and innovative data manipulation and reporting technology and software are incorporated in the devices. Countries need to develop technology assessment programs to facilitate faster policy development for adoption of novel technologies. Quality assurance schemes are needed for ensuring the quality of POC molecular tests and to monitor the quality of testing to maximize the impact of POC molecular tests.

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**Key issues**

- Many molecular technology platforms have been developed that could be used to improve the diagnosis of major infectious diseases and for monitoring progress toward disease elimination.
- More advocacy is needed to ensure that molecular technologies are applied to the detection of infectious diseases and antimicrobial resistance in resource-limited settings.
- Despite significant technological advances in the development of molecular diagnostics for resource-limited settings, many challenges remain in its delivery.
- Global and regional efforts are needed to lower barriers to market entry through streamlined clinical evaluations and harmonized regulatory approaches.
- Countries need to develop technology assessment programs to facilitate faster policy development for adoption of novel point-of-care molecular technologies.
- Novel financing mechanisms are needed for countries to scale up implementation and increase access to point-of-care molecular tests in resource-limited settings.

**References**

Papers of special note have been highlighted as: of interest


- The authors discuss the potential role of point-of-care (POC) tests in HIV and tuberculosis control programs. They consider advantages and disadvantages of POC testing compared with laboratory-based tests and existing diagnostic strategies, and highlight the need for integrated diagnostic services.


doi: 10.1586/14737159.2014.915748
• This study discusses issues pertaining to the selection and implementation of new tests for HIV and tuberculosis in low-resource settings with a view to maximizing impact and sustainability. It recognizes that stakeholders have a variety of needs and constraints and so considers the topic from different perspectives.
56. Peeling R, McNerney R. Increasing access to diagnostics through technology transfer and local production. WHO; Geneva, Switzerland: 2011
60. AHWP. Available from: www.ahwp.info/ [Last accessed 12 January 2014]
64. doi: 10.1586/14737159.2014.915748
66. Peeling R, McNerney R. Increasing access to diagnostics through technology transfer and local production. WHO; Geneva, Switzerland: 2011
70. AHWP. Available from: www.ahwp.info/ [Last accessed 12 January 2014]