Access to point-of-care testing (POCT) improves patient care, especially in resource-limited settings where laboratory infrastructure is poor and the bulk of the population lives in rural settings. However, because of challenges in rolling out the technology and weak quality assurance measures, the promise of human immunodeficiency virus (HIV)–related POCT in resource-limited settings has not been fully exploited to improve patient care and impact public health. Because of these challenges, the Joint United Nations Programme on HIV/AIDS (UNAIDS), in partnership with other organizations, recently launched the Diagnostics Access Initiative. Expanding HIV programs, including the “test and treat” strategies and the newly established UNAIDS 90-90-90 targets, will require increased access to reliable and accurate POCT results. In this review, we examine various components that could improve access and uptake of quality-assured POC tests to ensure coverage and public health impact. These components include evaluation, policy, regulation, and innovative approaches to strengthen the quality of POCT.

**Keywords.** point-of-care testing; access; quality assurance; policy; evaluation.

The Joint United Nations Programme on HIV/AIDS (UNAIDS), together with global and regional partners, launched the Diagnostics Access Initiative (DAI) to ensure increased access to quality diagnosis so that people infected with human immunodeficiency virus (HIV) can be effectively linked to quality treatment services [1]. The DAI emphasized the new UNAIDS targets of 90-90-90, which ensure that 90% of people living with HIV know their status, and 90% are on antiretroviral therapy (ART) with 90% exhibiting viral load suppression [2]. Affordable point-of-care testing (POCT) will play a critical role in ensuring these targets are achieved.

In public health, rapid and accurate detection of infections are critical for prevention and effective management of patients. Several interventions have demonstrated the importance of rapid diagnosis using POCT. For example, using a POCT device, the Alere PIMA CD4 showed increased retention of patients in care and increased ART initiation compared with the standard flow cytometric CD4 testing [3]. Similarly, rapid POCT of syphilis in pregnancy followed by administration of appropriate antibiotics can prevent thousands of fetal and neonatal deaths in developing countries each year [4, 5]. Use of sensitive and rapid laboratory-based and near-POC tuberculosis detection and drug susceptibility testing methods have been shown to decrease time to diagnosis as well as initiation of treatment in some settings [6–8]. In malaria programs, use of rapid and accurate POCT significantly reduces overtreatment of non-malarial cases with antimalarials such as occurs with presumptive and empiric treatment [9, 10].

To provide equitable access to quality HIV prevention and care services, robust diagnostic tools capable of rapid quality testing near patient care, such as POCT, are clearly needed. Point-of-care devices have the potential for great impact in global health programs but have many challenges (Table 1). The availability of new technologies has resulted in rapid development of new POCT devices, leading to additional challenges on how best to use them, including remote geographic locations, suitability of technologies, and uptake and quality assurance (QA) of testing.

The goal of this article is to explore the role of HIV-related POCT in providing access to quality patient care. We review lessons learned so far, including successes and challenges that can be applied to the successful uptake of HIV-related POCT. In addition, we provide considerations for appropriate implementation of POCT in resource-limited settings (RLSs) to ensure sustainable access to quality diagnostic testing to improve patient care.

**DEFINITION OF POCT**

POCT has a wide range of definitions depending on technology, functions, operational characteristics, geography, and whether it is performed in a facility or community setting [16]. The College of American Pathologists defines POCT as “tests that are
designed to be used at or near the site where the patient is located, that do not require permanent dedicated space, and that are performed outside the physical facilities of the clinical laboratories” [17]. The commonalities drawn from the multiple definitions are that POCT should increase patients’ access to diagnostic testing, should be performed close to the patient, and should provide results within a short turnaround time.

### IMPACT AND CHALLENGES OF ACCESS TO POCT IN GLOBAL HEALTH PROGRAMS

Quality-assured POCT will play a major role in the success of global health programs, including HIV/AIDS, tuberculosis, malaria, and syphilis. A summary of the impact and challenges of POCT in some global health programs is shown in Table 1.

#### Table 1. Impact and Challenges of Point-of-Care Testing in Global Health Disease Programs

<table>
<thead>
<tr>
<th>POCT</th>
<th>Author/Source</th>
<th>Study Design</th>
<th>Global Health Impacts/Outcomes</th>
<th>Major Challenges*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 testing</td>
<td>Jani et al [3]</td>
<td>Observational study with reduced pretreatment patient loss</td>
<td>Increased from 12% to 22% of patients initiating ART</td>
<td>Reduction from 64% to 33% of patients lost to follow-up</td>
</tr>
<tr>
<td>EIDb</td>
<td>Jani et al, [12]</td>
<td>Blinded cross-sectional study</td>
<td>Reduction of turnaround time for infant results</td>
<td>Improved early initiation and boosted coverage of infected infants on ART with better outcomes</td>
</tr>
<tr>
<td>Other POCT or near-POCT</td>
<td>Xpert MTB/RIF for TB</td>
<td>Churchyard et al [14]</td>
<td>Cluster-randomized trial to assess impact of Xpert MTB/RIF for TB</td>
<td>49% increased detection rate of TB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Boehme et al [6]</td>
<td>Feasibility, accuracy, and implementation study in RLSs</td>
<td>Identification of drug resistance TB in patients in RLSs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D’Acremont et al [15]</td>
<td>Review study supporting moving from presumptive malaria treatment</td>
<td>Increased uptake and coverage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ART, antiretroviral therapy; EID, early infant diagnosis; HIV, human immunodeficiency virus; MTB, Mycobacterium tuberculosis; POCT, point-of-care test; RDT, rapid diagnostic test; RIF, rifampicin; RLS, resource-limited setting; TB, tuberculosis; VL, viral load.

* Due to similarities of some challenges across POCTs, we used numbers to indicate where they apply in the major challenge column.

b Some EID and VL POCTs have CE (European Conformity) marking and are undergoing World Health Organization prequalification and/or field evaluations, with their likely impact or outcomes noted.
FACTORS FOR IMPROVED UPTAKE OF POCT

Because POCT technology has the potential to leap-frog laboratory diagnostics, similar to the experience of cellphones with landlines, it would require careful attention to identify suitable POCT to maximize their impact. For instance, POCT during the recent Ebola crisis in West Africa would have allowed quick diagnosis and triaging of infected cases for isolation and prevention of further transmission compared with laboratory diagnosis, which took several weeks [18]. By contrast, a near-POCT, Xpert MTB/RIF, appeared to show no difference in reduction of mortality of patients with tuberculosis at 6 months compared with laboratory microscopy-based detection [14]. However, early identification of resistant tuberculosis using Xpert MTB/RIF can help prevent further transmission of resistant strains. Several factors can influence the uptake and access of POCT. These factors are closely interlinked and include role of clinicians, national policy, role of academic and regulatory institutions, evaluation requirements, and regulation (Supplementary Figure 1).

Role of Clinicians in the Uptake of POCT

POCT is reshaping the delivery of healthcare in RLSs. For the clinician, the ability to perform a diagnostic test and immediately use the results to inform subsequent clinical management of the patient is a major advance in both clinical care and cost [16]. This reduces syndromic treatment by clinicians that often leads to wrong treatment or overtreatment of patients. For instance, malaria rapid diagnostic tests have been used to assist treatment with antimalarials and reduce the rate of treatment of all fevers with antimalarials, leading to huge drug waste and potential for drug shortages [15]. For the patient, the ability to obtain a diagnosis and clinical care in 1 visit is reassuring; it also saves on indirect costs (eg, patient transport cost or time lost from work) by saving the patient from having to return for results. Improved clinical patient outcomes as a result of POCT and clinical care could eventually lead to increased uptake of testing with significant impact on public health.

National Policy

The pipeline of POCT for diagnosing, staging, and monitoring HIV and other infectious diseases continues to grow [13]. Clear national policies are needed to guide the implementation of POCT in RLSs to ensure consistency, appropriate use, and QA. Unfortunately, there are no official government policies for implementation of POCT in most RLSs, and even where policies exist, they are not consistently applied. National policies should identify the appropriate department within the Ministry of Health (MOH) that will be responsible for standard regulatory issues including selection, evaluation, and placement of POCT diagnostics and postmarket surveillance (PMS). The policy should also define the approval process, procedures related to procurement, QA, and biosafety as well as human resources and training needs.

Role of Academic and Regulatory Institutions

National and international institutions will continue to play a pivotal role in advising MOH on strategies to improve the uptake of POCT by sharing policy/research findings and developing standards and policies that guide the use of POCT. Research institutions often facilitate product development and contribute preliminary evaluation data. The World Health Organization (WHO) has played a key role in assembling panels of experts to develop international norms, standards, and policies on the use of in vitro devices by member countries [19]. In the United States, the Food and Drug Administration (FDA) regularly publishes guidelines that advise and regulate the introduction and use of new diagnostic tests. There are also other institutions that, while they have no regulatory or guidance authority, can also contribute significantly to the uptake of POCT. The African Society for Laboratory Medicine (ASLM) is one such institution that could coordinate and streamline efforts among the many institutions for rapid uptake of quality POCT.

Evaluation of POCT

Once a new POCT is made available in the market by the manufacturer, it is critical to conduct an independent evaluation of its operational and performance characteristics in various settings to ensure the highest quality of testing. WHO has established a prequalification list of select POCT diagnostics for HIV and malaria that have undergone extensive evaluations at selected centers of excellence [20], and has implemented an additional policy development process for tuberculosis diagnostics [19].

Although evaluation processes for new diagnostic products vary, each typically consists of at least 3 phases prior to consideration of implementation [21, 22]: phase 1 to evaluate performance characteristics (eg, sensitivity, specificity); phase 2 to evaluate the performance of the test in field conditions where the test will be routinely used; and phase 3 to evaluate the costs and programmatic outcomes associated with routine use [16, 22]. This evaluation process will provide a reasonable indication of how the test will perform when implemented and expanded to multiple sites, as well as measure user acceptability, cost-effectiveness, and impact on public health. This is similar to new drugs or vaccines that undergo phase 1, 2, and 3 clinical trial evaluations for safety and efficacy prior to their approval; phase 4, involving ongoing studies of the vaccine or drug after it has been approved and licensed, can be likened to PMS of POCT devices to monitor performance while in use.

Independent evaluations other than that of the manufacturer are critical to informing end users’ decisions in selection of appropriate POCT technologies. Five independent evaluations of the PointCare NOW system for CD4 counting in HIV patients showed the performance to be inadequate for HIV clinical management in adults [23]. Additional lessons learned from previous POCT evaluations have demonstrated the need for coordinated evaluations and continuous PMS to inform needed decisions. The multiple concurrent evaluations of the PIMA CD4 and the...
quality issues with the Standard Diagnostics Bioline HIV-1/2 version 3.0 are 2 examples that can attest to these needs [24, 25].

Regulation of POCT
Regulatory guidance by the FDA or International Organization for Standards recommends quality management system (QMS) requirements for medical devices, including POCT devices [25]. Regulation of POCT technologies is a challenging area for most countries in sub-Saharan Africa where product registration is often slow and procedures are unclear [27]. Regulatory authorities often request documentation for a new product before its introduction into the market. At times the list of requirements for a new product is not standardized and may vary from one product manufacturer to another. Manufacturers also lack proper understanding of a country’s regulatory process and the level of detail and quality documentation required. Even after a new product may have undergone a protracted process, convening the approval body for a decision is slow and time-consuming. This delay often impedes the rapid approval of POCT that may be beneficial to patient care. Nonetheless, progress is being made; the Pan African Harmonization Working Group has been working with national regulatory authorities, ASLM, manufacturers, and other stakeholders to reduce regulatory barriers to quality-assured and safe POCT.

ENSURING QUALITY OF POCT

With increasingly large numbers of POCT being used outside the laboratory setting, and with their use involving different operators or cadres, innovative strategies are needed to monitor their quality for effective patient management. A comprehensive approach to ensure implementing quality management of POCT must be pursued [28]. It is highly recommended that a POCT QA plan to address the entire QA cycle be outlined and be part of the national policy prior to placement of POCT devices in the existing laboratory network. Several factors impacting quality include the following.

Quality Management System
A QMS that incorporates leadership, training, appropriate quality control (QC), standardized management tools, new lot validation, site supervision, and proficiency testing (PT) or external quality assessment (EQA) enables identification of facility, tester, or assay-associated errors for corrective actions and quality improvement.

External Quality Assessment
EQA is one component of a QMS and a valuable tool in the quality improvement process. Well-characterized serum or plasma PT samples from commercial vendors or reference laboratories have been used to monitor the quality of testing of HIV serology in EQA programs. This method poses logistical challenges due to cold chain requirements for these types of specimens, which, coupled with cost, make it difficult to sustain in large programs. A simple innovative technology using dried tube specimen (DTS) has been developed for QC and monitoring of HIV rapid testing and VL testing [29, 30]. The DTS technology has also been successfully expanded to other diseases including tuberculosis, malaria, and syphilis [31–33] and has been shown to be cost-effective [34]. Various PT methods and their advantages for monitoring quality of testing are summarized in Table 2.

Quality Control Specimens
DTS can also be used to prepare QC specimens (positive and negative controls) for various biomarkers mentioned above and distributed to POCT sites performing the tests [29]. Regular use of QC specimens permits instrument checks, confirms reagent quality, and verifies new kit lots while ensuring competency of the tester and accuracy of client results. To be effective, these data should be collected and reviewed regularly to assess performance of the POCT devices/reagents.

Standardized Data Management Tools
Because PT programs provide a snapshot of testing quality at a particular point in time, a comprehensive QA program should also include components designed to track routine performance prospectively. For example, standardized data management (eg, standardized HIV registers) has been proposed to monitor quality of HIV rapid testing in developing countries [28, 35], and standardized performance indicators have been proposed for mycobacteriology laboratories [36]. The data collected

Table 2. Proficiency Testing Methodologies for Monitoring Quality of Key Point-of-Care Diagnostic Testing

<table>
<thead>
<tr>
<th>PT Method (Specimen)</th>
<th>HIV</th>
<th>Syphilis</th>
<th>Malaria</th>
<th>TB (Xpert MTB/RIF)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum/plasma</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>NA</td>
<td>Refrigeration required, suitable in laboratory settings</td>
</tr>
<tr>
<td>DTS</td>
<td>+</td>
<td>NA</td>
<td>+</td>
<td>+</td>
<td>No refrigeration required; suitable for mobile unit, VCT, healthcare workers, health extension workers, and laboratory settings</td>
</tr>
<tr>
<td>DBS</td>
<td>+</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
<td>No refrigeration required; suitable in laboratory settings</td>
</tr>
<tr>
<td>DCS*</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No refrigeration required; suitable for mobile unit, healthcare worker, and laboratory settings</td>
</tr>
</tbody>
</table>

Abbreviations: +, available; DBS, dried blood spot; DCS, dried culture spot; DTS, dried tube specimen; EID, early infant diagnosis; HIV, human immunodeficiency virus; MTB, Mycobacterium tuberculosis; NA, not applicable; PT, proficiency testing; RDT, rapid diagnostic test; Rif, rifampicin; RT, rapid test; TB, tuberculosis; VCT, voluntary counseling and testing; VL, vial load.

* Limited to Xpert MTB/RIF.
with these standard tools should be regularly reviewed for errors and any necessary corrective action.

**Human Resources and Training**

A competent and adequate workforce is critical to ensure that POCT is correctly used in accessing communities/patients. Standard tools should be used to train laboratory and nonlaboratory testing personnel, as well as clinicians who will be requesting and acting upon test results [37]. Those trained on performing POCT should have a thorough hands-on training and then be assessed for competency. Successful trainees should be issued a certificate of competency valid for a specific duration. In addition to certifying POCT users, facilities using POCT should also be certified to indicate that they meet minimum requirements to conduct the particular POCT. Site certification has been successfully piloted in Cameroon for HIV rapid testing sites [38].

With POCT being used outside of a traditional laboratory setting, expansion of QA programs to monitor all testing sites would require innovative approaches. One of the obstacles is having an adequate number of trained staff. An innovative approach in which volunteer quality officers, who are compensated only during the time of their engagement, are used to provide intensive site monitoring should be explored. These trained volunteer quality officers can be tasked to collect QC and logbook data, distribute PT panels to sites and to non-laboratory testers, and provide on-the-spot corrective actions, as well as collect results and submit them to the MOH facility centrally or regionally responsible for coordinating the QA program. The volunteer quality officer innovative approach has been successfully implemented in Cameroon [38].

**Supply Chain Management**

Procurement should only include select POCT as included in the national guidelines and laboratory strategic plans. This is especially important as the procurement market in developing countries can be unregulated, coupled with donations of POCTs that are not in accordance with country needs [39]. This is often seen in many RLSs where it can be difficult to reject offers from donors, but such unplanned procurements have the potential to affect the quality of testing as a result of inadequate training or QA measures.

One of the greatest limitations of the most widely used POCT, HIV rapid test, is supply chain. This requires reliable inventory, consumption, and forecasting tools to allow for informed and planned procurement. This is critical as prolonged testing delays caused by stock-outs, for instance, of a test kit in a national HIV rapid testing algorithm can lead to the inability to follow the approved algorithm. Additionally, regional or district distribution hubs closer to end users should be encouraged.

**Implementing POCT Within the Laboratory Network System**

With the rapid expansion of POCT closer to the patient, some have argued that POCT is replacing laboratories or have started a POCT vs laboratory testing debate. On the contrary, POCT should be seen as an extension of the laboratory, and both are complementary. POCT will allow for equitable access of the population to quality diagnostic testing. The resulting increased testing volumes and sites can also burden an existing national laboratory network [40], which, if not sufficiently strengthened, may strain an already weak system. The DAI advocates for improving laboratory capacity and networks to achieve the control of the HIV/AIDS epidemic. It is clear that strong laboratory systems are needed for effective deployment of POCT (Supplementary Figure 1). Reference laboratories would eventually function as a training and supervisory hub for the POCT sites, send PT and QC materials, and analyze and review data within the QMS. POCT should be implemented as part of the existing laboratory networks, and, in some cases, may serve as a temporary backup for laboratory-based testing sites in the event of equipment malfunction or shortage of reagents.

Another innovative approach is connectivity of some POCT devices with wireless or Web-based systems that can be used to monitor and transmit QC results, error rates, and reagent consumption from POCT in peripheral locations to a central or regional laboratory, with feedback or planned corrective actions provided in real time [41]. Connectivity can enable monitoring of lot-to-lot variation, interinstrument variation, and interoperability variability, thus creating real-time information flow for use in improving on quality.

**Postmarket Surveillance**

Postmarket surveillance refers to monitoring the performance of a POCT after it has been shipped by the manufacturer to its intended recipient. This can be done through the routine monitoring of QC and performance indicators, as well as through testing of new lots as they are received in country, before they are distributed to various facilities and communities using well-characterized panels. PMS of POCT should not only be viewed as a regulatory requirement, but should also be considered a key and useful practice to monitor QA of the test. The importance of PMS was underscored when WHO removed the Standard Diagnostics Bioline HIV 1/2 3.0 Rapid HIV Test Kit from its list of approved rapid test kits and advised the recall of the underperforming batches [42]. PMS in the field provides continuous feedback that encourages accountability by manufacturers and also enables manufacturers to maintain a high standard of product quality to ensure consumer satisfaction.

**CONCLUSIONS**

POCT, when used appropriately, has the potential to transform patient care with a major impact on public health. Concerted efforts would be required to improve evaluations, regulatory processes, and workforce development for rapid uptake. Quality would remain critical as POCT is integrated into the laboratory network with innovative strategies to ensure continuous quality monitoring. Improved awareness of clinicians on relevant POCT would improve uptake for better patient management.
Supplementary Data
Supplementary materials are available at http://cid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyrighted and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes
Disclaimer. The findings and conclusions in this report are the views of the authors and do not necessarily reflect the official position of the Centers for Disease Control and Prevention (CDC).

Financial support. This work was supported by the President’s Emergency Plan for AIDS Relief through the CDC.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References