Pathology and laboratory medicine in low-income and middle-income countries 2

Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions

*Shahin Sayed, William Cherniak, Mark Lawler, Soo Yong Tan, Wafaa El Sadr, Nicholas Wolf, Shannon Silkensen, Nathan Brand, Lai Meng Looi, Sanjay A Pai, Michael L Wilson, Danny Milner, John Flanigan, Kenneth A Fleming**

Insufficient awareness of the centrality of pathology and laboratory medicine (PALM) to a functioning health-care system at policy and governmental level, with the resultant inadequate investment, has meant that efforts to enhance PALM in low-income and middle-income countries have been local, fragmented, and mostly unsustainable. Responding to the four major barriers in PALM service delivery that were identified in the first paper of this Series (workforce, infrastructure, education and training, and quality assurance), this second paper identifies potential solutions that can be applied in low-income and middle-income countries (LMICs). Increasing and retaining a quality PALM workforce requires access to mentorship and continuing professional development, task sharing, and the development of short-term visitor programmes. Opportunities to enhance the training of pathologists and allied PALM personnel by increasing and improving education provision must be explored and implemented. PALM infrastructure must be strengthened by addressing supply chain barriers, and ensuring laboratory information systems are in place. New technologies, including telepathology and point-of-care testing, can have a substantial role in PALM service delivery, if used appropriately. We emphasise the crucial importance of maintaining PALM quality and posit that all laboratories in LMICs should participate in quality assurance and accreditation programmes. A potential role for public-private partnerships in filling PALM services gaps should also be investigated. Finally, to deliver these solutions and ensure equitable access to essential services in LMICs, we propose a PALM package focused on these countries, integrated within a nationally tiered laboratory system, as part of an overarching national laboratory strategic plan.

Published **Online**
March 15, 2018
http://dx.doi.org/10.1016/S0140-6736(18)30459-8

This is the second in a **Series** of three papers about pathology and laboratory medicine in low-income and middle-income countries

See **Online/Comment**
http://dx.doi.org/10.1016/S0140-6736(18)30308-8, http://dx.doi.org/10.1016/S0140-6736(18)30310-6, and http://dx.doi.org/10.1016/S0140-6736(18)30457-4

See **Online/Series**
http://dx.doi.org/10.1016/S0140-6736(18)30458-6 and http://dx.doi.org/10.1016/S0140-6736(18)30460-4

Department of Pathology, Aga Khan University Hospital Nairobi, Nairobi, Kenya (S Sayed MMed); **Center for Global Health, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA** (W Cherniak MD, N Wolf BA, S Silkensen PhD, J Flanigan MD, K A Fleming FRCPath); **Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, USA** (N Brand BA); **Department of Pathology, National University of Singapore, National University Hospital, Singapore** (Prof S Y Tan MD); **ICAP at Columbia University, Mailman School of Public Health, New York, NY, USA** (Prof W E Sadr MD); **Faculty of Medicine, Health, and Life Sciences and Centre for Cancer Research and Cell Biology, Queens University, Belfast, UK** (Prof M Lawler FRCPath); **Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia** (Prof L M Looi FRCPath); **Columbia Asia Referral Hospital, Bangalore, Karnataka,**

Introduction

As discussed in the first paper of this Series,[1] health care in many low-income and middle-income countries (LMICs) is characterised by patchy and inequitable access to good quality pathology and laboratory medicine (PALM) services. Delays in diagnosis and initiation of appropriate treatment can compromise patient outcomes.[2,3] Furthermore, because PALM is integral to all aspects of health care, from diagnosis to policy development, the absence of a quality system will hinder the attainment of the Sustainable Development Goals (SDGs) and universal health coverage.

Common responses to this problem have been to try to make ad-hoc efforts to increase laboratory numbers, train more staff, and purchase more equipment. In the absence of long-term governmental allocation of appropriate resources, these approaches will inevitably fail. We recognise that financing for PALM is a key issue, on which we elaborate in the third paper of the Series.

Another response has been the creation of single-disease siloed programmes with built-in PALM services (eg, for tuberculosis, HIV, or malaria). However, the success of such programmes in reducing global incidence and mortality of these diseases has been, to some extent, at the expense of more general PALM services. The focus on specific diseases can lead to an internal brain drain that occurs when skilled staff leave public services to join other, usually private, organisations,[4] which can result in imbalances in human resource provision. In many LMICs, expansion of the private sector has been a de-facto response to these challenges, but this approach can increase the problem of inequitable access and, in the absence of regulation or mandatory accreditation, the quality of PALM services provided by the private sector has been highly variable.

Developing viable PALM solutions that are sustainable, affordable, and timely is a multilayered challenge that requires a combination of established and more innovative approaches. We discuss the potential solutions

Key messages

- Investment in human resources will be crucial to overcome the gap in access to quality pathology and laboratory medicine (PALM) services
- Information technology and point-of-care testing cannot compensate for weak health-care systems
- A PALM delivery package within an integrated network of tiered laboratories can help address the problems of access to PALM services in low-income and middle-income countries
- Research to map PALM challenges more accurately and to determine optimal solutions is urgently needed

India (S A Pai MD); **Department of Pathology and Laboratory Services, Denver Health, Denver, CO, USA** (Prof M L Wilson MD); **Department of Pathology, University of Colorado School of Medicine, Aurora, CO, USA** (Prof M L Wilson); **American Society for Clinical Pathology, Chicago, IL, USA** (D Milner MD); **and Green Templeton College, University of Oxford, Oxford, UK** (K A Fleming)

*Dr Fleming retired in September, 2008

Correspondence to: Shahin Sayed, Department of Pathology, Aga Khan University Hospital, Nairobi 00100, Kenya **shaheen.sayed@aku.edu**

See Online for appendix

to the four barriers identified in the first paper of the Series: insufficient human resources, shortage of education and training, inadequate infrastructure, and isufficient quality, standards, and accreditation.[1] This paper will also recommend a delivery package specific for LMICs for implementing the proposed solutions.

Insufficient human resources

The scarcity of trained pathologists in LMICs is a key gap that must be addressed. Three aspects are particularly relevant for addressing this barrier: increasing retention, task shifting, and short-term visitor programmes.

Increasing retention

Retaining workers in the public system in LMICs is challenging. A 2012 review of studies[5] done in LMICs that compared public with private health-care systems raised concerns about the increasing movement of public sector health-care workers into private practice. Although this review discussed the broader health-care workforce, its findings are also relevant to PALM. In a second study,[6] 1365 female health-care providers and managers in the public sector across 28 districts in rural Pakistan reported that dissatisfaction with salary, political interference, and shortage of medicines and supplies led professionals to exit the public health-care system. Solutions that could mitigate these issues include ensuring continued professional development and education, providing access to fair promotions, improving the physical work environment, providing financial incentives, and supporting access to educational facilities for employees' children.[6] However, in the absence of a robust public sector infrastructure for PALM in LMICs, the private sector can act as a safety net, providing good quality and not necessarily more expensive services.

Another approach to address retention of pathologists in rural or underserviced centres is to focus on universities with programmes that specifically target rural and underserviced regions. An example of this approach is THEnet (Training for Health Equity network), a joint WHO coalition that includes 12 international medical schools that was established specifically with a social accountability framework.[7] One member of THEnet is the Ateneo de Zamboanga University School of Medicine, located in a rural lower-resource setting in the Philippines. Since 1999, more than 80% of graduates have continued to practise in underserviced communities.[8] Although this programme caters to the general health-care workforce, it provides an example of how such an approach could be similarly adapted for PALM. Furthermore, apart from financial incentives for pathologists who might wish to work in these underserviced areas, advocating for the recognition of pathology as a clinical discipline in its own right is key to any retention strategy. The image of pathologists as specialists who are integral to the clinical decision-making process should be extensively promoted to attract greater numbers of young doctors to join the profession.

Providing opportunities to pathologists and trainees for mentorship and continued professional development is essential. In our survey of pathologists in LMICs, 108 of 267 (40·4%) respondents rated mentorship and faculty training as the number one solution to improving PALM services (appendix). A 2013 study[9] of graduates from the Fogarty International Center research training programmes at Makerere University, Uganda, and University of Nairobi, Kenya, identified mentorship as a crucial factor in the pursuit of a career in health research and maintaining their position as a faculty member—positions that are relevant to the trainer shortage issues previously outlined. Many international and national pathology associations provide a wide range of programmes for continued professional development, but, for many pathologists and pathology trainees in LMICs, programme attendance is constrained by cost, local commitments, and visa difficulties. These problems can be resolved by developing formal in-country training programmes delivered by international experts and augmented by online courses, thereby combining mentorship and continued professional development. Similar advantages come from planned or formalised attachments to renowned regional and international centres, for advanced training through sabbaticals and fellowships—provided by employee institutions and professional bodies with commitment to capacity-building for LMICs, such as the World Association of Pathology and Laboratory Medicine that, through its World Pathology Foundation, has funded fellowships (Gordon-Signy Fellowships) for early-career pathologists to train and be mentored at renowned centres in high-income countries since the 1970s.[10]

Task shifting and sharing

Task shifting and sharing, which involves distribution of specific skilled tasks to less specialised health-care personnel, can ensure a more effective and efficient use of the workforce and can work best in environments where regulations are properly enforced. In 2008, WHO convened the first conference on task shifting and sharing in LMICs in Addis Ababa, Ethiopia, and, in collaboration with the US President's Emergency Plan for AIDS Relief (PEPFAR) and the UN Program for AIDS Relief, produced a set of global recommendations and guidelines.[11] The report focused specifically on HIV, but the overarching principles can be applied across PALM. To close the divide, scalable task shifting and sharing programmes, such as training medical doctors and technologists to appropriately process surgical specimens for cancer diagnosis, could help to address the pathologist shortfall.[12] The processed samples and accompanying information can be transported along a tiered laboratory system to a centrally located pathologist or laboratory, where expertise can be aggregated. With

time, task shifting and sharing can create opportunities to attract young medical doctors to join the pathology discipline.

A phased programme to support cancer diagnosis was established in a rural hospital in Butaro, Rwanda, in partnership with Brigham and Women's Hospital (Boston, USA).[13] Two laboratory technicians underwent intensive and structured practical training for 2 months, which included grossing and processing fresh tissue samples, a task normally done by a pathologist or junior trainee doctor. During the pilot study period, a total of 437 tissue specimens were submitted, of which 244 (55·8%) were confirmed to be malignant. The programme has since expanded to include immunohistochemistry and telepathology.[13]

A study[14] done in rural Namibia reported how point-of-care (POC) testing for CD4+ cell count was shifted from the central laboratory to nurses and lay health-care workers, leading to improved turnaround time of results. Significantly, 92·2% of results were received by the patient on the same day, compared with 4·7% of standard laboratory CD4+ cell count results (p<0·001). Furthermore, there was up to 95% concordance between CD4+ cell count results done by the lay health-care worker and those done by the central laboratory.[14]

In our survey (appendix), 71 of 267 (26·6%) pathologists rated task shifting and sharing as one of the top three potential solutions to improving pathology services in LMICs. However, task shifting and sharing can only function if structural deficiencies within health-care systems in LMICs are addressed.[15] Additionally, concerns about adequate training in the specific tasks, appropriate allocation of tasks, supervision of the health-care workers, and motivation through financial incentives should be addressed to avoid compromising quality of care.[16]

Short-term visitor programmes

Globally, use of visiting individuals or teams of health-care providers and educators to expand and supplement local capacity is a common model.[17] Although this approach can be beneficial, negative aspects, such as non-sustainability, intermittency, and dependency of local communities on these stop-gap measures, need to be considered.[18] One approach to these issues is to ensure that visitor programmes align with the goals and directions of local ministries of health[17,19,20] and are based around a clear principle of local partner engagement, with a long-term commitment to transfer the roles of primary care provider to the local partners.[20] If developed through this collaborative and sustainable approach, these bridging initiatives could translate into long-term viable solutions.

Insufficient education and training

A key aspect to addressing the shortage of skilled PALM staff in LMICs is by increasing access to education and training opportunities—for example, by increasing the number and quality of pathology graduate teaching programmes and upscaling recruitment to those programmes. Although we recognise that this shortage is a global issue, the size of the gap in access to PALM services that needs to be filled in LMICs is huge compared with that in high-income countries. Various junior doctor training programmes for PALM exist in LMICs. Depending on the country, multispecialty training programmes are offered by universities or by public health-care systems. Additionally, monospecialty training (eg, haematology, anatomical pathology, and microbiology) is available in certain universities.

Our survey (appendix) indicated that 142 of 290 (49%) respondents had a PALM training programme at their institution; the majority of the programmes were based at academic teaching hospitals, and there was a dearth of such programmes in private or commercial laboratories. Increasing the number of PALM training programmes has challenges, such as a shortage of trainers, inability to attract trainees, and, crucially, insufficient funding. Achieving sustainable increases in trainer numbers will require incentives and mechanisms to make trainer posts more attractive and to use experienced pathologists in private and commercial laboratories to bolster teaching in academic centres. Recruiting more trainees will require the raising of the profile of PALM in medical schools—multiple studies[21–23] indicate that graduating medical students do not understand what the profession of pathology entails. It is particularly telling that, in Mwanza, Tanzania, public perception of pathologists is that they are doctors of the dead.[23] To address this misunderstanding, proposed solutions include exposing medical students to PALM during their preclinical years, providing in-class instruction that could later be supplemented with experiential learning.[22] Pathologists also need to take a more visible role in medical school activities—by having leadership roles in innovative curriculum design, being course directors and advisers to students on career choice, and by participating in multidisciplinary teams for decision making on patient care.

In this era of technological innovation, practising and future pathologists need to understand new technological developments to ensure their appropriate application in the clinical decision pathway.[24] Curricular content and structure must reflect 21st century developments in PALM. In parallel, bespoke accredited courses aimed at specific domains (eg, autopsy, molecular pathology) should be considered to supplement existing programmes. It will also be necessary to ensure the quality of pathology training through accreditation of programmes. For example, a study[25] from West Africa showed that there could be insufficient case volumes and case mixes in training programmes to fulfil course requirements. These quality metrics for training should also be built into general laboratory accreditation programmes.

In tandem with increasing pathologist numbers and quality of their training, a concerted effort to build capacity and improve the quality of allied laboratory staff (technicians, technologists, and scientists) is required. A summary report[26] on approaches to strengthening laboratory capacity for antimicrobial-resistance testing in LMICs indicated that individual laboratory staff skills could be improved effectively by repeated training with short courses, in conjunction with regular supervision and site visits.

Ultimately, many of the measures needed to increase the number of pathology training programmes require additional funding, which will inevitably constrain their expansion in the short term. One way of maximising the available resources would be to pool efforts across regions and countries, by use of curricular harmonisation and reciprocal recognition of pathology qualifications. These collaborations, such as north–south and south–south, can also help to share scarce resources. An example of a north-south collaboration is AMPATH, in which a consortium of North American academic health centres, led by Indiana University, have partnered with Moi Teaching and Referral Hospital in Kenya to develop a junior doctor programme for pathology at that hospital.[27,28]

For more on **PATH** see https://www.path.org/

Maximising education and training programmes to underpin workforce expansion can be achieved, as shown by the successful national strategy of the Malaysian health-care system. At independence in 1957, the country lost nearly 75% of health-care staff,[29] but over the course of 60 years it has worked to rebuild its health-care workforce. In 2007, the Pathology Lab Act was passed in parliament, codifying the importance of pathology standards and their implementation at national level.[30] As of 2015, there are more than 500 pathologists in the country (a ratio of one pathologist per 60 000 population), with training provided for five additional nations (Sudan, Yemen, Myanmar, Iraq, and Sri Lanka).[29]

Inadequate infrastructure

All aspects of PALM infrastructure are constrained to varying degrees in LMICs. New and innovative technologies hold considerable promise to help drive infrastructure solutions and should be considered.

Supply chain

A robust supply chain for laboratory consumables is necessary for a well functioning laboratory; problems with supply chains are a major issue in LMICs. Without commitment by ministries of health towards a robust, systematic supply chain, PALM solutions in LMICs cannot be implemented. There is surprisingly little research published on PALM supply chains in LMICs. One case study[31] that assessed the challenges of frequent stock-outs and testing delays focused on the 2007 Ethiopian Public Health Laboratory System Master Plan,[32] in which the government established a standardised national laboratory logistics system that was designed to meet the supply needs of individual laboratories, by creating efficient transport mechanisms and direct provision of supplies from regional hubs. The process harmonised test menus, test techniques, operating procedures, and laboratory equipment for each type of test and antiretroviral treatment facility in the system, thus providing patients with comprehensive care.[31] After the programme was initiated, there were no stockouts for antiretroviral treatments, and patients' waiting time for tests was reduced from 2–3 months to less than a day.

PALM solutions can also learn from national vaccine programmes, in which considerable efforts have been made to strengthen supply chains in LMICs. From 2007 to 2012, WHO in collaboration with PATH launched Project Optimize, aimed at strengthening vaccine supply chains by leveraging the expertise of private logistics companies and integrating national supply chains.[33] In Thailand, Project Optimize supported the creation of a vendor-managed inventory, first piloted in 28 of 76 provinces before being rolled out nationally. This initiative has proven to be cost-effective and has led to a more integrated supply chain.[34] Project Optimize has also supported Senegal to integrate all supply chains of their national health programmes into a single integrated system. This project was piloted in a single region, where it led to a 100% decrease in stockout incidents, from 56 events to 0 events after 3 years.[35] It is imperative that similar investments be made in supply chains for pathology laboratories, and there is a crucial need for rigorous evaluation of programme choices and assessement of programme outcomes to support these efforts.

Human resources for maintenance of medical equipment and devices

Because minimising equipment downtime is crucial, the role of biomedical engineers is essential for equipment maintenance. These professionals are also important for supporting safe and functional equipment and devices in a rapidly evolving landscape of technical innovation. Equipment leasing and reagent-based contracts that incorporate inbuilt maintenance clauses rather than outright purchase should be considered as a solution. Investment in biomedical engineering schools by national governments, in partnership with industry, as recommended by WHO Technical Series,[36] is another component of this solution.

Laboratory information systems

Strong and integrated laboratory information systems are crucial for quality control, efficient management of workload and supplies, and financial planning.[37] Although the costs of computing have plummeted, the requirements for data management, quality control, quality improvement, safety, and research have increased; it is seemingly impossible to imagine a modern laboratory functioning without the use of a laboratory information

system. Laboratory quality and management overall is greatly facilitated by access to aggregated reports of turnaround time, test failure rate, rejection rates, and so on. The capital investment required to add a laboratory information system or one designed for anatomical pathology (or both) to a laboratory is trivial compared with the gains that can be achieved, such as increasing quality and safety for the patient. Patient safety can improve because there will be less potential for errors in patient identification (and subsequent inappropriate treatment) and a reduction in manual clerical work—itself also a source of error. Appropriate software programs will also allow monitoring of turnaround times and the calculation of quality indicators and trends in quality assurance.[38]

Examples of the successful implementation of laboratory information systems in LMICs are scarce. In Peru, an online laboratory information system was developed to report results from the national referral laboratory to peripheral clinics for drug susceptibility testing of new tuberculosis cases. This system decreased turnaround time and culture conversion of patients who were treated for tuberculosis.[39] However, this approach was limited to a single disease and was not implemented across the entire laboratory.[39]

One substantial barrier to laboratory information system development is the infrastructure and software costs associated with their introduction.[40] A potential solution is the use of free and open source software, but many laboratories in LMICs find these options unfeasible, because of the expertise in information technology required, poor standardisation, frequent breakdowns, and insufficient support for maintenance of these systems.[41] Moreover, not all open source software systems have the ability to interface with laboratory analysers, thereby restricting their usefulness in certain settings. The creation of a free open sourced laboratory information system that is appropriate for an LMIC context would provide substantial benefits for global pathology integration.

Telepathology

Telepathology has the potential to address the problem of insufficient on-the-ground anatomic pathology expertise. This technology can allow remote users to provide anatomical pathology diagnoses by analysing digital images or dynamically examining a slide in real time. Although telepathology can be used for primary reporting of cases in areas with no resident

Panel 1: Molecular testing capabilities in low-income and middle-income countries (LMICs)

Viral load HIV testing

Quantitative viral load monitoring is the gold standard in high-income countries, but it is compromised in resource-limited settings by a dearth of centralised laboratories, appropriate infrastructure, and suitably qualified personnel, and by cost.[58] However, the development of the SAMBA semi-Q (simple amplification-based assay semi-quantitative test for HIV-1),[59] a molecular test that accurately measures viral load, is available as a nucleic acid amplification test on the semi-automated SAMBA I laboratory platform (DRW, Little Chesterford, UK) or as a point-of-care molecular assay on the SAMBA II fully automated system (DRW).[60] Comparative studies with other high sensitivity and high specificity laboratory-based tests revealed about 98% concordance for both SAMBA I and SAMBA II,[60] and this specificity, combined with robust reagents that are stable at high temperatures and high humidity, makes the SAMBA II point-of-care molecular platform an attractive option for viral load testing in low-throughput locations in LMICs.

Nucleic acid amplification and point-of-care molecular testing for hepatitis C virus

Nucleic acid amplification and next generation point-of-care molecular testing have been introduced for detection of hepatitis C virus in low-income and middle-income countries,[61,62] but issues such as cost, ease of sample collection, and transport are challenging.[61] Use of dried blood spots reduces sampling complexity, aids sample transport, and is increasingly being incorporated into diagnostic protocols for nucleic acid amplification and point-of-care testing.[63,64]

Point-of-care molecular testing for *Mycobacterium tuberculosis*

The Xpert MTB-RIF (Cepheid, Sunnyvale, CA, USA) is a point-of-care molecular test for diagnosis of *M tuberculosis* and resistance to rifampicin.[65] Xpert MTB-RIF is less sensitive than conventional laboratory tests in smear-negative and HIV-associated tuberculosis; however, a next generation assay (Xpert Ultra) has been developed and showed comparable overall performance but greater sensitivity than the previous assay.[66]

Molecular detection of *Plasmodium falciparum*

Next generation point-of-care testing using RealAmp, a portable device that integrates loop mediated isothermal amplification with real-time fluorescent detection has been successfully field tested in India and Thailand and showed higher efficiencies than conventional methods in detecting asymptomatic *P falciparum* infection.[67,68] The amplification method used in RealAmp does not require a PCR thermal cycler and, thus, is well suited to resource-limited settings.[56]

Molecular testing for human papillomavirus in cervical cancer

Testing for high-risk subtypes of human papillomavirus is becoming increasingly relevant in resource-limited settings.[69] Results of a randomised trial[70] in rural India indicated that single-round nucleic acid amplification testing for human papillomavirus could help reduce cervical cancer incidence and mortality by about 50%, whereas visual inspection with acetic acid or cytology-based screenings proved ineffective.

***Panel 2*: Standards, guidelines, and accreditation**

Diagnostic pathology and laboratory medicine (PALM) testing involves:

- Correct test selection, test ordering, specimen collection and transportation, and specimen processing (pre-analytical phase of testing)
- Doing tests, including direction to additional tests as necessary (analytical phase of testing).
- Reporting test results, interpretation, accurate and appropriate transmission of results, and consultation as needed (post-analytical phase of testing)

This infrastructure is made more complex by the fact that different tests require different approaches to each phase. Common biochemical tests, for example, have different pre-analytical, analytical, and post-analytical needs compared with anatomical pathology tests. Additionally, before tests can be done, necessary equipment must be selected and undergo quality review processes, staff members must be trained, and processes must be designed to ensure ongoing accuracy and quality.

These quality processes are driven by use of standards and guidelines. Standards are written documents that identify specific requirements for laboratory processes that must be followed without variation. These ensure sufficient test quality to allow test results to be comparable between laboratories. Guidelines, conversely, are written documents that describe general laboratory procedures and processes. Because they are more general, they allow for more flexibility in their use.

Accreditation is a process used to ensure the external validation of quality, with both technical and management components. The technical component provides guidance on doing high-quality testing, including specific quality assurance schemes, technical standards, and audits. The management component provides guidance for professional performance and assessments of competency, and guidance for creating effective management structures and systems for assessment and mitigation of risks.[76,77] Some of the national and international bodies providing accreditation include the National Accreditation Board for Testing and Calibration Laboratories of India and the College of American Pathologists in the USA.

pathologist—for example, in the initial phase of the telepathology programme in the Butaro Cancer Centre, Rwanda[42]—it is more commonly used to obtain a second opinion. For example, in China, a telepathology service has been developed to support cancer diagnostics, by linking 20 consultation centres with 80 national experts.[43] After 2 years, the telepathology service had provided 16 247 consultations, with 87% of these having a turnaround time within 48 h.[43] Telepathology can also provide professional and educational support for continued professional development. The Réseau en Afrique Francophone pour la Télémédecine network has been successful in using telepathology to create a network of interactive courses that take place in ten French-speaking African countries, in partnership with the University of Geneva, Switzerland.[44]

Barriers to the widespread adaptation of telepathology include inconsistent internet connectivity, high initial costs depending on image type required (from $100 to US$250 000), on-the-ground expertise in slide preparation, and equipment maintenance.[45] Furthermore, undefined minimum technical standards for image capture, storage, transmission, and viewing, coupled with inadequate competency assessments of pathologists for reporting cases on the basis of virtual images, patient confidentiality, and regulatory and legal requirements need to be addressed before adoption of this platform.[46] However, in settings where these barriers have been overcome, telepathology has proven to be an effective educational and diagnostic tool.[47,48]

Information chain

Poor communication between referring clinics and central laboratories can increase turnaround time and decrease quality of care.[49] To shorten turnaround times, two barriers must be addressed: the need for a referral system for quick and efficient test requests and transport of samples to the laboratory where diagnostic analysis is done, and the need for a standardised communication system that transmits test results back to the patient's clinic.

Successful public–private communication partnerships have been established in Ethiopia and Uganda for drug susceptibility testing for tuberculosis.[50,51] Both countries formed partnerships between their ministries of health, the US Centers for Disease Control and Prevention (CDC), and a private consultancy firm to create a referral network that used the national postal services for transportation of specimens to a central laboratory. These programmes led to an increase of greater than 8 times in referrals in Uganda (655 specimens in 2008 *vs* 5813 in 2011) and a decrease in turnaround time from 7 days to 2 days in Ethiopia.

Successful programmes that have improved report communication from laboratories back to referring clinics have predominantly used either mobile phone technology or web-based laboratory information systems. Short messaging services have been successful in reducing turnaround time in rural clinics in Swaziland,[52] where health-care facilities are not equipped with computers and internet, making the use of information systems unfeasible. However, this programme has not been fully implemented, because the messaging service has not replaced paper records and has not been incorporated into the clinic workflow.

Public–private partnerships

A striking feature of many LMICs is a strong and active private PALM sector. Indeed, in countries such as India, where the government spending on health care is low, over 70% of patients are treated in the private sector.[53] Therefore, most diagnostic tests are done in private laboratories.

To capitalise on private sector capacity and ensure a more efficient use of resources, private sector involvement in integrated networks of tiered laboratories (described later in this paper) should be explored, perhaps via public–private partnerships. These partnerships could involve outsourcing laboratory services to the private sector, providing subsidies to the private sector for service provision, placement of private laboratory equipment in public institutions, the private sector

Panel 3: Malaysian National Accreditation Scheme for pathology laboratories

In Malaysia, the National Accreditation Scheme for pathology laboratories was launched in December, 2004, after the creation of a memorandum of understanding between the College of Pathologists of the Academy of Medicine Malaysia and the Department of Standards Malaysia (DSM) in late 2002.

Against the background of expanding private pathology laboratories, the memorandum articulated the need for laboratories to comply with required standards of practice, including participation in quality assurance programmes, staff competency, safety, and continuous audit, and propelled 2 years of intense collaborative activity towards the realisation of the national scheme titled MS/ISO 15189, based on the international standard ISO 15189 of the International Organization for Standardization (ISO).

At that time, ISO 17025, the international standard for testing and calibration laboratories, was the standard adopted by many countries for accreditation of pathology laboratories. Recognition that pathology laboratories were not only analytical, but also had the additional responsibility of ensuring that tests were relevant to patient care (such as interpretation of test results, advice on choice of tests, advice on proper collection of samples, and so on) led to the development of ISO 15189 as a new standard for accreditation of medical laboratories. The fortuitous issue of ISO 15189 in 2003 and DSM's prior experience with ISO 17025 were helpful in the country's decision to adopt ISO 15189, placing Malaysia among the first low-income and middle-income countries to do so.

In 2003, a public forum brought together stakeholders (public and private laboratories and clients) to reach an understanding on the benefits of accreditation and the rationale for adoption of ISO 15189. Following this decision, 20 lead assessors and 60 technical assessors were formally trained with the help of International Accreditation New Zealand, and seven key documents were drafted to supplement ISO 15189 standards for the local setting: specific criteria for accreditation and specific technical requirements for cytopathology, histopathology, chemical pathology, haematology, medical microbiology, and virology. Additional documents expanded the fields covered to assisted reproduction and cytogenetics in subsequent years.

In April, 2005, the College of Pathologists published six practice guidelines in the *Malaysian Journal of Pathology* to support the accreditation process.[78] The six guidelines developed were:

- Retention of pathology records and materials
- Minimum qualification, training, and experience of professional personnel working in a pathology laboratory
- Laboratory construction and design
- Maintenance and operation of equipment in a pathology laboratory
- Safe laboratory practice
- Sample management

Although a voluntary exercise, accreditation is now well accepted in Malaysia because of strong peer support.

training public sector staff, and collaborative research. The specifics of such an approach should be tailored to local needs and situations and inbuilt clauses need to be in place to protect the public sector from being undermined by the private laboratories. Furthermore, mutually defined goals, building of trust, and continuous monitoring, learning, and evaluation are essential considerations for a successful and sustainable public–private partnership. An example of a successful model is the partnership between PEPFAR, the CDC, and Becton-Dickinson Company (Franklin Lakes, NJ, USA), which has strengthened laboratory systems in Kenya, Ethiopia, Mozambique, and Uganda, reducing—for example—turnaround times for antiretroviral treatment laboratory results by 71% in Ethiopia (7 days *vs* 2 days, for specimens referred in Addis Ababa).[54] To avoid conflicts of interest, a possible way to initiate public–private partnerships is by primarily involving non-governmental organisations and the corporate social responsibility divisions of companies (including those that are not related to the medical field).[55]

POC testing

POC testing, defined as near-patient testing or single-use testing that occurs outside the laboratory, is a rapidly expanding area that is and will continue to be a substantial part of PALM provision in many LMICs. Such testing usually is done by medical staff, nurses, or medical assistants, using small mobile testing devices on or close to the patient. In LMICs, POC testing has been used extensively to diagnose and help guide treatment. For example, patients with HIV or AIDS have benefited from extensive access to monitoring CD4+ cell counts by use of a POC testing platform.

Two developments in POC testing are of note. First, many of the newer tests are based on nucleic acid technology—eg, nucleic acid amplification tests and next generation POC molecular diagnostic platforms[56,57]—and have the potential to inform more effective PALM services and research in resource-limited settings (panel 1). Second, to overcome the problems of intermittent power supplies and reagent stockout, there is an increasing provision of POC devices with internal power and reagents.

The great advantage of POC testing is its short turnaround time. For certain indications, results can be available in less than 1 h or sometimes in a matter of minutes, facilitating rapid clinical decision making. Given that many patients in LMICs might only make a single clinic visit, the ability to see the potential patient, diagnose the condition, and treat the disease in that one visit is a major advance.[71] For example, in cervical cancer,

	Tier 1	Tier 2	Tier 3	Tier 4
Population served	30 000	50 000–200 000	3–6 million	..
Tests				
Test volume	<5000 per year	5000–10 000 per year	>20 000 per year	>20 000 per year
Typical clinical test package	12 tests or panels[83]	40 tests or panels[83]	100 tests or panels[83]	>100 tests or panels
Types of tests	POCT, prepare and forward FNAB and microbiology specimens	Clinical biochemistry, haematology, microbiology, anatomic pathology, and autopsy	Tier 2 tests plus specialised tests	Tier 3 tests plus specialised tests
Bellwether tests	Rapid HIV test, urinalysis, haemoglobin, pregnancy test, FNAB sample preparation	Electrolyte test, blood culture, FNAB, whole blood transfusion	Antimicrobial resistance testing, oestrogen receptor detection for breast cancer	Gene analysis
Typical turnaround time[83,84]	Critical: <90 min; routine: <1 day	Critical: <90 min; clinical laboratory: 1h–1 day; anatomical pathology: <5 days	Tier 2 turnaround times plus analysis of antimicrobial susceptibility and tumour biomarkers: 1 week	..
PaLM workforce	1–3 laboratory technicians	1 general pathologist, 6 laboratory technicians and pathology assistants	4 pathologists, 2 clinical scientists, 20 technicians and pathology assistants	Tier 3 workforce plus pathologist sub-specialist capacity
Surgical workforce	Primary care doctor, clinical officer or skilled nurse	General surgeon, anaesthesiologist or obstetrician	Specialty surgeons, gynaecologists, obstetricians, anaesthesiologist	Tier 3 workforce plus subspecialty surgeons
Typical surgical procedures	Minor surgery only	Basic trauma surgery package, basic emergency obstetric package, basic emergency general surgery package, general surgery package, obstetrics and gynecology package, specialist package[85]	Complex surgery, specialty oncology, specialty cardiovascular surgery, and so on;[85] Specialty and long duration anaesthesia, post-anaesthesia and critical care support	..
Infrastructure				
Information communications technology	Paper, mobile, or (preferred) electronic method	Paper, electronic, or (preferred) laboratory information system	Electronic or laboratory information system; telepathology (optional)	Tier 3 technology but with more data linkages to trials and registries
Typical equipment	Simple microscope, rapid diagnostic tests, POCT and single-use tests, specimen and patient identification, FNAB and FNAC, biopsy fixation	Automated blood and biochemistry analysers, microbiology analysers and incubators, blood typing, and refrigerators, tissue processor, and microtome for anatomical pathology	Automated tissue processor, equipment for full autopsy, immunohistochemistry station, frozen section; biobanking (optional)	Molecular biology and cytogenetics, immunofluorescence, flow cytometer, biobanking; electron microscopy (optional)
Public health and disease surveillance	Accumulate and forward incidence data to higher tier or public health authority	Report to public health authority or other registries, such as emerging diseases, AMR, cancer, and other NCD registries; hospital-based registry(optional)	Tier 2 tasks, ability to analyse data and report local disease trends; hospital-based registry	Research on disease incidence trends, including AMR and emerging diseases; population-based registry
Quality, standards, certification, and accreditation	Technicians supervised at a distance by pathologist; participates in EQA programme, progressing towards accreditation, such as SLIPTA	Technicians and pathologists supervise laboratory and tier 1 site, oversight by reference laboratory; participates in EQA programme, progressing towards accreditation, such as SLIPTA	National or international accreditation, such as ISO 15189 or other	Tiers 1–3 quality and standards, and specific quality assurance related to research studies; international accreditation, such as ISO 15189
Finance[83]				
Equipment cost (US$)	2000–5000	150 000–200 000	Varies according to functions	..
Annual laboratory budget	..	5·2% of hospital budget	7·3% of hospital budget	Biobank setup cost: US$ 3–5 million[86]

POCT=point-of-care testing. FNAB=fine needle aspiration biopsy. FNAC=fine needle aspiration cytology. AMR=antimicrobial resistance. NCD=non-communicable diseases. EQA=European quality assurance. SLIPTA=stepwise laboratory quality improvement process towards accreditation. ISO=International Organization for Standardization.

Table 1: **Proposed delivery package for pathology and laboratory medicine**

traditional approaches in LMICs have included visual inspection with acetic acid and cytology screening.[69,71,72] However, the detection of high-risk human papilloma virus (HPV) subtypes by POC testing is increasingly being used as a substitute.[67] Adopting a one-stop screen-and-treat approach is highly relevant,[72] directly countering the inadequate compliance with the repeated follow-ups required in conventional cytology screening programmes. Therefore, switching to POC molecular testing for HPV could be an effective strategy, particularly if incorporated into a same-day screen-and-treat protocol.[72] Another development is the recognition that, given the many similarities between POC testing methods, it is increasingly important to investigate the potential for shared POC platforms to diagnose multiple diseases and monitor therapeutic intervention rather than the disease-specific practices that are the norm in many LMICs. For example, existing instruments, such as GeneXpert (Cepheid, Sunnyvale, CA, USA), can be upgraded to run a suite of assays, facilitating the development of future disease-agnostic platforms to deliver multiple POC tests.

	Tier 1	Tier 2	Tier 3	Tier 4
Patient level	Turnaround time of test results available to the patient; cost of test for the patient; travel time of patient to accredited facility; unique patient identifier, numerical or biometric	Turnaround time of test results available to the patient; cost of test for the patient; travel time of patient to accredited facility; unique patient identifier, numerical or biometric	Turnaround time of test results available to the patient; cost of test for the patient; travel time of patient to accredited facility; unique patient identifier, numerical or biometric	Turnaround time of test results available to the patient; cost of test for the patient; travel time of patient to accredited facility; unique patient identifier, numerical or biometric
Quality, standards, certification, and accreditation	Stepwise laboratory improvement rating, such as SLIPTA; percentage of laboratory professionals with CME requirements	Stepwise laboratory improvement rating, such as SLIPTA; percentage of laboratory professionals with CME requirements	Percentage of laboratories meeting national or international standards, such as ISO 15189; percentage of laboratory professionals with CME requirements	Percentage of laboratories meeting ISO 15189; Percentage of laboratories conforming to international biobanking standards; percentage of laboratory professionals with CME requirements
Health systems coordination	Percentage of laboratories with SOP for routing specimens and results within the tiered network; ratio of tier 1 laboratories to population	Percentage of laboratories with SOP for routing specimens and results within the tiered network; ratio of tier 2 laboratories to tier 1 laboratories; percentage of hospitals doing general surgery that have tier 2 laboratories	Percentage of laboratories with SOP for routing specimens and results within the tiered network; ratio of tier 3 laboratories to tier 2 laboratories; percentage of teaching or training hospitals that have tier 3 laboratories	Percentage of laboratories with SOP for routing specimens and results within the tiered network; ratio of tier 4 laboratories to tier 3 laboratories
Disease specific indicators	Percentage of births with appropriate prenatal and newborn PLM screening; percentage of patients with hyperglycaemia with glycated haemoglobin test results; percentage of patients with tuberculosis undergoing multidrug resistance testing	Percentage of cancer diagnoses confirmed by tissue diagnosis; percentage of patients with hypertension with measured renal function; percentage of emergency blood transfusion requests fulfilled within 2 h	Percentage of breast cancer diagnosis with reported tumour markers; percentage of anatomical pathology cases with complete, standardised report (synoptic report); percentage of acute leukaemia with flow cytometry results	Proportion of eligible breast cancer cases undergoing molecular tests; Percentage of patients with renal transplant undergoing HLA crossmatch typing

SLIPTA=stepwise laboratory quality improvement process towards accreditation. ISO=International Organization for Standardization. CME=continuing medical education. SOP=standard operating procedures.

Table 2: **Assessing pathology and laboratory medicine systems**

It would be simplistic to assume that POC tests alone are a panacea for under-resourced PALM systems in LMICs. For drug-resistant tuberculosis, Cepheid's Xpert MTB-RIF test reduces turnaround time from months or weeks to days or hours, underpinning the timely treatment of patients. However, the experience from South Africa—which has considerably scaled up Xpert MTB-RIF testing—is instructive: it has proven difficult to link Xpert test results to health-care information systems, and delays have persisted in initiation of treatment,[73] which means POC testing cannot completely leapfrog systems-level weaknesses—these issues are considered in more detail in the third paper of this Series.

Staff implementing POC tests need training and oversight, particularly in selecting the appropriate tests and interpreting the results.[74] Guidance is needed as to which tests, of the multiple ones available for a particular indication or purpose, are appropriate and the circumstances in which the results are (and are not) reliable. A programme of quality assurance, allied to maintenance of the devices being used is paramount. POC tests do not obviate the need for strong PALM services, but should instead complement and be part of the local PALM system, as for the development of POC testing for tuberculosis.[65] This programme was in stark contrast to the unfocused initial development of rapid diagnostic testing for malaria, which was characterised by the introduction of myriad tests with highly variable specificities and sensitivities.[75] Embedding POC testing within national and regional PALM plans would help to ensure a culture of rigorous quality assurance and appropriate education and training in LMICs.

Insufficient quality, standards, and accreditation

The PALM system is complex, beginning with test selection, ordering, and sample collection, and ending in result interpretation, report dispatch, and consultation (when needed). Ensuring high quality across these different phases requires rigorous internal standards and guidelines. Validation that processes are being correctly observed is routinely achieved through participation in an external accreditation programme (panel 2). It is our position that all laboratories and associated individuals should participate in such programmes. Ministries of health need to be aware that accreditation is not a one-off expenditure, but is rather a recurring cost that must be factored in any discussion of quality and standards.

Several organisations offer international accreditation programmes for a fee. However, these are often not affordable in many LMICs. One alternative, at least for more developed countries, is the establishment of in-country accreditation programmes. Panel 3 describes one example from Malaysia of how a national laboratory accreditation programme was implemented, led by a strong and committed pathology professional leadership in partnership with the governmental accreditation agency.[78]

Another approach for laboratory quality improvement is the implementation of a mentoring programme, as occurred in Cambodia.[57] Following a capacity assessment of 28 public health laboratories across Cambodia, the CDC implemented a mentorship programme using short courses and work-based improvement projects. This was supported by site visits by mentors to teach

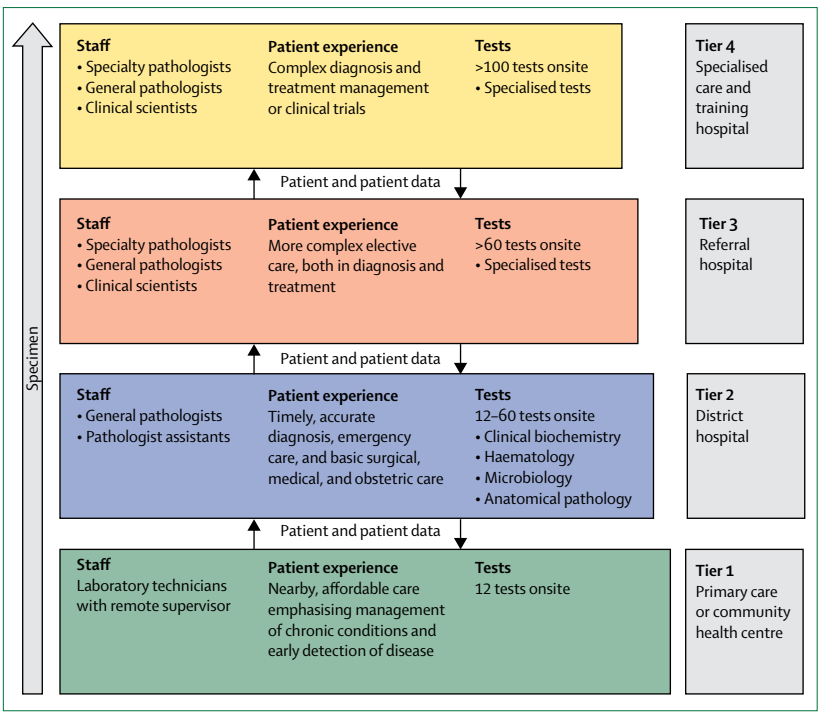

Figure: **Integrated network of tiered laboratories**
Tier 1 consists of primary care, health-care centres, or mobile laboratories serving mostly outpatients in a community, doing point-of-care and single-use tests and referring more complex work to either tier 2 or tier 3. It is staffed at the technician level. Tier 2 consists of laboratories in district hospitals that receive specimens from their own patients and receive referrals from tier 1 facilities. These laboratories usually have a surgical, medical, and pathology clinician and do a selected number of routine tests. Tier 3 consists of laboratories in regional or provincial hospitals that receive specimens from their own patients and receive referrals from tier 1 and tier 2 facilities. These laboratories ill have substantial numbers of pathology professionals and cover all routine testing in the major pathology disciplines. Teaching hospitals are expected to have at least one tier 3 laboratory. Tier 4 consists of laboratories in national or sophisticated teaching hospitals that receive specimens from their own patients and receive referrals from facilities from all other tiers. In addition to routine tests, these laboratories provide highly specialised tests and education and training for the network. In small countries, this facility might be a regional one shared by more than one country.

quality management systems to laboratory staff. This programme has since been scaled up to include an additional 12 laboratories.[79]

Given that the establishment of national accreditation programmes will not be feasible in every country, it would be helpful to develop an international agreement to make external accreditation programmes available to PALM services in LMICs free of charge, or at a nominal cost. Examples of such active programmes include the Strengthening Laboratory Management Towards Accreditation,[80] Stepwise Laboratory Quality Improvement Process Towards Accreditation,[81] and International Organization for Standardization 15189 programmes (appendix).[82]

A recommended PaLM delivery package focused on LMICs—the integrated network of tiered laboratories

To implement the solutions suggested in this paper and address inequitable access to PALM services, we propose the development of an evidence-based, LMIC-focused PALM delivery package based on an integrated network of tiered laboratories system (table 1). Furthermore, we suggest several measurable indicators to assess the effectiveness of this project in driving optimal PALM services (table 2).

This concept has previously been proposed as a framework for effective delivery of PALM services in LMICs.[83] The tiered approach is not unique to pathology; it has also been postulated for emergency medicine and general surgery.[85,87] Such a tiered system (figure) would span a continuum in which widely distributed primary care clinics, with minimal but relevant testing capabilities, are linked to a second tier of district hospitals with laboratories that offer a broader range of diagnostic testing. These, in turn, are linked to a third tier of larger hospitals, academic medical centres, or national laboratories with specialised diagnostic, teaching, and research capability.[83,84] POC testing should be appropriately incorporated into this system. Each tier should be interlinked and interdependent on the next, with a focus on providing access to the most cost-effective, high-quality testing that is appropriate for the clinical setting.[88] Within this framework, patients would move across tiers as clinically indicated, specimens would be moved to the required tier level for testing, and efficient communication systems would be created to facilitate transmission of data. The integrated network approach would also facilitate the standardisation of training, implementation of quality assurance programmes, financing, and infrastructure development. This framework should be the key structural component of all national PALM strategic plans.

Such a concept has been successfully adopted in the approach to the diagnosis and treatment of specific diseases. For example, in a programme led by the Asian Lymphoma Study Group, the role of the laboratory in diagnosing non-Hodgkin lymphoma, including level of expertise required and range of assays available, is articulated for each laboratory tier within the network.[89] The approach taken by the PEPFAR programme to improve access to HIV care, including diagnostic testing, in sub-Saharan Africa also provides useful lessons for creating integrated networks to improve access to care (panel 4). It would be prudent for PALM services in these countries to expand on the existing PEPFAR infrastructure, on which billions of dollars were expended.

Conclusion

There are substantial barriers preventing LMICs from providing patients with appropriate access to PALM services. In this paper, we describe several potential solutions to four of these major barriers. We believe that the solutions outlined are sufficiently flexible and generic to be relevant for the foreseeable future, and that LMICs will adapt or adopt those that best suit their unique circumstances.

Panel 4: Lessons from the HIV US President's Emergency Plan for AIDS Relief (PEPFAR) programme—how can we leverage resources?

The response to the global HIV epidemic encountered many of the same challenges that are obstructing access to high-quality pathology and laboratory medicine (PALM) services in low-income and middle-income countries (LMICs). Since its launch in 2004, PEPFAR has enabled more than 11·5 million people living with HIV to access life-saving antiretroviral therapy and prevented 2 million infants from acquiring HIV infection.[90] These remarkable public health achievements were accomplished in countries, mainly in sub-Saharan Africa, that many believed would be unable to support the scale-up of such complex programmes because of health-care systems characterised by weak infrastructure, insufficient workforce, and fragmented laboratory, procurement, and information systems.[91–94]

Increasing number of health-care workers, task shifting and task sharing

- The PEPFAR-funded medical education and nursing education partnership initiatives focused on revamping outdated curricula, building the capacity of instructors and faculty, and strengthening in-service training through innovative instructional methodologies;[93,95] almost 220 000 health-care workers received training to deliver HIV care and other health-care services
- The programme supported task shifting and task sharing from physicians to nurses and clinical officers and from nurses to community and other lay workers[96,97]

Improving infrastructure

- The PEPFAR programme invested in the physical infrastructure of laboratories to allow for provision of required services
- Effective procurement systems for essential equipment and supplies were put in place to sustain quality services
- Attention to the use of innovations, such as laboratory information systems and short messaging service printers, expedited the turnaround times of laboratory result reporting[98]

Integrated tiered systems of health-care delivery

- A matrix of tiered health-care facility and laboratory referral systems with rigorous external quality assessment schemes was established[99]
- A public-private partnership has been established to support laboratory infrastructure in four African countries with high HIV burden[90]

Accreditation of laboratories

- PEPFAR has also supported efforts to achieve international accreditation of laboratories through step-by-step mentorship and guidance throughout the accreditation process[100]

Perhaps most importantly, the HIV response has highlighted the value of conceptualising health-care services as continuums. This concept was epitomised by a focus on optimising every step across the continuum of prevention and care. It is only by such an approach that PALM services will be effective in LMICs and help achieve the desired effect of prevention and treatment interventions.[101,102]

Preparation of this paper has highlighted the substantial scarcity of accurate data on the current status of PALM services in LMICs. An accurate knowledge of the size and nature of the problem must inform potential solutions, therefore, research on this area is urgently needed. Additionally, a major programme of needs-assessment and research into areas such as the effectiveness, sustainability, affordability, and feasibility of possible solutions is needed.

Almost all aspects of PALM systems in many LMICs need re-inforcing. There is a role for a national strategic laboratory plan to coordinate these efforts and identify achievable goals within a specified timeframe. Such a plan should not simply focus on laboratories but should encapsulate the entire PALM system; this is addressed in detail in the third paper of this Series. Although the implementation of many of the individual solutions presented here need not await the creation of a national strategic laboratory plan, some aspects—for example, the

Panel 5: The African Society of Laboratory Medicine

The African Society of Laboratory Medicine is a pan-African professional body headquartered in Addis Ababa, Ethiopia, that is working with governments and local and international collaborators to strengthen African laboratory professionals through standardised training and certification.[103] The society, which is endorsed by the African Union, also supports enrolment of laboratories in quality improvement programmes, aims to establish harmonised regulatory frameworks for diagnostic products, and aims to build a network of public reference laboratories to improve early detection of diseases and promote collaborative research. Some of the key achievements of the society to date include:

- Audits of 160 laboratories across 22 African countries
- Establishment of a pan-African network of national public health reference laboratories in 30 countries across Africa
- Leading a ministerial call to action for laboratory strengthening that was signed by one third of African countries, in partnership with UNAIDS
- Launching a diagnostics access initiative to achieve the new UNAIDS 90-90-90 HIV treatment targets[103]

creation of an integrated network of tiered laboratories and accreditation—would be difficult in the absence of national strategic planning and regulatory and governance frameworks. For such system reinforcement, redesign, or both, it is a crucial and immediate requirement that governments in LMICs take an active role, supported by international organisations (eg, WHO, World Bank) and national stakeholders. One such coordinated effort has been the creation of the African Society for Laboratory Medicine in 2011, by stakeholders including WHO Regional Office for Africa, CDC, PEPFAR, UNAIDS, Clinton Health Access Initiative, and the American Society for Clinical Pathology (panel 5).

Growing populations, increasing disease burdens, and the magnitude of existing gaps in access to PALM services in LMICs mean that substantial progress in addressing these gaps will take years. It is, therefore, crucial not to delay, because barriers and issues will only increase with time. In view of the insufficient awareness of these problems, implementing national and international action will require a major advocacy effort. The third paper in this Series discusses in further detail the underpinning of national strategic laboratory plans, the role of advocacy and its political dimensions, and the costs and affordability of equitable, high-quality PALM services for LMICs.

Contributors

SSa, ML, LML, MLW, DM, JF, and KAF participated in design of the series and this second paper. SSa, WC, SYT, WES, NW, SSi, NB, LML, MLW, DM, and KAF assisted with initial literature search. SSa, MLW, and JF drafted the figures. SSa, WC, SYT, WES, ML, NB, SAP, and DM wrote some sections of the initial draft, and LML assisted in initial drafts of several sections. NW was responsible for the design, distribution, and analysis of the workforce survey, SSa, WC, SSi, ML, LML, MLW, JF, and KAF assisted with its design and analysis, and WC and SSi also assisted with the distribution of the survey. WC and NB assisted with revision of the sections during the writing process. WC, NW, SSi, LML, SAP, and DM provided reviews and critique during the writing process. MLW and KAF coordinated initial drafts with the other two papers in the series. SSa and KAF provided overall coordination of writing and revisions, with the assistance of ML, MLW, and JF.

Declaration of interests

We declare no competing interests.

Acknowledgments

The authors would like to thank the contribution of Sue Horton for her invaluable review and critique for this paper.

References

1 Wilson ML, Fleming KA, Kuti M, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a critical gap. *Lancet* 2018; published online March 15. http://dx.doi.org/S0140-6736(18)30458-6.

2 Bollyky TJ, Templin T, Andridge C, Dieleman JL. Understanding the relationships between noncommunicable diseases, unhealthy lifestyles, and country wealth. *Health Aff (Millwood)* 2015; **34:** 1464–71.

3 Jeon YH, Essue B, Jan S, Wells R, Whitworth JA. Economic hardship associated with managing chronic illness: a qualitative inquiry. *BMC Health Serv Res* 2009; **9:** 182.

4 Carter JY, Kihara HJ. Needs assessment for strengthening laboratory human resources capacity for universal access to HIV, malaria and TB services in three Sub-Saharan countries. 2010. http://apps.who.int/iris/bitstream/10665/44496/1/9789241500920_eng.pdf (accessed July 30, 2017).

5 Basu S, Andrews J, Kishore S, Panjabi R, Stuckler D. Comparative performance of private and public healthcare systems in low- and middle-income countries: a systematic review. *PLoS Med* 2012; **9:** e1001244.

6 Mir AM, Shaikh GR, Shaikh S, Mankani N, Hassan A, Sadiq M. Assessing retention and motivation of public health-care providers (particularly female providers) in rural Pakistan. 2013. http://www.popcouncil.org/uploads/pdfs/2013RH_RAF_MotivationStudy.pdf (accessed April 24, 2017).

7 Strasser R, Neusy AJ. Context counts: training health workers in and for rural and remote areas. *Bull World Health Organ* 2010; **88:** 777–82.

8 Strasser R, Kam SM, Regalado SM. Rural health care access and policy in developing countries. *Ann Rev Public Health* 2016; **37:** 395–412.

9 Bennett S, Paina L, Ssengooba F, Waswa D, M'Imunya JM. Mentorship in African health research training programs: an exploratory study of Fogarty International Center Programs in Kenya and Uganda. *Educ Health (Abingdon)* 2013; **26:** 183–87.

10 World Association of Societies of Pathology and Laboratory Medicine. World Pathology Foundation—Gordon Signy Fellowship. http://www.wasPALM.org/content/world-pathology-foundation-gordon-signy-fellowship (accessed Oct 13, 2017).

11 WHO. Task shifting: rational redistribution of tasks among health workforce teams. 2008. http://apps.who.int/iris/bitstream/10665/43821/1/9789241596312_eng.pdf (accessed July 30, 2017).

12 Knaul FM, Gralow JR, Atun R, Bhadelia A. Closing the cancer divide: an equity imperative. Boston: Harvard Global Equity Initiative, 2012.

13 Mpunga T, Tapela N, Hedt-Gauthier BL, et al. Diagnosis of cancer in rural Rwanda. Early outcomes of a phased approach to implement anatomic pathology services in resource-limited settings. *Am J Clin Pathol* 2014; **142:** 541–45.

14 Kaindjee-Tjituka F, Sawadogo S, Mutandi G, et al. Task-shifting point-of-care CD4+ testing to lay health workers in HIV care and treatment services in Namibia. *Afr J Lab Med* 2017; **6:** a643.

15 Mumtaz Z, Patterson P. Does task shifting among parts of a weak health system help? *Lancet Glob Health* 2017; **5:** e734–35.

16 Okyere E, Mwanri L, Ward P. Is task-shifting a solution to the health workers' shortage in Northern Ghana? *PLoS One* 2017; **12:** e0174631.

17 Hoenecke H, Lee V, Roy I. Pathologists overseas: coordinating volunteer pathology services for 19 years. *Arch Pathol Lab Med* 2011; **135:** 173–78.

18 Birrell I. Before you pay to volunteer abroad, think of the harm you might do. *The Guardian* (London), Nov 13, 2010. https://www.theguardian.com/commentisfree/2010/nov/14/orphans-cambodia-aids-holidays-madonna (accessed July 30, 2017).

19 Benediktsson H, Whitelaw J, Roy I. Pathology services in developing countries: a challenge. *Arch Pathol Lab Med* 2007; **131:** 1636–39.

20 Loh LC, Cherniak W, Dreifuss BA, Dacso MM, Lin HC, Evert J. Short term global health experiences and local partnership models: a framework. *Global Health* 2015; **11:** 50.

21 Adesina A, Chumba D, Nelson AM, et al. Improvement of pathology in sub-Saharan Africa. *Lancet Oncol* 2013; **14:** e152–57.

22 Hung T, Jarvis-Selinger S, Ford JC. Residency choices by graduating medical students: why not pathology? *Hum Pathol* 2011; **42:** 802–07.

23 Rambau PF. Pathology practice in a resource-poor setting: Mwanza, Tanzania. *Arch Pathol Lab Med* 2011; **135:** 191–93.

24 Castaneda C, Nalley K, Mannion C, et al. Clinical decision support systems for improving diagnostic accuracy and achieving precision medicine. *J Clin Bioinformat* 2015; **5:** 4.

25 Adeyi OA. Pathology services in developing countries—the West African experience. *Arch Pathol Lab Med* 2011; **135:** 183–86.

26 Liverpool School of Tropical Medicine. An analysis of approaches to laboratory capacity strengthening for drug resistant infections in low and middle income countries. 2017. https://www.lstmed.ac.uk/sites/default/files/centre/Lab%20capacity%20strengthening%20-%20summary%20-%20public%5B1%5D.pdf (accessed Oct 13, 2017).

27 Chite Asirwa F, Greist A, Busakhala N, Rosen B, Loehrer PJ. Medical education and training: building in-country capacity at all levels. *J Clin Oncol* 2016; **34:** 36–42.

28 Strother RM, Asirwa FC, Busakhala NB, et al. AMPATH-Oncology: a model for comprehensive cancer care in sub-Saharan Africa. *J Cancer Policy* 2013; **1:** e42–48.

29 Looi LM. In: Sayed S, editor. Challenges in the pathological assessment of cancer in low and middle income countries. UICC World Cancer Congress; Paris, France; Oct 31–Nov 3, 2016. 101M-T2.

30 Looi LM. The Pathology Laboratory Act 2007 explained. *Malaysian J Pathol* 2008; **30:** 01–10.

31 Nigatu A, Abdallah H, Aboagye-Nyame F, Messele T, Kidane-Mariam T, Ayana G. Case study: impact of the Ethiopian National Laboratory Logistics System on the harmonization of laboratory commodities. 2009. http://www.who.int/hiv/amds/amds_impact_ethiopian_lab.pdf (accessed April 25, 2017).

32 Ethiopian Health and Nutrition Research Institute, Federal Ministry of Health. Master plan for the public health laboratory system in Ethiopia. 2009. http://www.ephi.gov.et/images/downloads/Ethiopia%20Lab%20Master%20Plan_2nd%20Edition.pdf (accessed Oct 12, 2017).

33 WHO, PATH. Outsourcing vaccine supply chain and logistics to the private sector. 2012. https://www.path.org/publications/files/TS_opt_outsourcing_br.pdf (accessed July 30, 2017).

34 Riewpaiboon A, Sooksriwong C, Chaiyakunapruk N, et al. Optimizing national immunization program supply chain management in Thailand: an economic analysis. *Public Health* 2015; **129:** 899–906.

35 WHO, PATH. Optimize: Senegal report. 2013. https://www.path.org/publications/files/TS_opt_senegal_rpt.pdf (accessed Oct 13, 2017).

36 WHO. Human resources for medical devices, the role of biomedical engineers. 2017. http://www.who.int/medical_devices/publications/hr_med_dev_bio-engineers/en/ (accessed July 30, 2017).

37 Aller RD. Informatics, imaging and the pathologist's workstation. In: Henry JB, ed. Clinical diagnosis and management by laboratory methods. Philadelphia: WB Saunders, 1996: 92–124.

38 Kamat S, Parwani AV, Khalbuss WE, et al. Use of a laboratory information system driven tool for pre-signout quality assurance of random cytopathology reports. *J Pathol Inform* 2011; **2:** 42.

39 Blaya JA, Shin SS, Yagui M, et al. Reducing communication delays and improving quality of care with a tuberculosis laboratory information system in resource poor environments: a cluster randomized controlled trial. *PloS One* 2014; **9:** e90110.

40 Wagenaar BH, Sherr K, Fernandes Q, Wagenaar AC. Using routine health information systems for well-designed health evaluations in low- and middle-income countries. *Health Policy Plan* 2016; **31:** 129–35.

41 Kyobe S, Musinguzi H, Lwanga N, et al. Selecting a laboratory information management system for biorepositories in low- and middle-income countries: the H3Africa experience and lessons learned. *Biopreserv Biobank* 2017; **15:** 111–15.

42 Mpunga T, Hedt-Gauthier BL, Tapela N, et al. Implementation and validation of telepathology triage at Cancer Referral Center in rural Rwanda. *J Glob Oncol* 2016; **2:** 76–82.

43 Chen J, Jiao Y, Lu C, Zhou J, Zhang Z, Zhou C. A nationwide telepathology consultation and quality control program in China: implementation and result analysis. *Diagn Pathol* 2014; **9** (suppl 1)**:** S2.

44 Geissbuhler A, Bagayoko CO, Ly O. The RAFT network: 5 years of distance continuing medical education and tele-consultations over the internet in French-speaking Africa. *Intern J Med Informat* 2007; **76:** 351–56.

45 Fischer MK, Kayembe MK, Scheer AJ, Introcaso CE, Binder SW, Kovarik CL. Establishing telepathology in Africa: lessons from Botswana. *J Am Acad Dermatol* 2011; **64:** 986–87.

46 Lowe J. Telepathology: guidance from the Royal College of Pathologists. 2013. https://www.rcpath.org/resourceLibrary/telepathology-guidance-from-the-royal-college-of-pathologists-pdf.html (accessed Oct 30, 2017).

47 Mpunga T, Tapela N, Hedt-Gauthier BL, et al. Diagnosis of cancer in rural Rwanda: early outcomes of a phased approach to implement anatomic pathology services in resource-limited settings. *Am J Clin Pathol* 2014; **142:** 541–45.

48 UC Davis Health Newsroom. Telepathology program to improve cancer diagnosis in developing world. 2016. https://www.ucdmc.ucdavis.edu/publish/news/newsroom/11346 (accessed July 30, 2017).

49 Hawkins RC. Laboratory turnaround time. *Clin Biochem Rev* 2007; **28:** 179–94.

50 Joloba M, Mwangi C, Alexander H, et al. Strengthening the tuberculosis specimen referral network in Uganda: rhe role of public–private partnerships. *J Infect Dis* 2016; **213** (suppl 2)**:** S41–46.

51 Kebede Y, Fonjungo PN, Tibesso G, et al. Improved specimen-referral system and increased access to quality laboratory services in Ethiopia: the role of the public–private partnership. *J Infect Dis* 2016; **213** (suppl 2)**:** S59–64.

52 Jian WS, Hsu MH, Sukati H, et al. LabPush: a pilot study of providing remote clinics with laboratory results via short message service (SMS) in Swaziland, Africa. *PloS One* 2012; **7:** e44462.

53 Government of India, Ministry of Statistics and Programme Implementation. NSS Report no. 574: health in India. http://mospi.nic.in/sites/default/files/publication_reports/nss_rep574.pdf?download=1 (accessed Nov 25, 2017).

54 Shrivastava R, Gadde R, Nkengasong JN. Importance of public–private partnerships: strengthening laboratory medicine systems and clinical practice in Africa. *J Infect Dis* 2016; **213** (suppl 2)**:** S35–40.

55 Hernandez-Aguado I, Zaragoza GA. Support of public–private partnerships in health promotion and conflicts of interest. *BMJ Open* 2016; **6:** e009342.

56 Oriero EC, Van Geertruyden JP, Nwakanma DC, D'Alessandro U, Jacobs J. Novel techniques and future directions in molecular diagnosis of malaria in resource-limited settings. *Expert Rev Mol Diagn* 2015; **15:** 1419–26.

57 Vashist SK, Luppa PB, Yeo LY, Ozcan A, Luong JH. Emerging technologies for next-generation point-of-care testing. *Trends Biotechnol* 2015; **33:** 692–705.

58 United Nations. Political Declaration on HIV and AIDS: intensifying our efforts to eliminate HIV and AIDS. 2011. http://www.unaids.org/en/aboutunaids/unitednationsdeclarationsandgoals/2011highlevelmeetingonaids (accessed June 1, 2017).

59 Ritchie AV, Ushiro-Lumb I, Edemaga D, et al. SAMBA HIV semiquantitative test, a new point-of-care viral-load-monitoring assay for resource-limited settings. *J Clin Microbiol* 2014; **52:** 3377–83.

60 Goel N, Ritchie AV, Mtapuri-Zinyowera S, et al. Performance of the SAMBA I and II HIV-1 Semi-Q Tests for viral load monitoring at the point-of-care. *J Virol Methods* 2017; **244:** 39–45.

61 UNITAID. Hepatitis C: diagnostics technology landscape. 1st edn. 2015. http://unitaid-hepC-dx-techlandscape- report_2015.html (accessed April 19, 2017).

62 Pai NP, Vadnais C, Denkinger C, Engel N, Pai M. Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low- and middle-income countries. *PLoS Med* 2012; **9:** e100130618.

63 Snijdewind IJ, van Kampen JJ, Fraaij PL, van der Ende ME, Osterhaus AD, Gruters RA. Current and future applications of dried blood spots in viral disease management. *Antiviral Res* 2012; **93:** 309–21.

64 De Crignis E, Re MC, Cimatti L, Zecchi L, Gibellini D. HIV-1 and HCV detection in dried blood spots by SYBR Green multiplex real-time RT-PCR. *J Virol Methods* 2010; **165:** 51–56.

65 Boehme CC, Nicol MP, Nabeta P, et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. *Lancet* 2011; **377:** 1495–505.

66 WHO. WHO meeting report of a technical expert consultation: non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF. 2017. http://www.who.int/tb/publications/2017/XpertUltra/en/ (accessed June 1, 2017).

67 Hsiang MS, Greenhouse B, Rosenthal PJ. Point of care testing for malaria using LAMP, loop mediated isothermal amplification. *J Infect Dis* 2014; **210:** 1167–69.

68 Patel JC, Lucchi NW, Srivastava P, et al. Field evaluation of a real-time fluorescence loop-mediated isothermal amplification assay, RealAmp, for the diagnosis of malaria in Thailand and India. *J Infect Dis* 2014; **210:** 1180–87.

69 de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol* 2010; **11:** 1048–56.

70 Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *N Engl J Med* 2009; **360:** 1385–94.

71 Sankaranarayanan R, Esmy PO, Rajkumar R, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet* 2007; **370:** 398–406.

72 Denny L, de Sanjose S, Mutebi M, et al. Interventions to close the divide for women with breast and cervical cancer between LMICs and high-income countries. *Lancet* 2017; **389:** 861–70.

73 Holmes K, Bertozzi S, Boom BR, Jha P, eds. Major infectious diseases. In: Jamison D, Gelband H, Horton S, et al, eds. Disease control priorities, 3rd edn. Washington, DC: World Bank, 2017.

74 Shaw JLV. Practical challenges related to point of care testing. *Pract Lab Med* 2016; **4:** 22–29.

75 Wilson ML. Malaria rapid diagnostic tests. *Clin Infect Dis* 2012; **54:** 1637–41.

76 WHO Regional Office for Europe. The principles of quality assurance: report on a WHO meeting, Barcelona, 17–19 May 1983. 1985. https://searchworks.stanford.edu/view/10832571 (accessed Oct 13, 2017).

77 WHO. Manual for procurement of diagnostics and related laboratory items and equipment. 2013. http://www.who.int/diagnostics_laboratory/publications/130627_manual_for_procurement_of_diagnostics-001-june2013.pdf (accessed July 30, 2017).

78 College of Pathologists, Academy of Medicine of Malaysia. Pathology laboratory practice guidelines of the College of Pathologists. *Malays J Pathol* 2005; **27:** 51–74.

79 Perrone LA, Voeurng V, Sek S, et al. Implementation research: a mentoring programme to improve laboratory quality in Cambodia. *Bull World Health Organ* 2016; **94:** 743–51.

80 Noble M, Martin R, Ndihokubwayo JB. Transforming the quality of laboratory medicine through the Strengthening Laboratory Management Toward Accreditation program in 2014. http://www.ajlmonline.org/index.php/ajlm/issue/view/6 (accessed July 30, 2017).

81 WHO. WHO Guide for the stepwise laboratory improvement process towards accreditation in the African Region. 2013. http://www.who.int/tb/laboratory/afro-slipta-checklist-guidance.pdf (accessed July 30, 2017).

82 Schneider F, Maurer C, Friedberg RC. International Organization for Standardization (ISO) 15189. *Ann Lab Med* 2017; **37:** 365–70.

83 Fleming KA, Naidoo M, Wilson M, et al. An essential pathology package for low- and middle-income countries. *Am J Clin Pathol* 2017; **147:** 15–32.

84 Warner LC. Lab-in-a-Box: a guide to building anatomic pathology networks in resource-limited settings. *Am J Clin Pathol* 2017; **147:** 08–14.

85 Meara JG, Leather AJ, Hagander L, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet* 2015; **386:** 569–624.

86 Vaught J, Rogers J, Carolin T, Compton C. Biobankonomics: developing a sustainable business model approach for the formation of a human tissue biobank. *J Natl Cancer Inst Monogr* 2011; **2011:** 24–31.

87 Kobusingye OC, Hyder AA, Bishai D, Hicks ER, Mock C, Joshipura M. Emergency medical systems in low- and middle-income countries: recommendations for action. *Bull World Health Organ* 2005; **83:** 626–31.

88 Crook M. Clinical governance and pathology. *J Clin Pathol* 2002; **55:** 177–79.

89 Tan D, Tan SY, Lim ST, et al. Management of B-cell non-Hodgkin lymphoma in Asia: resource-stratified guidelines. *Lancet Oncol* 2013; **14:** e548–61.

90 US President's Emergency Plan for AIDS Relief. PEPFAR latest global results: factsheet 2016. 2016. https://www.pepfar.gov/documents/organization/264882.pdf (accessed Oct 13, 2017).

91 De Cock KM, El-Sadr WM, Ghebreyesus TA. Game changers: why did the scale-up of HIV treatment work despite weak health systems? *J Acquir immune Defic Syndr* 2011; **57** (suppl 2)**:** S61–63.

92 Palen J, El-Sadr W, Phoya A, et al. PEPFAR, health system strengthening, and promoting sustainability and country ownership. *J Acquir Immune Defic Syndr* 2012; **60** (suppl 3)**:** S113–19.

93 Middleton L, Howard AA, Dohrn J, et al. The Nursing Education Partnership Initiative (NEPI): innovations in nursing and midwifery education. *Acad Med* 2014; **89** (suppl 8)**:** S24–28.

94 Rabkin M, Kruk ME, El-Sadr WM. HIV, aging and continuity care: strengthening health systems to support services for noncommunicable diseases in low-income countries. *AIDS* 2012; **26** (suppl 1)**:** S77–83.

95 Manabe YC, Campbell JD, Ovuga E, Maling S, Bollinger RC, Sewankambo N. Optimisation of the Medical Education Partnership Initiative to address African health-care challenges. *Lancet Glob Health* 2014; **2:** e392.

96 Rabkin M, Lamb M, Osakwe ZT, Mwangi PR, El-Sadr WM, Michaels-Strasser S. Nurse-led HIV services and quality of care at health facilities in Kenya, 2014–2016. *Bull World Health Organ* 2017; **95:** 353–61.

97 Mwai GW, Mburu G, Torpey K, Frost P, Ford N, Seeley J. Role and outcomes of community health workers in HIV care in sub-Saharan Africa: a systematic review. *J Intern AIDS Soc* 2013; **16:** 18586.

98 WHO. SMS printers aid early infant diagnosis of HIV/AIDS in Nigeria CHAI's SMART. 2013. http://www.who.int/reproductivehealth/publications/mhealth/infant_diagnosis_hiv_nigeria/en/ (accessed July 30, 2017).

99 US President's Emergency Plan for AIDS Relief. Ethiopia operational plan report 2012. 2013. https://www.pepfar.gov/documents/organization/212142.pdf (accessed Oct 13, 2017).

100 Skaggs B, Pinto I, Masamha J, Turgeon D, Gudo ES. Implementing laboratory quality management systems in Mozambique: the Becton Dickinson-US President's Emergency Plan for AIDS Relief Public–private Partnership Initiative. *J Infect Dis* 2016; **213** (suppl 2)**:** S47–52.

101 McNairy ML, El-Sadr WM. A paradigm shift: focus on the HIV prevention continuum. *Clin Infect Dis* 2014; **59** (suppl 1)**:** S12–15.

102 McNairy ML, Lamb MR, Abrams EJ, et al. Use of a comprehensive HIV care cascade for evaluating HIV program performance: findings from 4 sub-Saharan African countries. *J Acquir Immune Defic Syndr* 2015; **70:** e44–51.

103 Peter T. Building an effective laboratory biosafety response in Africa. 2012. https://slmta.org/resource/biosafety/3-Day-1-Plenary/5-T-Peter-Day-1-1045am.pdf (accessed Oct 13, 2017).