Pathology and laboratory medicine in low-income and middle-income countries 3

Delivering modern, high-quality, affordable pathology and laboratory medicine to low-income and middle-income countries: a call to action

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Modern, affordable pathology and laboratory medicine (PALM) systems are essential to achieve the 2030 Sustainable Development Goals for health in low-income and middle-income countries (LMICs). In this last in a Series of three papers about PALM in LMICs, we discuss the policy environment and emphasise three crucial high-level actions that are needed to deliver universal health coverage. First, nations need national strategic laboratory plans; second, these plans require adequate financing for implementation; and last, pathologists themselves need to take on leadership roles to advocate for the centrality of PALM to achieve the Sustainable Development Goals for health. The national strategic laboratory plan should deliver a tiered, networked laboratory system as a central element. Appropriate financing should be provided, at a level of at least 4% of health expenditure. Financing of new technologies such as molecular diagnostics is challenging for LMICs, even though many of these tests are cost-effective. Point-of-care testing can substantially reduce test-reporting time, but this benefit must be balanced with higher costs. Our research analysis highlights a considerable deficiency in advocacy for PALM; pathologists have been invisible in national and international health discourse and leadership. Embedding PALM in LMICs can only be achieved if pathologists advocate for these services, and undertake leadership roles, both nationally and internationally. We articulate eight key recommendations to address the current barriers identified in this Series and issue a call to action for all stakeholders to come together in a global alliance to ensure the effective provision of PALM services in resource-limited settings.

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Introduction

These are exciting times for medicine, including for pathology and laboratory medicine (PALM). New opportunities are being provided by advances in technology. Molecular diagnostics will potentially radically reshape pathology as a discipline. However, these opportunities are tempered by resource constraints in health care. High-income countries face problems of ageing populations, slower economic growth than in the past, and the rising burden of non-communicable diseases. Low-income and middle-income countries (LMICs) are challenged in trying to move to universal health coverage while dealing with still-substantial infectious and growing non-communicable disease burdens. Globalisation is imposing new constraints on what national policy can achieve and exposing new areas in which international cooperation and action are needed. For PALM, globalisation implies issues as varied as multinational laboratory testing companies, emerging infectious disease threats that can be rapidly transmitted across national borders, and the internationalisation of production and marketing of diagnostic tests. In this paper, we examine the opportunities and challenges for PALM, looking forward to 2030, when the Sustainable Development Goals call for health coverage for all.

The first two papers[1,2] in this Series examined the current state of PALM in LMICs and highlighted the key challenges, as well as suggesting possible solutions over which the PALM community has at least some influence. This final paper examines the role of national planning, financing, and advocacy in the development and implementation of an innovative and affordable PALM strategy that enhances patient care globally (figure). We underline the key role that a global alliance can have in achieving this goal and provide specific recommendations for the five key stakeholder groups (pathologists and other laboratory professionals, physicians, policy makers, politicians, and the public).

Key messages

- Pathology and laboratory medicine (PALM) must be a component of the national health plan in every low-income and middle-income country (LMIC), and all countries need a national strategic laboratory plan
- Diagnostic tests are more affordable at large scale: the challenge in LMICs is balancing the volume with appropriate turnaround time
- Advanced technology and globalisation are underpinning wide-ranging changes in health care: pathologists must be at the apex of these developments and provide a systems perspective on PALM implementation
- Pathologists need to step forward into leadership and advocacy roles: if not, others will determine the future of PALM
- Global alliances have moved forward the agenda for vaccines and immunisations, AIDS, tuberculosis, and malaria: PALM could be a key partner in a proposed Global Alliance for Diagnostics
- Key indicators of success of the PALM system should be collected nationally and reported internationally by organisations such as WHO

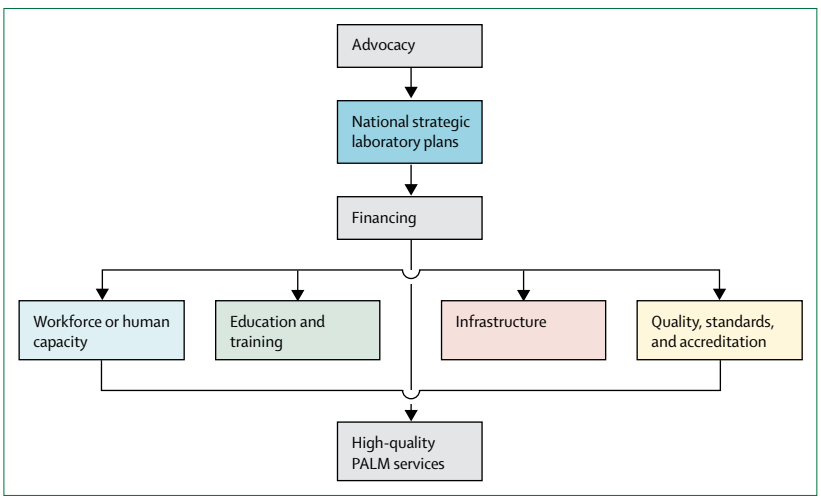

Figure: **Key factors underpinning high-quality, affordable pathology and laboratory medicine (PALM) services**

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National strategic plans for PALM systems

The solutions described in the second paper[2] of this Series are complex and require the participation of experts from many sectors to implement. A national strategic laboratory plan is required to coordinate these efforts and identify achievable goals to be reached within a specified timeframe. The Maputo Declaration on Strengthening Laboratory Systems, published in 2008, was one of the first documents to advocate for the development of a national strategic laboratory plan.[3] In response to this declaration, a report by WHO gave specific guidance on how to structure strategic national-level plans for PALM services,[4] and in the same year emphasised the importance of strengthening public laboratories for infectious disease control.[5] This guidance was reaffirmed in 2015 by the Freetown Declaration on Developing Resilient Laboratory Networks for the Global Health Security Agenda.[6]

The regulatory component of the strategic plan must carry the weight of government oversight and enforcement; without this stipulation, individual laboratories have little or no incentive to become accredited or to adhere to quality standards. As noted in the first paper[1] in this Series, inadequate regulatory oversight in Kampala, Uganda, resulted in hundreds of independent laboratories providing PALM testing, few of which met even basic quality standards.[7] Several of the examples in the second paper[2] highlighted the benefits of having a strategic plan. The existence of a plan in Malaysia has underpinned the increased deployment of human resources and the introduction of robust accreditation systems,[8] and in Ethiopia it has helped to overcome supply chain issues.[9] A national strategic laboratory plan, with pathologists appropriately involved in its design and implementation,[4] would allow countries to strategically implement the solutions to the key issues facing PALM. The national strategic laboratory plan would ideally be developed in close consultation with national plans (where available) for surgery, obstetrics, anaesthesia, and cancer, given the interdependencies among these areas.

Countries in sub-Saharan Africa have been slowly moving to develop national strategic laboratory plans. A study published in 2017 indicated that all of the 39 countries with national health plans in 2012 had highlighted aspects relating to laboratory issues in their plan; however, most of these plans had little of substance supporting PALM integration into national health-care delivery.[10] Only ten countries had a specific national strategic laboratory plan, although 13 more had begun the process of developing a plan. The same study indicated that by 2017, another six countries had started the process; thus, approximately 40% of sub-Saharan African countries have a national strategic laboratory plan either in place or under development.[10] However, less than five countries substantively covered financing in their national strategic laboratory plan.

Financing and costing: towards universal health coverage?

What does laboratory testing cost?

Estimates of the proportion of total health expenditures arising from laboratory tests range from about 3% to 6% across a range of high-income countries (5·0% in Spain,[11] 3·3% in the UK,[12] and 3·0% in Australia[13]) and two sub-Saharan African countries (3·5% in South Africa[14] and 3·3–4·6% in Uganda[15]). The USA is the exception, where laboratory tests account for an estimated 4·5–10·0% of health expenditures, although for Medicare the share is only 3·0%.[16] The overall median proportion of total health expenditures arising from PALM in these six countries is 4·0%. In Canada, the proportion of the hospital budget allocated to laboratory tests ranges from 2·7% in community hospitals to 6·0% in tertiary and teaching hospitals (Butany J, University of Toronto, personal communication).

Costs of individual tests vary considerably: biochemical tests are on average the least costly (pennies per test for common tests run on automated analysers), whereas the cost gradient increases with the more labour-intensive histopathology tests and molecular analyses for diseases such as cancer (hundreds or even thousands of dollars per test for one of the new molecular biology panels). Various factors affect test cost. Higher test volumes reduce test cost. For a standard biochemical test in the UK, compared with the highest-volume laboratories, cost per test approximately doubled for a laboratory running only 20% of the volume, and the cost quadrupled for laboratories running the test very infrequently;[12] a similar pattern was observed for histopathology tests in the UK[12] and for point-of-care testing using the Xpert test for tuberculosis in South Africa.[17] Test costs generally increase as turnaround time required decreases. Tests are least expensive if run in large batches on large analysers on a regular schedule; tests required at night or on weekends are more costly, as are tests that are run

individually or infrequently. Point-of-care tests (in most but not all cases) trade off higher cost for greater immediacy.[18] Since salaries increase with per capita income, test cost (and salary share within test cost) tends to increase with country income when holding other factors constant because consumables are traded and therefore have a more similar price across countries.[19]

Molecular point-of-care testing in LMICs

In the second Series paper,[2] we outlined the potential benefits of point-of-care testing in LMICs using new molecular technologies, including the reduction in test-reporting time and the lack of requirement for sophisticated equipment or specialist laboratory skills for test delivery. However, widespread application of these new technologies must be balanced against their cost in LMICs.[20] For example, point-of-care testing for HIV and subsequent linking of patients to care on the day that they are tested can potentially reduce loss to follow-up, lead to more rapid initiation of treatment, and hence reduce transmission. The question is whether LMICs can afford these new technologies. In South Africa, point-of-care testing for CD4 cell count to help inform antiviral therapy (at US$24 per test) has been shown to be cost-effective for initiation of treatment in pregnant women[21] and in the overall population.[22] One might expect similar results for the newly developed SAMBA viral load monitoring test ($17 per test).[23] In China, same-day point-of-care HIV testing followed by point-of-care CD4 testing and linkage to counselling (total cost $352 per person) was highly cost-effective.[24] However, both of these studies are for upper middle-income countries; affordability of testing and initiating treatment is a challenging issue, especially in low-income countries.

Point-of-care testing for tuberculosis has been greatly improved by the introduction of the Xpert MTB/RIF test, which detects *Mycobacterium tuberculosis* and resistance to rifampicin.[25] However, experience in South Africa, which has considerably scaled up Xpert MTB/RIF testing, is instructive: in addition to high budgetary costs, Xpert test results have sometimes proved difficult to link to health information systems and delays persist in initiation of treatment.[26] That is, point-of-care testing cannot completely overcome systems-level weaknesses.

For malaria, economic studies suggest that current-generation rapid diagnostic tests can be cost-effective in low-transmission environments, provided that physicians use test results to guide prescription of treatment. New next-generation point-of-care tests such as loop-mediated isothermal amplification[27] are similar in cost to current rapid diagnostic tests (<$1 per test) and, moreover, can help to reduce the overtreatment associated with such tests,[28] but cost-effectiveness must be confirmed by robust health economic studies. A cost of less than $1 per point-of-care test for malaria seems to be a lot more affordable than that of some of the tests discussed previously; however, when the number of malarial episodes per child aged under 15 years is 0·6 per year in urban areas (and 1·9 for children under 5 years of age in rural areas), as it is in high-endemicity countries in sub-Saharan Africa, affordability is still a concern.[29]

Testing for high-risk human papillomavirus subtypes as part of a same-day screen-and-treat protocol for cervical cancer is increasingly being carried out in LMICs.[30] However, although the desired single-visit approach might be cost-effective and affordable in densely populated areas,[31] a two-visit approach (with testing done locally but cryotherapy provided centrally) is more affordable for rural areas[32] and should be considered.

In low-income countries, point-of-care testing has often been used to bypass laboratory systems that are functioning poorly, particularly in the vertical programmes aimed at infectious disease. However, this short-term measure hinders the development of a sustainable solution, and this approach has proved to be inadequate in the management of new threats such as Ebola virus and the emerging burden of non-communicable diseases.

Affordable molecular pathology in LMICs

Innovative nucleic acid amplification testing approaches and next-generation point-of-care platforms are exciting developments with considerable potential in LMICs. However, economic studies are essential to determine when nucleic acid amplification or point-of-care tests are affordable, cost-effective, and an appropriate component of a well functioning PALM system in resource-limited settings. New diagnostic tests will be most relevant if they are complemented by continued market-shaping efforts to ensure that tests and accompanying new treatments are within the financial reach of patients in LMICs. In many LMICs (particularly the low-income countries), the development of basic pathology services and a functioning PALM system is first required, on which future molecular platforms can be built.

Who pays for laboratory tests, and why does it matter?

In health care, who pays is a key factor. In low-income countries, out-of-pocket payments account for the majority of health expenditures, and tend to fall with rising incomes, as public provision increases or insurance becomes more widespread. A reliance on out-of-pocket payments means that poor people underinvest in treatment, and they underinvest in diagnostic tests to an even greater degree (because they see more immediate value in treatment than in diagnosis). Thus, the importance of diagnostic testing to inform successful therapeutic intervention needs to be emphasised.

A relatively small number of test types, undertaken frequently, and in countries at all levels of income, form the backbone of screening and diagnosis for many diseases or conditions (table; panel 1; appendix pp 9–10). As discussed in the first paper[1] of this Series, in many LMICs, these services are either non-existent or

See Online for appendix

	All India Institute of Medical Sciences	Aga Khan University Hospital	Columbia Asia Referral Hospital	Denver Health	University College Hospital	University Malaya Medical Centre
Location	Delhi, India	Nairobi, Kenya	Bangalore, India	Denver, CO, USA	Ibadan, Nigeria	Kuala Lumpur, Malaysia
Public versus private	Public	Private	Private	Public	Public	Public
Year	2012	2016	2016	2015	2015	2015
Number of beds	1700	254	160	550	850	1060
Number of top 25 tests per year per bed	2217	1810	1769	1913	204	1906
Blood culture ranking	6–25	6–25	6–25	6–25	6–25	6–25
Blood type* ranking	>25	6–25	6–25	6–25	6–25	6–25
Calcium or phosphorus† ranking	1–5	6–25	6–25	6–25	6–25	6–25
CBC‡ ranking	1–5	1–5	1–5	1–5	1–5	1–5
Cytology ranking	6–25	6–25	>25	6–25	6–25	>25
ESR§ ranking	>25	6–25	6–25	>25	6–25	6–25
Glucose (blood)¶ ranking	6–25	6–25	6–25	6–25	6–25	6–25
HbA_{1c} ranking	>25	6–25	6–25	6–25	6–25	6–25
Lipid profile‖ ranking	6–25	6–25	6–25	6–25	6–25	6–25
Liver function ranking	6–25	6–25	6–25	6–25	6–25	1–5
PT/INR** ranking	6–25	>25	6–25	6–25	6–25	6–25
Renal function ranking	1–5	1–5	6–25	1–5	1–5	1–5
Surgicals (biopsies)†† ranking	6–25	6–25	6–25	6–25	6–25	>25
Thyroid function ranking	6–25	6–25	1–5	6–25	>25	6–25
Urinalysis ranking	>25	1–5	6–25	1–5	1–5	6–25
Urine culture or microscopy ranking	6–25	6–25	6–25	6–25	6–25	6–25

Data are previously unpublished. See appendix for full data. CBC=complete blood count. ESR=erythrocyte sedimentation rate. HbA_{1c}=glycated haemoglobin A_{1c}. PT/INR=prothrombin time and international normalised ratio. *Aga Khan University Hospital uses crossmatch but not blood type; Denver Health does crossmatch in addition. †University Malaya Medical Centre does both together; Denver Health and University College Hospital do phosphorus; and others do calcium. ‡Some tests also include a smear (haemogram). §Columbia Asia Referral Hospital combines ESR with CBC. ¶Combines fasting, post-prandial, and random. ‖All India Institute of Medical Sciences test is for cholesterol. **Columbia Asia Referral Hospital uses coagulation profile. ††Histological tests.

Table: **Analysis of the 16 most common of the top 25 diagnostic tests (by volume) in six hospitals**

inadequate, despite evidence that access to PALM services improves diagnosis and treatment outcomes in LMICs and that lack of access is a barrier to effective disease control.[33,34]

Our examination of the number of diagnostic tests run (calculated per bed per year in the hospital) across six hospitals in lower middle-income (India, Kenya, and Nigeria), upper middle-income (Malaysia), and high-income (USA) countries indicated that the University College Hospital in Ibadan, Nigeria, runs less than 12% as many tests as the other five hospitals evaluated (table; panel 1). National insurance coverage in Nigeria was only 4%[35] at the time of the study. Presumptive treatment (ie, treatment without a confirmed diagnosis) is particularly common in sub-Saharan Africa; many individuals bypass the health system and purchase the treatment that they think they need from a pharmacist or an unregulated pharmaceutical provider.[36] As indicated previously, diagnostic testing must form part of the decision-making process in this setting; this message must be supported through both increased advocacy for PALM and financial support to offset the burden to the individual patient.

Countries have experimented with various forms of capitation payments or norms on testing to control costs. In South Africa, a national reference price list serves as a guideline for practitioners and insurers; doctors can charge up to five times the reference list price, but private insurers will only reimburse the list price.[37] Argentina uses capitation payments from the Social Security organisation to the biochemists' professional association, which in turn reimburses individual laboratories undertaking tests.[38] Canada has commissioned cost-effectiveness studies on the frequency of selected diagnostic tests permitted for reimbursement and uses the results of these studies to discourage overuse.[39] China is piloting clinical pathways for selected conditions, which provide guidelines on which tests should—and should not—be ordered for cases treated according to the pathway and indicate a defined capitation payment for patients following the pathways.[40] In India, private medical insurance only covers diagnostic tests done during a hospital stay (or so-called prehospitalisation tests, occurring in the 30 days before admission), with the exception of angiography, which is covered when undertaken at any time: individuals who are covered can

receive a free check-up every 3–4 years after 4 years of coverage.[41] Some of these systems can have unintended (and sometimes undesirable) effects on health outcomes. For example, the National Health Insurance scheme in South Korea did not cover colonoscopy or sigmoidoscopy for colon cancer screening as of 2005, which led to overall low coverage of screening and the use of less accurate tests that both worsened health outcomes and increased treatment costs overall.[42] Nevertheless, it is important that country-adapted approaches ensure that patients have financial risk protection and do not face catastrophic health expenditures or impoverishment while seeking appropriate PALM services.

Setting appropriate incentives for providers for high-quality service is equally important, whether payment is from the public or private sector (panel 2). The organisation of laboratories (numbers, sizes, and types of test provided) has important implications for quality and is also strongly affected by how services are reimbursed (out-of-pocket expenditures and private and public insurance as well as their reimbursement structure).

Advocacy and public policy

Public policy directs action taken by administrative and executive groups, including governments, health-care regulators, research funders, and international bodies, in a manner consistent with law and international customs. As such, public policy has a major influence on health care, including how PALM can be undertaken. PALM has many commonalities with another major discipline of global health—surgery. Like surgery, PALM was missing from the Millennium Development Goals and remains invisible within the current Sustainable Development Goals. A lack of leadership from the PALM community has characterised health policy debate nationally and globally. Here, we analyse global PALM through the policy and politics of agenda-setting frameworks,[46] and identify what is required to embed PALM as a key component of a high-quality health system. We use six themes to organise the discussion: narrative politics, organisational politics, symbolic politics, economic politics, scientific politics, and politicians' politics.

Narrative politics

Understanding of the social standing of PALM and pathologists in health politics is crucial for improvement of visibility and leadership. No single event, no Big Bang, demarcates the beginning of pathology.[47] Over the past decade, molecular biology has driven considerable technical expertise and intellectual leadership away from classically trained pathologists to other clinical and non-clinical professionals, such as infectious disease clinicians and translational cancer scientists. By the late 1980s, the PALM narrative was almost entirely articulated by non-pathologists.[48] For example, an analysis of cancer research funding committees and health policy committees undertaken for this paper (panel 3) indicated that less than 3·0% of cancer research funding committee members and less than 1·2% of health policy committee members indicate

***Panel 1*: The top 25 diagnostic tests in six hospitals**

We analysed the top 25 tests by volume using data collected during the course of a recent year (table) for six tertiary-level hospitals (including tests for inpatients and outpatients). The results are summarised in the table, and the full data are available in the appendix. The hospitals range from four in lower middle-income countries (India, Kenya, and Nigeria), one in an upper middle-income country (Malaysia), and one in a high-income country (USA). Two are private hospitals, and the rest are public.

Key findings include:

- The top 25 tests account for about 78% of the total number of tests run in University Malaya Medical Centre (UMMC; Kuala Lumpur, Malaysia), and 71% in Denver Health (CO, USA; we do not have these data for the other hospitals).
- 16 tests from the top 25 are used in at least four of the six hospitals.
- The most common test in all but one of the hospitals is the complete blood count (CBC), which accounts for 11% of all tests by volume in Denver Health, and 20% in UMMC (it is the second most common test in Columbia Asia Referral Hospital [Bangalore, India]).
- Tests from all four main diagnostic areas appear in the top 25 (biochemistry, haematology, microbiology, and histopathology).
- Five of the six hospitals have at least one unique test that does not appear in the top 25 lists for other hospitals, reflecting local epidemiology. Examples are vitamin B12 in All India Institute of Medical Sciences (New Delhi, India); *Helicobacter pylori* in Aga Khan University Hospital (Nairobi, Kenya); drugs of abuse screen in Denver Health; platelet count in Columbia Asia Referral Hospital; and haemoglobin electrophoresis in University College Hospital (Ibadan, Nigeria).
- The epidemiological transition is visible, with tests for malaria, tuberculosis, hepatitis B, and hepatitis C in the top 25 list in four lower-income countries but not for the two higher-income countries, whereas the opposite is true for tests important for cardiovascular conditions (troponin and partial thromboplastin time).
- The number of tests per year, per bed show considerable similarity among five of the hospitals, but the public hospital in Ibadan runs only 9–12% as many tests per bed as the other hospitals, illustrating sharply the resource constraints in that region, as well as the silos created by free tests available elsewhere for major infectious diseases.

Data limitations include:

- One hospital (Denver Health) also includes data from outreach sites, although these data constitute only a small proportion of the total. Some of the other hospitals have outreach sites, but those data are not included.
- Most of these hospitals serve as referral hospitals and receive samples for specialised tests from other health facilities.
- As income increases, hospitals run more tests as panels: in Malaysia, the average panel test includes seven individual tests, which are run (and counted) as individual tests in the lower-income countries.
- Different countries do not always use the same test for the same condition (eg, the test for syphilis in Denver Health is an enzyme immunoassay screen, but other hospitals use the venereal disease research laboratory test); however, we have counted these as similar tests.
- Denver includes point-of-care tests in the totals; but these are not well captured in the data for the other hospitals; they are also less frequently used in the lower-income countries.

Panel 2: Impact of organisation of pathology and laboratory medicine on test cost and volume

How laboratories are organised varies with different health systems: laboratories are more centralised in systems in which there is greater reliance on single-payer public payment.[43] Countries often have many small private laboratories associated with clinics or physicians' offices, where a small range of tests (generally point-of-care tests) are done. Large-volume laboratories are often associated with hospitals (both public and private hospitals) or are national reference laboratories. Large-volume laboratories and hospital laboratories typically provide a wider range of the more specialised tests, although they also undertake the common tests.[15,43] In New Zealand, investor-led foreign (Australian) for-profit private companies are increasingly taking over the physician-led laboratories,[44] a tendency that might become more widespread elsewhere with globalisation and with more expensive molecular tests. Other types of laboratories include those operated by non-profit groups such as academic institutions, religious organisations, and others.

The small-laboratory sector accounts for a large proportion of the total number of laboratories but a smaller share of the total volume of tests. In Kampala, Uganda, 94% of laboratories are small and 52% of tests are done in small laboratories, whereas in the USA 75% of laboratories are small and 13% of tests are done in small laboratories.[43] One study[45] noted that prices charged by private laboratories in four different countries were almost invariably somewhat higher than those charged by public laboratories for the same test. This finding is not surprising, since private laboratories are required to make a profit, and public laboratories receive subsidies for various inputs, which is consistent with the lower volumes in many private laboratories.

Panel 3: Methods for bibliometric analysis

Various databases, including Web of Science, PubMed, and ECONLIT, and free text searches in Google and Bing search engines (accessed between Jan 7, 2017, and April 18, 2017) were searched for articles (original and review) published between Jan 1, 2000, and Dec 31, 2016, across several major fields relevant to global policy and pathology. These fields included economics (ECON) and pathology research policy such as tissue banking (RPOL), workforce (WFOR), technology of pathology (TPAH), and public policy (PPOL). Policy and economics are discrete subject search areas, but the breadth of pathology and policy literature germane to this area was defined by means of address words and contractions indicative of the widest possible definitions of this subject area,[49] for example, AD=(ECON*PATH* OR PATH* OR POLICY). Composite search fields were also created from several Web of Science subject areas in a snowball manner depending on the initial literature ranging findings. A bibliometric review was also conducted of previous *Lancet* Commissions to collate cross-cutting themes.

pathology as their primary discipline. According to our analysis, pathologists occupy almost no major leadership positions in international health funders, national research funders, clinical centres, or research institutes. Thus, it is incumbent upon the pathology community to address this imbalance and undertake leadership roles, so as to ensure PALM is appropriately incorporated into the health agenda.

Organisational politics

Beyond the social politics of PALM, how much influence does this domain have on wider health organisations? Although national and international organisations exist for PALM—eg, the UK Royal College of Pathologists, the College of American Pathologists, the European Society of Pathology, and the International Academy of Pathology—their scope, reach, and interaction with other major health organisations remain extremely limited. WHO, World Health Assembly, and UN communiqués and health policy documents between 2000 and 2016 contain no references to documents or policy statements from any of the standing PALM bodies. The great disconnect between PALM representative bodies and the ruling elites of research and health care in high-income countries reinforces the invisible narrative of PALM globally. Our bibliometric study (panel 3) found few examples of policy input from pathology organisations in international research and health agendas. For example, despite the crucial and central role of PALM in detecting the outbreaks of Ebola virus in west Africa between 2013 and 2016, all public narrative driving policy originated from infectious disease, epidemiology, or health systems communities.[50] Ebola virus outbreaks provide a cogent example of the assumed role of PALM, hidden within other organisational structures—in this case, the European Network of Infectious Diseases.[51] National and international pathology associations must look to gain ownership of the PALM agenda and play a more prominent part in authoring relevant health policy documents to help influence political change.

Symbolic politics

Symbolic politics—in which individuals or organisations use images and language as symbols to garner the support and power of the mass public—has been used effectively in numerous policy settings.[52] This type of politics relies on a cause-related marketing strategy that can promote important disease domains or medical approaches, and has been most effectively used in cancer.[53,54] Advocacy and activism that stem from this symbolism draw support from philanthropic organisations and dramatically alter the way in which a domain is perceived by the general public. However, this approach has not been developed much for PALM. In many countries, particularly emerging economies, this lack of symbolic politics, coupled to a series of mis-narratives, frame pathology not as the science behind the cure but as the technician of the autopsy.[55] Changing this perceived image in the advocacy discourse should be a key symbolic political aspiration and can be achieved by emphasising the central role of PALM in all aspects of medicine—eg, a slogan such as "no molecular pathology, no precision medicine" makes it clear that without molecular pathology, the exciting promise of precision medicine will not be realised.

Panel 4: Pathology and laboratory medicine (PALM) recommendations

Develop an evidence-based PALM delivery package for adoption in resource-limited settings

Action

All stakeholders must work together to develop, refine, and test an evidence-based PALM package based on a tiered delivery network that can be adapted to specific settings (eg, geographical and cultural).

Key actors

International associations of the PALM community and of clinical care professionals, international organisations (eg, WHO), patient advocates, and policy makers

Indicators to monitor progress

WHO to collect and report certain of such indicators, as determined by an appropriate expert group

- A reduced test turnaround time for key so-called bellwether tests at tier-two and tier-three laboratories (as defined in the second paper[2] of this Series)
- An increased number of functioning tier-two laboratories at district-level hospitals and functioning tier-three laboratories at referral hospitals
- A reduced turnaround time for getting results back from specimens referred from tier-two laboratories to tier-three laboratories, for specific tests

Embed appropriate PALM packages within national strategic laboratory plan frameworks

Action

Countries should produce an implementation strategy for the PALM package in the form of a national laboratory strategic plan. This plan should address the specific needs of the country: what needs to be done, who is responsible for implementation, and how it is financed. The plan should indicate the steps to implement a functional PALM system, with timelines and accountability, highlighting how public and private entities will contribute to the system.

Key actors

The national pathology community, clinical care professional representatives, patient advocates, and policy makers

Indicators to monitor progress

- An increased number of countries with a national laboratory strategic plan
- An increased number of countries with funding for the national laboratory strategic plan in place
- An increased number of countries with an annual national laboratory strategic plan report

Ensure that the necessary human resources are in place to support PALM delivery

Action

Countries should commit to producing adequate numbers of well trained high-quality PALM professionals, including pathologists, clinical laboratory scientists and technicians, technologists, and assistants.

Key actors

PALM practitioners and policy makers

Indicators to monitor progress

- An increased number of tier-two hospitals having a pathologist on site
- An appropriate ratio of laboratory technicians, technologists, and assistants to pathologists and clinical laboratory scientists at district hospitals and referral hospitals

Equip personnel with the appropriate skill sets and educational opportunities required to drive effective PALM service delivery focused on low-income and middle-income countries

Action

Education should be modernised to include health policy, management, and leadership training, and assessment of new technologies.

Key actors

PALM practitioners, educators, and policy makers

Indicators to monitor progress

- An increased percentage of the workforce engaged in continuing medical education or continuing professional development
- Existence of validated training programmes for country-specific task shifting

Establish appropriate infrastructure (including specialist equipment and effective laboratory information systems) to ensure high-quality service delivery within the PALM tiered framework

Action

Countries should commit to providing equipment and supplies to enable high-quality services appropriate to the tier within the network. This should include a commitment to information technology and laboratory information systems. Where appropriate, and where resources permit, telepathology services should also be embedded within the PALM system.

Key actors

Pathologists and clinical laboratory scientists and their associations, policy makers, and patient advocates

Indicators to monitor progress

- A reduced percentage of tests not done because of equipment failure and stock outs
- An increased percentage of tier-two laboratories that have a laboratory information system

Commit to a quality agenda that emphasises the need to meet national and international standards, supported by the establishment of national accreditation programmes

Action

All PALM professionals should commit to meeting international standards for certification and accreditation. Assessment of quality should include communications of results to patients and clinicians across the tiered network. Laboratories should

(Continues on next page)

(Panel 4 continued from previous page)
commit to meeting international and national accreditation, and engage in stepwise improvement towards that end.

Key actors
Pathologists, clinical care professionals, policy makers, patient representatives, and professional associations

Indicators to monitor progress
- A reduced turnaround time for test availability for medical decision making
- An increased percentage of laboratories using standardised reporting (synoptic reporting)
- An increased availability of test report data to support public health surveillance and quality assurance systems
- An increased percentage of laboratories engaged in stepwise improvement
- An increased percentage of laboratories accredited to international standards or national standards consistent with ISO 15189

Embed sustainable financing for PALM within national health budgets and ensure appropriate resource allocation within national strategic laboratory plans

Action
PALM should be specifically addressed in national health budgets. Provision of a standardised PALM package with sustainable financing should drive market efficiency and improve affordability.

Key actors
PALM professionals, national policy makers, health insurers (both for-profit and non-profit), and international donors

Indicators to monitor progress
- Countries to allocate at least 4% of their public health expenditure to PALM
- International donors to allocate at least 4% of their official development assistance for health to PALM

Ensure increased involvement of PALM professionals in health policy decision making, driven by enhanced pathology leadership at local, national, and global levels

Action
PALM professionals should increase their engagement with health policy makers and health-care and research funding bodies, and they should be represented on relevant committees to ensure that the PALM agenda is advanced. PALM professionals and their professional associations should engage with patient groups and the public to increase understanding of the important role of PALM in delivering optimal health care.

Key actors
PALM professionals and their associations, policy makers, patients, advocates, and the public

Indicators to monitor progress
- Increased PALM representation on, for example, health policy panels, funding panels (both health delivery and health research), and WHO committees
- Increased interaction with other health-care professionals on advancing the diagnostics agenda
- Increased engagement with patient groups and the public

Economic politics

The surgical community has devoted considerable effort to highlight that surgery is both affordable and cost-effective.[56] Similar efforts will be crucial for promoting the value of global PALM,[52] as articulated in the economics section of this paper.

Scientific politics

Scientific politics recognises that health policy agendas and sources of financial support for health policy priorities are based on scientific evidence.[52,56] Most scientific policy is articulated through national and international normative frameworks. The most obvious manifestation of these frameworks is through high-level commissions, published either through learned journals or UN–WHO committees. Over the past decade in global health, there have been a wide range of such outputs, ranging from policy dialogue around affordable cancer care to global surgery and major economic health transitions such as grand convergence for progressive universalism.[57–59] Little of this scientific political dialogue, we have found, overtly includes PALM, apart from specific nods in work such as the *Lancet* Commission on Global Cancer Surgery.[57] Indirectly, PALM in infectious disease, for example, has benefited from the dialogue driving funding into biodefence, pandemic influenza, and emerging disease threats; however, this discourse has been mostly focused on high-income settings.[58] The core of the global scientific political dialogue for PALM has been highly technocentric, focusing on diagnostic tests and pathology informatics (eg, telepathology and laboratory information systems).[59] This Series, we hope, will begin to redress this imbalance, positioning PALM as a key arbiter of improved disease control and better health in both high-income countries and LMICs.

Politicians' politics

Even with better social and organisational political framing, PALM needs to improve engagement with wider political elites. Politicians are key change agents and leaders whose actions influence the provision of public goods to their constituents. The policies that they design and implement determine how resources become available for national and global health. Global PALM has little to directly build on from a historical basis, but much to build on indirectly. Most political elites have not been engaged by the PALM community to consider the central role of

PALM in health systems and improved health outcomes, almost certainly because their understanding of the narrative is limited or has been influenced by other communities. Unsurprisingly, PALM was little in evidence in the Millennium Development Goals,[60] although some modest funding went to laboratory systems and there were efforts—eg, the Maputo Declaration[3] of 2008—to strengthen systems in Africa, where the gaps are largest.

Delivering on universal health coverage and the Sustainable Development Goals will be the main focus of both national and international action over the next decade. However, considerable tensions exist around this agenda and the degree to which it can be inclusive of discipline specialisations such as PALM.[61] In view of the broadness of progressive universalism (which includes eradication of poverty and systems strengthening), global PALM will need to engage politicians through specific advocacy and inclusion in high-level panels and agenda setting. Moreover, beyond multilateral organisations and national champions, the urgent human, structural, and economic needs for PALM in many LMICs require the rapid political engagement of major philanthropic donors such as the Wellcome Trust and the Bill & Melinda Gates Foundation to drive and empower change agents. This engagement is more likely to happen if pathologists themselves take on leadership roles and try to direct the agenda, instead of passively reacting to the major changes occurring.

Engage pathologists in national and international leadership

Pathologists must have leadership roles in the design and implementation of national strategic laboratory plans. Their technical expertise, allied to their experience of the key issues described in this Series, positions pathologists as the key architects and enablers of appropriate frameworks for a coherent and resilient PALM agenda. Pathologists can deliver realistic assessment of the current state of PALM in LMICs; prioritise next steps; determine the sequence of changes and pace of implementation of these changes; and help to evaluate outcomes and effectiveness of interventions. As a specific example, the Ministry of Health in Kenya has a Technical Working Group for Pathology, supported by the US National Cancer Institute, providing technical guidance and support for the Kenyan national cancer research and control programme.[62] This Working Group consists of pathologists from various disciplines, with representation from both the private sector and academic institutions, who have been involved from the outset in helping to develop this ambitious programme. Similar approaches are required to ensure pathologists influence and implement the PALM agenda globally within LMICs.

Pathologists must overcome their invisibility to the general public: patients receive the results of laboratory tests that can have major effects on their care, but never see or talk to the individuals responsible for those tests. Professional associations of pathologists need to engage in outreach to educate policy makers and the public as to the importance of PALM and how policies need to develop to support excellence in PALM. Pathologists must emphasise the centrality of their contribution as a clinical discipline to improved health care: if they are seen merely as providers of tests, then they might be bypassed by unplanned and uncoordinated growth of point-of-care testing, to the detriment of controlling health costs and improving outcomes.

At the international level, pathologists need to engage in the global health agenda, in conjunction with others who have shared interests. Diagnostic imaging practitioners (eg, radiologists) face similar issues of rapidly changing technology, some of which is becoming more affordable and within reach of LMICs. Radiologists similarly face funding constraints in that there is underinvestment in diagnostics in systems in which a large proportion of payment is out of pocket. Other disciplines (eg, surgery and radiotherapy) also have distinct but complementary challenges to the diagnostic domain. Thus, a commonality of purpose, based on developing shared goals and solutions to particular challenges in resource-limited settings, could substantially affect improvement of health outcomes in LMICs.

Recommendations

Affordable, high-quality universal health coverage in LMICs by 2030 cannot be achieved without reshaping the fragmented and under-resourced PALM system. To achieve the goal of strong, tiered, networked national and international PALM systems, relevant stakeholders

***Panel 5*: The role of global alliances**

- Global alliances can make a major contribution through advocacy. Bringing together the many stakeholders and achieving greater visibility are key to breaking down barriers such as those discussed in this Series.
- Gavi (originally the Global Alliance for Vaccines and Immunizations, founded in 2000) mobilised international funding for vaccines. Gavi's policy of requiring national co-funding, and an explicit trajectory towards graduation from Gavi support, has helped to ensure sustainability of immunisation systems as countries' economies develop.
- The Global Fund (founded in 2002) has consistently used strategies to shape markets for pharmaceutical and diagnostic products for major infectious disease.[64] The use of these strategies has helped to ensure best value for money, consistency in supply, and better coverage.
- The Global Alliance for Genomics and Health (founded in 2013) in its mission statement aims to accelerate progress in human health through sharing of genomic and clinical data.
- Global alliances can monitor progress towards agreed-upon targets.

***Panel 6*: Pathology and laboratory medicine in 2030: a clinical vignette**

A 44-year-old farmer from rural northern India attends the primary health-care clinic in the nearby large village. She has been told by her family and friends that her skin has become yellow over the past few days. She feels generally unwell and has noticed that her clothes have recently become a bit tight round her middle. She has been overweight for many years.

At the clinic, the nurse who examines her takes blood for testing in a point-of-care test machine in the clinic. A couple of hours later, the results show low haemoglobin, microcytic hypochromic anaemia, hepatitis C virus infection, abnormalities in liver function, the presence of a minor form of β thalassaemia, high blood sugar, and high glycated haemoglobin A_{1c}. In parallel, the data are automatically uploaded into the regional laboratory information system and an alert has notified the pathologist and physician in the district hospital that is part of the regional network. She is told she will need further investigation with a view to treatment at the district hospital.

Subsequently, she is scheduled for a liver biopsy, which is processed and stained overnight in the pathology and laboratory medicine department of the district hospital. The pathologist identifies marked fibrosis with much fat and iron in the liver. Given the complexity of possible causes, whole-slide images are sent via the laboratory information system to the specialist liver pathologist in the network's regional teaching hospital for further consultation.

A week later, the patient is informed via mobile telephony that she has type 2 diabetes and β thalassaemia minor with liver scarring resulting from a combination of hepatitis C virus infection, haemosiderosis (iron deposition in the liver due in her case to the excessive red blood cell breakdown in β thalassaemia), and non-alcoholic fatty liver disease.

Shortly afterwards, she is seen again in the district hospital and has genetic counselling and treatment for her β thalassaemia, while her liver disease and diabetes are treated by a combination of anti-hepatitis C drugs, venesection, and weight loss. Via regular follow-up tests in her community clinic, her response to therapy is monitored electronically by her doctor and pathologist in the district hospital.

Without treatment, this patient would have almost certainly died within several years due to a combination of diabetes and liver cirrhosis. However, accurate diagnosis and subsequent monitoring made possible by a well functioning pathology and laboratory medicine system enable effective therapy for her various conditions, resulting in years of productive life. This care has been provided at modest cost to the patient through the state's universal health coverage system.

including national policy makers, official development assistance funders, research funding organisations, clinical communities, the PALM community, patients, and the public must work together guided by eight key recommendations. These recommendations are to develop an evidence-based PALM delivery package for adoption in resource-limited settings; to embed appropriate PALM packages within national strategic laboratory plan frameworks; to ensure that the necessary human resources are in place to support PALM delivery; to equip personnel with the appropriate skill sets and educational opportunities required to drive effective PALM service delivery focused on LMICs; to establish appropriate infrastructure (including specialist equipment and effective laboratory information systems) to ensure high-quality service delivery within the PALM tiered framework; to commit to a quality agenda that emphasises the need to meet national and international standards, supported by the establishment of national accreditation programmes; to embed sustainable financing for PALM within national health budgets and ensure appropriate resource allocation within national strategic laboratory plans; and to ensure increased involvement of PALM professionals in health policy decision making, driven by enhanced pathology leadership at local, national, and global levels (panel 4).

Call to action: a global alliance

Future developments in modern PALM will underpin a step-change in clinical practice in high-income countries,[63] but their relevance, robustness, utility, and affordability for emerging economies need to be urgently developed as a vital component of universal health coverage. This Series, in identifying current problems in PALM in LMICs (first paper) and their potential resolution (second and last papers), has highlighted that the challenges are multifaceted, involving a diverse collection of stakeholders who must all contribute to deliver achievable solutions that position PALM as a key facilitator of universal health coverage. Many of these stakeholders are identified in the recommendations (panel 4). One key group that is not mentioned, but which is facing similar challenges and similar opportunities, is the imaging community. We would suggest that there are potential advantages in seeking to include such related communities in a broader diagnostics alliance.

Global alliances have successfully mobilised stakeholders to move forward the agenda for other areas of health (eg, major infectious diseases, vaccines and immunisations, and genomics and health, among others; panel 5). Therefore, we call on the international community to unite to form a global alliance, with a mandate to align efforts and advocate for accurate diagnosis in evidence-based systems. The formation of such an alliance is timely, with the recent announcement of WHO's initiative for development of an Essential Diagnostics List,[65] as well as recent calls for a Global Alliance for Medical Diagnostics[66] and a similar diagnostic initiative linked to the Coalition for Epidemic Preparedness Innovations.[67]

PALM in 2030—and beyond

Our Series started with a clinical vignette that emphasised the inequality divide that exists in the provision of optimal PALM services between high-income countries and LMICs. We finish with a clinical vignette that indicates what future health care might look like in resource-limited settings in 2030, in the presence of a functioning PALM system (panel 6).

However, this vision of the future will only happen if the recommendations that we have presented in this paper are acted on. Closing rather than widening the health divide between high-income countries and LMICs will only be

achieved if there is cooperation through a global alliance to ensure that access to high-quality PALM is within reach of everyone, using scale economies to help make tests affordable. Here, the pathologist plays a key part, by setting the standards for appropriate test type and frequency, by maximising the quality of the laboratory systems available, and by ensuring that scarce health testing resources are used in the best way possible. A modern, affordable, high-quality PALM system is essential for universal health coverage. We need to make it happen.

Contributors

SH, ML, and RS assisted with the initial literature search, drafted figures, participated in the design of the Series, wrote several sections of the initial draft of this paper, and provided overall coordination of writing and revisions of this paper. JF and KAF assisted with the initial literature search, participated in the design of the Series, coordinated the initial drafts of this paper and the other two papers in the Series, and provided overall coordination of writing and revisions of this paper. MAK, LML, and SAP assisted with the initial literature search, participated in the design of the Series, and provided overall review and critique in the writing process for this paper.

Declaration of interests

We declare no competing interests.

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