

An Essential Pathology Package for Low- and Middle-Income Countries

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ABSTRACT

Objectives: We review the current status of pathology services in low- and middle-income countries and propose an “essential pathology package” along with estimated costs. The purpose is to provide guidance to policy makers as countries move toward universal health care systems.

Methods: Five key themes were reviewed using existing literature (role of leadership; education, training, and continuing professional development; technology; accreditation, management, and quality standards; and reimbursement systems). A tiered system is described, building on existing proposals. The economic analysis draws on the very limited published studies, combined with expert opinion.

Results: Countries have underinvested in pathology services, with detrimental effects on health care. The equipment needs for a tier 1 laboratory in a primary health facility are modest (\$2-\$5,000), compared with \$150,000 to \$200,000 in a district hospital, and higher in a referral hospital (depending on tests undertaken). Access to a national (or regional) specialized laboratory undertaking disease surveillance and registry is important. Recurrent costs of appropriate laboratories in district and referral hospitals are around 6% of the hospital budget in midsized hospitals and likely decline in the largest hospitals. Primary health facilities rely largely on single-use tests.

Conclusions: Pathology is an essential component of good universal health care.

“As is your pathology, so is your medicine.”

—Sir William Osler

“It is difficult to deliver effective and high-quality care to patients without knowing their diagnoses.”¹

A young child living in sub-Saharan Africa (SSA) seeks treatment at a rural health care clinic with a 1-week history of fevers, night sweats, chills, and malaise. The child’s mother does not know if the child has lost weight in the recent past, but when weighed, the child is significantly below the expected weight for her age. No other family members, including other young siblings, report similar symptoms. Physical examination reveals a fever, mild increase in heart and respiratory rate, and enlarged lymph nodes along both sides of her neck. The clinic does not have access to imaging studies, and the only available pathology laboratory tests show that the patient does not have serologic evidence of human immunodeficiency virus (HIV) infection or malaria. She is mildly anemic as measured by a manual spun hematocrit. The physician wants to refer the patient to a hospital in a nearby city, but the family does not have the resources to do so. The physician offers to collect blood for pathology testing and send it to that hospital for testing, but because the hospital requires advance payment for pathology tests, the family again does not have the resources to do so. The physician completes the notes indicating that the differential diagnosis is broad (including tuberculosis, nontuberculous mycobacterial infection, disseminated fungal infection, Epstein-Barr virus infection [infectious mononucleosis], malignant lymphoma) and that accurate diagnosis requires

pathology investigations, including both microbiology and anatomic pathology. The family leaves the clinic, and the patient is lost to follow-up.

This scenario is played out daily in many countries across the world and illustrates one aspect of the crucial role that pathology has in ensuring effective health care—namely, diagnosis. Despite recent progress in controlling communicable disease, the need for pathology is becoming all the greater as the burden of noncommunicable diseases (NCDs) increases. For example, cancer, of which there were approximately 14 million new cases and 8.2 million deaths in 2012,² is impossible to treat accurately unless one knows the pathologic diagnosis. Cancer is predicted to increase by 70% by 2032, with more than 60% of these new cases arising in Africa, Asia, and Central and South America. Similarly, diagnosing and treating patients with diabetes mellitus—another developing epidemic in low- and middle-income countries (LMICs)—is impossible without the ability to measure levels of glucose in the blood. In addition, the diagnosis and risk stratification of cardiovascular disease also requires pathology (eg, troponin for heart attacks, cholesterol levels).

Given This, What Is Pathology?

The term *pathology* means “the study of disease.” Among many things, the knowledge gained from this study has led to the development of the many diagnostic tests used in clinical practice. These tests are performed on body fluids, including blood, urine, sweat, saliva, and sputum; on tissue biopsy specimens; and on cells obtained from fine-needle aspiration.

The diagnostic role is a key aspect of what pathology laboratories do and is fundamental to the effective working of any health care system. Indeed, a recent interview-based study of cardiologists and oncologists in Germany and the United States has indicated that 66% of clinical decisions are based on results from *in vitro* diagnostic tests.³ However, pathology also supports clinical care by assessing disease severity and prognosis (eg, determining the staging and grading of a cancer by histopathology), information fundamental to deciding and managing treatment plans for patients. Equally important is the role of the pathology laboratory in monitoring clinical response to treatment (eg, in renal failure, analysis of blood markers of renal function).

Beyond these more obvious roles, pathology also has a number of other key roles. One is quality assurance within the health care system. For example, even in 2013, autopsies showed around a 20% major discrepancy between the premortem clinical diagnosis and the autopsy diagnosis.⁴ Similarly, by examining surgical specimens, the surgeon

can learn if he or she is fully excising tumors or, by using microbiologic culture, can determine if the cause of a fever is being correctly identified. There is also a crucial role in disease surveillance (eg, identifying new and emerging diseases such as Zika virus) and in the maintenance of disease registries (eg, cancer registries) that help inform national health policy and allocation of resources. Finally, forensic pathology is integral to legal systems around the world.

To deliver all these roles, the pathology service comprises a number of disciplines and subspecialties, the main ones of which are described in **Table 1**. In the United States and most other parts of the world, these pathology disciplines are divided into two main groups: clinical pathology (also called laboratory medicine), which is largely concerned with analysis of blood and other fluids and involves clinical biochemistry, microbiology, and hematology, and anatomic pathology, which is concerned with cell and tissue analysis involving cytology, histology, and autopsy.

- In high-income countries (HICs), the pathology service typically has three levels of provision. The majority of the service is delivered from a central laboratory located in the hospital setting. The various components of such laboratories are supported by a common infrastructure, including specimen collection services, transport and reception, and a mechanism for transmitting the result of the test and any accompanying report to the ordering clinician (and patient). In addition, a laboratory information system (LIS) ideally is connected to the electronic patient record.
- In more rural environments, there may be smaller laboratories, offering a more limited repertoire of tests, as well as point-of-care testing (POCT) (see later) in the community setting.
- In addition to these two levels, a small number of laboratories, often in conjunction with university departments, will provide the most specialized tests. Such laboratories also undertake research, both in the field of pathology itself and in conjunction with other disciplines as part of a multidisciplinary team. They also organize and deliver education and training in pathology and related disciplines.

While the core of the laboratory activities may be considered “tests” or the analytical aspect of laboratory testing, it is important to recognize that there are important pre- and postanalytical⁵ aspects that are equally if not more important for generating accurate laboratory test results. As the terms imply, preanalytical activities occur before the actual testing; postanalytical activities occur after testing **Table 2**. This involvement spans the selection of the most appropriate tests or investigations, to the interpretation of their results and provision of clinical advice across the spectrum of

Table 1
Major Pathology Disciplines and Roles^a

Discipline	Role
Clinical biochemistry	Study of the biochemical basis of disease (eg, diabetes)
Cytopathology	Study of disease in individual cells (eg, cervical cancer)
Forensic pathology	Determination of cause and manner of death for legal purposes
Hematology	Study of blood disorders (eg, hemoglobinopathies)
Histopathology ^b	Study of disease in human tissue (eg, cancer)
Immunopathology	Study of the immunologic basis of disease (eg, allergy)
Medical microbiology	Study of infection (eg, tuberculosis)
Molecular pathology/genetics	Study of the molecular and genetic basis of diseases and heritable conditions
Pediatric/perinatal pathology	Study of the diseases of pregnancy, childbirth, and children
Transfusion medicine	Study of the collection, preparation, storage, and clinical use of blood products

^aA selection of the major disciplines, derived, in part, from <https://www.rcpath.org/>.

^bIncludes a number of subspecialties such as dermatopathology, neuropathology, and others that focus on diseases of a single organ or organ system.

Table 2
Phases of Analysis of Pathology Tests

Preanalytical phase

This includes selecting the appropriate test, obtaining the specimen, labeling with the patient's name, timely transport to the laboratory, accession in the laboratory, and processing prior to testing.

Postanalytical phase

This includes preparation of a report detailing the analysis and interpretation of the test, authorizing the report, transmission of the report to the clinician, and action by the clinician.

It is now recognized that in high-income countries, the largest proportion of errors in pathology occurs in the pre- and postanalytical phases. In the preanalytical phase, these errors include failure to ensure that the specimen is collected from the right patient and that the correct specimen type is collected—and at the right time. In the postanalytical phase, errors have included the wrong result being reported, the result not being “read” by the clinician, the wrong (or no) decision being made, or the wrong (or no) action being taken.

medical specialties. In practice, this may require a review of the patient's medical records and discussions with the ordering clinician. A good example of this is the multidisciplinary meeting (tumor board in the United States) where pathologists, surgeons, oncologists and radiotherapists, radiologists, nurses, and others involved in the care of a patient with cancer meet to review all the relevant information to decide on the best approach to therapy and management.

Pathologists may also provide leadership for hospital-wide quality assurance efforts, and increasingly, in many health systems, pathologists take on additional clinical roles (eg, as infectious disease doctors, managing patients with metabolic disorders, and specialized oncologists).

As can be seen from the above, pathology is not a stand-alone service. Its value is as an integral part of the system of care where the outcome for the patient and the operational and economic benefits for the system depend on all the parts (including pathology) working effectively together.

What Is the Situation of Pathology in LMICs?

The child described in the clinical vignette at the beginning of this chapter needed access to microbiology, hematology, and some immunology services and almost certainly would have needed access to the expertise of a

histopathologist. But as indicated in the vignette, access to diagnostic pathology services is not available in many countries and regions.

As in HICs, in the LMIC public sector, ideally there are three tiers of laboratories—primary, secondary and tertiary—with a small additional number of national or regional research or reference laboratories.⁶ The primary laboratories are widely distributed in the community and normally only perform a small number of simple clinical pathology tests. Laboratories at secondary and tertiary levels are progressively fewer in number, with tests of increasing complexity and capacity (including anatomic pathology), and are found in progressively larger centers of population. However, in many countries, especially the poorer ones, such a structure does not exist. There are many reasons for this, but the most important is the lack of human capacity, resulting in far too few laboratories to provide adequate population coverage at all the various levels.

Data on staffing are lacking for much of the world, but what data that do exist illustrate the problem. For example, in SSA, there are at least five countries with no anatomic pathologist. Recent surveys of the other countries of SSA have shown that the number of anatomic pathologists per patient population is approximately 1:1,000,000, or about 1/50 the ratio observed in the United States and United Kingdom.^{7,8} In China, in 2015, there were around 10,300 pathologists (all

disciplines) (Chinese Society of Pathology, 2015, unpublished data) with an estimated shortfall of the numbers needed for the size of population of between 60,000 and 120,000! In Myanmar, the ratio of pathologists per patient population is estimated to be 1:170,000 (Myanmar Society of Pathology, 2015, unpublished data). In countries in the upper middle-income bracket, the situation is somewhat better (eg, Malaysia 1:75,000),⁹ but the reality is that in all LMICs, the number of pathologists in relation to the population served is around an order of magnitude less than in HICs such as the United Kingdom and United States.

An additional problem to the staff shortages is that standards are very variable. Although the quality of the services, particularly that provided in large cities in middle- to upper middle-income countries, can be good, it is not infrequently seriously inadequate in both urban and rural areas.¹⁰

Outside the public sector, a characteristic of many LMICs is that there are often private laboratories (most of which are staffed by pathologists from the public sector) running in parallel to the public sector and providing services to the population. While the facilities in some of these laboratories can be as good as any internationally, many are much less satisfactory. In India, where 70% of the laboratories are private, only 1% are accredited.¹¹ In Uganda, in 2011, of more than 900 laboratories in Kampala, of which 96% were private, only 45 of all laboratories reached the first step on the five-step process to international accreditation.¹²

The result of all the above is that much of the population in LMICs does not have access to good-quality pathology. As those NCDs that are particularly reliant on pathology for diagnosis and management become more prevalent, this inevitably means there will be increasing misdiagnosis. This will result in unnecessary deaths and needless prolonged illness and distress, with associated social disruption and negative impact on gross domestic product (GDP) due to increasing and significant waste of scarce resources and prolonged and unnecessary time off work. The deficiencies also mean that data needed for disease surveillance and registries, as well as other types of population data needed to guide public policy and resource allocation, are not available. In addition, as good-quality pathology is necessary for the achievement of 11 of the 13 goals of the health-related Sustainable Development Goals (Table 3) from the United Nations (UN), attainment of these goals will be undermined.

An Essential Pathology Package

We next specify an essential minimal package of services that should be available in LMICs to provide access to pathology that is of reasonable quality, affordable, and timely to a majority of the population, especially that outside the main cities.

The key concept is of an integrated network of tiered laboratories providing widely accessible, sustainable, and good-quality pathology services to the general population (Table 4) and (Table 5). This model has similarities to the tiered model currently found in some LMICs,⁶ but the key aspect is that this must be an *integrated network* of laboratories. In other words, the laboratories in the various tiers should work together as one organization. This allows for more efficient and effective referral of patients across the network than would be the case with independent laboratories. It also allows advantages of scale such as sharing and purchase of equipment and reagents. Other benefits include better communication, exchange of staff and knowledge, provision of education/training, and opportunities for research. This all will result in development of a critical mass of expertise, while maximizing and optimizing scarce resources.

In 2008, such national integrated laboratory systems were proposed as a key development for pathology services in Africa in the Maputo Declaration on Strengthening of Laboratory Systems.¹³ Ethiopia was one of the first countries to develop such a model successfully, and the model has subsequently been endorsed in the Freetown Declaration of October 2015 as the cornerstone of effective health care.¹⁴ Although infectious disease was the focus of the original model, the principles are equally applicable to NCDs.

A key component in ensuring sustainability of such a model is the tier 4 laboratory (specialized center). These are the places where, in addition to specialized services, research, education, and training will largely be developed and provided, especially to the linked tier 1 and 2 facilities. Furthermore, innovations appropriate to the country's needs are most likely to be developed in these specialized centers. Without these fostering and supporting roles, the long-term sustainability of the lower tier laboratories will be impossible. Linking such centers to other centers of excellence, either regionally or abroad, to provide access to further expertise and resources is also important for continuing long-term development.

The model outlined in Table 5 should be regarded as the minimum that an LMIC should provide. Countries at higher levels of development can build on this model to deliver increased provision, as and how they wish, appropriate to their needs. Conversely, the model is also one to which low-income countries (LICs) can aim to move over time as resources become available and are invested.

Successful operation of the model will require five areas of activity, which, if not applied to the network, will compromise its function. These are leadership; education, training, and continuing professional development; emerging test technologies; quality management and accreditation systems; and reimbursement for pathology.

Table 3
Health-Related Sustainable Development Goals and Pathology

Sustainable Development Goals	Specific Pathology Examples
3.1: By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births	Testing for the most common causes of maternal mortality (eg, infections), blood transfusion, autopsy
3.2: By 2030, end preventable deaths of newborns and children younger than 5 years, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births	Testing and monitoring for most common causes of infant mortality (eg, infections), autopsy
3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases	Testing for communicable diseases (eg, human immunodeficiency virus, antiretroviral resistance, malaria blood tests)
3.4: By 2030, reduce by one-third premature mortality from noncommunicable diseases through prevention and treatment and promote mental health and well-being	Histo- and cytopathology for cancer diagnosis, hematology, and biochemistry for diabetes diagnosis and management. Pathology support for surveillance and other data platforms (eg, cancer registries)
3.5: Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol	Toxicology tests
3.6: By 2020, halve the number of global deaths and injuries from road traffic accidents	Autopsy reports, blood banks for transfusion support
3.7: By 2030, ensure universal access to sexual and reproductive health care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programs	Urine and blood pregnancy testing, sexually transmitted disease blood and urine tests
3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all	Pathology is essential for quality health care services
3.9: By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water, and soil pollution and contamination	Toxicology testing and diagnosis or related diseases
3.a: Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate	Testing for smoking cessation in urine
3.b: Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries and provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on TRIPS regarding flexibilities to protect public health and, in particular, provide access to medicines for all	Pathology systems provide data (eg, surveillance) and research platforms
3.c: Substantially increase health financing and the recruitment, development, training, and retention of the health workforce in developing countries, especially in least developed countries and small island developing states	Pathology workforce is an essential component of the health workforce
3.d: Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction, and management of national and global health risks	Surveillance for emerging disease and through cancer registries

Table 4
Definition of Laboratory Tiers

TIER 1—Primary care/health center laboratories serving mostly outpatients in a community, performing POCT/single-use tests and referring more complex work to either tier 2 or 3. It will be staffed at the technician level.
TIER 2—Laboratories in district hospitals that receive specimens from their own patients and receive referrals from tier 1 facilities. Usually will have a surgical, medical, and pathology clinician and perform a selected number of routine tests.
TIER 3—Laboratories in regional or provincial hospitals that receive specimens from their own patients and receive referrals from tier 1 and 2 facilities. They will have significant numbers of pathology staff and cover all routine testing in the major pathology disciplines.
TIER 4—Laboratories in national or teaching hospitals that receive specimens from their own patients and receive referrals from tier 1, 2, and 3 facilities. In addition to routine tests, they provide highly specialized tests and education and training for the network. In small countries, this facility may be a regional one shared by more than one country.

Note: As each country and region will have a somewhat different burden of disease and availability of staff, there may be some shifting of capacity across the tier boundaries. For example, if trained staff were available (eg, via a regular visit by the tier 2 pathologist), then fine-needle aspiration cytology could be performed and reported in a tier 1 laboratory.

Table 51
Pathology Tiers^a

Laboratory Features	Tier 1	Tier 2 (Includes Tier 1 Capabilities)	Tier 3 (Includes Tier 2 Capabilities)	Tier 4 (Includes Tier 3 Capabilities)
Tests and test categories	POCT and single-use tests: malaria, TB, urinalysis, and pregnancy tests; blood glucose; hemoglobin/hematocrit; ESR; blood typing Slide microscopy (eg, malaria, wet preparation, stool parasites) Preparation of FNAC and tissue specimens to send to tier 2 facilities	Many routine diagnostic and prognostic tests Clinical biochemistry: urea and electrolytes; hemoglobin A _{1c} for diabetes; liver, renal, bone, and lipid profiles Hematology: CBCs, CD4 count, simple coagulation studies and thalassemia tests, support for whole-blood transfusion Microbiology culture: blood/urine/cerebrospinal fluid/sputum, simple antimicrobial susceptibility testing, serology for hepatitis A/B/C and common infections Anatomic pathology: FNAC, tissue biopsies, and surgical excisions—processing, H&E stain, and interpretation; hospital autopsy	All routine and some specialized tests Clinical chemistry: endocrine tests (eg, thyroid), cardiac markers (eg, troponin), BNP, dynamic function tests (eg, GTT), tumor markers (eg, AFP, Ca-125), blood gases, therapeutic drug monitoring (eg, cyclosporine levels), serum and urine electrophoresis Microbiology: additional antimicrobial susceptibility testing, fungal cultures, mycobacterial cultures, viral load Hematology: more advanced blood analysis (eg, component therapy, hemolysis, myeloma), bone marrow studies, hematologic malignancies, immunologic studies Anatomic pathology: special stains, including immunohistochemistry (eg, ER, PR for breast cancer), specialized autopsy	Specialized services as appropriate, surveillance, toxicology studies, support for transplantation, rare tumors, nutritional studies, support for clinical trials, mutational studies (cytogenetics, molecular analysis), gene analysis
Staffing	Laboratory technician(s) supervised by general pathologist from distance	General pathologist, laboratory technicians, laboratory assistants One of the technicians manages laboratory	Monospecialty pathologists, clinical scientists, specialized laboratory technicians, laboratory assistants, dedicated laboratory manager, possibly laboratory information systems coordinator, quality care manager. Facilities and responsibilities for education and training of all levels of medical and nonmedical staff	As for tier 3 plus clinical trial specialists, data specialists; additional specialist educational capacity
Communication infrastructure	Paper or electronic, mobile	Paper/electronic or (preferred) laboratory information system	Electronic/laboratory information system; telepathology (optional)	As for tier 3 but more data linkages to trials and registries
Equipment	Simple microscope Rapid diagnostic tests; POCT/single-use tests Specimen and patient identification FNAC and biopsy fixation	Automated blood/biochemistry analyzers, microbiology analyzers and incubators, and blood typing, including refrigerators, tissue processor, and microtome for anatomic pathology	Automated tissue processor, equipment for full autopsy, immunohistochemistry station	Molecular biology/cytogenetics; immunofluorescence; electron microscopy for renal disease Consider biobanking for research

(continued)

■ **Table 5** (cont)

Laboratory Features	Tier 1	Tier 2 (Includes Tier 1 Capabilities)	Tier 3 (Includes Tier 2 Capabilities)	Tier 4 (Includes Tier 3 Capabilities)
Turnaround time	Rapid, POCT, and single-use tests, 0-3 hours Send-outs—several days	An hour to several days (depending on test)	An hour to days (routine) 5 days (complex) 30-60 days (autopsy)	As per tier 3
Networks and surveillance	Accumulates and forwards incidence data to higher tier	Report to emerging disease, AST, cancer, and other NCD registries	Links to emerging disease, AST, cancer, and other NCD registries	Research on disease incidence trends, including AST, and emerging diseases

AFP, α -fetoprotein; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; ER, estrogen receptor; ESR, erythrocyte sedimentation rate; FNAC, fine-needle aspiration cytology; GTT, γ -glutamyltransferase; NCD, noncommunicable disease; POCT, point-of-care testing; PR, progesterone receptor; TB, tuberculosis.

^aAssumptions: (1) Tiers may be adjusted as necessary to reflect the local burden of disease/local practice patterns and availability of trained staff. (2) Changes in technologies over time can shift tests and workloads across tiers. (3) Tests are examples (as applied to broad groups of infectious disease, cancer, and other NCDs) and are not an exhaustive list.

Leadership

The effective and efficient operation of the pathology laboratory is a multidisciplinary effort involving a diverse range of professional groups. The pathology services are primarily delivered by three groups of professionally qualified staff—pathologists, clinical scientists, and technicians (sometimes referred to as technologists)—supported by assistants, a manager, and administrators and information technology specialists. In reality, in most places, the administrator/manager role is often undertaken by the clinical scientist or technician. The role of the pathologist is to provide leadership to the service, including strategic development advice on clinical management and to provide the interface between the laboratory and the clinical services. In some countries and in some specialties, these roles are shared with the clinical scientists. The pathologists and clinical scientists also take the lead in quality improvement and service development, as well as pathology-led research and development. The laboratory technologist is responsible for delivering the technical aspects of the service.

The goal of this joint effort is the provision of a service that is patient oriented and meets clinical needs. These clinical needs are defined by standards of care, the expectations of individual physicians, and, ultimately, their patients. Accordingly, laboratory leadership must ensure that all activities of the various persons working in the laboratory are monitored to ensure that a clinically relevant service is being provided. This is a key leadership responsibility required by the International Standards Organization (ISO) 15189:2012, the international reference document for best laboratory practice.¹⁵

Laboratory leadership requires not only an understanding of the workings of the laboratory but also an understanding of the clinical background of the patient. Thus, while the information produced by the laboratory is a product of its processes, personnel, and equipment, it is influenced by the

clinical setting in which the laboratory operates and from which it receives specimens. There are also patient-specific, disease-specific, and therapy-specific factors, all of which may have an important bearing on the information produced by the laboratory. The leadership of the laboratory must understand the interaction between these factors, especially as it affects how the information will be used for patient care.

The Joint Commission International's accreditation standards for hospitals state that for the purpose of clinical consultation and rendering of medical opinion, the laboratory should be led by a physician, preferably a pathologist.¹⁶ Pathologists, being clinicians, have insight into the thought processes behind requests for laboratory tests and the decisions that may be made with the information received. Not only is this insight invaluable in defining how laboratory services are organized and directed, but it is also crucial to provision of clinical advice on the further investigation and management of individual patients. Clinical scientists, who have had significantly similar training to clinical pathologists, may also provide this level of leadership.

Reflecting the integral role that pathology plays in the wider health care system, laboratory leadership should also be involved in the development of National Laboratory Strategic plans. These plans detail the long-term vision and mission of the nation's laboratory health services. To be effective, the development of this national health care blueprint must be cognizant of local disease burden, available clinical skills and services, clinical requirements for diagnosis and monitoring, and technical realities. The primary involvement of clinical laboratory leadership, in conjunction with other clinicians, is provision of guidance to define policy that delineates the organization, scope, and nature of the laboratory service according to the tiers providing health care in the country.⁶

Pathologists are also important in the provision of leadership at the operational level. This requires an ability to read and understand scientific and technological advances in the

field of medicine as well as improvements in laboratory technology. Changing clinical demands for patient care, as documented in new and revised versions of locally applicable clinical guidelines of care, require a laboratory director's involvement and an informed response. Similarly, advances in technical capacity of the laboratory, including the introduction of new tests and withdrawal of obsolete ones, must also be assessed in relation to their ability to improve the clinical effectiveness of the laboratory. Playing a leadership role in responding to such changes, the pathologist must have authority to alter any aspect of the laboratory's operations to ensure that the laboratory remains true to its goal of enhancing the quality of care that patients receive.

This role was recognized in a report of an independent review of the pathology services of one of the largest health care organizations in the world, the UK National Health Service.¹⁷ To ensure the long-term sustainability and development of the essential laboratory network, this role must be endorsed.

Education, Training, and Continuing Professional Development

Given the shortage of staff outlined earlier, educating and training larger numbers is clearly of paramount importance in developing a sustainable pathology network. As mentioned above, there are three main groups of staff: pathologists, clinical scientists, and technicians.

The Pathologist

Historically, education of pathologists from LMICs was undertaken in North America, Europe, and Australia, with the individual often residing in the HIC for the full duration of his or her training program. Although those funded by governments or charities were expected or required to return home at the end of their training, large numbers stayed in HICs. In contrast, clinical scientists and technicians were predominantly trained locally.

Pathologists are medically qualified practitioners who have undergone postgraduate education and training in pathology. There are three main models of training. In the first, pathologists are trained as generalists dealing with all aspects of pathology (ie, both clinical and anatomic pathology—this is sometimes called general pathology). The training usually is 2 to 4 years. In some countries, the course is a university degree. In the second, pathologists are trained only as either a clinical or an anatomic pathologist. The duration of the training is around 2 to 3 years. In LMICs, both of these two models are common. In the third, the pathologists are trained as mono-specialists. Thus, the pathologist is

trained as a hematologist, microbiologist, clinical biochemist, and so on. Such individuals tend to be employed in academic centers. The duration of training is usually a minimum of 4 years. This model is the least common in LMICs and reflects countries with more developed health care systems, such as South Africa. In much of South America, pathologists are only trained as mono-specialty anatomic pathologists, while the other disciplines of pathology are staffed by clinical scientists such as clinical biochemists.

Like all postgraduate medical education, these training courses are largely experiential in nature, with considerable hands-on involvement in pathology service delivery, supplemented by small group teaching and formal lectures.

The Clinical Scientist

In some countries, the clinical scientist performs a similar role to that of the medically qualified pathologist and follows a similar pathway of training and examination of competence. This is applicable in clinical biochemistry, immunology, microbiology, and virology. Clinical scientists may also be responsible for the performance of specialized techniques (eg, molecular genetics, toxicology investigations, and electron microscopy). Even where this is not the case, normally the individual will have earned a chemical, biological, or biomedical science degree, usually followed by a master's or doctorate in an area of specialization such as microbiology or clinical biochemistry. The total duration of training is between 4 and 8 years. There may be subsequent subspecialization into, for instance, virology.

The Technician/Technologist

Training of the technical staff is usually via college courses, often part-time and extended over a number of years (eg, 3-5 years). The education can be general, over all the specialties of pathology, or restricted to one of the major specialties (anatomic pathology, microbiology, etc), the latter being a feature of more developed services. In some countries, technical staff will not have formal qualifications and will have had only hands-on training in the laboratory.

In most countries, in addition to the professional qualification or appropriate university degree, the individual will need to be registered with the national registration body as an indication of required competence before being allowed to practice.

In the past 30 years, LMICs have increasingly developed their own pathologist postgraduate educational and training systems. For example, 21 countries in SSA have developed training programs in the past 25 years. In the 14 countries for which there are comparative data, pathologists

have increased from 70 in 1990 to 370 in 2015.¹⁸ Similarly, in Malaysia, pathologists have increased from around 50 in the 1980s¹⁹ to more than 500 now.⁹

However, in many countries, especially LICs, the shortage is such that it will not be possible to train enough pathologists to staff fully all relevant sections of the health care system even in the medium term. Accordingly, expansion of training of scientists and technicians and exploration of task shifting and task sharing with them are needed, with parallel development of shorter training programs focused on specific tasks (eg, cytology screening).

Once people are trained, a key need for maintenance of standards is programs of Continuing Professional Development (CPD). Many individuals and institutions run CPD events (often delivered by visiting individuals and organizations) on an informal basis, but systematic institutional/national programs of CPD are rare in LMICs (see section on accreditation). Indeed, one of the commonest requests for support from pathologists in LMICs is for provision and access to CPD. Without such programs, individuals can become out of date relatively quickly, especially as the pace of advance accelerates. To ensure the long-term sustainability of the pathology network, development of such programs is necessary.

Emerging Test Technologies

In all health care systems, the need for a medical test at any point in the care pathway requires that a specimen (eg, blood or urine) be collected and sent to a laboratory for analysis and interpretation. Laboratory testing can be either centralized or provided at the point of care or, more typically, a combination of both. The selection of which approach to take is driven, in part, by whether a given test is available at the point of care, test volumes (high numbers of tests usually can only be performed in a central laboratory), and whether it is critical to have test results available at the time of the patient encounter. This must be balanced, however, against the generally higher cost of providing laboratory testing at the point of care and, as described below, technical challenges in generating accurate test results at the point of care. As described elsewhere in this chapter, use of a tiered system of laboratory testing that focuses on the type of care provided within each tier, as well as the number of tests performed within each tier, can be used to design approaches to testing. For example, tier 1 facilities would benefit the most from testing at the point of care, in contrast to tier 3 facilities, which would benefit most from centralized laboratory testing (see below for description of tiers). As another example, test devices used for disease surveillance can be designed for centralized use only.

To provide both options for laboratory testing within a tiered system of health care delivery, increase and improve access to laboratory testing in general, and bring new diagnostic tests to the public, device manufacturers and a number of public-private partnerships have developed new technologies for laboratory testing. Key challenges for the development and use of emerging tests are shown in **Table 6**. In particular, because new devices must be used by persons in many LMICs with widely varying languages, backgrounds, training, and expertise, simplicity of specimen collection, device use, and interpretation and communication of test results are of critical importance.

POCT

Because POCT most frequently occurs at a distributed, noncentralized site, different technological and staffing approaches are needed: POCT usually is performed by medical staff, nurses, or medical assistants using small, mobile testing devices. This is compared with centralized laboratory testing, which is performed by specialized laboratory technicians using large-capacity (high-throughput) analyzers. Most point-of-care tests also can be described as “single-use” or “single-patient” tests because each patient specimen is typically tested using a single, disposable modular unit such as a cassette, which is in contrast to tests performed in central laboratories, where analyzers are designed to handle much higher numbers of tests from many patients. Although POCT technologies are broadly based on the same techniques employed with centralized laboratory analyzers, they have reduced reagent and sample volume requirements, rely on stabilization of reagents, and typically employ single-use cassettes for testing. Use of small specimen volumes in particular yields substantial challenges in designing systems that can yield consistent test results.²¹ As

Table 6
Effectiveness Criteria for Emerging Tests

New tests should provide results for a specified clinical problem to guide clinical decisions, for monitoring disease status or response to therapy, or to collect data for disease surveillance.
For tests designed to be used in clinical care, test results must be available in a time frame that will guide clinical decision making.
Tests must be easy to perform and results easy to interpret and communicate.
Target performance characteristics (eg, sensitivity, specificity, predictive values, precision, and accuracy) for the intended use(s) should be specified prior to test development.
Manufacturers' claims regarding test performance characteristics must be independently verified.
Test platforms must be usable and stable in locations of intended use.
Test platforms must meet procurement requirements for supply chain, maintenance, availability of quality control standards, durability, and stability in variable climatic conditions.
Test costs must be affordable in locations of intended use.

Derived, in part, from Wu and Zaman.²⁰

a result, POCT may not yield test results that are in agreement with those generated by larger laboratory analyzers. An obvious outcome is that results from POCT should be harmonized with those from a central laboratory analyzer so that health care providers are familiar with any variations in the results obtained by POCT.

In LMICs, POCT has been used extensively to help guide treatment of a number of diseases and conditions. For example, patients with HIV-AIDS have benefited from extensive access to POCT, which is cost-effective in extending life expectancy.^{18,22,23} Access to smear microscopy and/or rapid malaria diagnostic testing has played an important role in decreasing the morbidity and mortality from malaria.²⁴ For tuberculosis, access to rapid detection of infection and limited antimicrobial susceptibility testing has also played an important role in global efforts to diagnose and treat tuberculosis.²⁵

Future Diagnostic Technologies

In many LMICs, electricity supply can be intermittent, with frequent scheduled and unscheduled power cuts. Many laboratories and hospitals have backup facilities such as diesel generators, but they can also be unreliable. Because many laboratory analyzers require a reliable external power supply, such variable power supply causes considerable disruption. In addition, in rural areas, there is no power supply. In view of this, there is increasing focus on developing devices that require no power or have power generation built into the device itself.²⁶⁻²⁸ In addition, because of the challenges of supply chains and storage in many LMICs, there is increasing focus for developing POCT devices that require minimal or no reagents other than the device itself and that can be stored for long periods in hot and humid climates with no degradation of performance. For larger analyzers used in central laboratories, one goal is develop test platforms that can support a number of different assays, rather than platforms that are unique to one set of tests. Development of flexible platforms would minimize the number of devices needed, with the associated reduction in acquisition and maintenance costs, and it would allow for rapid introduction of new assays, a consideration of particular importance with emerging diseases in LMICs.

In the past, molecular diagnostic techniques were substantially more expensive and required technical expertise and laboratory infrastructure not available in most LMICs. Today, this field of diagnostics is rapidly evolving to the point where some tests are becoming practicable for use in LMICs.²⁹ It is likely this trend will accelerate in the upcoming years. In addition, access to these tests is becoming a routine part of health care delivery, as a number of diseases and conditions can only be detected using these methods.

For example, many cancers are now classified using molecular tests, and the use of some drugs requires molecular testing to determine if specific biomarkers are present, typically in cancers.

Future Data-Handling Strategies

Clinical laboratories generate large volumes of data, both as part of patient care but also for quality control and other laboratory management operations. As access to laboratory services increases in LMICs, it will not be possible to handle high volumes of data using paper reporting systems. Moreover, an integrated, tier-based laboratory system will require the ability to transmit data to and from multiple testing sites, as well as to forward results to clinicians and selected test results to patients (for self-monitoring), public health authorities, and disease registries. These data-handling needs will only be achieved by use of LIS.³⁰ Although the cost of many commercial systems is not affordable in LMICs, open-source systems are available that may provide opportunity for local use. Development of robust, reliable LIS that can be integrated with other parts of health care data systems should be a priority in all regions. Mobile phones may have a role here.

For pathology, part of the “data” used in diagnostic testing consists of images. This is true not only for surgical pathology (histopathology) and cytopathology but also for hematology (blood smear examinations), microbiology (many parasites are identified based on morphologic examination), microscopic examination of urine specimens, and, in particular, malaria smears. One approach for diagnostic testing, consultation, and quality control is the use of telepathology (ie, the transmission of images via Internet connections to remote sites). In the past, this technology was expensive and required access to bandwidth not available in most of the world. In the recent past, costs have decreased, and improved Internet connectivity is occurring in many regions.

Quality Management and Accreditation

As described earlier, access to quality pathology laboratory testing is an essential part of modern medical practice. However, imagine a situation where a laboratory issues an incorrect result or, worse, a fraudulent one. In some settings, most laboratories are not accredited and do not meet minimal standards for good laboratory practice. As a result, it is unlikely these laboratories consistently generate test results that are accurate or reliable. Bad testing is the worst that a laboratory can do, for by providing “pseudo-evidence” on which wrong diagnoses are made, the harm down the line can be tremendous, such as inappropriate treatment instituted, wasted

resources, and even loss of lives. Such situations give credence to the saying “no test is better than a bad test.”

Why does bad testing occur? As previously stated, laboratory testing is a complex process with preanalytical, analytical, and postanalytical phases variables (Table 2). Considering analytical influences alone, test methodologies affect the magnitude of false-positive and false-negative results. Sensitivity and specificity profiles influence choices for screening and confirmatory tests. The competence of personnel, regular quality control, state of equipment, and laboratory infrastructure and access to reagents affect accuracy of test results. A lapse in any step in the long chain of processes involved can result in an incorrect, potentially harmful test result. Ethics and accountability are as important in the laboratory as in any other facet of health care.

To control these variables, it is essential that laboratories commit to a quality management system and organization structure that ensures that tests offered are fit-for-purpose, standard operating procedures are documented and adhered to, personnel are suitably qualified and trained, and regular audits are conducted. Over the decades, the practice of interlaboratory comparisons such as external quality assurance (EQA) and proficiency testing (PT) schemes has evolved to encourage laboratories to perform against validated performance benchmarks. Many comprehensive EQA and PT schemes are now available regionally and globally (Table 7). These vary in strength: some are more educational, while others have a validation focus.

The practice of audit has also extended beyond internal activities to assessments by third parties against national and international peer-determined standards. Formal assessment of laboratories by independent external agencies against such standards, known as accreditation, is now the norm in developed countries, where requirements for laboratory practices are often backed by law (eg, Pathology Services Accreditation Act of 1984, Victoria, Australia). Apart from ensuring quality, accreditation status also affects profitability and marketability of a laboratory (eg, only accredited tests are reimbursed by health insurance; Health Insurance Act of 1973, Australia). Also, through mutual recognition agreements (eg, the Asia-Pacific Laboratory Accreditation Co-operation, the Inter-American Accreditation Cooperation, and the International Laboratory Accreditation Co-operation), tests performed by accredited laboratories are recognized by signatories across country boundaries.

In LMICs, the culture of interlaboratory comparison, audit, and accreditation has yet to take firm root. A 2013 survey reported that more than 90% of African countries had no laboratories accredited to international quality standards, and of laboratories accredited, over 90% were in South Africa.³¹ In many LMICs in South-East Asia (eg, Myanmar,

Laos, and Cambodia), laboratory accreditation has not been established. This is due, in part, to the fact that most LMICs do not have national health insurance schemes; hence, the incentive of reimbursements for accredited laboratories does not apply. In addition, most LMICs lack strong regulatory oversight over laboratory practice. Laboratory tests performed by public laboratories are heavily subsidized by government and frequently resource constrained, while private laboratories thrive from out-of-pocket payments. EQA/PT is not mandatory. The situation pitches profits against quality, and many LMICs struggle with the mushrooming of shop-lot type private laboratories with substandard practices and questionable accountability.

However, practices in many emerging economies (eg, Thailand, Argentina, Malaysia, Brazil) are rapidly changing, and laboratory accreditation is now actively sought. Although most started off by seeking accreditation from foreign agencies (eg, Australia’s National Association of Testing Agencies and the College of American Pathologists), this has proved unsustainable because of high expense. Today, government-backed national accreditation agencies adopting international standards, especially the ISO 15189 for medical testing laboratories, have taken over and at more reasonable cost. Examples of accreditation agencies are listed in Table 8.

Notwithstanding, legislation-backed regulation of laboratories in LMICs (such as in Thailand and Malaysia) is still the exception,^{9,32} and participation in EQA/PT schemes and accreditation is entirely voluntary. For these emerging economies, the impetus toward accreditation has been competition and market driven, especially in light of trade agreements

Table 7 Examples of External Quality Assessment Programs

With international subscribers	
Royal College of Pathologists of Australasia—Quality Assurance Programs—Australia	
National External Quality Assessment Services—United Kingdom	
College of American Pathologists—United States	
Randox International Quality Assessment Scheme—International	
International Academy of Pathology—International with Regional/National Divisions	
National/local schemes	
Ministry of Public Health—Thailand	
National Institutes of Health: human immunodeficiency virus testing, toxicology	
Bureau of Laboratory Quality Standards: clinical biochemistry, hematology, blood banking, microbiology, clinical microscopy, immunology	
Mahidol University—Thailand	
Faculty of Medicine Siriraj Hospital: coagulation	
Faculty of Medical Technology: clinical biochemistry, hematology, clinical microscopy, tumor marker, immunology, parasite, lead	
Laboratory Quality Assurance Scheme—Malaysia	
Chinese National Center for Clinical Laboratories—China	
Indian Association of Medical Microbiologists—India	
National Health Laboratory Service—South Africa	

Table 8
Examples of Accreditation Bodies

The College of American Pathologists—Laboratory Accreditation Program USA
Joint Commission International
National Association of Testing Authorities—Australia
South African National Accreditation System
United Kingdom Accreditation Service
Clinical Pathology Accreditation—United Kingdom
International Accreditation New Zealand
Comite Francais d'Accreditation—France
Standards Council of Canada
China National Accreditation Service for Conformity Assessment—People's Republic of China
Hong Kong Accreditation Service
National Accreditation Board for Testing and Calibration Laboratories—India
Bureau of Laboratory Quality and Standards—Thailand
Medical Technology Council—Thailand
Department of Standards Malaysia—Malaysia
General Coordination for Accreditation—Brazil
Bureau of Accreditation—Vietnam
National Accreditation Committee—Indonesia

such as ASEAN Free Trade Area, World Trade Organization, and the imminent Trans-Pacific Partnership Agreement.

In Africa, because public laboratories are the main providers for the population, World Health Organization (WHO; in the African region) in 2009 introduced the Stepwise Laboratory Improvement Process Towards Accreditation checklist and the Strengthening Laboratory Management Towards Accreditation training curriculum. These were jointly developed with the Centers for Disease Control and Prevention, Clinton Health Access Initiative, and American Society for Clinical Pathology to motivate and assist laboratories toward accreditation status.³³ Although much remains to be done, these have transformed the laboratory mind-set and practice landscape in SSA.^{34,35}

The cooperation of the WHO, governments, and national professional bodies has been crucial in the global paradigm shift in laboratory testing toward quality and international standardization. However, many challenges remain for the LMICs, the most important being resource constraints, the establishment of national EQA/PT and accreditation schemes, and legislation-backed regulation of laboratories.

Ensuring the long-term good quality of the services provided by the essential pathology package (see later) requires adoption of an appropriate form of accreditation, within which EQA is embedded.

Reimbursement for Pathology

Pathology tests are almost universally costed according to the complexity and the volume of tests performed, often

referred to as the “cost per test” or “activity-based costing.” The burden of who pays for the tests varies across the world. It has a close relationship to the overall health reimbursement.

China has a large and complicated health care system, with a complex reimbursement system for pathology services. Although the national health care system accounts for most medical reimbursement, individual provinces and cities have their own, differing reimbursement policies. This is reflected in the big gap in health care benefits provided between the wealthy and poor regions in China.^{36,37} In Tianjin, a large city with a population of more than 13 million, the health care policy states that approximately 70% of the laboratory testing provided in the local hospitals is covered by the public medical insurance. The remaining laboratory tests have to be paid “out of pocket.” However, the government usually only reimburses basic laboratory tests, and because complex tests carry high price tags, only 40% of the actual cost of pathology testing is covered.^{35,38,39} In addition, there are restrictions on when a pathology test can be used. The result is that most of the cost of laboratory tests falls on the patient. In some rural areas, especially the underdeveloped regions of west China, the coverage of medical costs, including pathology services, is even less generous.

While state pathology reimbursement may be variable and modest in China, in contrast, in India, a country with more than 40,000 hospitals and 100,000 diagnostic laboratories, 70% of the health care delivery, including the laboratory service, is by the private sector. Public financing for health care is less than 1% of the GDP, and only 17% of the population is covered by any kind of health insurance. Thus, more than 70% of health expenditure, including pathology, is met by families, as out-of-pocket payment.⁴⁰

In SSA, the picture is mixed. In South Africa, 80% of the population have health care, including pathology, paid for by the government. Patients only make a payment if they can afford to. Around 7% have personal insurance, while the remainder pay out of pocket. A similar situation exists in Zimbabwe and Botswana. In East Africa, there is a mixture of government, insurance, and self-payment. In other countries, self-payment is commoner. Payment is made in advance for testing to occur, with patients and families purchasing the necessary supplies to perform the tests, in addition to paying the fee required for testing.

Some other LMICs have community-based health insurance that households can join. The coverage provided by these schemes varies; in Ghana, for example, the scheme covers only hospital-based services. In Bangladesh, insurance is operated by nongovernmental organizations and covers services in their own clinics. Whether or not laboratory tests are covered in these schemes depends on the details of the particular insurance scheme.⁴¹⁻⁴²

Irrespective of the type of the reimbursement system, the key factor, applying to all, is that both patients and clinicians worldwide have a tendency to prefer to use their limited financial resources in “therapy” instead of “diagnosis.” Thus, if payment is out of pocket, the tendency is for fewer, less complex, and lower quality tests, the opposite being the case when reimbursement is provided by national or private schemes. For all the reasons described earlier, inevitably this diminishes the eventual quality of the health care outcome. Moreover, it adversely affects the ability of health care systems and governments to standardize health care delivery, collect epidemiologic data, and assess the effectiveness of health care policy and interventions.

In view of this, to optimize the benefits of pathology provision, as little as possible of the reimbursement should be covered “out of pocket.” Indeed, where countries adopt a model of universal health care, we would propose that pathology reimbursement should be an integral component of the reimbursement system. Clearly, it will be important to ensure that in such a model, pathology costs (as all costs) are kept in check, for instance, by the institution of guidelines on the use of tests.

Economics of Pathology in Different Countries

Previous sections have commented that pathology is underresourced in ways that disadvantage the treatment of patients as well as the functioning of the health system. In this section, we analyze the costs of pathology laboratories using data from countries with different income levels and with very varied health systems ■ **Table 9**.⁴³⁻⁴⁵ These provide some interesting insights, although data are limited and not always readily comparable.

There are limited data available on the share of pathology costs in health costs. One study for the United States suggests that laboratory tests account for 4.5% to 10% of total health expenditures⁴⁶ compared with 5% for Spain,⁴⁶ 3.3% for the United Kingdom,¹⁵ and 3% for Australia.⁴⁷ The different payment system in the United States, where doctors receive payment per test (and are particularly conscious of potential litigation), means that the United States is likely an outlier among the high-income countries. In South Africa, the costs of pathology are around 3.5% of the total health care expenditure.⁴⁸ We have no data on the share of pathology costs in overall health expenditure in other LMICs.

Cost per laboratory test undertaken varies considerably. Important factors include the type of test, the volume of tests undertaken in the laboratory, the level of national income and hence salaries of technical personnel, whether the test is undertaken in the normal workflow or on an urgent/rapid-turnaround basis, and a hard-to-measure efficiency

factor. Since the level of the laboratory (tiers 1-4) affects the mix of tests undertaken, cost per test also varies with the level of the laboratory.

Some diagnostic areas are more standardized and more automated than others. Data from the United Kingdom⁵⁰ found that the median direct cost (ie, excluding equipment costs, costs of space, and overhead costs) of a specific routine test in biochemistry across a sample of laboratories was £1.00 compared with £2.40 in hematology, £6.90 in microbiology, and £48.10 in histopathology (2006-2007 costs). This latter cost reflects the need for a trained histopathologist to analyze and report the specimen, in contrast to the automated testing by large analyzers in, for example, biochemistry. In some areas, it has been possible to use equipment (eg, large analyzers) to drive down costs per test. In these areas, staff costs are a smaller proportion of test cost (68%-87% for biochemistry tests across different sites and 74%-89% for hematology, with one outlier). In other areas where automation is not as great, unit costs are higher, and staff costs are a higher proportion of test costs (72%-92% for microbiology and 93%-97% for histopathology⁵⁰). As science and technology changes, newer areas such as microbiology may well become more automated and less costly, but undoubtedly newer (and less automated) tests will continue to be developed.

There are strong economies of scale in laboratory testing in HICs⁴⁹ and LMICs.⁵⁰ However, the trade-off is that increased centralization of tests is also associated with increased turnaround time and potentially loss of patients to follow-up. In Table 9, the smallest laboratory performs about one test per person per day compared with 24 in a medium-sized laboratory in India and 43 (billable tests) in the largest laboratory in the United States. (No data on staff were available for Thailand: we have used 300 days worked per person per year as a rough guide for this calculation.)

Level of national income affects the technology used for doing tests and hence also the relative shares of different cost components. In LMICs, salary costs are lower relative to the cost of reagents and test kits, so tests tend to be less automated; despite this, staff costs form a smaller proportion of overall costs. In HICs, salary costs are higher relative to the cost of consumables, and there is more automation; despite this, salary costs form a higher proportion of overall costs (see Table 9: some caution in interpretation is needed, since the four laboratories examined in the table do not serve identical functions). Interestingly, in the United States, the ratio of staff to consumables in total costs has increased over time. The ratio was 40:60 in 1980 for one clinical biochemistry laboratory in a university hospital, but this had switched to 60:40 by 1990.⁵¹ It is likely that LMICs will follow a similar trend as increasing salaries increase automation.

Table 9
Structure and Annual Cost of Specialized (Tiers 3 and 4) Laboratories, Four Different Settings

Characteristic	Lilongwe, Malawi ⁴³	Tata Memorial Hospital, India, Hemopathology Laboratory ⁴⁴	King Chulalong-korn Memorial Hospital, Thailand ⁴⁵	Major Teaching Hospital, United States ^a
Types of test	91% histology, 9% cytology	Primarily hematologic malignancies	85% biochemistry; 15% hematology	Full service
Staff	2 pathologists, 2 laboratory technicians, 1 laboratory assistant	2 physicians, 2 senior residents, 6 scientists (2 PhDs), 2 technical officers (MSc), 13 technicians (BSc), 6 assistants (total = 31)	NA	7 pathologists, 7 technical supervisors, 19 phlebotomy, 4 blood bank, 18 molecular/microbiology, 26 chemical/hematology, 11 "processors," 25 outpatient laboratory technicians (total = 117, excluding administration)
Approximate population coverage	1 of only 2 such laboratories, country of 15 million	City of 21 million, state of 112 million, diagnostic center for region	City of 6.3 million	City of 650,000, state of 5.3 million
Annual number of tests	1,680	227,000	2.16 million	1.5 million billable (7 million total)
Annual budget, US\$ (year)	243,000 (2012)	976,270 (2012)	25.3 million in 2002 (2012 dollars)	18 million (2015) (2.7% of hospital budget)
Budget shares, %				NA ^d
Space, utilities	NA	2.8	1.9 (equipment + space)	
Equipment	22.6	11.2	13.2	
Staff	61.7	13.9	84.9	
Consumables	14.4	71.1	—	
Miscellaneous	1.2 ^b	1.1 ^c		

NA, no data available.

^aM. Wilson, MD, personal communication, May 2016.

^bCommunications costs (telepathology link with University of North Carolina).

^cQuality control (usually additional tests).

^dC. Price, PhD, personal communication, May 2016; data from a UK hospital trust suggest that the split is 72% staff, 26% equipment rental (ie, reagent cost), 1% equipment maintenance, and 1% other.

These variations in unit costs of tests suggest that estimating costs of an essential pathology package is not easy.

Estimated Costs for the Essential Pathology Package

As discussed above, it is not easy to cost a laboratory, as unit costs of tests vary (although there are systematic factors involved). We first estimate salary costs for technical staff, using WHO data **Table 10**⁵² for the average low- and lower middle-income country. We then construct stylized laboratories using a mix of expert judgment combined with published data summarized in Table 9. We combine this with the salary data and with the estimate that consumables in the laboratory cost approximately four times as much as salaries in Asia (this is a little lower than the ratio for the two big hospital laboratories in India and Thailand, summarized in Table 9). In Africa, the current ratio of consumables to salaries is more like 1:1 (M. Kuti, MBBS, personal communication, May 2016), but this is likely not to be optimal, as too few tests are currently undertaken. These yield estimates of recurrent laboratory costs of hospital budget of

just over 5% for the district hospital and just over 7% for a referral hospital. Our estimates can be compared with data for Ghana, where the share of laboratories in total hospital costs was 2.3% for a district hospital (117 beds, one doctor) and 4.1% for a referral hospital (100 beds, three doctors).⁵³ In India, by comparison, the shares were 7.3% for a district hospital (400 beds, 24 doctors) and 9.2% for a referral hospital (778 beds, 237 doctors).⁵⁴

We do not have enough data to estimate laboratory costs for primary health centers. One study of 12 government primary health centers in Ghana⁵⁵ estimates that laboratory costs (laboratory supplies only) cost less than 1% of the overall cost of the center. This excludes the cost of consumables for single-use tests that do not enter the laboratory.

We have too few published data to have confidence that these numbers apply in LICs. Professional salaries in LICs are about half the level (Table 10) compared with lower middle-income ones. However, it is unlikely the laboratories would be half the cost. Volumes of tests are likely to be lower, and unit costs therefore higher, by an unknown amount. The data from Malawi (S. Gopal, MD, personal communication, May 2016) show that salaries of laboratory personnel are closer to the levels of LMICs than the WHO

Table 10
Approximate Annual Salary (2010 US\$) of Pathology Staff by Country Income Category^a

WHO Employee Category/Corresponding Pathology Staff	Low Income, 2010 US\$	Lower Middle Income, 2010 US\$
2/laboratory assistant (secondary education/diploma)	2,220	4,800
3/laboratory technician (bachelor's degree)	2,870	6,170
4/scientific officer (master's degree)	4,550	9,800
Pathologist (physician with additional training)	13,650	29,400

^aAuthors' calculations using ongoing estimates from the World Health Organization (WHO).⁵² WHO data are from International Labour Organization salary databases. Equivalencies for technicians and construction of the top category (at three times the salary of category 4) by authors, using also unpublished data for Tata Memorial Hospital as a guideline.

Table 11
Estimated "Ingredients" for General Pathology Laboratories at Different Levels, Lower Middle-Income Country^a

Assumptions	Tier 1 Laboratory: Primary Health Facility	Tier 2 Laboratory: District Hospital	Tier 3 Laboratory: Referral Hospital
Facility description	5 health workers; no inpatients	100 beds, 5 surgeries/d, 500 outpatients/wk	2-400 beds, 15-20 surgeries/d, 1500 outpatients/wk
Approximate population served	30,000	50-200,000	3-6 million
Approximate annual hospital budget, US\$	150,000	6 million	18 million
Laboratory staff (excludes administrative support)	1 laboratory technician	1 general pathologist, 4 laboratory technicians, 2 laboratory assistants	4 pathologists, 2 clinical scientists, 12 laboratory technicians, 8 laboratory assistants, medical officer
Laboratory test volume/wk	100 slides plus POC tests	850	2,500
Equipment needs, US\$	2-5,000 (microscope; small devices)	150-200,000	Varies according to functions
Annual salary cost, US\$ (using Table 10)	4,800	63,680	259,440
Overall annual laboratory budget, assuming consumables: salaries is 4:1 in hospitals, US\$	NA	318.40 (ie, 5.3% of hospital budget)	1.3 million (ie, 7.2% of hospital budget)

NA, no data available; POC, point of care.

^aAuthors' best estimates, using economics ratios from Table 9, salaries from Table 10, and expert judgment. Published data were for hospitals; insufficient data were available to make complete estimates for primary health facility.

data predict. This is likely because technically qualified staff are sufficiently scarce, and if they were paid less, they would not remain in a public laboratory in a low-income country.

In summary, as stated above, our very rough estimates **Table 11** are that recurrent laboratory costs for a district hospital should be just over 5% of the hospital budget and just over 7% of the budget for a referral hospital. Of this, one-sixth is staff costs, with the balance being consumables. Costs for a tier 1 laboratory are more modest, but most testing at this level is single-use tests, and we do not have data on these. What is known from HICs is that single-use tests are generally more expensive on a "cost-per-test" basis compared with centralized testing.

Setting up the laboratory is estimated to cost \$2 to \$5,000 for a tier 1 laboratory, \$150 to \$200,000 for a tier 2 laboratory at a district hospital, and a considerably larger amount at a referral hospital (no estimates were made because of the wide variety of equipment choices available). By comparison, a specialized (primarily

histopathology) laboratory in Malawi cost \$150,000 to set up in terms of equipment and about half of this in addition to train two technicians in other countries (there is no training program currently in Malawi; S. Gopal, MD, personal communication, May 2016).

Conclusion

The differential diagnosis of the child in the vignette at the beginning of this article (ranging from tuberculosis to lymph node cancer) was wide, and each diagnosis would have required completely different treatments and management. Most of the possible diagnoses were life-threatening, and without the appropriate treatment, the prognosis for the child was poor. Conversely, with the right diagnosis and resultant treatment, the prognosis would have been good. Availability and access to timely good-quality pathology, as provided by the essential pathology package described above, would have provided that accurate diagnosis.

Key Messages

The key messages from this study are the following:

- Accurate diagnosis is the basis of effective health care. This requires access to good-quality pathology services as provided by the essential pathology package described above.
- Provision of the essential pathology package is affordable, at around 6% of the hospital's budget.
- A country cannot afford not to provide such a package. The cost of misdiagnosis is not just personal but also economic.
- Although addressing all the issues is a very long-term project, the progress of countries such as Malaysia shows that the problems are soluble.
- Analysis of the 13 targets in UN Sustainable Development Goal 3 (healthy lives and well-being) shows that effective pathology is necessary to 11 of them.
- Pathology is vital to national policy planning through, for instance, surveillance programs (eg, Ebola, Zika).
- Pathology is an integral part of any clinical care system, and without it, the system is greatly undermined. It is a cross-cutting discipline on which the other health disciplines depend.
- Pathology is also vital for research across communicable to noncommunicable diseases.
- Pathologists are diagnosticians who play a key role in linking the clinical services with the laboratory, providing leadership and capitalizing on the opportunities arising from the rapidly emerging, new technologies.

Recommendations

- Implementation of the essential pathology package is needed to address the lack of timely, accurate pathology in many LMICs.
- Given the rapidly increasing burden of NCDs, implementation is urgent.
- For the essential pathology package to achieve the benefits of shared knowledge, expertise, communication, and economies of scale, an integrated network is essential. Both the tier 1 and tier 4 levels are necessary.
- Sustainability and quality of the package depend on investment in education and training and in appropriate emerging technologies (including LIS).
- To ensure quality, standards of practice should be assessed across the network by an ongoing system of internal and external (accreditation) audit.
- Reimbursement systems, especially for universal health care, must include pathology to minimize “out-of-pocket” expenses and disincentives to appropriate use.

- Research to obtain more accurate data on the economic benefits of pathology and on the most cost-effective solutions is urgently needed.

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References

1. Murray CJL, Lopez AD. Measuring the global burden of disease. *N Engl J Med*. 2013;699:448-457.
2. Wild CP, Stewart B, eds. *World Cancer Report*. Lyon, France: IARC/WHO; 2014.
3. Rohr U-P, Binder C, Dieterle T, et al. The value of in-vitro diagnostic testing in medical practice: a status report. *PLoS One*. 2016;11:e0149856.
4. Kuijpers CC, Fronczek J, van de Goot FR, et al. The value of autopsies in the era of high-tech medicine: discrepant findings persist. *J Clin Pathol*. 2014;67:512-519.
5. Plebani M. Exploring the iceberg of errors in laboratory medicine. *Clin Chim Acta*. 2009;404:16-23.
6. World Health Organization—Regional Office for Africa and US Centers for Disease Control and Prevention (CDC). *Guidance for Development of National Laboratory Strategic Plans*. http://www.who.int/hiv/amds/amds_guide_dev_nat_lab_strat.pdf. Accessed May 25, 2016.
7. Adesina A, Chumba D, Nelson AM, et al. Improvement of pathology in sub-Saharan Africa. *Lancet Oncol*. 2013;14:e152-e157.
8. African Strategies for Advancing Pathology Group Members. Quality pathology and laboratory diagnostic services are key to improving global health outcomes improving global health outcomes is not possible without accurate disease diagnosis. *Am J Clin Pathol*. 2015;143:325-328.
9. Looi LM. The pathology act explained. *Malays J Pathol*. 2008;30:1-10.
10. Daramola AO, Bennett A, Abdulkareem F, et al. Breast cancer reporting in Lagos, Nigeria: implications for training and education in Africa [published April 6, 2016]. *J Glob Oncol*.
11. Singh D. Accreditation of diagnostic laboratories. *The Sangai Express*. September 28, 2013.
12. Elbireer AM, Jackson JB, Sendagire H, et al. The good, the bad, and the unknown: quality of clinical laboratories in Kampala, Uganda. *PLoS One*. 2013;8:e64661.
13. World Health Organization, Regional Office for Africa. 2008. The Maputo declaration on strengthening of laboratory systems. http://www.who.int/diagnostics_laboratory/Maputo-Declaration_2008.pdf. Accessed May 15, 2016.
14. The African Society for Laboratory Medicine. The Freetown Declaration. 2015. <http://new.aslm.org/programmes/global-health-security/freetown-declaration/>. Accessed April 27, 2016.
15. International Standards Organization (ISO). *Standardization of medical laboratories: requirements for quality and competence*. Geneva, Switzerland: ISO; 2012.
16. Joint Commission International. 2014. *Accreditation Standards for Hospitals*. 5th ed. <http://www.jointcommissioninternational.org/jci-accreditation-standards-for-hospitals-5th-edition/>. Accessed May 9, 2016.

17. Department of Health, UK. *Report of the Review of NHS Pathology Services in England*. London, UK: Department of Health (UK); 2006.
18. Nelson AM, Milner DA, Rebbeck TR, et al. Africa: pathology in the sub-sahara. In: Boyle P, Ngoma T, Sullivan R, et al, eds. *The State of Oncology in Africa 2015*. Lyon, France: iPRI Scientific Publication; 2016:4.
19. Jegathesan M, de Witt GF. Organisation of laboratory services in Malaysia. *Malaysian J Pathol*. 1982;5:1-5.
20. Wu G, Zaman MH. Low-cost tools for diagnosing and monitoring HIV infection in low-resource settings. *Bull World Health Org*. 2012;90:914-920.
21. Bond M, Richards-Kortum RR. Drop-to-drop variation in the cellular components of fingerprick blood: implications for point-of-care diagnostic development. *Am J Clin Pathol*. 2015;144:885-894.
22. Cassim N, Coetzee LM, Schnippel K, et al. Estimating implementation and operational costs of an integrated tiered CD4 service including laboratory and point of care testing in a remote health district in South Africa. *PLoS One*. 2014;9:e115420.
23. Hyle EP, Meye L, Kelly K, et al. The clinical and economic impact of point-of-care CD4 testing in Mozambique and other resource-limited settings: a cost-effectiveness analysis. *PLoS Med*. 2014;11:e1001725.
24. World Health Organization. *World Malaria Report*. 20th ed. Geneva, Switzerland: World Health Organization Press; 2015.
25. World Health Organization. *Global Tuberculosis Report*. 20th ed. Geneva, Switzerland: World Health Organization Press; 2015.
26. Pollock NR, McGray S, Colby DJ, et al. 2013. Field evaluation of a paper-based point-of-care fingerstick transaminase test. *PLoS One*. 30;8:e75616.
27. Whitesides GM, Wilding P. Lab on a stamp: paper-based diagnostic tools. Interview by Molly Webster and Vikram Sheel Kumar. *Clin Chem*. 2012;58:956-958.
28. Yetisen AK, Akram MS, Lowe CR. Paper-based microfluidic point-of-care diagnostic devices. *Lab Chip*. 2013;13:2210-2251.
29. St John A, Price CP. Existing and emerging technologies for point-of-care testing. *Clin Biochem Rev*. 2014;35:155-167.
30. National Pathology Programme. *Digital First: Clinical Transformation Through Pathology Innovation*. 2014. <https://www.england.nhs.uk/wp-content/uploads/2014/02/pathol-dig-first.pdf>. Accessed May 25, 2016.
31. Schroeder LF, Amukele T. Medical laboratories in sub-Saharan Africa that meet international quality standards. *Am J Clin Pathol*. 2014;141:791-795.
32. Wattanasri N, Manorama W, Viriyayudhagorn S. Laboratory accreditation in Thailand: a systemic approach. *Am J Clin Pathol*. 2010;134:534-540.
33. Gershy-Damet GM, Rotz P, Cross D, et al. The World Health Organization African region laboratory accreditation process. *Am J Clin Pathol*. 2010;134:393-400.
34. Yao K, Talkmore M, Luman ET, et al. The SLMTA programme: transforming the laboratory landscape in developing countries [published online September 16, 2014]. *Af J Lab Med*.
35. Alemnji GA, Zeh C, Yao K, et al. Strengthening national health laboratories in sub-Saharan Africa: a decade of remarkable progress. *Trop Med Int Health*. 2014;19:450-458.
36. Chen M, Zhao Y, Si L. Who pays for health care in China? The case of Heilongjiang Province. *PLoS One*. 2014;9:1-11.e108867.
37. Pan L, He P, Wu HF, et al. Investigation and analysis of city public hospital outpatient and inpatient medical expenses of inpatients and payment. *Chinese Gen Pract*. 2014;17:4127-4132.
38. Mao AY. Study on the impact of public health insurance system reform over 20 years in China, how patients' actual reimbursement rate changed. *Chinese Health Econ*. 2012;31:19-22.
39. Lei HD, Chen JB, Lu XS. Analysis on the personal burden of inpatients in a hospital in Tianjin. *Foreign Med Sci*. 2014;31:38-40.
40. The Hindu. Only 17% have health insurance cover. December 22, 2014. <http://www.thehindu.com/news/national/only-17-have-health-insurance-cover/article6713952.ece>. Accessed May 9, 2016.
41. Robyn PJ, Sauerborn R, Bärnighausen T. Provider payment in community-based health insurance schemes in developing countries: a systematic review. *Health Policy Plan*. 2013;28:111-122.
42. Soors W, Devadasan N, Durairaj V, et al. *Community Health Insurance and Universal Coverage: Multiple Paths, Many Rivers to Cross*. Geneva, Switzerland: World Health Organization; 2010. World Health Report Background Paper, 48.
43. Avivar C. Strategies for the successful implementation of viral laboratory automation. *Open Virol J*. 2012;6:151-121.
44. Centre for International Economics. The economic value of pathology: achieving better health, and a better use of health resources. http://www.thecie.com.au/wp-content/uploads/2016/04/Economic-value-of-pathology_-Final-Report-April-2016.pdf. Accessed May 12, 2016.
45. Pillay TS. Containing costs in the era of national health insurance—the need for and importance of demand management in laboratory medicine. *S Afr Med J*. 2012;103:24. <http://www.samj.org.za/index.php/samj/article/view/6383/4714>. Accessed June 27, 2016.
46. Department of Health, UK. *Report of the Second Phase of the Review of NHS Pathology Services in England*. London, UK: Department of Health (UK); 2008.
47. Cunnama L, Sinanovic E, Ramma L, et al. Using top-down and bottom-up costing approaches in LMICs: the case for using both to assess the incremental costs of new technologies at scale. *Health Econ*. 2016;25 (suppl 1):53-66.
48. Bengé H, Csako G, Parl FF. A 10-year analysis of revenues, costs, staffing and workload in an academic medical centre clinical chemistry laboratory. *Clin Chem*. 1993;39:1780-1787.
49. Aboagye AQQ, Degboe AKBObuobi ADD. Estimating the cost of healthcare delivery in three hospitals in southern Ghana. *Ghana Med J*. 2010;44:83-92.
50. Chatterjee S, Levin C, Laxminarayanan R. Unit cost of medical services at different hospitals in India. *PLoS One*. 2013 8:e69728.
51. Dalaba MA, Akweongo P, Savadogo G, et al. Cost of maternal health services in selected primary health centres in Ghana: a step-down allocation approach. *BMC Health Serv Res*. 2013;13:287-295.

52. Gopal S, Krysiak R, Liomba NG, et al. Early experience after developing a pathology laboratory in Malawi, with emphasis on cancer diagnoses. *PLoS One*. 2013;8:e70361.
53. Gujral S, Dongre K, Bhindare S, et al. Activity-based costing methodology as tool for costing in haematopathology laboratory. *Indian J Pathol Microbiol*. 2010;53:68-74.
54. Charuruks N, Chamnanpai S, Seublinvog T. Cost analysis of laboratory tests: a study of the central laboratory of King Chulalongkorn Memorial Hospital. *J Med Assoc Thai*. 2004;87:955-963.
55. Serje J. *Estimates of Health Sector Salaries Across Four Occupational Levels for UN Member States*. Geneva, Switzerland: WHO; 2015.