Cost, Capacity, and Care: History and Implementation Considerations of the WHO's Essential Diagnostics List

Laura Hallas

Plan II Honors Program

University of Texas at Austin

April 28, 2019

Supervisor: Dr. Stanley Reiser

Second Reader: Dr. Marc Lewis

Abstract

Author: Laura A. Hallas

Title: Cost, Capacity, and Care: History and Implementation Considerations of the WHO Essential Diagnostics List

Supervising Professor: Dr. Stanley Reiser, UT School of Public Health

Second Reader: Dr. Marc Lewis, UT Department of Psychology

Diagnostics are the gateway to healthcare, and major global health efforts such as the fight against HIV/AIDS dependent in large part on reliable and extensive diagnostic infrastructure. Despite this importance to global health, pathology and diagnostic medicine has been historically neglected amid significant global health initiatives. The May 2018 release of the WHO's essential diagnostics list is, therefore, a turning point in the history of global health programming and may hold specifically strong implications for the recently observed resurgence of HIV/AIDS cases in sub-Saharan Africa and Eastern Europe.

In this paper, I analyze the relationships between the 2018 EDL and past global health programming and propose specific benefits of the EDL to low- and middle-income countries, such as those in sub-Saharan Africa, when WHO-directed multi-government action helps to orient global health efforts. I also use existing literature concerning public health interventions in low- and middle-income countries to predict EDL impacts on four areas of need defined in recent pathology and laboratory medicine literature: human resources, education, infrastructure, and quality standards. Overall, I predict that the EDL will generate a more cohesive global health agenda toward pathology and laboratory medicine, and more evidence-based global health policies.

Key words: Diagnostics, Laboratory and Pathology Medicine, Global Health

Acknowledgements

There have been many individuals who have helped bring this thesis from an idea to a final version. I would first acknowledge Dr. Marc Lewis and Dr. Stanley Reiser for advising not only my thesis research but also my academic career as a whole. I would also like to thank Dr. Sarah Riley and the team at Pathologists Overseas for my early introduction to the fascinating field of global health and specifically the topic of pathology and laboratory medicine. Finally, I would like to thank Cathy and Jim Hallas, Christian Lumley, and the motley crew of 610 Maiden Lane for their support throughout my writing process.

Table of Contents

Introduction

Introduction and thesis objectives

Introduction

Ingrid didn't know what was wrong with her. She had been rapidly losing weight over the previous months, many days unable to even attend work. It was terrifying. As she watched herself slowly waste away, she knew she had to take action. She traveled from her rural village to Gaborone, the capital of Botswana, in 2002. There, her doctor offered her a diagnostic test, and for the first time she was able to put a name to her pain. Ingrid had HIV.

> 'When I was told I was HIV positive. I felt that relief within me. I was relieved that I knew what was wrong with me, because you do not know what is wrong with you and you can see yourself wasting away. That is the most scary part. That is what was really scary about [my experience with HIV]' (Ingrid, face-to-face interview by Smiley Pool, 2018).

There is power in naming disease. "Diagnostic medicine" is common shorthand for the more descriptive global health category of "Pathology and Laboratory Medicine," or PALM. PALM is broadly defined as any approach used to gather clinical information for the purpose of making a clinical decision (the diagnosis), and encompasses testing ranging from pregnancy tests to cancer biopsies. Diagnostic medicine is therefore the starting point for determining treatment and the monitoring of disease progression. Blood, urine, saliva, and even sweat all contain clues to our medical status and help healthcare professionals differentiate between diseases. By converting unknown maladies to named, well-defined diseases, medical diagnostics transform care. It is critical work.

Ingrid's diagnosis offers a particularly striking example of the power diagnostics have on both individual and population levels. When Ingrid, and then her young son, fell ill, there were limited options for adults to be tested and connected to the antiretroviral therapy necessary for

HIV treatment and no resources for children. In the early 2000s, the small sub-Saharan country of Botswana faced an epidemic of HIV/AIDS. Death touched everyone: doctors, teachers, parliamentarians, parents, children. The scale prompted President Festus Mogae to famously declare at the 2000 International AIDS Conference in Durban, South Africa that his country was "threatened with extinction.[1]" Without strong diagnostic infrastructure, the world had no chance of keeping up with the clip of this deadly infectious disease. Suddenly, entire regions of the world were forced to confront weak diagnostics infrastructure. Diagnostic testing rose to the forefront of the global health agenda.

Yet even amid trends that made the need for strong diagnostic infrastructure visible in a rapidly globalizing world, diagnostic medicine has not received the same care and attention afforded to the provision of treatment. UNAIDS cites evidence that 25 percent of the 36.9 million people living with HIV/AIDS have not been diagnosed.[2] Further, malaria, pneumonia, and other febrile illnesses are frequently misdiagnosed in low-resource environments—with deadly results. In fact, many poor, rural regions have no accredited laboratories or laboratory technicians at all; in some countries, even national laboratories struggle to maintain the quality control standards necessary for accurate diagnostic care. These gaps in infrastructure have far-reaching implications for health and human development. This thesis explores one new development in meeting this challenge for improved PALM care: The Essential Diagnostics List.

---

[1] Durban Algin. African president warns of extinction from Aids. The Telegraph. https://www.telegraph.co.uk/news/worldnews/africaandindianocean/botswana/1347791/African-president-warns-of-extinction-from-Aids.html. Published July 10, 2000. Accessed December 9, 2018.

[2] "AIDSinfo | UNAIDS." *AIDSinfo | UNAIDS*, aidsinfo.unaids.org/.

Thesis description

The World Health Organization's Essential Diagnostics List, released in May 2018, is both a long-awaited recognition of the critical role that diagnostics play in healthcare and a response to historical trends in global health. The Essential Diagnostics List, or the EDL, is a catalog of key laboratory tests created to boost global public health by promoting standardized usage of a set of highly effective and efficient diagnostic tests.[3] The EDL recommends 23 different diagnostic tests that help detect diseases such as HIV, malaria, and tuberculosis. The current first draft of the EDL has been created with expectations of future expansion, allowing each updated list to adapt to evolving world health conditions. As will be demonstrated, the very publication of this list is a historic turning point in the presence of diagnostic medicine within healthcare. Indeed, its existence has already made progress toward the dual goals of 1) raising awareness for global health policymakers and 2) narrowing diagnostic capacity building to a few key target areas, including HIV detection.[4] The unique focus of this particular global health initiative promises to propel the role of pathology and laboratory medicine to its rightful role in global health programming.

This study will characterize the publication of the Essential Diagnostics List in light of the history of diagnostic medicine, with an emphasis on global health responses to HIV/AIDS and Ebola. After providing this context, this thesis will determine where the 2018 Essential Diagnostics List may help to address contemporary needs in low- and middle-income countries. Criterion for analysis will be drawn from a recent Lancet series (entitled Pathology and Laboratory Medicine in Low-income and Middle-income Countries) describing the current

---

[3] *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018)*.
[4] Riley S. Essential Diagnostics List. Lablogatory. https://labmedicineblog.com/2018/05/07/essential-diagnostics-list/. Published May 4, 2018. Accessed October 30, 2018.

shortfalls of pathology and laboratory medicine in low- and middle-income countries.[5] The four main areas of observation as described by Wilson et al. are 1) Human resources and workforce capacity 2) Education and training 3) Infrastructure and 4) Quality, standards, and accreditation. These criteria are used in this thesis' analysis. This thesis represents the first extensive analysis of the WHO EDL in light of current literature on global health governance and predicts specific effects of the implementation of the EDL.

While the EDL is intended to be applicable in essentially any healthcare environment, this study will necessarily be narrowed and conducted with a specific context in mind. Specifically, analysis will be oriented toward the use of HIV diagnostics within a multi-tiered healthcare system in sub-Saharan Africa, while still incorporating broader lessons from low- and middle-income environments around the world. The choice of these parameters will both narrow the scope of this thesis to a manageable level of application, as well as provide the opportunity to draw on the rich literature of HIV/AIDS and Ebola response efforts—important subjects for the region. These two parameters of HIV/AIDS diagnostics and a regional focus on sub-Saharan Africa will narrow discussion of the EDL to a more manageable field of study while still allowing for generalizable results.

Limitations

Working in this theoretical framework and focusing specifically on sub-Saharan African HIV diagnostic capacity will necessarily involve several limitations. In discussing the history of PALM services in global health programming, it would be impossible to provide a full account

[5] Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

of the myriad pathways that have led to the EDL's development, and so analysis will remain relatively surface-level with the intention of capturing overall trends. Similarly, a focus on HIV testing as an example of PALM services does not provide a complete basis for endorsement or non-endorsement of the EDL's effectiveness, nor does focus on a single disease fully capture the fact that implementation the EDL might have positive externalities in the environment (ex: hiring an extra laboratory technician to meet HIV testing guidelines may also improve a clinic's ability to meet tuberculosis testing guidelines). Analysis will proceed with these limitations in mind, but it is my prediction that even with these restrictions, this thesis will still provide a valuable framework for analysis of the historical context and future impact of the WHO's EDL.

Defining Diagnostic Medicine

Before embarking on a study of global diagnostic medicine, it is first necessary to define the basic terms of the field. A more detailed analysis of contemporary issues in diagnostic medicine will occur in the third section of this paper.

Terminology

The terms "diagnostic medicine," "clinical pathology," "anatomic pathology" and "laboratory medicine," while related, have varying shades of meaning and field-specific connotations. However, all of these descriptors can be categorized under the broader umbrella of "pathology and laboratory medicine," or PALM, which is defined by Mosby's Medical Dictionary to be the branch of medicine concerned with the analysis of specimens of fluids, tissue, or other bodily substances outside of the body.[6]

[6] Laboratory medicine. (n.d.) *Mosby's Medical Dictionary, 8th edition*. (2009). Retrieved March 7 2019 from https://medical-dictionary.thefreedictionary.com/laboratory+medicine

Typically conducted in a laboratory setting, pathology and laboratory medicine uses an array of diagnostic tests ranging from handheld pregnancy tests to biopsies of cancerous tissue. In day-to-day patient interactions, the field largely consists of the "back of house" work that occurs when a physician sends a sample in for analysis In the context of a resource-poor health system, as is often found in low- and middle-income countries, diagnostic medicine may also occur largely outside of a formal laboratory setting, relying more on screening tools and point-of-care testing, such as a finger-prick malaria blood test.

Workforce

The breadth of required PALM services and the complexity of the care systems needed to maintain those services demands a well-trained and diverse workforce. At the highest level, staff with doctorates in fields such as pathology, chemistry, microbiology, or biochemistry work alongside medically-trained professionals (MDs) to run laboratories and implement quality control procedures. Supporting staff includes nurses, laboratory technicians, and medical or doctoral students. Depending on the healthcare environment, community health workers who visit patients directly to assist in screening and other public health activities may also play a role in providing patients access to diagnostic services. Finally, a basic functioning laboratory requires support staff in fields such as information technology and clerical administrative support (billing, coding etc.) to provide order and efficiency in healthcare environments where even salaries for health providers are not always a given.[7] As will be discussed later, PALM

[7] Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

workforce shortages in all of these categories are a major problem in many health systems today–including in the U.S.

Governance and Quality Control

Pathology and laboratory medicine services are most typically conducted within tiered healthcare systems, with a network of laboratories ranging from national laboratories, which determine national laboratory standards, to primary care settings where self-testing constitutes the majority of care. Ordered by the WHO from local (I) to national (IV), the below figure from the first draft of the EDL illustrates the tiered structure which most public health activity (and thus the EDL) is implemented.

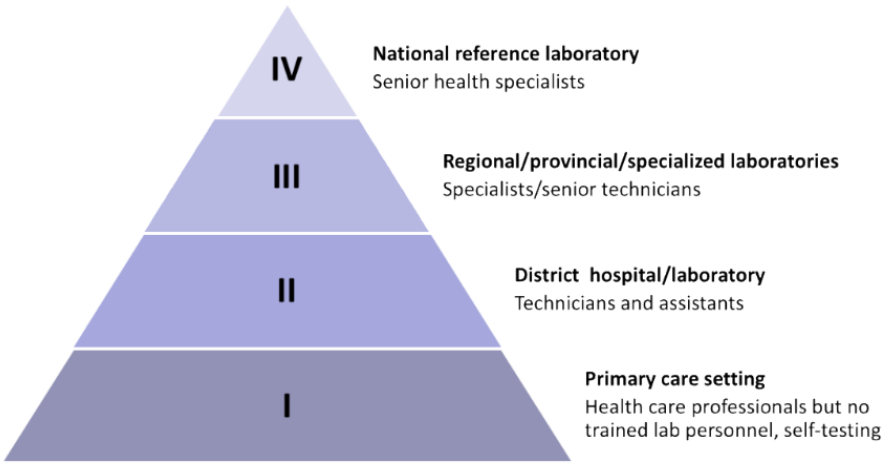

Figure 1: Tiered laboratory environment[8]

This hierarchical model allows for a downward flow of quality assurance, quality control, and external quality assessment schemes (EQAS). The details of these systems are not critical to this discussion, but notably the tiered laboratory model allows a top-down flow of documentation

[8] *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018).*

strategy, standard operating procedures, and quality control samples that standardize care within a country's healthcare system.[9] The recognized efficiency of such a tiered system is demonstrated by the successes of the United States' Laboratory Response Network, established in 1999. This program created a three-tiered model for US diagnostic care, composed of primary care "sentinel" laboratories which are the first line of patient care; hospital laboratories, which provide services similar to sentinel laboratories; reference laboratories that offer more specialized testing; and finally national laboratories that have the ability to identify the most infectious and specialized pathogens such as Ebola, as well as establish standardized controls for the rest of the country.[10]

Maintaining quality control systems is a truly international effort, as quality control sample and reagents often shared between countries. As such, quality control organizations within global powers such as the US and UK play a significant role in quality control activities for low- and middle-income countries. For example, the College of American Pathologists is acknowledged by the World Health Organizations as the world leader in laboratory quality assurance and accreditation and is involved in many international health activities surrounding diagnostic accreditation.[11] The UK's National External Quality Assessment Service serves a similar function. International support such as through these organizations has been essential to achieving some of the most significant PALM victories in the last decade, including the

---

[9] "Quality Assurance." *World Health Organization*, World Health Organization, 15 May 2017, www.who.int/diagnostics_laboratory/quality/en/.

[10] Centers for Disease Control and Prevention. Facts about the laboratory response network. 2014. https://emergency.cdc.gov/lrn/ factsheet.asp (accessed Oct 4, 2017).

[11] United States, Congress, Regional Office for Africa and United States Centers for Disease Control and Prevention. "Guidance for Development of National Laboratory Strategic Plans." *Guidance for Development of National Laboratory Strategic Plans*. https://www.who.int/hiv/amds/amds_guide_dev_nat_lab_strat.pdf

establishment of a national blood bank system in Ethiopia.[12] Lastly, the Royal College of Pathologists of Australasia (RCPA) has been influential in establishing quality control programs in countries such as Malawi.[13] These and other organizations must work alongside national governments and the WHO to implement PALM services.

Individual and Public Health Implications

It has been estimated that are 60,000 possible diagnoses,[14] 6,000 drugs and 4,000 medical and surgical techniques and procedures to address them.[15] The combinations thereof total well into the billions and thus necessitates a guiding process. Identifying diagnosis, and then determining treatment, has far-reaching implications for both individual and public health. Diagnosis is the first step towards an individual receiving medical treatment and allays the sinking feeling of the unknown that arises as patients travel from physician to physician hoping to receive information, any information, on what ails them. Diagnostics are empowering as well as medically critical. Figure 1 illustrates the care pathway as it relates to diagnostics, as it often serves as the first contact a patient has with healthcare system, and the link between multiple healthcare providers who are involved in delivering care.

---

[12] Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

[13] Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

[14] "ICD - ICD-10-CM - International Classification of Diseases,(ICD-10-CM/PCS Transition." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, www.cdc.gov/nchs/icd/icd10cm_pcs_background.htm.

[15] Gawande, Atul. "Cowboys and Pit Crews." *The New Yorker*, The New Yorker, 26 May 2011, www.newyorker.com/news/news-desk/cowboys-and-pit-crews.

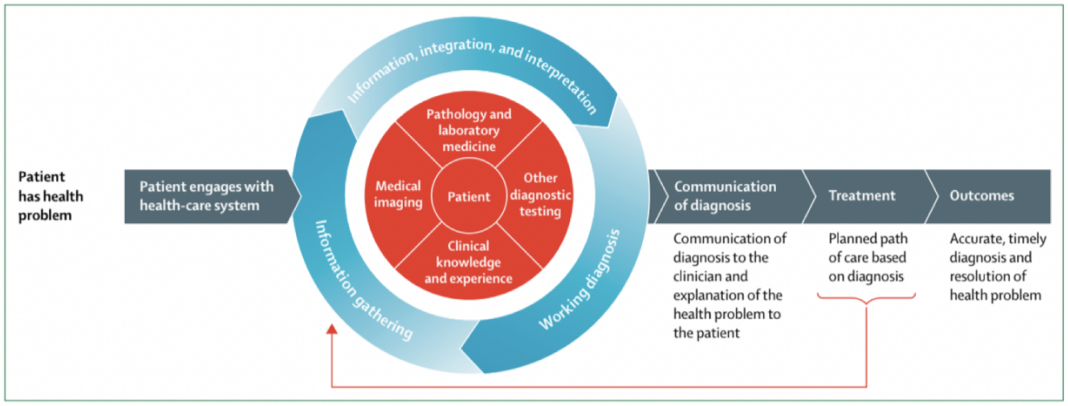

Figure 2. Wilson et al. description of diagnostic and treatment mechanisms [16]

The ability to reliably access accurate PALM services, and do so at a sufficiently low cost, is critical in limiting the period of illness for a patient, and therefore the disruption of their economic productivity. The field of health economics has long been concerned with the intersection of epidemiology and economics, particularly with the relationships of illness with poverty, GDP growth, and income per capita.[17] The economics valuation of morbidity (illness) and mortality (death) vary, but measures such as cost in dollars lost in wages, lost productivity, or years lost (either "healthy" life years" or absolute life years). There are also negative externalities of insufficient PALM services for one individual onto others' care. When an incorrect diagnosis leads to inefficient allocation of physician time, medical treatments, or existing diagnostic tools, other patients necessarily lose out on the potential benefits of those wasted resources. Economic considerations do not supersede the humanitarian value of maintaining health through accurate diagnostic systems but are nonetheless worth mentioning for their tangible impact on individual livelihood and national development. When a person must

[16] Ml W, Ka F, Ma K, Lm L, N L, K R. Access to pathology and laboratory medicine services: a crucial gap. *Yearbook of Paediatric Endocrinology*. 2018. doi:10.1530/ey.15.13.5
[17] Folland, Sherman, et al. *The Economics of Health and Health Care*. Routledge, 2017.

walk three days to reach quality diagnostic care or governments to not have standardized systems of provisioning PALM services, other aspects of a person's life suffer.

Lastly, population-level data on disease incidence and prevalence is used by international health organizations, national ministries of health, and local health initiatives, each of whom rely on strong diagnostic systems to identify healthcare needs and direct financial and human capital. Official diagnostics measures build data about disease presence in their areas of jurisdiction and help policymakers to allocate resources appropriately.[18] World Health Organization press releases, for example, cite "confirmed cases" that have been laboratory-tested in juxtaposition to "suspected cases." In those difference of definition are massive public health implications. Which groups gets funded, where doctors are sent, what diseases get studied — all of these depend in part on the availability of pathology and laboratory services to conclusively diagnose cases. With increased travel, as well as the expansion of supply chains for medicine and food across international borders, the ability to reliably detect and identify disease is of increasing importance to global health security. As should be clear, there are few subjects in healthcare and global health that are not touched by PALM services.

[18] Lesson 1: Introduction to Epidemiology. Centers for Disease Control and Prevention. https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section5.html. Published May 18, 2012. Accessed December 9, 2018.

Part I: Global Governance and PALM

Global Governance Organizations

Global Health and the WHO

"Global health" as we understand it today involves cooperation between international health organizations, national governmental initiatives, and local actors that is a fairly recent development in the longer history of medicine. Understanding the role of diagnostic medicine in global health first requires a broad-strokes understanding of global health programming trends. Urbanization and rapid economic growth following the industrial revolution brought public health into the public conscience, but also formed ideal conditions for disease to spread. With high-density environments, low-quality infrastructure, and intense socioeconomic stratification, "public health" as a field became preoccupied with disease-control and prevention programs, largely focusing on sanitation. This period too saw the first hints of what might be called "global health" when European governments committed resources to preventing and treating so-called "tropical" diseases in their southward colonies. This focus on sanitation and tropical diseases is reflected in the names of institutions founded in the late nineteenth and early twentieth century, such as the London School of Hygiene and Tropical Medicine. As germ theory and early vaccine researched continued to develop, these containment efforts became more and more effective, and the recommendations and guidelines of public health organizations held more and more weight in governmental programming.

With scientific and economic advancement came the need for global governance systems committed to tracking and controlling disease. The late nineteenth and early twentieth century saw the transition of the physician as healer to that of a physician-scientist — fostering an

understanding of the underlying pathology of disease with precision and scientific accuracy. Until the point, "diagnosis" in any formal sense merely described the deductive efforts of a physician as he matched a patient's complaints to known illnesses. With the shift came a flood of new discoveries of the microbes underlying then-common diseases such as cholera and tuberculosis.[19] The beginnings of globalization led too to the increase of international partnerships to address the spread of disease, and the pre-WWII era saw rise of several international health alliances and initiatives, including the Pan American Health Organization and the League of Nations. In 1948, the United Nations was established, shortly followed by the World Health Organization (a specialized agency of the United Nations). With the establishment of these two preeminent organizations, the remnants of WWII and European colonization drove popular support for a universalist approach to global health governance, and government accountability in meeting jointly-defined global health standards on a national level. What were once ungrounded health ideals became the legitimate subject of formal assembly subcommittees and internal memos. While the institutionalization of global health work did not instantly improve health by any means, there is little doubt that it provided a necessary forum for global health action.

The Alma-Alta Declaration

The 1978 Declaration of Alma-Alta further solidified the WHO's shifting focus toward preventative capacity-building and equipping primary healthcare systems rather than only focusing on acute health needs. The result of the International Conference on Primary Healthcare held in Alma-Alta, Kazakhstan, the Declaration outlined primary healthcare as a priority of the

[19] Frerichs RR. Who first discovered vibrio cholera? UCLA Fielding School of Public Health http://www.ph.ucla.edu/epi/snow/firstdiscoveredcholera.html. Accessed December 9, 2018.

international health community.[20] Examination of two major components of the Declaration provides insight into the way diagnostics were less emphasized than other direct forms of medical technology critical for health systems, namely immunization and provision of essential drugs, which were specifically mentioned in part VII of the declaration as shown below (emphasis added):

Declaration VII

> "... includes at least: education concerning prevailing health problems and the methods of preventing and controlling them; promotion of food supply and proper nutrition; an adequate supply of safe water and basic sanitation; maternal and child health care, including family planning; *immunization* against the major infectious diseases; prevention and control of locally endemic diseases; appropriate *treatment* of common diseases and injuries; and *provision of essential drugs"*

Unlike it's attention to "the provision of essential drugs," part VII of the Alma-Alta declaration did not attend to diagnostic medicine. Indeed, no portion of the declaration specifically cites diagnostic medicine as a health need. However, there are more general statements within the Alma-Alta Declaration that offer a basis for analysis of diagnostic medicine today, even though they were originally written merely as an endorsement on primary healthcare.

Declaration VI

> "Primary health care is essential health care based on *practical, scientifically sound and socially acceptable* methods and technology made universally accessible to individuals and families in the community through their full participation and *at a cost that the community and country can afford to maintain at every stage of their development* in the spirit of self-reliance and self-determination."

From Declaration VI, it can be concluded that diagnostic medicine must be "practical, scientifically sound and socially acceptable," and made available "at a cost that the community

[20] International Conference on Primary Health Care, Alma-Ata, USSR, 6-12 September 1978 . *Declaration of Alma-Ata*.

and country can afford to maintain." These principles from the Alma-Alta Declaration would come to serve as the ideological underpinnings of an argument for cost-effective diagnostics. With the ideals of the Alma-Alta Declaration in mind, it is then possible to examine the contemporary diagnostic medicine landscape and assess how the Essential Diagnostics List might bring primary health care closer to a model that is practical, scientifically sound, and affordable. This criterion is critical in assessing current diagnostic capacity.

The Millennium Development Goals

Per the Alma-Alta Declaration, the WHO and the United Nations had a broad mandate to set up concrete initiatives to improve global health and, in particular, access to primary healthcare. Global health governance organizations often accomplish these goals not through the brute-force method of fully identifying, funding, and carrying out a public health initiative, but by moving member states to action and organizing industry leaders. This agenda-setting capacity is therefore one of the most influential characteristics of global health organizations. By mobilizing the expansive network of private and governmental organizations toward a particular goal, (for example, eliminating maternal mortality) large global health organizations such as the WHO are able to organize at a high level while allowing local organizations to actually carry out logistics. The World Health Organization can release guiding documents that suggest individual nations reduce maternal mortality by 75 percent, and then it is local patient advocacy groups who actually drive young mothers to the hospital as they begin labor. This may seem to be evidence that the WHO and other large global health organizations are bureaucratic and/or ineffective in actually reaching those in need, but the Millennium Development Goals (MDGs) offer a valuable case-study in the way target statistics or initiatives set by the WHO and the UN can more

efficiently organize governmental funding and response than would have been the case without such guidance.

The Millennium Development Goals were a list of eight goals that emerged following 2000 United Nations Millennium Declaration, targeted for completion by 2015. All 191 member nations signed the declaration, and many more non-governmental organizations and private groups also oriented themselves to meet the stated goals. The eight goals were:

1. to eradicate extreme poverty and hunger;
2. to achieve universal primary education;
3. to promote gender equality and empower women;
4. to reduce child mortality;
5. to improve maternal health;
6. to combat HIV/AIDS, malaria, and other diseases;
7. to ensure environmental sustainability; and
8. to develop a global partnership for development.

Goals 4, 5, and 6 most explicitly address health metrics, and it is in the 15-year outcomes for these goals that the positive impacts of the MDGs can be best observed. Each MDG provided both a broad objective (to "reduce," "improve," or "combat") as well as specific benchmarks provided in UN documents. Goal 4 specifically laid out objectives to reduce the under-five mortality rate by two-thirds. Goal 5 defined improvement to maternal health as first; reduction by three quarters in the maternal mortality ratio, second; increasing the proportion of births attended by a health professional, and third; promoting universal access to reproductive health (increasing contraceptive access, decreasing adolescent birth rates). The decision-making process to determine which metrics to include and which to leave out was opaque, drawing criticism, but nonetheless resulted in specific goals.

While none of these (purposefully ambitious) goals were technically achieved by 2015, there were nonetheless massive improvements in the areas they sought to address. The

global under-five mortality rate declined by more than half within the designated time period of 1990 to 2015, dropping from 90 to 43 deaths per 1,000 live births.[21] Similarly, the maternal mortality ratio declined by 45 percent worldwide since 1990, with most of the reduction occurring since 2000. Much progress was made against HIV, tuberculosis and malaria as well. For example, new HIV infections fell by approximately 40 percent between 2000 and 2013, and the number of people receiving antiretroviral therapy (ART) globally increased from 800,000 in 2003 to 13.6 million in June 2014. Each marks a significant leap forward in these critical health metrics despite not reaching the technical numerical benchmarks laid out in 2000.

These positive results were initially dogged by questions of causality — how did world leaders know that their efforts to meet these target goals actually resulted in improvements instead of being the natural result of progress over time? The Brookings Institute investigated this question, and was able to illustrate that while improvements were already being made in each metric, the institution of the Millennium Development Goals allowed for a rapid acceleration in the progress being made.[22] Even more promising for global health leaders, the health-related aspects of the MDGs outperformed the other 5 non-health metrics, with more than 21 million "extra" lives saved from improvements in child mortality, maternal mortality, HIV/AIDS, and tuberculosis. Furthermore, Brookings found that progress in these three health metrics, as well as in the rest of the list, were most substantial in developing regions– about two-thirds of the 21 million lives saved were in sub-Saharan

---

[21] *The Millennium Development Goals Report 2015*. New York: United Nations

[22] McArthur J, Rasmussen K, McArthur J, Rasmussen K. How successful were the Millennium Development Goals? brookings.edu. https://www.brookings.edu/blog/future-development/2017/01/11/how-successful-were-the-millennium-development-goals/. Published January 11, 2017. Accessed February 5, 2019.

Africa.[23] Taken together, these two findings indicate not only that international action through the agenda-setting MDGs improved lives, but that it had the most impact in health-related areas of the list, and in developing regions where intervention was most needed.

For these conclusions to be applicable to the implementation of the Essential Diagnostics List, it is important to also address the logistical strategies that were able to gain such positive results for health in low-resource areas. First, the inherent creation of a specific list of goals added structure to an often-chaotic development environment. Tens of thousands of organizations exist to promote development worldwide, with few agenda-setting organizations to provide help reach larger goals– the WHO and UN are notable exceptions. The MDGs oriented development actors toward common health goals, which in some cases resulted in the creation of entirely new organizations. In 2004, the Millennium Challenge Corporation (MCC) became the most recent United States agency committed solely to development, existing entirely independent of the State Department and USAID (the U.S. agencies normally responsible for development projects). The MCC was established with bipartisan Congressional support and championed by President George W. Bush, who in 2003 would make another direct contribution to global health in the establishment of the President's Emergency Plan for AIDS Relief (PEPFAR), which remains the single largest financial and logistical commitment by a single nation to addressing an issue of public health importance. At its best-funded in 2007, the MCC received $2 billion from Congress to carry out its development goals across the 8 target areas, including public expenditure on health. The MCC established criterion for grant funding available to applicant countries contingent

[23] McArthur J, Rasmussen K, McArthur J, Rasmussen K. How successful were the Millennium Development Goals? brookings.edu. https://www.brookings.edu/blog/future-development/2017/01/11/how-successful-were-the-millennium-development-goals/. Published January 11, 2017. Accessed February 5, 2019.

on their success in pursuing the MDG criterion. This represented an innovative approach to development funding at the time, as previous development activities (including those pertaining to health) were largely decided by political factors.[24] In this capacity, the MCC served as a sort of "quality control" function for US MDG efforts — coordinating and assessing US-led investments and interventions while maintaining a macro-level focus on objective health metrics. For these reasons, the MCC has been widely praised for its effectiveness in using a more evidence-based approach to global health policy.

The implementation of the MDGs, and of the MCC improved the ability of many public health researchers and development workers to innovate within health development. With a targeted list of UN-selected health outcomes and a US-backed funding agency for administration of grants, applicants who were able to argue their research or interventions as furthering progress towards the MDGs could count on broader support not only from agencies such as the MCC, which directly fund MDG-related initiatives, but also the broader global public health community. This broader community recognized the MDG goals as legitimate, even if individuals were not working directly within the frameworks of the MDG in their own careers.

Implementation considerations for the Essential Diagnostics List can draw from the precedent set in 2000 by the Millennium Development Goals. These earlier WHO and UN initiatives illustrate that 1) global health organizations can trigger lasting improvements to health outcomes through their agenda-setting function, 2) national organizations and agencies

[24] Hook SW. Ideas and Change in U.S. Foreign Aid: Inventing the Millennium Challenge Corporation. *Foreign Policy Analysis*. 2008;4(2):147-167. doi:10.1111/j.1743-8594.2007.00062.

can profoundly influence health outcomes by incorporating WHO and UN criterion into programming, and 3) de-politicized, performance-based health goals effectively orient existing efforts and point up-and-coming research projects to areas of critical need.

Each of these conclusions must be considered in light of the inherent trade-off of creating a single, eight-item policy proposal (e.g. focus on HIV and malaria instead of diarrheal diseases necessarily disadvantages funding for the latter). Even so, the MDG has been effective to the extent that an international governing body can promote a public health initiative as desirable and, in doing so, motivate significant progress toward that goal. These observations offer strong support for the usefulness of the Essential Diagnostics List in the fight against HIV, malaria, and tuberculosis, as well as its ability to provide useful operational precedent for later global health programming.

The Sustainable Development Goals

The legitimacy and results of the MDGs were motivating enough for the UN to "renew" the concept with a second iteration, entitled the Sustainable Development Goals (SDGs). Enacted in 2015, the SDGs included health and wellbeing in its 2030 agenda.[25] Where the Millennium Development Goals were, by some accounts, literally drafted a cocktail napkin, the Sustainable Development Goals were very much goals "written by committee," using more formal avenues. Thus, they have been criticized for their relative complexity, at least as compared to the Millennium Development Goals. However, this approach did result in several significant benefits for health initiatives, including the creation of a "global price tag" for the "Health Sustainable Goals," those SDGs pertaining specifically

[25] Sustainable Development Goals:. Sustainable Development Knowledge Platform. United Nations. https://sustainabledevelopment.un.org/?menu=1300. Accessed February 5, 2019.

to health. Published in 2017, the global price tag estimates the costs of expanding primary health services to 67 low- and middle income countries.[26] The WHO study found that achieving a minimum level of progress toward the SDGs (called the "progress" scenario) would require increasing annual spending from $104 billion to $274 billion USD, and an "ambitious" scenario aiming at total achievement of SDG health targets would require an increase from $134 billion to $371 billion USD.[27] WHO analysis illustrates that most countries are financially able to meet both the "progress" and "ambitious" scenarios, providing evidence of the feasibility of such global health initiatives.

These findings are significant for pathology and diagnostic medicine. Analysis by the WHO recommends that in both the "progress" and "ambitious" scenarios health systems should make changes to address access to primary care capabilities, with 75 percent of the total cost earmarked for "building and operating new clinics, hospitals and laboratories; and buying medical equipment." These 2017 estimates indicated an increasing focus on the practicality of a cost-effective primary care plan that recognizes the centrality of diagnostics. Global health literature has long placed importance on first the MDGs and then the SDGs, but it is only in recent years that the broader global health community has emphasized the importance of PALM services in reaching these goals. Cost assessments, like that by the WHO, supports this shifted view.

---

[26] Global price tags. World Health Organization. https://www.who.int/choice/globalpricetags/en/. Published October 13, 2017. Accessed March 10, 2019.
[27] Q&A: Sustainable Development Goals Health Price Tag. World Health Organization. https://www.who.int/features/qa/sdg-price-tag/en/. Published July 17, 2017. Accessed March 10, 2019.

The International Health Regulations

The International Health Regulations provide another ongoing framework through which to understand the role of pathology and laboratory medicine. A legally-binding document for all 196* member states, the IHR was the first set of international guidelines specifically intended to address global health threats in a coordinated fashion. Ratified in 2005, the stated aims of the IHR are to provide a framework for defining and responding to a "public health emergency of national concern" without unduly interfering in international trade activities. While foreign investment in development infrastructure and public health capacity building has always existed in some form, the IHR plays a role similar to that of the Millennium Development Goals in that it focuses and organizes activity, including mandating that high-income countries supply low- and middle income countries with technical support for activities for disease surveillance, quality control, and other aspects of laboratory capacities.[28] The degree of detail regarding laboratory aid would evolve over time, which can be observed by comparing the growing number of mentions of the word "diagnostic" in the texts of the 2005 and 2015 documents, spaced ten years apart.

The 2005 edition of the IHR addresses diagnostic capacity more directly than any previous major WHO document, but even this distinction only comes with only two substantial mentions of diagnostic capacity.[29] The first, Article 46, is mentioned in Part VIII — General Provisions. The text reads:

> *Article 46: Transport and handling of biological substances, reagents and materials for diagnostic purposes* States Parties shall, subject to national law and taking into account relevant international guidelines, facilitate the transport, entry, exit, processing and disposal of biological substances and diagnostic specimens, reagents and other diagnostic materials for verification and public health response purposes under these Regulations.

---

[28] Siedner MJ, Gostin LO, Cranmer HH, Kraemer JD. Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic. *PLOS Medicine*. 2015;12(3). doi:10.1371/journal.pmed.1001804

[29] *International Health Regulations (2005)*. 3rd ed.; 2005.

Under this section, the IHR addresses the movements of "diagnostic specimens, reagents and other diagnostic materials" across international borders. This mandate, applied to all member nations, provides valuable legal protection for healthcare workers seeking to confirm diagnoses in this way, as well as assign a level of responsibility to higher-income nations to accept and aid in the processing of these samples.

Secondly, the 2005 edition of the IHR dedicates a specific subsection of its annex to the core capacity requirements for designated airports and other border crossings. These requirements are thereafter categorized into those that are required at all times, and those required only during a public health emergency of international concern. Of this first category, diagnostic capacity is addressed as the first core capacity:

> To provide access to (i) an appropriate medical service including diagnostic facilities located so as to allow the prompt assessment and care of ill travelers, and (ii) adequate staff, equipment and premises;

More specifically applied to the immediate needs of border crossings, this provision nods to the growing awareness in the political and global health community that disease could travel quickly across borders before being detected — well within a given incubation period or latency period. It was therefore critical to explicitly outline ways to prevent infectious disease from crossing "jurisdiction lines" into other states. The original IHR therefore provides a process of international travel and surveillance that respects state autonomy while still assisting global health diagnostic goals.

The International Health Regulations have undergone several editions since its earliest form, each offering increasing detail as to the role that diagnostic medicine is to play in international health response. A decade after the 2005 ratification, the 2015 International Health

Regulations Workbook provides specific practice scenarios to address diagnostic capacity, and then offers examples of possible actions to be taken by WHO member states. The topic of diagnostic medicine is examined most closely in the workbook subsection entitled "Core capacity 8: Laboratory." The IHR details different "capability levels" for epidemic response — from a level <1 to a level 3 — with corresponding levels of international responsibility.[30] Prompting questions for specific subtopics are included below, presented in the text of the IHR as a starting point for evaluating which actions should be taken, based on which capability level a member nation is operating. These prompting questions include:

> Is there reliable laboratory capacity in the country to test all samples related to this event? (This would include environmental and food samples in many of the scenarios.)
>
> Are adequately trained staff and materials available for the packing and transport of specimens?
>
> Are adequate biosecurity measures in place in laboratories where hazardous specimens will be examined?
>
> What laboratory level surveillance is in place? Would information be shared with other authorities (agriculture, food safety, etc.)?

Responses to these questions offer varying levels of capability. For example, responses for the first question might entail (capability level <1) that a policy is in place to ensure quality, or (capability 1) national and international laboratories together form a necessary network, or (capability 2) national laboratories successfully participate in external quality control activities,

---

[30] Core Capacity Workbook: A Series of Exercises to Assist the Validation of Core Capacity Implementation Levels.; 2015. https://apps.who.int/iris/bitstream/handle/10665/190819/WHO_HSE_GCR_2015.13_eng.pdf;jsessionid=DA6BFACDD3056E481BB6D78815DF9BD7?sequence=1

or (capability 3), all national laboratories are accredited to international standards. These prompting questions and specific responses provide a guiding framework for pathology and laboratory medicine the likes of which had not previously been observed in a document as binding as the International Health Regulations. The IHR therefore further legitimized the role of PALM in sustaining global health capacity.

Since 1948, there have been remarkable shifts in global health governance that have brought first primary care, then international health, then diagnostic medicine slowly into sharper focus. However, this evolution of documentation and policy did not evolve independently of the messier, pressing realities of disease and epidemics. To understand how global governance positions have been refined to address global health needs, and how diagnostic medicine fits into this evolution, it is thus critical to outline the impacts of major global health threats, most notably HIV/AIDS and Ebola, that led to the Essential Diagnostics List's development in 2018.

HIV and Global Health Policy

Origins of an epidemic

The HIV/AIDS epidemic has had an unprecedented impact on global health. The June 5, 1981 CDC Morbidity and Mortality Weekly Report featured five cases of a rare lung infection in young, white, previously healthy gay men in Los Angeles. The infection was found to be exacerbated by a dysfunctional immune system.[31] The case definition used for diagnosis would become infamous, even among lay Americans. Mysterious skin lesions, weight loss, fever,

[31] A Timeline of HIV and AIDS. HIV.gov. https://www.hiv.gov/hiv-basics/overview/history/hiv-and-aids-timeline. Published January 10, 2019. Accessed January 27, 2019.

sweating: each of these infamous symptoms sparked fear of this new plague. After the identification of the HIV virus in 1984, a diagnostic blood test could quickly confirm this collection of immunosuppressive symptoms as indicators of an HIV infection. Though some claim the virus has existed in humans since the 1930's, it wasn't until the 1980s that population health had been threatened by HIV/AIDS on a truly global scale.[32] The CDC report is considered to be the first to describe Acquired Immunodeficiency Syndrome, or AIDS. Public health surveillance of AIDS cases (characterized by measures such as mandatory reporting of HIV/AIDS cases to the CDC) began in 1982. It is impossible to understate the impact of the subsequent HIV/AIDS epidemic on health systems, scientific study, social institutions, and even geopolitics in the decades following this first report.

International response

The wide reach of the HIV/AIDS epidemic sparked public awareness and investment from major donor countries including the U.S. that translated into increased commitment to global health surveillance. From those earliest American diagnoses when HIV/AIDS was still known as GRID (Gay-Related Immunodeficiency), patient activism was a critical characteristic of the epidemic in the United States, Canada, and Europe. The LGBTQ+ community and in particular the gay community were instrumental in bringing popular attention to the disease. Their efforts fueled the search for a treatment for what was until the late 1990's a death sentence for those diagnosed. Initially this began with local efforts, but by the early 2000's the outsized impact of HIV/AIDs in sub-Saharan Africa led to several significant investments in global

[32] Where did HIV come from? | The AIDS Institute. https://www.theaidsinstitute.org/education/aids-101/where-did-hiv-come-0. Accessed January 27, 2019.

initiatives to strengthen public health surveillance efforts and contain the disease. As previously described in the case of Botswana, Africa faced the most devastating effects of the outbreak. Exacerbated by poverty, small populations, and a legacy of colonialism, HIV spread via trade routes and rapid urbanization to overtake the general population.[33] By the year 2000, more than a third of the adult population in Botswana faced HIV/AIDS. The scale of the epidemic prompted President Festus Mogae to famously declare at the 2000 International AIDS Conference in Durban, South Africa that his country was "threatened with extinction."[34] The situation in Botswana was not unusual — eSwatini (also known as Swaziland), Lesotho, South Africa, and Malawi all experienced HIV/AIDS at a level that crippled their population.

The international response to the HIV/AIDS epidemic was late, but emphatic. In 1994, the UN launched the Joint United Nations Programme on HIV/AIDS, the first program of its kind to work across UN agencies to address a single disease. The Global Fund to Fight AIDS, Tuberculosis and Malaria and George W. Bush's PEPFAR program were established within a year of each other (in 2002 and 2003, respectively), each marking significant funding and programming support for HIV/AIDS programs all over the world. PEPFAR was especially significant as it was (and remains) the largest global health investment by a single government for a single disease. At its 15th anniversary in 2018, the program supported more than 14 million

---

[33] Hallas L. Fighting AIDS in Africa How a president's initiative tamped down an epidemic. *The Dallas Morning News*. https://interactives.dallasnews.com/2018/life-and-hope-with-hiv/. Published November 21, 2018.

[34] Durban ALGin. African president warns of extinction from Aids. The Telegraph. https://www.telegraph.co.uk/news/worldnews/africaandindianocean/botswana/1347791/African-president-warns-of-extinction-from-Aids.html. Published July 10, 2000. Accessed December 9, 2018.

people globally on lifesaving anti-retroviral medication. When PEPFAR began, only 50,000 people in Africa were receiving treatment.[35]

The establishment of vertical health programs including PEPFAR and the Global Fund have thus had a transformative effect on both the availability of services and government engagement and investment. Both of these included improved surveillance of HIV and access to testing in their missions, and the financial support structure to further these aims. All told, development assistance for HIV/AIDS ballooned from $1.4 billion (USD) to $6.8 billion between 2002 and 2010.[36] However, even these massive figures do not totally capture the extent of global efforts, as low- and middle-income countries themselves invested heavily in their own infrastructure and epidemic control capacities. Through these efforts both by regional governments and international organizations, it became widely understood that diagnosis, prognosis, and guidance of therapy could not succeed without access to high-quality pathology and laboratory medicine.

While much has been gained in the past three decades, there remain significant needs regarding HIV testing and treatment, especially in sub-Saharan Africa. Of 36.9 million people with HIV/AIDS today, 25 percent do not know their status. The disease burden of HIV is not spread equally among all countries — approximately 70 percent of HIV infections are located in sub-Saharan Africa, despite the region holding only 12 percent of the world's population.[37] Finally, the 2018 International AIDS Conference made clear that HIV fatigue is growing among

---

[35]The United States President's Emergency Plan for AIDS Relief. PEPFAR: Accelerating Progress Toward HIV/AIDS Epidemic Control. https://www.pepfar.gov/15anniversary/index.htm. Accessed February 6, 2019.

[36] Ortblad KF, Lozano R, Murray CJ. The burden of HIV. *Aids*. 2013;27(13):2003-2017. doi:10.1097/qad.0b013e328362ba67

[37] Kharsany AB, Karim QA. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. *The Open AIDS Journal*. 2016;10(1):34-48. doi:10.2174/1874613601610010034

donors and governments who feel that the world's attention has lingered for too long on the disease. While there is no doubt that there are other serious public health concerns which have received less attention than the HIV/AIDS epidemic, this fatigue puts the progress made against the epidemic at serious risk. Fatigue or not– it is only strong laboratory capacity that has allowed health leaders to notice the creeping new infection rates in parts of Europe, Africa, and Asia in recent years. As has been increasingly emphasized in global health literature, diagnostics must play a key role in any future progress against HIV.[38]

Value of HIV as an indicator of diagnostic capacity

The significant resources put forth toward stopping the HIV/AIDS epidemic and the strategies used across the world to achieve this progress make HIV a valuable lens through which to view diagnostic capacity. After all, increased funding ultimately leads to research and better data. The scientific literature surrounding diagnostic outreach efforts, government programming, and pricing of materials have been emphasized much more in relation to HIV than to other diseases. Furthermore, HIV is infectious, and transmission occurs from host to host rather than relying on a vector like a mosquito. This means that diagnostic efforts can be viewed as more purely "human," with less need to monitor animal populations. This is not to say that human-transmitted diseases are not complex— sexually-transmitted infection is particularly fraught with stigma and fear— but merely that epidemic surveillance can be limited to a single species. Today, HIV/AIDS is a familiar, established example of the momentous importance of diagnostics in epidemic control and global health programming.

---

[38] Blum K. On the Road to an Essential Diagnostics List. AACC. https://www.aacc.org/publications/cln/articles/2018/april/on-the-road-to-an-essential-diagnostics-list. Published April 1, 2018. Accessed October 30, 2018.

Ebola and Global Health Policy

Epidemic and response

The 2014 Ebola outbreak had a similar galvanizing effect on diagnostic medicine, pushing national health systems and global leaders to improve diagnostic capacity. This was no ordinary tropical disease. On the whole, infectious diseases that primarily affect poor rather than rich countries are not common topic of conversation in the United States or other wealthy nations. This detachment has insidious effects such as the 10/90 gap, the observation that less than 10 percent of resources are dedicated to those conditions that are responsible for 90 percent of the global disease burden. But because most "tropical" diseases do not often cross into their jurisdiction, few politicians and health officials in Western Europe and North America have been pressed to answer for the quality of low- and middle-income countries' diagnostic capacities.

This changed with the 2014 Ebola epidemic. Ebola Virus Disease, what most simply call Ebola, is a viral hemorrhagic fever endemic to West Africa. Transmitted both zoonotically (i.e. from animals to humans) and from human to human, Ebola is spread through direct contact with infected bodily fluids, including blood and vomit.[39] Symptoms such as fever, sore throat, muscular pain, and headaches observed between two days and three weeks after infection are shared by more common diseases, including malaria and cholera. Specific diagnosis requires development of a cell culture, detection of viral RNA using polymerase chain reaction, and detection of antibodies. There is no cure for Ebola, meaning that treatment is largely limited to isolation procedures. Therefore, where a typical treatment pathway would proceed by physician

[39] Ebola (Ebola Virus Disease). Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html. Published December 27, 2017. Accessed February 23, 2019.

suspicion leading to laboratory confirmation followed by access to appropriate treatment, the primary focus of Ebola response is only on the first two steps.

The WHO reported a major Ebola outbreak in Guinea in March 2014, and just a year later, there were more than 22,000 Ebola cases and 9,000 Ebola deaths in Guinea as well as neighboring Sierra Leone and Liberia.[40] Ebola spread through travel, often by healthcare workers traveling to other African nations including Nigeria and Mali, as well as to Italy, Spain, the UK, and the United States. The United States became increasingly involved in Ebola response after recent Liberian immigrant Thomas Eric Duncan arrived at a Dallas emergency room with a fever and nausea in September 2014. After being sent home with antibiotic medication, he returned to the ER where he was eventually asked about his travel history and positively diagnosed with Ebola. He passed away on October 8. Duncan's death brought Dallas into the national spotlight, with President Obama citing Duncan's illness, as well as those of two Dallas nurses who had become infected during his care, in a request to Congress for $6 million of emergency funding for West Africa. Much of this was earmarked for ongoing capacity building– including diagnostic medicine.

While there were many competing causes to the outbreak, it has become clear in following years that pathology and laboratory medicine surveillance systems remained underfunded, even under the guidance of the International Health Regulations. During the Ebola outbreak, weak local laboratory capacity resulted in the need to fly-in foreign equipment, reagents, and expertise in the form of external organizations' leadership.[41] Any local capacities

---

[40] Siedner MJ, Gostin LO, Cranmer HH, Kraemer JD. Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic. *PLOS Medicine*. 2015;12(3). doi:10.1371/journal.pmed.1001804

[41] Goodfellow I, Reusken C, Koopmans M. Laboratory support during and after the Ebola virus endgame: towards a sustained laboratory infrastructure. *Eurosurveillance*. 2015;20(12):21074. doi:10.2807/1560-7917.es2015.20.12.21074

were diverted to caring for Ebola patients, neglecting the more mundane, but equally critical, laboratory needs of the normally-functioning healthcare system. As seen in Figure 3, the overall need was so great that only about half of total Ebola cases were ever confirmed by laboratory testing. As is often the case in instances of foreign intervention in public health, Ebola-affected countries were additionally saddled with the cruel paradox of having the benefit of new and advanced equipment thanks to the intensive spotlight on the region, but no sustained quality control procedures or sufficiently-qualified laboratory technicians to sustain this level of laboratory capacity.

Countries with Widespread Transmission and other Countries Affected During the Epidemic

Country	Total Cases (Suspected, Probable, Confirmed)	Laboratory Confirmed Cases	Total Deaths
Countries with Widespread Transmission			
Guinea	3,814	3,358	2,544
Liberia	10,678	3,163	4,810
Sierra Leone	14,124	8,706	3,956
Affected Countries			
Italy	1	1	0
Mali	8	7	6
Nigeria	20	19	8
Senegal	1	1	0
Spain	1	1	0
United Kingdom	1	1	0
United States	4*	4	1
Total	**28,652**	**15,261**	**11,325**

* While there were 11 patients with EVD in total treated in the United States, only four patients became ill after they arrived in the United States, either after exposure in West Africa or in a healthcare setting.

Figure 3. CDC description of Ebola cases, 2014 epidemic[42]

Global health leaders raised the alarm for the need for future capacity building. Thomas Frieden, then-director of the U.S. Centers for Disease Control and Prevention, wrote in the New

[42] Ebola (Ebola Virus Disease). Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html. Published December 27, 2017. Accessed February 24, 2019.

England Journal of Medicine in 2014 that "identifying infected persons quickly requires accessible diagnostic and treatment facilities."[43] As previously mentioned, President Obama, members of Congress, and other prominent politicians highlighted the role of global health preparedness domestically, significantly adding to the popular relevance of such discussions. Academic literature followed suit with more specific proscriptions, with papers such as that by Goodfellow et al. calling not only for a generalized strengthening of health systems, but also for tailored laboratory planning that allows regional laboratory systems to make capacity decisions best-suited to their needs. These, and more, offer examples of Ebola raising the profile of diagnostic medicine.

The Global Health Security Agenda (2014)

The Ebola epidemic directly led to the creation of the Global Health Security Agenda (GHSA) in 2014. The Ebola epidemic as well as other close calls with border-hopping infectious diseases such as Middle East Respiratory Syndrome (MERS) shocked the global health community in the mid-2000's. Goodfellow et al. writes in 2015 that the harsh lessons learned during the Ebola epidemic highlight the need for a "post-Ebola legacy" of laboratory support. It had become increasingly clear that more specific operational guidelines were needed in order to ensure proper alignment of national health priorities with those laid out in the IHR. Among the multitude of nation and regional-level reforms was the creation of the Global Health Security Agenda in 2014, a supplementary text to aid in application of the International Health Regulations. The problem lies in the fact that the International Health Regulations technically

[43] Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S. Ebola 2014 — New Challenges, New Global Response and Responsibility. *New England Journal of Medicine*. 2014;371(13):1177-1180. doi:10.1056/nejmp1409903

covered the areas of diagnostic capacity and global health security between international borders, but still did not offer extensive support as to how low-and-middle-income countries could be brought into compliance if their capacities were lacking.[44] The GHSA, created through partnerships with the WHO and 64 member nations (including the United States), outlines four specific elements focused on detection:[45]

1. Implement or improve disease surveillance
2. Implement or improve laboratory testing for virulent pathogens
3. Create accurate data systems and ensure timely reporting
4. Ensure presence of trained workforce.

Each of these elements offer guidance specifically for strengthening capacities of low- and middle-income countries to fight Ebola.

[44] Balajee SA, Arthur R, Mounts AW. Global Health Security: Building Capacities for Early Event Detection, Epidemiologic Workforce, and Laboratory Response. Health Security. 2016;14(6):424-432. doi:10.1089/hs.2015.0062

[45] Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S. Ebola 2014 — New Challenges, New Global Response and Responsibility. *New England Journal of Medicine*. 2014;371(13):1177-1180. doi:10.1056/nejmp1409903

Part II: Characterizing the Essential Diagnostics List

Thus far, this thesis has outlined the history of global health governance concerning diagnostic capacity in low-and-middle income countries and has pointed out specific examples of international legislation and global health scares that furthered the cause of diagnostic capacity worldwide. From this understanding, we may now assess the present role of the Essential Diagnostics List in 2018-2019 and determine the lists' role in addressing four primary areas of remaining need.

Low- and middle-income countries

Despite the incremental gains in diagnostic medicine made during the period from 1948 to present, there remain significant gaps in diagnostic care that have drawn the attention of pathology and laboratory experts in recent years. An April 2018 Lancet special series on global pathology services provides the most current comprehensive framework for the assessment of global pathology services, which can then be used, alongside additional case studies and theoretical evidence, to assess the potential impact of the May 2018 Essential Diagnostics List on the identified criterion. The three-part series featured voices from preeminent U.S. pathology leaders and was published in recognition of the accelerating efforts to meet the 2015 Sustainable Development Goals, previously outlined in this study. This most recent study will provide a roadmap to characterize current diagnostic needs in low- and middle-income countries.

Defining LMICs

Addressing the diagnostic capacity needs of low- and middle-income countries first requires defining the scope of this group. Low-income countries are categorized by the World

Bank Group as those countries with a GNI per capita of $995 or less.[46] Middle-income countries are those ranging from $995 per capita to $12,055. Middle-income countries represent a wide range of living standards and are thus further divided into low middle-income countries ($995 to $3,895 per capita income) and upper-middle-income countries ($3,895 to $12,055 per capita). This group is collectively referred to as LMIC in most development and global health literature. The term "low-resource settings" is functionally synonymous with LMIC countries within this study, and generally describes a healthcare setting where monetary factors constrain patients' ability to pay for care and providers' ability to supply all demanded services.

Overall, 138 countries are defined by the World Bank as low-income and middle-income.[47] More than 87 percent of the global population lives in these countries, and it is LMICs that are most severely affected by the 10/90 gap, the observation that less than 10 percent of resources are dedicated to those conditions that are responsible for the 90 percent of the global disease burden, which in turn is mostly burdened on LMICS. Low-income economies are largely clustered in sub-Saharan Africa and parts of Asia, including countries such as Burundi, the Central African Republic, Guinea, Malawi, Mozambique, Sierra Leone, Rwanda, Uganda, and Nepal. Analysis of current PALM conditions and potential impacts and implementation of the Essential Diagnostics List will focus on application in these areas. Lower-middle-income countries of interest include the Philippines, Ukraine, Ghana, Honduras, Nigeria, and India for their presence in PALM literature.

---

[46] World Bank Country and Lending Groups. How does the World Bank classify countries? – World Bank Data Help Desk. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519 -world-bank-country-and-lending-groups. Accessed February 26, 2019.

[47] Ml W, Ka F, Ma K, Lm L, N L, K R. Access to pathology and laboratory medicine services: a crucial gap. *Yearbook of Paediatric Endocrinology*. 2018. doi:10.1530/ey.15.13.5

While low- and middle-income countries are diverse and vary widely within their respective categories, they do share some similarities in their public health challenges. Low- and middle-income countries (as compared to upper-middle income and high-income countries) are disproportionately affected by communicable diseases, such as malaria, cholera, HIV, and many diarrheal diseases. Many of these diseases can only be definitively diagnosed by laboratory confirmation of their causative agents. Febrile illnesses represent a particular challenge, as many possible diseases share their symptoms (primarily fever). For this reason, conditions such as malaria and pneumonia can appear almost indistinguishable in a clinical environment. Only diagnostic services can provide a confident answer.

Challenges to PALM services in LMICs

In their 2018 paper entitled "Access to pathology and laboratory medicine services: a crucial gap" Wilson et al. describe four main categories of challenges related to PALM services which characterize the foundational barriers to improved PALM services in LMICs, 1) insufficient human resources and workforce capacity, 2) inadequate education and training, 3) inadequate infrastructure, and 4) insufficient quality, controls, and accreditation. Each of these challenges is the result of entrenched historical inequities and are exacerbated by a myriad of country-specific conditions, but their universal nature to LMIC healthcare systems offers hope that potential solutions to address these areas could result in scalable solutions.[48] The below considerations have resulted in substandard care and must be addressed in global health programming moving forward.

---

[48] Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

Insufficient human resources and workforce capacity

The first major area of analysis was that of human resources and workforce capacity within PALM services in LMICs. This field is characterized primarily by low levels of data — very few national governments keep up-to-date records of their current pathology workforce, and there are not many reliable alternative public records due to a dearth of certifying institutions and medical colleges (a subject which will be discussed further in the next subsection). In keeping with this study's overall focus on sub-Saharan Africa, it is this region of primarily LMICs that at present offers the best data. In 2016 sub-Saharan Africa, it was found that there was only about one anatomic pathologist to about 100,000 patients, 50 times fewer than in high-income countries.[49] This troubling statistic is representative of many anecdotal experiences of pathologists working abroad in countries such as Bhutan, which had only two pathologists at the time of one international nonprofit's intervention.[50] Nor can the problem be expected to be solved solely through incentive systems for pathologists in high and upper-middle income countries to work in LMIC environments – even the United States is experiencing a lack of qualified pathologists known as the Pathology Workforce Crisis exacerbated by the decrease in new pathologists being certified.

[49] Nelson AM, Milner DA, Rebbeck TR, Iliyasu Y. Oncologic care and pathology resources in Africa: survey and recommendations. J Clin Oncol 2016; 34: 20–26.
[50] Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

Inadequate education and training

The causes of the global pathologist shortfall may in part be explained by Wilson et al.'s second category of need: inadequate education and training. In 2013, there were only 168 medical schools in sub-Saharan Africa, and 11 countries had no medical school at all. The study notes that at currents education rates, it would take 400 years for the indigenous medical system to meet the regional demand for pathology services. Establishing training programs through external partnerships, as well as building internal capacities, has been an ongoing focus of pathologist groups such as Pathologists Overseas, which have worked within national education systems to build partner residency programs for Bhutanese students, a Haitian degree in Public Health and other educational partnerships.[51]

Inadequate infrastructure

In addition to human resources, physical resources and technology are often lacking in LMIC PALM settings. Space, adequate lighting, electricity, and clean water are all critical for powering testing machines and prepping samples and reagents.[52] Supply chains, including cold supply chains for biological materials, have specialized needs for transportation that often cannot be met in low-resource environments. Technical support is also necessary to maintain laboratory equipment. Many global health experts have been frustrated by benevolent attempts to donate new laboratory equipment from high-income countries, only to have those same pieces of

---

[51] Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

[52] Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

equipment sit unused because technicians do not have the appropriate training to use them, or because routine maintenance is not supported by local knowledge.

Insufficient quality, standards, and accreditation

As previously described, quality control standards and accreditation are critical for ensuring diagnoses are reliable, accurate, and reproducible within a healthcare system. However, few LMICs have standards for reproducibility standards, and one study of Ugandan laboratories in the city of Kampala illustrated that only 45, or 5 percent of the total, met or surpassed minimum WHO standards for the region.[53] Overall, few LMIC have standards for compliance with reproducibility standards, and those international accreditation programs that do exist are often too expensive to offer a practical solution.

The ongoing attention to the need for quality PALM services has led to some gains in the realm of quality control organization within Sub-Saharan Africa, namely through the Africa CDC and the African Society of Laboratory Medicine. Established in 2017, the Africa CDC aims to "improve surveillance, emergency response, and prevention of infectious diseases," and operates as a technical arm of the African Union.[54] New programs by Africa CDC such as the Regional Integrated Surveillance and Laboratory Network are well-placed to coordinate existing regional resources and organizations to improve diseases surveillance and epidemic readiness. The creation of Africa CDC has clear connections to the recent Ebola outbreak and continually pushes to meet the SDGs in sub-Saharan Africa, further illustrating the impacts of global health events on health policy. Individual countries including Thailand, Malaysia, and Kenya have also

[53] Ali M, Elbireer AM, Jackson JB, et al. The good, the bad, and the unknown: quality of clinical laboratories in Kampala, Uganda. PLoS One 2013; 8: e64661.
[54] Africa CDC. africacdc.org. http://www.africacdc.org/about/about-us. Accessed March 11, 2019.

developed internal standards and systems of accreditation that indicate rapid progress toward methods of quality control. The African Society of Laboratory Medicine (ASLM) has existed longer but has had a similar organizing effect on coordinating aid and advocacy activity within sub-Saharan Africa, particularly in response to the HIV/AIDS epidemic.[55] ASLM has audited 160 laboratories across 22 African countries and launched diagnostics access initiatives to meet the UNAIDS 90-90-90 HIV treatment targets.[56]

Two additional initiatives deserve notice for their success in establishing better quality-control in LMICs: SLMTA and SLIPTA. A joint program between the WHO Africa Collaborating Region, the US CDC, and other global actors, the Strengthening Laboratory Management Toward Accreditation (SLMTA) offers short courses, work-improvement projects, inexpensive site visits, and mentoring to member laboratories.[57] Average implementation requires only 16 months, a reasonable time-frame for laboratory managers hoping to come into compliance quickly with international standards. By 2017, 49 countries and more than 600 laboratories had enrolled across Latin America, Africa, and Asia, including 23 sub-Saharan African countries. Before SLMTA's launch, no government clinical laboratory outside of South Africa was accredited to international standards.[58] The Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) has similarly made accreditation more achievable for LMIC health systems by providing a framework for auditing laboratories at each "step" of

---

[55] Who We Are. ASLM. http://www.aslm.org/who-we-are/. Accessed March 25, 2019.
[56] Sayed S, Cherniak W, Lawler M, et al. Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions. *The Lancet*. 2018;391(10133):1939-1952. doi:10.1016/s0140-6736(18)30459-8
[57] SLMTA | Strengthening Laboratory Management Toward Accreditation. SLMTA | Strengthening Laboratory Management Toward Accreditation. https://slmta.org/. Accessed March 11, 2019.
[58] Nkengasong JN, Yao K, Onyebujoh P. Laboratory medicine in low-income and middle-income countries: progress and challenges. *The Lancet*. 2018;391(10133):1873-1875. doi:10.1016/s0140-6736(18)30308-8

laboratory advancement towards international standards.[59] These two programs need continued financial and governmental support to be scaled up but offer a model for future program developers hoping to close the gap between diagnostic medicine and the rest of the world. The International Organization for Standardization (ISO) works to interpret the SLIPTA and SLMTA checklists and bring countries into international compliance, such as its successful efforts to standardize Mozambique's national laboratory quality assurance program.[60]

Cost

The Wilson et al. description of current barriers for LMICs to improve diagnostic capacity inherently involves the issue of cost. Reimbursement models in LMIC settings are rarely primed to reward systems for quality improvements – most countries have point-of-care payment systems that do not assure healthcare providers of consistent reimbursement for their services. As a result, cost acts as a barrier to entry before diagnostic care can even be considered. For example, in Haiti, it is not uncommon for patients to be turned away at the door of a hospital if they do not have advance payment. This is not the result of the inhumanity of healthcare providers or (in most cases) government indifference to healthcare needs, but rather the reality that some source must cover the costs incurred in the operation of a health system in an LMIC, and incentivizing health care providers to remain in practice in a region or country similarly requires some form of regular salary. Even this essential element of maintaining a healthcare workforce cannot be assumed to exist in LMIC environments.

---

[59] SLIPTA Programme. ASLM. http://www.aslm.org/what-we-do/slipta/. Accessed March 11, 2019.

[60] Skaggs, Beth et al. "Implementing Laboratory Quality Management Systems in Mozambique: The Becton Dickinson-US President's Emergency Plan for AIDS Relief Public-Private Partnership Initiative." The Journal of infectious diseases 213 Suppl 2 (2016): S47-52.

Even the lowest-cost forms of diagnosis — rapid diagnostic tests— cannot be assumed to be affordable in a low-resource environment. For example, PEPFAR (the U.S. global health response to the HIV/AIDS epidemic) is one of the foremost providers of diagnostic testing for HIV and often uses rapid HIV tests to begin the process of a patient seeking care. However, even the small, white plastic rectangles that offer a two-lined positive or a one-lined negative result to a patient or community health worker cost $50 USD each to use. While low-cost compared to lab-based alternatives that require significantly more human and physical resources to operate, the $50 price tag is still far from affordable at the point of care. The reality of patient care in LMIC is still such that when faced with a $50 diagnostic test on a <$50/month income, a patient may choose to purchase multiple (cheaper) treatments rather than use up all allocated funding for a test, and then be unable to afford follow-up treatment. These hidden inefficiencies of the diagnostics and healthcare markets are critical considerations for any sweeping, top-down reforms. Groups such as Science With a Mission have sought to create diagnostic cassettes for a range of diseases including HIV and malaria for only $1 USD each, but even these promising efforts are years away from being a significant part of the global health pipeline.[61]

The Essential Diagnostics List

Despite progress, the contemporary pathology and laboratory environment in low- and middle-income countries is in dire need of coordinated intervention. Even those programs that work best regionally have not been scaled to reach the level of broad global health programming, nor, as has previously been established, have international organizations taken significant action

[61] Stafinski JM. Diagnostics. Science with a Mission. http://www2.sciencewithamission.org/diagnostics. Accessed March 11, 2019.

to coordinate laboratory medicine capacities on a broad basis. The following section will assess how the WHO's Essential Diagnostics List drew from previously successful global programming and was developed with a more comprehensive, at-scale, intervention in mind.

Replicating what works

The Essential Diagnostics List is an adaptation of a much earlier model, the Essential Medicines List. The origins, structure, and performance of this older sibling lay a strong argument for the EDL and provides evidence for the EDL's future effectiveness. First published by the WHO in 1977,* the EML was described as "a peaceful revolution" in global public health, significant for its assertion that some medicines are more useful than others and that essential medicines were often inaccessible to many populations, creating the need for a coordinated approach to their provision.[62] Ultimately, 205 medicines were chosen as meeting the criterion of "essential" The term "essential medicines" was defined as:

> "...those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety and comparative effectiveness. Essential medicines are intended to be available with the context of functioning health systems at all times, in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility."[63]

* While the WHO did not publish its draft of the Essential Medicines List for use by member nations until 1977, Tanzania had released its first draft of the Essential Medicines List as early as 1970. Development of international guidelines are seldom a purely top-down endeavor but are greatly shaped by the innovation of countries and organizations working on the ground.

[62] Laing R, Waning B, Gray A, Ford N, Hoen Et. 25 years of the WHO essential medicines lists: progress and challenges. *The Lancet*. 2003;361(9370):1723-1729. doi:10.1016/s0140-6736(03)13375-2

[63] WHO. The world drug situation. Geneva: World Health Organization, 1988.

The language of this eventual (and final) 2002 definition reflects the widespread disparities in global health previously discussed, reinforced by the use of similar language of "essential diagnostics" proposed in early WHO documentation. The EML was included in the Alma-Alta conference discussion as a key aspect of primary care provision, which in and of itself was valuable to the history of the Essential Diagnostics List (Alma-Alta conference discussed earlier).[64] The list has been updated every two years since 1977, and has expanded to include a separate Essential Medicines List for children, and includes hundreds of medications in the 2017 edition with uses ranging from poison antidotes to antipsychotics.

The EML is divided into "core" and "complementary" items.[65] The core list consists of "minimum medicine needs for a basic health-care system," focusing on so-called priority conditions as determined by "current and estimated future public health relevance, and potential for safe and cost-effective treatment." These medicines do not display the additional requirement of specialized training or diagnostic facilities. In contrast, the complementary list offers recommendations for essential medicines of priority diseases, but medicines whose administration requires specialist care — whether that be specialist training, medical care during the course of treatment, or specialized diagnostic and monitoring facilities. The ability of this list to expand as necessary reflects the ability of the list to address varied health needs over time — a living document of sorts. After initial criticism that the selection of tests was largely the work of experts, not of evidence, EML selection shifted toward an evidence-based approach in 1991 relying on the more objective considerations such as public-health relevance, efficacy, safety,

---

[64] Laing R, Waning B, Gray A, Ford N, Hoen Et. 25 years of the WHO essential medicines lists: progress and challenges. *The Lancet*. 2003;361(9370):1723-1729. doi:10.1016/s0140-6736(03)13375-2

[65] *Executive Summary: The Selection and Use of Essential Medicines 2017*. Geneva; 2017.

and cost-effectiveness that appeared in the 2002 definition of an "essential medicine." Today's EDL shares these concerns.

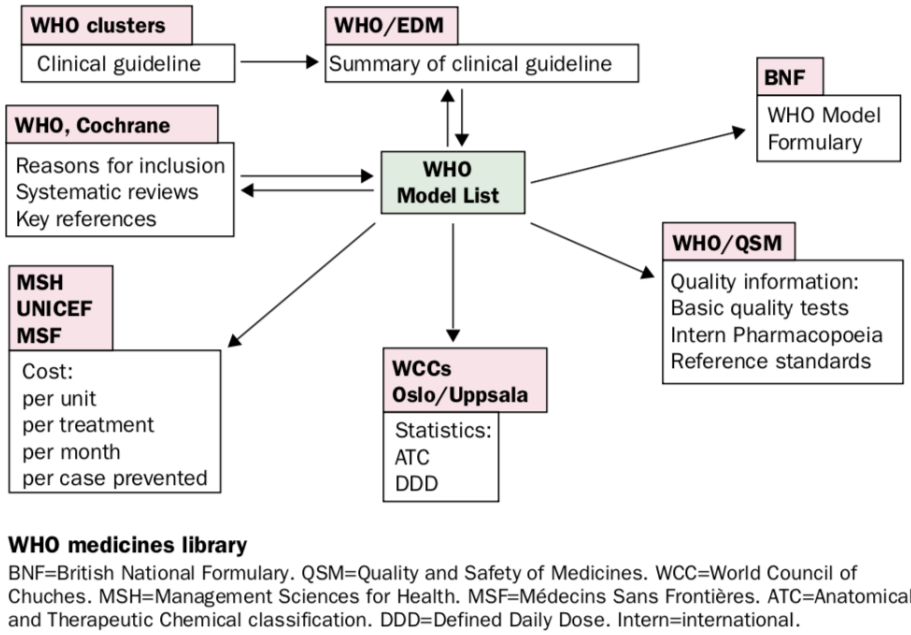

Figure 4. Development of the WHO Model List of Essential Medicines[66]

Successes of the EML

On the 30th anniversary of the EML, it is clear that the Essential Medicines List is an overall success. The release of the Essential Medicines list offered a welcome shift from the infectious-disease centric focus of the WHO in the 1960s and 1970s for which the WHO was increasingly coming under fire. The development of the EML signaled that global health organizations would commit themselves not only to acute infectious disease needs but also to the

[66] Laing R, Waning B, Gray A, Ford N, Hoen Et. 25 years of the WHO essential medicines lists: progress and challenges. *The Lancet*. 2003;361(9370):1723-1729. doi:10.1016/s0140-6736(03)13375-2

slower, more plodding progress necessary to build resilient health systems. The EML was widely adopted by 156 WHO member states, prompting the creation of national drug policies and quality control measures that did not exist before the EML's adoption.[67] Furthermore, the EML allowed the WHO Programme for International Drug Monitoring to form a network of 83 countries to provide global monitoring for drug safety, or in other words, quality control. Finally, the EML changed the pricing landscape of medicines. Previous to its adoption, there was virtually no publicly available price information about drugs and no information about cheaper generic options. With the guidance of the EML, there are now 33 countries who have carried out availability and pricing surveys, all of whom have made that information publicly available. As a result of these efforts and the ability of generics to compete with name-brand medicines, costs of those drugs named in the EML have dropped precipitously. Countries' common reliance on international trade law and membership in governing bodies such as the EML enabled the relatively simple act of the EML's publication to have a domino effect on the many structural factors that reduced access to medicines. By eliminating these barriers, the EML transformed the global health landscape to be more equitable, more transparent, and more effective system than it was 30 years ago.

Development of the EDL

Despite the successes of the EML, it would be 41 years before the WHO would release its diagnostic equivalent. Advocacy from prominent pathologist groups, and industry leaders such as Dr. Timothy Amukele of Johns Hopkins and Dr. Lee Schroeder of the University of

---

[67] The WHO Essential Medicines List (EML): 30th anniversary. World Health Organization. https://www.who.int/medicines/events/fs/en/. Published November 20, 2015. Accessed March 11, 2019.

Michigan, called for a worldwide essential diagnostics list in the model of the Essential Medicines List.[68] In 2016, Amukele and Schroeder joined other clinical pathologists to advocate for a model list of essential diagnostics in the New England Journal of Medicine. The article cited the successes of the EML in an argument for how a similar EDL might improve healthcare delivery.[69] The authors outlined a basic criterion that chosen tests be cost-effective, need-specific testing that would reflect the complexity and flexibility needed in building a functioning diagnostic system. Furthermore, they illustrate how proper use of the existing EML necessitates the use of 19 test categories, further illustrating the necessity of an EDL.

The next question for these "framers" of the first EDL was what kind of organization should carry out the EDL. While the World Health Organization ultimately houses the EDL and has been used an example throughout this study, that the WHO should control all significant global health activity is by no means a foregone conclusion. Though improved under its new director Dr. Tedros Ghebreyesus, the WHO is a highly bureaucratic and at times political institution that has a significant lag time on even the most pressing global health problems (as seen in its slow response to the Ebola outbreak). There is a legitimate debate to be had in whether such an ambitious project as the EDL should be carried out by the WHO, or by a nimbler, less political entities such as Gavi, the vaccine alliance challenging traditional dependence on large, governmental organizations in addressing health initiatives.

Despite these concerns, there exist clear arguments for the WHO to remain the point organization in implementing the EDL. First, global trust in the WHO means that its policy

---

[68] Blum K. On the Road to an Essential Diagnostics List. AACC. https://www.aacc.org/publications/cln/articles/2018/april/on-the-road-to-an-essential-diagnostics-list. Published April 1, 2018. Accessed October 30, 2018.

[69] Schroeder LF, Guarner J, Elbireer A, Castle PE, Amukele TK. Time for a Model List of Essential Diagnostics. *New England Journal of Medicine*. 2016;374(26):2511-2514. doi:10.1056/nejmp1602825

recommendations have unique weight among national governments and NGOs alike. This both increases the likelihood that policies will be carried out over the long term by governments, as well as signals to NGOs and nonprofits that they should align their activities with those of the WHO. The EDL also has the natural benefit of having its predecessor (the EML) having also been carried out by the WHO, meaning that the concept of such a list is not an entirely new venture.

Planning for the EDL began with a set of recommendations made in 2017 by the WHO's Expert Committee on the Selection and Use of Essential Medicines to help the creation of the first draft.[70] Specifically, the WHO Expert Committee on Selection and Use of Essential Medicines recommended the development of the EDL. The WHO additionally formed a Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD) to advise the creation of the list. The 16 members include representatives from all six WHO regions and have backgrounds in relevant laboratory testing.[71] SAGE IVD met twice in April of 2018 to guide the development of the EDL and provide oversight. The first meeting outlined the rationale for the EDL, narrowed the aims of the EDL to the subset of in-vitro diagnostics (devices used to examine specimens from the human body, outside the human body). The group's meeting in Geneva ultimately resulted in the executive summary, containing the first edition of the EDL.

---

[70] Blum K. On the Road to an Essential Diagnostics List. AACC. https://www.aacc.org/publications/cln/articles/2018/april/on-the-road-to-an-essential-diagnostics-list. Published April 1, 2018. Accessed October 30, 2018.

[71] Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD) 2019. World Health Organization. https://www.who.int/medical_devices/diagnostics/SAGE_IVD_2019_member_list/en/. Published March 14, 2019. Accessed March 23, 2019.

Composition

The EDL is made up of 23 in-vitro diagnostic tests, focused on the four major disease areas of HIV, malaria, tuberculosis and hepatitis B and C, which were emphasized in the WHO Impact Framework goal of providing coverage of essential health services for 1 billion more people by 2023.[72] Syphilis and HPV were also targets of the first edition of the EDL. The EDL also focuses on basic diagnostics for monitoring common conditions such as diabetes. The chosen tests themselves are grouped by the test discipline (such as serology, hematology, microbiology) and then specific test type (particular goal of the test such as blood count).[73] The EDL lists the test purpose, the assay format (the detection mechanism of the test, such as enzyme immunoassay), the specimen type (whole blood, urine), the facility level, and finally links to WHO guidance and recommended products when available (specific brands that might be prequalified by the WHO). Overall, the list is structured to address the first two levels of a multi-tiered health facility: primary health care and health care facilities with clinical laboratories.

Content - HIV testing

The WHO document of the first edition of the EDL contains both an explanation of the list's various elements as well as the list itself, presented in table "I.b Disease-specific IVDs for primary healthcare" which outlines the five categories listed above as applied to specific diseases (a second table supplies general IVDs for health care facilities with clinical laboratories). Figure 5 is a reproduction of the section of the table concerning HIV detection.

---

[72] Background Document Strategic Advisory Group of Experts on ... https://www.who.int/medical_devices/diagnostics/back-doc_WHO-model-list-essential-diagnostics-updt.pdf. Accessed March 23, 2019.

[73] *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018)*.

Diagnostic Test	Test Purpose	Assay format	Specimen type	WHO prequalified or endorsed products	WHO supporting documents
Antibodies to HIV ½ (anti-HIV test)	HIV self-testing	Rapid Diagnostic Test (RDT)	Oral fluid, Capillary whole blood	INSTI HIV Self-Test, **OraQuick** HIV Self-Test	Guidelines on HIV self-testing and partner notification (2016) Consolidated guidelines on HIV testing services (2015) WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection, module 10 for testing providers (2017)
	For diagnosis of HIV infection	RDT	Oral fluid, Capillary whole blood		
Combined HIV antibody/p24 antigen (anti-HIV/p24 Ag) test	For the diagnosis of HIV infection	RDT	Capillary whole blood	Genie, **OraQuick**, First Response, **Alere**, DPP, ELISA, Murex	Consolidated guidelines on HIV testing services (2015)

Figure 5. Partial reproduction of the first edition of the WHO EDL[74] (Bolded tests discussed below.)

[74] *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018).*

The tests are categorized by either their detection of the antibodies which the immune system develops in response to the presence of an antigen (in this case HIV), or their detection of both the antibody and the antigen in the sample (combined test). Both types of HIV, 1 and 2, are included in these testing menus, reflecting the differing prevalence of type 1 (mostly found in North America and Europe) and type 2 (primarily found in Africa).[75] Antigen testing and combined testing is preferable for its ability to detect the virus directly in the blood, instead of waiting for antibodies to form, which can take up to six months after infection.[76] Some tests, such as OraQuick (bolded above), allow for testing either oral fluid (which contains antibodies but not antigens) or whole blood (from a finger prick). The inclusion of an oral self-test reflects the realities of blood testing being generally unappealing and difficult to administer. Many patients fear an infection from the process of a finger prick itself, and blood samples are easy to misapply.[77]

Challenges to cost-effectiveness

One possible limitation of the EDL is that some of the tests featured on the EDL would still be too expensive for some LMICs to provide — a key concern considering the EDL's focus on cost-effectiveness. As previously discussed, even relatively low-cost materials such as rapid diagnostic tests can be out of reach for low-resource environments. For example, individual studies of HIV programming reveal that even "low-cost" tests such as the OraQuick and Alere (both bolded in Figure 6) rapid diagnostic tests can be practically out of reach in some

---

[75] What tests look for - HIV-1 and HIV-2. HIV & AIDS Information: What tests look for. http://www.aidsmap.com/HIV-1-and-HIV-2/page/1322970/. Accessed March 24, 2019.
[76] HIV/AIDS - Illinois Department of Public Health. http://www.idph.state.il.us/aids/materials/10questions.htm. Accessed March 24, 2019.
[77] Ibitoye M, Frasca T, Giguere R, Carballo-Diéguez A. Home testing past, present and future: lessons learned and implications for HIV home tests. *AIDS Behav*. 2014;18(5):933-49.

environments. A comparative study of rural Thailand and Ghana showed that even amid policy efforts to encourage HIV tests before marriage, cost can be a barrier. The tests in Ghana cost US $4, Ghana Cedi 30,000 when the minimum wage was only 5,500 Cedis/day.[78] Though conducted in 2004, this paper points out the unique challenges of providing testing services to the most vulnerable (poorer, more rural) population in sub-Saharan Africa even as compared to other LMIC environments in the world such as Thailand. Sub-Saharan African countries consistently rank among the poorest in the world, have the lowest Human Development Index rankings, and have some of the highest levels of inequality in the world. It is the smaller, hard-to-reach populations with high persistent HIV prevalence which have been thus unreached by existing global health efforts.

This challenge to affordability has resulted in the ongoing evaluation of current widely-used rapid diagnostic tests (such as OraQuick and Alere as cited in the EDL), and exploration into lower-cost options such as the Science With a Mission antibody test (mentioned in previous section). While individual purchases of each type of test vary wildly based on discounts, purchasing organization, and current global health programming, below are available price information per test, along with the sensitivity and specificity measurements for cross-validation procedures conducted at Washington University Institute for Public Health as part of an internship with Pathologists Overseas ($n<20$). This small-scale validation served not to replace a more rigorous analysis, but to illustrate at a small level the cost-effectiveness of each test. As shown, the downward cost pressure from innovators such as Science With a Mission could go a long way in improving diagnostic access in future iterations of the EDL is able to gain the accepted status of the OraQuick test.

---

[78] Aheto DW, Gbesemete KP. Rural perspectives on HIV/AIDS prevention: a comparative study of Thailand and Ghana. *Health Policy*. 2005;72(1):25-40. doi:10.1016/j.healthpol.2004.06.013

	OraQuick (antibody)	Alere (combined)	Science With a Mission (antibody)
Cost (USD/test)	$3-6[79]	$15-25[80]	$1
Sensitivity, Specificity (whole blood)	100,100	100, 100	100, 100

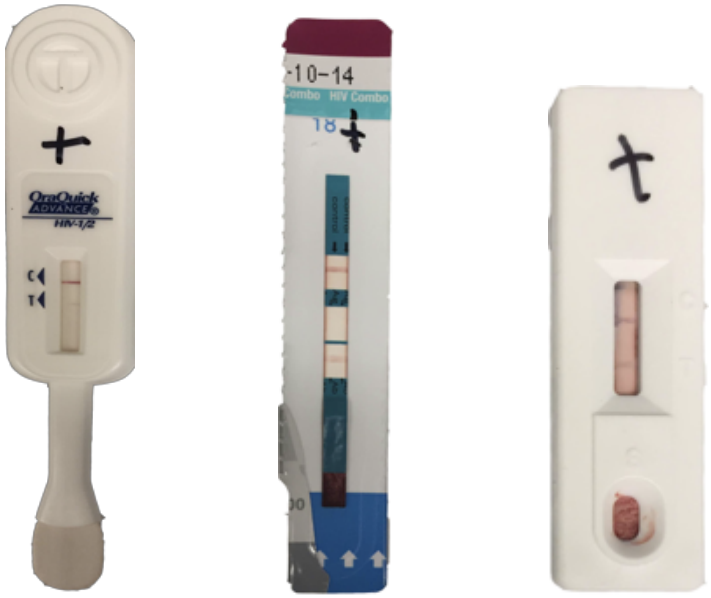

Figure 6. HIV tests with associated costs and accuracy.

[79] Number of countries adopting HIV self-testing policies rises sharply. World Health Organization. https://www.who.int/hiv/mediacentre/news/hiv-self-testing-increases/en/. Published July 25, 2017. Accessed March 24, 2019.
[80] Alere Determine HIV-1/2 Ag/Ab Combo Test - Diagnostic Tests and Clinical Products, Diagnostic Tests and Controls. Alere Determine HIV-1/2 Ag/Ab Combo Test 25 Tests:Diagnostic Tests and. https://www.fishersci.com/shop/products/alere-determine-hiv-1-2-ag-ab-combo-test-25-tests/23046614. Accessed March 25, 2019.

Evidence for cost-effectiveness

Despite these challenges to affordability, especially LMICs in sub-Saharan Africa, recent histories of HIV program expansion offer strong evidence that adoption of above tests would significantly contribute to PALM capacity, including meeting the criterion laid out by the Lancet series. A 2016 systematic review and meta-analysis of point-of-care HIV tests (like those included in the EDL) found that use increased retention between testing and treatment and shortened turnaround time between testing and treatment. In Mozambique found a .7-year increase in the projected life expectancy compared to conventional testing with an incremental cost ratio of life-year saved of $500 (USD).[81] A South African mobile unit found similar results, with an increase of .71 years and an ICER/life-year saved of $2400 USD. Similar results were found in Mozambique.[82] Applied to misdiagnosis, a previously discussed challenge in LMIC environments, more than five times the number of timely, correct diagnoses.

Similarly, there is a strong cost-effectiveness argument for investment in human capital that would necessarily result in the implementation of these tests. While the rapid diagnostic tests detailed above are advantageous for reaching remote, rural sites with few health workers, other laboratory-based tests are still necessary for confirmation of diagnoses as well as quality control within a tiered health system. However, a study of laboratory quality control in Myanmar illustrates that investments in human capital, in part orchestrated by NGOs and international

---

[81] Vojnov L, Markby J, Boeke C, Harris L, Ford N, Peter T. POC CD4 Testing Improves Linkage to HIV Care and Timeliness of ART Initiation in a Public Health Approach: A Systematic Review and Meta-Analysis. PloS one. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4866695/. Published May 13, 2016. Accessed March 25, 2019.

[82] Hyle EP, Jani IV, Lehe J, 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 Medicine*. 2014;11(9). doi:10.1371/journal.pmed.1001725

groups, significantly improved testing abilities, cutting the proportion of laboratories reporting at least one aberrant test result from 9.2% to 5.4% within seven years.[83]

While further study is needed, there is support in the literature for the ability of a strategic diagnostic list such as the EDL to cover the majority of healthcare needs in the country at relatively low cost when compared to other healthcare expenditures. The 2016 NEJM article points to high-resource settings such as the US, where Medicare part B ascribed only 3 percent of payments to laboratory expenditures and were able to carry out 80 percent of the testing volume with only 2 percent of the laboratory tests available. This indicates that the majority of diagnostic needs were met at relatively low cost and cover the majority of the population's medical needs.[84] Similar proportions of health expenditure exist in South Africa and Uganda, where 3.5 percent and 3.3-4.6 percent, respectively, of overall health expenditures were spent on PALM services. While the implementation of a higher-quality PALM plan may require initial costly investments, for human resources etc., these figures indicate that countries would not need to significantly increase expenditure over the long run to improve healthcare, especially with a focus on cheaper, more common tests such as the HIV tests included in the EDL.

Changes to the EDL

Critical to the conception of the EDL is the ideal of countries' autonomy in determining the goals of their healthcare programming. This expansion and specialization process has been critical to the success of the Essential Medicines List and thus has been adapted for the EDL. The

---

[83] Kyaw LL, Nozaki I, Wada K, Oo KY, Tin HH, Yoshihara N. Ensuring accurate testing for human immunodeficiency virus in Myanmar. *Bulletin of the World Health Organization*. 2014;93(1):42-46. doi:10.2471/blt.14.138909

[84] Schroeder LF, Guarner J, Elbireer A, Castle PE, Amukele TK. Time for a Model List of Essential Diagnostics. *New England Journal of Medicine*. 2016;374(26):2511-2514. doi:10.1056/nejmp1602825

SAGE IVD committee which determined the first edition of the EDL has created a process for inclusion, change, and deletion of diagnostics from the EDL, available on the WHO website.[85] The application period to propose changes to the EDL for inclusion in the second edition of the EDL spanned from July-December 2018.[86] The SAGE IVD group met again from March 18-22, 2019, to discuss the changes. While the results of these discussions have not yet been released, the process for revision laid out in Figure 7 and executed by the SAGE IVD committee in March of 2019 creates a framework for specializing the EDL to fit the needs for specific stakeholders while still maintaining international standards and steered by a group of experts from all involved WHO regions. These are all preconditions for successful global health programming and indicate that the EDL will be supported in perpetuity.

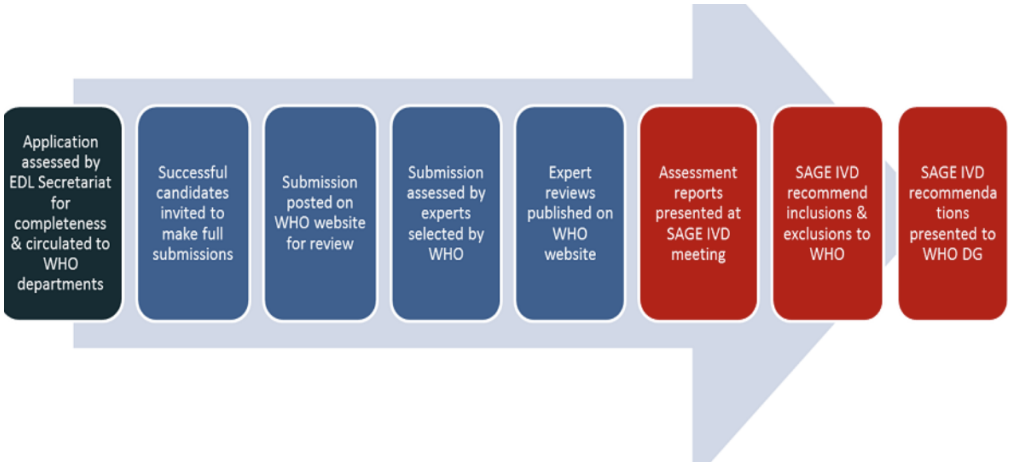

Figure 7. Process for additions to EDL (Source, WHO)

[85] Procedure to update the WHO Model List of In Vitro Diagnostics. World Health Organization. https://www.who.int/medical_devices/diagnostics/selection_in-vitro/edl-model-lists/en/. Published January 31, 2019. Accessed March 26, 2019.
[86] 2nd Meeting of the Strategic Advisory Group of Experts on IVDs. World Health Organization. https://www.who.int/medical_devices/diagnostics/selection_in-vitro/selection_in-vitro-meetings/sage-ivd-2nd-meeting/en/. Published March 20, 2019. Accessed March 24, 2019.

The EDL in its environment

With the Sustainable Development Goals in mind, the 2018 Lancet series of pathology and laboratory experts set out to outline significant areas of need within the field of pathology and laboratory medicine. Though each pertains to a specific area of need within LMIC PALM services, discussion surrounding each emphasizes the need for international cooperation in light of an increasingly globalized healthcare environment, as well as the need for a coordination of resources to meet the gap of PALM services currently experienced worldwide. There is evidence that the Essential Diagnostics List will directly improve the attainment of these four goals, and thus meet a critical need in global health programming. These predictions are summarized in Figure 8.

Insufficient human resources and workforce capacity	Inadequate education and training	Inadequate infrastructure	Insufficient quality, controls, and accreditation
● Widespread focus on PALM capacity improves retention[87] ● WHO member states have improved infrastructure for collaboration	● Local industry leaders such as Africa CDC expand professional training and mentorship ● EDL raises awareness of field of pathology among medical students and policymakers	● Harmonization of testing procedures and equipment recommendations simplifies supply chain planning ● Pressure to show results encourages laboratory information systems development ● POC testing bypasses many infrastructure challenges	● Codification at national level encourages standardization ● Cost-effectiveness criterion encourage non-arbitrary decisions ● WHO implementation introduces automatic oversight

Figure 8. Predicted impact of EDL on Wilson et al. PALM challenges

[87] Sayed S, Cherniak W, Lawler M, et al. Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions. *The Lancet*. 2018;391(10133):1939-1952. doi:10.1016/s0140-6736(18)30459-8

Insufficient human resources and workforce capacity

The Essential Diagnostic's List emphasis on multiple diseases and introduction through an international health body indicate it will be useful in fighting the current lack of human resources and low workforce capacity within PALM. The history of vertically-focused global health programs, primarily focused on HIV, malaria, and tuberculosis has resulted in the movement of the few PALM professionals that do exist in countries to move to the private sector or foreign-run programs that pay better. As a result, the more basic, publicly-run laboratory functions are often left understaffed, or without professionals at all. For example, a survey of rural Pakistani health-care providers cited dissatisfaction with a shortage of medicines and supplies and dissatisfaction with salary as reasons they or colleagues exited the field.[88] However, there was evidence that advocating pathology as a distinct and critical medical specialty improves retention rates within the field. As the EDL is, by definition, PALM-focused and publicly led, we can expect to see an effect of increased retention with its implementation.

Inadequate education and training

As Sayed et al. notes in their Lancet article, knowledge of pathology careers is severely limited among even medical students – in Tanzania pathologists are considered to be "doctors of the dead," primarily conducting autopsies.[89] Similarly, Malaysia's 2007 Pathology Lab Act raised the profile of pathology services amid the healthcare workforce and government alike,

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

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

resulting in a national push to increase the number of pathologists working in Malaysia.[90] The effects were felt not only in Malaysia, where the ratio of pathologists reached one pathologist per 60,000 people but also had the spillover effect of providing training for five additional nations. Similar to the previous category of human resources, the inherent capacity building required to staff some of the EDL's more involved diagnostic procedures (those that need standalone laboratory equipment) would raise awareness of PALM medicine in what medical training does exist in a country, as well as create incentives for more of such training to take place. Groups such as the Africa CDC, the African Society for Laboratory Medicine, and global partnerships between training programs offer fellowships and training programs that would contribute to strengthening the global PALM workforce. These same groups will be intimately involved with the implementation of the EDL and thus have a mutually reinforcing effect.

Inadequate infrastructure

Sayed et al. point to the development of laboratory software in Peru's national referral laboratory system as indicative of the benefits to the turnaround time for systems which build operational systems that work between different laboratories, thus improving infrastructure. While long-term infrastructure improvement is the goal, this is an ongoing process that will not meet the needs of patient populations today. The EDL accounts for this, and the inclusion of many rapid diagnostic tests and other point-of-care testing services (POC) promises to bypass the most pressing infrastructure challenges of LMIC environments such as power outages,

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

transportation challenges, and reagent stockout.[91] Recent developments to make RDTs cheaper and more efficient include the pursuit of lower-cost options such as those produced by Science With a Mission, new nucleic acid technology, and tests with no need for external power or reagents.

Insufficient quality, controls, and accreditation

As described in Sayed et al., the adoption of PALM at the national legislative level, or even just familiarity at that high level, can vastly improve quality control by encouraging national quality control programs. The EDL, which was approved and shaped by member nations working at the national level, would necessarily structure implementation in a top-down fashion. While less nimble, only this directional implementation would ensure quality control and accreditation through a hierarchical, tiered health system. Additionally, the fact that the EDL's testing recommendations are based on cost-effectiveness decision-making eliminates some of the arbitrariness surrounding PALM services in LMICs. As Dr. Sarah Riley discusses in an online blog post about the EDL, decisions about which testing services to provide in resource-limited environments may be as arbitrary as reflecting the pet project of an absentee lab director, or the capacities of donated equipment.[92] This kind of inefficient decision-making could, of course, still occur under the EDL, but the frameworks of cost-effectiveness and tailored care would make these instances much less likely, and rightfully bring additional scrutiny on poor decision-making.

---

[91] Sayed S, Cherniak W, Lawler M, et al. Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions. *The Lancet*. 2018;391(10133):1939-1952. doi:10.1016/s0140-6736(18)30459-8

[92] Riley S. Essential Diagnostics List. Lablogatory. https://labmedicineblog.com/2018/05/07/essential-diagnostics-list/. Published May 4, 2018. Accessed October 30, 2018.

Conclusions and future directions

This study has outlined the historical lack of diagnostic medicine in global health programming, analyzed the gaps in care this neglect has created and described how the new Essential Diagnostics List is structured to meet this need. This study has thus come to two significant conclusions concerning the EDL's place in global health programming. First, the long history of both global health programming as well as recent incidences of high-profile diseases has created an environment that both focuses on primary care and necessitates increased global coordination for PALM services, conditions which led to the development of the EDL. Secondly, this study concludes that the makeup and focus of the Essential Diagnostics List will serve to meet the four critical areas of need identified in a recent Lancet analysis of PALM services in low- and middle-income countries.

The Essential Diagnostics List is less than a year old, its long-term impacts still unknown. It is too early to tell precisely how the EDL is currently affecting government programming, pharmaceutical pricing, quality control metrics — the list goes on. The long-term impacts of the EDL have huge potential but, at this time, little concrete evidence. Future analysis of the WHO's EDL would do well to track individual countries' compliance with EDL availability, population utilization of these services, and supplier pricing and cooperation in providing the testing materials. The policy-centric analysis could assess how frequently the EDL was cited in national public health policymaking and by politicians, thus assessing the impact of the EDL on countries' leadership.

Discussion of PALM services and policies can feel removed, bureaucratic even. However, at the heart of UN resolutions, policy papers, and needs assessment ultimately find their value in individual patients such as Ingrid, the HIV patient quoted at the beginning of this study. Pathology and laboratory medicine alleviates patient fears, quickens access to treatment,

and saves lives. Making these basic tenets of healthcare a reality for millions more people will require concerted effort to implement the EDL, and an understanding of the global governance environment we live in. This study has built on the work of industry leaders and global health policymakers to contextualize a promising new movement in global health. Delivering on this promise will be the subject of many more studies in the future.

References List

1. Durban ALGin. African president warns of extinction from Aids. The Telegraph. https://www.telegraph.co.uk/news/worldnews/africaandindianocean/botswana/1347791/African-president-warns-of-extinction-from-Aids.html. Published July 10, 2000. Accessed December 9, 2018.

2. "AIDSinfo | UNAIDS." *AIDSinfo | UNAIDS*, aidsinfo.unaids.org/.

3. *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018).*

4. 92. Riley S. Essential Diagnostics List. Lablogatory. https://labmedicineblog.com/2018/05/07/essential-diagnostics-list/. Published May 4, 2018. Accessed October 30, 2018.

5. ,7, 12, 48, 52 Wilson ML, Fleming KA, Kuti MA, Looi LM, Lago N, Ru K. Access to pathology and laboratory medicine services: a crucial gap. The Lancet. 2018;391(10133):1927-1938. doi:10.1016/s0140-6736(18)30458-6

6. Laboratory medicine. (n.d.) Mosby's Medical Dictionary, 8th edition. (2009). Retrieved March 7 2019 from https://medical-dictionary.thefreedictionary.com/laboratory+medicine

8. World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018).

9. "Quality Assurance." *World Health Organization*, World Health Organization, 15 May 2017, www.who.int/diagnostics_laboratory/quality/en/.

10. Centers for Disease Control and Prevention. Facts about the laboratory response network. 2014. https://emergency.cdc.gov/lrn/ factsheet.asp (accessed Oct 4, 2017).

11. United States, Congress, Regional Office for Africa and United States Centers for Disease Control and Prevention. "Guidance for Development of National Laboratory Strategic Plans." *Guidance for Development of National Laboratory Strategic Plans*. https://www.who.int/hiv/amds/amds_guide_dev_nat_lab_strat.pdf

13. Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

14. "ICD - ICD-10-CM - International Classification of Diseases,(ICD-10-CM/PCS Transition." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, www.cdc.gov/nchs/icd/icd10cm_pcs_background.htm.

15. Gawande, Atul. “Cowboys and Pit Crews.” *The New Yorker*, The New Yorker, 26 May 2011, www.newyorker.com/news/news-desk/cowboys-and-pit-crews.

16. Ml W, Ka F, Ma K, Lm L, N L, K R. Access to pathology and laboratory medicine services: a crucial gap. *Yearbook of Paediatric Endocrinology*. 2018. doi:10.1530/ey.15.13.5

17. Folland, Sherman, et al. *The Economics of Health and Health Care*. Routledge, 2017.

18. Lesson 1: Introduction to Epidemiology. Centers for Disease Control and Prevention. https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section5.html. Published May 18, 2012. Accessed December 9, 2018.

19. Frerichs RR. Who first discovered vibrio cholera? UCLA Fielding School of Public Health http://www.ph.ucla.edu/epi/snow/firstdiscoveredcholera.html. Accessed December 9, 2018.

20. International Conference on Primary Health Care, Alma-Ata, USSR, 6-12 September 1978 . *Declaration of Alma-Ata*.

21. *The Millennium Development Goals Report 2015*. New York: United Nations

22. , 23. McArthur J, Rasmussen K, McArthur J, Rasmussen K. How successful were the Millennium Development Goals? brookings.edu. https://www.brookings.edu/blog/future-development/2017/01/11/how-successful-were-the-millennium-development-goals/. Published January 11, 2017. Accessed February 5, 2019.

24. Hook SW. Ideas and Change in U.S. Foreign Aid: Inventing the Millennium Challenge Corporation. *Foreign Policy Analysis*. 2008;4(2):147-167. doi:10.1111/j.1743-8594.2007.00062

25. Sustainable Development Goals: Sustainable Development Knowledge Platform. United Nations. https://sustainabledevelopment.un.org/?menu=1300. Accessed February 5, 2019.

26. Global price tags. World Health Organization. https://www.who.int/choice/globalpricetags/en/. Published October 13, 2017. Accessed March 10, 2019.

27. Q&A: Sustainable Development Goals Health Price Tag. World Health Organization. https://www.who.int/features/qa/sdg-price-tag/en/. Published July 17, 2017. Accessed March 10, 2019.

28. Siedner MJ, Gostin LO, Cranmer HH, Kraemer JD. Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic. *PLOS Medicine*. 2015;12(3). doi:10.1371/journal.pmed.1001804

29. *International Health Regulations (2005)*. 3rd ed.; 2005

30. Core Capacity Workbook: A Series of Exercises to Assist the Validation of Core Capacity Implementation Levels.; 2015. https://apps.who.int/iris/bitstream/handle/10665/190819/WHO_HSE_GCR_2015.13_eng.pdf;jsessionid=DA6BFACDD3056E481BB6D78815DF9BD7?sequence=1

31. A Timeline of HIV and AIDS. HIV.gov. https://www.hiv.gov/hiv-basics/overview/history/hiv-and-aids-timeline. Published January 10, 2019. Accessed January 27, 2019.

32. Where did HIV come from? | The AIDS Institute. https://www.theaidsinstitute.org/education/aids-101/where-did-hiv-come-0. Accessed January 27, 2019.

33. Hallas L. Fighting AIDS in Africa How a president's initiative tamped down an epidemic. *The Dallas Morning News*. https://interactives.dallasnews.com/2018/life-and-hope-with-hiv/. Published November 21, 2018.

34. Durban ALGin. African president warns of extinction from Aids. The Telegraph. https://www.telegraph.co.uk/news/worldnews/africaandindianocean/botswana/1347791/African-president-warns-of-extinction-from-Aids.html. Published July 10, 2000. Accessed December 9, 2018.

35. The United States President's Emergency Plan for AIDS Relief. PEPFAR: Accelerating Progress Toward HIV/AIDS Epidemic Control. https://www.pepfar.gov/15anniversary/index.htm. Accessed February 6, 2019.

36. Ortblad KF, Lozano R, Murray CJ. The burden of HIV. *Aids*. 2013;27(13):2003-2017. doi:10.1097/qad.0b013e328362ba67

37. Kharsany AB, Karim QA. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. *The Open AIDS Journal*. 2016;10(1):34-48. doi:10.2174/1874613601610010034

38. Blum K. On the Road to an Essential Diagnostics List. AACC. https://www.aacc.org/publications/cln/articles/2018/april/on-the-road-to-an-essential-diagnostics-list. Published April 1, 2018. Accessed October 30, 2018.

39. Ebola (Ebola Virus Disease). Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html. Published December 27, 2017. Accessed February 23, 2019.

40. Siedner MJ, Gostin LO, Cranmer HH, Kraemer JD. Strengthening the Detection of and Early Response to Public Health Emergencies: Lessons from the West African Ebola Epidemic. *PLOS Medicine*. 2015;12(3). doi:10.1371/journal.pmed.1001804

41. Goodfellow I, Reusken C, Koopmans M. Laboratory support during and after the Ebola virus endgame: towards a sustained laboratory infrastructure. *Eurosurveillance*. 2015;20(12):21074. doi:10.2807/1560-7917.es2015.20.12.21074

42. Ebola (Ebola Virus Disease). Centers for Disease Control and Prevention. https://www.cdc.gov/vhf/ebola/history/2014-2016-outbreak/index.html. Published December 27, 2017. Accessed February 24, 2019.

43. Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S. Ebola 2014 — New Challenges, New Global Response and Responsibility. *New England Journal of Medicine*. 2014;371(13):1177-1180. doi:10.1056/nejmp1409903

44. , 45. Balajee SA, Arthur R, Mounts AW. Global Health Security: Building Capacities for Early Event Detection, Epidemiologic Workforce, and Laboratory Response. Health Security. 2016;14(6):424-432. doi:10.1089/hs.2015.0062

46. World Bank Country and Lending Groups. How does the World Bank classify countries? – World Bank Data Help Desk. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519 -world-bank-country-and-lending-groups. Accessed February 26, 2019.

48. Ml W, Ka F, Ma K, Lm L, N L, K R. Access to pathology and laboratory medicine services: a crucial gap. *Yearbook of Paediatric Endocrinology*. 2018. doi:10.1530/ey.15.13.5

49. Nelson AM, Milner DA, Rebbeck TR, Iliyasu Y. Oncologic care and pathology resources in Africa: survey and recommendations. J Clin Oncol 2016; 34: 20–26.

50. Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

51. Volunteer Projects. Pathologists Overseas. https://www.pathologistsoverseas.com/projects-1. Accessed March 10, 2019.

53. Ali M, Elbireer AM, Jackson JB, et al. The good, the bad, and the unknown: quality of clinical laboratories in Kampala, Uganda. PLoS One 2013; 8: e64661.

54. Africa CDC. africacdc.org. http://www.africacdc.org/about/about-us. Accessed March 11, 2019.

55. Who We Are. ASLM. http://www.aslm.org/who-we-are/. Accessed March 25, 2019.

56. 87. 91. Sayed S, Cherniak W, Lawler M, et al. Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions. *The Lancet*. 2018;391(10133):1939-1952. doi:10.1016/s0140-6736(18)30459-8

57. SLMTA | Strengthening Laboratory Management Toward Accreditation. SLMTA | Strengthening Laboratory Management Toward Accreditation. https://slmta.org/. Accessed March 11, 2019.

58. Nkengasong JN, Yao K, Onyebujoh P. Laboratory medicine in low-income and middle-income countries: progress and challenges. *The Lancet*. 2018;391(10133):1873-1875. doi:10.1016/s0140-6736(18)30308-8

59. SLIPTA Programme. ASLM. http://www.aslm.org/what-we-do/slipta/. Accessed March 11, 2019.

60. Skaggs, Beth et al. "Implementing Laboratory Quality Management Systems in Mozambique: The Becton Dickinson-US President's Emergency Plan for AIDS Relief Public-Private Partnership Initiative." The Journal of infectious diseases 213 Suppl 2 (2016): S47-52.

61. Stafinski JM. Diagnostics. Science with a Mission. http://www2.sciencewithamission.org/diagnostics. Accessed March 11, 2019.

62. 64. 66. Laing R, Waning B, Gray A, Ford N, Hoen Et. 25 years of the WHO essential medicines lists: progress and challenges. *The Lancet*. 2003;361(9370):1723-1729. doi:10.1016/s0140-6736(03)13375-2

63. WHO. The world drug situation. Geneva: World Health Organization, 1988.

65. *Executive Summary: The Selection and Use of Essential Medicines 2017*. Geneva; 2017

66. The WHO Essential Medicines List (EML): 30th anniversary. World Health Organization. https://www.who.int/medicines/events/fs/en/. Published November 20, 2015. Accessed March 11, 2019.

68. 70. Blum K. On the Road to an Essential Diagnostics List. AACC. https://www.aacc.org/publications/cln/articles/2018/april/on-the-road-to-an-essential-diagnostics-list. Published April 1, 2018. Accessed October 30, 2018.

69. Schroeder LF, Guarner J, Elbireer A, Castle PE, Amukele TK. Time for a Model List of Essential Diagnostics. *New England Journal of Medicine*. 2016;374(26):2511-2514. doi:10.1056/nejmp1602825

71. Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD) 2019. World Health Organization. https://www.who.int/medical_devices/diagnostics/SAGE_IVD_2019_member_list/en/. Published March 14, 2019. Accessed March 23, 2019.

72. Background Document Strategic Advisory Group of Experts on ... https://www.who.int/medical_devices/diagnostics/back-doc_WHO-model-list-essential-diagnostics-updt.pdf. Accessed March 23, 2019.

73. 74. *World Health Organization Model List of Essential In Vitro Diagnostics First Edition (2018)*.

75. What tests look for - HIV-1 and HIV-2. HIV & AIDS Information: What tests look for. http://www.aidsmap.com/HIV-1-and-HIV-2/page/1322970/. Accessed March 24, 2019.

76. HIV/AIDS - Illinois Department of Public Health. http://www.idph.state.il.us/aids/materials/10questions.htm. Accessed March 24, 2019.

77. Ibitoye M, Frasca T, Giguere R, Carballo-Diéguez A. Home testing past, present and future: lessons learned and implications for HIV home tests. *AIDS Behav*. 2014;18(5):933-49.

78. Aheto DW, Gbesemete KP. Rural perspectives on HIV/AIDS prevention: a comparative study of Thailand and Ghana. *Health Policy*. 2005;72(1):25-40. doi:10.1016/j.healthpol.2004.06.013

79. Number of countries adopting HIV self-testing policies rises sharply. World Health Organization. https://www.who.int/hiv/mediacentre/news/hiv-self-testing-increases/en/. Published July 25, 2017. Accessed March 24, 2019.

80. Alere Determine HIV-1/2 Ag/Ab Combo Test - Diagnostic Tests and Clinical Products, Diagnostic Tests and Controls. Alere Determine HIV-1/2 Ag/Ab Combo Test 25 Tests:Diagnostic Tests and. https://www.fishersci.com/shop/products/alere-determine-hiv-1-2-ag-ab-combo-test-25-tests/23046614. Accessed March 25, 2019.

81. Vojnov L, Markby J, Boeke C, Harris L, Ford N, Peter T. POC CD4 Testing Improves Linkage to HIV Care and Timeliness of ART Initiation in a Public Health Approach: A Systematic Review and Meta-Analysis. PloS one. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4866695/. Published May 13, 2016. Accessed March 25, 2019.

82. Hyle EP, Jani IV, Lehe J, 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 Medicine*. 2014;11(9). doi:10.1371/journal.pmed.1001725

83. Kyaw LL, Nozaki I, Wada K, Oo KY, Tin HH, Yoshihara N. Ensuring accurate testing for human immunodeficiency virus in Myanmar. *Bulletin of the World Health Organization*. 2014;93(1):42-46. doi:10.2471/blt.14.138909

84. Schroeder LF, Guarner J, Elbireer A, Castle PE, Amukele TK. Time for a Model List of Essential Diagnostics. *New England Journal of Medicine*. 2016;374(26):2511-2514. doi:10.1056/nejmp1602825

85. Schroeder LF, Elbireer A, Jackson JB, Amukele TK. Laboratory diagnostics market in East Africa: a survey of test types, test availability, and test prices in Kampala, Uganda. PLoS One 2015; 10: e0134578.

86. Procedure to update the WHO Model List of In Vitro Diagnostics. World Health Organization. https://www.who.int/medical_devices/diagnostics/selection_in-vitro/edl-model-lists/en/. Published January 31, 2019. Accessed March 26, 2019.

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

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

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

Biography

Laura Hallas is passionate about improving global health through law and policy, which led to her working at Washington University's Institute of Public Health, the U.S. State Department, and Dell Medical School. A longtime writer, she also pursued journalism alongside public health research, both as the editor-in-chief of The Daily Texan and as an intern at The Dallas Morning News. Laura will spend the next two years in the UK as a Marshall Scholar, where she will pursue degrees in public health policy at the London School of Hygiene and Tropical Medicine and the University of Oxford.