Factors affecting access to quality HIV diagnostic services in Liberia from a laboratory perspective

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A thesis submitted in partial fulfilment of the requirement for the degree of Master of Science in International Health

By

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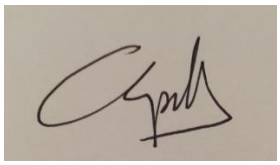

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List of Abbreviations

AIDS	Acquired immune deficiency syndrome
ANC	Antenatal Clinic
ART	Antiretroviral treatment
ARV	Antiretroviral drug
CCM	Country Coordinating Mechanism
CD4	Cluster of Differentiation 4
CDO	Country Diagnostic Officer
DBS	Dried Blood Spot
DHIS	District Health Information System
DHS	Demographic and Health Survey
DIC	Drop-In Center
EDTA	Ethylenediaminetetraacetic acid
EID	Early Infant Diagnosis
EQA	External Quality Assessment
EVD	Ebola Virus Disease
GAVI	Global Alliance for Vaccines and Immunization
GF	The Global Fund to fight Aids, Tuberculosis and Malaria
GDP	Gross Domestic Product
HMIS	Health Management Information System
HNSP	HIV National Strategic Plan
HTC	HIV Testing and Counselling
HTS	HIV Testing Services
HIV	Human Immunodeficiency virus
IHR	International Health Regulations
JEE	Joint External Evaluation
LMIS	Logistics Management and Information System
LIMS	Laboratory Information Management System
MOH	Ministry of Health

MSM	Men having Sex with Men
NAC	National Aids Commission
NACP	National Aids Control Program
NBSP	National Blood Safety Program
NDD	National Diagnostic Division
NDU	National Diagnostic Unit
NGO	Non-Governmental Organisation
NHSP	National HIV Strategic Plan
NTCP	National Tuberculosis Control Program
NPHIL	National Public Health Institute of Liberia
NPHRL	National Public Health Reference Laboratory
NRL	National Reference Laboratory
PCR	Polymerase Chain Reaction
PLHIV	People Living with HIV
PMTCT	Prevention of Mother to Child Transmission
POC	Point-of-Care
RDT	Rapid Diagnostic Test
SARA	Service Availability and Readiness Assessment
SLIPTA	Stepwise Laboratory (Quality) Improvement Process Towards Accreditation
SLMTA	Strengthening Laboratory Management Toward Accreditation
SPNHLSL	Strategic Plan for the National Health Laboratory System of Liberia
SW	Sex Workers
TB	Tuberculosis
USA	United States of America
USAID	United States Agency for International Development
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Program
VL	Viral Load
WHO	World Health Organization

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Abstract

Background: The 2014 Ebola epidemic in Liberia has exposed the country health system weaknesses, in particular regarding its laboratory capacity. Meanwhile, Liberia is still lagging behind the 2020 UNAIDS 90-90-90 target: at the end of 2019, only 57% of the number of estimated people living with HIV know their HIV status, 56% of them are on antiretroviral treatment, while no data is available on viral load suppression.

Objectives: Identify factors affecting access to quality HIV diagnostics in Liberia, from a laboratory perspective.

Method: Literature review.

Results: A reform of the laboratory system has been initiated recently, with the creation of the National Public Health Institute of Liberia and the elaboration of strategy and policy documents to guide the development of a National Laboratory System. Yet, responsibilities for moving the agenda forward and funding needs are not defined. Stock-outs of health products and equipment dysfunction affect the delivery of diagnostic services and require urgent action. HIV testing and counselling services are offered in 65% of the 765 facilities of Liberia and are therefore not accessible to all. For Viral Load and Early Infant Diagnosis testing, the placement at county level of GeneXpert machines for integrated use (HIV, Tuberculosis, Ebola Virus Disease) seems relevant to reduce test result turnaround times while keeping services accessible, yet reported levels of biological monitoring of people living with HIV remain very low, with 12% of patients with documented Viral Load results in 2018. A new sample transportation system, put in place by Riders for Health for public health surveillance purposes, seems to deliver promising results though it is unclear clear whether it benefits the HIV program. Shortages of qualified laboratory staff need to be quantified and could be addressed with further implementation of task-shifting (for example HIV testing by community health volunteers). In the context described above, the absence of evidence of a functional quality assessment system for HIV diagnostics is a concern, though initial steps to implement the WHO AFRO Stepwise Laboratory (Quality) Improvement Process Towards Accreditation have been undertaken. Overall, the literature review highlighted limited research done for Liberia, in particular regarding the implementation of HIV Testing and Counselling and laboratory practices at health facility level regarding ordering, sample collection and use of test results.

Conclusion: The development of a National Laboratory system in Liberia has just begun and needs to be accelerated, starting with the definition of a costed plan and accountability framework. Significant supply chain weaknesses resulting in frequent stock-outs are a critical bottleneck, requiring a sector-wide solution, while the shortage of qualified laboratory staff has to be quantified and addressed. Research on laboratory practices, test turnaround times and use, needs to be undertaken.

Keywords: Diagnostics, HIV, Laboratory, Liberia, Laboratory system

Wordcount: 13187

1. Background

Geographical context

Liberia is a West African country covering 111,000 square kilometres (see Figure 1-(1)). Its Atlantic coastline is 360 mile long and it has borders with Sierra Leone, Guinea-Conakry and Ivory Coast. (2) Liberia is divided into fifteen counties, which, in turn, are subdivided into 92 second-level administrative divisions called districts. (3)

Figure 1 – Map of Liberia (1)

Political context

Liberia was founded by free people of color and later former slaves, whose emigration from the United States of America was funded and organized by the American Colonization Society, claiming territory from the existing indigenous population. The Republic of Liberia was established on July 26, 1847. Between 1847 and 1980, both political and economical power remained in the hands of the descendants of the black colonists, known as Americo-Liberians, leaving Liberia indigenous population out. (4) Profound inequalities and ethnic tensions created by this society led to two civil wars between 1989 and 2003, which destroyed infrastructure and led to the shutdown of public services (health, education) in large part of the country. (5)

Since the end of the war, significant efforts were undertaken to consolidate peace and stability. In 2018, the peaceful transition of power from one elected president (Nobel Peace prize Ellen Johnson Sirleaf) to the newly elected president (George Weah) has been a positive signal and set the grounds for further development efforts. (2)

Economic context

Liberia is a low-income country, with a reported Gross National Income per capita of US$ 370. The economy of Liberia, dominated by agriculture and mining, is slowly transforming, with the emergence of a services sector. (2) Liberia ranked 181st out of 189 countries in the latest United Nations Development Programme (UNDP) Human Development Index and 155th in the Gender Inequality Index (2019). (6)

Poverty levels remain very high, with 72% of the rural population and 32% of the urban population below the poverty rate measured at the national poverty line in 2016. (7) Its population of 4.6 million is very young, result of both a high fertility rate (4,3 births per woman

in 2018) and a low life expectancy (63,8 years in 2018). (8) The Gini coefficient for Liberia was 35,3 in 2016. (9)

Health situation

Maternal mortality stands at 661 for 100,000 live births in 2017 (down from 1,072 in 2013). Infant mortality 32,4 per 1,000 live births in 2019, down from 54 in 2013. The under-5 mortality is 84,6 per 1,000 live births. (10) Leading causes of mortality in 2019 are Malaria, diarrheal diseases, neonatal disorders, lower respiratory infections, heart disease and HIV/AIDS. (11)

Health system

The decade-long civil wars had a dramatic impact on the health system, with major infrastructure destructions, health personnel loss and partial or complete halt of health services depending on the regions. (2) Since the end of the civil war, several reforms were implemented in order to increase access of Liberians to quality healthcare, with the introduction of the Basic Package of Health Services, later upgraded to the Essential Package of Health Services. (12)

Liberia is divided into 5 regions, 15 counties covering 92 health districts. Liberia's health system is structured into three levels of service delivery: primary level with 671 health clinics, secondary level with 58 health centres and county hospitals, and tertiary level consisting of a limited number of regional and referral hospitals (total number of hospitals in Liberia: 36). (3)

The laboratory system comprises five public health laboratories (the National Reference Laboratory, four regional laboratories in Bong, Nimba, Maryland and Lofa counties) and 401 clinical laboratories (285 public, 116 private, 1 at the public-private tertiary facility level). The clinical laboratories provide services ranging from Rapid Diagnostic tests ('RDT') to advanced diagnostics, using automated analysers. (13)

In 2017, expenditure on health per capita amount to US$ 65 and represent 8% of the GDP. Out of pocket expenditure represent 40% of health expenditures while development assistance for health expenditures represent 42 %. (11)

Partnership landscape

Liberia health sector benefits from strong support from a large number of multilateral and bilateral partners (USAID, World Bank, Global Fund, GAVI, etc.). The Ebola outbreak underlined the need to ensure investments were being made in health systems strengthening, in order for all programs to be supported. (14)

HIV in Liberia

In order to end the HIV/AIDS epidemic, UNAIDS has globally set three targets to be achieved by all countries by the end of 2020: 90% of all people living with HIV should know their HIV status, 90% all people with diagnosed HIV infection should receive sustained antiretroviral therapy and 90% of all people receiving antiretroviral therapy should have viral suppression. (15)

In 2019, it is estimated that 43,000 adult and 3 600 children under 14 live with HIV in Liberia: 57% know that they are HIV-positive and, out of those, 56% are on antiretroviral treatment

('ART') and no data is reported regarding viral suppression. Coverage of adult and children on ART overall is 34%. 90% of pregnant women needing ARV for PMTCT are on ART, yet final transmission rate including during breastfeeding is 14,5%. Coverage of early infant diagnosis ('EID') is low at 22%. (16)

HIV-AIDS is the sixth cause of mortality in Liberia: estimated number of deaths due to HIV/AIDS was 1,900 in 2019, a reduction of 45% since 2010. Overall adult prevalence rate is estimated at 1,5% while prevalence rates in key-population ('KP') groups are much higher (see Table 1- (16)). Incidence rate is estimated at 0,74 per 1,000 population and has reduced by 35% since 2010. (11)(16).

Group	Estimated prevalence rate	Estimated n# of PLHIV
Adult aged 15 to 49	1,5%	47 000
Men Having Sex with Men ('MSM')	19,8%	14 771
Sex workers ('SW')	9,8%	15 984
Injecting Drug Users ('IDU')	3,9%	160

Table 1 - Estimated HIV prevalence in 2019 in Liberia

Ensuring people know their HIV status and how to prevent themselves from getting infected is a first pillar of the HIV response. Results of the Demographic and Health Survey 2019/2020 for Liberia show that only 50% of the men and 32% of the women surveyed had ever been tested for HIV and received the results. (17)

2. Problem statement

Results reported by UNAIDS for Liberia at the end of 2019 fall short of the 90/90/90 target, with no data reported at all regarding viral suppression, indicating significant progress remains to be done for that third indicator. Multiple factors contribute to these insufficient results in the fight against the HIV epidemic, which relate to different programming areas of the HIV response and range from the care service delivery model to the insufficiency of the supply chain systems to stigma and discrimination, to name only a few. (16)

Nevertheless, while much remains to be done to ensure all Liberians accept and voluntarily seek HIV testing, it is essential, for these interventions to be both impactful and ethical, that all systems are in place for them to access quality HIV diagnostic services and receive appropriate clinical services including ART in order to reach viral suppression. (18) A recent audit of the Liberia portfolio of grants undertaken by the GF highlighted that deficiencies in the supply chain systems and in the laboratory system in particular were contributing to low EID coverage of and under-utilization of viral load ('VL') equipment in the facilities visited. (19)

Since the Maputo Declaration on Strengthening of Laboratory systems in 2008, laboratory services have improved in a number of countries in Sub Saharan Africa, however progress has been uneven and many countries still experience significant challenges: equipment not fully functional due to lack of maintenance; stock-out of laboratory products (tests, reagents, consumables); unavailability of trained human resources; inefficient sample transportation system resulting in delays between testing and results reporting. In 2014, the Ebola epidemic in West and Central Africa underlined the weaknesses of the national health system in Liberia, particularly its laboratory services. (20)

Issues affecting the laboratory system in Liberia are wide and range from inadequate institutional arrangements, lack of skilled workforce, dysfunctional equipment to insufficient supply chain and information systems. (21) Since the end of the outbreak, increased attention has been paid to the laboratory system, with the development of national policy and strategy documents, as well as with the creation end 2016 of the National Public Health Institute of Liberia ('NPHIL'). (22)(23) The NPHIL Strategic Plan recognizes the limited laboratory capacity to detect, notify and respond to most infectious diseases of public health concern and underlines the need to develop a bio-surveillance and laboratory diagnostic system. (13)

As reaching the 90/90/90 target requires laboratory services delivering quality HIV Diagnostics at scale (both testing services and clinical management such as VL testing, CD4 and routine biological monitoring), it is important to understand in more detail the strengths and gaps on the laboratory side and how they contribute to the success or failure of a major disease control program.

Justification:

Literature found highlights key deficiencies of the laboratory system, but the question of how gaps identified constitute barriers to early diagnosis of HIV and adequate clinical monitoring of PLHIV has not been researched in detail

While other aspects of the HIV response in Liberia could have been researched, the gaps identified in the laboratory systems will be the area of research of this thesis, as a strong laboratory system is a pre-condition to ensuring an HIV control program can reach its goals.

3. Objectives

The objective of my research will be to identify, from a laboratory and supply chain systems perspective, the factors influencing access to quality HIV diagnostic services in Liberia and issue recommendations to improve both access to and quality of such services.

Specific objectives include:

- To analyse the governance, strategy, policy and financing aspects, with regards to the laboratory system and the HIV program in Liberia;
- To analyse how the current set-up influences access to HIV diagnostic services, both HIV testing services and clinical monitoring diagnostic tests;
- To identify what Liberia can learn from neighbouring countries and countries in Eastern and Southern Africa having achieved high level of VL diagnostic coverage among PLHIV in order to scale up its clinical management diagnostic services;
- To issue recommendations to improve access and quality of the laboratory systems for HIV diagnosis in Liberia to the Ministry of Health ('MOH') of Liberia, the National Public Health Institute of Liberia, the donor community and to health service/ laboratory managers.

4. Methodology

The method followed will be literature research.

4.1 Search strategy

For all objectives, the search engines used for the search and the inclusion criteria are detailed below:

Key Search terms	MESH: 'Laboratory', 'Policy', 'Laboratory personnel', 'Health workforce', 'HIV', 'Diagnosis', 'Diagnostic services', 'Diagnostic errors', 'Laboratory Proficiency Testing', 'Quality assurance Healthcare', 'Health services accessibility', 'Point of care testing', 'Viral Load', 'Sustained virologic response', 'Retention in care', 'Child', 'Vulnerable population', 'Interventions', 'Policy', 'Best practices', 'Eastern Africa', 'Southern Africa', 'Sierra Leone', 'Guinea'. Non-MESH: 'laboratory system', 'laboratory services', 'laboratory supply chain', 'laboratory workforce', 'laboratory financing', 'diagnostics quality assurance', 'governance', 'laboratory strategy', 'HIV program', 'HIV diagnostic', 'HIV testing', 'HIV self-testing', 'access to HIV testing', 'testing', 'access to HIV diagnostics', 'clinical management of HIV', 'CD4 monitoring', 'Viral Load monitoring', 'early infant diagnosis', 'PMTCT', 'ART retention', 'HIV drug resistance', 'Key-populations', 'Sex workers', 'MSM', 'children', 'HIV viral suppression', 'scale up, 'success', 'lessons learnt'. The key-words above will be searched for Liberia specifically and also independently.
Databases used for the Search	Pubmed, Google scholar, Microsoft Academic Search, Refseek
Inclusion criteria	Published in English, French or Spanish Published papers, snowballing article references Published since 2010

Grey literature from the MoH of Liberia, WHO, UNAIDS, GF and other national/international bodies of relevance will be searched and used. As this data is not validated, it is understood that bias may exist, however information available from these sources is interesting and sometimes the only source available.

4.2 Conceptual framework

After looking at different frameworks (WHO Building blocks, Lesveque model), I have decided to use an adapted version of the Conceptual framework for testing process and associated errors in sample processing after Hickner and al and Carraro and Plebani, because it is based on the three phases of the Diagnostic-Therapeutic loop (Pre-analytical, Analytical and Post-Analytical) and as such addresses well the specifics of an individual test processing and factors associated with positive patient outcome following the performance of a test. (24)

However, that framework does not allow for the review of several aspects of the laboratory system itself which are important to analyse barriers to access and which are well defined in the WHO Building Blocks framework.

I have therefore decided to adapt the conceptual framework to include aspects linked to governance, strategy and policy, and financing, in an additional phase, called the pre-pre-analytical phase, as shown below.

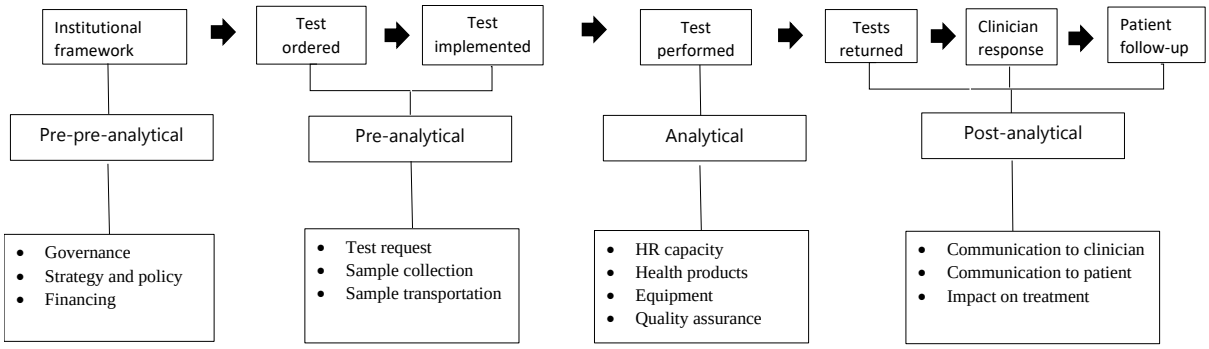

Figure 2– Adjusted framework based on Conceptual framework for testing process and associated errors in sample processing after Hickner and al and Carraro and Plebani (24)

- Pre-pre analytical phase: governance, strategy, policy and financing, will be reviewed to understand their influence on the access to HIV diagnostic services.
- Pre-analytical phase: we will review the test commissioning and sample collection and transportation when applicable.
- Analytical phase: we will review the actual delivery of the test, from the HR capacity, availability of laboratory products and equipment and quality assurance processes perspectives.
- Post-analytical phase: we will review how test results are communicated and whether they lead to appropriate treatment decisions.

In each of the phase, both HIV testing and clinical monitoring of HIV will be reviewed.

5. Results section

5.1 Pre-pre analytical phase – Institutional framework for HIV diagnostics

In this section, we will assess how governance, strategy, policy and financing for both the laboratory system and the fight against HIV are impacting access to quality HIV diagnostic services.

5.1.1 Governance

The way organizations are structured and their relationships influence their ability to coordinate actions and share accountability for the results. (25)

Governance for the laboratory system

Before the Ebola epidemic, supervision of medical laboratory operations in Liberia were under the responsibility of the National Diagnostic Division ('NDD'), reporting to the Chief Medical Officer of the MOH. The National Reference Laboratory ('NRL'), created in 2010, was also hierarchically located within the MOH, though we were not able to identify through our research to whom the NRL was reporting to exactly. (22)

End 2016, following the Ebola epidemic, the creation of the National Public Health Institute of Liberia ("NPHIL") was enacted. (13) When creating a National Public Health institute, each country decides of its governance system: the review of the establishment of five National Public Health Institutes in Sub-Saharan Africa has shown that models followed varied widely, in particular regarding the autonomy towards the MOH. (26) In Liberia, the NPHIL is largely autonomous, with a reporting responsibility only towards the MOH, without however specifying to whom exactly. This autonomy can allow for independence in oversight of health operations through surveillance and in setting strategic goals and priorities for research. Nevertheless, it can also make the collaboration with the different departments of the MOH more difficult as information and samples related to outbreak alerts are coming from clinical laboratories. Being outside of the MOH, budgetary allocation may also prove to be more difficult to obtain. (27)

The National Reference Laboratory, renamed National Public Health Reference Laboratory (" NPHRL"), is now part of the NPHIL and has the responsibility to strengthen public health diagnostic capacity for diseases of public health concern. (22) It currently is able to carry out laboratory diagnosis of epidemic-prone diseases and houses the National TB Reference laboratory which performs culture and drug susceptibility testing of TB bacteria. Its responsibilities also include performing quality assurance and referral testing as well as training and supervision of public health regional laboratories and integrated disease surveillance teams at county and district level. (28)

The 2008 Maputo declaration on strengthening laboratory systems was stressing the importance of establishing a dedicated department of laboratory systems within the MOH. (29) A review of the type of laboratory governance of 39 sub-Saharan African countries done from national strategy and policy documents issued until 2010 highlighted the variety of models followed, with only 5 (13%) having a dedicated Laboratory Directorate in the MOH. Other models included a shared Directorate for laboratory and other services (33%), a

Research/provider institution in charge or a situation where multiple departments within the MOH had some form of responsibility for the laboratory system (18%). The article strongly recommended to pursue efforts for the creation of a Directorate for Laboratory Services as a way to ensure prioritization of the development of regulations, accreditation plans and definition of norms and standards. (30)

In that review, Liberia was identified as having multiple departments dedicated to laboratory within the MOH. It is not clear whether this classification related to the fact the NRL was also within the MOH or to the fact laboratory operations were also sometimes directly coordinated by vertical programs, such as the National Aids Control Program ('NACP'), National Tuberculosis Control Program ('NTCP') and National Blood Safety Program ('NBSP'). (30)

Finally, the development of a structured National Laboratory System for Liberia remains at its early stage: a Technical Working Group for the National Laboratory System is planned in the new organogram to ensure alignment between all stakeholders and coordination between the NPHIL and the different departments within the MOH (including the NDD and the NACP). However, we could not find evidence confirming this Working Group is operational. (23)

Governance for the HIV response

The National Aids commission ("NAC"), established in 2010 and chaired by the President of the Republic of Liberia, coordinates the decentralized and multi-sectoral HIV response and advocates for funding of the HIV response, while the Country Coordinating Mechanism ("CCM") mandate is to supervise the implementation of the GF grants and submit request for funding to GF. All sectors/partners involved in the HIV response are represented in both the NAC and the CCM, with the NAC being also a CCM member. While the mandate of the CCM is more focused on the GF grant processes, overlaps do exist between the two bodies' mandates, in terms of coordination of and advocacy for the HIV response. (31)(32)

The NACP, located within the MOH, oversees the clinical response to the HIV epidemic, including coordinating access to diagnostic and care for all targeted population. International and local Non-Governmental Organizations manage HIV community-based prevention activities towards KP, such as Men who have sex with Men ("MSM") and sex workers ("SW"), including provision of HIV testing and counselling services ('HTC') and referral for care. (33)

While the NDD and NACP both operate under the MOH umbrella, a clear framework for collaboration between the two departments on the HIV diagnostics area could not be identified in the documents reviewed. (23) The National Laboratory System Policy mentions that "some" laboratories fall directly under the responsibility of the NACP, but it has not been possible to identify which ones they refer to exactly as it was not stated in the document. (22)

5.1.2 Strategy and policy

Strategy and policy for the laboratory system

After a five year gap following the first plan covering 2011-2015, the second Five Year Strategic Plan for the National Health Laboratory System of Liberia ('SPNHLSL') has been recently finalized in October 2019 and covers the period 2019-2024. It underlines twelve strategic objectives, covering priority areas for the laboratory system, detailing for each one

output and priority actions required, in line with the National Laboratory Policy issued in July 2019. (23)

Key-activities planned in the SPNHLSL (development of the organization structure of the National Laboratory System, compilation of an exhaustive listing of all laboratory facilities, definition of a testing menu) show that the development of an harmonized and structured laboratory system is still at a very early stage. (22)(23) While it stresses strategic objectives, priority actions and expected output, the Strategic Plan does not include any element of cost nor any operational details and we could not locate any such document through our research. The Monitoring Framework defined is basic and only makes reference to high-level outcomes, with no clear accountability framework for targets set. In addition, it does not include specific sections addressing Point of Care ('POC') testing, Partnership and Community, which was noted in other countries. (23) (34)

Strategy and policy for HIV response

The current National HIV strategic plan ('NHSP') covers the period 2015-2020. As outlined in the strategy, HTC services are to be provided through multiple channels: antenatal care clinics (Option B+ is followed), family planning clinics, health facilities, TB clinics, as well as through programs managed by civil society organisations (for KP). Clinical care for PLHIV, including CD4 count and VL analysis, is managed in ART centres where HIV + patients are referred to. Specific outreach activities are planned for identified KP (SW, MSM, IDU). (35)

When reviewing the HNSP, little information is available about the laboratory-related challenges and gaps of the HIV response. Several activities are nevertheless mentioned in specific sections: for example, the Blood Bank program section details activities to undertake to improve performance (training, equipment, quality assurance, etc); the Treatment and Care section underlines the need to improve the quality of laboratory services, including CD4 count and in-country availability of EID. Stock-out of RDTs is also referred to as an obstacle to reaching testing targets while quality assurance activities are mentioned. (35)

Currently the HNSP does not specifically address laboratory-related challenges as a cross-cutting issue. In Section 8.1 which details the 5 main Health System Strengthening challenges impacting the HIV program, no specific laboratory-related issue is mentioned or explained; the laboratory services only appear in the Procurement and Supply chain strategies detailed, which mention the strengthening of coordination between pharmacists and county diagnostic officers ('CDO', part of the County Health teams supervising health services), and the need to incorporate laboratory reagents and consumables in the Logistics Management Information System ('LMIS') and Health Management Information System ('HMIS'). (35)

Moreover, the HNSP does not make any mention in the text of the NDD nor the NPHRL, which questions the linkage between the different structures. In the technical working groups set up to elaborate the HNSP, there was no representation of the NDD or the NPHRL for both the Prevention and Care working groups. The only representation we could find was that one NDD representative participated in the Strengthening Health Care system working group and one in the HNSP validation retreat.(35)

The stages of development of the HNSP and of the SPNHLSL are quite different. A review of national health policies and plans from 39 sub-Saharan African countries of the period 2010 to 2012 highlighted that most laboratory issues were addressed in the context of HIV and AIDS

and that the level of progress on developing laboratory policies seemed to vary depending on the scale of HIV prevalence and Pepfar presence, which seem consistent with the Liberia case with an HIV prevalence of 1,5 % and no Pepfar presence. (30)

5.1.3 Financing

Financing of the laboratory system

In the 10 national laboratory policies reviewed in the study, limited information was generally available on the budget needed and budget available for laboratory services on a consolidated basis (government and partner). (30) This is the case for Liberia where no financial information is disclosed either in the National Policy or in the SPNHLSL. (22)(23)

The study performed on 39 countries identified evidence of a budget line for the laboratory services in 2 countries only. (30) No dedicated budget line for laboratory services exist in Liberia and it is not clear which systems and personnel will be used to conduct fiscal/budgetary planning and accounting for the laboratory system while this was identified as key-issues for other countries. (30)(34)

Financing of the HIV NSP

The HNSP, which serves as a basis of funding requests to donors, includes an estimated costing per intervention (prevention, care, treatment) and totals US$ 189 million for five years. Details on the costing of the activities or the assumptions followed are not available in the document. (23)

The GF is the main funder of the NSP, with a funding allocation for joint TB/HIV application of about US$ 30 million for 3 years for the period 2018-2020, with the government of Liberia and other partners, such as USAID also contributing to financing the plan. (33) The grant agreement mentions that the grant includes activities to improve the laboratory and diagnostic capacities, including VL, CD4, TB testing and EID. (36)

5.2 Pre-analytical phase – Preparing for the HIV diagnostic test

In this section, we will focus on the step of ordering the test, collecting the sample and transporting it to the laboratory when needed. The willingness of people/ patients to be tested and other barriers to do so are not going to be discussed.

5.2.1 Service provider knowledge/willingness to commission a diagnostic test

In order to perform the diagnosis of HIV, from an institutional perspective, the commissioner needs to have the knowledge, capacity and willingness to do so.

5.2.1.1 HIV testing

In Liberia, in 2018, 36 hospitals (100%), 50 health centres (86%) and 409 clinics (61%) were offering HTC services as per the Service Availability and Readiness Assessment performed ('SARA'). Lowest scores in terms of coverage were found in Margibi and Montserrado counties with respectively 35% and 36% coverage. (3) The 2020 HIV Testing Services ('HTS') guidelines mention the Opt-out Provider-initiated counselling and testing as the preferred strategy. (37)

Health facility density varies from 1,3 per 10,000 inhabitants for the counties of Bong, Nimba and Grand Bassa to 3,6 for the county of Sinoe, which raises concerns on the equity of access to services of the Liberian population in 2018. When comparing, per county, the percentage of facilities providing HTC services and the health facility density, no specific correlation however can be found: for example, 59% of the 75 facilities of Nimba (health facility density of 1,3) provide HTC while 61% of the 35 facilities of Sinoe (density of 3,6) provide HTC. (3) In rural counties, it is estimated 60% (1.2 million people) of the population lives more than 5 km from the nearest health facility. (38)

The overall Health Workforce density per 10,000 population was assessed in the SARA as 10,7, i.e.less than 50% of the WHO recommendation of 23 and again showed significant disparities between counties. Health workforce cadres considered in the assessment were Physicians/doctors, physicians assistants, nurses and midwifes, therefore we do not have an assessment of the availability of laboratory staff available. (3)

Only 20% of the health facilities offering HTC had all 5 tracer items tested for HTC available (Guidelines available, at least 1 staff trained, room with visual and auditory privacy, HIV diagnostic capacity, condoms), with the lowest score related to training of staff (32%) and to a less extent to availability of guidelines (75%). (3)

In Malawi, a review of Provider-Initiated HTC ('PIHTC') highlighted that, in most cases, HIV testing was proposed based on symptoms displayed by the patient and not on a routine opt-out basis. Barriers to HTC most frequently reported included test kit shortages, inadequate physical space and inadequate number of counsellors, with an overall length of time reported to perform HTC of 55 minutes. (39) In Tanzania, similar barriers were reported, with a third of the health workers interviewed reporting that HTC was too demanding to health workers. (40) In Namibia, limited awareness of policy by health workers and limited support/mentoring received post-training were also highlighted as a barrier for providers to initiate HTC. (41)

Apart from the SARA findings, no specific review or study of barriers to PIHTC in Liberia could be found in the different searches done. Yet, the low level of training of staff on HTC reported in the SARA, in the context of critical shortage of health workers, could potentially point out to similar issues in the context of Liberia. (3)

Higher level of PIHTC have been reported in different studies for ANC and TB clinics, with perceived factors being clearer policy guidelines and providers feeling they have a reason to offer HTC due to the pregnancy and the risks linked to the HIV/TB co-infection. (39) (42) This seems consistent with results reported for the PMTCT and TB programs in Liberia, though the latter still fall short of the target set (in 2018, 74% of HIV+ women knew their HIV status; in 2016, 74% of TB patients had been tested for HIV). (19) (43)

EID remains vastly underperformed: in 2019, only 22% of infants born to women living with HIV received a virological test for HIV within two months of birth. (16) Studies undertaken in Burkina Faso, Kenya and South Africa have shown that, at the institutional level, understaffing, insufficient knowledge of HIV testing guidelines and laboratory sample collection techniques as well as poor communication between ANC, delivery and postnatal facilities were barriers to providers initiating EID. (44) (45).

A systematic review and meta-analysis performed showed that community-based HTC done by community health volunteers reach population in their catchment area with higher coverage than facility-based HTCs, though most of the studies found referred to home and facility HTC and focused on general population. (46) In Liberia, HIV testing by peer counsellors for KP started to be implemented in 2016, with the concurrent establishment of Drop-In-Centres for referral for confirmatory testing and care and treatment. However the program has been experiencing challenges, with 59% of the reactive cases not subject to confirmatory testing and 41% of positive cases not initiated on ART. (19)

5.2.1.2 Commissioning the laboratory tests required for the care of a PLHIV

Once diagnosed, HIV positive patients should have a monthly appointment during the first six months of treatment and then once every three months, while VL monitoring should be done every six months during the first year and then every year thereafter. (47)

In 2018, 32 hospitals (89%), 41 health centres (71%) and 188 health clinics (28%) were providing treatment follow-up services for persons on ART as per the SARA. Mean diagnostic capacity of various tests essential in general service provision to clients was assessed at 39% overall. Only 4% of facilities surveyed had capacity to diagnose for all 8 tracer items (haemoglobin, blood glucose, malaria, urine dipstick- glucose, urine dipstick- protein, HIV RDT, syphilis, urine test for pregnancy). (3) While no conclusion can be directly drawn from these figures in relation to the commissioning of laboratory tests for HIV care, they point out to limited availability of basic diagnostic services on-site.

While guidelines were available in 83% of the health facilities providing care and support to PLHIV, only 42% had one staff training in ART prescription and management over the past two years. Documentation of VL or CD4 count was reported for only 4% and 12% of the patients respectively. (3) The interruption of availability of the molecular testing capacity during the Ebola outbreak, shortly after the start of its implementation in 2013, may have hampered initial efforts to promote the request for VL testing. (48)

In a qualitative study done in Malawi regarding implementation of VL monitoring, the main barriers identified by providers were the workload generated and reporting requirements, while a strong facilitator was the satisfaction to use laboratory results to guide clinical management. (45) Though Malawi and Liberia settings are different in terms of HIV prevalence and maturity of the HIV program, the negative impact generated by the workload may also exist in Liberia.

5.2.2 Specimen collection and transportation

RDTs are generally performed on site, while VL, EID and CD4 will often require samples to be transported to a higher level. In low-resource settings, collection and transportation of biological specimens, requiring complex handling and temperature monitoring, remain challenging. (49)

5.2.2.1 Specimen collection

To perform an HIV RDT, a sample of blood needs to be drawn from the patient, intravenously of via finger prick, the latter making it possible for trained lay providers to collect the samples. (37) (50)

The first molecular testing capacity for HIV VL and EID was established in Monrovia in 2013 with the installation of a Polymerase Chain Reaction ('PCR') machine. Challenges faced with central testing during the Ebola outbreak underlined the need for POC diagnostic systems in order to resolve challenges linked to specimen collection, transportation and long turnaround times. (48)

The introduction of GeneXpert technologies was initiated for the TB program and increased during the Ebola Virus Disease ('EVD') outbreak to improve EVD testing capacity. Difficulties faced by Liberia in implementing molecular HIV testing led to the decision to promote the integrated use of the GeneXpert platforms for HIV, TB and EVD. (48)

The HIV Treatment Guidelines 2020 detail different sample collection procedures: for CD4, whole blood in Ethylenediaminetetraacetic acid ('EDTA') tube needs to be drawn while, for VL and EID, Dried Blood Spots ('DBS') are being used. (47)

To maintain sample stability for CD4 testing, blood collected in an EDTA tube needs to be used within 6 to 48 hours depending on the machine, with temperature control. (47) The short timeline between collection and sample use, coupled with the fact that only 62% of the health facilities have access to a power source (it is not mentioned if the ones with power have a functional refrigerator), could represent a challenge for remote health facilities and a potential threat to sample quality. (3)

For VL and EID, DBS are used for specimen collection. (47) If well packed, DBS specimens can bear extreme temperatures, which represents a significant advantage over other methods of specimen collection (whole blood/plasma) in contexts where transportation systems are weak and cold chain maintenance a challenge. Several surveys comparing VL test results using DBS and plasma have concluded on the strong correlation of ribonucleic acid levels using the two methods. (51) A survey in Malawi however identified that use of DBS for VL testing had significantly higher odds of longer test phase turnaround time (time elapsed between receipt at the laboratory and testing) compared to plasma: this could be due to lack of training, difficulties

of preparation or priority given to plasma specimens due to habit and cold chain requirements. (52)

Finally, a National Rapid assessment of the laboratory system in Sierra Leone also reported that only 13% of the health facilities surveyed had the ability to pack the specimen as per the appropriate guidelines. (53) While we could not find such data for Liberia, the similarity of the contexts could point out to the same difficulties.

5.2.2.2 Specimen transportation

Transport conditions in Liberia are difficult, due to limited tarred roads (6%) and weather conditions (heat, humidity, rainy season leading to impracticable roads), making the transportation of biological specimens as per requirements challenging. (54)

The Joint External Evaluation ('JEE') of International Health Regulations ('IHR') Core Capacities of Liberia undertaken by WHO in 2016 gave a score of 3 (out of 4) to the specimen referral and transport system, underlining a reasonable performance. This scoring reflected the existence of a partnership with the organization Riders-for-Health, which supports the transport of clinical and public health specimens from health care facilities to regionally or centrally based laboratories. (55)

The implementation of the Riders for Health program started out of the Ebola outbreak in March 2015: it includes vehicle fleet management services of the MOH fleet of 534 vehicles (281 motor vehicles, 183 motorcycles and 70 sample courier motorcycles), including the creation of six maintenance hubs across Liberia, and the implementation of a national sample transport system using 60 couriers picking from 302 pick-up points, connecting health centres to the laboratories at the regional level. This system is based on a "Relay system" and "Hub and spoke" method. Entirely funded by USAID, the system sustainability could be challenged, should this funding be stopped. (56)

Centralized and decentralized models both have advantages and disadvantages (see Table 2 - (57)). In Liberia, the use of DBS for VL and EID has allowed for the decision to use an hybrid model, with equipment located at county level. (48) For CD4 and other tests requiring whole blood in an EDTA tube, it is not clear where instruments are located while the requirement of receipt and use of the sample at the laboratory within hours of collection advocates for a more decentralized approach, requiring an efficient sample transportation system. (47)

	Advantages	Disadvantages
Decentralized	• Patients' timely access to diagnostics and results • Current focus on decentralization • Does not limit growth	• Complexity of quality systems • Complexity of instrument service and support • Infrastructure challenges
Hybrid		
Centralized	• Quality is maintained through less complicated means • High throughput, low cost instrumentation is utilized	• Limits for growth • Specimen or patient transport • Complex information systems

Table 2 - Advantages/disadvantages of centralized and decentralized approaches to VL/EID (55)

The NPHIL reports that, in the first and second half of 2017, laboratory results were received respectively within 7 and 4 days of initial alert. (28) The website of the Riders organization mentions that an average of 78% of samples would now arrive at laboratories within 24 hrs of collection, versus 25% before (exact period not mentioned), though no research is available to corroborate this finding for Liberia. (56) In Uganda, the implementation of a similar sample transportation system for EID (creation of hub networks covering 20 to 40 health facilities, one

motorbike and rider per hub) resulted in a decrease of both the sample delivery time and result transit time from 12 days to 5 days. The overall turnaround time went down from 39 to 14 days as laboratory turnaround time was also reduced due to laboratory consolidation efforts. (58) However, we could not find documented evidence through our research that the Riders for Health system was actually being used for sample transportation for the HIV program in Liberia.

Unmanned Aerial Systems (Drones) are increasingly considered as potential delivery system in countries with poor road conditions and extreme weather. A survey done in the US positively assessed the utilisation of Drones for routine transport of chemistry and haematology laboratory specimens, concluding on test results accuracy, though noting reduced precision for some analytes. (59) However, environmental conditions in Liberia are different from the US and sample transport requirements for VL and EID testing different than the ones in the survey so accuracy of VL and EID test results following transportation with Drones in Liberia would have to be tested. In addition, the risk of accidents and unavailability of adequate equipment and packaging to maintain samples at the right temperature should also be considered. (60)

5.3 Analytical phase – Performing an HIV diagnostic test

In this section, we will analyse the availability and quality of the main contributors to the actual performance of the test: human resources, health products, equipment and quality assurance

5.3.1 Human Resource capacity

In its National Health and Social Welfare Policy for 2011-2021, the MOH had projected needs for different category of health cadres for 2021: for the laboratory staff, projected need was for 190 laboratory technicians, 288 laboratory assistants and 415 laboratory aides, hence a total of 893 laboratory-related staff, e.g. 6% out of the expected total need of 15,626 health staff. (61) The revised implementation plan of the Health Workforce Program issued after the Ebola outbreak for the period 2015-2021 focuses on five cadres of health professionals (community health workforce, health managers, midwives, nurses and physicians) which do not include laboratory staff. It makes reference in one instance in the text to a goal of expanding laboratory assistants and physician assistants, but without giving any more detail or plan for it. (62)

An analysis made of Liberia HR investment plan and of the ones similarly drawn by Guinea and Sierra Leone post-Ebola, underlines the budgetary challenges that the plans' intended growth represent in contexts of limited fiscal space but also areas which have to be further worked on and resolved for such investments to bring the expected outcome: uneven distribution of resources between rural and urban settings, ratios between health cadres (doctors to nurses, etc) as well as pre-service training, in-service training and motivation. (63)

Through our research, we could not find any assessment of the number of staff currently employed in laboratory functions in Liberia so we cannot identify in more detail where gaps currently are. We found one assessment of availability of trained laboratory staff for TB in Liberia from a study done in TB laboratories through onsite TB proficiency testing: out of the total 107 TB laboratories, 14 could not participate in the study due to lack of trained staff member able to perform the test (13%); in 40% of the remaining participating facilities (e.g. 35 laboratories, 35% of total), laboratory aides conducting TB testing were not formally trained in laboratory science and were using job aides without full detail of the testing procedures while 12% of facilities had a laboratory technologist, 31% a laboratory technician and 17% a laboratory assistant. (64)

In Liberia, only two pre-service laboratory institutions located in Monrovia and one in Bong county offer laboratory training curriculum in Liberia (two diplomas, one associate and one bachelor degree, number of graduates per year is not known). (23) Retention of staff remains a challenge, with government workers experiencing low wages and delays in salary payment and the difficult conditions experienced in hardship/rural areas. A Health Worker Retention Study is planned in the HR investment plan for 2015-2021 to assess the rates and factors driving retention and attrition. (62)

In Sierra Leone in 2016, an assessment of laboratory staff done in 20 of the 21 government hospitals and 78% of the health centres highlighted that 30% of them did not have a laboratory staff, while being expected to perform clinical diagnostic services with a laboratory worker. In addition, only 30% of the laboratories had staff which were paid by the government, with the rest of laboratories being paid through other sources, including primarily GF. (53)

To address the shortage of healthcare staff, particularly acute in low-resource settings such as Liberia, task shifting has been recommended by WHO. (65)(66) In Liberia, HTS Guidelines issued in June 2020 include HIV screening by community health assistant and promotor, though implementation is not confirmed to have started. (37) A systematic review highlighted high concordance of testing results when performed by laboratory staff or lay providers in South Africa and Malawi, with respectively 23 out of 3896 samples and 4 out of 2911 samples showing discordant results, though the available evidence was found to be limited. (67)

Regarding POC VL testing, a randomized control trial undertaken in an urban clinic in South Africa assessed that implementation of POC VL testing with task shifting versus standard laboratory VL testing led to improve both the viral suppression as well as the retention in HIV care. However all participants came from the same clinic, were enrolled at their 6 months visit (thereby excluding patient not returning to care after ART initiation) and the task shifting was to an enrolled nurse trained for two years versus a registered nurse with a four-year training. South Africa being a high burden country, replicability to other settings with low prevalence, with smaller volumes and different cost implications, would have to be further studied. (68) In Zimbabwe, a cross-sectional retrospective study on 46 sites on implementation of point-of-care for EID reported similar results in terms of internal quality control failure rate and turnaround time between non-laboratory and specialized laboratory-trained operators, hence suggesting task-shifting to nurses can be implemented without compromising testing quality, though the accuracy of test results by both cadres has not been assessed in this study. (69)

5.3.2 Availability of test kits, laboratory products and reagents

The supply chain system is an ecosystem of organizations, technology and activities set up to ensure that a product is made available at the place and time when it is needed as cost-efficiently as possible; it fulfils two goals: delivering the products but also gathering information on needs and consumption for program planning purposes. (70)

Supply chain weaknesses are referred to as a main bottleneck to service delivery, due to frequent stock-out of drugs and health products, in the different strategic plans developed. (14)(35) An audit performed in 2019 by the GF reported that 20 out of the 25 facilities visited were experiencing stock-out of key-commodities for the three diseases (HIV, TB and Malaria) despite stocks being available at central level. Stock-out of HIV commodities was reported in 48% of the facilities visited, with an average stock-out period of 68 days and a maximum of 404 days, while the low rate of utilisation of GeneXpert machines (10%) was attributed to stock-out of cartridges at all facilities. (19) No information is provided in the report on which HIV commodities are exactly taken into account nor on the methodology followed to compute the stock-out, yet findings indicate that constant availability of the required health products is a material issue. Stock-out and procurement delays of EID and VL reagents are also reported as one of the main causes of testing unavailability. (48)

In the South East region, due to the frequent stock-out of laboratory supplies and consumables, a WhatsApp platform set up by the CDOs is in use to identify available stock in case of emergency, underlining challenges faced. (71)

Quantification and procurement

No specific process for a national quantification of laboratory products in Liberia has been identified through our research while, for HIV commodities, a national committee is in charge

of quantification. Procurement of HIV laboratory products funded by GF is done through international procurement agents. (33)

Storage and distribution

The National Drug Service, in charge of storing and distributing medicines and health products acquired by the government of Liberia, moved in 2018 from its historical location within the compound of the JFK Hospital in Monrovia to a new central warehouse built near Monrovia (Caldwell) with international support. Despite having been recently completed, an audit from the GF five months after the transfer of GF-funded commodities to this new warehouse showed that no inventory procedures, tools or management system were in place. The report also underlines that a parallel supply chain management system, managed vertically by the HIV disease program, is in place for laboratory products. (19) The latter points out to significant system weaknesses at central level, raising concerns over the ability of the system to collect and use data for quantification, procurement and planning purposes. At the decentralized level, the low availability of a reliable power source (in 82% of the hospitals, 73% of the health centres and 61% of the clinics) question the likelihood of having well-ventilated storage spaces. (29)

HIV RDTs must be stored in health facilities in the conditions recommended by the manufacturers, generally within a range of between 2 and 25-30 degrees Celsius. While we do not have data on storage conditions in health centres, results of the SARA 2018 indicating that 62% of facilities had a reliable source of power and that basic equipment was not available in all facilities cast a doubt on the fact that all facilities performing HIV testing with RDTs have a well-ventilated storage space, where temperature does not exceed 25-30 degrees. (3) A study undertaken in Malawi on three HIV RDTs concluded that excess temperature (37 degrees during 28 days) did not affect the sensitivity and specificity of the tests. Yet, it should be underlined that this study did not take into account the humidity factor nor the fact that HIV RDTs could be stored at excess temperature during a longer period of time. (72) Furthermore, a systematic review by WHO of rates and causes of HIV misdiagnosis on all continents identified the use of inappropriate, damaged or expired test kits as one of the main contributing factors. (73)

Management information system

Setting up a solid Laboratory Information Management System ('LIMS') is essential to manage inventories, track consumption patterns and needs and ensure timely resupply of health products to avoid stock-outs and expiries. In Liberia, through the DHIS2 system, aggregated data is consolidated for clinical laboratory data; a pilot is underway for an electronic laboratory information system at the NPHRL and another hospital. (23) In Sierra Leone, no specific form or reporting system for laboratory commodity was identified during the assessment done in 2016. (53)

In Ethiopia, in order to address frequent stock-out of reagents and long turnaround time of results to patients, a laboratory logistics management information system was established. (74) While the implementation of this system is mentioned as having significantly reduced stock-outs and turnaround times, an assessment done on 43 facilities highlighted stock-out situations for at least one laboratory commodity in 37% of the facilities, with 61% of them reporting occurrence of stock-out during the last 6 months and 50% not using stock tools/bin cards at the hospital and health centres level, underlining the need for training at decentralized level.

However the sample size was relatively limited and all facilities sampled were located in Addis Ababa. (75)

In Uganda, the National Reference Laboratory has set up an electronic LIMS for EID and VL with ordering of laboratory supplies available online. (34) Malawi also established in 2012 a Laboratory Information Management system (LIMS) to collect laboratory data on all HIV VL and EID tests, which reports, among others, on turnaround times by step of the lab testing process, on rate of rejection, positivity rate. (52) (76)

5.3.3 Availability of functional equipment

The JEE of IHR Core capacities of Liberia in 2016 had concluded that the lack of available functional equipment in the laboratories was a significant challenge in Liberia, with no mechanism in place for maintenance and repair of the equipment. (55)

The choice and placement of instruments required for HIV care needs to be carefully thought through in order to ensure accessibility and cost-effectiveness. (75) A review of harmonization efforts of instruments in HIV laboratory systems undertaken by 8 African countries since the Maputo declaration highlighted varying levels of successes and a common set of recurring challenges across countries, with the greatest diversity of manufacturing brands found for chemistry and haematology, while equipment for CD4 and VL/EID appeared less diverse possibly due to the WHO pre-qualification requirement imposed by international donors funding those equipment. (77) Instrument downtime due to lack of maintenance or servicing is also recognized as a challenge for VL scale-up in Sub-Saharan Africa. (78)

In Liberia, one molecular PCR testing platform (Abbott) is available in Monrovia and GeneXpert machines, able to perform VL and EID testing, are currently placed in the 15 counties. (48) Unfortunately, we could not find information on the number and placement of the CD4, haematology and chemistry machines so no comment can be made on the actual level of brand diversity for these instruments.

In 2015, an article reports that Liberia had two biomedical engineers, which led to prolonged repair times, particularly for equipment located in rural areas or with parts to be replaced. (79) While this represents a low capacity, it does not correlate with the assessment of the JEE of IHC core capacities that no system is in place. (55) After the Ebola outbreak, the MOH has created a new cadre of health professional within the county health teams: fifteen biomedical engineering technician ("BMET"), responsible for the functionality of equipment and supervised by the Health Technology Management Unit of the NDD, were sent for training in Kenya and deployed to each county. (23) (71)

Availability of qualified staff and parts being referred to as major issue for equipment repair, a study of 2529 engineering requests on medical equipment in 60 hospitals located in 11 different countries in Africa, Europe, Asia, and Central America, led to identify that 72% of the equipment could be repaired without import of spare part and that skills required for 66% of them did not need the full skills required from a BMET degree, and recommended the creation of the new profile of biomedical technician's assistant in low-resource settings. (80) However this review did not include complex equipment, such as CD4 or VL/EID machines. Indeed, for the GeneXpert machines installed in Liberia, the absence of an in-country authorized service

provider able to perform regular calibration of the machines has been mentioned as a challenge to optimal machine utilization. (48)

5.3.4 Quality management system

HIV misdiagnosis bears significant consequences, whether it is a false positive diagnosis with severe impact on the patient life or a false negative diagnosis leaving an HIV-infected person unable to receive the care required and at risk of further spreading the disease. Errors in performing tests can also lead to incorrect clinical assessment, inappropriate treatments and worse patient outcome. In Liberia, there is no national system of licensing of public and private laboratories, based on clear standards defined and independent review process. (23)

The JEE of IHR Core Capacities of Liberia gave in 2016 the lowest mark of 1 to the laboratory quality system, with one of the priority action recommended being to actually develop such a quality management system, implying none was actually in place in 2016. (55)

Different factors affect the accuracy of HIV diagnosis with an HIV RDT: the quality of the HIV RDT (both at manufacturing and upon use, after transport and storage), the test selection and algorithm used and the quality of the testing procedure itself. (81) A systematic review performed to assess the causes and extent of HIV misdiagnosis identified rates of false HIV positive rates ranging from 2,6% to 10,3% in three studies and instance of false HIV negative cases (rate of 2% in South Africa, Zimbabwe, Tanzania) in three other studies, though underlining the limited number of studies available. Factors related to poor quality of HIV testing were technical errors such as labelling and recordkeeping, user errors in performing or interpreting the HIV RDT, suboptimal testing strategy and poor management and supervision. (73) In Liberia, until recently, the testing strategy recommended the result of a third assay to rule-in HIV infection as a tie-breaker test, which did not follow WHO recommendations and was identified as a source of misdiagnosis; this has now been revised in the new HTS Guidelines issued in June 2020. (17) (37)

The NPHRL is responsible for the implementation of the quality assurance system, as well as for supervision and monitoring of the four regional public health laboratories and referral testing. (23) Supervision of clinical laboratories at the hospitals, health centres and clinics is the responsibility of the CDOs (no information or assessment on the skillset of CDOs could be found). (82)

External quality assurance ("EQA") forms an integral part of a quality management system and generally consists of a mix of external proficiency testing, external experts supervision and retesting of a subset of specimens in another competent laboratory or site at higher level. (81) In Liberia, results reported from external proficiency testing performed in the TB program were that 75% of the 80 TB sputum microscopy laboratories participating did not have an acceptable result, with only two facilities scoring 100%. Only 31% of the laboratory were keeping slides for rechecking by the TB programme. (64) We have not found evidence through our research that an EQA program was in place for HIV diagnostics in Liberia; supervision activities are referred to in several documents, however we do not know what they entail and could not find evidence of proficiency testing undertaken for HIV diagnostics.

A review of the results of HIV proficiency testing exercises in Zambia over a two-year period highlighted a reduction of incorrect test results from 69 to 31 per 1000 tests. However, the site selection had not been randomly done and targeted sites increased from 550 in the first year to

680 in the second, while response rate also increased from 51 to 71%, in a context of high attrition and turnover of staff. The article mentions however that performance improved among sites that participated in both PT cycles, without providing however any data on this. (83) In Haiti, a review of the implementation of an EQA program for HIV RDTs between 2006 and 2011 reported an increase in the number of laboratories reaching a score above 80% from 49 in 2006 to 145 in 2011 (out of a total enrolled throughout the program of 680). While these results demonstrate an improvement in the overall level of proficiency, despite the laboratories not being consistently the same responding every year, it is unclear how the score of 80% as "proficient" has been set, given that a score below 90% is generally considered as unacceptable. (84)

Liberia HTS Guidelines plan that internal quality assurance be performed (i.e.etesting by another provider within the same facility for an agreed % of tests performed) and that proficient testing be implemented on a national scale for all HTC counsellors under supervision of qualified laboratory personnel. (37) No data could be found to ascertain whether this is taking place, and, if so, with which results.

Recognizing challenges faced in low-resource settings and the low number of laboratories meeting internationally-recognized accreditation, WHO and partners designed the WHO AFRO Stepwise Laboratory (Quality) Improvement Process Towards Accreditation (SLIPTA), which is a framework for clinical, medical and public health laboratories in developing countries, aiming at achieving the requirements of the International Organization for Standardization (ISO) 15189 clinical laboratory standard. (85)

Early 2017, the MOH of Liberia started to implement the SLIPTA: two cohorts of trainees attended the initial training (staff from NDD, NPHRL, CDOs, laboratory supervisors of county hospitals). (15) Subsequent audits took place in eight county hospitals and two regional hospitals, which highlighted major gaps and weaknesses at all level (scores not available). (23) The German cooperation is currently supporting eight county hospitals in the South East region with mentoring through regular visits and group trainings and has reported that 3 hospitals had reached in 2019 a one star rating (out of a maximum of 5). (72)

The Strengthening Laboratory Management Toward Accreditation (SLMTA) programme, is a competency-based programme based on workshops, supervision and mentoring, aiming at creating quick and practical laboratory improvements, measured at entry and end by a SLIPTA audit. A review of the implementation of this programme in 302 laboratories in 47 countries in Africa, the Caribbean Region, Central and South America, and Southeast Asia, showed an increase in checklist scores (from 39% at baseline to 64% at exit) during the programme time between 2010 and 2013. However data was not yet available for more than half of the 617 laboratories enrolled in the programme which had not yet finished it and sustainability of the progress beyond the program could not be assessed. (86)

5.4 Post-analytical phase – How test results are used

Laboratory results are important to most medical decisions. In this section, we will review the communication of laboratory test results to clinicians and patients as well as how they are taken into account to determine patient care.

5.4.1 Communication of test results to clinicians

While rapid communication of laboratory test results is essential to optimize patient care, our research identified limited data related to communication of test results to clinicians in Liberia. One retrospective study of GeneXpert testing data for HIV VL over the period December 2015 to March 2017 reported a short turnaround time of one day between the moment the sample arrived at the laboratory and the time test results were received by the requesting unit. However, the article does not specify whether samples tested were coming from the facility performing the test or whether they had also been received from other facilities as well. (48) The absence of data on HIV patients with suppressed VL in the Liberia 2019 UNAIDS Factsheet underlines difficulties faced in obtaining reliable data for that intervention. (16)

On its website, the organization Riders for Health reports that, in Liberia, test results are communicated by email or text message from the laboratory to the rural community health center. (56) The 2018 SARA highlighted that only 77% of the 36 hospitals, 31% of the 58 health centres and 7% of the 671 health clinics had a computer with internet while availability of communication equipment was higher (88% of the 36 hospitals, 63% of the 58 health centres and 51% of the 671 health clinics). (3) Based on this assessment, it is not clear how rural community health centres receive such communication, though one explanation could be that private mobile phones of staff are used, which may not have been considered as facility communication equipment in the survey, raising therefore potential privacy concerns.

In a cross-sectional study undertaken in one hospital in Ethiopia, 7% of the errors in the total testing process were attributed to excessive turnaround times and lack of timely reporting of critical values. (87) In a study done in Malawi, the turnaround time for HIV VL testing was negatively associated with the use of DBS instead of plasma as well as with certain months and certain laboratories. (52)

Regarding EID, a systematic review of factors associated with accessibility of EID services in sub-Saharan Africa identified the long turnaround time for PCR test results as a barrier to implementation, with median time between sample collection and results communicated to the attending health worker being between 1,3 and 7,7 months in the studies performed. (88) In South Africa, a survey across primary health care physicians reported that late receipt of the laboratory test results represented a challenge for 51% of the physicians surveyed. (89)

5.4.2 Communication of test results to patients

Results from the Demographic and Health Survey 2019-2020 in Liberia highlight that 4,3% of the women surveyed and 1,7% of the men surveyed had been tested but had not received their results. (17)

Liberia HIV Treatment Guidelines require to actively communicate to a patient, by phone or through a home visit, any detectable VL results (above detection limit, even if <1000) as soon

as the result is received at the site. (47) We have not been able to identify data related to the communication of results to patients in Liberia; as a proxy, we have considered that patients enrolled in care and who have been lost to follow-up would not be able to receive their test results.

In 2019, an audit done in 25 health facilities reported that 49% of the patients who were initiated in care during or before 2018 were classified as Lost to Follow-up, which is due to many different factors which we will not study here. (19) As of April 2016, estimates for retention among patients initiated on ART was reported to be 69.9% at 12 months compared to 24.7% among patients not on ART, with these rates going down to 56.8% and 14.3% at 24 months, and to 48.7% and 9,4% at 36 months. (90) In a study done by the NGO Partner in Health to measure the impact of its community health interventions, which include socio-economic support, in three health facilities in Maryland county, lost to follow-up rate is reported as being 36% in 2013 (before Ebola) and 14% in the first semester of 2015 (after Ebola but still pre-intervention) while the post-intervention rate went down to 8%, showing a significant improvement in retention. (91)

A systematic review of retention in care after antiretroviral therapy initiation covering the period 2008-2013 in low- and middle-income countries led to an estimated 36-month retention at 65% in Africa, 80% in Asia, and 64% in Latin America and the Caribbean. With 49% after three years, Liberia is performing lower than the average reviewed in all regions. (92)

The low retention rates reported raise concern about treatment adherence and development of drug resistance. As retention was lower for patients which were not on ART, the adoption and implementation of Test and Treat in Liberia may positively impact the overall retention rate going forward. (90)

5.4.3 Impact of test results on treatment

With Test and Treat, a positive HIV diagnosis should lead to immediate referral to an ART Center for treatment. In Liberia, as of 2018, 495 facilities were offering testing services and 245 ART services, which means need for referral to another site, thereby creating the risk to lose patient before they enrol into care. (3) At the end of 2019, 15 000 people living with HIV were on ART following their positive diagnosis. (16)

A review of facility-based registers in 8 health centres in Rwanda identified that only 42% of the patients having tested positive to HIV had enrolled in care within 90 days of the HIV diagnosis and that the presence of an ART clinic at the HIV testing site was positively contributing to increase enrolment. (93)

Being able to interpret test results, considering clinical history, physical examination and symptoms, is essential to assess changes to make to a patient treatment. A survey across primary health care physicians in South Africa in 2015 reported difficulties in interpreting test results in 17% of diagnostic encounters while a similar survey in the US resulted in such difficulties in 8% of the cases, though the response rate in the US survey was low (5,9% of 1 768 physicians surveyed). (89) (94) In the US survey, weekly collaboration/communication with laboratory staff was happening for only 6% of the physicians while the South African survey identified interpretive comments from the laboratory, published guidelines and the existence of a dedicated laboratory phone line as contributing to increased use of the test results. (89) (94) An exploratory study done in 4 health facilities in Tanzania also highlighted limited

collaboration and communication between clinician and laboratory professionals, with differences in education levels causing clinicians' mistrust in the laboratory test results, though sample size was small and interviewees limited to the ones present onsite. (95)

Receipt of VL results is critical to monitor treatment efficacy and identify early on potential drug resistance. A cross-sectional study performed in 2013 in two hospitals in Monrovia on patients on ART for more than one year and presenting clinical and/or immunological failure highlighted high prevalence of resistance-associated mutations of 63% and 71% among the tested group. However, this study only included patients who presented signs of treatment failure. In addition, patients were attending two major hospitals providing care and treatment for PLHIV, which cannot be considered representative of the health facilities situation in Liberia, at a time when VL testing was not yet operational in Liberia. (96)

Identifying early potential drug resistance is critical to optimize switches to second-line regimens and minimize transmission of HIV drug resistance. A study done among 116 newly HIV-1-infected patients at one hospital in Monrovia assessed the prevalence of Transmitted Drug Resistance in recently diagnosed and untreated patients at 5,9% in 2014. (97) In Sierra Leone, a study done on 215 patients in November 2017 in one hospital in Freetown reported even higher disturbing drug resistance rates of 22.4% for ART-naive patients and 56% for ART-experienced patients. (97) Differences between the drug resistance rates between the two countries may be due to the fact that the Liberia study was performed pre-Ebola and the Sierra Leone one post-Ebola, with potential disruption of treatment during the Ebola crisis a potential source of increased drug resistance.

6. Discussion

Multiple factors, at the governance, strategic and operational levels, affect the delivery of HIV diagnostic services in Liberia. We will discuss below positive aspects and barriers identified, as well as lessons which can be learnt from other countries.

Governance, strategy and network design

On the laboratory system side, positive steps have been noted recently with the creation of the NPHIL end 2016 as well as with the development in 2019 of the National Laboratory Policy and the Five Year Strategic Plan for the National Health Laboratory System. However, while a National Strategic Plan is available, the absence of a costed action plan reduces the chances of a coordinated and prioritized implementation. (23) In addition, if the recent set-up of the NPHIL has made the separation between public health and clinical laboratory operations clearer, the NDD, responsible for the supervision of the clinical laboratory operations in the MOH, seem to be missing key-attributes to perform its mission such as budget development, control on funding and supply chain resources and decisions. (23) This seems important as a review of national health policies and plans from 39 sub-Saharan African countries of the period 2010 to 2012 resulted in a recommendation to pursue efforts for the creation of a Directorate for Laboratory Services to ensure adequate prioritization of laboratory strategic activities. (30) Within the MOH, the lack of participation of the NDD in the 2015-2020 HIV strategic development process highlighted the absence of coordination, essential to ensure quality HIV diagnostics. (35)

The absence of clear definition of the testing menu to be available at each tier of the laboratory system, based on needs (both for clinical diagnosis including HIV and surveillance), and on the mapping of existing capacity, does not set a clear framework for HIV diagnostic operations. (23) When discussing network optimization, the options to use a centralized or decentralized system carry distinct advantages and disadvantages, with the centralized model making it easier to have qualified staff and implement a quality management system, and the decentralized model more favourable to shorter turnaround times and with reduced need for sample transportation. (57) Regarding HTC, services are decentralized at the health facility level, which seems appropriate given the need for immediate turnaround time and referral to care. (37) For HIV VL and EID testing, Liberia has made the hybrid decision to integrate the use of the GeneXpert equipment with TB and EID at the county level while maintaining PCR molecular diagnostic capacity at central level (for other tests required to ensure the clinical monitoring of PLHIV, we could unfortunately not find data regarding the current situation). (48) Given challenges linked to road transport and availability of specialized staff, such placement appears reasonable.

Operational set-up for delivery

In Liberia, in 2018, 36 hospitals (100%), 50 health centres (86%) and 409 clinics (61%) were offering HTC, meaning that these services are not available to all Liberians. In addition, only 20% of the health facilities offering HTC had all 5 tracer items for HTC available. (3)

Referral for care from sites performing HTC is required as 245 sites are providing ART services in 2018, i.e. 49% of the number of HTC sites, which results in a risk to lose patients to follow-up. (3) In the KP program started in 2016, 41% of positive cases identified were not initiated on ART. (19)

For the PLHIV in care and treatment, access to CD4 and VL testing seems very limited with only 4% and 12% of patient file with documented results in the 2018 SARA, which could be due to insufficient knowledge of existing services, lack of training of staff and inefficient sample transportation system. (3) Retention remains a significant issue, with only 49% of patients initiated on ART estimated to still be in care after 3 years in 2016, well below the regional averages. (90)(92) Though multiple factor outside of the laboratory area affect retention, the inability to adequately perform clinical biological monitoring and reported stock-out of HIV commodities may have contributed to the low retention of patients in care.

Limited availability of qualified staff in Liberia, with a health workforce density estimated at less than half of WHO recommendation, and retention issues, impact service delivery. (2) We could not find evidence of an assessment of the laboratory staff currently in function, and the laboratory cadre was not included in the revised implementation plan for 2015-2021 issued after the Ebola outbreak. Evidence found from a TB proficiency testing study identified that 13% of the laboratories part of the study did not have staff able to perform the tests while task-shifting to laboratory aides which had not been trained was occurring in 35% of them. (64)

For HTC to general population, with the challenges faced in Liberia, implementation by community health volunteers, which a systematic review assessed as reaching higher coverage than facility-based HTCs, could be explored. (39)(40)(46) In doing so, Liberia can learn from its own experience with the Key-Population program, in which peer counsellors are performing HTC with referral to specific Drop-in Centres established for these target groups, and for which issues linked to lost to follow-up and quality assurance have been noted. (19) It can also build on the pilot program of Partner in Health in the South East Region which has concluded that active support of HIV+ people on treatment by community health volunteers had a positive impact on retention. (91)

For VL testing and EID, countries such as South Africa and Zimbabwe have introduced task-shifting with point-of-care equipment, with positive results on retention rate and VL suppression and no identified negative outcome on quality. Though Liberia is a low HIV prevalence setting facing different challenges in term of number of patients and number of VL tests than South Africa and Zimbabwe, those findings can be worth considering, in a context of specialized staff shortage. (68)(69)

Major supply chain and logistic issues affect the delivery of HIV diagnostic services in Liberia. Almost half of the facilities visited by the GF during its audit of Liberia grants were experiencing stock-out of HIV commodities, while the low utilization rate of the GeneXpert machines (10%) was attributed to stock-out of cartridges at all facilities. Weak inventory management practices at the central warehouse, lack of national quantification for laboratory products and the absence of a laboratory LMIS, impact the ability of the system to adequately plan the supply and to monitor stock levels to prevent stock-outs. (19) Ethiopia and Uganda have implemented electronic LMIS respectively for laboratory commodities and HIV and VL testing, with report of reduction of stock-out and turnaround time reduction. (34)(74) Given the limited computerization of health facilities in Liberia, implementation up to the health facility level appears difficult but could be considered up to the county level.

The creation of a new cadre of workers called ‘biomedical engineering technician’ testifies of the challenges faced and importance given to ensuring all equipment remain functional. (23) However, while these BMET staff may be able to fix laboratory standard equipment, it may not be the case for more complex equipment, as illustrated by calibration issues faced for

GeneXpert machines. (48) Liberia being a relatively small country with limited equipment, the in-country presence of a local representative tasked by the manufacturer to service the equipment is not guaranteed and joining efforts with neighbouring countries to secure timely support may be a way forward to prevent down time. Buying reagents under a service contract, including maintenance, as suggested by HIV donors, could also be considered though no documented evidence that downtime has reduced thanks to that has been found. (78)

The implementation of the Riders for Health sample transportation program in Liberia following the Ebola outbreak in March 2015 is reported to have reduced laboratory test result turnaround time for public surveillance to 4 days following the initial alert. (28) While no evidence could be found that this system is fully in use for clinical HIV samples in Liberia, the implementation of the same program in Uganda for VL and EID resulted in a decrease of both the sample delivery time and result transit time from 12 days to 5 days. (58)

The lack of evidence of implementation of an EQA program for HIV diagnostics is of concern, given the implementation of decentralized/hybrid approaches and increased recourse to task-shifting, in a context of HTC expansion and intended scale-up of VL and EID testing. Different studies have underlined the benefits brought by strong EQA programs in reducing diagnosis errors and increasing motivation of health workers. (83) (84) The beginning of implementation of the SLIPTA program is however a positive development, as a study assessed positively the results of its implementation in 302 laboratories in 47 countries where it had taken place. (86)

Limited information is available regarding the communication of diagnostic tests to health workers and patients in Liberia (only information available is from the DHS survey 2019-2020 in which 4,3% of the women and 1,7% of the men surveyed did not receive the result of their HIV RDT after being tested). (17) With a quick turnaround time identified as a key element to ensure testing is done and results are used, the implementation of instant communication methods, such as text messages, emails, to communicate test results would beneficially impact the program, provided privacy concerns are addressed, though possibility to do so may be constrained by existing communication equipment at facility level. (3)

Limitations

An important limitation of this study is the lack of publicly available data and research done in Liberia, which has led me to use proxies and research from neighbouring countries to inform the analysis. Time available, with work and family life, has also been a constraint as well as lack of opportunity to validate results with key-informants in country.

7. Conclusion

The absence of a structured National Laboratory System and the limited importance given to laboratory matters in the HIV NSP point out to a relative neglect of the laboratory issues until the Ebola outbreak.

Since then, progress has been noted on several fronts, with the creation of the NPHIL, development of policy and strategy documents for the laboratory system, implementation of the Riders for Health sample transportation program and the integration of GeneXpert machines for HIV, TB and EVD at county level. However, despite this progress, significant problems remain.

The absence of a clear accountability framework and costed plan to implement activities of the Strategic Plan for the National Laboratory System questions its future operationalization, which is essential to structure and optimize the laboratory network and bring much needed improvements, including increased coordination between the different governmental actors.

Major logistic and supply chain issues, leading to frequent stock-outs of health products and equipment downtime, need to be addressed to ensure no testing opportunity is missed and quality of services can be guaranteed, in a context where EID and laboratory monitoring of PLHIV remain vastly underperformed. Shortages of qualified laboratory staff have to be quantified and strategically addressed through curriculum development and/or further task-shifting, together with implementation of a strong quality assurance component.

Finally, scarcity of available literature for Liberia identified during the review calls for action to fill the knowledge gaps, in particular regarding implementation of PITC, laboratory practices at health facility level and quality assurance activities implementation.

8. Recommendations

- To the MOH of Liberia:

    1. Develop a costed action plan to implement the National Strategic Plan for the laboratory system, including responsible parties; map existing contributions, and prioritize remaining gaps; definition of a testing menu per tier of the system and identification of HR gaps should be considered as priority actions;
    2. Prioritize plans to strengthen the laboratory supply chain including: (i) inventory management, (ii) national quantification, (iii) LIMS implementation; (iv) equipment inventory and maintenance plan and (v) assessment of the HIV sample transportation system for integration with the Riders for Health program;
    3. Develop an Operational Research agenda to address implementation of PITC, testing turnaround times, and laboratory practices at health facility level (ordering, sample collection, return and use of test results);
    4. Consider point of care testing at the community level to increase HTC coverage.

- To the NPHIL / NPHRL:

    5. Establish a strong quality assurance program, in close coordination with the MOH and ensure close coordination with the clinical laboratories;

- To health service/ laboratory managers:

    6. Ensure ordering of the laboratory tests follow HIV testing and treatment guidelines and adequate documentation;
    7. Monitor and document turnaround times, from test ordering to return of results; encourage dialogue between clinicians and laboratory staff to improve interpretation of the test results;
    8. Set up internal quality assurance mechanisms to detect potential mistakes., including ensuring task delegation in case of qualified staff shortages.

- To the donor community:

    9. Consider contributing to the financing of the Laboratory Strategic Plan, once a more detailed prioritized budget is available;
    10. Advocate for a stronger National Diagnostic Division with an increased mandate in terms of budget and resources management.

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