Title: The Feasibility and Acceptability of a New Fluorence Microscopy Technology for TB Diagnosis in Fragile States: A Somaliland Case Study

Author: Halima Mohamed

Supervisors:

Professor Anne Mills

Professor Mishal Khan

Thesis submitted in accordance with the requirements for the degree of Doctor of Philosophy

University of London

2021

Department of Global Health and Development

Faculty of Public Health and Policy

London School of Hygiene & Tropical Medicine

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Name: Haliam Mohamed
Student ID: 254039
Signed: Halima Mohamed
Dated: 17/06/2021

Acknowledgements

My deep-felt gratitude goes to my supervisor Professor Dame Anne Mills for her outstanding guidance, professionalism, and encouragement throughout the course of this work, without which I could not have done it. Professor Dame Anne Mills, thank you very much for your patience, understanding and unconditional and outstanding support, and most importantly for believing in me and the importance of my work and making sure that I finished my degree. I would like to thank Dr Katherine Fielding who provided useful statistical input and made a valuable contribution to my thesis writing. Special thanks to Drs Mishal Khan and Laura Hammond for their critical comments and constructive feedback on the structure, content and the quality of thesis writing, which I needed the most.

Many thanks to the Research Degree Coordinator for all the support I received during my study at the School. My special thanks to the Degree Program Coordinator Office staff for their extensive support throughout my study period. My sincere thanks to the Transferable Skills Instructors at the LSHTM Library for their help with thesis writing methods, styles and the use of research tools and statistical software for data collection and interpretation of results throughout the entire time of my research.

Abstract

Background: Tuberculosis is a growing public health problem and one of the major causes of death globally, killing close to 1.5 million people each year and infecting another 10.4 million, particularly in settings with weak health systems. The best way to cut TB transmission is to identify infectious TB cases early, in order to diagnose and treat them effectively. To overcome the growing TB challenge, global control efforts have shifted from disease burden reduction to eradication, with the gradual introduction of robust diagnostic technologies in high TB burden countries (HBCs), including fragile states. One such technique was the light-emitting diode fluorescence microscopy (LED). However, empirical evidence linking LED with feasibility and acceptability for regular utilization in fragile states appeared lacking.

Aim: The primary aim of this study was to help improve access to good quality care (diagnosis and treatment) for TB patients in fragile states, specifically in the north-west of Somalia (Somaliland) which had introduced and implemented LED technology for regular TB testing at primary care facilities as a pilot intervention.

Methods: The study utilised a theory-informed mixed method approach for data collection and analysis and included systematic literature review, analysis of routine data, key informant interviews and facility observations.

Findings: The literature review revealed a weak relationship between LED technology usage and increased TB case detection in resource-poor and fragile health system settings, but otherwise little evidence of feasibility and acceptability. The analysis of routine data on LED implementation and use found no difference in the proportion of patients with negative and positive outcomes between LED and the traditional ZN technology. Iinterviews with facility staff found health workers' attitudes, perceptions and opinions on LED use generally positive. However, staff attitudes were largely negative toward the future introduction and implementation of new technologies for routine utilisation without improving the systematic and programmatic readiness of the existing health system. Interviews with policy-makers identified serious resource, structural and environmental constraints to the feasibility of LED use in fragile health systems.

Conclusion: This study is the first of its kind in a fragile state to assess the feasibility and acceptability of LED, and shed light on constraints to both feasibility and acceptability of new technologies such as LED. The findings of this study add to an existing body of knowledge from other settings related to the diagnostic performance and operational feasibility of LED as a diagnostic strategy to improve patient access to quality TB diagnosis.

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List of abbreviations

AFRO	**African Region of World Health Organization**
AFB	Acid Fast Bacilli
AUCDC	African Centre for Disease Control, African Union
CDC	Centre for Disease Control and Prevention
CI	Confidence Interval
COOPI	Cooperazione Internazionale
DOTS	Directly Observed Treatment Short-Course
EURO	European Region of the World Health Organization
EMRO	Eastern Mediterranean Region of the World Health Organization
ETS	End TB Strategy
EPTB	Extra Pulmonary Tuberculosis
EQA	External Quality Control
FP	False Positive
FN	False Negative
FS	Fragile States
FBP	Fund-Based for Peace
GF	Global Fund
HCWs	Healthcare Workers
HPs	Health Professionals
HIV	Human Immunodeficiency Syndrome Virus
HIV-TB	HIV-Tuberculosis
HBCS	High Burden Countries
IQA	Internal Quality Control
IQRs	Interquartile Range
IAF	Impact Assessment Framework
KIs	Key Informants Interviews
LMICS	Low and Middle Income Countries
LSHTM	London School of Hygiene & Tropical Medicine
LED	Light-Emitting Diode Fluorescence Microscopy
MeSH	Medical Subject Headings
MDGs	Millennium Development Goals
MDR-TB	Multi-Drug-Resistant Tuberculosis
MOH	Ministry of Health

NGOs	Non-Governmental Organizations
NTP	National TB Program
OR	Odds ratios
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PLHIV	People Living with Human Immunodeficiency Syndrome Virus
PTB	Pulmonary Tuberculosis
PSR	Physicians of Social Responsibility
QC	Quality Control
QI	Quality Improvement
QA	Quality Assessment
QUADAS	Quality Assessment for Diagnostic Accuracy Studies
RR	Rifampicin Resistant
SEARO	South East Region of the World Health Organization
SSIs	Semi-Structured Interviews
SF	State Fragility Index
STS	Stop TB Strategy
TAM	Technology Acceptance Model
THE UNION	International Union Against Tuberculosis and Lung Disease
TP	True Positive
TN	True Negative
TB	Tuberculosis
WHO	World Health Organization
WEPRO	Western Pacific Region of the World Health Organization
WV	World Vision
WHO-STOP	World Health Organization Stop Tuberculosis Partnership
TB	Tuberculosis
ZN	Ziehl Neelsen

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Chapter One: Introduction to tuberculosis, tuberculosis control, fragile states and Somaliland

1.1 Introduction

This chapter provides a descriptive background of tuberculosis (TB) as an infectious disease, including its transmission and prevention as well as a brief overview of current global TB control strategies[1, 2]. Tuberculosis (TB) is a growing public health problem, and a leading cause of death from a single infectious disease agent globally[3-5]. TB is caused by *Mycobacterium tuberculosis or M. tuberculosis,* and if not properly treated one person with the disease can pass the disease to others[6]. The World Health Organization (WHO) estimates that 10 million people fall ill and 1.5 million die of TB annually worldwide respectively[7]. Not only does TB kill, it also destabilizes the livelihoods of families and communities around the world[2-4, 8]. The most effective way to cut TB transmission is to find, diagnose and treat infectious cases early and effectively. Improving access to good quality, reliable diagnosis and treatment for those affected by TB is key to achieving this goal[9, 10].

Over the last few decades, global control efforts have mainly focused on TB burden reduction in the so-called "high TB burden countries" (HBCs)[3, 8] [11]. However, TB also presents major public health crises in fragile states (FS) – that is, countries with complex political, social and economic instabilities. Empirical evidence on TB control challenges in fragile states is presently lacking in the current TB literature. Section two of this chapter presents a brief description of TB, different types of TB and the transmission of the disease. Sections three to five provide a brief overview of the current global TB burden problem and describe different Stop TB control strategies, including the End TB Strategy for 2015-2035. Sections 6 and 7 discuss the use of rapid TB diagnostic technologies and control challenges in fragile states. Sections 8 and 9 provide a brief description of Somalia as a fragile state and discuss the burden of TB in Somaliland, focusing on the adoption, introduction and implementation of new diagnostic technologies for TB diagnosis in these settings. The last sections of the chapter present a brief overview of the thesis, aims and objectives, and research questions.

1.2 A brief description of tuberculosis

The signs and symptoms of TB include weight loss, a persistent cough lasting more than three weeks, fatigue and night sweats[12]. In most cases, a person with latent TB might not show any signs or symptoms of TB but can still pass the disease to others[12].

There are two known forms of TB: 1) *pulmonary tuberculosis* (PTB) and 2) *extra-pulmonary tuberculosis* (EPTB). These types of *M. tuberculosis* affect different parts of the human body with varying severity, infectiousness and symptoms[13, 14]. The most common form of *M. tuberculosis* is pulmonary tuberculosis[14]. Pulmonary TB (PTB) mostly involves the lungs, but can also affect other organs of the body such as the brain, intestine, kidneys or spine[15]. Approximately 60-80% of clinical disease is PTB worldwide[2]. The PTB disease might result from primary infection (i.e., the first time the host experienced the infection) or secondary infection (i.e., resulting from a reactivation of latent infections, sometimes from people who have had prior TB infections)[12, 16].

TB is an airborne disease that is transmitted through inhalation when an infected person spits, coughs or sneezes into the air[17]. If left untreated, a person infected with TB can transmit the disease to 10-15 people a year[3, 12, 18]. Conditions contributing to person to person TB transmission include the infectiousness, frequency and duration of exposure and the socio-economic and environmental conditions of the infected person[11, 12]. One of the most effective ways to cut TB transmission is early and rapid diagnosis and effective treatment of all infectious cases[19].

1.3 The global burden of tuberculosis

In 2018, the WHO estimated that 10 million and 1.6 million people were infected and died of TB worldwide respectively[6]. While the burden of TB varies across countries and regions from fewer than five to more than 500/100K population, on average 133 new TB cases were reported annually per 100K population globally (Table 1.1 & Figure 1.1)[7].

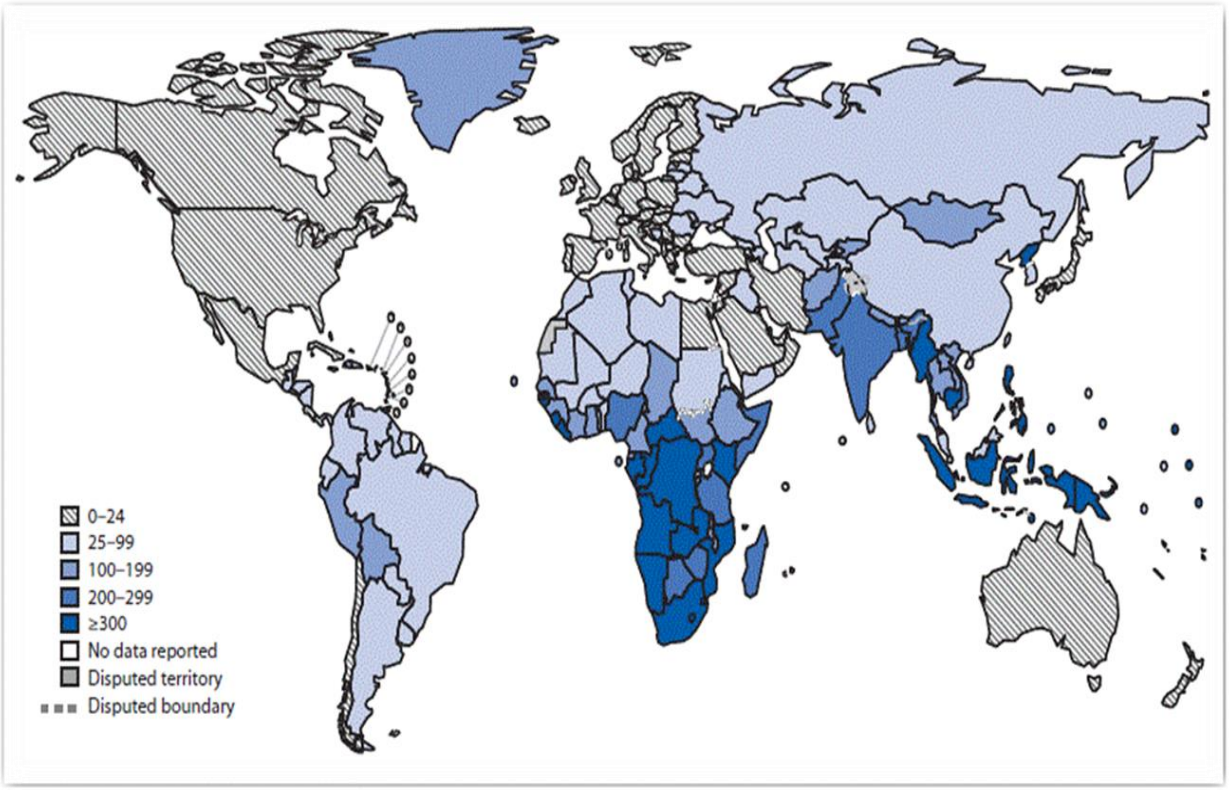

Figure 1.1 ***Estimated tuberculosis incidence worldwide***
Source: *WHO TB Report 2017*

Whilst the true burden is unknown, WHO estimates that two million new cases of childhood TB occur each year worldwide[2]. Of these, 1.1 million (10% of the world TB infections) are in children under five years of age[20-22]. Although TB affects people of all sexes and ages, the highest TB burden levels are in males aged 15 years and over. These accounted for 57% of all TB cases compared to 32% in females and 11% for children under 15 years. People living with HIV (PLHIV) accounted for 8.6% of all TB cases reported worldwide. TB was also the leading cause of death among PLHIV with 0.3 million deaths reported annually in the world (Table 1.1)[7, 22, 23].

Table 1.1 ***Estimated number of incident tuberculosis (TB) cases, incidence, and percentage of deaths among all TB cases, TB cases among persons with human immunodeficiency virus (HIV) infection, and rifampicin-resistant (RR) or multidrug-resistant (MDR) TB cases, by World Health Organization (WHO) region – 2018***

WHO region	All TB cases			TB cases among persons with HIV infection			RR or MDR TB cases		
	No. (x1,000)	Incidence*	Deaths, no. (x1,000) (fatality§)	No. (x1,000)	Incidence†	Deaths, no. (x1,000) (fatality§)	No. (x1,000)	Incidence*	% RR or MDR among all TB cases
Global (all regions)	**10000**	**133**	**1570 (15.7)**	**920**	**2.4**	**300 (32.6)**	**558**	**7.4**	**5.6**
AFRO	2480	237	665 (26.8)	663	2.5	252 (38.0)	90	8.6	3.6
PAHO	282	28	24 (8.5)	30	0.87	6 (20)	11	1.1	3.9
EMRO	771	113	92 (11.9)	9.8	2.5	3 (30.6)	41	6.0	5.3
EU	273	30	29 (10.6)	33	1.4	5 (15.2)	109	12.0	40.0
SEARO	4440	226	666 (15.0)	152	4.2	28 (18.4)	192	9.7	4.3
WPRO	1800	94	97 (5.4)	31	2	5 (16.1)	114	6.0	6.3

* Cases per 100,000 populations.
† Cases per 100 persons with HIV infection.
§ Per 100 TB cases.
ǂ Source**:** https://www.cdc.gov/mmwr/volumes/68/wr/mm6811a3.htm. Accessed on March 5th 2020.

Geographically, low and middle-income countries (LMICs) are hardest hit by the TB epidemic. Nearly 91% of TB new cases occurred in the South-East Asia (44%), Africa (24%) and the Western Pacific (18%) regions, with much smaller percentages in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%). Over 95% of TB deaths were reported in the South East Asia (SEARO) and Sub-Saharan Africa (AFRO) and Western Pacific (WPRO) Regions (Table 1.1)[2, 3, 5].

In 1998, the WHO introduced the concept of high burden countries (HBC). This has been widely used in the context of TB to track disease levels and distribution, and to help focus control interventions in countries reporting 80% of the global TB incidence [24-26]. This concept was later used for HIV/TB and MDR-TB infections and co-infections reporting. By 2015, three types of HBC lists had emerged and were used to estimate TB, HIV-TB co-infections and MDR-TB burden levels [3, 26].

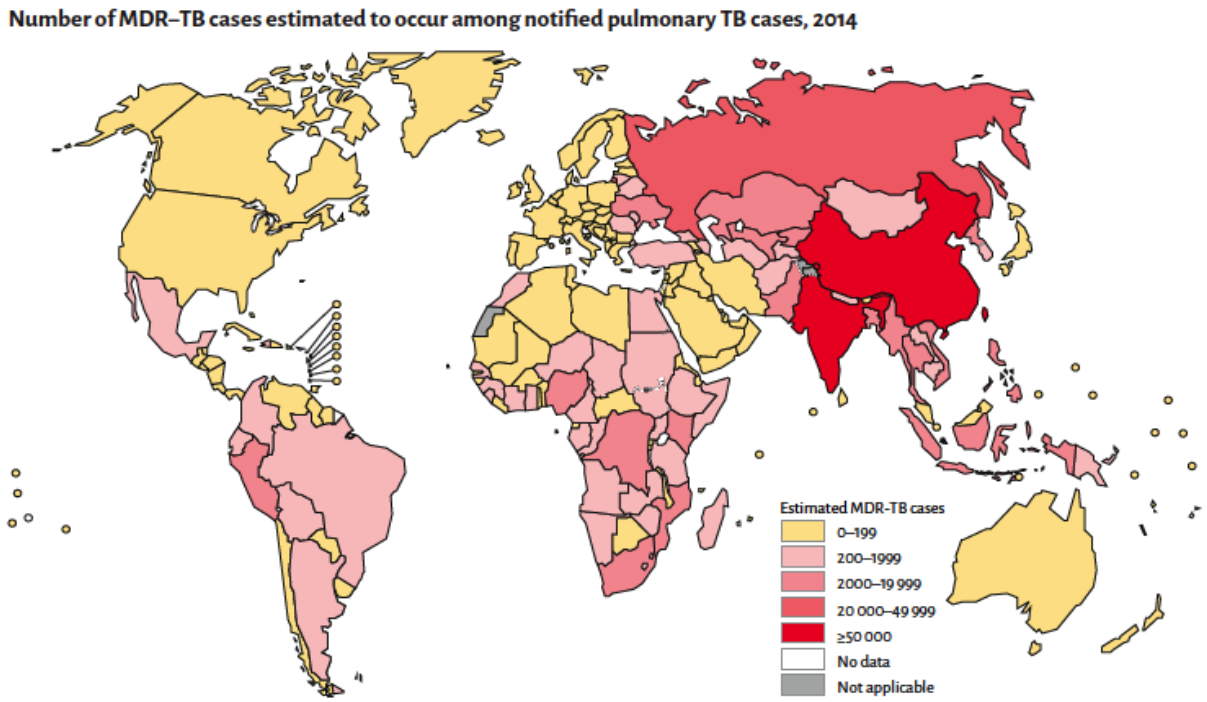

Figure 1.2 ***The estimated number and distribution of new MDR-TB cases reported in 2014.***
Source: WHO: Global tuberculosis report 2014 (who.int).

In 2019, 28 out of the 30 HBCs with the highest TB-HIV infection and co-infection rates were in the AFRO and SEARO regions [27]. The proportion (40%) of TB cases with multi-drug-resistant (MDR-TB) and Rifampicin-resistant (RR) TB were highest in the EURO region (Table 1.1) [7]. The AFRO region reported the highest proportion (27%) of TB cases among PLHIV (Table 1.1) [3, 28, 29].

Table 1.2 Estimated incidence of MDR/RR-TB in 2018 for top 30 high MDR-TB burden countries, WHO regions and globally

	Estimated % of new cases with MDR/RR-TB		Estimated % of previously treated cases with MDR/RR-TB		Incidence of MDR/RR-TB				
Country	***Best estimate[b]***	***Uncertainty interval***	***Best estimate***	***Uncertainty interval***	***Number (in 1000s)***	***Uncertainty interval***	***Rate[c]***	***Uncertainty interval***	***% of RR-TB with MDR-TB***
Angola	2.4	1.1–4.2	15	11–19	3.9	1.7–7.1	13	5.4–23	84
Azerbaijan	12	11–13	26	24–27	1.3	0.94–1.6	13	9.5–16	73
Bangladeshd	1.5	0.9–2.3	4.9	3.0–7.9	5.9	3.2–9.6	3.7	2.0–5.9	99
Belarus	37	34–39	69	66–73	1.4	1.0–1.7	14	11–18	100
China	7.1	5.6–8.7	21	20–21	66	20–21	4.6	3.5–6.0	74
DPR Korea	2.2	0.82–4.2	16	9.1–25	5.2	2.5–8.8	20	9.9–34	88
DR Congo	1.7	1.1–2.6	9.5	8.8–10	6.0	3.0–10	7.2	3.6–12	55
Ethiopia	0.71	0.62–0.80	16	14–17	1.6	1.0–2.2	1.4	0.96–2.0	100
India	2.8	2.3–3.5	14	14–14	130	77–198	9.6	5.7–15	69
Indonesia	2.4	1.8–3.3	13	9.0–18	24	17–32	8.8	6.2–12	99
Kazakhstan	27	26–28	64	63–66	4.8	3.0–6.9	26	16–38	59
Kenya	1.3	0.74–2.0	4.4	3.7–5.2	2.3	1.1–4.1	4.5	2.1–7.9	62
Kyrgyzstan	29	27–31	68	66–71	3.0	2.4–3.6	47	39–57	100
Mozambique	3.7	2.5–5.2	20	5.2–40	8.3	4.4–14	28	15–46	82
Myanmar	4.9	4.7–5.1	20	19–21	11	7.4–16	21	14–30	100
Nigeria	4.3	3.2–5.5	15	11–19	21	12–32	11	6.4–16	73
Pakistan	4.2	3.2–5.3	16	15–17	28	18–40	13	8.4–19	90
Papua New Guinea	3.4	1.7–5.0	26	15–36	2.0	1.2–2.9	23	7.6–13	78
Peru	6.3	5.9–6.7	20	19–22	3.2	2.4–4.1	10	7.6–13	80
Philippines	1.7	1.1–2.5	16	13–20	18	7.7–32	17	7.3–30	73
Republic of Moldova	29	26–31	60	56–64	1.4	1.1–1.6	34	28–40	93
Russian Federation	35	34–35	71	70–71	41	26–59	28	18–40	90
Somalia	8.7	6.1–12	47	29–65	4.0	2.2–6.3	27	15–42	61
South Africa	3.4	2.5–4.3	7.1	4.8–9.5	11	7.2–16	19	12–28	62
Tajikistan	21	19–24	38	34–42	1.9	1.4–2.4	20	15–26	95
Thailand	2.3	1.3–3.4	24	18–31	4.0	2.3–6.1	5.7	3.3–8.8	76
Ukraine	29	28–30	46	45–48	13	13	29	18–41	78

Uzbekistan	15	14–16	34	32–36	4.7	3.2–6.6	15	9.9–20	57
Viet Nam	3.6	3.4–3.8	17	17–18	8.6	5.4–13	9.1	5.7–13	83
Zimbabwe	3.9	3.5–4.3	14	8.9–20	1.5	1.1–2.0	10	7.4–14	71
MDR-TB HBCs	**3.6**	**2.7–4.6**	**18**	**8.9–30**	**438**	**371–510**	**9.3**	**7.9–11**	**78**

* Numbers shown to two significant figures if under 100 and to three significant figures otherwise.
a. MDR-TB is a subset of RR-TB (78% globally).
b. Best estimates are for the latest available year.
c. Rates are per 100 000 population.
d. Estimates for Bangladesh are interim, pending final results from the national drug resistance survey of 2018–2019.
ǂ Source: https://www.who.int/tb/publications/global_report/en/. Accessed 05-03-2020.

Though the disproportionate rise and distribution of TB burden levels in different countries could be linked with population size, the highest TB, TB/HIV and MDR-TB infections and co-infection rates were reported in countries with much smaller populations [30]. It is not yet clear why some countries tend to have higher TB and HIV burden levels than others[3, 24, 31]. While few countries were dropped from the 2006 HBCs list, ten more countries joined the list of HBCs in 2015 with the highest number of TB, MDR-TB cases and co-infections reported[2, 32, 33]. Based on these disease burden estimates, TB became the first infectious disease ever to be declared a global health emergency by WHO, in 2015[34-36].

1.4 **The Stop TB control strategies and their impact**

To deal with rising global TB burden levels, WHO declared a global emergency in 1993 and launched the Stop TB Strategy (STS) in 1996 [37]. The primary objectives of the Stop TB Partnership Strategy were to halt global TB deaths and reduce prevalence by 50% by the year 2015, in line with the Millennium Development Goals (MDGs)[37]. The successful implementation of the STS depended heavily on one specific strategy: “Directly Observed Treatment Short-Course” (DOTS)[37, 38] [38]. The WHO promoted the DOTS strategy as the most cost-effective and preferred TB control strategy in resource-poor settings [39, 40]. Improving access to quality diagnosis and treatment care for all patients affected by TB at the primary care level in each country was one of the key pillars of the DOTS strategy [41]. The central aim was to detect 70% of new TB cases and successfully treat 85% of detected TB cases [38, 42, 43]. DOTS was marketed as the only TB control approach to combine a diagnostic and treatment

protocol (short-course drug therapy) with a delivery policy (direct observation) [41].

As a result, between 2006 and 2015, close to 50 million deaths were averted and TB incidence and prevalence rates fell by 1.5% per year, mainly in countries with strong health systems[3, 5]. However, in resource-poor settings, TB burden levels rose to disturbing levels, particularly in the SSA and SEA regions [1, 3]. In the DOTS period (1993-present), while TB case notification rates increased, over three million cases remained undiagnosed or missed in the community each year around the world[3, 5]. One in two people worldwide is presently infected with latent TB[3, 44]. WHO estimates that 10% of those will become ill with TB in their lifetime (approximately 5% in the first 2 years and 5% in their lifetime) [2, 3]. Only one in four and one in two of TB and MDR-TB detected cases respectively were cured[45].

The number of countries reporting more than 1000 TB, TB/HIV and MDR-TB cases per 100,000 population per year rose during the DOTS period [3, 4]. In many HBCs, case detection and cure rates remained unchanged, mainly due to low TB case finding and treatment success rates[1-3]. Critics argued that the projected DOTS and STS effects were entirely based on contextual comparisons: future projections and clinical impressions supported by estimations and common sense, and not on scientific grounds[46]. New survey data from a few HBCs in the SEA and AFRO regions showed that TB and HIV burden levels were much higher than previously predicted, and that more robust control strategies were urgently needed[3, 5].

1.5 **The End TB Strategy 2015-2035**

In 2016, to sustain progress and further accelerate current TB control global efforts, WHO launched the End TB Strategy (ETS)[3, 4]. Under the ETS, the focus of global TB control shifted from control to disease eradication, guided by locally tailored response strategies (Table 1.3[3, 47].

Table 1.3 ***The WHO End TB Strategy Indicators - A world free of Tuberculosis***

Indicators	**2020**	**2025**	**2030**	**END TB 2035**
Percentage reduction in the absolute number of TB deaths (compared to 2015 baseline levels)	35%	75%	90%	95%
Percentage reduction in the TB incidence rate (compared to 2015 baseline levels)	20%	50%	80%	90% (approx., 10/100K pop)
Percentage of TB-affected households experiencing catastrophic cost due to TB (level in 2015 unknown)	0%	0%	0%	0%

Source: WHO global TB report 2016: http://www.who.int/tb/publications/global_report/en/ last accessed October 2019.

To bring rising TB burden levels down, integrated patient-centred care and prevention, guided by bold policies and supportive national systems, is critical to successful TB control[3]. The main principles advancing the ETS are improved access to robust and quality diagnosis, and treatment policies for all TB patients through universal healthcare coverage[3]. Most crucially, the use of innovative technologies for rapid TB diagnosis in resource-poor and HBCs was deemed critical to achieve 90% and 80% of global TB incidence and death reduction by 2030 respectively, and eliminate TB by 2035[3].

1.6 **The use of rapid technologies for TB diagnosis**

Modern technologies for TB diagnosis started with Robert Koch, who first discovered the tubercle bacillus diagnostic technique in 1882[48]. Franz Ziehl and Friedrich Neelsen made diagnostic discoveries based on Robert Koch's work, and later introduced the Ziehl and Neelsen smear microscopy (ZN) staining diagnostic technique in the 1890s[49]. While considerable advances have been made over the decades, leading to a number of new TB diagnostic technologies, smear microscopy (ZN) remains the most commonly used and widely available technique for TB diagnosis in resource-poor settings[50, 51]. However, ZN has low sensitivity, is time-consuming, contains toxic products, and requires technicians working in darkrooms to increase magnification for acid-fast bacilli (Figure 1.3, image a)[52].

a)

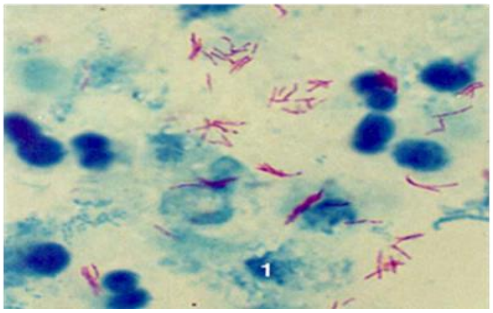

Image a) shows purple staining under ZN, which is hard to see in comparison with the mycobacteria tuberculosis stained under LED in image b).

b)

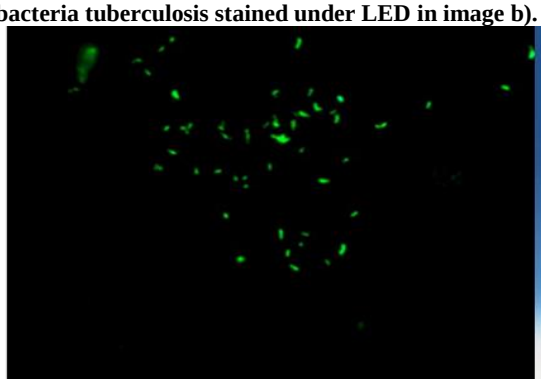

Image b) shows highly visible yellow-green TB bacilli against a dark background under LED microscopy.

Figure 1.3 ***The magnification difference in mycobacterium TB staining with ZN and LED***

To overcome the limitations of ZN microscopy, WHO introduced light-emitting-diode fluorescence microscopy (LED) in many resource-poor settings as an alternative strategy[53]. To accelerate TB control efforts, WHO recommended replacing ZN with LED as an alternative method for rapid TB diagnosis in resource-poor settings[54]. LED microscopes have better magnification for microscopic detection of acid-fast bacilli (AFB) using auramine staining, which increases sensitivity by 10% compared to ZN microscopy[55, 56]. They also have several practical advantages over ZN microscopes, making LED microscopes the preferred choice for routine TB testing in resource-poor settings[57]. The use of LED technology permits better smear reading and the detection of TB bacilli bacteria under low to medium power lenses, and takes much less time for operators (laboratory technicians) than ZN microscopy (Figure 1.3, image b)[3, 57]. Although the ZN method is highly specific, reliable and the cheapest method available in resource-poor settings, it has low sensitivity and detects only 50% of existing infectious TB cases[58]. ZN microscopy sensitivity is significantly reduced in the diagnosis of pulmonary TB among extra-pulmonary TB and HIV-infected patients, which is a major constraint to TB control efforts in many resource-poor settings[59]. Comparatively,

the LED technology is argued to be low-cost, more sensitive, reliable, easy to use and suitable for rapid TB diagnosis in weak health system settings[60].

To facilitate a smooth transition from ZN to LED, countries were required to improve and prepare the delivery capabilities of existing health system infrastructures, particularly laboratory service capacities, to support, sustain and integrate new technologies into mainstream healthcare services. Improving the delivery capabilities of the existing health systems infrastructures required the recruitment, training and retainment of a competent health workforce, specifically laboratory staff, to use the new diagnostic technologies at all levels of the care delivery process. It was envisaged that such approaches would help countries to improve access to quality, reliable and continued TB care services as well as intensify case detection in their respective settings[61, 62].

While the use of LED resulted in favourable gains in access to quality care and case detection outcomes in stable contexts, limited or no evidence appears to be available on the suitability, acceptability and operational feasibility of new TB diagnosis technologies like LED in countries affected by protracted civil unrest, political and economic instabilities (also known as fragile states)[63]. The next section of the chapter discusses the burden and challenges of TB control in fragile states[64].

1.7 **Fragile states and challenges of TB control**

A nation is characterized and ranked as a "fragile state" if it is experiencing either protracted or sudden social, economic and political fluxes caused or contributed by a combination of war, drought/famine and climatic change resulting in significant or excessive loss of human life[65-70]. The concept of fragile states emerged originally from the international donor community and is widely used to apply and adopt aid policies to countries experiencing developmental, humanitarian and security complexities, particularly those in the global south[68]. The next few paragraphs provide a brief description of the term *fragile states* and its use, as well as rankings of the 20 most fragile states. This is followed by a brief analysis of the TB burden and case detection outcomes of 20 fragile states, examining whether there is a significant change in overall TB burden in fragile states over the last decade.

Table 1.4 ***The world's 20 most fragile states and their fragility rankings based on socio-economic indicators – 2019***

Fragility Ranking		*Cohesion indicators*			*Economic indicators*			*Political indicators*			*Social indicators*			*SFI*
	Country	Security apparatus	Functionalized elite	Group grief	Economic decline	Uneven development	Human flight and Brain drain	State legitimacy	Public services	Human rights/rule of law	Demographic Pressure	Refugees and internal displacement	External intervention	Total Fragility Score
1	Yemen	9.3	9.4	8.5	8.6	8.5	7.4	8.9	8.7	8.3	8.8	8.4	8.4	110.93
2	Somalia	9.1	10.0	9.3	9.3	8.3	7.9	9.7	9.7	9.7	8.9	8.9	9.6	113.36
3	South Sudan	8.2	9.9	9.9	9.2	8.9	6.6	9.6	9.6	9.7	9.4	10.0	10.0	113.82
4	Syria	8.9	9.5	9.0	6.9	7.7	7.0	9.3	6.8	9.3	6.7	9.7	7.0	110.38
5	DR. Congo	9.6	9.3	9.2	8.4	8.2	7.5	9.1	9.3	8.8	9.6	8.8	8.9	109.85
6	CAR	9.5	8.6	8.2	8.3	9.2	5.7	9.3	9.2	9.8	7.4	9.4	9.4	112.45
7	Chad	9.4	9.8	8.9	8.2	9.1	8.2	9.6	9.6	8.7	7.9	9.5	8.7	109.52
8	Sudan	9.7	9.0	9.9	7.7	8.7	8.5	9.7	9.0	9.6	8.9	9.8	9.8	110.44
9	Afghanistan	9.7	9.0	9.2	8.2	7.8	7.5	9.4	8.9	8.6	9.0	9.3	10.0	99.80
10	Guinea	8.8	9.6	8.6	9.2	7.7	7.4	9.6	9.5	7.7	8.7	8.2	7.4	102.4
11	Haiti	7.7	9.6	6.5	8.7	9.7	8.8	9.7	9.7	7.6	9.5	7.7	10.0	105.3
12	Iraq	10.0	9.6	9.6	6.6	7.3	9.5	8.2	8.7	8.6	9.9	9.7	9.7	105.4
13	Nigeria	9.2	9.6	9.2	8.0	8.6	7.2	8.6	9.2	8.9	9.1	7.5	6.5	101.6
14	Burundi	8.8	8.2	7.9	8.0	7.2	6.3	8.8	8.0	8.8	9.3	8.6	9.0	98.9
15	Ethiopia	8.4	8.7	9.1	7.0	6.5	7.6	8.2	8.8	9.0	9.8	9.3	9.3	101.1
16	Cameroon	8.5	8.7	8.2	8.2	8.7	7.3	7.4	7.1	8.2	8.2	8.3	8.2	97.0
17	Eritrea	7.2	8.1	7.1	8.1	7.8	8.3	9.3	8.4	9.0	8.8	8.3	7.7	98.1
18	Niger	8.7	8.9	8.0	7.5	8.5	7.3	9.5	9.5	6.5	9.0	7.9	8.1	97.4
19	Guinea Bissau	8.9	9.6	5.2	8.3	9.1	8.1	9.2	9.4	7.5	8.6	7.3	8.3	99.5
20	Uganda	8.2	8.9	8.4	6.9	6.5	7.2	8.1	7.7	8	8.4	8.7	8.3	95.3

The FSI scores denote 0 = No fragility and 10 = extreme fragility.
Source: State Fragility Index: Global Report, 2019.

According to the State Fragility Index (SFI) produced by US-based Fund for Peace (FBP) in 2019, there are 20 fragile states in the world today, comprising 15 African countries, five Asian countries and one in the Americas (Haiti). The FBP estimated that more than 270 million people lived in the world's 20 most fragile states in 2019. The SFI assesses countries based on 12 social, political and economic indicators, which provide scores on the highest fragility levels ranging from zero to ten (0 = no fragility) and (10 = extreme fragility)[71]. As depicted in table 1.4 and figure 1.4, countries in dark red are classified as the most fragile countries with highest fragility scores[64, 67]. The SFI explicitly elucidates how protracted civil wars, peace accords, environmental calamities (i.e., frequent droughts and famines), and political volatilities pushed some countries toward instabilities or to the brink of complete state collapse (Table 1.4 & Figure 1.4 and 1.5) [64, 67, 68].

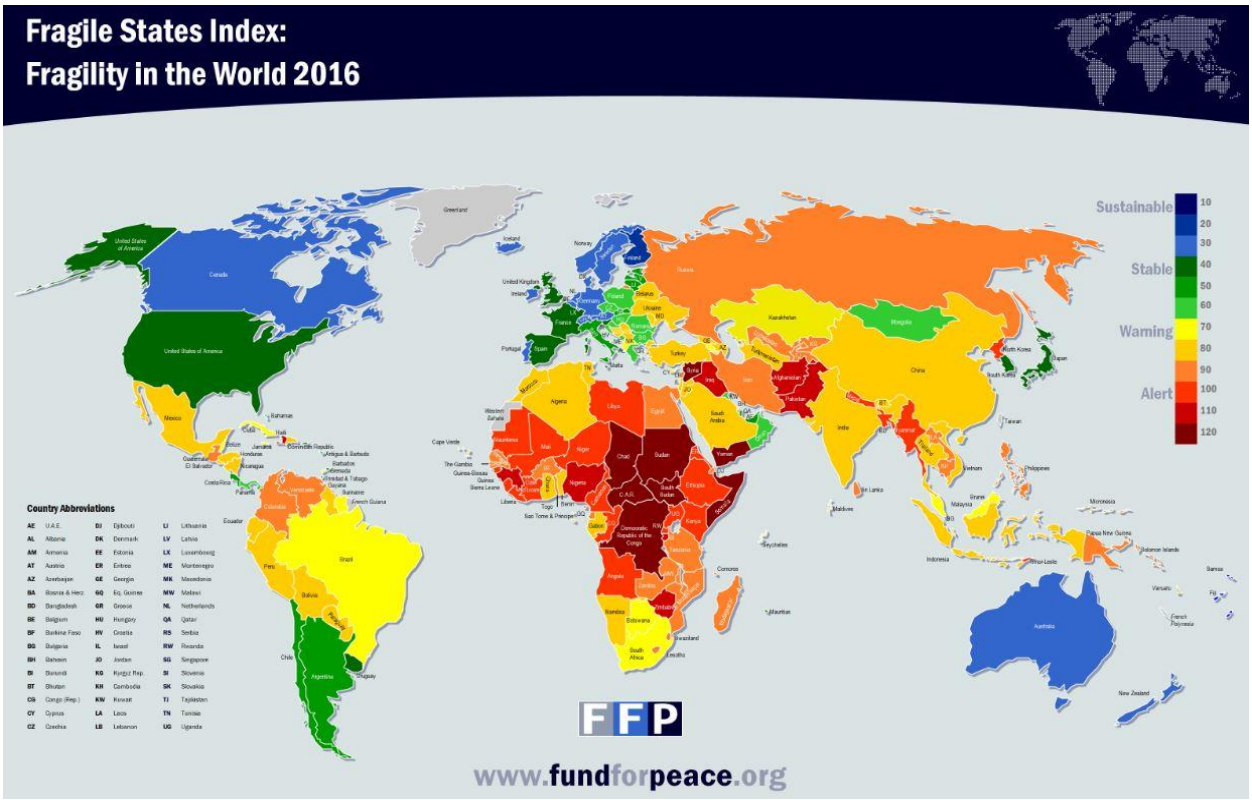

Figure 1.4 ***The world's top 20 states with the highest fragility (2019).***
Source: https://en.wikipedia.org/wiki/Fragile_States_Index. Last accessed on 05/03/202.

Consequently, the proliferation of social, political, environmental and economic instabilities result in weak social cohesion and feeble state institutions. These undermine not only the state's ability, but

also the legitimacy and effectiveness of the state to deliver basic public services such as accessible, affordable and equitable health services to its citizens[68].

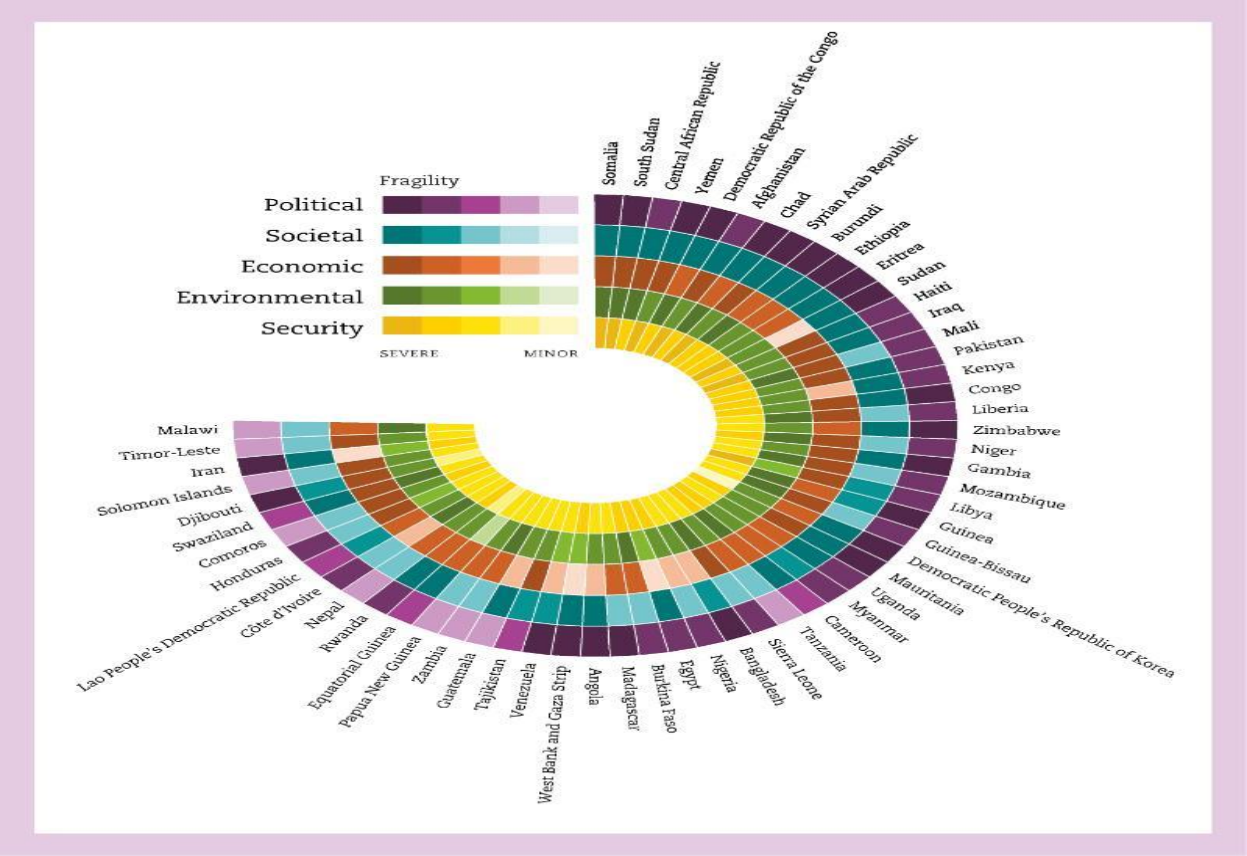

Figure 1.5 ***The world's countries and their corresponding rankings in the State Fragility Index***
Source: http://www.oecd.org/dac/conflict-fragility-resilience/. Last accessed on 27/03/2019.

In fragile states, the control of infectious diseases such as TB and HIV faces enormous challenges due to a lack of functioning or the collapse of health services in general to meet the needs of an increased number of vulnerable people[72]. According to the WHO report on TB and HIV, infections and co-infections remained staggeringly high in the top 20 fragile states[2, 73]. In most of these countries, case notification and TB burden levels (incidence, prevalence, mortality) have either remained unchanged or risen with some of the highest MDR-TB and HIV/TB co-infections rates reported[74]. In this report, it is clear that the TB burden levels in fragile states is a particularly worrying public health problem and requires appropriate responses guided by evidence-based practical solutions (Tables 1.5 & 1.6) [50, 75, 76].

Table 1.5 Estimated TB deaths in the world's twenty most fragile states– *2019*

Country	**Pop. (m)**	**Deaths TB only (absolute no. in thousands)/yr.**	**Death TB only (rate/100K)/yr.**	**Deaths HIV+TB only absolute no. in (thousands)/yr.**	**Deaths HIV+TB only (rate/100K)/yr.**
South Sudan	12	3(1.8-4-5)	24(14-37)	.77(.49-1.1)	6.3(4-9.1)
Somalia	15	8.7 (6,1-12)	67(44-115)	.23(.19-.46)	2.1(1.3-3.2)
CAR	4.6	2.7(1.5-4.2)	59(33-92)	2.5(1.3-4)	54(29-87)
Yemen	28	1.9(1.3-2.6)	6.9(4.9-9.3)	.026(.01-.053)	.09(.03-.19)
Sudan	40	5.6(3-9.1)	14(7.5-23)	.28(.098-.57)	.72(.25-1.4)
Syria	18	.23(.22-.23)	.12(.12-.13)	.01(.01-.01)	0(0-01)
DR. Congo	79	53(31-80)	67(39-101)	8.5(4-15)	11(5.1-19)
Chad	14	4.5(2.7-6.9)	31(18-48)	1.3(.61-2.1)	8.7(4.2-15)
Afghanistan	35	11.85 (6.7-17)	33 (19-49)	.096(.06-.24)	.28(.05-.71)
Iraq	37	1.2(.84-1.7)	3.3(2.3-4.6)	.01(.01-.01)	.02(.01-.02)
Haiti	11	.19(.052-1.4)	8.4(4.8-13)	.75(.57-.95)	6.9(5.2-8.8)
Guinea	12	3.3(1.9-4.9)	26(16-40)	2(1.3-2.9)	16(10-23)
Nigeria	186	120(67-180)	62(36-95)	39(23-58)	21(12-31)
Zimbabwe	16	1.2(.71-1.7)	7.2(4.4-11)	4.4(3.6-6.1)	27(19-38)
Ethiopia	102	26(16-37)	25(16-36)	4(2.7-5.4)	3.9(2.6-5.3)
Guinea Bissau	1.8	1.4(.8-2.1)	76(44-116)	1.2(.73-1.8)	66(40-98)
Burundi	11	2(1.2-3.1)	19(12-29)	.52(.33-.75)	4.9(3.1-7.1)
Pakistan	193	44(34-55)	23(18-29)	2.1(.98-3.6)	1.1(.51-1.9)
Eritrea	5	.64(.29-1.1)	13(5.9-23)	.075(.036-13)	1.5(.72-2.6)
Niger	21	4(2.4-6.1)	20(12-30)	.39(.24-.57)	1.9(1.2-2.7)

*MDR= TB is resistant to most powerful available TB drugs (Rifampicin and Isoniazid
*RR denotes TB is resistant to rifampicin only. Source: WHO Global TB Report 2019.

Table 1.6 Estimated incidence of TB in the world's twenty most fragile states **– *2019***

Country	**Pop. (m)**	**Incidence TB only (absolute no. in thousands/yr.)**	**Incidence TB only (rate/100K)/yr.**	**Incidence HIV+TB only (absolute no. in thousands)/yr.**	**Incidence HIV+TB only (rate/100K)**	**Incidence MRD-RR-TB only (absolute no. in thousands)**	**Incidence of MDR-RR/TB (rate/100K)**
South Sudan	12	18(12-26)	146(95-209)	2.2(1.4-3.1)	18(11-26)	.66(.43-.9)	5.4(3.5-7.5)
Somalia	15	39(25-55)	336(175-585)	.59(.37-.86)	4.1(2.6-6)	3.9(2.2-6.3)	27(15-42)
CAR	4.6	19(12-27)	407(263-587)	6.2(3-3-9.9)	134(73-215)	.18(.0-41)	4(.0-8.9)
Yemen	28	13(12-15)	48(42-54)	.09(.59-.13)	.33(.21-.47)	.36(.18-.55)	1.3(.65-2)
Sudan	40	32(18-51)	82(46-129)	.83(.54-1.2)	2.1(1.4-3)	1.2(.58-1.9)	3.1(1.5-4.7)
Syria	18	3.8(2.9-4.8)	21(16-26)	.01(.01-.01)	.02(.01-.03)	.37(.23-.51)	2(1.2-2.8)
DR. Congo	79	254(165-363)	323(209-461)	20(13-29)	26(17-37)	7.6(3-9-11)	9.7(4.9-15)
Chad	14	22(14-32)	153(99-219)	2.8(1.8-4)	20(13-28)	.76(.16-1.4)	5.3(1.1-9.4)
Afghanistan	35	65(42-93)	189(122-270)	.28(.18-.41)	.82(.53-1.2)	3.3(1.2-5.4)	9.5(3.6-15)
Iraq	37	16(14-18)	43(37-48)	.02(.02-.02)	.04(.03-.05)	1.2(.88-1.5)	3.2(2.4-4.1)
Haiti	11	20((17-24)	188(156-222)	3.1(2.5-3.6)	28(23-34)	.77(.44-1.1)	7.1(4.1-10)
Guinea	12	22(14-31)	176(114-252)	5.4(3.4-7.8)	43(28-63)	.7(.14-1.3)	5.9(1.1-11)
Nigeria	186	407(266-579)	219(143-311)	63(40-93)	34(21-50)	20(12-29)	11(6.4-15)
Zimbabwe	16	34(24-44)	208(152-273)	23(15-32)	139(90-199)	1.9(1.3-2.3)	12(8-16)
Ethiopia	102	182(128-245)	177(125-239)	14(9.6-19)	13(9.4-18)	5.8(3.1-8.5)	5.7(3-8.3)
Guinea Bissau	1.8	6.8(4.4-9.7)	374(242-534)	2.2(1.4-3.2)	120(75-175)	.2(.017-.39)	11(.93-21)
Burundi	11	12(8-18)	118(76-169)	1.5(.96-2.2)	14(9.1-20)	.42(.27-.58)	4(2.5-5.5)
Pakistan	193	518(335-741)	268(174-383)	6.9(3.2-12)	3.5(1.6-6.2)	27(17-37)	14(8.8-19)
Eritrea	5	3.7(1.7-6.4)	74(34-129)	.22(.14-.31)	4.4(2.9-6.3)	.14(.028-.26)	2.9(.57-5.2)
Niger	21	19(12-27)	93(60-132)	.95(.6-1.4)	4.6(2.9-6.6)	.66(.14-1.2)	3.2(.67-5.7)

*MDR= TB is resistant to most powerful available TB drugs (Rifampicin and Isoniazid.
*RR denotes TB is resistant to rifampicin only.
*Source: WHO global TB Report 2019.

TB control efforts in such settings face numerous resourcing (people, money, information) and structural (operational, systematic and programmatic readiness) difficulties[77, 78]. Dependency on international aid (when aid stops, programs stop) and a lack of functioning health systems to support the delivery of quality TB care are key contributing factors to the rising TB and HIV burden levels in fragile health system settings[79-81]. Thus, frequent interruptions of TB care services have contributed to the spread of TB infections and the proliferation of more complex forms of TB, such as MDR-TB and HIV-TB co-infections[80, 82]. Such prevailing challenges impede both access to and delivery of basic services including quality, reliable and sustained healthcare services to states' populations[83-85]. As these challenges continue to take a toll, TB control efforts become more challenging and complex due to health systems' capacities to deliver accessible and quality care services[86].

As illustrated in table 1.7 the top ten of the world's 20 most fragile states with the highest fragility scores reported some of the lowest proportions of TB cases detected.

Table 1.7 ***Proportion of TB cases detected (all forms) in the world's 20 most fragile states over the last 10 years.***

Country	2006 Appendix A: (%)	2007 (%)	2008 (%)	2009 (%)	Appendix B: 2010 (%)	2011 (%)	2012 (%)	2013 (%)	Appendix C: 2014 (%)	2015 (%)	2016 (%)
South Sudan	-	-	-	-	-	47	53	39	49	56	60
Somalia	**39**	**35**	**38**	**33**	**29**	**33**	**33**	**35**	**35**	**37**	**47**
CAR	23	0	31	42	35	31	48	53	60	59	53
Yemen	55	59	61	67	73	72	82	84	77	59	71
Sudan	63	63	52	55	55	52	51	52	54	55	63
Syria	63	63	63	63	63	63	63	63	63	63	63
DR. Congo	52	52	53	55	54	50	48	48	48	48	51
Chad	0	36	41	48	53	57	55	57	55	54	49
Afghanistan	52	57	55	49	51	50	49	51	51	56	64
Iraq	61	59	67	68	69	62	59	57	54	52	46
Haiti	39	40	42	44	44	51	60	65	59	64	64
Guinea	43	47	50	42	55	56	56	55	56	57	58
Zimbabwe	60	57	56	69	76	70	68	72	69	71	81
Ethiopia	48	51	57	62	66	69	66	62	59	71	69
Guinea Bissau	**41**	**0**	**39**	**39**	**38**	**34**	**31**	**32**	**36**	**32**	**33**
Burundi	44	47	52	57	60	54	56	61	58	55	61
Pakistan	41	52	54	57	56	55	55	58	62	63	69
Eritrea	61	61	61	61	61	61	61	61	61	61	61
Niger	44	49	49	54	54	56	59	60	58	55	52
Nigeria	**23**	**26**	**26**	**26**	**24**	**24**	**25**	**25**	**22**	**22**	**22**
Source: WHO TB report 2016.											

Countries like Somalia, Nigeria and Guinea Bissau (all high TB and HIV burden) reported some of the lowest TB case detection rates with the highest deaths. An inability to deliver and sustain basic health care services imposes enormous challenges for fragile states[78].

In fragile states, the control of these infectious diseases requires robust and innovative strategies that extend beyond the traditional models and policies for disease control in stable settings[87, 88]. Dealing with complex health system challenges depends heavily on having sufficient resources (human, financial, information). It also requires existing health systems to be ready to support and sustain control efforts at a local level. A lack of functional health systems and a competent health workforce; widespread shortages of medicine and medical equipment; and inadequate financial resources are all widely prevalent in fragile states[84, 89].

While the persistent inadequacies of functioning health systems remain a major hindrance to the effective prevention, control and management of TB efforts in fragile settings, the launch of the Global Fund (GF) over the last decade led to a substantial increase in TB funding in fragile states[90]. With this new funding commitment, a large proportion of TB control funding went to the introduction, implementation and utilization of new technologies for routine TB diagnosis to intensify TB case detection and treatment[91, 92]. Despite increased funding for TB control, TB case detection rates remained largely unchanged in all fragile countries (Table 1.6). Arguably, the impact of increased funding on TB control outcomes in resource-poor settings including fragile states remains unclear[90].

The perceived narrative is that rising TB burden levels correlate with population size: countries with larger population sizes tend to have higher TB burden levels than those with smaller population size[93]. However, Guinea Bissau has one of the smallest population sizes but had some of the biggest TB burdens. Somalia, Nigeria and Guinea Bissau reported the lowest case detection rates with TB over the last decade (Table 1.6). The next few paragraphs briefly look at Somalia as a fragile state: its socio-demographic profile and the estimated TB burden and current model of control interventions.

1.8 **Somalia as a fragile state**

Somalia is a fragile state located in the Horn of Africa with a population of 15 million[94]. Predominantly nomadic, 50% of its population live in remote areas on less than a dollar a day[95, 96]. Somalia has been a failed state for over two decades due to prolonged and protracted civil unrest, economic stagnation, extreme poverty and underdevelopment[5, 62, 97-100]. The country is presently

divided into three separate administrations: South-Central Somalia, Puntland and Somaliland. There is no centralised government, as each zone is run by a separate administration (Figure 1.6)[95].

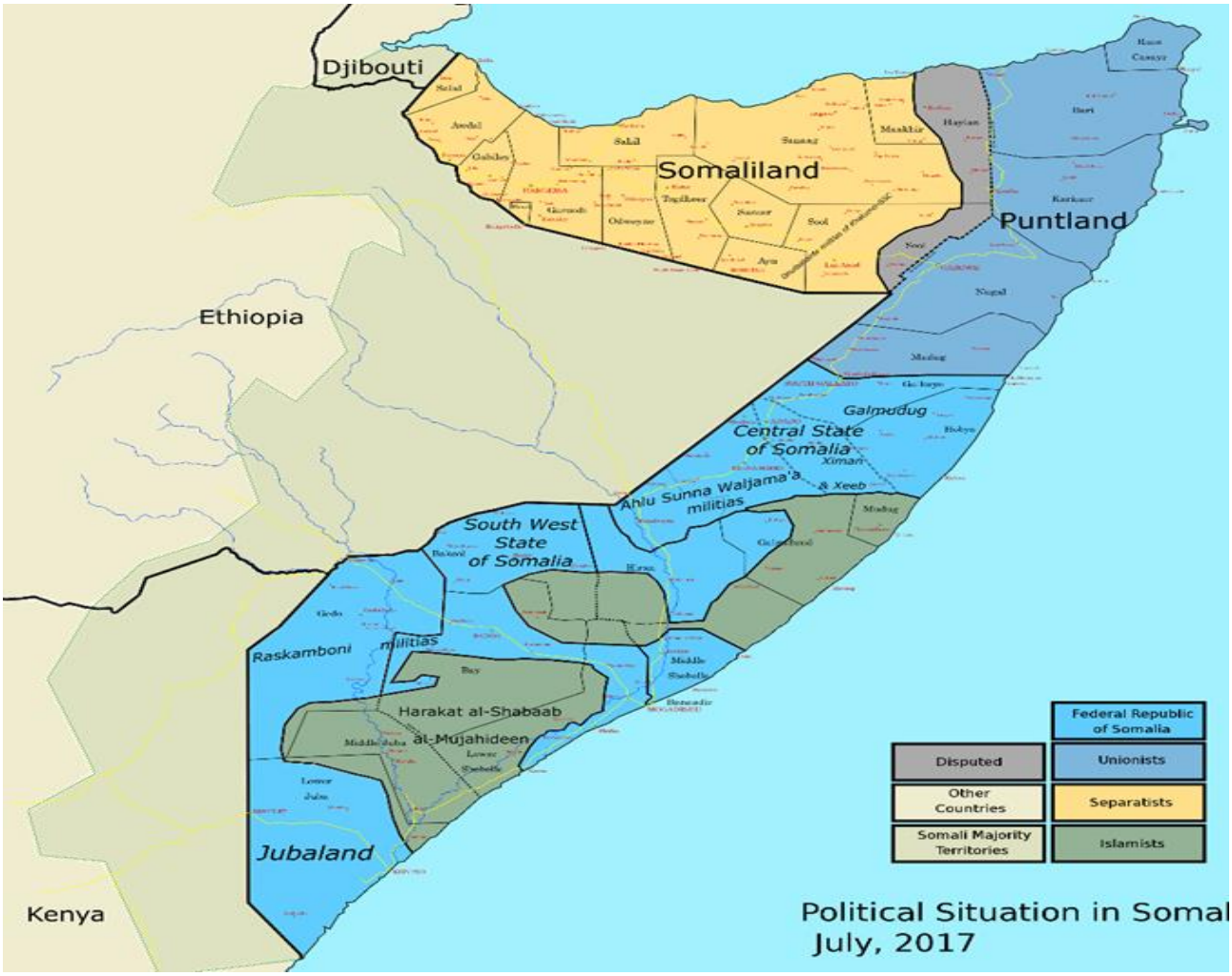

Figure 1.6 ***Somalia's zonal divisions and administrative systems (2017). Last accessed October 2020.***
Source: Somalia political map - Bing Maps

In the FSI in 2019, Somalia ranked second and scored over nine for every category in the fragility index indicators[101]. Observed fragility scores or rankings of Somalia stress how protracted civil wars, peace accords, environmental calamities (i.e., frequent droughts and famines) and political volatilities pushed this country toward instability, which led to complete state collapse[70].

In the following sections, special emphasis will be given to the current health system structure and functions and how the national TB program (NTP) functions/fits or is embedded within the wider health system both at the Somalia and Somaliland levels.

1.9 **The State and Structures of the Current Health Care System of Somalia**

Over the past almost four decades, Somalia has continued as one of the world's most enduring humanitarian crises, causing enormous distraction and damage to health and development systems [102]. Prolonged political, economic and security volatilities have caused the country's health system to collapse and become extremely fragmented[5, 103]. Since the collapse of the Central Government in 1991, no national or centralised health system can provide adequate public health protection and quality, and accessible and affordable primary healthcare, to all citizens [104]. Access to primary public service healthcare has either been non-existent or suboptimal, functioning mostly only in urban areas[103, 105].

At present, Somalia's health system is organised into three central zonal administrations: South-Central Somalia, North-East (Puntland) and North-West (Somaliland) (Figure 1.6). Each zone has its own administrative health system structure, namely ministries of health (MOHs) with varied health service delivery capacities and capabilities, and underlying support systems within and across the three zones [104]. While the provision of essential primary care services has improved in Somaliland and Puntland, the situation in South Central Somalia remains volatile and fragmented with disturbingly suboptimal service delivery capacities [106].

The care service delivery of the health system is structured theoretically into a four-tier system: regional referral hospitals, district hospitals, maternal and child health centres (MCHs) in large towns and cities, and health centres which operate at the village level. However, regional hospitals and primary health care facilities are limited in number and inadequately distributed with varied functional and care service delivery capacities [106]. According to the UNICEF Somalia health report, while accurate estimates of facility-population ratio are unknown, it is estimated that the density of health facilities is 1.7 per 10,000 populations compared to 11 per 10, 000 population in neighbouring Ethiopia [107] . This can be broken down to 0.76 public facilities and 0.93 private facilities per 10,000 population [108]. Moreover, Somalia's health service provision remains fragmented and concentrated in major towns or areas with better security [102, 109, 110].

Somalia's total health expenditure (i.e., the total sum the country spends on health, including government expenditure, private expenditure, out of pocket payments and donor support) and changes over time are presently unknown due to lack of relevant data. However, the recent UNICEF health survey report stated that the total health expenditure of the Somali government is estimated to be about $33 (USD) per person per year, a tiny amount, as available resources are inequitably distributed across the country [106]. It is estimated that the Somali government spends less than 1% of its total expenditure on health [106].

The recent UNFPA and UNICEF health survey reports suggest that out-of-pocket spending is high [106, 108]. Most people rely on services meant to be free of charge at public or not-for-profit private health facilities, namely non-governmental organisations (NGOs), but in practice people often have to pay for certain services (e.g., for drugs, laboratory work) [106, 108]. According to the UNFPA 2020 survey health report, nearly 48% of households reported that they had to pay for their health expenses from their income Of these, 25% said that their family or friends paid for their care, 14% had to borrow money, and 11% were obliged to sell their assets to cover health expenditures[106]. Only 2% of the households interviewed in the survey reported that they could draw on health insurance to pay for health expenses [106]. Moreover, the tax base in Somalia remained almost non-existence, making the financing of the health system highly donor-dependent [106].

1.10 **The Structure and Delivery of TB Care Services in Somalia**

The provision of TB care services is presently structured and managed under one Somalia national tuberculosis program (NTP) with funding and technical assistance coming from the Global Fund (GF) and the WHO respectively for the entire Somalia including Somaliland. World Vision International is the principal recipient for the distribution and management of funds from the GF for the entire Somalia NTP. The NTP acts as the responsible agent for all TB care service through public, private and NGO provider arrangements [111, 112]. The public sector responsibilities include developing and implementing TB control policies, strategies, and guidelines for diagnosing and managing TB care service provision [113, 114].

Because the NTP lacks the resource, operational and functional capacity to deliver comprehensive and sustainable TB care at all levels, most TB care services are currently provided by entities outside the public sector practice, namely private and NGO sectors [102, 114, 115]. Private and NGO practices

have increased, largely unregulated[116, 117]. The decline of the public health sector in the early 1990s has become deeply entrenched in the health system which formerly played a significant role in TB care service provision in Somalia [118].

Therefore, private practices have become the only available and accessible form of health care, including TB care, to the vast majority of the Somali population, particularly in areas where the public sector does not operate[116, 117, 119]. These private practices are diverse groups of local pharmacies, private medical clinics, traders of medical supplies and traditional healers [112]. These private practices are not integrated into or regulated by the public sector[120]. Inappropriate prescriptions and violation of ethical guidelines on patient care have been widely reported in private practices [111, 112].

The NGO sector fills an important gap in Somalia's collapsed/sub-optimal health care system [112, 114, 121, 122]. In the early days of the Somalia crisis, countless NGOs arrived to provide emergency health services [114]. Today, approximately 80-90% of TB care services are provided by NGOs (local and international NGO entities) [109, 123, 124]. However, the provision of TB care in the NGO sector operates largely apart from the rest of the NTP TB control activities. The lack of necessary systematic and regulatory oversight creates parallel and fragmented care delivery systems [120].

According to the WHO TB report in 2020, the number of TB Care Service Units (TCUs) increased from 44 in 2016 to 95 in 2019, with at least one TB centre in each region in the three zones: Somaliland, Puntland and South-Central Somalia [114]. However, TB control activities in the country have faced considerable resource, structural and operational challenges [114, 125, 126]. Firstly, most TB control activities have been funded and managed by outside entities [114, 125, 126]. Secondly, the functional and delivery capacity of the health facilities has remained sub-optimal and fragmented, and generally under-equipped [114, 125, 126]. Thirdly, most healthcare workers are not sufficiently trained and have received no or limited renewed training and development since the collapse of the central government in the early 1990s [114, 125, 126]. Fourthly, the NTP guidelines for diagnosing and managing TB infections are not effectively implemented by the different TB care providers [112].

In Somalia, laboratory services cannot do rapid diagnoses, and cannot implement new diagnostic strategies both at the peripheral and national levels [127]. Even before the political, social, environmental and economic upheaval in the early 1990s, Somalia's diagnostic laboratory facilities operated at suboptimal capacities with no proper internal and external quality assurance mechanisms

[112, 114, 128]. The only national reference laboratory (NRL) supporting the peripheral laboratory services in all Zones of Somalia operates from Nairobi in neighbouring Kenya [114, 115].

In 2011, the Physicians for Social Responsibility (PSR-Finland) established a regional reference laboratory facility in Hargeisa, Somaliland to support all TB laboratory diagnostic facilities in all zones of Somalia [115, 129]. Like any other fragile or recovering state, Somalia suffers from an acute shortage of skilled and knowledgeable laboratory personnel [114]. The vast majority of laboratory service personnel have either emigrated to other countries or work at private practices in Somalia [102, 109, 130, 131].

Somalia is a high TB burden country with 49000 new TB cases and an incidence rate of 350 per 100K/ population reported annually (Table 1.8) [3]. The TB burden has been on the rise over the last decade and 80% of the reported TB cases occur in the productive age group (15-44 years). Based on the estimates of a nation-wide survey in 2011, Somalia has one of the highest MDR-TB cases in the world with 5% and 41% new and previously treated TB cases respectively with MDR-TB each year [132]. Somalia has joined the top 30 MDR-TB high burden countries with an average of 9% TB/HIV co-infection rates reported also each year (Tables 1.5 - 1.7) [5, 11, 87, 133-140].

Table 1.8 ***Estimated TB burden in Somalia (2000-2018).***

Year	Total no. TB cases reported/year	Estimated new TB cases/100K/yr	Total no. TB deaths reported/year	TB deaths/100K /yr	TB/HIV deaths /100K/yr
2000	31000	346	1100	125	8
2001	32000	346	1100	120	8
2002	33000	347	1150	118	8
2003	34000	347	1100	109	7
2004	35000	347	950	96	6
2005	36000	347	920	94	6
2006	38000	346	1050	100	7
2007	38000	347	1100	106	7
2008	39000	347	1100	101	7
2009	41000	347	1230	109	7
2010	42000	347	1300	115	7
2011	43000	348	1300	113	6
2012	44000	347	1350	109	6
2013	45000	346	1350	106	6
2014	45000	333	1300	102	6
2015	46000	333	1350	99	4
2016	47000	327	1350	97	3
2017	48000	374	1380	101	1.2
2018	49000	375	1380	100	1.4

Source: WHO TB report 2016/http://www.who.int/tb/country/data/download/en/ accessed 2016.

Over the last decade, Somalia's TB case detection rate increased somewhat, from 39% in 2006 to 47% in 2016 (Table 1.8) [5]. This increase in case detection was mainly due to an increased number of trained healthcare personnel at TB care facilities and improved access to quality-assured drugs for TB patients[141, 142]. However, key challenges remain unaddressed, including low case detection, sub-optimal disease surveillance systems, lack of effective quality internal and external assurance mechanisms, poor case management practices (mainly in the private sector), and limited access to quality TB care services in all regions of Somalia. To address the growing TB problem, the NTP of Somalia developed a comprehensive five-year plan to scale up TB case detection and treatment success rates through improved access to rapid and quality diagnosis and treatment services combined with a sound recording and reporting strategy. Using Somaliland as a pilot site, the NTP introduced LED and mobile GeneXpert for TB diagnosis over a 12-month period (April 2012 – May 2013).

1.11 **The current state of the health system of Somaliland**

Somaliland is the north-west region of Somalia with a population of 3.5 million. A self-declared state and former British colony, it gained its independence in 1960 and joined Somalia the same year [96]. After decades of dictatorship followed by a long civil war, Somaliland declared its independence from the rest of Somalia in 1991[143]. Though receiving no international recognition, Somaliland enjoyed peace, security, political and economic stability for over two decades compared to other regions of Somalia[96, 143, 144].

Despite its *de-facto* independence from the rest of Somalia for over three decades now, Somaliland's health system remains as part of the larger health system of Somalia. While Somaliland's health system has been slightly progressing over the last few decades, significant challenges remain in both the provision and access to basic healthcare services [145]. Like the rest of larger Somalia, the Somaliland health system is poorly structured and funded with deficiencies in planning and management of care delivery services [146].

Moreover, the fragmentation and the absence of national unified health system governance for larger Somalia has affected the capacity of regional health authorities to regulate the private sector and to partner NGOs to deliver quality healthcare services to populations in remote and rural areas[147]. Much provision that does exist is either funded or/and provided by international organizations with

most of the funding coming from bilateral donors and earmarked through WHO and UNICEF in Somalia [104].Qualified health professional staff are in short supply, with limited training and accreditation programs available, and drugs and equipment are sparse in Somaliland [119].

The existing Somaliland health system is essentially privatized, and it is confined to major towns, leaving the poor majority in the remote and rural areas without of accessible, affordable and sustainable health care. This dual health system has been dominated by the private sector whilst the government owned hospitals are often depicted as disorganised and inefficient [117]. Consequently, less than 30% of the population in Somaliland has access to some sort of healthcare services[106, 108]. The private sector has promoted a plethora of clinic and hospital facilities, some of dubious quality and relevance to the health needs of the population, largely unregulated and the quality of services provided is rudimentary [116, 117]. Most services are provided for direct payment, limiting access to quality and affordable care to the poor.

1.12 **Somaliland and the burden of TB**

In Somaliland, although TB burden levels are virtually unknown, they are thought to be historically linked to socio-economic conditions of the Somali population[111, 148]. The TB case detection rate is low, while MDR-TB and HIV infections and co-infections are thought to be rising.

The aim of the NTP pilot programme referred to above in section 1.10 was to introduce LED and GeneXpert into Somaliland to increase TB case detection from 47% to 65% by improving access to quality diagnosis and treatment services to TB patients throughout the country. While LED and GeneXpert use for diagnosis show promising gains in reducing the TB burden in stable settings, it is not yet clear whether the use of new diagnostic technologies will have any added benefit in reducing TB burden levels in fragile states. Not only do these technologies need to be effective, affordable and accessible to all populations, but they are also likely to need sustained resources, structural capacity and capability, as well as the environment to support and sustain the routine utilisation of such new technologies.

1.13 **Research problem and overview of the thesis**

The present global plan outlines the main policies and strategies used for the prevention, control and management of TB disease. An integral element to the current global TB control plan is the development and deployment of new diagnostic technologies for routine use to halt the rising TB

prevalence levels in HBCs[149-152]. In light of this, several approved and innovative new diagnostic technologies, including LED, were enthusiastically adopted, introduced and implemented in HBCs resource-poor settings, including Somalia, over the last two decades[153-160].

However, limited empirical evidence is available on the feasibility and acceptability of new diagnostic technologies for routine TB testing in countries with fragile health systems. Failure to recognise the importance of the programmatic and systematic readiness of existing health systems to support and sustain the applied diagnostic interventions may undermine not merely the delivery process but the quality diagnosis for patients[79].

The primary aim of this thesis was to improve access and quality of diagnosis for TB patients in fragile states, with particular emphasis on Somaliland. The research objectives and questions were to:

1. Systematically review all existing and relevant literature on the feasibility and acceptability of LED for routine TB diagnosis in fragile states.
2. Investigate differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities.
3. Assess the knowledge, attitudes, perceptions and practices of healthcare workers regarding LED use for TB diagnosis at primary care facilities in Somaliland.
4. Identify key resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis at primary care facilities in Somaliland.

In line with the research objectives and corresponding questions, the body of the thesis is organized and presented in the form of eight chapters.

Chapter 1 has provided an introduction to tuberculosis (TB) as a human disease, including a basic description of different types and how the disease is transmitted, and discussed its control in the modern era. Chapter 2 provides details of the methodology used for the collection and analysis of the data, with specific statistical methods in line with the research questions and objectives, together with the theoretical framework.

Chapter 3 presents the findings from the systematic review of existing literature on the feasibility and acceptability of new TB diagnostic technologies in resource-poor and fragile states, with particular emphasis on the LED diagnostic technology for routine TB testing in fragile states. Chapter 4 describes

the findings of data analysis on LED and ZN use for routine testing at nine TB care facilities in Somaliland.

Chapter 5 presents the results of the health workers' knowledge, attitudes, perceptions and practices regarding the acceptability of LED technology for routine use at TB care facilities in Somaliland. Chapter 6 sets out the views of key informants on the resourcing, structural and environmental constraints to the feasibility of the introduction, implementation and utilisation of new TB technologies in fragile health system settings, using Somaliland as a case study.

Chapter 7 briefly summarises, discusses and interprets the findings in light of the research questions and objectives. Chapter 8 presents the concluding remarks and puts the work in context as it discusses the relationship between the applied diagnostic technologies and their implications for patients' diagnostic test outcomes in fragile health systems, together with any potential implications of the study for future TB control programs.

1.14 **Research questions**

The following questions framed the research activities:

1. To what extent is the introduction and use of new technologies for TB diagnosis feasible and accepted in fragile health states?
2. To what extent is the use of LED for routine TB diagnosis feasible and accepted in primary care facilities in Somaliland?
3. Do the knowledge, attitudes, perceptions and practices of healthcare workers towards LED use influence patients' TB diagnosis at primary care facilities in Somaliland?
4. What are the resourcing, structural and environmental constraints to feasibility and acceptability of LED use for TB diagnosis in Somaliland?

Chapter Two: Aims, objectives and methodology

This chapter is divided into, and presented in, five main sections: (1) study aims and objectives, (2) the conceptual framework and theoretical background, (3) methodology, (4) ethical considerations and (5) limitations.

2.1 Aims and objectives

The single overarching aim of this study was to improve access to quality of diagnosis for TB patients in fragile health system settings, with particular emphasis on Somaliland. The primary research objectives and questions were to:

1. Systematically review all existing and relevant empirical literature on the feasibility and acceptability of LED for routine TB diagnosis in fragile states.
2. Investigate differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities.
3. Assess the knowledge, attitudes, perceptions and practices of healthcare workers regarding LED use for TB diagnosis at primary care facilities in Somaliland.
4. Identify key resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis at primary care facilities in Somaliland.

2.2 Research questions

1. To what extent is the introduction and use of new technologies for TB diagnosis feasible and accepted in fragile health states?
2. To what extent is the use of LED for routine TB diagnosis feasible in primary care facilities in Somaliland?
3. What are the knowledge, attitudes, perceptions and practices of healthcare workers on LED use for TB diagnosis at primary care facilities in Somaliland?
4. What are the resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis in Somaliland?

2.3 **Conceptual framework and relevance of theoretical background**

The objectives and questions of this research drew inferences from the Technology Acceptance Model (TAM) and the Impact Assessment Framework (IAF) to explore the feasibility and acceptability of new technologies for routine TB diagnosis[161, 162].

One such new diagnostic technology, LED, was introduced by the WHO in 2011 as an alternative to ZN for regular TB diagnosis at the primary care level[163].

Over the last few decades, improving access to quality diagnosis for people suspected with TB and treating them successfully in a timely fashion in resource-poor settings has become the priority and cornerstone of global TB control[50]. While extensive literature has been established on the accuracy, efficacy and effectiveness of LED in resource-poor settings, research on feasibility and acceptability of new technologies in fragile states appears to be limited. The feasibility and acceptability of new TB diagnostic technologies for regular use such as LED in countries experiencing complex humanitarian crises, also known as fragile states, is unclear in the current TB literature[164-168]. Before getting into greater details of the theoretical background of the proposed conceptual framework, a brief description of the terms *feasibility* and *acceptability* is provided.

Feasibility is regarded as the degree to which applied interventions are technically feasible and can achieve the intended outcomes within the estimated resources (people, money and time) in a specific context[169-171]. Three questions generally guide feasibility assessment: can the intervention work (efficacy)? Does it work for the intended purpose (effectiveness)? Will it work in the real world (in all contexts)[169, 170]. Acceptability, on the other hand, is regarded as the degree to which an intervention is perceived as useful and easy to use by potential users[172, 173]. The theoretical orientation of this inquiry is grounded in multi-construct theoretical frameworks: the Technology Acceptance Model (TAM) and the Impact Assessment Framework (IAF)[123, 162, 174-176].

2.4 **The Technology Acceptance Model**

The Technology Acceptance Model is a systems theory to understand user motivation, and it is determined by three factors: *perceived usefulness, perceived ease of use* and *attitudes/behaviour* toward the applied technology intervention[162, 177]. The TAM was applied to explore the perceived views of intended end users toward LED technology acceptance for routine TB diagnosis within a

fragile health system context. The aim was to understand the *perceived ease of use*, *perceived usefulness and attitudes* among technology users.

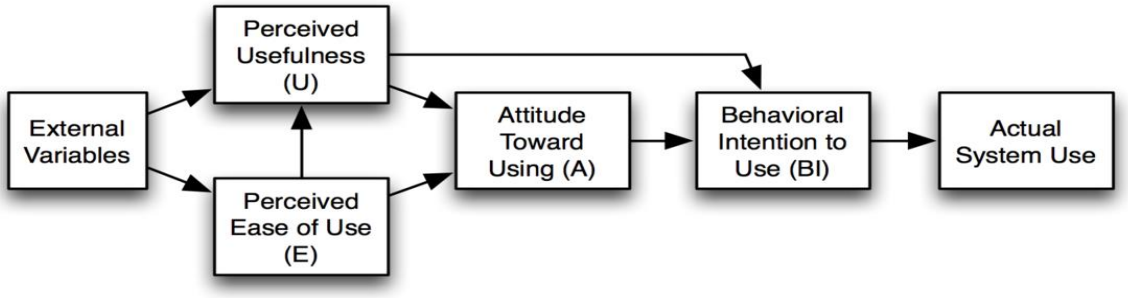

Figure 2.1 ***The technology acceptance model (Davis, 1986)***

These included those stakeholders providing primary care services and policy-making for TB care in Somaliland. Technology acceptance was determined by assessing the knowledge, attitudes, perceptions and practices of technology users on the LED technology for routine TB diagnosis at primary care facilities in Somaliland. Figure 2.1 summarises the TAM and its application and relevance to the proposed research.

2.5 **The Impact Assessment Framework (IAF)**

The IAF was applied to understand critical policy-making decisions for introducing and implementing LED for TB diagnosis in resource-poor settings[123, 174, 175]. To understand factors that help or hinder the introduction and use of LED technology for routine TB diagnosis in fragile settings, this research drew its inference from the IAF to link feasibility with acceptability [123, 174, 175]. This research examined the four system elements critical to the successful introduction, implementation and utilisation of the applied technology in a fragile health system environment.

The four critical elements were context (fragile settings), infrastructural capacity (the health system's capability to support and sustain the delivery of TB diagnostic services), processes (strategies used for the deployment and utilisation of new tools) and outcomes (diagnosis/treatment provided to the intended beneficiaries – TB patients). It examined the extent to which pre-existing health systems have systematic and programmatic readiness. This includes, but is not limited to *resource* (people, money,

time, information) *capacities*, *structural capabilities* (physical space) and the *conducive environment* to support and sustain the introduction and implementation of new TB diagnostic technologies in a fragile context with limited resources[123, 174, 175, 178].

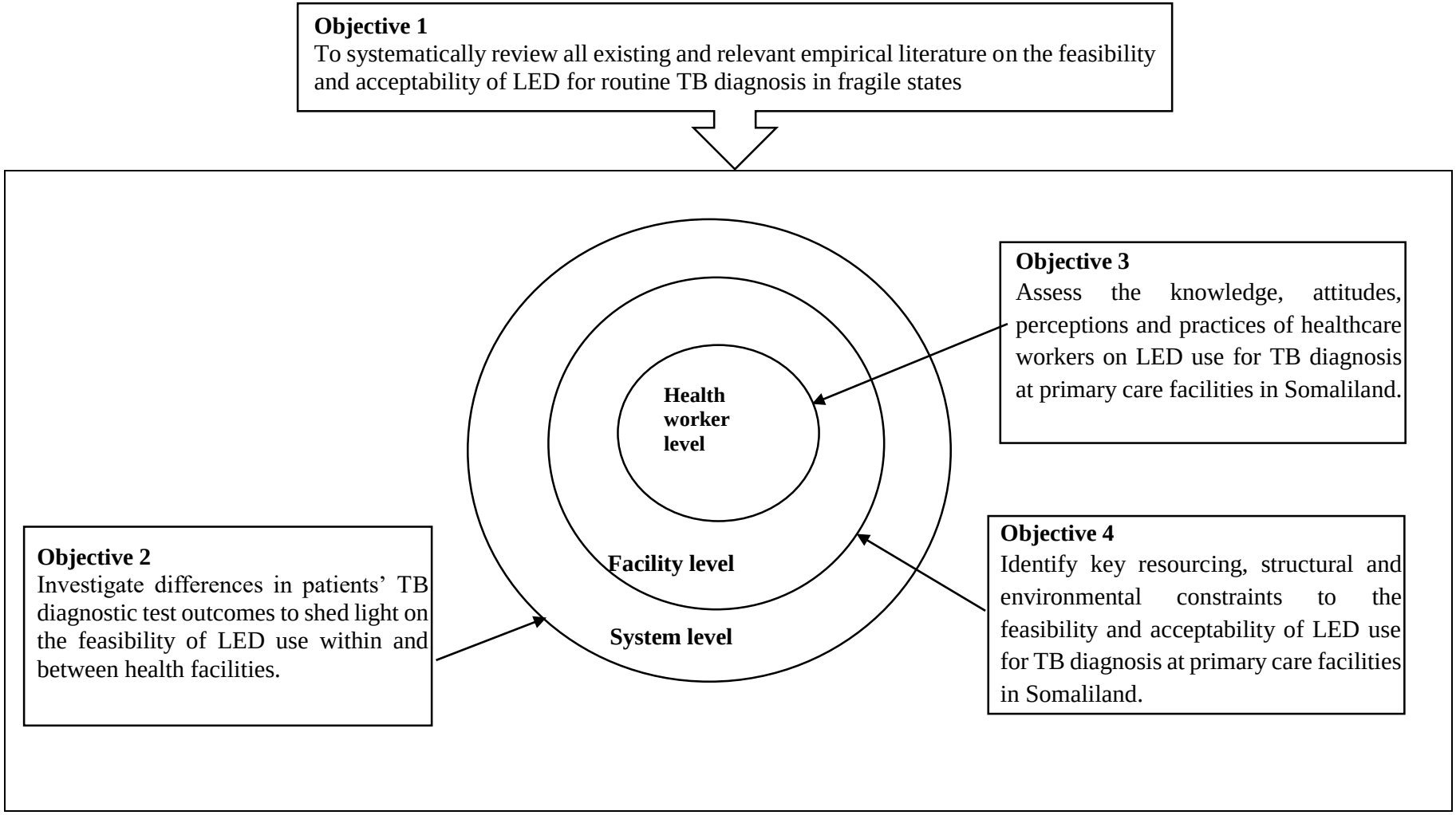

Figure 2.2 ***The conceptualized relationship between objectives on the feasibility and technology acceptability of LED in fragile health systems***

Therefore, the applied theoretical models provided the researcher with an opportunity to build the basis of this inquiry. They also allowed the researcher to appraise key health system features that influence feasibility and acceptability of the introduction, implementation and uptake of new TB diagnostic technologies such as LED in fragile health system settings[177, 179].

Objectives 3 and 4 generated vital information from interviews with policy-makers and primary care providers involved in TB care services. These interviews provided useful insights on key factors that influence the feasibility and acceptability of new TB technologies in fragile health system settings. Facility-based clinical data (quantitative) generated through the parallel implementation of new (LED) and old (ZN) TB diagnostic technologies was analysed to draw valuable insights regarding technology acceptability by end users in facilities. Furthermore, these theoretical frameworks helped the researcher construct the conceptual framework and research objectives together with corresponding questions for the proposed research (Figure 2.2).

Figure 2.2 depicts the main elements of the conceptual framework and the four objectives. The findings of objective 1 (systematic review of the literature) guided the analysis of diagnostic data on LED and the development of the data collection tools (interview guides) used for objectives 3 and 4, and feasibility and acceptability of new technologies in fragile health system settings.

2.6 **Methodology**

This research utilized a mixed-method approach for the collection, analysis and interpretation of primary and secondary data in line with the research objectives, questions and main methods which are presented in table 2.1.

Primary data used for this study came from the following sources: quantitative data (facility-based clinical data) from nine TB diagnostic service facilities in Somaliland, and qualitative data from semi-structured interviews with primary care providers and health professionals. Secondary data were elicited through the review of policy, technical and operational documents and on-site visit observations: the findings are presented in chapters 4-6. A systematic review of the existing and relevant empirical literature on the feasibility and acceptability of introduction, implementation and utilization was conducted for one particular technology (LED) for routine TB diagnosis in a resource-limited fragile health system context.

Table 2.1 ***The linkage between research objectives, research questions and corresponding methods***

Research objectives (RO)	**Research question (RQ)**	**Main methods**	**Analytical tool**
Objective 1: To systematically review all existing and relevant empirical literature on feasibility and acceptability of LED for routine TB diagnosis in fragile states.	**RQ 1:** To what extent is the introduction and use of new technologies for TB diagnosis feasible and accepted in fragile health states?	Systematic review	- Thematic analysis - Qualitative analysis
Objective 2: Investigate differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities,	**RQ 2:** To what extent is the use of LED for routine TB diagnosis feasible in primary care facilities in Somaliland?	Quantitative analysis of facility-based data	Descriptive statistical analysis
Objective 3:.Assess the knowledge, attitudes, perceptions and practices of healthcare workers on LED use for TB diagnosis at primary care facilities in Somaliland.	**RQ 3:** What are the knowledge, attitudes, perceptions and practices of healthcare workers on LED use for TB diagnosis at primary care facilities in Somaliland?	- Semi-structured interviews/ - Observational data collection - Document review	Thematic analysis
Objective 4: Identify key resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis at primary care facilities in Somaliland.	**RQ 4:**What are the resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis in Somaliland?	In-depth interviews and document review	Thematic analysis

2.7 A systematic literature review of the feasibility and acceptability of new TB diagnostic technologies in fragile states (Objective 1 and Question 1)

This study systematically reviewed, synthesised and appraised all existing and relevant empirical (qualitative, quantitative and mixed methods) evidence that met pre-specified eligibility criteria on the feasibility and acceptability of the introduction and implementation of light-emitting diode fluorescence microscopy (LED) for routine TB diagnosis in resource-poor settings. The WHO introduced and recommended the LED technology in resource-poor and high-TB burden countries in 2006. The aim was to replace the conventional Ziehl-Neelsen microscopy (ZN) for routine TB diagnosis to improve access to quality diagnosis and ultimately escalate TB case finding in resource-constrained and high TB burden settings[180]. New technologies such as LED need health systems to be effective and acceptable to both patients and intended users (laboratory technicians) for routine use in resource-constrained settings [54, 148, 171, 181]. This review investigated the extent to which the introduction and implementation of new technologies for routine TB diagnosis were both feasible and accepted by their potential end users (health workers) at all levels of the care delivery system in fragile health systems.

To strike a balance between broad, specific and systematic searches, the review, synthesis and appraisal of relevant empirical evidence on feasibility and acceptability was limited to literature in the English language indexed in various medical and health sciences databases for published data or studies from 2006 to the present. In addition, unpublished (grey) literature was identified from contacts with experts, conference and dissertation abstracts, reference lists of key papers and hand searched for in relevant book chapters as well as relevant websites.

The review of existing and relevant evidence on the feasibility and acceptability of the LED diagnostic technology was determined in three ways. First, patients' diagnostic test outcomes achieved through LED technology use and other testing techniques were compared. Second, resource availability (people, money, time), structural capability (systematic and programmatic readiness, integrated care services) and the supportive environment (organisational communication and collaboration strategy and policy contexts) established to enhance quality of TB care services in a fragile health system context were reviewed. Third, acceptability was determined from a technology acceptability point of view by user motivation (the intended or end user), influenced by perceived usefulness, perceived ease of use and attitudes towards using the applied technology (LED) in fragile health system settings. The review specifically examined how *increased positivity rates* in patients' diagnostic outcomes were linked with the feasibility and acceptability of the introduction, deployment and utilisation of LED in settings with weak health systems.

The search strategy and selection criteria followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statements and checklist as well as the reporting format, where relevant. Because TB is a subject of high interest and a simple search could generate multitudes of results, a carefully selected collection of keywords (search strings) were used to whittle down available and relevant empirical research on the subject for review. The researcher constructed a theory-informed conceptual framework to assess the feasibility and acceptability of LED technology in a fragile health systems context. Review questions were framed around the population, intervention(s), methods, comparator(s) and outcomes of the studies included in the review.

The elements of the review objectives and questions, together with the study design, were then refined to determine the specific inclusion and exclusion criteria used in the selection of studies for review. Data extracted from reviewed studies were analysed for overall and sub-group feasibility and acceptability by tabulating the diagnostic test outcomes of each study included in the review. The tabulation of diagnostic test outcomes (*true positive, true negative, false positive and false negative*) analysis generated through LED testing and reported in all included studies was used for group and sub-groups and the results presented in 2x2 contingency tables. In addition, relevant qualitative data was compiled, tabulated and analysed. More details on data and statistical analysis are presented in chapter 3.

2.8 **Differences in patients' TB diagnostic test outcomes within and between health facilities to shed light on the feasibility of LED use (Objective 2 and Question 2)**

Method: Facility-based diagnostic data quantitative analysis

Setting: Nine TB diagnostic facilities in six regions of Somaliland

Patients: 14176 patients presumptive of TB who provided specimen samples for TB testing at nine laboratory facilities that implemented LED in parallel with ZN for routine TB diagnosis in Somaliland.

Data and data sources: Data on paired samples (dependent samples) from 14176 patients aged a year and older who were tested for TB with ZN and LED at nine diagnostic facilities for 12 months period (April 2012 to May 2013) were obtained from the Somaliland National TB Program database for analysis. Data on the diagnostic test results of paired samples from 14176 patients who provided specimens for examination at the nine laboratory facilities were extracted and uploaded into an MS Excel spreadsheet.

Data analysis: The analysis of the paired samples was done at the 1st, 2nd and 3rd specimen-level for overall test results and at the patient-level restricted to positive and negative subsets. The differences in the paired proportion of subsets of positive and negative by each technology were analysed using the standard formula. The exposure variable was the testing technologies (ZN and LED) and the outcome of interest was the differences in test results of the paired proportions at the specimen and patient levels. The expected outcomes were proportions and differences in patients' positivity rates between LED and ZN.

Statistical analysis: Data on demographic and diagnostic outcomes of all TB patients tested for TB were analysed using STATA statistical software version 15.1, Houston TX, 2017[182]. The proportions of patients' test outcomes stratified by gender and facility, including all tests with inconclusive diagnostic outcomes, were cross-tabulated, and the summarised findings presented in contingency tables, together with age expressed as median with interquartile range (IQR). All patients with inconclusive test outcomes (i..e., 'missing', 'scanty' or 'not done') by LED and ZN were excluded from the patient-level analysis.

The difference between the paired sample proportions was calculated from the numbers of concordant (s) and discordant pairs (r) divided by the total number of pairs (n). The hypothesis of the paired sample proportions was grounded on the assumption that the proportion of patients with positive and negative outcomes was higher with LED technology testing than ZN testing.

Differences in proportions of the paired samples were determined again at the specimen and patient level but restricted to subsets with negative and positive test outcomes using the χ^2 test with odd ratios (ORs) along with their 95 % confidence intervals (95 % CIs). All tests were two-tailed. The outcome parameters were estimated, summarised and presented in tables. Further details on data and statistical analysis are presented in chapter four (facility-based diagnostic data analysis). Both the study and use of diagnostic data for analysis were authorised and approved by the Somaliland National TB Control Program of the Ministry of Health. The lead researcher guaranteed that all data collected will be anonymized and securely protected with the utmost confidentiality.

2.9 **Knowledge, attitudes, perceptions and practices of healthcare workers on LED use for TB diagnosis at primary care facilities in Somaliland: a Somaliland healthcare worker survey (Objective 3 and Question 3)**

Method: Qualitative approach

Study site: This study took place at four TB care facilities in two large urban towns and cities in Somaliland between December 2018 and January 2019 (Figure 2.3 & Table 2.2).

Figure 2.3 ***The distribution of LED intervention centres selected for study in Somaliland***

The selection criteria for study sites was based on the LED intervention status and Somaliland security travel restrictions as advised by the LSHTM and UK-Foreign and Commonwealth Office. Facilities selected for the study were Berbera, Gabiley, Hargeisa TB Hospital and Hargeisa-Finsoma.

Data collection: Semi-structured interviews (SSIs) with primary healthcare providers (*n* = 25) working in TB care facilities for primary data collection.

Table 2.2 ***List of TB care facilities and their supporting agencies in Somaliland***

No.	TB care facilities and their geographical locations	Supporting agency	LED recipient
01	Berbera	COOPI- Inpatient	Yes
02	Gabiley (outside Hargeisa)	World Vision-inpatient	Yes
03	Hargeisa	KJRC- Inpatient	Yes
04	Hargeisa Finsom	PSR Finland- Inpatient	Yes

Source: Somaliland National TB Program (MOH-Somaliland).

Strand one: semi-structured interviews (SSI) with healthcare providers working at TB care facilities

The eligible study population for interviews were all staff working at all facilities (n= 4) selected for study.

Sampling technique: Purposeful sampling

A total of 25 participants comprising laboratory technicians (*n* = 15), primary care physicians (*n* = 6) and nurses (*n* = 4) were to be purposefully selected from four TB care facilities for face-to-face interviews utilising the SSI interview guide. The selection of the study participants for interviews was solely based on the length of experience in TB and LED technology use. The research team briefed the participants to clear any lingering confusions and concerns about the study. Each participant was given a written copy of the consent form in their preferred language to sign. The consent forms provided participants with information about the purpose of the study, the use of interview data, access to the data and the point of contact for clarifications or further questions. The informed consents were translated from English into Somali (the local language) for participants.

All study participants were informed about the recording of the interviews, the risks and benefits involved in their participation and the lead researcher ensured all participants understood this. The purpose was to keep study participants actively engaged in the interview discussions to provide useful insights on constraints to technology acceptance for routine use. The principal investigator asked specific questions about the feasibility and acceptability of the introduction and use of LED technology for routine TB diagnosis in Somaliland. Key user motivation issues such as perceived usefulness, perceived ease of use, attitudes toward technology acceptance (the percieved use and ultimately actual use) of the new diagnostic technology by health facility staff at the TB care facility level were assessed. The interviewer tried not to lead participants to any preconceived notions or encourage participants to provide particular answers by expressing approval or disapproval of what health workers said.

Participants were assured that their confidentiality would be protected and that data collected would be used for research purposes only. All interviews were conducted in private locations with no outsiders present and in a relaxed manner. The aim was to keep participants at ease and comfortable to maximise responses and ensure all interviews proceeded smoothly in a structured way. Each interview took 40-60 minutes, was recorded and subsequently uploaded to a data storage device, and kept in a safe and secure location with password access only. All audio recordings and the interview scripts were kept in safe and secure locations without the names of interviewees on transcripts. In addition to SSIs, field notes were taken to capture any valuable information mentioned during the interviews.

Interview guide: An interview tool was developed, tested and used to guide the interview discussions to ensure that all study questions were answered accordingly and purposefully. The interview guide was generally constructed according to the Technology Acceptance Model (TAM) framework and asked study participants to provide explanations about their knowledge, attitudes, perceptions and practices towards the use of LED technology application for TB diagnosis at the facility level. Finally, the study respondents were asked to provide recommendations, suggestions and viable solutions for improvements of TB care delivery in a fragile health system setting like Somaliland. The interview tool combined an outlined, simple semi-structured interview script with a list of open-ended questions relevant to the research topic. The questions used in the interview guide for semi-structured interviews are presented in the Appendix to chapter 2.

Compiling and organising interview data: All data and relevant information elicited from the interview transcripts, and field notes, were organised, transcribed and compiled into a Word

document and Nvivo for analysis. Organising data in such a manner provided an opportunity for the research team to acquire individualised documents with all of the interviewee's discussions organised under each question. To draw a clear line between the relationships across different interview transcripts and field notes, data were grouped, merged and organised into major categories (themes) in accordance with the research objectives, questions and theoretical framework for analysis.

Strand two: site visit observations

Data collection: On-site visit observations at the same TB care facilities (n=8)

Sampling technique: The site visits took place in four TB care facilities (Hargeisa TB Hospital, Gabiley TB centre, Finsoma TB centre and Bebera TB Hospital). Two site visits were made to each facility. All data acquired through site visit observations were read, proofread, verified and written legibly in the native language of the study subjects (Somali) before leaving the study sites. The site visit took place between December 2018 and January 2019 at the above-stated TB care facilities (Table 2.2). The first site visits to each facility covered the introduction to the research team, the purpose of the study, set plans for future site visits and information collection. The principal investigator administered all site visits with the help of a research assistant for note-taking.

Observations guide (checklist): A site visit checklist was developed and used to guide observations to capture insights on day-to-day operations, interactions, use and compliance with guidelines, standard operating procedures, and to understand systems issues and challenges in routine LED technology use for TB diagnosis at the facility level. The site visit observations were used to gather knowledge of the day-to-day interactions, experience, practices and behaviours of healthcare workers in the use of new technologies including LED for routine TB diagnosis at the facility level. On-site visit observations were also intended to explore key constraints to the routine use of new technologies, including staff competence, the use of guidelines, protocols and standard practices at the facility level. Particular attention was paid to user motivation issues such as perceived usefulness, perceived ease of use, and attitudes toward technology acceptance (use and actual use) by health facility staff, using the observation checklist.

To analyse and synthesise the site visit observation data, the researcher adopted the thematic framework-based analysis approach by creating numerous codes and coding processes (i.e., organising the data into chunks before bringing meaning to the chunks). The codes served as labels to compile and assemble data and integrate major emerging themes in the data. This type of analytic

approach allowed the researcher to eliminate less useful themes, identify relevant themes and sub-themes and link them them into the theoretical models of this research for thematic analysis. The frequency distribution of the findings was tabulated, summarised and displayed and presented in tables and figures. More details of the thematic analysis and the study findings are presented in chapter 5 of the thesis.

Documents review: The document review looked at operational data, program monitoring, evaluation templates, infection control guidelines, standard operating procedures for diagnosis, treatment and case management, infection control protocols and training manuals for facility staff. Reviewed documents were developed/contributed by various agencies involved in TB care delivery (WHO STOP-TB, Global Fund, World Vision and NTP-Somaliland). Documents reviewed were mainly operational documents (standard operating procedures, guidelines, training manuals and protocols for different laboratory functions/tasks (i.e., documentation of patients' diagnostic/treatment outcomes and LED technology use and maintenance) at the facility level. More details about the interview process and data collection tools are provided in chapter 5.

2.10 Key resourcing, structural and environmental constraints to feasibility and acceptability of LED for TB diagnosis in Somaliland (Objective 4 and Question 4).

Method: Qualitative approach

Study site: The study took place at the managerial offices of healthcare professionals selected for the in-depth interviews in Hargeisa, Berbera and Gabiley in Somaliland between December 2018 and January 2019.

Data collection: In-depth interviews with key informants (policy, managerial, technical and coordination teams) complemented the key policy document review. The interview guide was constructed according to the impact assessment framework (IAF) where study participants were asked to provide explanations about key resourcing, structural and environmental constraints to the feasibility of the introduction of new technologies for TB diagnosis[161, 162]. Approximately 20-30 interviews were planned to be conducted with key informants (KIs) – healthcare professionals from various TB care providers (i.e., public, private and NGOs) in policy, managerial and technical positions. Participants were informed about the purpose of the interviews, as indicated in the informed consents in the study protocol.

The principal investigator was assisted by a note-taker, and each interview took 40-60 minutes. All conversations were recorded with the consent of the study participants. At the beginning of each

interview, key informants were asked about their roles and responsibilities in strategic and policy formulation for TB care service provision as well as their perceptions towards TB diagnostic service delivery in Somaliland. Subsequently, the principal investigator gradually advanced the interviews with detailed and probing questions on various topics in TB diagnostic services. See the interview guide in the Appendix for chapter 2.

Data analysis: The interview data were imported into NVIVOv 12 software and were coded manually. The quality and cleanness of the interview transcripts were thoroughly checked by listening to the recorded interviews. With the help of transcriber(s), all interview interactions were recorded on the interview recorder, including all interruptions (noise, unexpected noises). The principal investigator then identified and summarised meanings and meaning units in a paragraph format with similar contents. Preliminary codes across comparable or similar meaning clauses emerging from transcripts were merged and thematically analysed. More details on the framework-based thematic and content analysis are presented in chapter 6.

2.11 Ethical approval of the research protocol

The proposed research was approved by the London School of Hygiene & Tropical Medicine Ethics Committee and the Somaliland Ministry of Health Research Ethics Office. All potential research subjects received oral and written information about the aims and objectives of the proposed research. All potential research subjects signed a consent form before their participation in the research activities. All research subjects were free to decline, accept or withdraw from participation in this research whenever and wherever they chose to do so. All excluded data on subjects who rescinded their participation in the study were safely stored on secured servers.

Chapter Three: Feasibility and acceptability of new tuberculosis diagnostic technologies in fragile states: a systematic literature review

3.1 Introduction

This chapter presents the findings from a review of the literature on the feasibility and acceptability of new TB diagnostic technologies in resource-poor and fragile states. This review aimed to determine the feasibility and acceptability of one particular TB diagnostic technology called light-emitting diode fluorescence microscopy (LED) for routine TB testing in fragile states.

While exploring and reviewing the relevant literature, the author found that while extensive research existed on various aspects of LED performance in stable settings, limited literature was available on the feasibility and acceptability of LED technology for routine TB diagnosis in fragile states. Consequently, the search was extended to the feasibility and acceptability of LED in resource-poor and fragile states to maximise the value of the search. In addition, the formulation of the review research objectives and questions helped the construction of the conceptual framework discussed elsewhere in the thesis.

The review question was framed in terms of the population, intervention(s), comparator(s) and outcomes of studies included in the review. These elements, together with the study design, were then refined to determine the specific inclusion criteria used to select the retrieved studies. The review questions were: (1) To what extent is the introduction and utilisation of LED technology for TB diagnosis feasible, and accepted in resource-poor and fragile health system settings? (2) What are the main gaps in the existing literature on the feasibility and acceptability of LED-FM in resource-poor and fragile health system settings? (3) How does current research on TB diagnosis define, theorise about, analyse, assess and measure the feasibility and acceptability of complex healthcare interventions in resource-poor and fragile health systems?

The terms of feasibility and acceptability were defined and theorized from a healthcare perspective.

3.2 Review framework and methods

Review framework

This review drew inferences from How to Design Feasibility Studies (Bowen et al., 2009) and the Technology Acceptance Model (Davis et al.,1985) for feasibility and acceptability assessment respectively[162, 169, 170]. These frameworks were adopted to guide the assessment of how the studies selected for review defined and theorised the feasibility and acceptability of the implemented interventions in their own analysis from a resource-poor and fragile state perspective.

The review defined feasibility as “the likelihood an intervention can be done, can work or should proceed with the concerned strategy and purpose in a specific context” with existing resources[1, 2, 74, 183]. The review’s feasibility assessment framework was adopted from Bowen et al (2009), regarding design and evaluation of studies on the feasibility of health care interventions, and the potential challenges faced by implementers, program designers (policy-makers) and deliverers (primary care providers). According to Bowen et al. the feasibility assessment framework elucidates that the success and failures of any applied intervention are often influenced by the resources and structure available locally. They are also influenced by the knowledge, attitudes, perceptions and practices of program designers, deliverers and the immediate environment in which these actors operate. Health systems consist of three levels that facilitate, support and sustain the introduction, implementation and uptake of the applied interventions: the system, facility and provider levels.

Existing literature provides no clear and context-specific definition for the term acceptability from a provider’s and user’s perspective, and there are many ambiguous definitions used in the healthcare literature. The review defined acceptability as “the conformity to the wishes, desires and expectations of patients and responsible members of intended beneficiaries or users”. The TAM is concerned with technology acceptance or user motivation influenced by the usefulness of, ease of use, and attitudes towards use of the applied technology. Technology precedes use whereby acceptance is incumbent on the attitude of the individual, which is influenced by other factors [2, 3, 6, 7, 24, 184]. Therefore, technology acceptance is a multi-faceted construct that reflects the degree to which these constructs are considered in the planning, delivering or receiving of the intervention to ensure the feasibility based on previous experience or/and anticipated outcome including user responses to interventions concerned[135, 185].

Feasibility and acceptability are inextricably linked and essential for viability analysis to ensure that the applied intervention is operationally, technically and economically feasible, justifiable and accepted by the intended users. The feasibility framework argues that for any applied technology to be feasible, it needs to be accepted, implemented, used (demand), integrated and practical with a potential to expand in any given context[169, 170, 186, 187].

3.3 **Methodological assessment of reviewed studies**

To systematically theorise, synthesise, appraise and bring together the principal findings of the reviewed studies in a narrative manner, this review combined inductive (data-driven) with

deductive (theory-driven) procedures to assess literature on the feasibility and acceptability of LED technology. Inductive theorisation focused on how and to what extent empirical literature formed/influenced theory-based analysis for feasibility and acceptability assessment of new TB diagnostic technologies including LED-technology for routine utilisation in the given context[188, 189]. The deductive synthesis appraised the premise theory applied in the individual studies reviewed to understand large bodies of empirical evidence, as well as to help explain differences among the reviewed studies on relatively the same or similar question(s)[190].

Preliminary scoping searches identified no empirical evidence focusing on the feasibility and acceptability of new or optimised TB diagnostic technologies, including LED technology, in a fragile health system context. However, a few studies were identified that considered the feasibility and acceptability of the new or optimised TB diagnostic technologies alongside other factors such as adoption, performance, efficacy and the diagnostic accuracy of such diagnostic technologies in resource-poor settings. Therefore, the search for feasibility and acceptability of new TB diagnostic in fragile state was expanded to resource-poor health system contexts.

The feasibility assessment framework elucidated how the success and failures of applied interventions are influenced by critical infrastructural features (resourcing and structural) of the existing health system[169, 170]. It equally attempted to illuminate how individual studies selected for review separated feasibility study from feasibility analysis for assessment. The review assessment was also concerned with the extent to which individual studies considered key feasibility attributes: acceptability, demand, implementation, practicality, adaption, integration, expansion and limited efficacy.

Therefore, this systematic review involved, and was enhanced by, the application of scientific inductive and deductive theorisation processes. These were used in ways that limit bias, help assemble and critically appraise and synthesise all relevant studies that addressed a scientific research question on various aspects of LED technology use for TB diagnosis[191-195]. Such an approach helped establish and gain an in-depth understanding of how existing literature defined, theorised, assessed and measured the feasibility and acceptability of the introduction and implementation of the LED technology for routine use in resource-poor settings. It specifically determined how individual studies selected for review framed, defined, assessed and verified their research objectives, questions and methods of data collection and analysis of their research findings.

3.4 **Search strategy**

This search focused on both published and unpublished literature indexed in four databases: Global Health databases (EBSCO), Med-line/OvidSP, PUB-MED and Cochrane Library. All studies that used qualitative, quantitative or mixed methods were included. Unpublished (grey) literature was identified from contacts with experts, conference and dissertation abstracts, reference lists of critical papers and hand searches of relevant book chapters as well as searches of relevant websites. Because TB is a subject of high interest and a simple search could potentially generate thousands of results, carefully selected search strings were used to whittle down relevant literature.

The author further used "Medical Subject Headings (MeSH)" terms for search in both Med-Line and Pub-Med, including text search. In search engines with no MeSH terms (i.e., Google Scholar and Cochrane Library), exploding searches were used to find all relevant literature. In doing so, MeSH terms were combined with automated and manual searches and the full text was extracted after reviewing each abstract retrieved. Such searches were later expanded to all different sources to capture all relevant literature on the feasibility and acceptability of LED technology use for routine TB testing or diagnosis in resource-poor and fragile state settings. All study types were included in the search, as this search was conducted in the full text of each study.

To identify relevant studies in the grey literature, the author searched *OpenGrey* and the websites of critical agencies or organisations that have technical expertise in delivering health programs, particularly those tackling TB in conflict-affected or fragile states and resource-poor settings. These agencies were the International Union Against Tuberculosis and Lung Disease (The Union), the World Health Organization STOP-TB Partnership (WHO-STOP TB), and Médecins Sans Frontières (MSF). Pre-selected subject experts on TB diagnosis in fragile states at academic and research institutions, NGOs, UN agencies (WHO-STOP TB), and centres of disease control (USA, E-CDC, AU-CDC) or otherwise were consulted where relevant. Additionally, the author hand searched for unpublished material in the grey literature, including reports, manuscripts, conference or working papers through Google Scholar for .pdf, .doc, and documents with combined titles of technologies, diagnostics, tools, tuberculosis (in English), and/or fragile state(s).

Furthermore, the author looked through reference lists of critical papers, searched by hand for relevant book chapters and searched relevant websites. Qualitative, quantitative and mixed methods study types were included in the search and reviewed. All studies, articles, publications and abstracts with any information on LED diagnostic technology, methods or/and tools in resource-poor settings including fragile states, populations affected by conflict, armed conflict, complex

humanitarian crises, complex emergencies and internally displaced people or populations were carefully screened and checked for eligibility. Lastly, the author screened the bibliographies of all selected and included studies. Table 3.1 in the Appendix to chapter 3 presents the search terms, strings, concepts and variations for all databases that were searched.

3.5 Period for review

The review period was restricted from 2006 to 2018. The reason for choosing 2006 to the present is because the technology was introduced in 2006. Publications were limited to the fragility period of each country or setting as defined and measured in the state fragility index (where relevant) and followed the backward literature searching identified through the searches stated above[196-199]. Both ″state fragility″ and ″fragility period″ terms were defined and determined in chapter 1 of this thesis. A fragile state has weak state capacity or weak state legitimacy, leaving citizens vulnerable to a range of shocks, including lack of access to basic healthcare services[200]. Initial searches were conducted in November 2017 and later updated in July 2018. All studies not in the English language were excluded.

3.6 Screening of the selected citations and eligibility criteria

Two reviewers collectively and independently screened individual study titles and abstracts included in the relevant accumulated abstracts from various databases and in the grey literature in two rounds. In the first round of the screening process, all duplicates of the selected abstracts were removed in Endnote and each abstract reviewed by the lead researcher against the inclusion and exclusion criteria (Table 3.2, Appendix 3). After removing duplicate records, 201 abstracts were eligible for further screening. All relevant studies reporting research findings on LED performance compared to other microscopy devices or technologies with sufficient scientific rigor and details/information about the individual research methods used were included for review. All retrieved studies were checked for duplication, uploaded, stored and tracked on Endnote Software version X9.

To assess the reliability of the screening process, a second reviewer independently reviewed 100% of the selected abstracts. Both reviewers then reached 100% agreement on all selected abstracts for full text review. All studies meeting the pre-defined inclusion criteria were then moved to full text review and validated. In the second round, a comprehensive and independent full text review of the eligible studies was performed first by the lead researcher and subsequently by a second reviewer. All descriptive and comparative studies and systematic reviews on the feasibility and acceptability of LED for the diagnosis of pulmonary tuberculosis conducted in resource-poor settings, including

fragile settings, were selected and included for full text review. All discrepancies in the preliminary full-text review were again resolved through discussions between the two reviewers.

3.7 **Data extraction**

The lead researcher used a specific data extraction template and strategy according to the review objectives and questions. Data extraction for qualitative evidence was typically iterative, as the reviewer read all primary papers identified and retrieved for review, followed by data synthesis and interpretation in several cycles to identify key themes in the selected studies. The lead researcher retrieved all selected studies that met the inclusion criteria and extracted data on definitions, methods for data collections and analysis, theoretical frameworks and measurement for assessment of feasibility and acceptability using a data extraction form. A second reviewer subsequently and independently reviewed 50% of the included studies for full text review and extracted information/data using a similar data extraction format used by the lead reviewer.

Additional studies were included if the study evaluated, assessed or provided data/information on accuracy (sensitivity and specificity), or data on feasibility, acceptability, adoption, introduction, implementation and performance of LED for routine TB diagnosis in fragile states. All studies with sufficient and relevant information on knowledge, perception, attitudes, and practices of health care providers about the perceived usefulness, and reported ease of use of LED by users at primary care facilities in fragile states were later included for review.

Information on study designs, populations and measures of association for LED use, performance and outcomes for included studies was extracted for analysis. Detailed information was sought for extraction on the study settings (health systems), participants, the intervention delivered given the context (fragile states), and feasibility and acceptability. The aim was to aid and help retain data interpretation and synthesis in the specific context in which the data were generated and embedded. Particular attention was paid to the frequency of specific themes emerging from data collection with particular study participants (i.e., laboratory technicians, nurses or doctors, technical/implementation staff, managerial and policy-making teams) in the introduction and utilization of new technologies for TB diagnosis in fragile health system settings.

The first reviewer assessed, recorded and checked for consistency for all selected studies for review. A second reviewer verified all extracted data from selected studies for consistency between the first and second reviewers. All differences and disagreements arising from the selected studies across viewers were resolved.

3.8 **Quality assessment of review results**

For quality assessment of the extracted studies, definitions and measurements of feasibility and acceptability indicators were first determined. To explore how individual authors defined, theorised, measured, assessed, synthesised and analysed feasibility and acceptability in individual studies, the lead researcher extracted definitions from each of the included studies, including systematic reviews. The methodological quality of individual articles was assessed in all studies selected for full text review. The Cochrane Tool of Quality Assessment for Diagnostic Accuracy Studies (QUADAS) was used for all studies selected for review[201]. All studies chosen for review were scrupulously and independently assessed, and rated for quality by the first and second reviewer. The QUADAS checklist comprised 14 questions. Of these, each included study was given one of the yes, no or cannot tell answers for each question (Table 3.3, Appendix 3). If the study received yes answers for the first three questions, the study met the objectives of the review. Quality assessment and analysis (QUADAS) of the results of the extracted evidence for each study reviewed are presented in table 3.4 in Appendix 3.

Another quality assessment tool applied was based on the Bowen et al. (2009) feasibility assessment framework (FAF)[169, 170]. The quality of the included studies was assessed based on key feasibility attributes such as *acceptability, demand, implementation, practicality, adaption, integration, expansion* and *limited-efficacy* (Table 3.5 and 3.6 in Appendix to chapter 3)[169, 170]. The reviewer specifically examined the types of information provided on *technology acceptance* and *actual usage* for the intended purpose in a fragile health system. All studies that did not meet the feasibility criteria were excluded from the data extraction tables.

Subsequently, studies were appraised for risk of bias within individual studies and across studies. Risk of bias within individual studies was assessed in two ways: (1) looking at the methods used, and at what level (study or outcome level) the risk of bias was appraised, and (2) checking to see if authors provided any specifications about how the study result was intended to be used. For risk of bias across studies, studies were appraised for any risk that could potentially affect the cumulative evidence (i.e., publication bias and selective reporting within studies). Considerable attention was paid to any risk of bias that could potentially downgrade evidence for individual studies and across studies in the quality assessment process. Key elements assessed included inconsistencies, severe indirectness, imprecision and the likelihood of publication bias.

3.9 **Assessment of feasibility and acceptability in reviewed literature**

All studies selected for review were assessed for feasibility on crucial principles of acceptability, demand, implementation, practicality, adaptation, integration, expansion and limited-efficacy testing at all levels of the care delivery process (individual, facility and health system levels)[169, 170]. Specifically, eligible studies were also assessed for acceptability on potential user motivation influenced by the *perceived usefulness*, *perceived ease of use* and *attitudes towards usage* of the LED technology for routine use. The search, quality screening, review, syntheses and analysis of the selected studies mainly focused on how and what tools, processes, measures, indicators, theoretical frameworks and methods were used to assess feasibility and acceptability of the LED technology in settings where it was introduced. It explicitly assessed the extent to which existing and relevant literature addressed the human (people, money and time), and material cost (operational, technical, regulatory) as well as the environmental (organizational buying, culture) viability of the new technology introduced and implemented for routine utilization in fragile health system settings. The full details of the summary of selected articles are presented using the Preferred Reporting Items Systematic Review and Meta-Analysis (PRISMA) format in Figure 3.1.

3.10 **Statistical analysis**

A standardized data extraction form was developed and used for statistical analysis. The reviewer tabulated the true positives (TP), false positives (FP), false negatives (FN) and true negatives (TN) for each study reviewed. The tabulation of outcomes included all studies that reported yield from sub-group analysis including HIV-infected TB patients generated through LED testing, and a 2x2 contingency table was constructed. All participants with incomplete and irrelevant data such as missing, contaminated and non-TB were excluded from the feasibility analysis. A review manager (5.2) was used to generate forest plots and calculate and display sensitivity and specificity results together with their corresponding confidence intervals (CIs).

In addition, data on LED diagnostic accuracy reported by individual studies were divided into sub-groups based on implementation sites of LED in different countries or settings: referral laboratory, peripheral laboratory, hospital facility, or primary care facility, or the combination of all types of healthcare facilities that provided data for use to authors of individual studies. The sub-group analysis aimed to determine whether the LED sensitivity and specificity outcomes were influenced by the type and location of the diagnostic facility. The analysis criteria included the article type and use of LED technology, year of publication, study location, the use of definitions for feasibility and acceptability and the conceptual theories and conceptual frameworks behind the studies.

3.11 **Results**

Characteristics of included studies

A total of 201 articles were identified through the searches of various databases and retrieved for full text review. Of these, 159 articles were identified through systematic searches in five databases: Embase (n = 36), Pub-Med (n = 50), Medline (n= 41), Global Health (n= 29) and Cochrane (n= 3). An extra 42 references were identified through searches in the grey literature, including the websites of specialised agencies or institutions such as WHO (*n* = 9) and Médecins Sans Frontières (*n* = 3). After screening titles and abstracts of the retrieved articles, 186 studies were duplicates or did not meet the inclusion criteria and were excluded from full text review. A total 15 studies were eligible and included for full-text review. The breakdown of the search, screening and selection process for the review was depicted in figure 3.1.

All studies eligible for full-text review (n=15) were carefully screened for feasibility and acceptability relevance, and quality appraised. The findings of the included studies for full text review are presented and the results summarised in table 3.1. Of the 15 studies selected for full-text review, 67% (10/15) were observational studies, which evaluated/assessed the accuracy or operational performance of LED technology use for TB testing in various resource-poor settings, including various fragile states[29, 60, 76, 202-218]. One was a meta-analysis study using the diagnostic data of 14 countries[219]. Of these, 7 countries were either in conflict or recovering from conflict at the time of the study[202]. Four and 11 of the remaining 15 studies utilised data from TB-only and TB-HIV co-infected patients' diagnostic data respectively[29, 76, 204, 205, 207-213]. The summary of descriptions and outcomes of all studies reviewed for analysis are displayed in table 3.7 in the appendix to chapter 3.

Table 3.1 ***Main findings of the 15 articles selected for literature on feasibility and acceptability of LED for routine TB testing in fragile states***

Study	Settings and participants	Time frame	Objectives or questions of study	Main findings
Affolabi, D. et al. (2010)	Benin	Not stated	To compare performance between ZN and LED in routine TB testing	- LED performed significantly better than ZN - Reported to be accepted/more appreciated by users - Regarded as more user-friendly - LED acceptance among inexperienced lab-techs was reported as the main obstacle to routine use at peripheral labs - Routine use of FM severely restricted by the short life/high cost of the mercury vapors - Difficult maintenance and lamp adjustments, need for a dark room, and strict requirements for electrical power supply for new technology (LED) use.
Albert, H. et al. (2010)	Uganda	Jan 2009-Mar 2009	To compare the performance of three LED, Lumin-FM and ZN in TB detection on slides prepared from the sputum of TB suspects.	- FM showed modest increase in sensitivity and similar specificity vs ZN - Slide-reading substantially quicker under FM than ZN and FM was rated highly by labs-techs - Difference in operational performance across testing tools - Operational characteristics should be considered prior to the introduction and implementation of new tools - FM was highly acceptable to Ugandan technologists, although differences in operational performance of the three systems were reported.
Albert, H. et al. (2013)	Uganda	Jan 2009-Mar 2009	This study sought to compare the operational performance of three FM methods compared to light microscopy in a cohort of HIV-positive tuberculosis (TB) suspects at an urban clinic in a high TB burden country.	- Routine performance of LED - Specificity LED was significantly lower than compared ZN - LED rated attractive to users - Operator-dependent factors remain critical regardless of system use - User acceptance of new technologies is vital to successful uptake and roll-out - Variations in operational characteristics reported and could affect user acceptability (ease of use, availability of objects for use) - Smear preparation quality, staining and slide reading time could have contributed to low LED sensitivity - LED specificity rated as same as ZN - Training for users prior to introduction and implementation needs further investigation.
Bonnet, M. et al. (2011)	Kenya	2009-2010	The study aimed to compare the performance of LED-FM versus Ziehl-Neelsen (ZN) microscopy and to assess the feasibility of LED-FM at a low level of care in a high HIV prevalence country.	- No increase in sensitivity - Shorter reading time, user acceptance and ease of use aids LED introduction at a facility level - Feasibility was assessed based on inter-reader agreement, reading time and technicians' acceptability assessed feasibility - Higher acceptance and ease of use helped the introduction of new technologies at peripheral laboratories in resource-poor settings

Bonnet, M. et al. (2011)	Kenya	2008-2009	This study aimed to evaluate the performance of combined LED-FM and NaOCl sputum sedimentation for TB detection at a peripheral level of health services.	- Neither increased sensitivity nor improved performance in routine TB testing at point of care - Acceptance among laboratory technicians was slighter better at referral laboratory facilities.
Cattamanchi, A. et al. (2011)	Uganda	2009-2010	This study aimed to determine whether two alternative approaches can increase smear-positive case detection by increasing the efficiency (single-specimen microscopy) or sensitivity (light-emitting diode [LED] fluorescence microscopy [FM]) of TB suspect evaluation.	- No difference in sensitivity and specificity between the two testing strategies - More studies needed on patients and health system costs - LED reported more useful for single-specimen method and remedied concerns raised about operational feasibility at facility level.
Chang, E. W. et al. (2016)	Meta-analysis	2000-2014	This study aimed to determine the diagnostic accuracy of LED for tuberculosis detection and explore potential factors that might affect its performance.	- LED specificity is high and should not deter its introduction in peripheral lab services - Methodology factors and differences in LED procedure or device use could also affect its performance at all levels of laboratory services - The choice of a reference standard for comparison can influence performance estimates - LED specificity is high and should not be a barrier to device introduction, particularly among peripheral healthcare settings where this technology is meant to be used.
Cuevas, L. E. et al. (2011)	Yemen, Ethiopia, Nigeria, Nepal	2008-2009	The aim of this study was to assess the sensitivity/specificity of LED for the diagnosis of pulmonary TB and whether its performance varies with the timing of specimen collection.	- Sensitivity/specificity of ZN and LED did not vary: LED showed significantly lower sensitivity and specificity than ZN in routine use - The use of different sputum collection techniques influences neither sensitivity nor specificity of LED in a resource-poor setting - The introduction of LED should be accompanied by appropriate training, quality management, and monitoring of performance at the facility level.
Everett, C. K. et al. (2010)	Ethiopia	2011-2012	Study aimed to evaluate the performance of LED for the diagnosis of PTB in HIV positive individuals.	- LED fluorescence microscopy has better performance for the diagnosis of PTB in HIV positive individuals compared to conventional ZN microscopy.
Gelalcha, A. G. et al. (2017)	Ethiopia	Jan 2017-Aug 2017	This study aimed to evaluate these tools for TB detection in individuals visiting Ambo Hospital, west-central Ethiopia.	- LED sensitivity is higher compared to results quoted by recent systematic reviews although it appears to be lower than what was cited in the WHO recommendations - The high specificity of LED in the study area is encouraging and is expected to boost its reliability and uptake.
Getachew, Konjit et al. (2015)	Ethiopia	2011-2012	This study aimed to evaluate the performance of LED for the diagnosis of PTB in HIV positive individuals.	- LED has better performance for the diagnosis of PTB in HIV positive patients compared to ZN - Findings support the use of LED in HIV positive population as recommended by the WHO

				LED has better sensitivity for the diagnosis of PTB in HIV positive individuals as compared to conventional ZN microscopy. LED can be used as an alternative to conventional ZN microscopy.
Marzouk, M. et al. (2013)	Tunisia	Apr -Nov 2011	The objective of the study was to compare the performance of conventional fluorescence microscopy (CFM) and light-emitting diode (LED) fluorescence microscopy (FM) for detection of acid-fast bacilli (AFB) in clinical samples.	- Negative-positive inter-reader agreement of LED and ZN was excellent, but detection of scanty AFB was higher under LED - Slide reading time was identical for LED and ZN - Easy to use for lab-techs - Although it was not faster than ZN, the higher detection of scanty AFB smears combined with ease of use supports the consideration of LED microscopy by all tuberculosis diagnostic laboratories, as a replacement for conventional fluorescence microscopes.
Nyaruhirira, Alaine et al. (2015)	Rwanda	2009-2010	The study aimed to determine the acceptability and effectiveness of LED in a low resource setting.	- Inter-reading agreement perfect between compared technologies - LED reduces time needed for examination by more than half.
Perez-Tanoira, Ramon et al. (2017	Ethiopia	2012-2013	This aimed to evaluate the feasibility of LED use for increased sensitivity and reducing time for analysis, compared to ZN.	- LED showed ease of use in high burden and resource-poor settings like Ethiopia - Laboratory technicians demonstrated high acceptance of LED and reduced time needed for examination by more than half - LED microscope also excelled in terms of user-friendliness and acceptance by users - LED use for routine TB testing reduced the time needed to analyze each sample compared with ZN.
Taddese, Boja (2017)	Ethiopia	2013-2014	The aim of the study was to compare the results of sputum smears by LED against ZN stained sputum smears using TB culture as a reference test.	- LED showed better sensitivity than ZN - Consistency across tools compared was reported to be promising - Easy to perform, saves time and a better choice for sputum microscopic examination.

Approximately 80% (12/15) of the studies selected for full text review were conducted in countries or settings that were either affected by, or recovering from, conflict at the time of studies [29, 60, 76, 203, 204, 208-214, 216-218, 220]. About 27% (4/15) either compared or evaluated LED overall performance at the primary care level[204, 205, 214, 218]. The majority of the included studies reported no information on the risk of bias, patient selection, sampling methods and reference standards used for analysis.

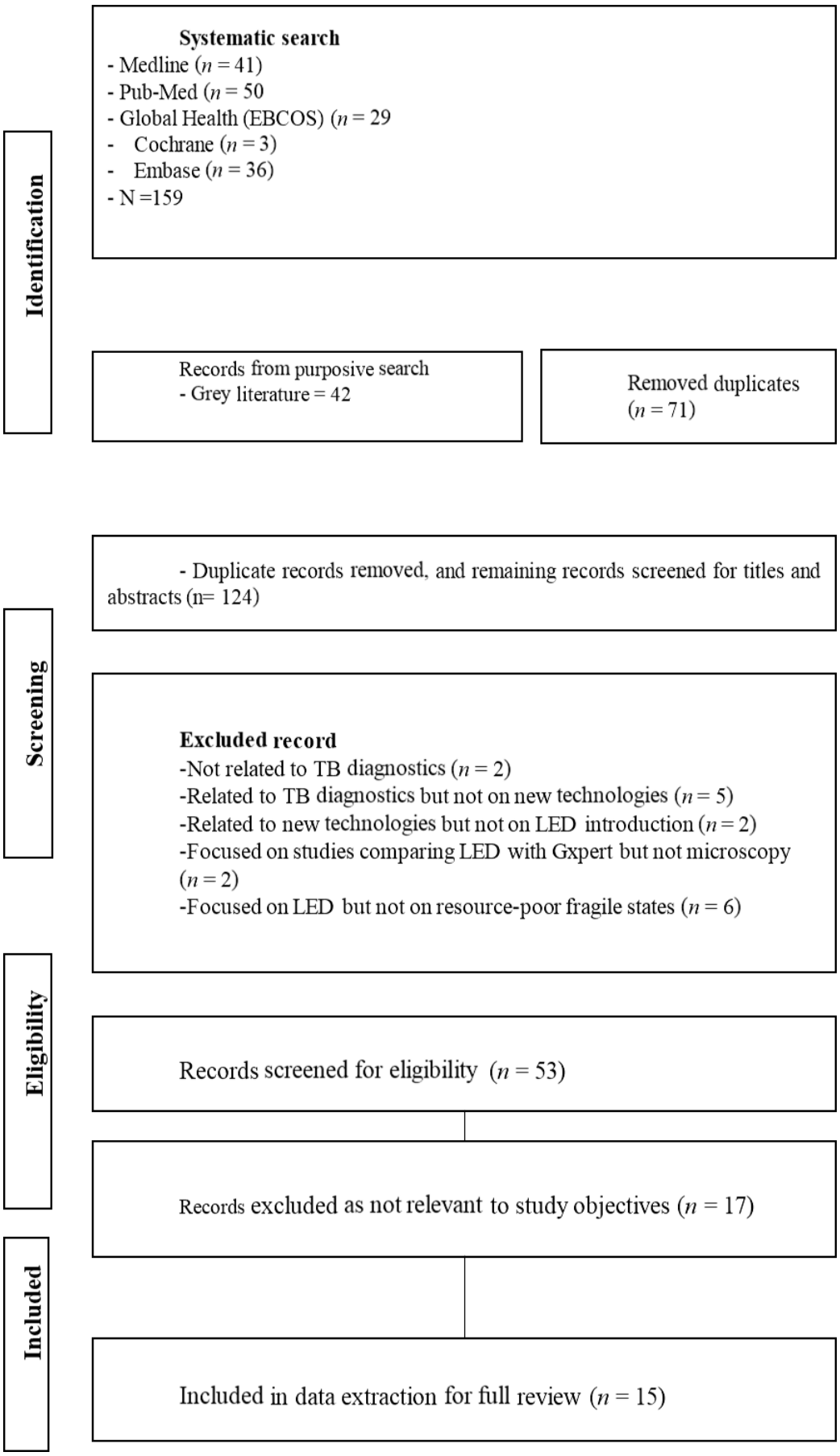

Figure 3.1 ***Selection process of articles for review in a PRISMA flow chart***

3.12 Feasibility and acceptability assessment in resource-poor fragile health system contexts

The different methods applied to develop theoretical frameworks were not always clearly stated and described systematically in the studies. Inconsistencies in the theorization of feasibility and acceptability concepts can impede the development of valid assessment instruments[221, 222]. The vast majority of the studies assessed the operational performance, mainly the diagnostic accuracy (sensitivity and specificity) of the LED technology against several new, optimized or old/conventional TB diagnostic tools for routine TB diagnosis in various settings. The reviewed studies used various measures as indicators to assess feasibility and acceptability from resource-poor settings. None of the studies reviewed had clearly defined, theorized or systematically appraised feasibility and acceptability of the LED technology for routine use.

The methodological quality of individual reviewed studies was discussed in one (7%) of the 15 in regards to LED operational performance and acceptability in a resource-poor context[223]. Eleven (69%), three (19%) and two (13%) of the reviewed studies assessed or meant to assess performance, feasibility and acceptability respectively [29, 203-206, 213, 214, 216, 217, 224]. Ten (63%) of the studies reported also that they assessed feasibility, acceptability or both using self-reported user-acceptance measures, including user responses and the views and experiences of intended users, namely laboratory technicians[208-211, 223, 225]. Only one study stressed the importance of theory-informed feasibility and acceptability analysis of the performance of the LED technology for routine use in resource-poor and high-burden settings[223]. The studies also failed to articulate or provide evidence of the theoretical, operational, technical and financial feasibility of the applied technology in a real-world setting.

Frequent measures used as indicators of LED technology performance included the incremental gains in case detection, detection sensitivity, specificity, user acceptance, user preferences, operator dependency, satisfaction, suitability and user perceptions. Studies that evaluated the feasibility of LED implementation and diagnostic performance in resource-poor settings discussed primarily user-acceptance issues (i.e., inter-reader agreement, user preferences, reading time, and operator acceptance)[29, 76]. Most of the studies reviewed used accuracy (sensitivity and specificity) of the LED technology in TB testing as the determining factor for feasibility. These studies assessed LED technology feasibility fundamentally from solely operator acceptance (i.e., reported fast reading times, ease of use of LED) and argued that acceptance levels could benefit the future introduction of LED in similar settings[204, 205].

Although most of the studies took place in resource-poor settings, none of them clearly addressed the feasibility and acceptability of the introduction and implementation of LED technology for routine use from a fragile health system context. For example, the feasibility, implementation and performance of the LED technology was solely assessed objectively by using quantifiable and measurable outcomes (i.e., frequency of use, the proportions of patients with positive, negative and scanty results) generated through actual usage of the LED technology at the intervention facilities[76, 204, 205]. The degree to which LED was acceptable (a subjective measurement) and could be implemented for routine use was solely based on users' perceptions and practices regarding the applied technology (i.e., self-reporting of user acceptance, usefulness, ease of use). No study assessed the feasibility of actual usage of the technology itself, or wider health system issues. Such assessments appeared to have been influenced by the opinions, beliefs, perceptions and behaviours of the end user at the facility level without much consideration given to the programmatic and systematic readiness of the wider healthcare system in fragile states[29, 60, 202-205, 208-211, 216-218, 225].

For instance, studies that assessed technology acceptance among intended users focused on performance (accuracy) in routine TB diagnosis at referral laboratory facilities, largely in urban settings. These studies reported that technology acceptance was primarily influenced by largely operator-dependent factors (user friendliness, user acceptance, inter-readability and inter-variability of specimen slides among laboratory technicians) at the facility level[29, 76, 203].

Other studies stressed the need for larger implementation studies on the routine use and utilization of LED in peripheral health facilities (peripheral laboratory settings) to determine whether the use of new technologies such as LED for regular testing is suitable in such environments in regards to resource availability and health system capability[207-211]. Another study assessed the diagnostic accuracy of LED technology use for TB detection in 17 resource-poor countries, including 10 fragile states, and declared the LED technology feasible for routine use[202]. This study intended to explore factors that could potentially impede performance of LED, and reported no potential barriers to LED introduction in resource-limited settings where such technology was initially intended to be routinely used[202]..

The overall sensitivity and specificity analysis

The majority of the included studies assessed technology accuracy by comparing sensitivity and specificity rates of the LED with all commercially available microscopy devices at all types and levels of healthcare facilities in different parts of the world (Table 3.8, Appendix 3). A total of 6947 participants, out of 8073 enrolled participants from 15 studies, were included in the detection sensitivity and specificity analyses.

The reported study-specific detection sensitivity and specificity rates ranged from 40% to 94% with specificity levels ranging from 87% to 100% (Table 3.3). Comparatively, the pooled sensitivities and specificities of LED for the 15 studies in the analysis were 71% and 94% (95% CI: 53-83; 90-96) respectively. Despite a high acceptance of LED technology among end users, sensitivity and specificity rates remained unchanged relative to that of the ZN technology, and consistent with results reported in previous studies[215, 226-229].

Table 3.2 ***Diagnostic accuracy (sensitivity and specificity) outcomes for all included studies on LED technology for review***

Number.	Author name (year)	Setting	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
1.	Affolabi, D. et al (2010)	Benin	806	15	61	985	.45[.43-47]	.55[.52-57]
2.	Albert, H. et al (2010)	Uganda	53	1	12	127	.27[.21-.34]	.66[.59-.72]
3.	Albert, H. et al (2013)	Uganda	75	6	6	69	.31[.27-.36]	.69[.64-.74]
4.	Bonnet, M. et al (2011)	Kenya	68	25	12	287	.95[.93-.98]	.72[.62-.83]
5.	Bonnet, M. et al (2011)	Kenya	68	25	9	287	.78[.69-.86]	.87[.83.67-.91]
6.	Cattamanchi, A. et al (2011)	Uganda	146	8	85	221	.50 [.46-.55]	.50[.45-.55]
7.	Chang, E. W. et al (2016)	Multi-country	1317	108	256	2180	.67[.61-.63]	.96[.93-.99]
8.	Cuevas, L. E. et al (2011)	Multi-country	385	166	144	1660	.22[.21-24]	.78[.76-79]
9.	Everett, C. K. et al (2010)	Ethiopia	15	5	155	167	.62[.56-.69]	.100[.90-.100]
10.	Gelalcha, A. G et al (2017)	Ethiopia	35	10	37	287	.78[.63-.89]	.98[.98-.100]
11.	Getachew, Konjit et al (2015)	Ethiopia	148	2	34	175	.82[.76-.87]	.97[.93-.99]
12.	Marzouk, M. et al (2013)	Tunisia	12	14	25	31	.93[.85-.100]	.100[.99-.100]
13.	Nyaruhirira, Alaine et al (2015)	Rwanda	26	31	14	134	.75[.38-.100]	.99[.96-.100]
14.	Perez-Tanoira, Ramon et al (2017)	Ethiopia	56	24	28	538	.53[Not reported]	.52[Not reported]
15.	Taddese, Boja (2017)	Ethiopia	99	22	8	121	.80[.74-.88]	.93[.88-.97]

*True positive (TP), false positive (FP), false negative (FN), true negative (TN).

Sub-group analysis

For the sub-group analysis, pooled sensitivity and specificity estimates were calculated to determine to what extent the type and location of the diagnostic facility influenced LED use for routine TB diagnosis within and across settings.

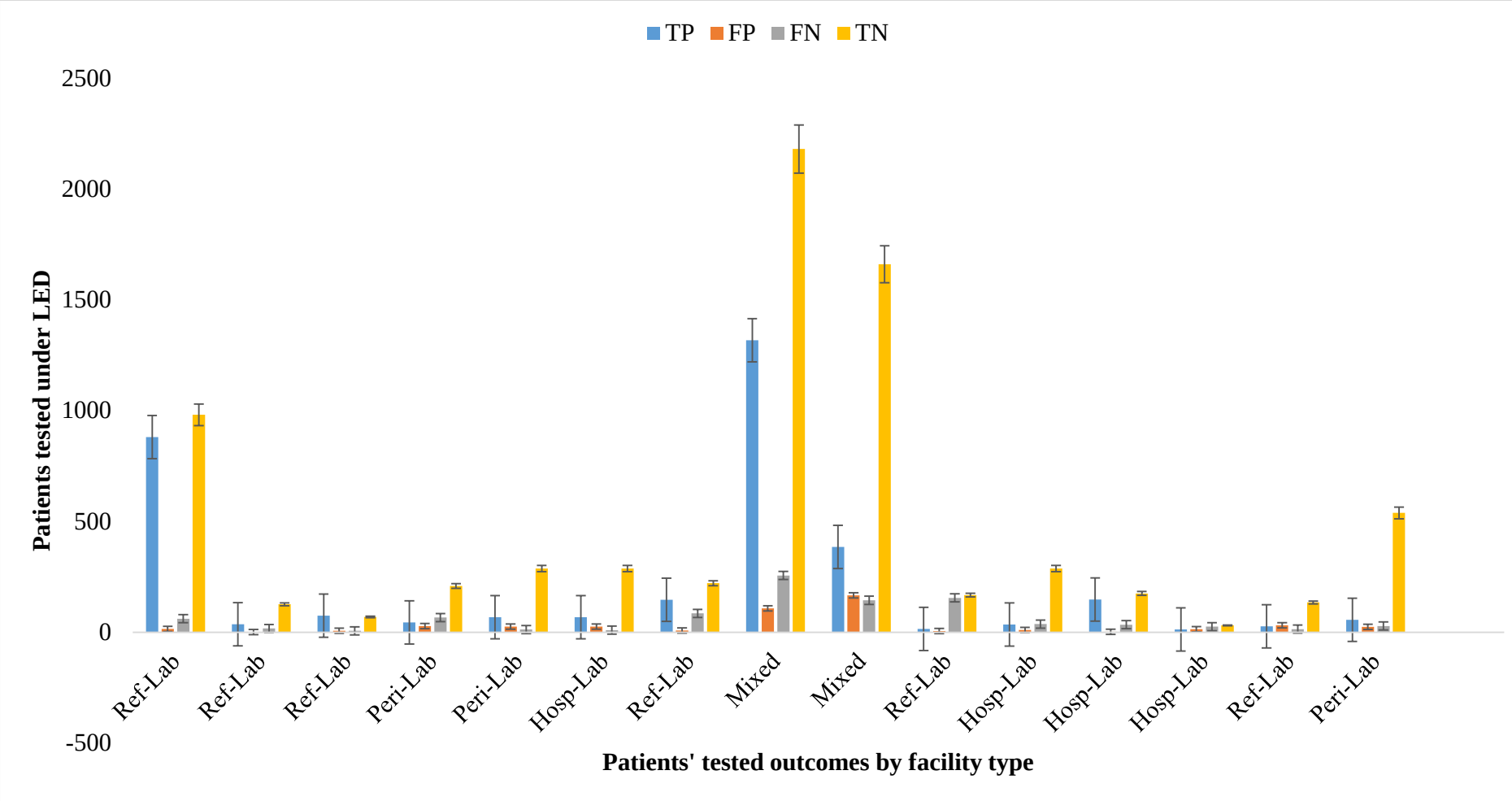

Figure 3.2 ***Sub-group tested outcomes by facility type and location***

*True positive (TP), false positive (FP), false negative (FN) and true negative (TN).

Approximately 38%, 32%, 19% and 19% of the included studies were conducted in referral laboratories (Ref-Lab), hospital laboratories (Hosp-Lab), peripheral laboratories (Peri-Lab) and combination of different healthcare (Mixed) facilities respectively. Studies evaluating LED implementation in similar settings reported higher sensitivity and specificity levels in higher levels of the healthcare system (reference labs and specialty hospitals) than in lower level health facilities (Table 3.4 & Figure 3.2). The highest positivity rates (50%) were reported by studies conducted at, or that used data from, mixed health facilities (referral labs, peripheral labs, primary care centres and hospital outpatient clinics). Because there were fewer than four studies, pooled estimates were not calculated for HIV and TB-HIV-co-infected patients. About 50%, 35%, 10% and 5% of the TB cases were reported by studies conducted at different types and levels of health facilities (mixed), followed by referral, hospitals and peripheral laboratories respectively (Figure 3.2)[29, 76, 203, 204, 217].

Table 3.3 ***Sensitivity and specificity for sub-group analysis by intervention facility type and setting***

Number.	Author (year)	Setting	Intervention facility	Sensitivity (95% ICs)	Specificity (95% CIs)
01	Affolabi, D. et al. (2010)	Benin	Ref-Lab	.94[.92-.95]	1.00[.90-.99]
02	Albert, H. et al (2010)	Uganda	Ref-Lab	.68[.54-.80]	.99[.96-1.00]
03	Albert, H. et al (2011)	Uganda	Ref-Lab	.40[.33-.48]	.93[.90-.95]
04	Bonnet, M. et al (2010)	Uganda	Peri-Lab	.40 [.31-.50]	.88[.83-.92]
05	Bonnet, M. et al (2011)	Kenya	Peri-Lab	.73 [.63-.82]	.98[.94-.98]
06	Cattamanchi, A. et al (2011)	Kenya	Hosp-lab	.78[.69-.86]	.88[.84-.91]
07	Chang, E. W. et al (2016)	Meta-analysis	Mixed	.63 [.57-.69]	.97[.93-.98]
08	Cuevas, L. E. et al (2011)	Multi-country	Ref-Lab	.67 [.60-.63]	.96[.93.98]
09	Everett, C. K. et al (2010)	Ethiopia	Peri-Lab	.73 [.69-.77]	.90 [.89-.92]
10	Gelalcha, A. G et al (2017)	Ethiopia	Ref-Lab	.62 [.57-.75]	.98 [.90-1.00]
11	Getachew, Konjit et al (2015)	Ethiopia	Hosp-Lab	.78 [63-.89]	.99 [.98-1.00]
12	Marzouk, M. et al (2013)	Tunisia	Hosp-Lab	.82[.76-.87]	.97[.93-.99]
13	Nyaruhirira, Alaine et al (2015)	Rwanda	Hosp-Lab	.93[.85-1.00]	1.00[.901.00]
14	Perez-Tanoira, Ramon et al (2017)	Ethiopia	Ref-Lab	.75[.38-1.00]	.99[.96-1.00]
15	Taddese, Boja (2017)	Ethiopia	Ref-Lab	(Not reported)	(Not reported)

In terms of study type and settings, the studies that were conducted at lower level health facilities, namely peripheral primary care centres, represented only 5% of the reviewed studies and reported lower pooled sensitivity and specificity[204, 217].

The highest sensitivity and specificity rates were reported in two studies that were conducted at national reference laboratories in two countries (Uganda and Benin)[203, 208-211].

The vast majority of the studies reviewed found no significant variations in detection performance (sensitivity and specificity) in all settings in which the LED technology is introduced and implemented. For example, a study comparing LED performance as measured by its detection accuracy (sensitivity and specificity) to various commercially available microscopy devices reported shorter reading time for lab techs to interpret specimen slides under LED technology and recommended it as the most suitable technology testing strategy in TB high burden countries. In the same study, it was reported that LED detection sensitivity fell far short than initially anticipated in similar settings[207-211]. Another study rated staining, reading and examination time of sputum slides together with the technician's acceptance towards LED usage for routine testing, but not *actual usage of LED* [204, 205]. Another study assessing the feasibility of LED technology stressed the importance of training for technology users, namely laboratory technicians, prior to the LED introduction, and how training could influence technology acceptance and performance among users[29]. Two studies addressed the need for integrated internal quality assurance (IQA) and external quality assurance (EQA) into the larger laboratory service system to improve diagnostic performance of new technologies in routine TB under programmatic conditions[29, 76].

3.13 **Conclusion**

The aim of this review was to establish a clear and comprehensive understanding of the feasibility and acceptability of LED technology for routine TB diagnosis in fragile states. It specifically attempted to determine how existing TB diagnostic literature defined, theorised and measured feasibility and acceptability of the LED technology for routine TB diagnosis. To the best of the author's knowledge, this review is the first of its kind to assess the feasibility and acceptability of LED technology use for routine TB diagnosis in resource-poor settings, including fragile states.

The chapter has presented a critical review of the relevant scientific and grey literature on the feasibility and acceptability of LED use for TB testing in resource-poor fragile states. It systematically reviewed existing and relevant evidence on the feasibility and acceptability of LED technology for routine TB testing in resource-poor and fragile states. It also tried to identify knowledge gaps in the TB literature on the feasibility and acceptability of LED in fragile states, as well as to identify opportunities for future research. For LED technology to be feasible in resource-poor fragile health system settings, it needs to be accepted and used by its intended end users in

health systems with the capacity and capability to support the introduction and implementation as well as sustain incremental gains.

Chapter Four: The operational feasibility of LED use for routine TB testing at primary care facilities in Somaliland

4.1 Introduction

This chapter presents the findings of the analysis of the facility-based laboratory data from patients presumptive and tested for tuberculosis (TB) at nine laboratory diagnostic facilities in Somaliland. This analysis assessed the diagnostic performance and operational feasibility of light-emitting diode (LED) fluorescence microscopy technology used for routine TB testing in Somaliland. The use of smear microscopy for regular testing remains a critical component of TB diagnosis in resource-poor fragile health system settings, including Somaliland[3, 163, 230-233]. The aim of the LED endorsement and introduction by WHO was to increase case detection outcomes through increased access to quality diagnosis for TB patients at the first point of care[5].

Since its inception, the LED technology has been introduced, implemented for a decade and has now replaced the conventional direct smear microscopy ZN technology for routine TB testing in many resource-poor countries, including fragile states[163]. The use of LED technology as an alternative diagnostic strategy to ZN has been tested and evaluated elsewhere[204, 205, 215, 232-234]. However, the diagnostic performance and operational feasibility of its routine use for TB testing in fragile health system context have never been assessed. This analysis investigated the diagnostic performance and operational feasibility of LED use for routine TB testing in Somaliland. It specifically investigated the difference in proportions of patients' diagnostic test outcomes between LED and ZN across nine TB diagnostic facilities in Somaliland.

The diagnostic performance determined whether the LED technology use for routine TB testing improved TB case finding at the facility level in fragile health systems[235]. More information on the fragile health system is provided in the subsequent chapter[236, 237].

4.2 Objective

To investigate the differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities.

4.3 Methods

This study adopted a quantitative analytical strategy utilizing clinical binary data from nine TB care facilities in Somaliland. Ethical approval and authorization for the study and use of data for analysis was obtained from the Ministry of Health and the London School of Hygiene & Tropical Medicine.

Design

This study utilised facility-based diagnostic paired data from 14176 patients presumptive of TB who submitted specimens for testing at nine of the ten TB diagnostic facilities that implemented LED technology in parallel with ZN technology for 12 months (April 2012-May 2013) in Somaliland. The LED technology introduction and implementation was part of a larger WHO-STOP-TB Partnership TB REACH-supported intervention in Somaliland, which ran between April 2012 and May 2013.

In this intervention, patients were asked to submit three sputum samples over two consecutive days using the *spot-morning-spot* sputum collection strategy for examination. The first specimen (**spot)** was received on the 1st day of the patient's visit to the diagnostic facility. The second (**morning**) and third (**spot**) specimen were collected from the patient in his/her second visit to the diagnostic facility. All patients' specimen samples were prepared and examined by ZN first and subsequently by LED. For the first specimen examination exercise, two smears were created from the specimen collected on the first day and examined first by ZN and second by LED. The same specimen examination process was used for the second and third specimen examination for ZN and LED. A mmaximum of six smears were examined for each patient: three examined with ZN and three with LED for each patient.

Setting

Data used for analysis came from nine of the ten diagnostic facilities that introduced and implemented the LED technology in six regions of Somaliland (one TB care facility per region) with each estimated to have approximately 10,000 to 400,000 population. One facility did not provide diagnostic data on the LED implementation in parallel with ZN due to unspecified reasons. The selection and eligibility of the study facilities were based on LED and ZN parallel implementation for routine TB testing for a minimum of 12 consecutive months (April 2012-May 2013).

4.4 Study population

The study population comprised 14176 patients presumptive of TB aged one year or older with a persistent cough lasting more than two weeks, night sweats, fever or/and weight loss who provided specimens for testing at the nine TB diagnostic facilities that introduced LED for diagnosis. The demographic characteristics of the study population are presented in Appendix 4, Table 4.1.

4.5 **Data analysis of paired samples**

The diagnostic test results from 14176 patients (providing a total of 42528 test results) tested for TB were entered into MS Excel. Data on demographic profiles and test outcomes by facility, year, gender and age by technology for the sample was compiled and entered into MS Excel and later uploaded into STATA version 16, Houston TX, 2019 for analysis.

The analysis of paired proportions (paired samples) utilized the diagnostic test results of ZN and LED testing methods for detecting TB disease in the specimen subsets from all specimens (n = 42528) at the specimen level and patient level. The exposure was the new diagnostic technology (LED vs ZN) and the outcome was the test results at the specimen and patient level. The most appropriate method for analysis of such paired data was to consider the test results of each pair of subsets by each technology: each pair had five possible outcomes (not done, missing, unknown, negative and positive) at the specimen level and two possible outcomes (negative and positive) at the patient level.

Missing specimens were defined as specimens from patients with known name, patients' identification numbers and facility visit dates entered in the TB register at notification with one or more examined missing specimen test outcomes[238]. These specimen results were classified as *missing* and given a numeric value of ″7″, and excluded or dropped from the analysis.

Unknown specimens were defined as specimens with known patients' name, identification numbers and and facility visit dates entered in the TB register but with no confirmed diagnostic test results notified in the register at notification. All these specimen outcomes were classified as *unknown* and given a numeric value of "9" and excluded from the analysis[238].

The difference between *missing* and *unknown* test outcomes was that missing specimens had test outcomes with conclusive diagnostic test outcomes (negative or positive) at examination with known patients' names, identification numbers and facility visit dates but no test outcomes recorded in the TB register at notification. For example, one or more specimens examined for TB had confirmed negative or positive test outcomes but somehow these were not recorded in the TB register at notification[238].

Unknown specimen test outcomes, on the other hand, were test outcomes that were neither recorded as *missing* nor *not done* in the TB register at notification. For example, one or two patients' specimens were examined but had unreliable or insufficient clinical material to make a clinical judgement or decision for individual TB patients[239]. *Missing* and *unknown* values are common patterns in the WHO TB case notification country reports: these can have a significant impact on

statistical inferences or potential conclusions drawn from such analysis if not handled appropriately[240].

Not done (unexamined) specimens were defined as specimens from patients with known names, identification numbers and facility visit dates in the TB register but one or more unexamined specimens. In this analysis, all these specimens with unknown examined specimen test results were classified as *not done*, given a numeric value of "8", and excluded from the specimen level analysis.

Positive tests at the patient-level were defined as the presence of acid-fast bacilli (AFB) or TB disease in at least one of the specimen samples[241]. ***Negative*** tests at the patient-level were defined as an absence of AFB in a minimum of two sputum microscopy smear examinations. Further details on the WHO case definitions are presented in the working definitions section in the Appendix to chapter 4.

For the specimen-level analysis, two summaries were performed. First, all diagnostic test results generated by ZN and LED, including all tests with inconclusive results (i.e., *missing, unknown and not done*) were cross-tabulated and summarized in tables. In the second specimen level of analysis, the analysis was restricted to negative and positive results only. Note: all specimens (1^{st}, 2^{nd} and 3^{rd} specimens) were paired samples from the same patients (i.e., paired data generated through matching).

For the patient-level analysis, patients' test results were changed from specimen counts to a case count (patient count). Patients' test results were dichotomised and categorised as individuals based on disease condition (positive or negative). All test results with inconclusive (i.e., non-positive, non-negative results) were excluded from the analysis. In other words, the analysis of the subsets tests was restricted to only patients with negative and positive outcomes for ZN and LED for the entire intervention period. The outcome parameters (proportions, the difference in proportions or patients' positivity rates) were estimated, summarised and presented in 2x2 tables. This was to determine the overall incremental gains in patients' test outcomes with LED use for the entire intervention period.

Data clarifications and handling *missing, unknown* and *not done* values

In the analysis, specimen test outcomes were notified under one of five test outcome categories: *missing, not done* (sputum not examined), *unknown, negative and positive*. A large number of patients' test results was reported as *not done*, mostly under ZN. This was mainly due to a lack of precise protocol or implementation and evaluation plan for the proposed intervention. There was

no protocol developed for the introduction, implementation and utilisation for routine use of the technology in the first place.

Although inconclusive results, defined as any *missing, not done and unknown*, are directly related to testing accuracy, they are still essential considerations in the assessment of the overall clinical diagnostic performance and operational feasibility of the technology assessed (LED).

Therefore, all inconclusive test outcomes (*unknown, not done and missing*) were excluded from the patient-level analysis but included in the specimen analysis. Excluding test outcomes with inconclusive outcomes from the analysis helped to handle information biases and ultimately yield the least unbiased performance and feasibility estimates.

It should be noted that due to the lack of explicit study protocol use at the design and implementation stage of the intervention concerned, the importance of clustering was ignored in the analysis of paired data. Therefore, estimates associated with clustering of the population sample proportions might or might not be highly significant. It is, hence, essential to calculate and present proportion estimates as accurately as possible.

The primary outcome of interest

The primary outcome of interest was the difference in the proportion of specimens and patients with positive test outcomes by ZN and LED technology for the entire intervention period.

4.6 Statistical analysis

Data on demographic and clinical diagnostic outcomes for individual patients from all diagnostic facilities were uploaded into MS Excel spreadsheet and subsequently analyzed using statistical software (STATA version 16, Houston TX, 2019)[182]. The proportion of test results by technology for the entire intervention period was cross-tabulated by facility, year, gender and age together with their corresponding median interquartile ranges (IQRs) for specimen and patient-level analysis using the standard formula for binary-paired data. All patient diagnostic outcomes were first cross-tabulated for all possible outcomes by technology for comparative analysis and the results presented in tables and figures.

The main emphasis for specimen-level and patient-level analysis was placed on the test outcomes with positive test results on which the two testing technologies did not agree, or *the discordant pairs*, which were calculated from the numbers of discordant pairs (r) and (s) and total number of pairs (n). In doing so, the proportion (*p*) of patients who tested positive with the disease (*d*) in the

proportion (n) of the sample population (N) was computed as *d*/*n*. Differences in proportions of test outcomes with positive and negative results at the specimen-level and patient-level by each diagnostic technology with 95% confidence intervals (95% CIs) together with their estimated odds ratios (ORs) and p-values were calculated using the standard formula (r-s)/n. The working hypotheses were as follows:

Null hypothesis: The proportion of patients with negative and positive test outcomes for the two populations (ZN-tested and LED-tested) are equal. **Alternative hypothesis:** The proportion of patients with negative and positive test outcomes for the two populations (ZN-tested and LED-tested) are not equal.

The difference in the diagnostic test results between the two paired proportions was computed from the number of discordant pairs at alpha (α) = .05 significance level and 95% confidence intervals (95% CIs) using the standard formula: *difference between paired proportions* = $\frac{(r-s)}{n}$, standard error = *s.e(difference)* = $\frac{\sqrt{(r-s)2}}{n}$ and odds ratios (ORs) with their corresponding 95% CIs). A McNemar's chi-square (χ^2) test for paired proportions with 1 degrees of freedom (df.1) was calculated using the standard formula: $\chi^2_{\text{paired}} = \frac{(r-s)2}{s-r}$, $(df = 1)$.

4.7 **Results**

Between 2012 and 2013, a total of 42528 specimens were collected from 14176 patients presumptive of TB. As shown in table 4.1, more patients were tested for TB in the first year (2012) than the second year (2013) of the LED implementation. Of the patients who provided specimens for examination, 62% (8746/14176) and 38% (5425/14176) were males and females respectively with a median age of 50 years (IQR, of 30-70 years) (Table 4.1). By facility, the highest specimen examinations were reported by three facilities: Hargeisa TB Hospital (38%) Borama (14%) and Burco (13%) (Table 4.1 & Table 4.2 in Appendix to chapter 4).

Table 4.1 ***Summary statistics of patients assessed for TB using LED vs ZN technologies in Somaliland (2012-13).***

Facility	**N**	**(Column %)**	**Median age (IQR)**			**Row % Gender (n)**		**Row % enrolled in 2013 (n)**
			Lower quartile	*Median quartile*	*Upper quartile*	*Females*	*Males*	
Overall	14176	(100)	30	50	70	38 (5425)	62 (8746)	58 (8228)
Borama	1942	(14)	30	50	70	44 (840)	57 (1101)	62 (1195)
Gabiley	1187	(8)	35	50	70	48 (565)	53 (621)	43 (507)
Hargeisa TB Hospital	5429	(38)	32	50	70	37 (1994)	64 (3434)	56 (3021)
Finsoma	1067	(8)	30	50	70	41 (435)	60 (631)	50 (530)
Berbera	535	(4)	28	48	72	33 (174)	68 (361)	53 (282)
Sheikh	824	(6)	30	50	70	47 (381)	54 (443)	44 (358)
Burco	1894	(13)	30	50	72	31 (583)	69 (1310)	96 (1817)
Odweyne	544	(4)	29	41	62	33 (179)	68(365)	0
Lasanod	754	(5)	30	39	56	37 (274)	64 (480)	69 (518)

Approximately 90% and 52% of patients' specimens were examined by LED and ZN respectively. Of these, 82% (8%) were negative (positive) with LED only, compared to 48% (4%) with ZN only for the entire intervention period.

Of these, 54% (6%) and 35% (3%) were negative (positive) with LED and ZN respectively at the 1st, 2nd and 3rd examination. Of these .9% (129/14176), 1% (100/14176) and .01% (10/14176) of the specimens were positive with LED but negative with ZN testing at the 1st, 2nd and 3rd examinations respectively. About 41% (5810/14176) of the specimens were *not done* with ZN testing at the 1st and 2nd examination. And 34% (4801/14176) of specimens were reported as *not done* at the 3rd examination (Figure 4.1).

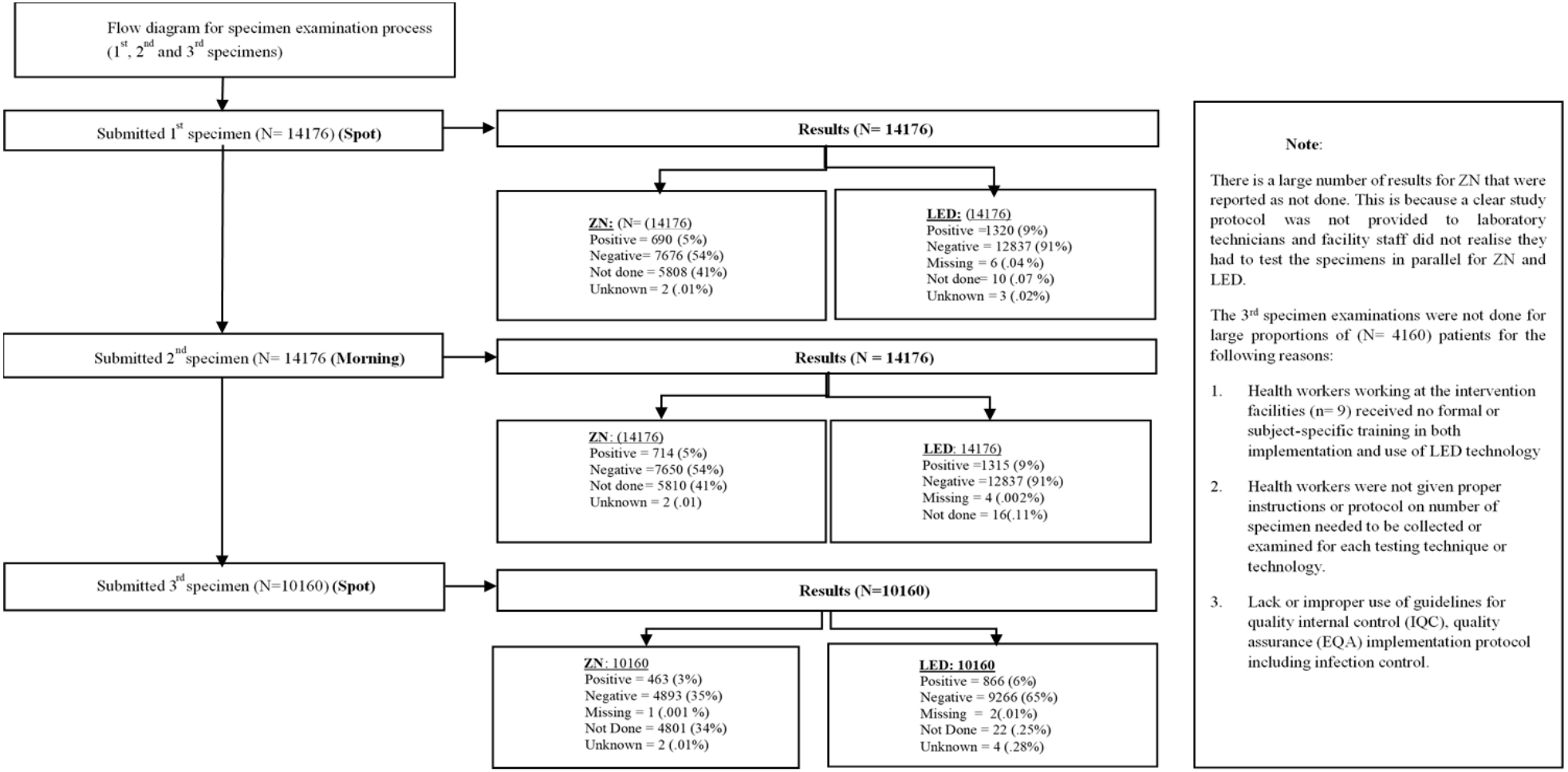

Figure 4.1 ***Flow chart for patients' specimen examination process using LED and ZN technologies in Somaliland (2012-13).***

Table 4.2 ***Cross-tabulations of examination test results (ZN vs LED) for the 1st, 2nd and 3rd specimens (specimen count) in Somaliland (2012-13).***

(a)- 1st specimen examination results through parallel ZN microscopy vs LED microscopy (N = 14176)

Testing technology (N= 14176)	***LED microscopy***					
ZN microscopy	Negative	Positive	Missing	Not done	Unknown	Total
Negative	**7547**	**129**	**0**	**0**	**0**	**7676**
Positive	**1**	**688**	**0**	**1**	**0**	**690**
Missing	0	0	0	0	0	0
Not done	5289	503	6	9	1	5808
Unknown	0	0	0	0	2	2
Total	**12837**	**1320**	**6**	**10**	**3**	**14176**

(b) 2nd specimen examination results through parallel ZN microscopy vs LED microscopy (N=14176)

Testing technology	***LED microscopy***					
ZN microscopy	Negative	Positive	Missing	Not done	Unknown	Total
Negative	**7550**	**100**	**0**	**0**	**0**	**7650**
Positive	**0**	**713**	**1**	**0**	**0**	**714**
Missing	0	0	0	0	0	0
Not done	5287	502	3	16	2	5810
Unknown	0	0	0	0	2	2
Total	**12837**	**1315**	**4**	**16**	**4**	**14176**

(c): 3rd specimen examination results through parallel ZN microscopy vs LED microscopy (N= 10160)

Testing technology	***LED microscopy***					
ZM microscopy	Negative	Positive	Missing	Not done	Unknown	Total
Negative	**4883**	**10**	**0**	**0**	**0**	**4893**
Positive	**1**	**461**	**1**	**0**	**0**	**463**
Missing	0	1	0	0	0	1
Not done	4382	394	1	22	2	4801
Unknown	0	0	0	0	2	2
Total	**9266**	**866**	**2**	**22**	**4**	**10160**

Note: A large number of specimens were labelled as missing, unknown and not done under ZN testing. Patients were considered diagnosed with TB if at least one of their sputum samples was ZN or LED smear-positive.

In table 4.2 (a-c), the cross-tabulation analysis shows marginal change in specimens' test outcomes between LED and ZN, particularly in positive test results for LED.

The highest proportion of specimens with inconclusive test outcomes, namely *not done* at the 1st, 2nd and 3rd examinations, were reported with ZN. The large number of *not done* specimens with ZN was mainly attributed to a lack of, or inadequate, intervention protocol uses by facility staff (laboratory technicians). As shown in table 4.3, when the specimen level analysis was restricted to only specimens with negative and positive results, excluding all inconclusive test outcomes (*missing*, *unknown* and *not done* test outcomes) for the entire intervention period, the specimen test outcomes remained unchanged.

Table 4.3 ***Comparison of cross-tabulated positive and negative subsets specimens examined by ZN and LED technology excluding all specimens with inconclusive test outcomes (i.e., missing, unknown and not done) values reported (specimen count); Somaliland (2012-13).***

Ccomparison of specimen results from the 1st, 2nd and 3rd examination by LED and ZN combined for the entire intervention period					
Specimen examination strategy	**Technology**	**LED**			
1st specimen (Spot)	ZN	*Test outcomes*	*Negative n/N = % (95% CIs)*	*Positive n/N = % (95% CIs)*	*Total n/N = % (95% CIs)*
		Negative	7547/8365= 90 (89-90)	129/8365 = 2(1-2)	7676/8365 = 91(91-92)
		Positive	1/8365 = .01(3.03e-.06)	688/8365= 8(8-9)	689/8365 = 8(7-9)
		Total	7548/8365 = 90(89-90)	817/8365 = 10(9-10)	8365/14176 = 59(58-60)
		LED			
2nd specimen (morning)	ZN		*Negative*	*Positive*	*Total*
		Negative	7550/8363= 90(89-90)	100/8363 =1(.9-1)	7650/8363= 91(90-92)
		Positive	0/8363	713/8363= 9(8-9)	713/8363= 9(8-9)
		Total	7550/8363= 90(89-90)	813/8363= 10(9-10)	8363/14176 = 59(58-60)
		LED			
3rd specimen (Spot)	ZN		*Negative*	*Positive*	*Total*
		Negative	4883/5355 =91(90-91)	10/5355 = .2(.09-.30)	4893/5355 = 91(90-92)
		Positive	1/5355 = .09(4.73e-.001)	461/5355 = 8(8-9)	462/5355 = 8(8-9)
		Total	4884/5355 = 91(90-91)	471/5355 = 8(8-9)	5355/14176 = 38(36-39)

*Table 4.3 summarizes the cross-tabulation by ZN only and LED only restricted to specimens' negative and positive test results.

Of these with negative and positive results at the first examination, 90% (7547/8365, 95% CIs, 89-90%) and 10% (688/8365; 95% CIs, 1-2%) were negative and positive by both technologies, respectively. About 16% (129/817) were negative by ZN but positive with LED; 8% (689/8365) were positive by both technologies. Only 1 specimen was positive with ZN but negative on LED. At the 2nd specimen examination, the total number of specimens examined for TB by both technologies decreased from 8365 to 8363.

Approximately 90% (7550/8363; 95% CIs, 89-90) and 10% (813/8363; 95% CIs, 9-10%) specimens were negative and positive by both technologies respectively. Of the 813 specimens positive by both technologies, 1% (100/8363; 95%, .9-1%) were negative with ZN but found positive with LED. On average, 10% (713/836; 95% CIs, 9-10) of specimens were TB positive by both technologies.

However, the proportion of specimens examined at the 3rd examination further declined from 59% to 38%. Of the 5355 specimens examined, 91% (4884/5355; 95% CIs, 90- 91%) and 8% (471/5355; 95% CIs, 8-10%) were negative and positive for TB respectively. Of these, 2% (10/5355; 95% CIs, .09-.30%) were negative with ZN but positive with LED (Table 4.3 & Table 4.8 in Appendix to chapter 4).

When the analysis changed from specimen-level to patient-level, 8864 patients were tested for TB. Of these, 85% (7550/8864; 95% CI, 84% - 86%) were negative and 8% (669/8364; 95% CI, 7-8%) positive for TB by both technologies. This means that patients' positivity rate increased by approximately 2% (144/8364; 95% CIs,1-2%) with LED use compared to 8% (670/8364; 95% CIs,7-8%) by both technologies. The results are presented in Table 4.4 & Table 4.11 in Appendix to chapter 4.

Table 4.4 ***The comparison of ZN and LED technologies for detecting TB in patients (patient-level analysis); Somaliland (2012-13).***

Testing technology	**LED**		
ZN	*Positive*	*Negative*	Total
Positive	669	1 (r)	670
Negative	144 (s)	7550	8194
Total	813	7551	8364

*The diagnostic test results of 8364 patients who were tested for TB using both technologies were used for the patient-level analysis.

The difference between the proportion of patients with negative and positive results with LED and ZN technology was calculated based on the discordant pairs: $\frac{(r-s)}{n} = \frac{(1-144)}{8364}$ =.-017 (95% CIs, -.2- -1.4%). With a $\chi 2$ of 141 (P<.001), there is strong evidence that the percentage positive is higher by LED versus ZN (Table 4.4).

As presented in table 4.5, the specimen level analysis was again restricted to negative and positive subsets. No difference was observed between the two paired proportions. Of the 22044 specimens examined by both technologies, 90% (19986/22044; 95% CI, 90-91%) and 9% (2058/22044; 95% CI, 9-10%) were negative and positive by both technologies respectively. Of these, 90% (1819/22044; 95% CI, 90- 91%) were negative and 8% (1819/22044, 95% CI, 8% -9) positive for TB with ZN. Table

4.5 ***The comparison of ZN and LED technology for detecting TB disease combined (specimen level analysis) restricted to negative and positive outcomes; Somaliland (2012-13).***

Technology		LED		
ZN		*Positive*	*Negative*	Total
	Positive	1819	5	1824
	Negative	239	19981	20220
	Total	2058	19986	22044

Eleven percent (239/2058; 95% CI, 10-13%) of specimens were positive by LED only, but were initially negative with ZN. Comparatively, ZN found five specimens positive that were negative with LED. It should be noted that the proportion of positive sample diagnoses was the highest when both techniques were used concurrently and lowest when ZN was used alone. The difference between the paired proportions computed as (r-s)/n was only -.01% (5-239)/22044; 95% CIs; -1-.9%), $\chi^2 = 224$ ($P<.0001$). Facility level data are in tables 4.6-9 in Appendix for further reference.

4.8 Conclusion

This analysis investigated the diagnostic performance and operational feasibility of LED for TB routine testing in Somaliland. This analysis utilized paired data from patients presumptive and tested for TB at nine diagnostic facilities that introduced and implemented LED for routine TB diagnosis in Somaliland. Specifically, it compared proportions and the differences in proportions in patients' positivity rates between ZN and LED testing at the specimen and patient level. The exposure variable was the testing technologies (ZN and LED), and the outcome variable was the test results (negative and positive results).

Overall, the proportion of positive sample diagnoses was highest when both methods were being used concurrently, and lowest with ZN-only usage. Despite reported gains in previous similar settings (resource-poor), the overall diagnostic yield (patients' positivity rates) did not exceed 2% with LED technology use in Somaliland.

Chapter Five: Health care workers' knowledge, attitudes and practices regarding light-emitting diode fluorescence microscopy use for routine tuberculosis testing in fragile states

5.1 Introduction

This chapter presents the findings from objective 3, which explored the knowledge, attitudes, perceptions and practices of healthcare workers on light-emitting diode fluorescence use for routine tuberculosis (TB) testing. Though the main focus of this chapter was to determine the knowledge, attitudes, perceptions and practices of healthcare workers on technology acceptance, it also explored factors that helped or hindered the introduction, implementation and routine use of new diagnostic technologies for TB diagnosis at the primary care level in Somaliland.

The current global plan for TB control hinges on improving both access to, and delivery of, quality care for millions of people around the world[28, 29, 137, 242]. The introduction of new tools for TB diagnosis was regarded as a critical step to improving access to, and delivery of, quality diagnoses for people affected by TB in high burden settings. While available TB literature is rife with empirical evidence validating the importance and usefulness of newly adopted technologies for TB diagnosis, it has failed to address barriers to their introduction, implementation and routine utilization as well as acceptance of these technologies by intended users in a fragile health system context [243-247].

One of such technologies introduced is light-emitting diode fluorescence microscopy (LED) to replace the conventional Z-N microscopy (ZN) for routine TB diagnosis in resource-constrained and fragile health systems. The use of LED as an alternative strategy for routine TB diagnosis has been widely adopted, introduced and mostly implemented in many resource-poor settings including fragile health states[163, 248-250]. The operational feasibility of LED technology to replace ZN for routine TB diagnosis, and acceptance by intended users (front-line health workers) in settings with weak health systems remains unclear[48, 141, 251]. The review of existing and relevant literature found no empirical evidence, including framework-based qualitative studies, on the operational feasibility of LED technology for routine utilization in a fragile health system context.

To inform the design and implementation of new healthcare technologies including TB diagnostic technologies such as LED, this study explored the knowledge, attitudes, perceptions and practices (KAPs) of intended users, namely healthcare workers (HCWs), working at four TB care facilities in Somaliland.

5.2 **Methods**

This is an exploratory study utilizing theory-informed qualitative data collection and an analysis approach to elicit data from HCWs on potential barriers to the acceptance and routine utilisation of LED in fragile health system settings. The main data collection techniques were semi-structured interviews, site visit observations combined with field notes and a document review. Primary data were elicited through semi-structured interviews (SSIs) with healthcare workers (n =25) working at four TB care facilities in Somaliland in the period December 2018-January 2019 Secondary data were extracted from document review, and field notes that were taken during the site visit observations and SSIs.

All data collection tools (interview and site visit guides) were pre-tested for clarity, validity, consistency and rigor and measures were formulated to tackle potential limitations or threats to the internal and external validity of the study findings. The aim was to control for information bias or recall bias that potentially affected the data quality, and check the time needed to complete individual interviews to allow engagement in conversation without interruptions[252, 253]. All study participants were informed about the purpose of the interviews before interview dates. Informed consents were obtained from all study HCWs before the interviews. All interviews were conducted (all interviews were audio-recorded) by the principal investigator (Halima Mohamed) in a standard format, either at the workplaces/facilities or at a private location preferred by study participants. Names of study subjects were removed from each interview transcript, and all data were kept in safe and secure locations.

The interview question guide consisted of four sections with specific questions on knowledge, attitudes, perceptions and practices, and this was then combined with a site visit observation checklist. Each of the knowledge questions had two possible/potential responses: *adequate or inadequate* in TB care service provision including LED technology use. The attitudes questions had two possible user responses: *positive* or *negative*, and the opinion questions also had two possible responses: *favourable or unfavourable* towards the technology concerned among the intended users (health workers). The perceptions questions were used to elucidate the *perceived usefulness* and *perceived ease of use* of the LED technology used by the intended users. Variables determining HCWs' views on practices in LED use included, but were not limited to, the acceptability and frequency of use of LED technology, HCWs' use and adherence to standard operating procedures (diagnostic, treatment and patient care, including infection control measures and quality control), and recording and reporting guidelines at the facility level.

The study population consisted of primary care physicians (n = 6), nurses (n = 4) and laboratory technicians (n = 15) working at four TB care facilities that introduced and implemented the LED technology for routine TB testing in Somaliland.

The health workers were purposefully selected for the SSIs based on their profiles (work, experience, roles and responsibilities) in TB care service provision at the facility level at the time of the study. Health facilities were selected based on their LED use and on convenience (security and travel restrictions). More details on the study population and data collection tools are presented in the methods section in chapter 2 (methods).

5.3 Theoretical framework

This study adopted a framework-based qualitative primary and secondary data collection and analysis technique using the technology acceptance model from Davis, 1985 and the Braun and Clarke's (2006) six steps thematic analysis framework (Figure 5.1) [161].

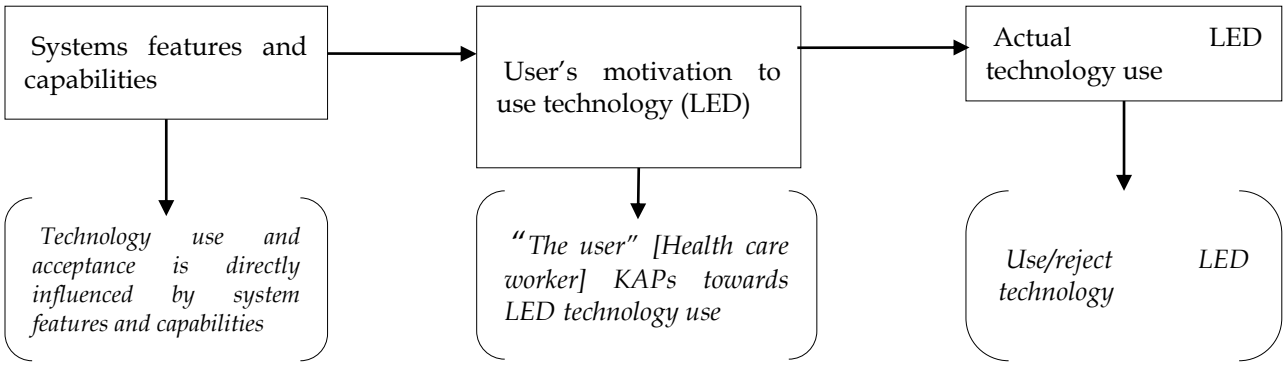

Figure 5.1 ***The conceptual model for technology acceptance***
Source: Davis, 1985.

5.4 Data analysis

Data from interviews, site visit observations, field notes and document review were analysed through thematic (inductive) and content (deductive) analytic methods using NVivo v12 software. The use of combined framework-based analysis helped the researcher familiarise themselves with data and data corpus, generated initial codes, searched for themes, identified patterns defined and reviewed relevant themes[254]. In this process, all identified themes on *technology acceptance* as explained by *perceived usefulness, perceived ease of use, perceived barriers and attitudes towards using, and how these perceived factors influenced the actual use of LED technology for routine TB diagnosis* were coded, collated, organised, grouped and merged into categories. The coding served as labels to compile and assemble the data, and integrate major emerging themes in the dataset (Table 5.1 in Appendix 5).

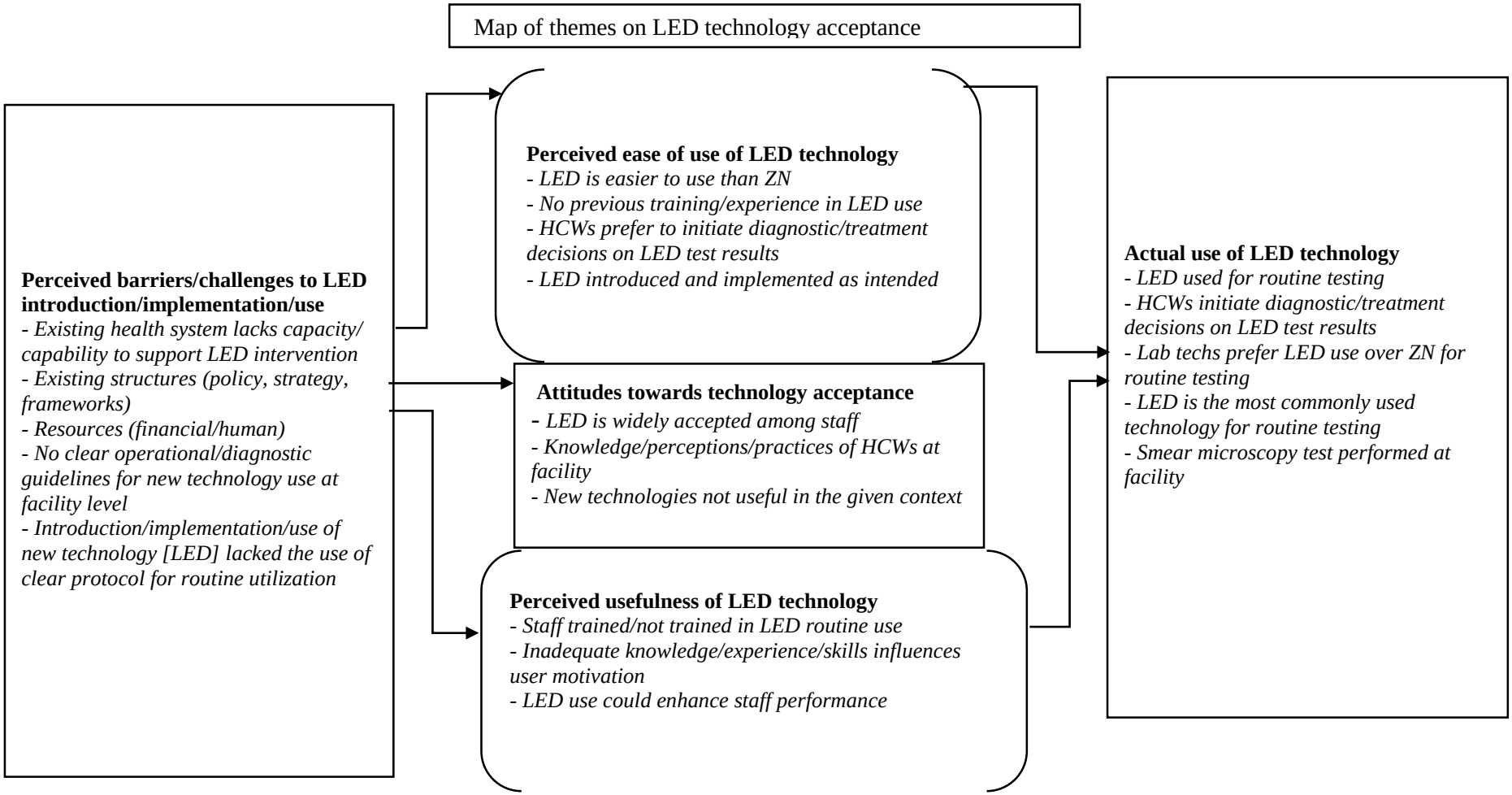

Figure 5.2 ***Mapping the content of, and relationship between, themes on technology acceptance (2018-2019).***

As summarised in Figure 5.2, & Tables 5.1-5.4 in the appendix to chapter 5, all persistent thoughts, views, explanations and interpretations of technology acceptance and use identified in coded scripts were thematically mapped. The data was then organised into meaningful groupings to identify important phrases in line with the research conceptual framework and objective/questions. The cumulative frequencies of themes were quantitatively analysed, tabulated and summarized in the Appendix to chapter 5.

Equally, content analysis of data from documents and field notes entailed skimming, identifying patterns, extracting data and generating segments, quotations, and passages in the data scripts. The data extraction process from a descriptive to an analytic state prepared the data for comprehensive and crosscutting intuitive, interpretive and inclusive content analysis. For this analysis, strict textual interpretation was adopted for the coded themes from reviewed documents and field notes. The use of content analysis helped describe, interpret and narrate the data captured in the documents review and field notes[21, 22].

Finally, all the extracted and coded segments generated through thematic and content analysis were appraised and synthesized to provide context-specific insights, interpretations and explanations about current TB care practice at the facility level[255, 256]. This helped the researcher draw conclusions from relevant theories or existing research findings on technology acceptance and appreciate how the findings of this analysis complement the existing body of knowledge in practice (i.e., technology acceptance), ultimately improving patient care at the facility level in a fragile health system context[257]. The frequency distribution of the findings was tabulated, summarized and displayed in tables and figures. This helped identify factors influencing participants' cohesive understanding of constructs and provide answers to critical research questions on technology acceptance for routine use in a fragile health system context.

5.5 **Results**

Table 5.1 presents the demographic characteristics of the study participants. In total, 55 health workers were approached for the semi-structured interviews at four TB care facilities in three regions of Somaliland. Of these, 25 health workers agreed and 30 refused to participate in the study. The high refusal rates of health workers approached for interviews were primarily influenced by the lack of, or inadequate information on, both the use and usefulness of the LED technology for routine TB

diagnosis. Lack of time, or time conflict and work pressure were common or principal reasons for HCWs' refusal to participate in the study.

Furthermore, most of the health workers who refused to participate in the study were nurses and physicians: they indicated that they were neither prepared nor informed fully about the usefulness of the technology applied (LED technology). Most of the health workers interviewed for study were laboratory technicians (n=15), primary care physicians (n= 6) and nurses (n= 4) who worked at the largest care facility in Hargeisa, Somaliland. Most of the nurses and laboratory technicians who declined participation in the study were new recruits and argued that they were not sufficiently informed about the LED technology application and purpose.

16/25 and 9/25 of participants were male and females respectively. About 14/25 and 10/25 of health workers reported a diploma and bachelor of science level education respectively. Only 1/25 of health workers reported a masters and higher level education. Another 6/25 of staff were certified in general health services alone. 16/25 had received no formal training in TB care, compared to 9/25 who did have TB training. About 5/25 of the staff interviewed had worked in their current positions/roles for less than 2 years. Most had held their current positions/roles for 210 years respectively. Only 7/25 of the staff had held their current posts for over 10 years.

Table 5.1 Socio-demographics and characteristics of study participants, health worker study, selected facilities, Somaliland (2018-2019).

Variable		**Frequency (N= 25)**	**Percent (%)**
Age	21-35	15	60
	36-45	6	24
	46-55	4	16
Sex	Males	16/25	64
	Females	9/25	36
Education status	MSc and above	1/25	4
	BSc	10/25	40
	Diploma	14/25	56
Training in TB care	No formal training in TB care	16/25	64
	Formal training in TB care	9/25	36
Duration in current position/role	<2 years	5/25	20
	2-4 years	7/25	28
	5-10 years	10/25	40
	>10 years	7/25	28
Present role at this facility	TB nurse	4/25	16
	Laboratory technician	15/25	60
	Physician	6/25	24
Work experience in TB care (including diagnosis)	Previous experience	0	0
	<2 years	5/25	20
	3-4 years	9/25	36
	6-10 years	4/25	16
	>10 years	7/25	28

The vast majority (24/25) of HCWs had received no routine or refresher training in LED and protocol use since its inception in 2012.

Knowledge in TB care, use and maintenance of LED technology

Table 5.2 summarizes the frequency distribution of health workers' responses to knowledge competencies in LED technology use and TB diagnosis in general. Knowledge is defined as the fact or condition of knowing something with familiarity gained through experience or association[258]. Nearly 24/25 of health workers reported inadequate training in LED technology use and maintenance. No health workers reported prior experience in TB care including diagnosis.

Table 5.2 ***The frequency distribution of health workers' responses to attitudes and knowledge questions on LED use and TB diagnosis (2018-2019).***

Variable (knowledge competencies of staff)	Frequency (n/N= 25)	Percent (%)
Adequate knowledge in TB care (including diagnosis)	13/25	52
Inadequate knowledge in LED use for routine testing	12/25	48
Adequate knowledge in LED for routine testing	07/25	28
Inadequate training in LED technology use and maintenance	24/25	96
Favourable opinion of LED use for routine TB testing	14/25	56
Unfavourable opinion of LED use for routine TB testing	11/25	44
Need to improve ownership of TB control program	16/25	64

Overall, health workers rated their knowledge competencies in the use and maintenance of LED technology, as well as TB care in general, as low. Across all professions, physicians appeared more knowledgeable in TB care (i.e., diagnostic and treatment) services relative to their professional counterparts (i.e., lab technicians and nurses). The physicians reported knowledge levels in TB care service provision through medical education at various medical schools and subsequently from working at different health facilities in the country. Nearly half (12/25) of health workers regarded their knowledge competencies in LED use for routine diagnosis as inadequate, and 7/25 as adequate.

The perceived staff knowledge deficit in the use and maintenance of LED technology was believed to be linked with mainly a lack of locally available resources.

"*My knowledge and experience in diagnosis or TB care general were minimal when I first joined. They do not teach or train you in the management of important diseases such as TB in medical schools because there are resources to cover staff training. Now, I know more about all aspects of TB care*

than when I joined here, and I enjoy it very much. I would love to get more training and experience to improve my knowledge in TB care in the future. It is all about the training, experience and frequent practice at work. But we do not have resources to train staff." (Somali TB physician.)

Attitudes towards LED technology use

Attitude is defined as how people feel about specific subjects or issues[259]. The health workers' responses to questions about their attitudes towards LED use are presented in table 5.3 in Appendix to chapter 5. Overall, health workers voiced a favourable opinion of LED technology use for routine TB diagnosis and professed the new technology as an important means for improving patients' diagnostic outcomes in a resource-poor fragile context. Over half of the staff interviewed had a favourable (14/25) opinion of LED technology utilization for TB diagnosis. Little over half (16/25) of staff believed that LED use helped to reduce their daily laboratory workload and improved staff performance, as well as patients' diagnostic outcomes at their health facilities.

Eighty percent of the health workers stressed the importance of local partners involved in planning TB control activity in the country. Close to 88% of health workers raised concerns about the lack of formal training in the use and maintenance of new technologies including LED for regular use, particularly at the health facility level.

"There are varied views on the new technology introduction and regular use in settings like ours. It is entirely unclear whether the recommended and introduced new technologies are suitable to a fragile health system context. In my opinion, some people think that any tool or technology donated by our donors or principal recipient (World Vision and the Global Fund) should be accepted with no objections, because even though these technologies might not work here, they are better than nothing. I do not think we should accept any tool or technology without training for staff and upkeep costs. These technologies might not be suitable for the environment where we operate or fulfil our technical and operational needs" (Somali chest physician.)

Perceptions and opinions of HCWs towards LED technology use

Perception is the person's primary form of cognitive contact with the world around him/her[260, 261]. This definition was used to assess health workers' perceptions of LED for regular use in fragile health systems. The health workers' responses to perception questions are presented in Figure 5.3 & Table 5.4 in Appendix 5. Generally, health workers were unclear whether the use of advanced and complex technologies for TB diagnosis achieved the intended purpose (increased case finding) given stated

barriers in a fragile health system context. Overall, staff perceptions on LED implementation and use were evenly split. Half (2/4) of the nurses and physicians and 3/6 of laboratory technicians regarded LED as widely accepted by staff for routine diagnosis. Comparatively, almost half of laboratory technicians (8/15), nurses (2/4) and physicians (3/6) said LED technology was not widely accepted by staff at the facility level. Genexpert and LED technologies were reported as the most common diagnostic tests performed for routine TB diagnosis.

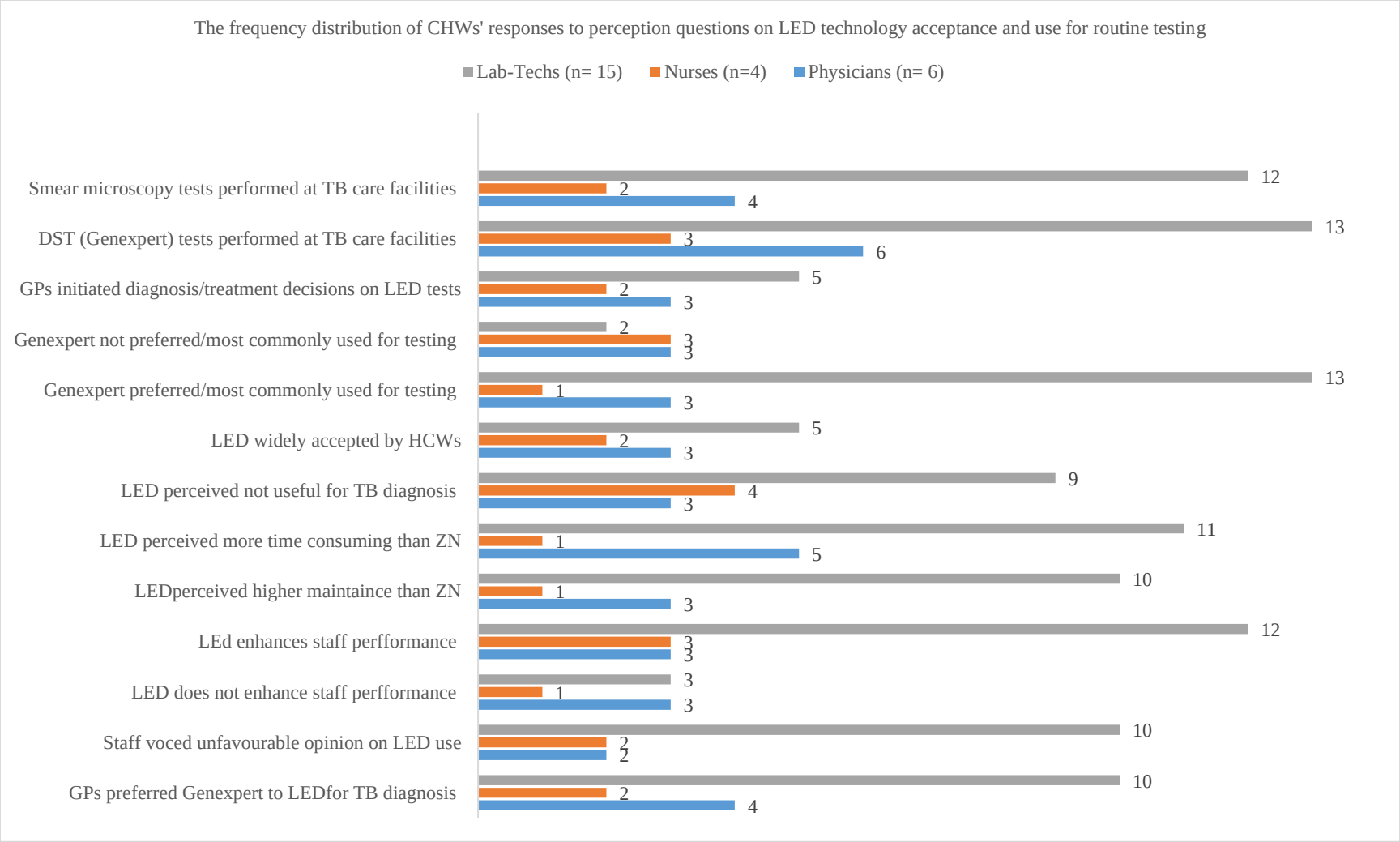

Figure 5.3 ***The frequency distribution of HCWs' responses on opinions and perceptions of LED use for routine TB testing (2018-2019).***

about 4/6 physicians preferred Genexpert for TB diagnostic and treatment initiations compared to less than half (2/6) who preferred LED. The physicians' reluctance to use LED technology was thought to be influenced largely by unfamiliarity with the new technology application. Physicians believed the application of too many technologies at once not only overwhelmed an already weak health system but also hindered TB care service delivery due to resource constraints in the given context (Figure 5.3 & Table 5.4 in Appendix to chapter 5).

Over (14/25) of staff said LED had not been implemented as initially intended due to problems associated with resource scarcity, coupled with the weak structural capacity of the existing health systems to support the implementation, management and utilization of these complex interventions in a fragile health system context. The vast majority of the HCWs (19/25) said that LED did enhance their performance in TB diagnosis or patient care. Only 7/25 of HCWs said LED use did not improve their performance in TB diagnosis (Figure 5.3 & Table 5.4 in Appendix 5).

Most laboratory technicians (9/15) and half the physicians (3/6) and nurses (2/6) viewed LED technology as necessary, applicable and useful. However, a significant number of laboratory technicians (10/15) and physicians (3/6) and nurses (1/4) perceived LED as higher maintenance than ZN. Approximately 1/4 of nurses, 8/15 of physicians and 4/6 of laboratory technicians regarded LED as more time consuming than ZN in TB testing.

More importantly, a large number of physicians (3/6), nurses (2/4) and laboratory technicians (6/15) voiced unfavourable opinions of the importance and applicability of LED technology use for routine TB testing in a fragile health system setting such as Somaliland. Almost all (22/25) of staff interviewed raised concerns about the lack of information on the use and maintenance of the technologies concerned at the facility level (Figure 5.3 & Table 5.4 in Appendix to chapter 5).

The vast majority of health workers interviewed were concerned about the lack of frontline staff involvement in the planning process for the implementation, deployment and utilisation of such complex technologies as future intended users.

"You know these advanced technologies will enable us, I mean laboratory technicians to run effective and sophisticated diagnostic tests and communicate these results to primary care physicians in real-time. After that, primary care facilities will demonstrate how quality TB care can be delivered to populations in need, which would ultimately improve the health outcome of people. This is the dream

for all health workers in the country. Unfortunately, that is not happening now and it is very sad. But, that is how things are in Somaliland" (Somalia laboratory technician.)

While most of the health workers had a favourable opinion towards LED and introduction and use, they felt the systematic and programmatic readiness of existing laboratory services should be prepared to support the implementation and management of such complex technologies in fragile health system settings.

Practices of HCWs regarding LED technology implementation and routine use

Healthcare practice or 'best practice' is defined as the activities, disciplines and methods used available to identify, implement and monitor the available evidence in health care[262]. The site observations were used to assess not only the use of the applied technology (LED) but the overall use of standard operating procedures for the TB care service provision including the prevention and control of TB at the facility level. The results from the site observations were thematically and quantitatively analyzed, tabulated and summarized in Figure 5.4.

Data used for analysis were elicited from site visit observations (quantitative) and field notes (qualitative) utilising a checklist/guide by watching the actions, interactions and operational performance of staff on duty at the various facilities visited. Key practice elements assessed at the study facilities during observations included: staff competencies in LED technology acceptance/routine use, documentation of patients' diagnostic outcomes, the use of standard operating procedures and protocols for laboratory bio-safety, infection control and the collection and handling of diagnostic specimens in patient care areas as well as the laboratory facilities. Quality assurance (QA), quality control (QC) (internal/external) and quality improvement (QI) checks included the reliability of electricity and the physical space/location of diagnostic facilities at TB care facilities. In total, 8 site visit observations (2 visits per facility) were administered at the four TB care facilities in two regions of Somaliland.

The cumulative information elicited from the site visit observations and field notes was intended to explore and provide useful highlights on factors that helped and hindered standard laboratory diagnostic practice in day-to-day TB care service provision, including the use of new technologies such as LED at primary care facilities in Somaliland. Overall health workers' practice competencies in all aspects of TB care delivery were mostly inadequate across facilities visited. Nearly all laboratory diagnostic facilities visited lacked the necessary resources (competent health workforce, financial) and

an infrastructural capacity to support and sustain as well as reinforce the use of the required standard practices to deliver reliable and quality diagnostic and treatment services to patients (Figure 5.4). An overwhelming majority of facility staff were worried about the lack of routine and standard QC and QA checks at their laboratory facilities. Half (2/4) of the health facilities visited lacked adequate equipment, reagents, supplies and spare parts available or kept at laboratory facilities.

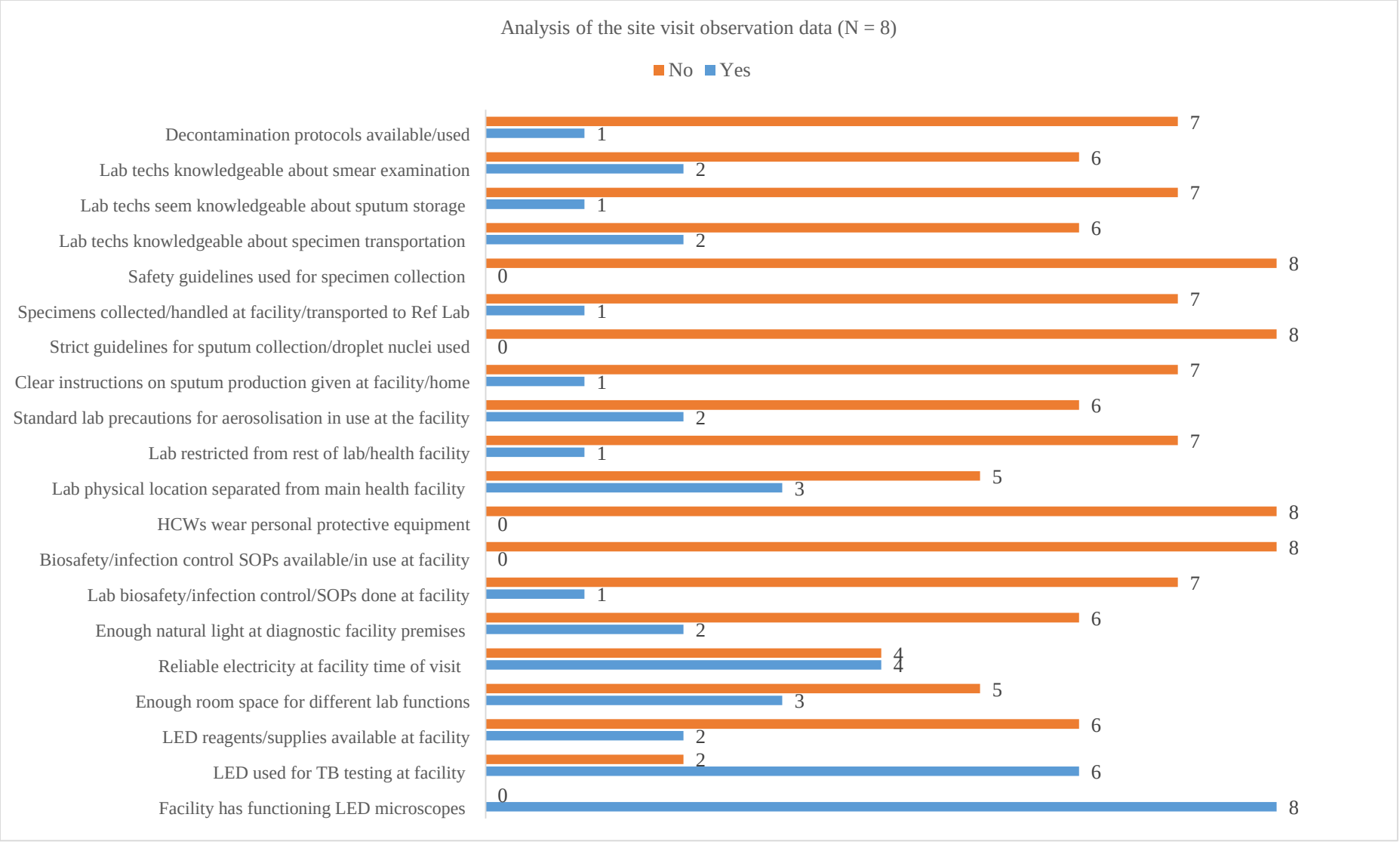

Figure 5.4 ***The frequency distribution of the observed events/responses during site visit observations (2018-2019).***

Not all staff working at the health facilities studied wore personal protective equipment (laboratory gowns, masks and gloves) when collecting and handling specimens or interacting with patients at TB care facilities, as this equipment was unavailable at their facilities. All of the health facilities visited had functioning LED microscopes that were used for routine TB diagnosis. Frequent interruption to the supply of consumables or reagents and maintenance was a significant constraint to the routine utilization of LED microscopes, mostly at peripheral facilities in Somaliland.

Waste management and safety disposal guidelines/protocols were neither available nor adequately followed at all facilities visited. During site observations, over half of laboratory staff said that they did not follow waste management and safe disposal measures due to a lack of availability of standard protocols/guidelines or protocols at the facility level. The required safety guidelines for specimen handling, including the collection, processing and transportation of specimens were not followed at facilities visited. Presumptive patients were not separated/isolated from non-presumptive patients in most of the facilities visited. Most of the patients' diagnosis and treatment rooms lacked proper ventilation, aeroionisation and decontamination systems at most of the health facilities visited.

Health workers expressed concerns about the use of the new technologies due to a lack of, or inadequate, infection control measures to prevent further transmission of TB at healthcare facilities. All staff working at facilities visited raised concerns about the lack of infection control measures or use of protocols at the facility and needed these problems addressed urgently. Most of the patients' rooms in almost all TB care facilities visited lacked reliable electricity to operate LED microscopes or storage systems, and also lacked the physical space to separate or isolate presumptive patients from non-presumptive patients, as well as a proper ventilation system. The observed shortage of laboratory equipment, reagents, supplies and spare parts, particularly for the technology concerned (LED), as well as the lack of standard laboratory diagnostic protocols or guidelines, was mainly attributed to a deficiency of resources, including human technical expertise, financial support and information on procurement and supply chain management.

Consequently, the health workers' conceptualised views on new technology acceptance and use reflected the lack of systematic and programmatic readiness of the existing health system to support and sustain the utilisation of the applied technologies for routine use. In an interview a physician stated that:

"You know we do not have adequate resources or systems for us to make use of these technologies. I have already stated this in your previous questions. I have told you that our facility lacks the

structural and resource capacities necessary to support the introduction, implementation and utilisation of these new technologies like LED, mobile chest x-rays and Genexpert. But we do not have the resources or system to support the routine use of these tools. In my opinion, the system should be prepared first or before introducing sophisticated technologies in settings as such. Maybe they would work after that". (Somali TB physician.)

Key barriers to good laboratory practice included, but were not limited to, a lack of quality control and quality assurance systems available at the facility level. For example, no specimen slides were prepared for quality control and assurance checks with the use of LED for routine diagnoses at the TB laboratory facilities. The reported inadequacy of quality control and quality assurance checks jeopardised the reliability, validity and quality of diagnostic outcomes and ultimately, patient care. Lack of quality control and quality assurance systems was an important concern for all facility staff.

Another critical concern that emerged in the interview discussions, field notes and site visit observations was the adoption of multiple technologies for routine utilisation concurrently without improving the systematic and programmatic readiness of existing health systems, particularly laboratory diagnostic services at all levels. For this particular reason, health workers were noticeably concerned about overcoming the challenges of new technologies without the human, financial and infrastructural capacities needed to support and sustain their implementation and routine utilization.

"The current plan for further technology use for TB diagnosis is not working for our patients' need, in my opinion. We have received a wide array of products so-called 'improved diagnostic tools', but none of them works in this environment due to a lack of programmatic and systems support to both manage the tools already in use and rapidly integrate the new technologies at the facility level. That is what we need to benefit from these advanced technologies". (Laboratory technician in charge.)

5.6 **Conclusion**

This study explored the health workers' knowledge, attitudes, perceptions and practices regarding LED technology acceptance and utilisation for routine diagnosis in TB care facilities in Somaliland. The health workers' attitudes, perceptions and opinions on LED use appeared to be generally positive. Most health workers who participated in the study were fairly clear and consistent about the factors that helped and hindered acceptance and utilisation of LED technology for TB diagnosis at the facility level. Staff opinions were split over LED technology acceptance and use, which bred

negative attitudes toward the future introduction and implementation of new technologies for routine utilisation at the primary care level. Primary care physicians, for example, viewed LED technology as a valuable tool for TB diagnosis in a fragile health system context: a tool that could potentially improve patients' diagnostic outcomes and ultimately reduce errors in diagnostic and treatment process. Laboratory technicians and nurses, however, placed higher priority on operational and systematic issues, including the need for standard protocols and procedures, staff training in new technology use, maintenance and infection control.

Chapter Six: Health professionals' views on resourcing, structural and environmental constraints to the feasibility and acceptability of LED

6.1 Introduction

This chapter presents the findings from objective 4, which explored the views of health professionals (HPs) on the feasibility of using light-emitting diode fluorescence (LED) for routine TB diagnosis in fragile health system settings.

The prevention and control of tuberculosis (TB) in fragile and resource-poor settings requires a multi-sectoral responsibility and is often a challenging task to achieve[63]. As a result of this effort, the last few decades have seen the introduction of several new health technologies for TB diagnosis for high burden, resource-poor settings[153-160, 263]. In such resource-poor settings, the control of TB is heavily dependent on smear microscopy, as it is relatively easy to use, inexpensive and suitable for resource-poor environments [233]. Modern and innovative diagnostic technologies cover a diverse range of products intended to enable resource-poor settings to improve quality diagnosis at mainly primary care services and ultimately intensify TB case finding in high burden areas[60, 248, 264].

One such new technology is LED technology, which has been recommended and introduced for routine TB testing in high burden countries, including fragile states[184, 265-268]. Since its inception, LED technology has been widely adopted and implemented in many resource-poor settings, such as Somaliland[153-160]. However, deployment, uptake and use of the LED technology for routine TB diagnosis has fallen far short of the levels predicted by the WHO and its TB control collaborators[163, 269, 270]. This is partly because the introduction and predicted utilisation levels of these technologies advanced faster than improvements to existing delivery capacities, organisational cultures and resources in settings with weak health systems[87, 271]. In short, improving access to quality diagnosis for people affected by TB has been hugely challenging as it requires concerted and coordinated efforts from all those involved in TB care service provision[272]. While the accuracy (sensitivity and specificity) of the LED technology has already been proven in previous studies, limited or no research is available on the resourcing (training capability, level of expertise), infrastructural (equipment, laboratory delivery capacity) and procurement (i.e., reagents, consumable) implications of introducing such sophisticated healthcare technologies in a fragile health system[123, 174, 175].

As found in chapter five of this thesis, technology acceptance by the intended user is broadly influenced not only by the ease of use of the applied technologies but also the existing health system's capacity to support its introduction, implementation and routine utilisation at the primary care level.

This chapter assessed feasibility in terms of three aspects: the resourcing (financial and health workforce), structural (system-wide operational, technical capacities) and environmental (physical facilities, the organisational culture and conditions, stakeholder involvement and engagement) contexts in which these complex technologies were introduced and used. For intended recipients (HPs) to recommend further introduction and deployment, such complex interventions must show that they are feasible structurally and environmentally, given the resources available locally. Previous TB diagnostic technology evaluations have assessed feasibility based on its efficacy (accuracy or incremental gains) under ideal circumstances. Instead, this analysis appraised potential hindrances to the feasibility of TB diagnostic technologies in non-ideal world conditions with a particular emphasis on fragile health system settings[63, 273, 274]. To do so, it explored the views of healthcare professionals in operational, managerial, technical and policy-making positions in TB care service provision in Somaliland.

6.2 **Method**

HPs' interviews were used to obtain information about their views and practices with regards to the resourcing, structural and environmental constraints to the feasibility of LED use for routine utilisation in Somaliland.

Theoretical framework: the impact assessment framework

This study drew its inference from the impact assessment framework (IAF) and used it as a tool for analysis[175]. The research questions were developed from two of the five IAF layers: health system and policy analysis, and provided the main themes and direction for analysis (Table 6.1). These questions were formulated out of the IAF to factor in resourcing, structural and environmental constraints to the feasibility of new TB diagnostic technologies such as LED in fragile health system settings. While the feasibility analysis was not a full-blown system-wide enquiry, the health system and policy analysis layers of the IAF were applied to articulate the extent to which the existing health system of Somaliland met basic requirements for technologies' introduction, uptake and utilisation[123, 174, 175]. These layers examine the health system requirements of a new intervention, for example human resources, infrastructure, operating procedures, quality assurance, procurement and maintenance[123, 174, 175].

Understanding the broader (outer) context for technology introduction, which rests on the relationship between resourcing, structural and environmental components, is critical[123, 174, 175]. With this in mind, this analysis conceptualised critical constraints to the feasibility of the introduction and utilisation of the LED technology, whose implementation and suitability depended on a whole host of influential factors at different levels in the wider health system context. With the caveat that new TB diagnostic technologies are suitable and feasible in a diverse range of settings, the use of the IAF also aided interpretation of the study findings and the interactions that helped or hindered adoption, implementation and utilisation of LED technology in Somaliland. The use of the IAF provided a platform for rigorous feasibility analysis and helped identify the resourcing, structural and environmental constraints and bottlenecks that potentially impede not only the implementation (feasibility) but also acceptance and utilisation (real world) of the applied new technologies in fragile resource-limited settings.

Study design

A key informant interview guide was developed with questions focused on resources, infrastructural capacities and environmental conditions, and perceived challenges to introduction, uptake and use of the LED technology.

Table 6.1 ***The use of the impact assessment framework for feasibility analysis***

Layer of assessment	Kinds of questions being addressed	Previous studies addressing these questions (see Chapter 3)
1. Efficacy analysis	How well does the new tool work regarding accuracy? How many additional cases were identified that would otherwise would not have been identified? How many additional cases will actually start (and complete) treatment as a result of using the new tool?	15 studies have addressed the accuracy of LED technology
2. Equity analysis	Who benefits from the new tool (ambulant vs. hospitalised, poor/less poor, men/women, adults/children)? Why do these benefits accrue (level health system in which new diagnostic is deployed, change in time to issue of results, change in patients' costs)?	Not the focus of the present study
3. **Health systems analysis**	What are the human resource implications of introducing the new technology (training, number and cadre of staff)? What are the infrastructural implications (equipment, laboratory layout, safety installations)? What are the procurement implications (reagents, consumables and documentation)? What are the implications for quality assurance (internal and external)?	**This is the focus of the present study**
4. Scale-up analysis	What is the expected impact, to determine further scale with the new technology? Cost savings to health provider/health system Cost saving to patients about income Effects of transmission of improved infection control as a result of the new technology	Not the focus of the present study
5. Policy analysis	What other similar technologies are available or likely to become available? How do the similar technologies compare in their projected performance within each of the layers above?	**This is the focus of the present study**

*Source: Mann et al, 2010

Study setting

This study took place at the public, private, charitable and non-governmental organisations' administrative offices at the national and regional, district health and laboratory diagnostic facilities in three urban towns of Somaliland over the period 2012-2013 The participating facilities were part of the TB-REACH LED technology introduction intervention in Somaliland for the period of 2012-2013.

6.3 Study population

The study population consisted of purposefully selected HPs with managerial, coordination, technical advisory and policy-making responsibilities for various public, private, charitable and non-governmental organisations, agencies and stakeholders (local and international) involved in TB care service provision in Somaliland.

6.4 Data analysis

This study adopted a framework-based qualitative approach for the thematic content analysis of data extracted from 20 interviews, and document review. Most of the documents reviewed were strategic, policy and operational documents developed by several stakeholders involved in TB care delivery (i.e., WHO STOP-TB, Global Fund, World Vision, and NTP-Somaliland). Interview data were transcribed verbatim and loaded into NVivo 12 software for thematic analysis. The identity and confidentiality of all study participants were anonymised and preserved. This helped depict the views of HPs on crucial resourcing, structural and environmental constraints to the feasibility and acceptability of the introduction, implementation and utilization of LED for routine TB diagnosis in Somaliland. The cumulative frequency of codes (HPs' responses to research questions) on LED were mapped together, tabulated, quantitatively analysed, summarised and presented in tables and displayed in graphs where relevant (Figure 6.1 in Appendix to chapter 6).

The analysis of this inquiry drew its inferences from the impact assessment framework (IAF) by G. Mann et al. (2010). The thematic and content analysis of data focused on linking evidence on human resources (skilled health personnel, money, time) with infrastructural (systematic and programmatic readiness, including procurement of laboratory supplies) constraints to the introduction of the new technologies for routine diagnosis in resource-limited settings. Figure 6.1 provides clear illustrations about the mapping of the thematic and content analysis of feasibility and acceptability technology introduction, uptake and routine utilization of LED.

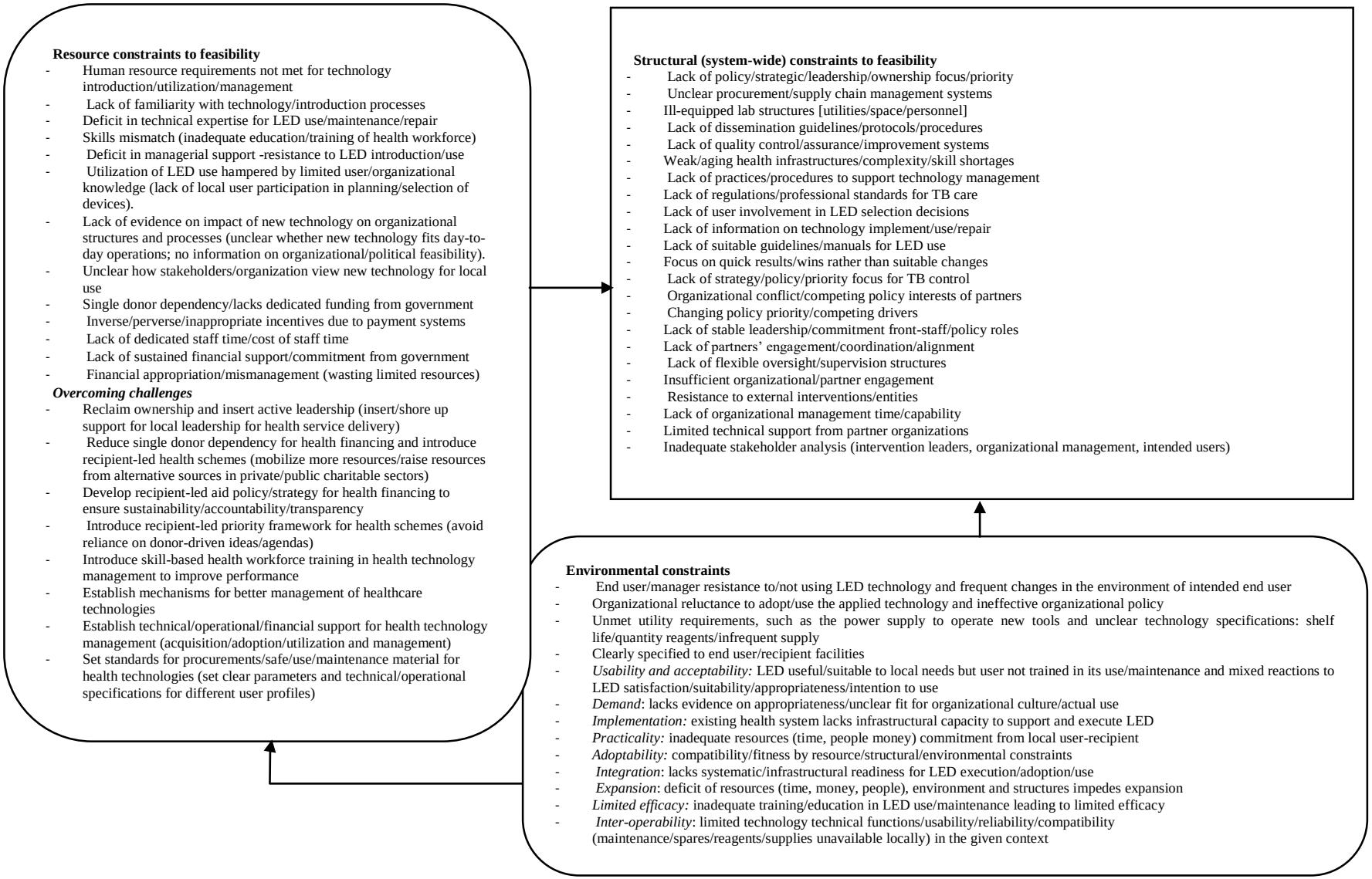

Figure 6.1 ***Mapping of the emerging themes in the health professionals interviews on the feasibility of technology introduction, uptake and routine utilisation, Somaliland (2018-2019).***

The use of the framework-based analysis helped provide precise descriptions of both the process and steps embraced for a thorough and systematic thematic and content analytical approach, guided by inductive/deductive theoretical analysis of data elicited from interviews, field notes and document review. This type of analytical approach helped establish a clear understanding of HPs' views on key resourcing, structural and environmental constraints to the feasibility of LED technology introduction, implementation and utilisation for routine TB diagnosis in a fragile health system context[162].

To become familiar with the overall body of data/data corpus, all data extracts from interview transcripts, field notes and document review scripts were read several times to identify recurrences of patterns, themes and clauses and to develop coding categories. The recognised coded categories were applied to a similar text and transformed into meaningful and conventional analysis utilising ″an open coding″ format with no pre-set codes[275, 276]. Tables 6.1 & 6.2 in Appendix 6 present the summary of the HPs' responses to interview questions.

6.5 **Results**

Table 6.2 presents the demographic and other characteristics of the study participants. In total, 60 health professionals (HPs) with diverse managerial, technical and coordination responsibilities within various organisations involved in TB care service provision in Somaliland were approached for the key informant interviews. Approximately 40 out of the HPs approached refused and 20 agreed to participate in the study. Table 6.2 (bottom row) provides details on the number of HPs who refused or agreed to participate in the HPs' interviews in Somaliland.

The vast majority of the HPs were males (n = 17). Most of the HPs interviewed were Ministry of Health (MOH) policy makers (10/20), TB program managers (5/20), program coordinators (11/20) and technical advisors (2/20). About 18/20 of the HPs interviewed had held their current roles for 2-5, 6-10 and over 10 years respectively. Only 2/20 of the HPs worked had held their current posts for less than 2 years (Table 6.2). None of the HPs interviewed reported previous experience in TB care (diagnosis and treatment) prior to their current posts.

Overall, HPs interviewed for the study were clear and consistent about factors impeding the feasibility of LED technology in Somaliland. All (n = 20) of the HPs interviewed reported participation in the implementation and use of LED technology for routine TB diagnosis at their respective facilities. Nearly half (8/20) of the HPs rated Genexpert and LED as the most commonly used tools for TB

diagnostic tests at their facilities. Nearly half of the HPs said that mobile X-rays and culture respectively were most preferred and used for routine TB diagnostic tests at their facilities.

Table 6.2 ***Socio-demographics and characteristics of the study participants – health professionals, Somaliland (2018-2019).***

Variable			**Frequency**	**Percent (%)**
Age	25-35		05/20	25
	36-45		10/20	50
	46-55		02/20	10
	56-65		02/20	10
	66+		01/20	5
Sex	Males		17/20	85
	Females		03/20	15
Education status	MSc and above		6/20	30
	BSc		14/20	70
Years in current position/role	<2 years		2/20	10
	2-5 years		8/20	40
	6-10 years		6/20	30
	>10 years		4/20	20
Years worked in health care	<2 years		1/20	5
	2-5 years		3/20	15
	6-10 years		7/20	35
	>10 years		9/20	45
Work experience in TB care (including diagnosis)	*Previous experience*			
	<2 years		5/20	25
	2-5 years		2/20	10
	6-10 years		10/20	50
	>10 years		3/20	15
Roles and professional affiliations of HPs	***Breakdown of HPs***	***Approached for interview***	***Agreed***	***Refused***
	HPs (MOH level)	20/60 (34%)	9/20 (45%)	20/60 (33%)
	Program coordinators (organizational level)	11/60 (19%)	4/20 (20%)	10/60 (17%)
	Technical advisors (MOH/GF/WV (focal points))	10/60 (17%)	2/20 (10%)	12/60 (20%)
	TB program managers (for Somaliland only)	19/60 (31%)	5/20 (25%)	18/40 (45%)

*MOH=Ministry of Health, WV=World Vision and GF = Global Fund.

According to responses from HPs interviewed, key constraints to the feasibility of LED introduction, uptake and use were mainly lack of resources (human and financial), system-wide structural issues and lack of a supportive environment. Inadequate resources (human, financial, knowledge, information), suboptimal capacity in systematic and programmatic readiness (physical laboratory structures, supply chain, policy and regulatory mechanisms, leadership and governance capacities) of existing health systems, coupled with distractive environmental conditions, were perceived as significant constraints

to the introduction, implementation and utilisation of LED in a resource-limited fragile health environment.

HPs' perceptions towards LED technology usability

Table 6.3 depicts the frequency distribution of HPs' views on LED technology usability for routine TB diagnosis in Somaliland. Overall, the participants' views on LED acceptance and usability in a local context were mixed. Only 3 out of 20 of the HPs interviewed believed LED technology was widely accepted by facility staff. The vast majority of HPs believed LED technology was not widely accepted at the facility level. Close to 13/20 of HPs believed that LED had not been implemented as initially intended, compared to 7/20 who thought otherwise.

Table 6.3 ***The frequency distribution of HPs' responses to interview questions on perceptions on LED technology feasibility for routine utilisation in Somaliland (2018-2019).***

HPs responses to perception questions on LED technology implementation and use	Frequency (N=20)	n/N [%]
- LED not implemented as intended due to weak structural capacity	13	13/20 [65]
- LED implemented as initially intended	7	7/20 [35]
- LED could potentially increase TB case detection	6	6/20 [30]
- LED useful for TB diagnosis	10	10/20 [50]
- Not suitable to local conditions	12	12/20 [60]
- Suitable to local TB care needs/conditions	8	8/2 [40]
- LED is easy to use	14	14/20 [70]
- Not used for routine testing	15	15/20 [75]
- LED used for routine testing	5	5/20 [25]
- Lack of confidence of facility staff in LED use	17	17/20 [85]
- Widely accepted among staff for routine use	3	3/20 [15]
- LED not better than ZN in case finding	11	11/20 [55]
- Low LED acceptance attributed to staff resistance	13	13/20 [65]
- Frequent disruption to reagents/supplies for LED	17	17/20 [85]
- LED technology not widely accepted at facility level	17	17/20 [85]
- Confused protocol in LED use/maintenance	16	16/20 [80]
- Not useful for TB diagnosis in a fragile health system environment	10	10/20 [50]
- Lacking information on installation and safety/operation checks for routine use	16	16/20 [80]
- Acceptance tests and full/proper functions of tools not specified/verified with end users	15	15/20 [75]
- Calibration/testing for specific equipment/tools not specified to potential users	13	13/20 [65]
- Training/information on basic/advanced maintenance/repair not shared with end users	19	19/20 [95]
- Spare parts/post warranty do not meet minimum required for technology acquisition	17	17/20 [85]
- Lack of operating manuals with information on access to spares for LED routine maintenance	19	19/20 [95]
- Technology fails to meet basic requirements for disposal of hazardous materials	18	18/20 [90]
- Technology neither consistent nor compatible with existing practice	17	17/20 [85]
- Lacks information on risk clarification on technology use/maintenance by user	15	15/20 [75]

Comparatively, HPs perceived LED technology as not suitable (12/20) and suitable (8/20) for regular use in a fragile health context. When HPs were asked about their views on any benefits of LED technology, over half (13/20) of the health professionals perceived LED as potentially useful to TB diagnosis compared to half of health professionals who viewed it as not beneficial at all. The perceived challenges to LED technology usability at primary care facilities included unclear guidelines (12/20), confusing protocol (16/20) and a lack of confidence (17/20) among health workers in technology use (all levels). Over 12/20 of HPs indicated that weak structural capacity coupled with frequent interruptions of reagents/supplies and consumables were critical obstacles to LED routine use in a fragile health system (Table 6.3).

Resource constraints to the feasibility of LED in fragile health systems

Table 6.4 depicts the frequency distribution of HPs' responses to questions about resource constraints to the feasibility of LED introduction, implementation and utilisation in Somaliland. Close to 18/20 of HPs indicated that the existing health system lacked the operational capacity, technical expertise and financial means to support both the use and maintenance of advanced technologies such as LED in fragile health system settings. A significant proportion (10/20) of the policy, managerial and technical teams believed scarce resources (financial and human) impeded or hampered the feasibility of LED or any other newly introduced healthcare technology. All HPs interviewed indicated that there was a lack of access to education or training support for HPs to make informed and strategic policy decisions.

As indicated in table 6.4, most of the HPs voiced concerns about the unsettling deficit of a competent health workforce with the technology-related knowledge and mix of skills to support TB care services in Somaliland. Seventy percent of the HPs reported a lack of effective leadership, governance and managerial oversight for the deployment and management of new technologies in a fragile health system environment as a major hindrance to the feasibility of LED utilisation. Ninety-five percent of the HPs believed the shortage of qualified health workforce for the use and maintenance of such technologies not only impeded feasibility but also affected both the quality of care and ultimately the intended outcomes.

Eighty percent of HPs said lack of incentives and motivational compensation, combined with severe delays of staff salaries, hindered the implementation and routine utilisation of new technologies at the primary care level.

"The problem we have with staff competence, and ultimately performance, has to do with incentives and compensation for staff working in TB care. Because at present, the vast majority of staff working at the point of care is not paid for their work. Even for those paid for their work are often subjected to 8-10 months' delay. The principal recipient is aware of this problem, and nothing has been done about it to date. Now, how can I convince my staff to keep working and perform well? I cannot. This is a major bottleneck to TB care delivery of quality including diagnosis to our patients". (Somali policy-maker.)

Consequently, 15/20 of HPs felt the single donor dependency for health financing constrained the feasibility of the implementation and utilisation of all programs, including new technologies, in the given context. Close to 19/20 of those interviewed believed that aid dependency for health financing contributed to increased inequality in health service provision and weakened local ownership respectively (Table 6.4).

Table 6.4 ***Perceived resource constraints to LED operational feasibility (introduction and utilisation) in Somaliland (2018-2019).***

HPs responses to questions on resource constraints (thematic codes)	**Frequency** n/N [%]
Human resource constraints	
- Deficit in health workforce with LED technology-related knowledge/skills in Somaliland	19/20 [95]
- Lack of local technical/operational expertise to support LED implementation/management	18/20 [90]
- Lack of administrative support for LED technology introduction/implementation/utilization	17/20 [85]
- No continuous skill-based/education/training for professional development in TB care services	19/20 [95]
- Shortage of qualified/skilled health workforce in the use/maintenance of healthcare technologies	19/20 [95]
- Lack of local leadership/ownership/governance of health service delivery/management	14/20 [70]
- Failure to assume responsibility for health service levels (facility/regional and national)	12/20 [60]
Financial resource constraints	
- Lack of financial incentive/compensation/inadequate pay and benefits for staff	16/20 [80]
- Lack of resources to execute regulatory/guidelines for QC/QA/QI functions (all levels)	13/20 [65]
- Health policy teams lack access to education/support to make informed decisions	20/20 100]
- Lack of sustainable health financing/suffers from single donor dependency funding	19/20 [95]
- Single donor dependency poses serious barriers to sustainable TB care services	15/20 [75]
- Aid induces dependency/weakens local ownership/autonomy to design/implement policies	16/20 [80]
- Local authorities have lost control of TB programs to donors/principal recipient entities	19/20 [85]
- Aid dependency increasing health inequality in healthcare service provision	19/20 [95]

Nearly 16/20 of staff interviewed thought that local authorities losing ownership of TB programs to external entities had become a challenge:

"The national TB program and Ministry of Health have no ownership, control or accountability of the TB program at all. We virtually have no say in the planning, development, management or rights to TB program ownership. We do what the donors and principal recipient of the Global Fund grant want. All of the program decisions and responsibilities remain in their control. We have what they say at quarterly review meetings, often outside of the country, and in luxury hotels. They are never here. The only time they come here is when they need a letter to be signed for them". (Somali policymaker at MoH).

Consequently, 12/20 of HPs expressed concerns about the lack of active role or failure of local authorities to assume responsibility for TB care service delivery activities. Over 12/20 of HPs related low feasibility to failure in meeting the basic requirements for human resources, physical infrastructures and financial capacities for TB care service provision, including the introduction of new diagnostic technologies at the local level. Approximately 16/20 of these HPs said that they never received consistent professional support and the necessary guidance needed for the management of specialised care services such as TB care in a fragile health system setting (Table 6.4).

Structural constraints to the feasibility of LED technology implementation and utilisation

Table 6.5 summarises the HPs' responses on structural constraints to LED feasibility for regular use. The WHO defines health care structure as institutions that deliver healthcare services to fulfil the health needs of the target population, including elements contributing directly or indirectly to the system and system boundaries (i.e., the network of connected interactions that temporally close it, represent limits, and contribute to the overall structure of the system)[277-279].

In the present study, the structural constraints to the feasibility of the introduction, implementation and utilisation of LED technology were mainly appraised from system and programmatic readiness perspectives. Nearly all (19/20) of HPs believed that a lack of clear policy/strategic priority/direction was a key constraint to the implementation of sophisticated healthcare technologies, including TB diagnostic technologies, for routine utilisation in Somaliland. Another 16/20 of the HPs saw the absence of strong leadership and governance from local authorities as a key obstacle, not only to the introduction, implementation and utilization, but also the management, of such complex technologies in weak health system settings.

Table 6.5 ***The frequency distribution of HPs' responses to questions on structural (system-wide) constraints to LED feasibility in Somaliland (2018-2019).***

HPs response to structural constraint questions (N= 20)	**Frequency of responses n/N [%]**
- Lack of strategic/policy/priority/direction for TB control in Somaliland	19/20 [95]
- Lack of strong leadership/governance from local authorities for TB control	16/20 [80]
- Low user acceptance thwarted the introduction/utilization of new technologies (LED)	18/20 [90]
- Obstructive organizational culture for stakeholder participation (buy-in; engagement)	17/20 [85]
- Lack of systematic/programmatic readiness to support technology	19/20 [95]
- New tools induce pressure and burden on an already weak health system	15/20 [75]
- Lack of a good procurement/supply chain system for technology use	17/20 [85]
- Imbalance between health needs, priorities and available resources	18/20 [90]
- Frequent interruption of available reagents/supplies/maintenance for LED use	17/20 [85]
- Lack of a clear resource mobilization strategy for TB control	14/20 [70]
- Lack of performance monitoring/evaluation frameworks for practice (at all levels)	12/20 [60]
- Acceptance/feasibility/usability of LED hindered by stakeholders' resistance	15/20 [75]
- Technology not tested for feasibility prior to introduction and rollout	13/20 [65]
- Utility requirements not met (lack of/inadequate/unreliable power supply to operate new tools)	19/20 [95]
- Local HPs lack access to safe quality materials/tools to comply with accepted standards	17/20 [85]
- Health technologies procurement (supply chain) handled by external entities	16/20 [80]
- Inadequate storage space and inventory for new tools/technologies (at all levels)	18/20 [90]
- Resistance to change in workflow in laboratory diagnostic services	19/20 [95]

Ninety percent of those interviewed believed the effective implementation and use of new technologies had been considerably curtailed by low user acceptance among health workers at the point of care. About 17/20 of HPs thought both the feasibility and acceptability of new technology were hindered by obstructive organizational cultures, for example the lack of buy-in and stakeholder engagement.

HPs also linked low user acceptance of technology (18/20) with a lack of organizational support (17/20) and stakeholder resistance to change (15/20) respectively. Eighty-five percent of the HPs said the adopted technologies, including LED technology, were neither appropriate nor compatible with existing practice and context.

Consequently, the lack of strong governance, coherent leadership, buy-in and stakeholder engagement for the introduction of new technology resulted in a lack of coordination, and an unclear strategic direction and policy framework. Nearly 19/20 of those interviewed said that current TB care service structures (at all levels) lacked the necessary systematic and programmatic support to execute the deployment, utilisation and management of complex healthcare technologies in a fragile health system. Another 14 out of the 20 of the HPs interviewed related the lack of a clear and coherent strategy for resource mobilisation to support the routine use of new health technologies, including LED. The perceived deficit of a competent health workforce was a key constraint to the introduction, implementation and utilization of the LED technology for routine use in the given context:

"My worry about the use of sophisticated technologies such as LED is to do with health system capability and readiness, a competent health workforce and their compliance to standard guidelines for technology, which will no doubt be the driving force of both the development and introduction stages. It all comes down to the operational feasibilities, staff salaries, and the costs and capacity of the health system to support the implementation and management of complex technologies. A competent health workforce is key to improving the care service delivery capability of the health system. Otherwise, these technologies are not going to be practical for the majority of these facilities". (Program TB coordinator.)

HPs linked the diminished capacity of existing health system structures to the imbalance between physical structures and staff and the available resources to meet health needs and priorities respectively. Sixty-five percent of HPs stated that recommended healthcare technologies are never tested for potential feasibility prior to their introduction in fragile system contexts. A technology is applicable to local needs in the context of given resources and infrastructural capacities and capabilities, as well as

the supportive environment necessary for the introduction and utilisation of these technologies in a fragile health system environment.

"The most critical component of TB care system is the delivery capacity of existing laboratory services and networks. But laboratory services should provide quality and reliable diagnostic services to their populations through integrated laboratory network functions. Such integrated systems and networks need to be built through the regular day-to-day operations of the National Tuberculosis Program at all levels. An equally important element in effective TB control is the implementation of systematic and efficient good laboratory practices and quality assurance schemes at all levels of laboratory networks. All these important elements stated above are missing from the current TB care delivery, which makes the system deficient". (TB laboratory service officer.)

More than half (17/20) of the HPs indicated that frequent interruptions of the supply chain (reagents, supplies and maintenance) for new health technologies, including LED microscopy, Genexpert and mobile X-rays, induced unique constraints not only to feasibility and utilisation but also ongoing care delivery systems. Almost all (19/20) of HPs were concerned about the lack of established priorities in the selection, introduction, suitability and management of new health technologies for routine utilisation in a fragile health system setting. For example, more than half (15/20) of all those interviewed felt they never received necessary support from their managerial and policymaking colleagues, or felt unsupported in their work (Table 6.5)

The vast majority of HPs were primarily concerned about the introduction of an array of advanced technologies without preparing the existing health system prior to introduction and with no proper plan for alignment with the existing primary care context. Lack of prior feasibility analysis of the new technology (LED) overwhelmed the existing care delivery system, which caused a struggle to integrate the new technology into routine practice:

"If the national and local health system structures and laboratory diagnostic services are all ill-prepared or lack the necessary capacity to support the implementation of complex healthcare technologies such as LED, Genexpert and now mobile X-rays for regular use, the introduction of these technologies is not only unsuitable for such weak systems, it de-capacitates these. This makes a bad situation worse in attempting to meet the unmet health needs of our populations". (TB program officer).

Environmental constraints

Table 6.6 presents the perceived responses to environmental constraints. Environment constraints in a health system context refer to the political and economic environment, including the organisational culture, stakeholder engagement and commitment, the health workforce, regulatory standards and financial capacities. HPs indicated that environmental constraints to health services delivery, including TB, are many in Somaliland and often overwhelming. In such settings, the existing health system is too fragile not only to support and sustain new technologies or interventions, but also to deliver good quality health services to populations in need[103, 280, 281]. These constraints include limitations on strategic and policy priorities and focus (external/internal), stakeholder involvement and engagement, social requirements and expectations, cultural or economic arrangements and technological or legal requirements.

Table 6.6 ***Frequency distribution of HPs' responses to questions on environmental constraints to the feasibility of LED utilisation in Somaliland (2018-2019).***

HPs' responses to environmental constraint questions	Frequency n/N [%]
- Stakeholder resistance to new technology application with no clear implementation plan	17/20 [80]
- Lack of supportive environment including political, financial and structural means	16/20 [85]
- Operating temperatures (resistance to humidity, dust levels) in accordance with local conditions	16/20 [80]
- Basic requirements not met for transportation/storage of new technologies at the facility level	12/20 [60]
- Culture of blame rather than active stakeholder engagement/ownership/leadership in TB care services	13/20 [65]
- Shelf life/quantity reagents/supply not often clearly specified to end user/recipient facilities	14/20 [70]
- Construction/structural changes, utility requirements not considered at facility level	17/20 [85]
- Healthcare facilities don't decide on the need for equipment	17/20 [85]
- Healthcare facilities not consulted about need of health technologies	15/20 [85]
- New technologies can be destructive to existing routine/ongoing diagnostic services	18/20 [85]
- Acceptability/feasibility determined from the perspective of the supplier, not the user	16/20 [80]
- Principal recipient plans/sets priorities for needed technologies	19/20 [95]

Almost 19/20 of HPs indicated that key environmental constraints such as delivery capacities of the existing laboratory structures (support services), resources and leadership implications for stakeholder

involvement in delivering specialised care (including TB care) had proven extremely challenging in the fragile health environment.

More than half (16/20) of HPs considered stakeholder resistance to adaptive problem solving or organisational acceptance to adopt new technologies for routine utilisation as a critical constraint to feasibility. Sixteen out of 20 of the HPs interviewed for this study emphasised the need for a supportive environment (politically, financially and structurally) as a priority for the adoption/deployment of new technology in fragile health system settings. A large proportion of the HPs said that technology users or recipient health systems often do not meet the basic and necessary environmental requirements (structural, storage, space, operating temperatures and resistance to high humidity or dust levels).

"You see, the fragile nature of the environment we operate in impedes our work in health service delivery, including TB care, partly because we often lack the commitment and support of all stakeholders, namely providers and users of TB care services alike. The general view of health workers on the current practice, I must say, is not overwhelming positive and needs drastic change for the system to make use of new technologies". (Technical TB control advisor.)

Most of the HPs appeared mostly unconvinced about the true motive behind the introduction of sophisticated health technologies such as LED for routine use without much consideration to its operational and technical feasibility including assessment, selection, procurement, installation, maintenance and training for its safe use. Eighty-five percent of HPs believed that new technologies have proven to be destructive to existing routine/ongoing diagnostic services and that it is vital to understand how the proposed techniques are perceived by different involved stakeholders in its routine use at all levels of the care delivery system. Equally important, those interviewed identified organisational (17/20) and stakeholder resistance (15/20) respectively to adopting and using new technologies without clear operational protocols.

Most of the HPs (18/20) reported that unclear policy/strategy focus and priorities, together with competing interests, impeded feasibility of LED implementation and regular use. Whereas, 13/20 of all HPs believed the culture of blame combined with the absence of active leadership stalled both the adoption and management of LED technology in such a challenging environment. Seventy percent of the HPs indicated that shelf-life/quantity reagents/supply usage was not often clearly specified to the end user/recipient facilities. The volatile nature of the health system environment often leads to

frequent changes in political leadership, organisation of health service delivery and partner engagement and involvement, which in turn affects the care delivery process (Table 6.7).

Overcoming challenges in new diagnostic technology

Table 6.7 presents the HPs' perceived challenges and solutions for the introduction and utilisation of new healthcare technologies, particularly for TB diagnosis. Almost all HPs who participated in the study identified several solutions to overcome perceived difficulties with the introduction, implementation and regular use of new technologies in settings with weak health systems. Nearly all (19/20) of the policy, technical and operational teams said that reclaiming ownership of the national TB control program is critical to overcoming current challenges.

A significant proportion (17/20) of HPs believed in reducing or ending dependency on single donor funding for healthcare financing and identifying alternative resources. Almost half (13/20) of health workers interviewed thought that developing locally-led policy, strategic priorities and frameworks (i.e., reducing reliance on donor-led ideas/agenda) for specialised care services such as TB would help local health authorities overcome current challenges.

Table 6.7 ***Frequency distribution of responses to questions on overcoming challenges faced in LED introduction and utilisation in Somaliland (2018-2019).***

HPs responses to questions on changes needed at national, regional and facility level	***Frequency n/N [%]***
- Reclaim ownership – reduce donor involvement in service delivery process	19/20 [95]
- Ensure aid comes in the form of general government budget support rather than selective schemes	18/20 [80]
- Introduce recipient-led health schemes (control program) to reduce dependency	11/20 [55]
- Reduce/end reliance on single donor funding for health (TB control)	17/20 [85]
- Develop recipient-led aid and policy/strategy for health financing to ensure sustainability	15/20 [75]
- Develop a locally-led priority framework for health (avoid reliance on donor ideas/agendas)	13/20 [65]
- Identify alternative sources for funding (raise funding from local sources – private sector)	10/20 [50]
- Focus donor aid on capacity building only (building/improving health infrastructures)	12/20 [60]
- Introduce locally driven accountability frameworks for different stakeholders	15/20 [75]
- Encourage support for country leadership for health service delivery	12/20 [60]
- Introduce skill-based health workforce training/assessment to improve performance	14/20 [70]
- Seek practical advice on all aspects of health technology acquisition and utilization	13/20 [65]
- Establish technical/operational/financial support systems for technology management	16/20 [80]
- Set guidelines for procurement/safe use/maintenance of healthcare technologies	12/20 [85]
- Ensure the availability of spare parts/maintenance materials for new technologies	17/20 [70]
- Set technical/operational specifications for different user profiles	13/20 [65]

Furthermore, 12/20 of the HPs said any donor funding should be used solely for capacity-building schemes, compared to 13/20 who said that inserting active ownership would help local partners overcome critical challenges. About 17/25 of them believed that developing recipient-led aid policy/strategy for health financing is vital to ensure sustainability. However, only 12/20 of the HPs considered that raising funds from alternative sources, including the private sector, together with increased government budget allocations, was the best way to tackle the single donor dependency problem. The end user characteristics (i.e., motivation, financial incentives, and physical capacity of the facility) were noted as critical barriers to technology introduction and utilisation at the facility level.

The majority (13/20) of the HPs interviewed stated that introducing locally-driven accountability frameworks for different stakeholders in TB care delivery is the most effective solution for overcoming challenges related to feasibility. Another 14/20 of HPs highlighted introducing skill-based training/assessment for health workforce competence and 17 out of the HPs interviewed stated that seeking technical and operational expertise on specifications for different new technology user profiles (resource, structural capabilities). Most HPs interviewed had a clear idea of practical ways to overcome the challenges faced for LED introduction and uptake for routine utilisation in a fragile health system context (Table 6.7). Most of the HPs noted the introduction of new technologies for routine use was mostly supplier-driven rather than driven by the diagnostic needs of intended recipients, which in turn limits the acceptability of the technology by the end user (providers and HPs).

In the interview discussions, HPs were largely critical of supplier-driven technologies and a failure/reluctance to deliver interoperable technologies for routine utilisation in resource-constrained settings:

"I think the most important thing for us here is what is perceived useful for our practice and help us improve patient care and not just overwhelm or litter the system with more complex gadgets that do not mean anything to the welfare of our patients. Yes, we are interested and open to trying new ideas, including the adoption of technologies to improve and deliver quality diagnosis to our population in need of quality care. However, the question one needs to ask is how useful are these technologies to our local needs or are these technologies just an extra burden for an already fragile system?" (Policymaker.)

The HPs interviewed were profoundly concerned about the genuine motives behind the introduction of new technologies in settings with weak health systems. Each of these technologies was conditioned with donor interest regardless of its operational feasibility and acceptability. Another essential element

that emerged in the discussions was the supply chain, and maintenance issues, as neither reagents nor spare parts for LED technology (or any other technology) were procured by the supplier or available in the country.

6.6 **Conclusion**

To understand factors that helped or hindered the implementation and utilisation of LED technology for TB diagnosis in fragile resource-limited settings, this analysis adopted a framework-based analysis (IAF) to link the feasibility and use of diagnostic tools with feasibility in fragile health system settings[282-284]. In doing so, this chapter focused on the analysis of three crucial elements critical to feasibility: context (environmental context), infrastructural capacity (health system capacity to support and sustain), and resourcing constraints (health workforce, financial, information) with a particular focus on fragile, resource-poor settings.

The study explored the views of the HPs on resourcing, structural and environmental constraints to the feasibility of LED technology introduction, implementation and utilisation in Somaliland. The use of framework-based qualitative analysis helped identify themes, sub-themes, patterns and trends emerging in the analysis and helped paint a clear picture of the key constraints to the feasibility of complex new technologies in fragile health systems.

Chapter Seven: Discussion of main findings of the thesis

7.1 Introduction

This chapter summarises, discusses and interprets the main findings in line with the study questions, objectives and existing literature on the subject of study. It further presents comprehensive insights into the research findings in an attempt to improve access to and the quality of diagnosis for TB patients in fragile health system settings, with particular emphasis on Somaliland.

Tuberculosis (TB) is a growing public health problem and one of the top causes of death globally, killing close to 1.5 million people each year[74]. Another 10.4 million were infected with the disease globally[74]. To overcome this challenge, global control efforts have shifted from disease burden reduction to eradication with the introduction of more robust diagnostic technologies, mainly in high TB burden countries (HBCs) including fragile states[32]. One such technique recommended and introduced for robust diagnostic technologies in HBCs was light-emitting diode fluorescence microscopy (LED), designed to replace the older and widely used Ziehl-Neelsen (ZN) microscopy method for routine TB testing[157, 163]. LED technology is one of several TB diagnostic technologies that have been endorsed and recommended by the World Health Organization (WHO) for use in many high-TB burden resource-constrained settings, including fragile states, for over a decade now[285].

More importantly, TB presents significant public health crises in countries with complex political, social and economic instabilities, also known as fragile states. The most effective way to cut TB transmission is to find, effectively diagnose and treat infectious TB cases early[286]. TB diagnosis in resource-poor settings relies heavily on the ZN testing technique[287]. Although ZN testing has proven to be a reliable and effective technique for routine TB diagnosis in resource-poor settings, it has low sensitivity and detects only 50% of infectious TB cases[150, 157, 158, 286, 287].

7.2 Aims and objectives and rationale of study

The burden and control of TB in fragile states have been overlooked in the current TB literature, and the impact of TB control interventions, including new diagnostic technologies, on population health outcomes remains unclear in these settings. The primary research objectives and questions of this thesis were the following:

1. To systematically review all existing and relevant empirical literature on the feasibility and acceptability of LED for routine TB diagnosis in fragile states.
2. To investigate differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities.

3. To assess the knowledge, attitudes, perceptions and practices of healthcare workers on LED use for TB diagnosis at primary care facilities in Somaliland.
4. To identify key resourcing, structural and environmental constraints to the feasibility and acceptability of LED use for TB diagnosis at primary care facilities in Somaliland.

As set out in the methods section (chapter 2), the theoretical orientation of this study was grounded on multi-construct conceptual frameworks of feasibility and acceptability of healthcare interventions, with a particular emphasis on the introduction and routine utilization of new technologies. The objectives and questions of this research were constructed using the Technology Acceptance Model (TAM) and the Impact Assessment Framework (IAF) to explore the feasibility and acceptability of new TB diagnostic technologies in resource-poor settings including fragile states[135, 169, 170, 288]. The TAM was applied to explore the perceived views of potential users (primary care providers) toward the use of new technologies for TB diagnosis in a fragile health system context[177, 289]. The IAF was adopted to explore and provide explanations about key resourcing, structural and environmental constraints to the feasibility of introducing new technologies for TB diagnosis in settings with weak health systems[175].

The applied theoretical models provided the researcher with an opportunity to build the basis of this inquiry and to appraise key health system features that could potentially influence the feasibility and acceptability of introducing new TB diagnostic technologies successfully in fragile health system settings[177, 179]. Both theoretical frameworks draw their inferences from diverse teachings and schools of thoughts on the feasibility and acceptability of complex interventions, including the introduction and utilization of new technologies in different health system settings with varied infrastructural capacities[19].

The conceptual framework for the study depicted in figure 2.2 shows the other elements of the thesis. Objective 1 of this study was to systematically review the relevant literature on the feasibility and acceptability of new technologies for TB diagnosis in settings with weak health systems. Objective 2 investigated the differences in patients' TB diagnostic test outcomes to shed light on the feasibility of LED use within and between health facilities in Somaliland. The analysis of secondary data helped the researcher build on the existing and relevant literature on the feasibility and acceptability of new TB diagnostic technologies for routine utilization in resource-poor settings. All research findings from all objectives of the study were examined, synthesised and interpreted, using inductive and deductive reasoning to generate policy recommendations. Objectives 3 and 4 were developed to generate vital information on feasibility and acceptability from stakeholder interviews (primary care providers and policymakers) involved in TB care. These

serve to provide useful insights about key factors that influence the feasibility and acceptability of new TB technologies in fragile health system settings.

Objectives 3 and 4 adopted a theory informed strategy for data collection, involving:

1. Semi-structured interviews with health workers to assess knowledge, attitudes, perceptions and practices, combined with site visit observations.
2. Key informant interviews with policy and technical and operational teams working for various agencies, combined with a review of strategy, policy and operational documents.
3. The adoption of a framework-based thematic and content analysis.

7.3 **Summary of main findings**

The key findings of all study objectives were constructed and guided by the conceptual framework in figure 2.1.

Chapter 3 (Literature review)

1. No research has examined the feasibility and acceptability of LED technology for routine utilisation in TB diagnosis in fragile health system settings. The extent to which effective introduction, implementation and utilization of LED technology is feasible and acceptable in resource-poor environments is yet to be determined.

2. Existing literature on LED usage in TB diagnosis largely investigated a diverse set of factors associated with LED uptake, acceptability and diagnostic accuracy. The literature did not, however, explore details of prevailing resourcing, structural and environmental constraints affecting the feasibility and acceptability of LED use in resource-poor and fragile states.

3. A strong consensus existed among all studies reviewed that users were more likely to accept technology if it was likely to increase their diagnostic performance, but more reluctant to use technology that was likely to increase their workload. Existing literature revealed a weak relationship between LED technology usage and increased TB case detection in resource-poor settings.

Chapter 4

1. No significant differences were observed in the proportion of patients with negative and positive outcomes between the LED and ZN technologies across facilities in Somaliland. The difference between the proportion of patients with negative and positive outcomes under LED and ZN technology did not exceed 1.7% (95% CIs, .015-.020) compared with $\chi 2$ = 641 (P>0.001).

2. A lack of standard operating procedures or protocol use, and a deficit in knowledge about LED use among laboratory technicians were thought to have contributed to the observed patients' diagnostic outcomes and operational performance of LED use in Somaliland.

3. The findings of this analysis contradict results reported in previous performance studies in resource-poor settings, where the LED technology has shown a higher positivity rate than ZN. The findings of this analysis suggest that the introduction and implementation of sophisticated diagnostic technologies such as LED might not be effective for routine utilisation without improving the systematic and programmatic readiness of the existing laboratory infrastructures.

Chapter 5

1. The semi-structured interviews with facility staff revealed that health workers' attitudes, perceptions and opinions regarding LED use appeared to be generally positive. However, staff attitudes were largely negative toward the future introduction and implementation of new technologies for routine utilisation at the primary care level without improving the systematic and programmatic readiness of existing delivery functions of healthcare facilities, particularly primary care.

2. Critical barriers to new technology introduction and utilization at the facility level included perverse incentives (delayed staff salaries), stakeholder resistance to new ideas/intervention without a clear plan for resource mobilization, diminished structural capacity (policy, technical, operational), and a lack of local partner engagement and involvement to support, facilitate and sustain the introduction, implementation and utilization of the applied technology.

3. Primary care physicians viewed LED technology as a valuable tool for TB diagnosis in a fragile health system context, which could potentially improve patients' diagnostic outcomes, and ultimately reduce errors in the diagnostic and treatment process. Laboratory technicians and nurses, however, placed higher priority on operational and systematic issues including the use of standard protocols and procedures, staff training in new technology use including maintenance and infection control, and the provision of an uninterrupted and sustained supply chain (reagents, spare parts and consumables) for continued technology utilization.

4. There was suboptimal use of basic laboratory biosafety guidelines and standard operating protocols for routine laboratory functions, including the prevention and containment of unintentional exposure to pathogens, toxins or/and their accidental release. Such exposures were widely prevalent and reported across all the facilities studied. Inadequate laboratory

equipment, reagents, supplies and spare parts available at laboratory facilities were reported as key barriers to the diagnostic performance and operational feasibility of LED technology use.

5. The findings portray the overall knowledge-related competencies as inadequate. This affected both staff and diagnostic performance for everyday use of the applied technologies. Inadequate resources (people, money, time) combined with a lack of robust laboratory systems and networks to support and sustain the delivery of quality diagnostic services were key constraints to poor operational feasibility and diagnostic performance of the LED technology. Specific areas of deficiencies were staff knowledge and competencies in the use and maintenance of the new technology (LED) together with a lack of functional TB care delivery capacities.

Chapter 6

1. The findings of this sub-study revealed serious resourcing, structural and environmental constraints to the feasibility of LED introduction, implementation and utilization for regular use in a fragile health system environment. While policy-makers recognised the potential benefits of LED as an innovative technology for TB diagnosis, they were mostly concerned about the operational feasibility of such sophisticated technologies for regular use in fragile health system environments. Policy-makers believed that the routine use of new healthcare technologies (not only for TB control, but also for any other disease management) required functional systems, sustained resources (people, money, time/commitment) and an environment conducive to supporting ongoing healthcare services and robustly integrating new ones at all levels of the health system.

2. Although the introduction and use of new technologies such as LED could potentially help improve the quality of TB management and care, their dissemination at the primary care level has been proven to be problematic. System-wide issues such as the lack of a competent health workforce, and the absence of a coherent policy and systematic and programmatic readiness, were key constraints to the feasibility of introducing, implementing and utilising new diagnostic technologies in Somaliland.

3. Policy-makers interviewed believed that complex technologies such as LED would not work in a fragile health system environment without improving the delivery capacity of the existing health system, particulary laboratory structures to support the routine use of these technologies. *"To make new diagnostic technologies work in settings with weak health systems like ours, we need to improve both manpower capability and system readiness to support implementation and sustain routine utilization"* a Somaliland policy-maker stated.

4. A key constraint to both diagnostic performance and operational feasibility of the applied technogies was a dependency on donors for financial, technical and operational support, which undoubtedly undermined continued and sustained TB care services provision on the ground. The availability of sufficient resources (health workforce, knowledge, information) together with improved systematic and programmatic readiness of existing health services were deemed critical to support and sustain complex interventions such as routine LED technology use in a weak health system context. Key informants stressed the need for clarity concerning the balance between the pressing need for more robust diagnostic technologies and their operational feasibility in fragile health system settings.

5. The vast majority of policy-makers interviewed believed that the introduction and utilization of new technologies for TB diagnosis would require a locally-driven policy and strategic priority agenda, including reducing reliance on donor dependancy for technical and financial support for specialised care services. The development of locally-driven alternative and suitable strategies for resource-mobilization from local sources, combined with sustained political and financial commitment from local health authorities, were perceived as practical solutions to overcome current financial and technical challenges.

7.4 Discussions and interpretation of main findings

Interpretation of the main findings

The findings of this research were generated through a systematic review of existing literature, the analysis of routine program data and the collection and analysis of theory-informed qualitative and quantitative data. The analysis and interpretation of the findings of this study were conducted and presented in the form of four feasibility and acceptability questions (as illustrated in chapters 3-6). Empirical research findings were to inform the reader how the findings of the present study conflict with or complement the existing literature on the feasibility and acceptability of new technologies, particularly LED for TB diagnosis in resource-poor settings, in line with the theoretical construct of the thesis. The researcher tried to provide explanations for the observed inconsistencies between the findings of the present study and the existing literature on the feasibility and acceptability of the introduction and use of LED for routine diagnosis in weak health system settings.

Chapter 3

Discussion

The main findings of the systematic review of all studies that met the eligibility criteria were systematically reviewed, synthesised, appraised and summarised, primarily from a feasibility and acceptability perspective. Most of the reviewed studies used the terms of feasibility and acceptability interchangeably and solely focused on the diagnostic performance or accuracy (sensitivity and specificity) as perceived by the intended user. First and foremost, the analysis of most the studies reviewed primarily focused on LED sensitivity and the ability of the technology to correctly identify those with the disease (true positive rate), and the specificity or the ability of the LED technology to correctly identify patients without the disease (true negative rate)[203].

The quantitative findings of the reviewed literature were later used to generate a single estimate. The author adopted a meta-analysis approach as a statistical technique to determine the feasibility and acceptability of LED use for routine TB diagnosis in fragile health system settings[29, 290]. The aim was not only to increase the statistical power of individual studies to detect differences within and between groups but also derive conclusions about the reviewed body of research on the feasibility and acceptability of LED technology for routine use in resource-poor fragile state settings.

The findings of the systematic review of existing and relevant literature on LED technology for routine TB testing showed no credible and convincing evidence on increased case detection rates in settings where it was introduced[29, 60, 76, 202, 204, 205, 207-211]. The findings of the systematically reviewed studies on LED introduction for routine TB testing also revealed an overall group pooled sensitivity (72%) and specificity (95%) that were much lower than those previously claimed or reported by the WHO[213, 214, 216-218, 223-225].

The sub-group analyses of the systematic review of existing literature on the difference between LED and ZN performance showed that the sensitivity and specificity of LED appeared to be lower in settings where it was applied. This difference was greater in primary care facilities than in the referral facilities. The systematic review findings are sharp reflections of the limited feasibility and acceptability of LED implementation and utilisation for routine TB diagnosis at primary care health facilities and peripheral laboratories where this technology was initially intended to be used[163].

Key factors in the reviewed studies explaining diminished feasibility and acceptability of LED included a lack of or inadequate training for the intended users (laboratory technicians) prior to

technology introduction, a lack of maintenance and the absence of the streamlined or integrated quality assurance programs (internal and external) that were considered vital in resource-poor health system settings in all studies reviewed. In addition, the views of key TB partners or stakeholders potentially involved in both the introduction and implementation of the LED technology for routine use were not addressed in the feasibility assessments or acceptability analysis in all most of the studies reviewed [60, 212-214, 216-218, 225].

None of the studies reviewed clearly defined or objectively measured the feasibility and acceptability of LED technology introduction, and its implementation for regular use in weak health system contexts. Most definitions or measures offered in the reviewed studies were performance definitions of feasibility and acceptability of LED technology rather than technical or resource-based (people, money, time) and structural (systematic and programmatic readiness issues). Operator acceptance, user acceptance, user preferences, user satisfaction, user uptake (laboratory technicians) and accuracy (sensitivity and specificity) were used to infer the review authors' definitions of acceptability.

Most of the studies reviewed relied heavily on quantitative performance analysis and either evaluated, assessed or compared LED performance, namely accuracy (sensitivity and specificity) in TB case detection with other microscopy devices to determine the feasibility of future technology use. None of the reviewed studies (n=15) defined, theorized, or adequately synthesized feasibility and acceptability from a health system perspective. Most of the studies assessed feasibility and acceptability according to operator preference and diagnostic accuracy, or according to a combination of feasibility and acceptability perspectives.

Few of the reviewed studies assessed the acceptability of LED technology for routine use in great length and none of the studies concentrated on or emphasized feasibility issues (i.e., the systematic and programmatic readiness of existing health systems to support and sustain such complex interventions in resource-poor and fragile settings). This review revealed that acceptability and feasibility assessments of the technology were primarily confounded with the concept of satisfaction (user acceptance) rather than taking a holistic and systematic analytic approach. No study showed or stressed the need for feasibility assessment prior to the introduction and implementation of the technology in the given context.

Bowen et al. have stressed that for any applied technology to be feasible, it needs to be accepted, implemented, used (demand), integrated into larger primary care services delivery and practical, with a potential to expand in any given context[169, 170]. Equally, the evidence base on LED

technology introduction, implementation and use for routine TB diagnosis in fragile and resource-poor settings seemed compromised by methodological limitations and inconclusive.

The aim of this review was to establish a clear and comprehensive understanding of the feasibility and acceptability of LED technology for routine TB diagnosis in fragile states. It specifically attempted to determine how existing TB diagnostic literature defined, theorised and measured feasibility and acceptability of the LED technology for routine TB diagnosis. To the best of the author's knowledge, this review is the first of its kind to assess the feasibility and acceptability of LED technology use for routine TB diagnosis in resource-poor settings, including fragile states.

Limitations

Despite the use of a systematic and rigorous search strategy for peer-reviewed scientific and grey literature to reduce potential selection and confirmation bias, the risk of introducing spectrum bias during the selections of studies remained high. A fundamental limitation that emerged from the review of the literature was that almost all studies had assessed a single index test – "test accuracy" (sensitivity and specificity), although they intended to determine the feasibility and acceptability of LED use for routine TB testing. It was particularly challenging to combine, compare and draw inferences from the findings of different studies reviewed due to varied study designs. The use of grey literature or unpublished literature increases the threat to validity (both external and internal) and could lead to misrepresentation of the review findings as it does include the findings of all existing research on the feasibility and acceptability of LED. Thus, there is a risk of not arriving at accurate conclusions on the quality of the source.

Furthermore, the findings of the systematic review revealed that the TB diagnostic literature was strongly dominated by quantitative analysis of the LED technology performance. A limitation was that the range of specific feasibility and acceptability issues discussed in the retrieved studies appeared to be broad across all studies. Though many of the studies reviewed seemed to be relevant to new TB diagnostic technologies and performance practices, most of the analysis relied heavily on quantitative performance analysis to find explanations for technology acceptance outcomes. However, it failed to shed light on dominant systems' or feasibility issues (overall health system capacity and capability characteristics). This made it difficult for the reviewer to draw clear and context-specific conclusions on the feasibility of technology for routine utilisation in fragile health system settings.

The relatively small sample of the reviewed studies on feasibility and acceptability of the LED technology use for TB diagnosis, mainly in stable settings, limited the extrapolation of the statistical analysis results to overall feasibility and technology acceptance in other contexts. In other words,

this reduces one's confidence that the review results can serve as a parameter for technology acceptance in a fragile health system context, in spite of the abundant literature available on LED performance in stable settings.

The search of the systematic review was limited to only studies in the English language. Thus, a significant number of peer-reviewed studies and grey evidence in languages other than the English language might have been missed. While the reviewed studies varied in quality and scope, the methodological challenges together with possible solutions were influenced by (i) sources, (ii) study quality, (iii) quality assessment (i.e., publication bias and assessment of heterogeneity), (iv) presentation of study results, and finally (v) the possible implications of the findings on policy, practice and future research. Reviewing the methodological quality of meta-analysis in the included studies was a major challenge. To address this challenge, data from individual studies were not used more than once, as this would undermine the statistical power of the review findings and future inferences[291]. It would also run the risk of producing misleading and overly precise estimates[292]. To overcome this challenge, the reviewer unpicked each of the reviewed studies and subsequently combined all results of individual studies.

Chapter 4

Discussion

The WHO and its global TB control partners claimed that the introduction of LED use for routine TB testing could increase case detection outcomes in settings where it has been applied, particularly in resource-poor high TB burden ones[215, 264, 293] The WHO and its TB control partners claimed that the increased sensitivity and specificity, which in turn contributed to increased TB case detection, associated with LED use was equivalent to other internationally recognised reference standards such as culture and Genexpert[225, 249, 293]. In this claim, the global TB control partners argued that LED technology offered the best benefits of any fluorescence microscopy technology without the catastrophic maintenance costs associated with the routine use of new TB diagnostic technologies in settings with weak health systems[248, 264, 294].

The analysis of clinical data on LED implementation contradicted the reviewed literature on the sensitivity and specificity of LED technology. The present study found LED accuracy was worse than in the literature with also poorer ZN case detection outcome than initially claimed. This implies the issue is not just LED implementation but diagnostic practices more broadly. The proportion of patients for which fewer than all three samples were positive was highest with ZN use alone, likely reflecting slightly lower sensitivity. The number of specimens with inconclusive (missing, unknown and not done) results by LED was considerably lower than under ZN. This can

be partly attributed to a lack of protocol use for the comparison of LED and ZN technologies coupled with inadequate training and experience in the new technology use for users (laboratory technicians).

When both techniques were used concurrently, and both results recorded, a slight variation of only 1.7% (P< 0001) was observed in patients' diagnostic test outcomes (Table 4.10 in Appendix to chapter 4). The lack of observable difference between the testing techniques could be attributed to several factors. First, laboratory users were not blinded to ZN results during specimen examination using LED. It was thought that the unmasked comparison might have led to potential subsequent alterations of ZN test outcomes if they differed. Second, false negatives of one technique being detected by the other might be reflective of increased positivity rates by LED, which could have led to altered test results through ZN testing.

Third, analysis of the clinical data also showed where the individual tests were applied separately or in parallel, and an increase in patients' positivity rates in LED-only were slightly higher than ZN-only ones. Fourth, the lack of difference in patients' positivity rates between the two technologies could be associated with inadequate user (laboratory technicians) knowledge, experience and training in the routine use and maintenance of LED coupled with a lack of clear standard operating procedures for use. Such variability in end user expertise could also be reflective of observed laboratory facility variations. More details on end user variability are presented in the next section.

The findings of this analysis contradict results reported in previous performance studies in resource-poor settings. The analysis in this thesis was inclined to attribute the null finding of an incremental gain in patients' positivity rates with LED in part to recording, reporting mechanisms and the lack of clear intervention protocol use for technique to technique comparison.

It emerged in the semi-structured interviews with facility staff (in chapter 5), that a 2-4 days basic training in LED technology was given to a small number of laboratory technicians with no clear intervention protocol. Presumably, most of the specimens were collected and examined by laboratory technicians with insufficient training and experience in using the new technology (LED) and without the use of clear intervention protocols or standard operating procedures. Due to the lack of clear intervention protocol use, the specimen reading, recording, and reporting of patients' test results changed under ZN once the original reading of LED results started. This was a frequently reported problem across all intervention facilities throughout the intervention period.

Limitations

Using facility-based clinical data included the following possible limitations: incompleteness, concordance, timeliness and accuracy of available data, as well as the validity of documented patient categories (new or follow-up patients) and consistency of documented test results. During the first attempt of data cleaning, the researcher realised that available data could only be analysed for limited variables: *positive*, *smear negatives*, *scanty* and *not done*. This was a significant disadvantage, which limited both the scope and flexibility of the analysis.

A critical concern about the facility-based data analysis to estimate differences in patients' diagnostic outcomes in the given contexts is that data from vital routine information systems is known to be imprecise due to measurement errors, misclassifications and improper use of the intervention protocol. This could lead to misleading or spurious estimations of the true differences in patients' positivity rates between the two technologies.

Considerable limitations to recording and reporting of the diagnosis at notification (facility level) led to inconclusive test outcomes, namely 'not done' with ZN use, due to a lack of clear protocol use for the comparative intervention of the two technologies. This was an indication of user preference for LED technology routine utilization among the intended users (laboratory technicians) in the field. Whilst this analysis was inclined to attribute the observed finding of no difference in the proportion of patients with negative and positive outcomes in part to recording mechanisms and the lack of a genuine sample-by-sample head to head comparison, it remains unclear, however, which of the two diagnostic technologies was better than the other**.**

A fundamental limitation to the study findings was the lack of a well-designed intervention protocol explicitly outlining data collection, recording, and reporting patients' diagnostic outcomes, which could have in turn helped reduce all forms of biases. For example, there was no protocol outlining the purpose and design, timelines and the comparative nature of the LED introduction and implementation to all participating and potential stakeholders. As a result, facility staff appeared confused about the purpose and intended outcome and about both the use and the comparison of the new technology (LED) with the old (ZN) for routine TB testing at intervention facilities.

The present intervention was intended to be a feasibility study but failed to provide clear standard protocols and procedures for the implementation, introduction and utilisation of the proposed intervention at all levels in the care delivery system. Such methodological weaknesses might introduce selection biases that could distort the accuracy, reliability and validity of the data on patients' test outcomes. Other important limitations of the study include data extraction from

routine program records with the possibility of missing, unknown, unexamined or scanty patients' diagnostic test records from both new and follow-up examinations, assuming that deficiencies in recording and reporting have affected patients' test results.

The lack of a clear intervention protocol used for comparative testing by the two technologies runs the risk of this analysis producing erroneous or misleading results. This clearly jeopardised the quality, validity and reliability of intervention data for both performance and feasibility analysis. The resulting significant data flaws also limited both the scope and flexibility of the analysis for operational feasibility and acceptability purposes.

Inconsistent recording and reporting of patients' diagnostic test outcomes were widely persistent and prevalent in the data, which clearly undermined the consistency, quality and validity of the data. This was a significant flaw which limited both the scope and flexibility of the analysis for the intended outcomes. The amount of data recorded and reported as *not done*, mainly under ZN testing at the time of reading, was unfortunate as it limited the possibility of a direct comparison between the two technologies.

The lack of blinding during concurrent LED and ZN usage led to widespread inconsistencies of patients' diagnostic test outcomes where slides initially recorded as negative were sometimes recorded as positive or unknown or unexamined when the corresponding other slide was read as positive or negative. In such circumstances, head to head comparisons seemed meaningless and flawed, particularly at facilities with higher caseloads (i.e., Hargeisa TB Hospital, Borama and Gabiley TB diagnostic facilities). For example, data acquired through LED and ZN testing were neither masked, quality assured nor quality controlled. Because blinding was perceived by primary care providers as neither feasible nor achievable, it might have been difficult for facility staff (lab technicians) not to be influenced by the intentional or unintentional selection of recording or reporting of test results during the intervention.

The comparison of the two technologies with no reference standard (i.e., the parallel use of culture) made the inference of these study findings particularly challenging and questionable. The use of culture would have given a more accurate estimate of sensitivity for both techniques.

Although a large number of specimens with *not done* test outcomes were presumably due to lack of study protocol use, there were a relatively small number of specimens with missing and unknown test outcomes. Restricting test results to either positive or negative, however, fails to represent both the diagnostic performance and the reality of such findings in clinical practice. More crucially, the results from diagnostic tests by the two technologies compared did not exclusively fall into positive and negative categories. This helped the calculation of proportions and differences in proportions

of the paired tests to summarise the discriminatory performance of tests (i.e., positive and negative values) using ZN and LED technology.

Further, a large proportion (41%; 5808/14176 for the 1st specimen) of specimens in the dataset were recorded as unexamined for ZN, and thus excluded from the analysis. Such gaps in the data could have influenced data collection motivations for staff, where staff collecting data might have miss-classified or recorded test results differently for different patients and testing technologies.

Further, the analysis of data at the specimen level (Table 4.5) did not take clustering at the facility and patient level into account. Lack of clustering at the planning and designing stages of the LED implementation removed cluster level variability, which also resulted in potentially spuriously low ($P<.0001$) with overly narrow CIs. This in turn could underestimate the intervention effect variability[295]. This means that the observed diagnostic outcomes could be attributed to non-ignorable clustering in practice. Within this, correlation between patient outcomes within clusters may occur for two reasons. First, patients with similar demographic characteristics are more likely to seek care from similar diagnostic facilities. Second, the clusters (facilities) themselves exert a certain level of influence on the outcome, where certain diagnostic facilities are more likely to have negative and positive outcomes due to the standard of care received.

No quality control and assurance systems were established to effectively and systematically monitor the performance of laboratory diagnostic services to ensure the validity, reliability and generalizability of data generated through parallel testing for this particular intervention. Establishing proper quality control and an assurance system could have helped to ensure the reliability and reproducibility of the data as well as the accurate recording and reporting of patients' diagnostic results. While the performance of the 'index test', or the technology whose performance was under study (LED), was viewed as the intervention, the scope of the anticipated incremental gain in patients' diagnostic test outcomes appeared unclear at the outset.

Finally, though not part of the laboratory data analysis, there were considerable inconsistent recording and reporting issues attributed to user preference for both ZN and LED routine use for routine TB testing within and across facilities in the field. Even without a demonstrable increase in case detection, LED technology users reported a reduced time to call sputum specimen slides negative (the bulk of the time being consumed in slide reading) and more comfortable reading.

Chapter 5

Discussion

Prior to the present study, the feasibility and acceptability of LED technology use for routine TB testing has never been determined in terms of resource availability, structural capacity and the capability (systematic and programmatic readiness) of existing health system settings to support and sustain the implementation in settings with weak health systems.

According to the findings on acceptability of the present study, staff opinions were split concerning LED technology acceptance and use, which bred negative attitudes toward the future introduction and implementation of new technologies for routine utilisation at the primary care level. Primary care physicians, for example, viewed LED technology as a valuable tool for TB diagnosis in a fragile health system context: a tool that could potentially improve patients' diagnostic outcomes and ultimately reduce errors in diagnostic and treatment process. Laboratory technicians and nurses, however, placed higher priority on operational and systematic issues, including the use of standard protocols and procedures, staff training in new technology use, maintenance and infection control.

While overall health workers' attitudes, perceptions and opinions regarding LED use were mostly positive, a deficit in staff knowledge and practice competency in new technology use for routine TB diagnosis were key factors to LED technology acceptability. The lack of a competent health workforce coupled with a lack of structural capacities and financial commitment at all levels of the TB care delivery system were reported as key barriers to technology acceptability and the routine use of the applied technology.

The deficit of or suboptimal use of standard operating procedures (SOPs) and measures for different laboratory functions, including inadequate use of personal protective equipment while on duty, was a particular concern for all staff working at all facilities visited. Inadequate use of laboratory biosafety guidelines and protocols for the handling of and containment of unintentional exposure to pathogens and toxins (or/and their accidental release) were widely prevalent and reported across all facilities. There was a profound need for formal and informal training (continued/refresher training) among staff for the use and maintenance of complex and sophisticated technologies such as LED.

Inadequate laboratory equipment, reagents, supplies and spare parts available at laboratory facilities were reported as key barriers to the diagnostic performance and operational feasibility of LED technology use. Reducing the frequent interruption of supply chains (reagents, spare parts and consumables) for continued technology utilization was perceived by laboratory technicians to be a

means of improving patient health outcomes at the point of care. Such problems were widely prevalent and reported across all the facilities studied.

Limitations

This study has several limitations, which also imply the need for further research. First, the external validity of the data analysis might have been affected by the cross-sectional nature of the study and the relatively small sample size. Second, the use of a framework-based qualitative analysis approach could have resulted in the misinterpretation of segments of data due to content and thematic aggregation. The use of data gathered through direct on-site observation on practice competence and performance could have overstated adherence to guidelines. Third, the study participants' recruitment through program coordinators or managers, and their gatekeeping role, might have played a role in the high refusal rate among health care workers (HCWs) and might have introduced selection bias into the process[55].

Fourth, the external validity might be affected by the use of purposive sampling technique coupled with a relatively small sample size. One significant weakness was that 50% of the Somaliland population lives in remote, rural and peri-urban towns, and the selection of the small number of HCWs from four facilities in three urban cities might not be a reliable representative of the rest of the country. Fifth, the use of semi-structured interview data may have resulted in sections of data being misinterpreted due to the use of content and thematic analysis. Because the number of study participants is small and selected from only four out of nine TB care facilities that implemented the intervention in question, this might not be representative of the views of all health staff working in TB care in Somaliland. Nevertheless, the use of rigorous qualitative research methods for the collection and analysis of data might minimise the effects of such limitations.

Another issue is that of reflexivity: the degree to which the researcher's status, profile, position and interaction with study participants (health workers) prior to the present study could have influenced the collection, analysis and quality of data and the ultimate study findings. In other words, how the researcher's or study subjects' roles, preconceptions, beliefs, values, assumptions and positions could have influenced not only the nature of the research process, but also the findings, is a potential limitation[56, 57]. Another limitation is the Hawthorne Effect, where the observer's interaction with the observed facility staff could have compromised the accuracy and quality of observation data during site visits[3, 58, 230].

The findings presented here were elicited through objective and interpretive (interview data, on-site observation data) and contextual (document review, field notes) data collection and analysis techniques, which might affect the validity, reliability (consistency) and accuracy of these

findings[59, 296]. Another significant and potential limitation is the interpretive nature of the results. These could have been influenced not only by the way the views, thoughts and observed accounts and interactions of the study participants (health workers) were captured/measured, categorised, grouped, coded for thematic and content analysis, accurately reflected and reported, but also by the way these were portrayed by the researcher[62]. While a high refusal rate could be a threat to internal and external validity, it was challenging to assess the influence of the researcher's position/status and health workers' reasons for accepting or refusing interviews[63]. Thus, a clear conclusion cannot be drawn whether the observed high refusal rates among health workers were inextricably linked with the roles, position and previous interactions of the study subjects and the researcher, or were about the presence or absence of researcher bias at this point[67, 160, 297].

Chapter 6

Discussion

To understand factors that helped or hindered the implementation and utilisation of LED technology for TB diagnosis in fragile resource-limited settings, this analysis adopted a framework-based analysis (IAF). The single overarching aim of this study was to improve access and quality of diagnosis for TB patients in fragile health system settings, with particular emphasis on Somaliland. In doing so, this analysis tried to understand three crucial elements critical to feasibility: context (environmental context), infrastructural capacity (health system capacity to support and sustain), and resourcing constraints (health workforce, financial, information) with a particular focus on fragile, resource-poor settings.

Although most of the health professionals (HPs) acknowledged the potential benefits of innovative technologies such as LED for TB diagnosis, they were mostly concerned about the feasibility of the application and regular use of sophisticated technologies in a resource-poor, fragile health system environment. Previous studies on feasibility and LED technology acceptance for daily use focused on accuracy analysis (sensitivity and specificity), primarily focusing on performance rather than the operational, technical, resource and environmental constraints to feasibility in a fragile health environment[29, 181, 213, 216, 217]. The findings of this analysis revealed serious resource, structural and environmental constraints to LED technology feasibility, which were also supported by previous research conducted in resource-poor settings[29, 203, 215, 230, 298, 299].

Furthermore, the appropriate technology doctrine stresses that for any technology applied to work in a resource-poor setting, it needs to be compatible with the social and economic conditions of environments in which these technologies are used[300-302]. The technology is deemed

appropriate if it is suitable in local structural and environmental conditions, and can be used easily with locally available resources, with tools and processes that are maintained and managed by the intended users or beneficiaries [300-302]. Almost all of the HPs interviewed for this study believed that complex technologies such as LED would not work in a fragile health system environment without preparing and strengthening the existing health system structural capacities.

Critical barriers identified in this study revealed both at the individual and group level (user, manager, policy-maker) were perverse incentives (delayed staff salaries) and a lack of technical expertise (i.e., knowledge, skills, experience in technology use/maintenance) for the introduction, implementation and utilization of the applied technology. System-wide issues such as a deficit of competent health workforce and a lack of coherent policy/strategy and infrastructural capacity, as well as a lack of systematic and programmatic readiness, were key constraints to the feasibility of new technology introduction, implementation and utilisation in fragile health settings. It is critical to understand the interplay between the demand for more robust, rapid technologies for TB diagnosis and the prevailing question about the appropriateness of such technologies in fragile states.

While the need for more robust and rapid diagnostic tools in resource-poor settings, including countries with fragile health systems, is undeniably imperative, the findings of the present study echoed the importance of involving potential stakeholders (i.e., technology end users, technical, operational and managerial teams) in all stages of the technology development, introduction and implementation. Such a process of involvement provides opportunities for managing potential expectations and challenges that may arise in the process of the technology application.

The findings of this study add to an existing body of knowledge from other settings related to the diagnostic performance and operational feasibility and diagnostic performance of LED as an alternative diagnostic strategy to improve patient access to quality diagnosis[181]. With involvement of stakeholders, TB control efforts are more likely to succeed and be supported and sustained through improved local capacities in weak health system contexts.

Limitations

The use of purposeful sampling (non-probability sampling) technique in this research has several known limitations. First, the purposeful sampling technique is highly prone to researcher bias, where the sampling nature of the study population was solely based on researcher judgment. Although potential researcher-driven purposive sampling biases could have been minimized through the use of clear inclusion/exclusion criteria based on the theoretical framework and expert elicitation, reducing researcher biases would be challenging despite the type and rigor of data

collection and analysis techniques applied. Second, although the use of purposeful sampling provided an opportunity to generate averages in the data analysis with often low margins of error, it also ran the risk of generating inferential statistical biases. It might also be challenging to defend the representative nature of the sample, which also undermines the generalizability of the research.

Third, the subjective and non-probability sampling nature of the unit selection (health workers, organizations, study sites and context) for study makes it more difficult to defend the lack of representativeness of the sampled population. As a result of this, it will be challenging to convince the potential readers that the applied researcher judgment is sound and appropriate. Therefore, diminished external validity relating to the implementation of the findings outside the specific context (fragile health system setting) of the study means it might be difficult to convince the reader that the use of non-probability sampling has achieved adequate theoretical or analytical rigor for generalization[70].

Another critical limitation was to do with the difficulty of getting access to potential study participants (health professionals) and clear answers from policy makers and external agencies during the interviews. The vast majority of healthcare professionals interviewed were reluctant to report on weaknesses related to resourcing, systematic and programmatic challenges, and worried about losing their jobs.

7.5 **Overall discussion of the study findings**

The findings of the present study deliver new highlights on the key priorities and constraints to the adoption, deployment and utilization of new healthcare technologies including diagnostic ones in weak health system settings. The key health system features influencing health system functions of a country such as Somaliland are the production and mobilization of vital resources (i.e., competent health workforce, sustainable financing and production/availability of information on prevailing population health needs).

The findings of the existing TB literature attributed the deficit of health staff knowledge as not unique to diagnostic technology, but also found in all aspects of TB control in many resource-poor settings[303, 304]. These findings also portray the overall knowledge and related competencies among staff as inadequate[35, 296, 305, 306]. The deficit of vital resources, structural and programmatic capability and readiness affected both user acceptance and operational feasibility of the applied technologies for routine utilization including the diagnostic performance for everyday use in settings with weak health systems[228, 307-312].

Previous research on health systems types and functions, highlighted key elements that help or hinder the introduction and implementation of complex health interventions including healthcare technologies (competent health workforce, structural and financial abilities) and the use of novel technologies[313]. The findings of such research helped create a comprehensive understanding of how well health systems perform and factors that influence health system performance in resource-poor settings[228, 314].

Equally, although context-specific, the findings of the present study contrast with the findings of several previous studies that assessed the acceptability, feasibility and operational performance of LED technology in similar resource-poor settings[38, 42, 315-317]. Studies that assessed the feasibility and acceptability of LED implementation and utilization for routine use in resource-poor environments, for example, primarily focused on user or operator acceptance (i.e., perceived usefulness, ease of use)[318, 319]. However, they failed to address the importance of the systematic and programmatic (structural, environmental and resourcing) constraints to routine utilization of such sophisticated technologies in a fragile health system context, which are addressed here[19, 49, 50, 52, 137]. These studies broadly examined feasibility and acceptability from the diagnostic accuracy (sensitivity and specificity) aspects of LED technology by focusing on utility and yield in patient diagnostic outcomes but also stressed the need for further research on the implementation of quality assurance procedures at the time of introduction[44-48].

Other studies highlighted the need for further and broader field interventions to assess the feasibility and acceptability of LED introduction and routine utilization as an alternative testing technology to conventional techniques, namely ZN, in resource-poor settings[20, 21, 38, 53].

The findings of the present study are in agreement with previous literature on LED technology elsewhere that showed similar deficiencies in health workers' knowledge concerning new diagnostic technology use in settings where it was applied[54, 56, 57, 313]. Specific areas of deficiencies identified in the present findings were staff knowledge and competencies in the use and maintenance of the new technology (LED) together with a lack of functional care delivery capacities in Somaliland. Previous research stressed the importance of improving health workers' proficiency in TB care service provision through training, and how such a strategy would help address gaps in knowledge competencies among staff[50, 228, 320, 321].

The findings also reaffirm previous research stressing the importance and need for improving the systemic and programmatic readiness of the existing health system, particularly laboratory facilities, to support and sustain both the implementation and routine utilization of such complex healthcare technologies, for both resource-rich and resource-constrained settings[58, 59, 317]. The

findings of the reviewed literature provided crucial highlights on the feasibility and acceptability of LED use for routine TB diagnosis in settings where it was introduced. In the present study, the researcher has tried to shift the focus of feasibility analysis from a *user-preference-based* focus to an overall health system capability analysis. The researcher shifted from user preferences and expectations (knowledge, attitudes, perception and practices of the intended user) to an overall health system capability analysis (resourcing, structural, environmental), in order to support the introduction, implementation and management of new TB diagnostic technologies such as LED.

Availability of the necessary infrastructural capacity was vital to effectively facilitate and sustain the introduction, implementation, and utilization of the applied technology such as LED in fragile health system settings. The vast majority of staff voiced a knowledge deficit in use and repair as a critical constraint to LED technology use at the primary care level. Another critical issue to note in the analysis of this study was that all laboratory technicians working in intervention facilities were on a performance-based incentive scheme: each laboratory technician was expected to read 25-35 slides per day with no clear protocol/guidelines.

While the intention might be to improve and help deliver the quality diagnostic services to population in need of quality TB care, the introduction of performance-based incentives could have influenced user behaviour[76]. The use of incentives could be both powerful and useful to improve performance and ultimately, population health outcomes in resource-poor settings. However, careful attention should have been paid to the intended and unintended consequences of performance-based staff incentives[322-326].

The observed diagnostic performance and operational feasibility outcomes in Somaliland were reflective of many examples of failed interventions or more mixed results for overall TB care service delivery practices in resource-poor and fragile health system settings[153-160, 263]. These problems were especially prevalent when the introduction and implementation of a diagnostic technology changed organisational structures[263]. Such changes may take several years to produce a clear impact at the health system level, but it may also be difficult to identify the material and financial constraints to feasibility and acceptability, as well as the effects of such changes in a fragile health system environment.

State of art research supports the findings of the present study as it clearly illustrated that the majority of LMICs including fragile states do not fit neatly into the traditional categories of health system typologies[318]. In particular, the health systems of LMICs including fragile states tend to be fragmented, with different arrangements for different population groups[304]. The control of TB infections in fragile settings is much more complex, and not only that, it requires enormous

resources (human and financial), but also innovative programmatic policies, strategies and plans that go beyond the traditional models of TB control practices often measured by progress against predefined targets. In an era of extreme austerity, the welfare problem has grown so much that international assistance for emergency aid has become a sustainable basket for millions around the world, and Somalia is no exception[327]. Consequently, implementing LED successfully required enormous resources (human and financial), and strong and well established health system infrastructures that could facilitate effective TB care delivery.

7.6 Overall strengths and limitations of the study

Strengths of the study

The strengths and weaknesses of this study were the following:
Mixed-method research is the combination of qualitative and quantitative approaches to the research methodology in a single study or multi-phased study[63]. The use of mixed methods for the collection and analysis of data allowed the researcher to obtain basic data and trends regarding the problem (tuberculosis) being studied without the complications of using random sampling[328]. The use of multiple approaches for the collection, analysis and inference of the research findings maximizes the implications of the findings. The application of this approach brings complementary strengths and less-overlapping weaknesses, in turn creating a bridge between qualitative and quantitative research approaches in TB control in a fragile health system context.

Importantly, the use of qualitative and quantitative research approaches together enhances representation, which increases the researcher's ability to extract adequate information from the underlying data. Legitimation, on the other hand, increases the validity (internal/external) of data interpretation[329]. A wide range of sampling techniques can be used across such qualitative research designs: purposive sampling techniques that range from homogeneous sampling through to critical case sampling and expert sampling[330, 331] . Such an approach equips the researcher with the rationale to generalise the findings of study to similar populations and ensures whether such generalisations can be theoretical, analytic and/or logical in nature.

Such an approach also provided the researcher with a wide range of non-probability sampling techniques to draw on for a clear and concise conclusion of the research findings given in a resource-poor fragile health system context. To reduce potential bias in the data collection process, qualitative aspects of the exploratory study (semi-structured interviews with health workers at delivery and policy levels) placed major emphasis on human elements of the research in order to

identify, control and reduce all types of researcher (confirmation bias) and participant bias (preventing subjects answering questions to present themselves in the best possible light).

7.7 **The overall limitations of the study**

The overall study has several limitations. This research sought to understand the extent to which the introduction, implementation and deployment of one new diagnostic technology (LED) for routine TB testing is feasible and acceptable in a fragile health system setting. Each country that has adopted new technologies, including TB diagnostic ones, has its unique challenges or own particular circumstances, so generalising the findings of this study from one fragile health system setting would be difficult. A few limitations specific to fragile health systems have and specifically a health system governance problem influenced by the current political situation between Somalia and Somaliland, emerged from this study:

1. Information on not only the feasibility and acceptability but also the adoption and management of new TB diagnostic technologies, particularly LED in fragile states, was either extremely limited or unavailable in Somaliland.

2. The number of countries or settings that had adopted and introduced LED technology for routine use since its inception in 2012 was unknown.

3. The interpretation of the validity and reliability to ascribe credibility level of the routine clinical data on the introduction, implementation and utilization of LED technology for routine testing in a fragile health system context was difficult. Such a prevailing limitation goes beyond listing the magnitude and direction of random and systematic errors and validity problems.

4. A challenge unique to Somaliland was the security-related travel restrictions to outside main urban towns and cities to collect representative data on the operational feasibility and acceptability of the technology applied (LED) in a fragile health system context.
5. Conducting high level research in a fragile state was proven to be problematic due to prevailing systematic and programmatic deficiencies in existing health services, including poor data recording and reporting at health facilities selected for study in Somaliland.

6. The use of non-probability for the selection of study participants (health workers, organisations, study sites and context) makes it difficult to defend the lack of representativeness of the sampled population. As a result of this, it would be challenging to convince potential readers that the applied researcher judgment was deemed sound and appropriate.

7. Diminished external validity, reliability, applicability and generalizing relating to the implementation of the findings outside fragile health system settings make it difficult for the researcher to convince the reader that the use of non-probability sampling has achieved adequate theoretical or analytical rigour for generalisation[55].

The use of mixed methods which included the use of purposeful sampling (non-probability sampling) technique in this research was highly prone to researcher bias, as the sampling nature of the study population was solely based on researcher judgement. Irrespective of the type of purposive sampling used, the study findings could still be prone to researcher bias (selection bias, information bias and confounding)[332]. Even if the study was highly valid and not subject to potential sources of biases, it is important to stress the extent to which the study findings generalize to similar populations in given contexts[2, 24]. Another critical weakness leading potentially to several types of bias was the use of a mixed-methods approach which assumed mixing of different techniques for data collection and analysis was required and the resulting triangulation of research responses might undermine the quality of the findings.

In a fragile health system context, poor study design or incongruence between aims and methods increase the chance of bias, which can occur when the researcher's or participants' personal beliefs influence the choice of research objective, research question and methodology of the study[333-335]. Data collection is another critical shortfall to note in this dataset with a potential designer, implementer and user bias: this could have influenced the information or data collected from individual study subjects[336, 337]. In the broadest context, it is crucial to recognise potential bias at all intervention stages. This is necessary both for the study's integrity and application of the methods undertaken, as well as the precision to which the findings can accurately reflect the data.

Chapter Eight: Conclusions and recommendations for policy and practices and future research

8.1 Introduction

In resource-poor fragile health system settings, TB transmission is uniquely affected by influences such as population movement, continued civil unrest, poor living conditions, a lack of or inadequate access to quality care (diagnosis, treatment), frequent interruption of applied interventions and the diminished delivery capacity of the existing health system[80]. The feasibility and acceptability of the introduction, implementation and utilization of novel technologies for the routine use of TB diagnosis in resource-poor and fragile health systems is not clearly articulated in the current TB control literature.

The capacity of existing health systems to support, sustain and facilitate such sophisticated technological interventions in fragile health system settings plays a significant role in technology acceptance and ultimately use by the intended users at the facility level. The North-West region of Somalia (Somaliland) is one such settings that introduced LED for routine utilization. The systematic review of existing literature in chapter 3 revealed that the feasibility and acceptability of the introduction and implementation of LED technology use for routine TB diagnosis in fragile and resource-constrained settings has been confused by both policy and providers with the construct of user satisfaction or acceptance. This confusion has arisen because of the lack of consideration given to wider systematic and programmatic aspects of existing healthcare delivery capability.

Important elements of the healthcare system studied in this thesis included resources (skilled people, money, information), structural capability (systematic and programmatic readiness) and environmental feasibility (values, norms, stakeholder engagement and relationships). Such analysis helped to shed light on the extent to which the existing system can support, sustain and manage the implementation and routine utilization of new technologies in weak health systems.

8.2 Conclusions of the thesis

New technologies such as LED have been endorsed, introduced and recommended by the WHO as the most effective and efficient technology for routine TB diagnosis in resource-poor high TB burden settings, including countries with weak health systems[153-160, 163, 264]. The WHO and its global TB control partners projected that, with the use of new sophisticated technologies such

as LED for routine TB diagnosis, case detection in TB high burden countries would increase, and TB burden and death rates would be reduced relative to pre-LED introduction levels[32, 163]. Since its inception in 2006, many resource-poor and high TB burden countries have adopted, introduced and implemented the LED technology for routine TB diagnosis. A significant number of these countries were either in or recovering from protracted complex emergencies (political, social and economic), mostly in the African region. The central aim of this study was to shed light on key constraints to the introduction and use of LED technology for routine testing and how that influenced TB case findings in a setting with a weak health system.

To address this aim, this study used framework-based qualitative and quantitative data collection and an analysis approach to assess the performance, operational feasibility, acceptability of potential users (primary care providers) and diagnostic performance of LED in Somaliland. The use of such a framework has helped contribute to a clearer picture of the key constraints to the feasibility and acceptability of complex new technologies in fragile health systems. Although it is challenging to causally link increased case detection and an overall decline in the TB burden with the feasibility and acceptability of LED introduction and utilization for routine TB diagnosis, overall case detection and disease levels have remained unchanged in settings with weak health systems. According to the WHO annual TB reports over the last few decades, the level of the TB burden, as measured by country-specific TB case detection rates, has either remained unchanged or marginally decreased in all other WHO geographical regions over the last two decades, but has increased in Africa[2, 74, 183]. More people are now infected, living with and dying from TB and TB related illnesses, than ever in the African region, and the region currently shows disturbing drug-resistance levels[2, 74, 183, 202, 332, 338-340].

The findings of the systematic review in this study identified considerable knowledge gaps in both the peer-reviewed and grey literature, which made a feasibility and acceptability assessment of the introduction and routine use of LED technology challenging. The level of evidence established in all reviewed studies failed to accurately define, theorise, assess or measure the feasibility and acceptability of the introduction and utilization of healthcare technologies, including LED, in settings with weak health systems.

A large proportion of the studies reviewed both in the peer-reviewed studies and grey literature came mostly from resource-poor stable environments. Most of the studies used quantitative methods such as surveys, experiments and modelling. Only a few of the reviewed studies used qualitative methods (i.e., interviews, observations). None of the studies that assessed ″feasibility″

discussed essential resourcing, infrastructural and environmental factors influencing the successful implementation of LED in fragile states. Equally, no studies assessed potential constraints to the feasibility and acceptability of LED and the systematic and programmatic readiness of existing health systems. No empirical evidence was found on programmatic and systematic considerations or corrective measures for the future introduction and implementation of LED in fragile health systems. Consequently, higher quality context-specific evidence was needed on the feasibility and acceptability of new technologies such as LED, as a base for further advances and guidance on TB diagnosis in fragile health system settings.

The findings of clinical data analysis on LED implementation (question 2 of the present study) revealed no observable differences in patients' diagnostic test outcomes between the two testing techniques compared (LED vs ZN). Thus, it was possible that the lack of difference in the observed patients' test outcomes between the two diagnostic techniques might be attributed to the deficit of operational, technical (skilled health workers) and infrastructural capacities (physical structures, including laboratory diagnostic testing capacities). They might also have been influenced by the geographical location of diagnostic facilities coupled with a lack of, or inadequate use of, clear standard operating procedures at the facility level for routine technology use. Chapters 5 and 6 provide useful highlights on structural, resourcing (people, money and time) and environmental constraints to the use of new and sophisticated healthcare technologies such as LED in settings with weak health systems.

In resource-poor settings, including fragile states, smear microscopy for TB diagnosis is the fastest, cheapest and the most reliable method for the detection of TB [57, 316, 341]. The findings of the clinical data analysis of the present study suggest that the introduction of sophisticated diagnostic technologies such as LED might be feasible, accepted and useful for routine utilisation in resource-poor settings such as Somaliland. However, the use of new or optimized diagnostic technologies such as LED will not work without the systematic and programmatic readiness and the capability of the existing system to support and sustain the introduction, implementation and more crucially the routine utilization of such complex health technologies in settings with weak health systems. While some aspects of laboratory improvement will be needed or sufficient in varied capacities across settings based on the characteristics of the applied new technologies, there is an overall unmet need: inadequate knowledge, skills and experience among care providers, technical and policy teams and difficulties in the retention of trained health personnel.

The findings of the interviews with frontline staff showed that overall knowledge among staff about LED technology for everyday use was inadequate, which in turn affected the diagnostic performance and operational feasibility of the applied technology. Inadequate resources (people, money, time) combined with a lack of robust laboratory systems and networks to support and sustain the delivery of quality and diagnostic services were key constraints to operational feasibility and the diagnostic performance of LED technology. Key prevailing perceptions on technology usability at the facility level were that most of the new technologies introduced were either not easy to use or lacked clear or agreed guidelines/protocol for use and maintenance.

In addition, the vast majority of health workers were profoundly concerned about the true motive of introducing new technologies in settings with weak health systems like Somaliland. These healthcare professionals believed that the introduction and use of new technologies for routine TB testing alone has not worked without preparing the resourcing and structural capability of the existing health system in fragile health system settings. Another barrier encountered in the introduction and implementation process of LED was that each of the technologies was conditioned with donor interest.

During the discussions with health workers at different levels of the health system, it became apparent in the study findings that the introduction and implementation processes in place for new technology utilisation affected the intended outcomes (improved TB case detection) in Somaliland. One of the most common barriers to LED technology utilisation was resistance from health workers (at all levels) to due to a lack of, or delayed, staff salaries and other disincentives. Therefore, the findings of the present study provided useful highlights on key priorities and constraints to new technology adoption, deployment and the utilisation process in a fragile health system context.

While the need for more robust and rapid diagnostic tools in resource-poor settings, including countries with fragile health systems, is undeniably imperative, the findings of the present study echoed the importance of involving and engaging all potential stakeholders (i.e., technology end users, technical, operational and managerial teams) in all stages of the technology development, introduction and implementation. Such a process will provide opportunities for managing potential expectations and challenges that may arise in the process of the technology application. Though the rate of technological development may be an essential aspect of TB diagnosis and clinical practice in general, it is unlikely to be useful in settings with limited structural and resourcing capacities.

To date, traditional methods for assessing the impact and effectiveness of TB control interventions focus on measuring and reporting program effectiveness. These methods produce mixed and

conflicting results on progress without revealing the prevailing realities that can reflect how interventions work or fail in a particular context. Most of the challenges identified in this study were linked with *supplier-driven* (the technology introduction was based on marketing purposes) rather than *beneficiary-driven* (intended users were not consulted/involved) applications of new healthcare interventions. The lack of introducing interoperable technologies for routine utilisation in resource-constrained settings impedes acceptability of applied technologies should reflect of the true motives behind LED introduction in fragile health system settings.

In summary, this study is the first of its kind in a fragile state to assess the feasibility and acceptability of LED, and shed light on constraints to both the feasibility and acceptability of the deployment and management of new technologies such as LED in the pursuit of increased case detection outcomes. The findings of this study add to an existing body of knowledge from other settings related to the diagnostic performance and operational feasibility of LED as an alternative diagnostic strategy to improve patient access to quality diagnosis. The findings of the present study provide useful highlights on the key constraints to new technology adoption, deployment and the utilisation process, and priorities to be considered for improving access to quality TB care (diagnosis and treatment) in a fragile health system context.

While the use of more robust and rapid TB diagnostic tools in resource-poor settings are undeniably desirable, the findings of this study reinforce the importance of stakeholder engagement (i.e. health professionals, care providers and target beneficiaries) with all stages of technology development, introduction, implementation and routine utilization. Active stakeholder engagement and involvement will provide opportunities for managing potential expectations and challenges that arise in the process of technology application. With such an approach, TB control efforts are likely to succeed and be supported and sustained through improved local capacities in fragile health system contexts.

To conclude, the introduction and use of sophisticated diagnostic technologies alone will not be sufficient for reducing the current TB burden levels in resource-poor fragile states. The deployment and management of healthcare technologies, not only for TB control but also any other disease conditions, requires functional systems, sustained resources (people, money, time/commitment) and a conducive environment that can support and strengthen ongoing healthcare services and robustly integrate new ones at all levels of the health system. The availability of sufficient resources (health workforce, knowledge, information) together with the improvement of the systemic and programmatic readiness of existing health systems to support and sustain complex interventions in fragile health system settings is undoubtedly critical.

The findings of health workers' interviews indicated that reducing or ending dependency on single donor funding for healthcare financing and the identification of alternative resources would improve both program performance and local ownership. Developing locally led policies and strategic priorities would help local health authorities overcome current challenges including reducing reliance on donor-led ideas and agenda-specialized care services.

8.3 **Recommendations for policy and practice**

Policy recommendations for TB control partners about the introduction and utilisation of LED and other technology for routine TB diagnosis in fragile states (e.g., Somaliland)

The research specifically explored the introduction of LED, but also asked key informants more broadly about issues with the introduction of new technologies for TB diagnosis. Hence, this section provides policy recommendations for TB control partners thinking about introducing new technology, including LED, for TB diagnosis in settings with weak health systems. The following points are emphasised:

1. Any future introduction and utilization of new TB diagnostic technologies should ensure that the existing systems meet the basic operational, technical and structural conditions to support and sustain the use of the applied technology.
2. Prior to introducing new diagnostic technologies, feasibility and acceptability should be considered, as should the capacity to assimilate them into existing healthcare structures and workforces.
3. End-user characteristics (e.g., the facility's physical capacity, staff motivation, financial incentives etc.) were found to be critical factors affecting technology introduction, implementation, and utilisation at the facility level in a setting with a weak health system.
4. Based on the findings of the health professionals' sub-study, local health authorities should be more involved and engaged in all stages of technology introduction and utilisation, including:
   - The development of locally-led policy, strategic priorities and frameworks for the introduction and utilization of new TB diagnostic technologies such as LED in resource-poor settings.
   - Ending or reducing single donor funding dependency for healthcare financing for complex health interventions to be supported and sustained.
   - Mobilizing and sustaining funds from alternative sources combined with increased government or local budget allocations to tackle the single donor dependency problem.

Policy recommendations for TB global partners (WHO, Global Fund)

For new technology such as LED to work in settings with weak health systems, critical feasibility and acceptability conditions need to be met at all levels of the adoption, introduction, and implementation processes. The following points are emphasized:

1. Based on the findings of both the health workers and health professionals' sub-studies, TB control partners, including WHO and the Global Fund, should obtain accurate empirical evidence on the feasibility, acceptability and suitability of introducing new TB diagnostic technologies prior to their routine use in settings with weak health systems.
2. Training of health workers in the use of the new technology, establishing external and internal quality assurance, establishing adequate reporting and recording systems, as well as maintaining uninterrupted and sustainable supply chains, is critical to sustainability and routine utilization of the applied technologies.
3. International TB control entities and their local counterparts should learn from, and adapt to, local conditions prior to implementation, if preferred strategies for the introduction and routine utilization of new technologies are to be effective in target areas and achieve intended outcomes.

Implications for future research

The present study's findings addressed feasibility and acceptability issues relevant to the introduction and management of LED in settings with weak health systems. The following further ideas are worthy of consideration for future research:

1. Consideration of the systematic and programmatic readiness of existing fragile health systems to support the introduction and implementation of complex health technologies such as LED.
2. Studies providing comprehensive and country-specific empirical analyses on how innovative technologies can work in fragile health systems are urgently needed to shed light on the applicability and feasibility of new diagnostic technologies or tools.
3. Study of the operational, technical, and structural requirements of recommended new technologies in TB care services provision from the perspectives of beneficiaries, providers, and policy makers
4. While the focus of this study was not aid effectiveness, it was clear from interviewees that future research should look at the shortcomings of aid dependency and its impact on the achievement of intended outcomes, including issues around achieving local ownership of new interventions in a fragile health system context.

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APPENDIX TO CHAPTER 2 (Survey tools)

Consent form for participant (interviews)

Title of Project: The Feasibility and Acceptability of New Technologies for TB Diagnosis in Fragile States: A Somaliland Case Study

Name of PI/Researcher responsible for project: Halima Mohamed

Statement	**Please initial or thumbprint* each box**
I confirm that I have read and understood the information sheet dated 26-10-2018(version 2) for the above-named study. I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
I understand that my consent is voluntary and that I am free to withdraw this consent at any time without giving any reason and without my/the participant's employment status or legal rights being affected.	
I understand that relevant sections of my information and data collected during the study may be looked at by authorised individuals from [London School of Hygiene & Tropical Medicine], where it is relevant to my/the participant's taking part in this research. I give permission for these individuals to have access to these data or information.	
I understand that data about/from me/the participant may be shared via a public data repository or by sharing directly with other researchers, and that I will not be identifiable from this information	
I understand that the data or/and information collected from me/the participant will be used to support other research in the future, and may be shared anonymously with other researchers, for their ethically-approved projects	
I give permission for a copy of this consent form, which contains my/the participant's personal information, to be made available to the research institution (LSHTM) for monitoring purposes only.	
I agree to my/the participant's employer being informed of my participation in the study.	
I agree to me/the participant taking part in the above named study.	

Printed name of participant/Representative	Signature of participant/Representative	Date

Printed name of person obtaining consent	Signature of person obtaining consent	Date

The participant/representative is unable to sign. As a witness, I confirm that all the information about the study was given and the participant/representative consented to taking part *(*only required if the participant/representative is unable to read or write).*

Printed name of impartial witness*	Signature of impartial witness*	Date

Participant information sheet for interviews

Title of Project: *<The Feasibility and Acceptability of New Technologies for TB Diagnosis in Fragile States: A Somaliland Case Study>*

Introduction

We would like to invite you to take part in a research study. Joining the study is entirely up to you. Before you decide, you need to understand why the research is being done and what it would involve. One of our team will go through this information sheet with you, and answer any questions you may have. Ask questions if anything you read is not clear or you would like more information. Please feel free to talk to others about the study if you wish. Take time to decide whether or not to take part.

What is the purpose of the study?

The London School of Hygiene and Tropical Medicine (LSHTM) are conducting research on the feasibility and acceptability of Light-emitting diode fluorescence microscopy (LED-FM) in Somaliland. The purpose of this study is to improve access and quality of TB diagnosis for TB patients in fragile states, with particular emphasis on Somaliland.

Why have I been asked to take part?

You have been invited because you are one of 50-60 healthcare workers and professionals who either are working at 10 TB care facilities implementing the LED-FM technology use for routine TB testing or managing TB diagnostic services in the organizations identified and selected for taking part in interviews

You should already have been approached or asked by your employer or organization to take part in this study assessing the feasibility and acceptability of LED-FM which was introduced in Somaliland 2012.

Do I have to take part?

No. Your participation in this study is voluntary. It is up to you to decide to take part or not. If you do not want to take part, that is ok. You will still be employed at your organization and your decision will not affect your employment or employment status.

We will discuss the study together and give you a copy of this information sheet. If you agree to take part, we will then ask you to sign a consent form.

What will happen to me if I take part?

If you agree to participate, the researcher (Halima Mohamed) will ask you to sign an informed consent form. The researcher will arrange for you to meet with the PI (Halima Mohamed) for further clarification about what it is involved. A follow-up interview will be conducted either immediately after you have signed the informed consent or at your preferred location. Please note all your conversations during the interview will audio-recorded using an audio-recorder. The purpose of the recording conversations is to allow the researcher to capture all the information discussed during the interview, which is important for them to analyse later. The interview will take about 40-60 minutes.

What will I have to do?

You are required to answer the questions based on your personal experience during the interview on LED-FM technology use for routine testing or your involvement in policy development and decision making in TB care service delivery in Somaliland. However, you are free to refuse to answer any questions which you feel are uncomfortable and you can stop the interview at any time.

What are the possible risks and disadvantages?

During the interview, at times, you could be asked questions about certain sensitive topics which may upset you. You can refuse to answer any questions which you feel uncomfortable with, or you can stop the interview anytime you wish do to so.

What are the possible benefits?

We cannot promise the study will help you but the information we get from the study will help our knowledge and understanding of this research area <improve the quality and access of TB diagnosis for patients in Somaliland >.

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researcher <Halima Mohamed> who will do her best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting < Patricia Henley at rgio@lshtm.ac.uk or +44 (0) 20 7927 2626>

Can I change my mind about taking part?

Yes. You can withdraw from the study at any time. You just need to tell your employer or organization that you do not want to be in the study anymore. Your refusal will not affect your employment or status within organization.

If you withdraw from the study we will destroy all your </tape recorded interview>, but we will need to use the data collected on you up to your withdrawal.

What will happen to information collected about me?

All information collected about you will be kept private. Only the study staff and authorities who check that the study is being carried out properly will be allowed to look at information about you. Data may be sent to other study staff in London <or in Somaliland> but this will be anonymised. This means that any information about you which leaves the LSHTM for publication purpose, will have your name and address removed so that you cannot be recognised.

Your organization will send some details about you to the study team in London or Somaliland who will store it securely.

At the end of the project, the study data will be archived at LSHTM. The data will be made available to other researchers worldwide for research and to improve TB care service knowledge and patient care. Your personal information will not be included and there is no way that you can be identified.

What will happen to the results of this study?

The study results will be published in various journals so that other organizations can learn from them. Your personal information will not be included in the study report and there is no way that you can be identified from it.

Who is organising and funding this study?

<London School of Hygiene & Tropical Medicine> is the sponsor for the research and they have full responsibility for the project including the collection, storage and analysis of your data.

Who has checked this study?

All research involving human participants is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by The London School of Hygiene and Tropical Medicine Research Ethics Committee ***(***<https://www.lshtm.ac.uk/research/research-governance-integrity/ethics>***).** *The Somaliland Ministry of Health Ethics Office has also reviewed the study and have agreed that it is okay for us to ask people to take part.*

1. Further information and contact details

Thank you for taking time to read this information leaflet. If you think you will take part in the study, please read and sign the consent form. If you would like any further information, please contact [Halima Mohamed] who can answer any questions you may have about the study.

2. Who you should approach if unhappy with the study? All question or concerns you have about the study will be addressed by following:

Halima Mohamed
London School of Hygiene & Tropical Medicine
15-17 Tavistock Place
WC1H 9SH
London, UK
Tel: +44 (02) 072994704 (W)
Tel: +44 7849405516 (M)
Email: Halima.Mohamed@lshtm.ac.uk
Email: Famohamed10@gmail.com

3. Who you should approach if still unhappy with the study? Please ask

Patricia Henley
LSHTM Ethics Office
Email:*rgio@lshtm.ac.uk*
Tel: +44 (0) 20 7927 2626

OR

Using the LSHTM Complaint Procedures, which you can obtain from this web site for more details: https://www.lshtm.ac.uk/research/research-governance-integrity/ethics or contact the Somaliland Ministry of Health.

Consent form for on-site facility observations

Title of Project: The Feasibility and Acceptability of New Technologies for TB Diagnosis in Fragile States: A Somaliland case study

Name of PI/Researcher responsible for project: Halima Mohamed

Statement	**Please initial or thumbprint* each box**
I confirm that I have read and understood the information sheet and informed consent for on-site observations dated (26-10-2018.) for the above-named study. I have had the opportunity to read/consider the information on site-observation visits, asked questions and have these answered satisfactorily.	
I understand that my consent is voluntary and that I (the manager or person-in-charge) at this facility can withdraw from this consent at any time without giving any reason and without my/the participant's employment or status or legal rights being affected.	
I understand that relevant sections of my data collected during on-site facility observations may be looked at by authorised individuals from the London School of Hygiene and Tropical Medicine/facility manager for taking part in site-observations for the proposed research. I give my full permission or authorization for the proposed individuals to have access to these records or collect more data.	
I understand that data about/from me/the participant may be shared via a public data repository or by sharing directly with other researchers, and that my personal identities will not be identifiable from this information collected during observations.	
I understand that data or information collected from me/the participant during on-site observations will be used to support other research in the future, and may be shared anonymously with other researchers, for their ethically-approved projects	
I give permission for a copy of this consent form, which contains my/the participant's personal information, to be made available to the London School of Hygiene and Tropical Medicine for data collection and confidentially monitoring purposes only.	
I agree to my/the participant's employer being informed of my participation in the study.	
I agree to me/the participant taking part in on-site observations as part of the above named study.	

Printed name of participant (facility-in-charge)	Signature of participant (facility-in-charge)	Date

Printed number of person obtaining consent	Signature of person obtaining consent	Date

The participant is unable to sign. As a witness, I confirm that all the information about the study was given and the participant consented to taking part *(*only required if the participant is unable to read or write)*

Printed name of impartial witness*	Signature of impartial witness*	Date

Information sheet for on-site facility observations

Title of Project: *<The Feasibility and Acceptability of New Technologies for TB Diagnosis in Fragile States: A Somaliland Case Study>*

Introduction

We would like to invite you to take part in on-site facility observations as part of a research study. Joining the study is entirely up to you. Before you decide, you need to understand why the research is being done and what it would involve. One of our team will go through this information sheet with you, and answer any questions you may have about the on-site-facility observations. Ask questions if anything you read is not clear or you would like more information about the proposed on-site-facility observations. Please feel free to talk to others about these observations of the study in general, if you wish. Take time to decide whether to take part in the on-site-facility observations.

What is the purpose of the study?

The London School of Hygiene and Tropical Medicine (LSHTM) are conducting research on the feasibility and acceptability of Light-emitting diode fluorescence microscopy (LED-FM) in Somaliland. The purpose of this study is to improve access and quality of TB diagnosis for TB patients in fragile states, with particular emphasis on Somaliland.

Why has my facility been asked to take part in the on-site observations?
Your facility has been invited to take part in the on-site-facility observations because you are one of the four facilities implementing the LED-FM technology use for routine TB testing selected for taking part in the on-site-facility observations. You should already have been approached or asked by your employer or organization to take part in the on-site-facility observations as part of a study assessing the feasibility and acceptability of LED-FM technology use for routine TB testing which was introduced in Somaliland 2012.

Does my facility have to take part in the on-site-facility observations?

No. Your facility's participation in the on-site-facility observations as part of the stated above study is voluntary. It is up to you to decide on whether your facility takes part or not. If you do not want your facility to take part, that is ok. You will still be employed at your organization and your decision will not affect your employment or employment status at the facility.

We will discuss the study together and give you a copy of this information sheet. If you agree on your facility to take part in the on-site observations, we will then ask you to sign a consent form.

What will happen to my facility if it takes part in on-site observations?

If you agree on your facility to participate in the on-site observations, the researcher (Halima Mohamed) will ask you to sign an informed consent form. The lead researcher (Halima Mohamed) will arrange for you to meet with her for further clarification about what is involved in the on-site observations. A follow-up on-site observation visit will be conducted either immediately after you have signed the informed consent or at your preferred time. The researcher will return for a further 2-3 visits. Each on-site-facility observation will take about 40-60 minutes. All on-site observations will take place at your facility at dates, times agreed, and approved by you (the person-in-charge or

facility manager). All facility staff will be notified about the date and time of the on-site observations well in advance.

What will I have to do as a person-in-charge?
You are required to give permission for the on-site observations at your facility on LED-FM technology use for routine testing or your involvement in LED-FM use at your facility. However, you're free to refuse give permission or deny access to your facility to participate in the on-site observations. You are can stop these observations to be conducted at your facility at any time.

What are the possible risks and disadvantages?

During the observations, at times, your staff could feel unconfortable with someone sitting or walking in the facilty which may upset some staff. Your staff at the facility can ask you to have the observations at your facility stopped anytime they wish do to so.

What are the possible benefits?

We cannot promise the study will help your facility but the information we get from the on-site observations will help our knowledge and understanding of the introduction of new technologies such as LED-FM for routine TB testing in fragile health system settings like Somaliland. Thus, information collected through on-site observations will help us improve the quality and access of TB diagnosis for TB patients in Somaliland.

What if something goes wrong during on-site observations?

If you have a concern about any aspect of the on-site observations, you should ask to speak to the lead researcher<Halima Mohamed>, who will do her best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting < Patricia Henley at rgio@lshtm.ac.uk or +44 (0) 20 7927 2626>

Can I change my mind about my facility taking part in on-site observations?

Yes. You can cancel all on-site observations at your facility or withdraw from the study at any time. You just need to tell your employer or organization that your facility will not take part in the on-site-facility observations anymore. Your refusal will not affect your employment or status within organization.

If your facility withdraws from the study we will destroy all your <on-site facility observations>, but we will need to use the data collected on the facility up to your withdrawal.

What will happen to information collected during on-site observations about my facility?

All information collected about your facility during on-site observations will be kept private. Only the study staff and authorities who check that the observations are being carried out properly will be allowed to look at information about your facility. Data collected during the on-site observations may be sent to other study staff in London <or in Somaliland> but this will be anonymised. This means that any information about your facility, which leaves the LSHTM for publication purpose, will have your facility name and address removed so that you cannot be recognised.

Your organization will send some details about your facility to the study team in London or Somaliland who will store all data or information acquired through the on-site-facility observations securely.

At the end of the study, all on-site-facility observation data will be archived at LSHTM in a safe and secured databases with password access. The data will be made available to other researchers worldwide for research purposes only and to improve quality TB diagnosis, knowledge, and patient care. Your facility information will not be included and there is no way that your facility's information can be identified.

What will happen to the results of this study?

The study results will be published in various journals so that other organizations can learn from them. Any specific information about your facility will not be included in the study report and there is no way that you can be identified from it.

Who is organising and funding this study?

<London School of Hygiene & Tropical Medicine> is the sponsor for the research and they have full responsibility for the project including the collection, storage and analysis of your data.

Who has checked this study?

All research involving human participants is looked at by an independent group of people, called a Research Ethics Committee at the London School of Hygiene & Tropical Medicine, to protect your interests. This study has been reviewed and given favourable opinion by The London School of Hygiene and Tropical Medicine Research Ethics Committee (<https://www.lshtm.ac.uk/research/research-governance-integrity/ethics>*). The Somaliland National Tuberculosis Program (NTP) of the Ministry of Health Ethics Office has also reviewed the study and have agreed that it is okay for us to ask people to take part.*

4. Further information and contact details

Thank you for taking time to read this information leaflet. If you think your facility will take part in the study, please read and sign the consent form. If you would like any further information, please contact [Halima Mohamed] who can answer any questions you may have about the study.

5. Who you should approach if unhappy with the study? All question or concerns you have about the study will be addressed by following:

Halima Mohamed
London School of Hygiene & Tropical Medicine
15-17 Tavistock Place
WC1H 9SH
London, UK
Tel: +44 (02) 072994704 (W)
Tel: +44 7849405516 (M)
Email: Halima.Mohamed@lshtm.ac.uk
Email: Famohamed10@gmail.com

6. Who you should approach if still unhappy with the study? Please ask

Patricia Henley
LSHTM -Ethics Office
Email:*rgio@lshtm.ac.uk*
Tel: +44 (0) 20 7927 2626

OR

Using the LSHTM Complaint Procedures, which you can obtain from this web site for more details: https://www.lshtm.ac.uk/research/research-governance-integrity/ethics or contact the Somaliland Ministry of Health.

On-site visit observations to laboratory diagnostic facilities

Name of facility: _____ Date: _____/_____/_____/ Time started: _____ Time ended: _____

LED-FM implementation at laboratory facilities **Section I**	**YES**	**NO**	**DK**	**Unclear**	**Other (Specify)**
1. Functional LED-FM microscopes available at this facility at the time of observation					
2. LED-FM in use for routine TB testing at this facility					
3. Microscopy reagents, supplies and spare parts are available and kept at lab-facility					
4. Diagnostic rooms provide enough space for different lab functions					
5. Storage for microscopes is available at the facility					
6. The TB test results of individual patients performed are documented on a daily basis at the facility					
7. The facility has electricity at the time of visit					
8. There is enough natural light at all diagnostic facility premises					
Laboratory Biosafety, Infection Control and standard operating procedures					
9. Biosafety and infection control guidelines with clear standard operating procedures available and in use at facility					
10. Waste management procedures including safe disposal for waste materials mechanism in use at the facility					
11. Health staff wear recommended personal protective equipment (gloves, masks, gowns)					
12. The physical location of lab facility is separated from other labs or health facility					
13. Access to Lab restricted from rest of lab/health facility					
14. Standard laboratory precautions for aerosolisation of TB bacilli droplet nuclei in use at the facility					
15. Patients given proper and clear instructions on sputum production at both the facility and at home					
16. Strict guidelines for droplet nuclei are in use (i.e., sputum being collected in the open air)					
17. Sputum specimens collected, and handled safely at the facility and when transported to reference labs					
18. Laboratory technicians follow the safety guidelines for sputum collection at the time of visit					

19. Laboratory technicians seem knowledgeable about specimen transportation at the time of visit					
20. Laboratory technicians seem knowledgeable about sputum storage at the time of visit					
21. Laboratory technicians seem knowledgeable about smear examination and staining at the time of visit					
22. Appropriate decontamination protocols available and in use					
23. There is enough ventilation at the facility					
Section II (*look at previous records-document review done during 1st visit only)*					
Basic recording and reporting information system functions at the facility level	**YES**	**NO**	**DK**	**Unclear**	**Other (Specify)**
24. Estimates of population served by this TB care facility available					
25. Total number of people notified in the previous year at this facility available					
26. Total number of people notified this year at this facility available					
27. New smear-positive pulmonary TB documented					
28. New smear negative-pulmonary TB documented					
29. Total smear-positive started treatment documented					
Quality Assurance (QA)	**YES**	**NO**	**DK**	**Unclear**	**Other (Specify)**
30. Panel testing (results compared to other labs in network-Intermediate and reference labs) done regularly					
31. Blind re-checking and on-site evaluations (re-reading smears) performed properly and regularly at the time of visit					
32. Routine Internal QA done at the facility level					
33. Routine External QC done at the facility					
34. Routine Quality Monitoring (QM) done at the facility					
35. Routine Quality improvement (QI) done at the facility					

Interview guide for healthcare providers

(Nurses)

Name of Interviewer_____ Interviewee number_____

Location _____ Organization type _____

Date ____/_____/_____

1. Please tell me your current roles and responsibilities in TB care at this facility.
2. Can you describe your experience and knowledge in TB testing?

Prompt: what is your role in TB diagnostic services?

3. What are the tools used for routine TB testing at your facility?

Prompt: Does this include LED-FM?

4. Please explain about your experience in LED-FM use for TB testing.
5. What are your views about LED-FM use for routine TB testing? Do you think it is useful? If so, how and why?
6. Now that LED-FM has been introduced, what is your opinion/perception towards LED-FM acceptance among staff? Please describe?
7. Can you tell me if you have ever received training and/or information on LED-FM use or TB diagnosis in general? If so, what type of information did you receive? If not why?
8. If you were to change anything, what would you like to see changed in TB diagnostic services:
   a. At the facility level?
   b. At the regional level?
   c. At the national level?

Any comments or questions?

----------*Thanks and close*----------

Interview guide for healthcare providers

(Physicians)

Name of Interviewer_____

Interviewee number _____ Location_____

Facility Type_____Date _____/_____/_____

1. Please tell me about your position?

   Prompt: How long have you been in this position?

2. Tell me about your current and previous experience in TB care.

   Prompt: What is your role and responsibility in TB care service provision at this facility?

3. Please explain the types of diagnostic services provided at this facility.

   Prompt: What are the types of TB tests performed at the facility?

4. Have you ever received any formal educccation or training in TB care?

   Prompt: what knowledge/skills/experience the worker has in TB diagnosis?

5. Please tell me about the tools you use for routine treatment decisions? Prompt: why?

6. Can you please tell me about LED-FM acceptance and usage among staff?

   Prompt: what are the barriers to acceptability?

7. Please tell me if LED-FM is feasible for routine use? Prompt: what are the barriers to feasibility?

8. How do you describe staff knowledge and skills in LED-FM use for routine TB diagnosis?

   Prompt: what are areas of deficiency?

9. In your opinion, does LED-FM use influence your routine diagnosis and treatment decisions for individual patients?

   Prompt: How and why?

10. Can you tell me about whether your facility has adequate resources/systems to support LED-FM implementation for routine use?

    Prompt: Please describe the barriers to LED-FM routine use?

11. If you were to change anything, what would you like to see changed in TB diagnostic services:

    a. At the facility level?

    b. At the regional level?

    c. At the national level?

Anything to add? Any other questions?

----------*Thanks and close*----------

Interview guide for healthcare providers

(Laboratory technicians)

Name of Interviewer_____ Interviewee_____

Location _____ Organization type _____

Date ____/_____/_____ _____

1. What is your current position at this facility? How long have you been in your current position?
2. Can you tell me about your previous experience in TB diagnosis?
3. What are your specific responsibilities in TB diagnostic services?
4. What are the types of TB tests performed here?

Prompt: What tools do you use for routine TB testing?

5. Can you tell me if LED-FM was introduced to your facility?

Prompt: Was it implemented as initially intended? [If so, or not, how and why?]

6. Is LED-FM presently used for routine TB testing at your facility? If not, why?
7. What are your opinions/perceptions on the routine use of LED-FM technology?
8. Are laboratory technicians sufficiently trained in LED-FM use? If not, what are areas of deficiencies?
9. Can you tell me if LED-FM is accepted among facility staff? If not, what are the barriers to acceptance?
10. In your opinion, which tool(s) do you consider as the most reliable tool for TB testing? And why?
11. Have you ever received any refresher training or feedback for LED-FM use from policy maker or manager? If so, what was the feedback?
12. In your opinion, can you tell me if LED-FM use for routine TB testing enhances your daily work performance?
13. Can you tell me about the challenges you faced with LED-FM use?

Prompt: How can these challenges be overcome?

14. If you were to change anything, what would you like to see changed in TB diagnostic services:
    a. At the facility level?
    b. At the regional level?
    c. At the national level?

Anything to add? Any other questions?

---------- *Thanks and close*----------

Interview guide for key informants

(Policy, managerial, technical and coordination teams)

Name of Interviewer: _____ Interviewee number: _____
Location: _____ Organization type: _____
Date: ____/_____/_____ _____

1. What are your roles and responsibilities in TB care services in your organization?
2. How many TB care facilities your organization supports? How many of these provide diagnostic/treatment services?
3. What types of TB diagnostic tests are performed in your facilities? Please describe these tests?
4. Has your organization participated in LED-FM introduction through the TB-REACH project in 2012?

   Prompt: If not, why? If so, is LED-FM still being used for routine TB testing at all recipient facilities?
6. What factors have supported LED-FM implementation?

   Prompt: Please describe how and why?
7. What difficulties did LED-FM implementation face?

   Prompt: Please describe these difficulties and why?
8. Was LED-FM implemented as intended/planned? If so, or not, how and why?
9. Can tell me if facility staff received sufficient training in LED-FM use? If so, what was this training? If not, why and what are the gaps?
10. Please describe if your laboratory services have the *resources* and structure capacities to support LED-FM implementation? If not, what are the gaps?
11. Can you tell me if LED-FM is accepted among staff at primary care facilities?

    Prompt: what are the barriers to acceptability?
12. Are there policies or guidelines for LED-FM implementation? If not why?
13. What systems are in place for procurement of LED-FM supplies/maintenance?

    Prompt: Please explain who's responsible for these services?
14. Overall, what were the challenges your organization faced in LED-FM implementation?

    Prompt: Please describe how these challenges could be overcome?
15. Overall, what is your opinion of LED-FM use in Somaliland?
16. If you were to change anything, what would you like to see changed in TB diagnostic services:
    a. At the facility level?
    b. At the regional level?
    c. At the national level?

Anything to add? Any other questions?

----------*Thanks and close*----------

APPENDIX TO CHAPTER 3

Table 3.1 ***Search strategy, strings, and review of the literature used in Medline (Pub-Med), CABI-Global Health Databases (EBSCO) and Web of Science Databases***

Searched database	Concepts	Search terms	Search results
PUB-MED	*Concept 1(C1)*	(Tuberculosis*) OR (TB OR Mycobacterium TB*) OR (Mycobacterium Tuberculosis*) OR (mycobacterium*) OR (Pulmonary TB OR Pulmonary*) OR (MTB*) OR (M Tuberculosis*) OR (Pulmonary Tuberculosis*) OR (tuberculosis*) OR (m tuberculosis*) OR (mycobacterium tuberculosis*)	1063348
		AND	
	Concept 1 (C2)	(Light emitting diode fluorescence microscopy*) OR (FM*) OR (Led Fluorescence microscopy*) or (FM*) OR (FM Microscopy*) OR (FM Microscopy*) OR (LED fluorescence Microscopy*) OR (FM*)	77
		AND	
	Concept 3 (C3)	(Feasibility*) OR (feasibility*) OR (feasible*) OR (introduction*) OR (implementation*) OR (performance*) OR (evaluation*) OR (utilization*) OR (introduction*) OR (operational*) OR (constraints*) OR (obstacles*) OR (barriers*)	*4939449*
		AND	
	Concept 4(C4)	(Acceptability*) OR (acceptability*) OR (acceptable*) OR (accepted*) OR (useful*) OR (easy*) OR (perceived*) OR (attitudes*) OR (healthcare*) OR (providers*) OR (laboratory*) OR (services*) OR (technicians*) OR (Labs*) OR (Facility*) OR (Facilities*) OR (Laboratories*) OR (Routine*) OR (laboratories*) OR (Lab techs*)	3910354
		AND	
	Concept 5(C5)	(Complex Emergency*) OR (Crisis*) OR (War*) OR (Conflict*) OR (Armed Conflict*) OR (Fragile State*) OR (Unstable*) OR (Chronic Complex Emergency*) OR (Conflict Affected*) OR (Fragile OR Insecurity*) OR (Violence*) OR (Humanitarian Crisis*)	1192839
		AND	
	Concept 6 (C6)	(Somalia*) OR (South Sudan*) OR (Sudan*) OR (Afghanistan*) OR (DRC*) OR (Syria*)OR (Chad*) OR (CAR*) OR (Yemen*) OR (Iraq*) OR (Haiti*) OR (Guinea*) OR (Nigeria*) OR (Zimbabwe*) OR (Ethiopia8) OR (Guinea Bissau*) OR (Burundi*) OR (Pakistan*) OR (Eritrea*) OR (Niger*)	10084563
	C1 and C2	Tuberculosis and LED	71
	C1 And C2 And C3	Tuberculosis and LED and Feasibility	53
	C1and C2 AND C3 and C4	Tuberculosis and LED and feasibility and acceptability	36
	C1and C2 and C3 and C4 and C5	Tuberculosis and LED and Acceptability and feasibility and fragile states	0
	C1 and C2 and C3 and C4 and C5 and C6	Tuberculosis and FM and feasibility and acceptability and fragile states and individual countries	0

Table 3.1 ***Search strategy, strings, and review of the literature used in Medline (Pub-Med), CABI-Global Health Databases (EBSCO) and Web of Science Databases*** **(Continues).**

Searched database	Concepts	Search terms	Search results
GLOBAL HEALTH databases (EBSCO)	*Concept 1(C1*	Tuberculosis OR TB OR Mycobacterium TB OR Mycobacterium Tuberculosis OR mycobacterium OR Pulmonary TB OR Pulmonary OR MTB OR M Tuberculosis OR Pulmonary Tuberculosis OR tuberculosis OR m tuberculosis OR mycobacterium tuberculosis	150975
		AND	
	Concept 2(C2)	Light emitting diode fluorescence microscopy OR FM OR Led Fluorescence microscopy or FM OR FM Microscopy OR FM Microscopy OR LED fluorescence Microscopy OR FM	60
		AND	
	Concept 3(C3)	*Feasibility OR feasibility OR feasible OR introduction OR implementation OR performance OR evaluation OR utilisation OR introduction OR operational OR constraints OR obstacles OR barriers*	498412
		AND	
	Concept 4(C4)	*Acceptability OR acceptability OR acceptable OR accepted OR useful OR easy OR perceived OR attitudes OR healthcare OR providers OR laboratory OR services OR technicians OR Labs OR Facility OR Facilities OR Laboratories OR Routine OR laboratories OR Lab techs*	669861
	Concept 5(C5)	Complex Emergency OR Crisis OR War OR Conflict OR Armed Conflict OR Fragile State OR Unstable OR Chronic Complex Emergency OR Conflict Affected OR Fragile OR Insecurity OR Violence OR Humanitarian Crisis	0
		AND	
	Concept 6(C6)	*Somalia OR South Sudan OR Sudan OR Afghanistan OR DRC OR Democratic Republic of Congo OR Syria OR Chad OR Central African republic OR CAR OR Yemen OR Iraq OR* Haiti OR Guinea OR Nigeria OR Zimbabwe OR Ethiopia OR Guinea Bissau OR Burundi OR Pakistan OR Eritrea OR Niger	0
	C1 and C2	*Tuberculosis and LED*	55
	C1 and C2 and C3	*Tuberculosis and LED and feasibility*	*40*
	C1 and C2 and C3 and C4	*Tuberculosis and LED and feasibility and acceptability*	*29*
	C1 and C2 and C3 and C4 and C5	*Tuberculosis and LED and feasibility and acceptability and fragile states*	*0*
	C1 and C2 and C3 and C4 and C5 and C6	*Tuberculosis and LED and feasibility and acceptability and fragile states and individual countries (n=20)*	*0*
	C1	Tuberculosis OR TB OR Mycobacterium TB OR Mycobacterium Tuberculosis OR mycobacterium OR Pulmonary TB OR Pulmonary OR MTB OR M Tuberculosis OR Pulmonary Tuberculosis OR tuberculosis OR m tuberculosis OR mycobacterium tuberculosis	*766673*
		AND	

MED-LINE/OvidSP	*C2*	Light emitting diode fluorescence microscopy OR FM OR Led Fluorescence microscopy or FM OR FM Microscopy OR FM Microscopy OR LED fluorescence Microscopy OR FM	*58*
		AND	
	C3	*Feasibility OR feasibility OR feasible OR introduction OR implementation OR performance OR evaluation OR utilisation OR introduction OR operational OR constraints OR obstacles OR barriers*	*2905001*
		AND	
	C4	*Acceptability OR acceptability OR acceptable OR accepted OR useful OR easy OR perceived OR attitudes OR healthcare OR providers OR laboratory OR services OR technicians OR Labs OR Facility OR Facilities OR Laboratories OR Routine OR laboratories OR Lab techs*	*2624517*
		AND	
	C5	Complex Emergency OR Crisis OR War OR Conflict OR Armed Conflict OR Fragile State OR Unstable OR Chronic Complex Emergency OR Conflict Affected OR Fragile OR Insecurity OR Violence OR Humanitarian Crisis	*260098*
		AND	
	C6	*Somalia OR South Sudan OR Sudan OR Afghanistan OR DRC OR Democratic Republic of Congo OR Syria OR Chad OR Central African republic OR CAR OR Yemen OR Iraq OR* Haiti OR Guinea OR Nigeria OR Zimbabwe OR Ethiopia OR Guinea Bissau OR Burundi OR Pakistan OR Eritrea OR Niger	*275596*
	C1and C2	*Tuberculosis and LED*	*53*
		AND	
	C1and C2 and C3	*Tuberculosis and LED and feasibility*	*41*
		AND	
	C1 and C2 and C3 and C4	*Tuberculosis and LED and feasibility and acceptability*	*31*
		AND	
	C1 and C2 and C3 and C4 and C5	*Tuberculosis and LED and feasibility and acceptability and fragile states*	*0*
	C1 and C2 and C3 and C4 and C5 and C6	*Tuberculosis and LED and feasibility and acceptability and fragile states and individual countries*	*0*
	C1	Tuberculosis OR TB OR Mycobacterium TB OR Mycobacterium Tuberculosis OR mycobacterium OR Pulmonary TB OR Pulmonary OR MTB OR M Tuberculosis OR Pulmonary Tuberculosis OR tuberculosis OR m tuberculosis OR mycobacterium tuberculosis	643727
		AND	
	C2	Light emitting diode fluorescence microscopy OR FM OR Led Fluorescence microscopy or FM OR FM Microscopy OR FM Microscopy OR LED fluorescence Microscopy OR FM	11,538
		AND	
	C3	*Feasibility OR feasibility OR feasible OR introduction OR implementation OR performance OR evaluation OR utilisation OR introduction OR operational OR constraints OR obstacles OR barriers*	7 879 370

COCHRANE		*AND*	
	C4	*Acceptability OR acceptability OR acceptable OR accepted OR useful OR easy OR perceived OR attitudes OR healthcare OR providers OR laboratory OR services OR technicians OR Labs OR Facility OR Facilities OR Laboratories OR Routine OR laboratories OR Lab techs*	4 581 846
		AND	
	C5	Complex Emergency OR Crisis OR War OR Conflict OR Armed Conflict OR Fragile State OR Unstable OR Chronic Complex Emergency OR Conflict Affected OR Fragile OR Insecurity OR Violence OR Humanitarian Crisis	957 478
		AND	
	C6	*Somalia OR South Sudan OR Sudan OR Afghanistan OR DRC OR Democratic Republic of Congo OR Syria OR Chad OR Central African republic OR CAR OR Yemen OR Iraq OR* Haiti OR Guinea OR Nigeria OR Zimbabwe OR Ethiopia OR Guinea Bissau OR Burundi OR Pakistan OR Eritrea OR Niger	437 029
		AND	
	C1 and C2	*Tuberculosis and LED*	303
	C1+C2+C3+C4+C5+C6	*Tuberculosis and LED and feasibility and acceptability and fragile states and individual countries*	*4*

Table 3.2 ***Inclusion and exclusion criteria for articles recruited for review***

Inclusion criteria	**Exclusion criteria**
1. Quantitative, qualitative, mixed method and literature review studies including a meta-analysis in the English language only. 2. Provided information/data on feasibility, acceptability, adoption, introduction, implementation and performance of LED for routine TB diagnostic in fragile states. 3. Included sufficient and relevant information on knowledge, perception, attitudes and practices of healthcare providers, including users' perceptions of LED's usefulness and ease of use at primary care facilities in fragile states. 4. Provided information/data on specific factors influencing the feasibility and acceptability of new TB diagnostic technologies at a policy-making level in fragile states. 5. Reported information on or relevant to TB screening, testing, diagnosis and control in either resource-poor setting or fragile states. 6. Provided relevant data or information on LED technology use for diagnostic with "hypothesis testing" if the investigators compared data between technologies and/or across periods. 7. Examined accuracy (sensitivity and/or specificity) and evaluated, assessed or determined the impact of LED on basic pulmonary TB testing (including HIV-positive). 8. Compared LED testing outcomes to those of microscopy tools or technologies (not assays) and demonstrated scientific rigor. 9. Reported primary research findings on TB diagnostic technologies in fragile states with sufficient scientific details or information of the individual research methods used. 10. All references deemed relevant to the subject of interest from articles or studies encountered in the search were included for review.	1. All studies (all types) that used statistical testing hypothesis and determined differences in diagnostic outcomes between LED and ZN testing tools or technologies in different fragile health system settings or geographical locations. 2. All studies, articles, data, or information or unknown sources on the subject of interest not in the English language were excluded from the review. 3. Reports, data, information or/and any other information on immigrant refugees in high-income countries; any data, information and reports on refugees (in camps) or in a high-income country; any information on specific populations in crisis or displacement or conflict-affected or migrants. 4. Studies that failed to adopt rigorous scientific research methods (i.e., studies failed to pass the quality assessment questions checklist – see the quality assessment checklist for details in table 8). 5. Studies that are solely presenting the author's opinion with no substantiated independent evidence on the research subject. 6. Literature superseded or outdated by new empirical evidence on the feasibility and acceptability of LED. 7. Studies that failed to provide adequate information or evidence on the feasibility, acceptability, introduction, implementation, and utilization of new TB diagnostic technologies for routine TB diagnosis in fragile states. 8. Reviews of literature with no new or relevant data, information or analysis on the subject of research.
All systematic reviews (including critical synthesis reviews) of a healthcare intervention were included in the review. A systematic review was defined as "a review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research and to collect and analyse data from the studies that are included in the review". Participant samples included all recipients and deliverers of healthcare interventions.	

Table 3.3 ***The QUADAS quality assessment question of the selected studies for systematic review***

Questions	**Yes**	**No**	**Cannot tell**
1. Was the spectrum of patients representative of the patients who will receive the test in practice?			
2. Were selection criteria clearly described?			
3. Is the reference standard likely to correctly classify the target condition?			
4. Is the time period between the reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?			
5. Did the whole sample, or a random selection of the sample, receive verification using a reference standard of diagnosis?			
6. Did patients receive the same reference standard regardless of the index test result?			
7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?			
8. Was the execution of the index test described in sufficient detail to permit replication of the test?			
9. Was the execution of the reference standard described in sufficient detail to permit its replication?			
10. Were the index test results interpreted without knowledge of the results of the reference standard?			
11. Were the reference standard results interpreted without knowledge of the results of the index test?			
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?			
13. Were uninterpretable/intermediate test results reported?			
14 Were withdrawals from the study explained?			

Table 3.4 ***The QUADAS questions for quality assessment of the selected studies for the systematic review in chapter 3***

Name of author of study	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**	**Q14**
Affolabi, D. et al.(2010)	YES	YES	YES	YES	YES	YES	YES	NC	YES	NO	YES	YES	YES	NO
Albert, H. et al (2010)	YES	YES	YES	YES	YES	YES	YES	YES	YES	NC	YES	NO	NO	NC
Albert, H. et al (2013)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	NO	NC
Bonnet, M. et al(2010)	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	NO	NC
Bonnet, M. et al (2011)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	NC
Cattamanchi, A. et al (2011)	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES	NO
Chang, E. W. et al (2016)	YES	YES	YES	YES	YES	YES	YES	NO	YES	NO	YES	YES	YES	NC
Cuevas, L. E. et al (2011)	YES	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	NO
Everett, C. K. et al (2010)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
Gelalcha, A. G et al (2017)	YES	YES	YES	NO	NC	NC	NC	NO	NC	NC	NC	NC	NC	NC
Getachew, Konjit et al (2015)	YED	YES	YES	YES	YES	YES	YES	YES	YES	NC	NC	YES	YES	NC
Marzouk, M. et al (2013)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NC	YES	YES	NC
Nyaruhirira, Alaine et al (2015)	YES	YES	YES	YES	YES	YES	YES	YES	NC	NC	NC	NC	NC	NC
Perez-Tanoira, Ramon et al (2017)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NC
Taddese, Boja (2017)	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NC

*NC = Not clear

Table 3.5 ***FAF assessment attributes adopted from Bowen et al. (2009) of the selected articles for the systematic review in chapter 3***

Terms for feasibility	The study asks	Outcomes
Acceptability	Assesses how the intended beneficiaries or recipients (planners, deliverers, and end user) react (accept or reject) to the applied intervention	Satisfaction Intention to use Perceived appropriateness Fit within the organizational culture Perceived positive or negative effects on the organisation
Demand	Assesses the estimated use of the applied intervention given context	Actual use Expressed interest or intention to use Perceived demand
Implementation	Is concerned with the extent or the likelihood that the applied intervention can be fully implemented as planned or intended in an uncontrolled environment or setting	Degree of execution Success or failure of exclusion The amount, type of resources needed to implement Factors affecting implementation ease or difficulties/constraints Efficiency, speed, or quality of implementation
Practicality	Explores the extent an intervention can be delivered given resources (human, financial, time) and commitment	Positive/negative effects on target participants The ability of participants to carry out intervention activities Cost analysis
Adaption	Explores possibilities for opportunities to change or modify contents or procedures to be appropriate or suitable to a specific context/environment or new situation	The degree to which similar outcomes are obtained in the new format process outcomes comparison between intervention in use and the new one in two populations
Integration	Assesses need for change to integrate new program/intervention/process into an existing infrastructure or program (i.e., organizational, social, physical environment) to determine true feasibility	Perceived fit with infrastructure Perceived suitability
Expansion	Examines the suitability and potential success of an already-successful intervention in a new context/setting or population	Costs to organization and policy bodies Fit with organizational goals and culture Favourable or adverse effects on the organization Disruption due to expansion component
Limited-efficacy testing	Concerned with the feasibility of applied intervention given study design and how that leads to limitations (i.e., statistical power)	Intended effects of the program, process on crucial intermediate variables Effect-size estimation Maintenance of changes from the initial change

Table 3.6 ***The FAF assessment questions adopted from Bowen et al. (2009) of the selected articles for the systematic review in chapter 3***

Attributes	Number	Questions
Acceptability	Q1	To what extent is the new idea, program process or measure judged as suitable, satisfying or attractive to program deliverers, policy actors or potential end users (target beneficiaries)?
Demand	Q2	To what extent is a new idea, program, process or measure likely to be used (how much demand is likely to exist)?
Implementation	Q3	To what extent can a new idea, program, process or measure be successfully delivered to intended participants in some defined, but not adequately controlled, context?
Practicality	Q4	To what extent can an idea, program, process, or measure be carried out with intended participants using existing means, resources, and circumstances and without outside intervention?
Adaption	Q5	To what extent does an existing program or process measure performance when changes are made for a new format or with a different population?"
Integration	Q6	To what extent can an idea, program, process or measure be integrated within an existing system?
Expansion	Q7	To what extent can a previously tested program, process, approach, or system be expanded to provide a new program or service?
Limited efficacy	Q8	Does a new idea, program, process, or measure show promise of being successful with the intended population, even in a highly controlled setting?

Table 3.7 ***Names, summary description and outcomes of interest of the systematically reviewed articles***

Author (year)	Study aims	Setting	Design	Sample size	Time frame	Study population (inclusion criteria)	Location of intervention	Outcome measured/questions addressed
Affolabi, D. et al. (2010)	To compare the performance of Frean FluoLEDTM and LW LuminTM light-emitting diode (LED) fluorescence microscopy modules.	Benin	*Cross-sectional*	1937	2008-2009	TB patients	Lab-based	Detection sensitivity of LED vs ZN in routine TB testing
Albert, H. et al. (2010)	This study compared the performance of three commercial light emitting diode (LED)-based microscopy systems (PrimostarTM LED , LuminTM and AFTERH) for fluorescent detection of Mycobacterium tuberculosis with ZN microscopy on slides prepared from the sputum of TB suspects.	Uganda	*Cross-sectional*	193	2009-2010	TB patients	Lab-based	Detection sensitivity of LED vs ZN in routine TB testing
Albert, H. et al. (2013)	We sought to compare the operational performance of three FM methods compared to light microscopy in a cohort of HIV-positive tuberculosis (TB) suspects at an urban setting	Uganda	*Cross-sectional*	627	2009-2010	TB-HIV	Lab-based	Compared performance of LED and ZN in routine testing
Bonnet, M. et al. (2011)	To compare performance of LED versus ZN to assess the feasibility of LED at a low level of care in a high HIV prevalence country.	Kenya	*Cross-sectional*	497	2008-2009	TB patients	Lab-based	Operational performance of LED against ZN
Bonnet, M. et al. (2011)	This study aimed to evaluate the performance of combined LED and NaOCl sputum sedimentation for TB detection at the peripheral level of health services.	Kenya	*Cross-sectional*	497	2008-2009	TB patients	Lab-based	The LED yield in TB-positive smears compared to direct microscopy (ZN)
Cattamanchi, A. et al. (2011)	To determine whether two alternative approaches can increase smear-positive case detection by increasing the efficiency (single-specimen microscopy) or sensitivity (light-emitting diode [LED], fluorescence microscopy [FM]) of TB suspect evaluation.	Uganda	Cross-sectional	464	2009-2010	TB patients	Lab-based	Compared diagnostic accuracy of four pre-specified strategies (LED) in routine TB testing
Chang, E. W. et al. (2016)	We aimed to determine the diagnostic accuracy of LED-FM for tuberculosis detection and explore potential factors that might affect its performance.	Global	Meta-analysis		2000-2014	TB patients	Lab-based	Assessed diagnostic accuracy of LED for TB diagnosis Explored potential factors affecting LED performance
Cuevas, L. E. et al. (2011)	The aim of this study was to assess the sensitivity/specificity of LED for the diagnosis of pulmonary TB and whether its performance varies with the timing of specimen collection.	Yemen, Ethiopia, Nigeria, Nepal	Cross-sectional	2445	2008-2009	TB patients	Lab-based	Assessed sensitivity and specificity of LED against ZN
Gelalcha, A. G et al. (2017)	This study aimed to evaluate these tools for TB detection in individuals visiting Ambo Hospital, west-central Ethiopia.	Ethiopia	Cross-sectional	362	Jan–Aug 2015	TB-HIV	Lab-based	The high specificity of LED in the study area is encouraging and is expected to boost its reliability and uptake.

Getachew, Konjit et al. (2015)	This study aimed to evaluate the performance of LED for the diagnosis of PTB in HIV positive individuals.	Ethiopia	Cross-sectional	178	2011-2012	TB/HIV patients	Lab-based	Sensitivity and specificity of LED for PTB in HIV patients
Marzouk, M. et al. (2013)	The objective of the study was to compare the performance of conventional fluorescence microscopy (CFM) and light-emitting diode (LED) with fluorescence microscopy (FM) for detection of acid-fast bacilli (AFB) in clinical samples.	Tunisia	Cross-sectional	180	Apr-Nov 2011	TB patients	Lab-based	Compared performance of LED and ZN in routine TB diagnosis
Nyaruhirira, Alaine et al. (2015)	The study aimed to determine the acceptability and effectiveness of LED (LED) in a low resource setting.	Rwanda	Cross-sectional	37	2009-2010	TB patients	Lab-based	Acceptability and effectiveness of LED against ZN in resource-poor settings
Perez-Tanoira, Ramon et al. (2017	This aimed to evaluate the feasibility of LED use for increased sensitivity and reducing time for analysis compared to ZN.	Ethiopia	Cross-sectional	1126	2012-2013	TB patients	Lab-based	Increased sensitivity and reduced reading time of samples under LED vs ZN
Shete, P.B et al. (2017)	This assessed the feasibility of a streamlined strategy for improving tuberculosis (TB) diagnostic evaluation and treatment initiation among patients with presumed TB.	Uganda	Cross-sectional	1212	2015-2016	TB patients	Lab-based	Evaluated the feasibility and implementation of each component in a resource-poor fragile state such as Uganda; additional outcomes included the time to-diagnosis and time-to-treatment of smear-positive and Genexpert-positive patients
Taddese, Boja (2017)	The aim of the study was to compare the results of sputum smears by LED against ZN stained sputum smears using TB culture as a reference test.	Ethiopia	Cross-sectional	248	2013-2014	TB patients	Lab-based	Sensitivity of LED vs ZM in TB routine use for TB diagnosis

Table 3.8 ***Characteristics of included studies for review in chapter 3***

Study (ref)	Study design	Subjects (specimens)	Country	Settings	HIV/TB-status	Reference standard	Compared devices	Scanty smears LED/ZN/Fraen/Lumin	Sensitivity (%)	Specificity (%)
Affolabi, D. et al.(2010)	Cross-sectional	1937	Benin	Ref-Lab-based	TB-patients	Unclear	LED	LED= 34 Frean = 67	52	43
Albert, H. et al (2010)	Cross-sectional	193	Uganda	Ref-Lab-based	TB-Patients	Culture	LED vs ZN, Fraen	LED = 6, ZN= 2 Fraen= 6, Lumin= 7	ZN= 77.4 LED = 37	ZN = 40.9, LED = 80.6, FraenFraen = 99
Albert, H. et al (2013)	Cross-sectional	627	Uganda	Ref-Lab-based	TB-Patients	Culture	ZN, LED Fraen, Lumin	ZN= 12, LED =11, Frearn =16, Lumin=12	ZN= 31, FM= 33, LED = 42 Lumin =39	ZN =94, FM=99, LED=93, Fraen = 91, Lumin = 91
Bonnet, M. et al(2010)	Cross-sectional	497	Kenya	Peri-Lab-based	TB-patients	Culture	ZN vs LED	ZN= 15, LED= 21	LED =73 ZN =72	LED =97, ZN =96
Bonnet, M. et al (2011)	Cross-sectional	497	Kenya	Peri-Lab-based	TB-patients	Culture	ZN, LED	LED= 22, ZN = 16	LED =79 ZN =72	LED =89, ZN=97
Cattamanchi, A. et al (2011)	Cross-sectional	464	Uganda	Ref-Lab-based	TB-patients	Culture	LED vs ZN	Unclear	LED = 64 ZN = 56	LED =96, ZN =98
Chang, E. W. et al (2016)	Meta-analysis	7451	Multi-country	Multi-settings	TB-patients	Mixed	Various	Unclear	LED = 67 (pooled)	LED=97 (pooled)
Cuevas, L. E. et al (2011)	Cross-sectional	2445	Multi-country	Peri-Lab-based	TB-patients	Mixed	LED vs ZN	Unclear	LED =73 ZN =70.5	Unclear
Ngabonziza, Semuto et al (2016)	Cross-sectional	648	Ethiopia	Ref-Lab-based	TB-HIV-patients	Culture	LED vs ZN	Unclear	LED=38 ZN = 56	LED= 43, ZN= 58
Gelalcha, A. G et al (2017)	Cross-sectional	362	Ethiopia	Ref-Lab-based	TB	Cult	LED vs Genexpert	Unclear	LED=78	LED =100
Getachew, Konjit et al (2015)	Cross-sectional	178	Ethiopia	Ref-Lab-based	TB-HIV-patients	Culture	LED vs ZN	Unclear	LED =63, ZN 30	LED =95, ZN=90
Marzouk, M. et al (2013)	Cross-sectional	180	Tunisia	Ref-Lab-based	TB-patients	Culture	LED vs ZN	LED =5, ZN=13	LED =80 ZN 83	LED =98,ZN=98
Nyaruhirira, Alaine et al (2015)	Cross-sectional	37	Rwanda	Ref-Lab-based	TB-patients	Culture	Unclear	Unclear	Unclear	Unclear
Perez-Tanoira et al (2017	Cross-sectional	1126	Ethiopia	Ref-Lab-based	TB-patients	Culture	LED vs ZN	Unclear	Unclear	Unclear
Taddese, Boja (2017)	Cross-sectional	248	Ethiopia	Ref-Lab-based	TB-patients	Culture	LED vs ZN	Unclear	LED=94, ZN =66	LED =93, ZN =96

*ZN=Ziehl-Nelsen, LED= Light emitting Diode fluorescence Microscopy, FM= Fluorescence Microscopy or conventional microscopy, Lumin, culture (LJ).

APPENDIX TO CHAPTER 4

Table 4.1 ***Socio-demographics and characteristics of study participants (N =14176)***

Variable	**Gender (m=0; f=1**	**Frequency**	**Percent**		
Gender	Males	8746	61.70		
	Females	5425	38.27		
	Unknown	5	0.04		
	Total	14176	100.00		
Age group	**(Male =0, Female = 1, Missing = 7)*				
	Age	Males (%)	Females (%)	Unknown (%)	Total (%)
	0-19	189 (2)	105 (.74)	12 (.09)	294 (2)
	20-39	3619 (26)	2103 (15)	9 (.06)	5722 (40)
	40-59	1778 (13)	1108 (9)	10 (.07)	2886 (20)
	60-79	1268 (9)	827 (6)	13 (.09)	2095 (15)
	80-99	250 (2)	85 (.59)	5 (.03)	335 (3)
	100+	14 (.09)	4(.02)	1 (.007)	18 (.12)

Table 4.2 ***The total number of patients who submitted specimens for examination by age and by facility***

Age group	Borama (%)	Gabiley (%)	HTH (%)	Finsoma (%)	Berbera (%)	Sheikh (%)	Burco (%)	Odweyne (%)	Lasanod (%)	Total
0-19	426 (13.9)	318 (10.4)	1191 (38.7)	289 (9.4)	80 (2.6)	100 (3.3)	402 (13.1)	91 (2.9)	182 (6.3)	3079 (21.8)
20-39	695 (12.2)	392 (6.9)	2156 (37.7)	412 (7.2)	225 (3.9)	519 (9.0)	743 (12.9)	294 (5.2)	288 (5.0)	5724(40.5)
40-59	429 (14.9)	229 (7.9)	1063 (36.7)	185 (6.4)	150 (5.2)	165 (5.0)	402 (13.9)	117 (4.1)	147 (5.0)	2887 (20.4)
60-79	327 (15.6)	213 (10.2)	850 (40.5)	145 (6.9)	79 (3.8)	38 (1.9)	295 (14.1)	41 (1.9)	108 (5.2)	2096(14.9)
80-99	376 (15.5)	246 (10.1)	989 (40.7)	180 (7.4)	80 (3.3)	40 (1.7)	346 (14.3)	41 (1.7)	136 (5.6)	2434(17.3)
100+	4 (22.3)	2 (11.2)	9 (50.0)	2 (11.2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.6)	18(0.3)
Total	1930 (13.7)	1187 (8.4)	5406 (38.3)	1067 (7.6)	535 (3.8)	824 (5.9)	1893 (13.3)	543 (3.9)	754 (5.4)	14139(99.7)

Table 4.3 ***The frequency distribution of specimens' diagnostic outcomes by ZN and LED technology***

Frequency distribution of specimen examination by LED technology			
Outcomes	**Freq.**	**Percent**	**Cum.**
Negative	12837	90.55	90.55
Positive	1320	9.31	99.87
Missing	6	0.04	99.91
Not done	10	0.07	99.98
Unknown	3	0.02	100.00
Total	14176	100.00	
. tab led2			
Test outcomes	**Freq.**	**Percent**	**Cum.**
Negative	12837	90.55	90.55
Positive	1315	9.28	99.83
Missing	4	0.03	99.86
Not done	16	0.11	99.97
DK	4	0.03	100.00
Total	**14176**	**100.00**	
.tab led3			
Test outcomes	**Freq.**	**Percent**	**Cum.**
Negative	9266	91.20	91.20
Positive	866	8.52	99.72
Missing	2	0.02	99.74
Not done	22	0.22	99.96
Unknown	4	0.04	100.00
Total	**10,160**	**100.00**	

Frequency distribution of specimen examination outcomes by ZN technology			
Test outcomes	**Freq.**	**Percent**	**Cum.**
Negative	7676	54.15	54.15
Positive	690	4.87	59.02
Not done	5808	40.97	99.99
Unknown	2	0.01	100.00
Total	14176	100.00	
. tab zn2			
Test outcomes	**Freq.**	**Percent**	**Cum.**
Negative	7650	53.96	53.96
Positive	714	5.04	59.00
Not done	5810	40.98	99.99
Unknown	2	0.01	100.00
Total	14176	100.00	
. tab zn3			
Test outcomes	**Freq.**	**Percent**	**Cum.**
Negative	4893	48.16	48.16
Positive	463	4.56	52.72
Missing	1	0.01	52.73
Not done	4801	47.25	99.98
Unknown	2	0.02	100.00
Total	10160	100.00	

Table 4.4 ***Specimen examination status and disease classifications for ZN technology***

Specimen examination outcomes	**Frequency**	**%**	**Specimen examination outcomes**	**Specimen examination status according to WHO case definitions and disease classifications**
--.	2742	19.34	Negative at 1st and 2nd and scanty 3rd specimen examinations	Negative – meets the WHO case definition for **negative** status
---	4885	34.46	Negative at all 3 specimen examinations	Negative – meets the WHO case definition for **negative** status
--+	1	0.01	Negative at 1st 2 specimens, but positive at 3rd examination	Negative – meets the WHO case definition for **negative s**tatus
--8	1	0.01	Negative at 1st 2 specimens with not done at 3rd examination result	Negative – meets case definition for **negative** status
-+.	43	0.3	Negative at 1st specimen, positive at 2nd with unexamined smear result at 3rd	Unexamined smear – meets the WHO case definition for not done smear status
-+-	2	0.01	Negative at 1st but positive at 2nd specimen but negative at 3rd specimen examination	Negative – meets case definition for **negative** status
-++	2	0.01	Negative at 1st specimens but positive at 2nd and 3rd examinations	Positive – meets the WHO case definition for **positive** status
+-.	18	0.13	Positive at 1st specimen, negative 2nd but smears not examined at 3rd examination	Unexamined smear – meets the WHO case definition for **not done smear** status
+--	3	0.02	Positive at 1st specimen but negative 2nd and 3rd specimen examinations	Negative – meets case definition for **negative** status
++.	204	1.44	Positive at 1st and 2nd specimens but scanty at 3rd examination	Positive – meets the WHO case definition for **positive** status
++-	3	0.02	Positive at 1st and 2nd specimens but negative at 3rd examination	Positive – meets the WHO case definition for **positive** status
+++	459	3.24	Positive at all 3 specimen examinations	Positive – meets WHO case definition for **positive** status
++7	1	0.01	Positive at 1st and 2nd specimens, but result missing for 3rd examination	Positive – meets the WHO case definition for **positive** status
+8.	1	0.01	Positive at 1st specimen, not done at 2nd specimen and scanty at 3rd specimen	Unexamined smear – meets the WHO case definition for not done smear status
+88	1	0.01	Positive at 1st specimen 2nd and 3rd specimen reported not done	Unexamined smear – meets the WHO case definition for not done smear status
88.	1008	7.11	1st and 2nd specimens not done with scanty 3rd	Unexamined smear – meets the WHO case definition for not done smear status
88+	1	0.01	1st and 2nd not done with positive 3rd examination	Unexamined smear – meets the WHO case definition for not done smear status
888	4799	33.85	All 3 specimens were not done or unexamined	Unexamined smear – meets the WHO case definition for not done smear status
999	2	0.01	All 3 specimens examinations were reported as unknown	Unexamined smear – meets the WHO case definition for not done smear status
Total	**14176**			

Table 4.5 ***Specimen examination status and disease classifications for LED technology***

LED	Frequency	%	Specimen examination outcomes	Specimen examination status according to WHO case definitions and disease classifications
--.	3571	25.19	Negative at 1st and 2 specimen examinations) – meeting the WHO definition for smear-negative (SM-)	Negative – meets the WHO case definition for **negative** status
---	9254	65.28	Negative at all 3 specimen examinations) – meets WHO case definition for SM-	Negative – meets the WHO case definition for **negative** status
--+	4	0.03	Negative at 1st 2 specimens and positive at 3rd specimen examination) – meets WHO case definition for SM+	Negative – meets the WHO case definition for **positive** status
--8	1	0.01	Negative at 1st 2 specimen examinations with 3rd smear unexamined, but still meets the WHO case definition for SM-	Negative – meets the case definition for **negative** status
-+-	2	0.01	Negative at 1st and 3rd specimen examinations, but positive at 2nd examination – meets WHO case definition for SM+	Negative – meets the WHO case definition for **negative** status
-++	5	0.04	Positive at 2nd and 3rd specimen examination and negative at 1st examination	Positive – meets the WHO case definition for **positive** status
+-.	1	0.01	Positive at 1st and negative 2nd examination but 3rd specimen unexamined – meets the WHO case definition for SM+	Unexamined smear – meets the WHO case definition for not done smear status
+--	5	0.04	Positive at 1st but negative at 2nd and 3rd specimen examinations	Negative – meets the WHO case definition for **positive** status
+-+	1	0.01	Positive at 1st and 3rd specimen examinations but negative at 2nd examination	Positive – meets the WHO case definition for **positive** status
++.	439	3.1	Positive at 1st and 2nd specimen examinations but unknown at 3rd examination. But meets the WHO case definition for SM+	Positive – meets the WHO case definition for **positive** status
++-	5	0.04	Positive at 1st and 2nd specimen examinations but negative at 3rd examination	Positive – meets the WHO case definition for **positive** status
+++	854	6.02	Positive at all 3 specimen examinations	Positive – meets the WHO case definition for **positive** status
++7	2	0.01	Positive at 1st and 2nd specimen examinations but missing results for 3rd examination	Positive – meets the WHO case definition for **positive** status
++8	5	0.04	Positive at 1st and 2nd specimen examinations with missing results for the 3rd examination	Positive – meets the WHO case definition for **positive** status
+7+	1	0.01	Positive at 1st and 3rd specimen examination with missing results for 3rd examination	Positive – meets the WHO case definition for **positive** status
+88	6	0.04	Positive at 1st specimen examination with unexamined specimens at 2nd and 3rd examinations	Unexamined smear – meets the WHO case definition for smear not done status
+99	1	0.01	Positive at 1st specimen but with unknown results at 2nd and 3rd examinations	Unexamined smear – meets the WHO case definition for smear not done status
7+.	2	0.01	Result missing at 1st specimen but with unknown results at 2nd and 3rd examinations	Unexamined smear – meets the WHO case definition for smear not done status
7++	1	0.01	Missing results at 1st specimen but positive at 2nd and 3rd examinations	Positive – meets the WHO case definition for **positive** status
77.	3	0.02	Result missing at 1st and 2nd specimen examinations but 3rd unexamined – WHO case definition for further test analysis	Unexamined smear – meets the WHO case definition for smear not done status
888	10	0.07	All 3 specimens are recorded as not done (not examined)	Unexamined smear – meets the WHO case definition for smear not done status
999	3	0.02	All 3 specimen examination results are recorded as unknown	Unexamined smear – meets the WHO case definition for smear not done status
Total	**14176**	**100**		

Table 4.6 ***The proportion of patients with negative, positive, missing, not done and unknown diagnostic results by ZN-microscopy stratified by facility for the entire intervention period***

Technology	**1st specimen examination**					
Facility	***Negative (proportion, 95% CIs)***	***Positive (proportion, 95% CIs)***	***Miss (proportion, 95% CIs)***	***Not done (proportion, 95% CIs)***	***Unknown (proportion, 95% CIs)***	***Total (proportions, 95% CIs)***
Borama	1026 (.6, .51- .6)	58 (.03, .03- .04)		856 (.5, .4- .5)	2 (.002, .02- .004)	1942 (.05, . .05- .05)
Gabiley	1122 (.95, .93- .96)	65 (.06, .05- .07)		0	0	1187 (.03, .03- .03)
HTH	1757 (.32, .31- .33)	253 (.05, .04- .06)		3419 (.63, .62- .65)	0	5429 (.13, .13- .14)
Finsoma	496 (.45, .45- .51)	46 (.05- .03- .06)		525 (.49, .46- .53)	0	1067 (.03, .03- .03)
Berbera	490 (.92, .89- .94)	45 (.09, .07- .11)		0	0	535 (02, .02- .02)
Sheikh	591 (.72, .67- .74)	39 (.05, .04- .07)		194 (.24, .21- .27)	0	824 (.02, .02- .03)
Burco	1059 (.56, .54- .58)	117 (.07, .05- .07)		718 (.37, .36- .40)	0	1894 (.05, .05- .05)
Odweyne	435 (.78, .78- .84)	13 (.03, .03- .04)		96 (.12, .15- .23)	0	544 (.02, .02- .02)
Lasanod	700 (.93, .91- .95)	54 (.07, .06- .09)		0	0	754 (.02, .01- .02)
Total	**7676 (.54, .54- .55)**	**690 (.05, .05- .06)**		**5808 (.41, .42- .42)**	**2 (.01, .001- .005)**	**14176 (.34, .33- .34)**
2nd specimen examination						
Facility	***Negative (Proportion, 95%CIs)***	***Positive (Proportion, 95% CIs)***	***Miss (Proportion, 95% CIs)***	***Not done (Proportions, 95% CIs)***	***Unknown (Proportion, 95% CIs)***	***Total (Proportion, 95% CIs)***
Borama	1027 (.53, .50- .55)	57 (.06, .04- .07)		856 (.83, .80- .85)	2 (.001, .002- .007)	1942 (.03, .03- .03)
Gabiley	1123 (.94, .93- .95)	64 (.05, .04- .06)		0	0	1187 (.03, .02- .03)
HTH	1756 (.33, .31- .33)	253 (.05, .04- .06)		3420 (.62, .61- .64)	0	5429 (.12, .12- .13)
Finsoma	494 (.46, .43- .49)	48 (.05, .04- .06)		525 (.49, .46- .53)	0	1067 (.02, .02-03)
Berbera	490 (.92, .88- .93)	45 (.08, .06- .11)		0	0	535 (.01, .01- .02)
Sheikh	595 (.73, .69- .75)	35 (.04, .03- .05)		194 (.23, .20- .26)	0	824 (.02, .02- .03)
Burco	1033 (.54, .52- .56)	142 (.08, .06- .08)		719 (.34, .35- .40)	0	1894 (.05, .04- .05)
Odweyne	434 (.79, .76- .83)	14 (.03, .02- .04)		96 (.12, .14- .22)	0	544 (.01- .01- .02)
Lasanod	698 (.92, .90- .94)	56 (.07- .05- .09)		0	0	754 (.01, .01- .02)
Total	**7650 (.54, .53- .55)**	**714 (.54, .53- .55)**		**5810 (.40, .41- .42)**	**2 (.001, .001-.005)**	**14176 (.33, .32- .34)**
3rd specimen examination						
Facility	***Negative (Proportion, 95%CIs)***	***Positive (Proportion, 95% CIs)***	***Miss (Proportion, 95% CIs)***	***Not done (Proportions, 95% CIs)***	***Unknown (Proportion, 95% CIs)***	***Total (Proportion, 95% CIs)***
Borama	1025 (.53, .50-.55)	58 (.02, .02- .04)	0	857 (.44, .41-.46)	2 (.001, .0001- .003)	1942 (.04- .04- .05)
Gabiley	1123 (.94, .93-.95)	64 (.054, .04- .06)	0	0	0	1187 (.02, .02- .03)
HTH	1757 (.32, .31- .33)	251 (.04, .04- .05)	1 (.001, 4.66e- .001)	3420 (.63, .62- .64)	0	5429 (.12, .12- .13)
Finsoma	498 (.45, .43-.49)	45 (.04, .03-.05)	0	524 (.49, .46-.52)	0	1067 (.03, .02- .03)
Berbera	490 (.91, .88-.93-)	45 (.08, .06- .12)	0	0	0	535 (.01, .01- .02)
Total	**4893 (.48, .47- .49)**	**463 (.04, .04- .04)**	**1 (.001, 2.49e-06- .0005)**	**4801 (.47, .46- .48)**	**2 (.001, .002- .007)**	**10160 (.23, .23-.24)**

Table 4.7 ***The proportion of patients with negative, positive, missing, not done and unknown diagnostic results by LED-microscopy stratified by facility for the entire intervention period***

	1st specimen examination					
Facility	**Negative (proportions, 95% CIs)**	**Positive (proportions, 95% CIs)**	**Miss (proportions, 95% CIs)**	**Not done Appendix D: (proportions, 95% CIs)**	**Unknown (proportions, 95%CIs)**	**Total (proportions, 95% CIs)**
Borama	1831 (.94, .93- .95)	100 (.05, .04- .06)	0	8 (.004, .001- .008)	3 (.002, .003- .004)	1942 (.04, .04- .05)
Gabiley	1117 (.94, .92-.95)	70 (.06, .04- .07)	0	0	0	1187 (.02, .02- .03)
HTH	4848 (.89, .88- .90)	580 (.10, .09- .11)	0	1 (.001, 4.66e-06- .001)	0	5429 (.12, .13- .13)
Finsoma	980 (.91, .90- .93)	85 (.07, .06- .09)	1 (.001, .001- .005)	1 (.001, .001- .005)	0	1067 (.02, .02- .03)
Berbera	490 (.91, .88- .93)	45 (.08, .06- .11)	0	0	0	535 (.01, .02- .02)
Sheikh	736 (.89, .87- .91)	88 (.10, .08- .12)	0	0	0	824 (.02, .02- .02)
Burco	1650 (.87, .85- .88)	239 (.12, .11- .14)	5 (.002, .0008- .0061)	0	0	1894 (.045, .04, .05)
Odweyne	499 (.91, .89- .93)	45 (.08, .06- .10)	0	0	0	544 (.02, .01- .02)
Lasanod	686 (.90, .88- .92)	68 (.09, .07- .11)	0	0	0	754 (.02, .02- .0190289
Total	12837 (.90, .90- .91)	1320 (.09, .08- .09)	6 (.0004, .0001- .0009)	10 (.0007, .0003- .0012)	3 (.0002, .0004- .0006)	14176 (.04, .03- .04)
Facility	***Negative***	***Positive***	***Miss***	***Not done***	***Unknown***	***Total***
	2nd specimen examination					
Borama	1828 (.94, .92- .95)	102 (.05, .04- .06)	0	8 (.004, .001- .008)	4 (.002, .0005- .0052)	1942 (.04, .04- .05)
Gabiley	1119 (.94, .93- .95)	68 (.05, .05- .08)	0	0	0	1187 (.02, .03- .03)
HTH	4847 (.89, .88- .90)	574 (.10, .09- .11)	1 (.0001, 4.6e-06 - .00102)	7 (.002, .0005 - .0026)	0	5429 (.13, .12- .13)
Finsoma	981 (.91, .90- .93)	85 (.08, .06- .09)	0	1 (.0009, .00002- .00521)	0	1067 (.03, .02- .03)
Berbera	490 (.92, .88- .93)	45 (.08, .06- .11)	0	0	0	535 (.02, .01- .02)
Sheikh	736 (.89, .87- .91)	88 (.10, .08- .12)	0	0	0	824 (.01, .01- .02)
Burco	1651 (.87, .85- .88)	240 (.12, .11- .14)	3 (.001, .0003- .0046)	0	0	1894 (.05, .04- .05)
Odweyne	499 (.91, .89- .93)	45 (.08, .06- .10)	0	0	0	544 (.01, .01- .02)
Lasanod	686 (.90, .88- .92)	68 (.09, .07- .11)	0	0	0	754 (.01, .01- .02)
Total	12837 (.90, .90- .91)	1315 (.09, .08- .09)	4 (.0002, .00007- .00072)	16 (.001, .0006- .0018)	4 (.0002, .00007- .00072)	14176 (.33, .32- .34)
	3rd specimen examination					
Facility	***Negative (proportions, 95% CIs)***	***Positive (proportions, 95% CIs)***	***Miss (proportions, 95% CIs)***	***Not done (proportions, 95% CIs)***	***Unknown (proportions, 95%CIs)***	***Total (proportions, 95% CIs)***
Borama	1825 (.93, .92- .94)	104 (.05, .04- .06)	0	9 (.004, .002- .008)	4 (.002, .0005- .005)	1942 (.04, .04- .05)
Gabiley	1117 (.94, .92- .95)	70 (.05, .05- .07)	0	0	0	1187 (.02, .03- .03)
HTH	4848 (.89, .88- .90)	567 (.10, .09- .11)	2 (.0003, .00004- .00133)	12 (.002, .001- .0038)	0	5429 (.13, .12- .13)
Finsoma	986 (.92, .90- .93)	80 (.07, .05- .09)	0	1 (.0009, .00002- .00521)	0	1067 (.03, .02- .03)
Berbera	490 (.91, .88- .93)	45 (.08, .06- .11)	0	0	0	535 (.02, .01- .02)
Total	9266 (.91, .90- .91)	866 (.08, .07- .09)	2 (.0002, .00003- .00071)	22 (.003, .002- .004)	4 (.0004, .0001- .0010)	10160 (.24, .23- .25)

Table 4.8 The proportions of patients with specimens with negative and positive outcomes by ZN and LED and by gender

ZN1	**Gender**		
Diagnostic outcomes	***Males (Proportions, 95% CIs)***	***Females (Proportions, 95% CIs)***	***Total (Proportions, 95% CIs)***
Negative	4592 (.90, .89- .91)	3082 (.94, .93- .94)	7676 (.91, .91-.93)
Positive	496 (.09, .08- .10)	194 (.05, .05-.06)	690 (.08, .07-.08)
Total	**5088 (.60, .59- .61)**	**3276 (.39, .38- .40)**	**8366 (.59, .58-.59)**
ZN2	**Gender**		
Diagnostic outcomes	*Males*	*Females*	*Total*
Negative	4573 (.10, .09-.10)	3075 (.93, .92-.94)	7650 (.91, .90- .92)
Positive	513 (.10, .09-.11)	201 (.06, .05- .07)	714 (.08, .08-.09)
Total	**5086 (.60, .59-.61)**	**3276 (.39, .38- .40)**	**8364 (.59, .58- .59)**
ZN3	**Gender**		
Diagnostic outcomes	*Males*	*Females*	*Total*
Negative	2855 (.89, .88-.90)	2036 (.93, .92-.95)	4893 (.91, .90- .92)
Positive	324 (.10, .09-.11)	139 (.06, .05- .07)	463 (.08, .07-.09)
Total	**3179 (.59, .58-.60)**	**2175 (.40, .39-.41)**	**5356 (.37, .36- .38)**
Led1	**Gender**		
Diagnostic outcomes	*Males*	*Females*	*Total*
Negative	7790 (.89, .88-.89)	5042 (.93, .92-.93)	12837 (.90, .90-.91)
Positive	941 (.10, .10-.11)	379 (.06, .06-.07)	1320 (.09, .08-.09)
Total	8731 (.61, .60- .62)	5421 (.38, .37-.39)	14157 (.99, .99- .100)
Led2	**Gender**		
Diagnostic outcomes	*Males*	*Females*	*Total*
Negative	7792 (.89, .88-.89)	5040 (.93, .92-.93)	12837 (.90, .90-.91)
Positive	939 (.10, .10-.11)	376 (.06, .06- .07)	1315 (.09, .08- .09)
Total	8731 (.61, .60-.62)	5416 (.38, .37-.39)	14152 (.99, .99-.100)
Led3	**Gender**		
Diagnostic outcomes	*Males*	*Females*	*Total*
Negative	5516 (.59, .58- .60)	3746 (.40, .39-.41)	9266 (.65, .64-.66)
Positive	614 (.70, .67-.73)	252 (.29, .26-.32)	866 (.06, .05-.06)
Total	**6130 (.60, .59-.61(**	**3998 (.39, .38-.40)**	**10132 (.71, .70- .72)**

Table 4.9 ***Comparison of proportions of patients with negative, positive and unknown test outcomes by facility***

Technology	**ZN**				**LED**			
Facility	**Negative (n/N, 95% CIs)**	**Positive (n/N, 95% CIs)**	**Unknown (n/N, 95% CIs)**	**Total (n/N, 95% CIs**	**Negative (n/N, 95% CIs)**	**Positive (n/N, 95% CIs)**	**Unknown (n/N, 95% CIs)**	**Total (n/N, 95% CIs)**
Borama	1027 (.52, .50 .55	57 (.03, .02- .04)	859	**1943 (.13, .13- .14)**	1828 (.94, .92- .95)	102 (.05, .04- .06)	12 (.006, .003- .010)	**1942 (.13, .13- .14)**
Gabiley	1123 (.94, .93- .95)	64 (.05, .04, .06)	0	**1187 (.08, .07- .09)**	1118 (.94, .92- .95)	69 (.05, .04- .07)	0	**1187 (.08, .07- .08)**
HTH	1756 (.32, .31- .33)	253 (.21, .19- .23)	3420 (.62- .64)	**5429 (.38, .37-.39)**	4847 (.89, .88- .90)	575 (.10, .09- .11)	7 (.001,.005- .002)	**5429 (.38, .37-.39)**
Finsoma	496 (.46, .43- .49)	46 (.04, .03- .05)	525 (.49, .46- .52)	**1067 (.07, .07- .08)**	983 (.92, .90- .93)	83 (.07, .06-.09)	1 (.009, .0023- .0052)	**1067 (.07, .07- .08)**
Berbera	490 (.91, .88- .93)	45 (.08, .06- .11)	0	**535 (.03, .03- .04)**	490 (.91,.88- .93)	45 (.08, .06- .11)	0	**535 (.03, .03- .04)**
Sheikh	587 (.71, .68- .74)	31 (.03, .02- .05)	206 (.25, .22- .28)	**824 (.05, .05- .07)**	736 (.89, .87- .913)	88 (.10, .08- 12)	0	**824 (.05, .05- .06)**
Burco	1026 (.54, .51- .56)	109 (.05, .04- .06)	759 (.40, .37-.42)	**1894 (.13, .12-.13)**	1650 (.87, .85-.88)	238 (.12, .11-.14)	6 (.003, .001- .006)	**1894 (.13, .12-.13)**
Odweyne	434 (.79, .76- .83)	13 (.02, .01- .04)	97 (.17, .14-.21)	**544 (.03, .03- .04)**	499 (.91, .89- .93)	45 (.08, .06- .10)	0	**544 (.03, .03- .04)**
Lasanod	695 (.92, .90- .93)	51 (.06, .05-.08)	8 (.01, .004- .020)	**754 (.05, .04- .05)**	686 (.90, .88-.92)	68 (.09, .07- .11)	0	**754 (.05, .04- .05)**
Total	7634 (.53, .53- .54)	669 (.04, .04- .05)	5874 (.41,.40- .42)	**14176 (.99, .99-.99)**	12837 (.90, .90- .91)	1313 (.09, .08- .09)	26 (.001, .001-.002)	**14176 (.99, .99- .99)**

Table 4.10 ***The total number of patients with positive, negative and unknown (missing, unknown and not done) diagnostic test results by technology and by facility***

Technology	**ZN**			**LED**		
Facility	**Negative (n/N, 95% CIs)**	**Positive (n/N, 95% CIs)**	**Unknown (n/N, 95% CIs)**	**Negative (n/N, 95% CIs)**	**Positive (n/N, 95% CIs)**	**Unknown (n/N, 95% CIs)**
Borama	1027	57	859	1828	102	12
Gabiley	1123	64	0	1118	69	0
HTH	1756	253	3420	4847	575	7
Finsoma	496	46	525	983	83	1
Berbera	490	45	0	490	45	0
Sheikh	587	31	206	736	88	0
Burco	1026	109	759	1650	238	6
Odweyne	434	13	97	499	45	0
Lasanod	695	51	8	686	68	0
Total	7634	669	5874	12837	1313	26

Table 4.11 ***The proportion of patients with positive and negative test results by ZN and LED technologies***

	LED technology		
ZN technology	**Exposed**	**Unexposed**	**Total**
Exposed	1819	5	1824
Unexposed	239	19981	20220
Total	2058	19986	22044

McNemar's chi2(1) = 224.41 Prob > chi2 = 0.0000
Exact McNemar significance probability = 0.0000

	Proportion with factor		
	Cases	**.0827436**	
Controls	**.0933587**	**[95% Conf. Interval]**	
difference	**-.0106151**	**-.0120423**	**-.009188**
ratio	**.8862974**	**.8724023**	**.9004138**
rel. diff.	**-.0117082**	**-.013249**	**-.0101674**
odds ratio	**.0209205**	**.0067313**	**.0495057 (exact)**

Working definitions to chapter 4:

Tuberculosis (TB): Tuberculosis is a re-emerging zoonotic disease caused primarily by Mycobacterium tuberculosis[286, 342].

TB is a potentially fatal contagious diseasethat can affect almost any part of the body but is mainly a n infection of the lungs[12].

Having *Mycobacterium tuberculosis* complex can be identified from a clinical specimen, either by culture or by molecular tests, such as Genexpert MTB/RIF or line probe assay[286].

A definite case of tuberculosis: A definite case of TB (defined above) is one in which a health worker (clinician or medical practitioner) has diagnosed a patient with TB and has decided to treat the patient with a full course of TB treatment[343]. A patient with *Mycobacterium tuberculosis* complex can be identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay. In countries that lack the laboratory capacity to routinely identify pulmonary TB with one or more initial sputum smear examinations positive for acid-fast bacilli is also considered to be a "definite" case, provided that there is a functional external quality assurance system with blind rechecking[344].

***Presumptive of TB**:* A person to be evaluated for TB; sometimes used to define a person who presents with symptoms or signs suggestive of TB[344]. The most common symptom of pulmonary TB is a productive cough for more than two weeks, which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

***Case notification**:* Notification refers to the obligation of health workers to register the name of each person diagnosed with TB, usually in the TB register. Data on the number of cases are then reported at regular intervals to national health authorities[344].

Case detection rate: This is referred to as the number of reported cases per 100,000 persons per year divided by the estimated incidence rate per 100,000 per year. When a person is diagnosed with TB, they should be registered and reported within the national TB surveillance system and then to the World Health Organization [345, 346]. TB incidence is uncertain and not measured but estimated: therefore, the case detection rate is uncertain. A new indicator to assess case detection known as "the

patient diagnostic rate" has been proposed and introduced and used to estimate TB infection level in a country[347].

Unknown specimens: These were defined as specimens from patients with a known facility visit date and identification number in the TB register but with no confirmed diagnostic test results in the register. These specimens were classified as *unknown*, given a numeric value of "9", and excluded from the analysis.

Missing specimens: These were defined as specimens from patients with a known diagnostic test (either negative or positive) with a facility visit date and identification number in the TB register but with one or more missing diagnostic test results[348]. These types of specimens were classified as *missing* and were given a numeric value of ″7″. These specimens were excluded or dropped from the analysis. The difference between missing and unknown test outcomes is that missing data (or missing values) is referred as the diagnostic tests with one or more missing test outcomes recorded in the TB register for a specific variable in the observation of interest[238, 240]. *Missing* and *unknown* values are common patterns in the WHO TB case notification country reports: these can have a significant impact on statistical inferences or potential conclusions drawn from such analysis if not handled appropriately.

Not done (unexamined) specimens: All specimens from patients with a known identification number in the TB register where there were one or more unexamined specimens were classified as *not done* and excluded from the analysis. In this analysis, all these specimens were classified as *not done*, were given a numeric value of "8", and excluded from the specimen level analysis.

Scanty specimens : If microscopic examinations revealed the presence of acid-fast bacilli or TB disease in at least one specimen examined for each individual patient they were regarded as ″definite positive″[239]. The WHO and its global TB control partners advise facility health workers to record all tests with unclear results as a *″scanty″* or 'doubtful' result for further diagnostic analysis[344]. Therefore, all observations with fewer AFB than the number needed to qualify as a ″positive″ result were classified as *″scanty″*, and thus excluded from this analysis[239].

Patients' positivity rate (patient diagnostic rate): This is the rate at which prevalent cases are detected by control programs and can be measured as the number of reported cases per 100,000 persons per year divided by the prevalence per 100,000[347, 349].

Smear positive TB case: The revised definition of a new sputum smear-positive pulmonary TB case is based on the presence of at least one acid-fast bacilli (AFB+) in at least one sputum sample in countries with a well-functioning external quality assurance (EQA) system[241].

Smear negative TB case*:* A patient with a minimum of two sputum microscopy smear examinations negative for AFB, but with a chest-X ray suggesting TB, and this is unresponsive to a course of broad-spectrum antibiotics (except in a patient with strong clinical evidence of HIV infection)[344].

Data analysis: The process of evaluating data using analytical and logical reasoning to examine each component of the data provided. It is a process of inspecting, cleansing, transforming and modelling data to discover useful information, informing a conclusion and supporting decision-making[350].

Specificity*:* This is the proportion of those that do not have the condition for which the diagnostic test is negative[235]. To study specificity, a separate study would have to be conducted in which subjects were drawn from the population of individuals without the disease. The data from such a study could be analysed with this procedure by changing the meaning of positive and negative[235]. Instead of positive meaning that the person had the disease, positive would mean that the diagnostic test result matched the true condition of the subject. Likewise, negative would mean that the diagnostic test result did not match the subject's true condition. In the procedure printouts, you would substitute specificity for sensitivity[235, 237].

Prevalence: This quantifies the proportion of individuals in a population who are ill with TB at a specific point in time. It is usually given as the number of affected individuals per 100 00[344].

Screening: This refers to the systematic identification of people with active TB in a predetermined target group by the application of tests, examinations or other procedures that can be applied rapidly [351]. Among those with potential TB, the diagnosis needs to be established through the application of diagnostic tests and clinical assessment with high combined specificity[344].

APPENDIX TO CHAPTER 5

Table 5.1 ***Generated codes for emerging themes in responses to interview questions in HCWs' interviews***

Themes (Interview questions)	Initial codes
1. Current position at facility	- Clinical (normal) - Qualified Nurse (Head nurse) - Inventory Nurse - DOTS Nurse (infection control) - General outpatient (OPD) Nurse - Auxiliary nurse - Counselling nurse - Ward aid nurse - Triage nurse
2. Duration in this current position at facility	- 0-5 years - 6-10 years - Over 10 years
3. Previous knowledge/experience/skills in TB care (including diagnosis)	- No previous experience in TB care - Had experience in TB care - Worked in TB care before but not trained - Worked in TB care facilities but not on TB - Trained in TB but never worked in TB care - Had experience and training in TB care
4. Knowledge/skills/experience in TB diagnosis	- Highly knowledgeable in LED use - Adequately knowledgeable - Limited knowledge in LED use - No knowledge in LED use - Highly experienced/skilled in LED use - Not skilled/experienced in LED use - Formally trained in LED use
5. Barriers to acceptability of LED use	- Resources are inadequate (human, financial and structural) - Lack of training in new technology use is a significant barrier - Health system (laboratory) lacks infrastructural capacity to support - New technologies overwhelm an already weak system - Existing system cannot support LED introduction and use - Health system not sufficiently prepared to implement LED - LED maintenance/spare parts unavailable locally
6. Describe your knowledge and skills in LED use	- Sufficiently knowledgeable in LED use - Highly knowledgeable - Limited knowledge in LED use - No knowledge in LED use - Highly skilled in LED use - Not skilled in LED use at all - Formally trained in LED use

Table 5.1 ***Generated codes for emerging themes in responses to interview questions in HCWs' interviews (continued)***

Themes (Interview questions)	Initial codes
7. Role/responsibility	- Patients registration - Triage at OPD - Assist patients with sputum production (specimens) - Preparation and examination of specimens - Documentation of patients' tests and treatment results - Patient diagnosis and treatment counselling - Perform tests for different tests
8. Previous experience in TB care (including diagnosis)	- No previous experience in TB diagnosis - Had some experience in TB diagnosis - Worked in TB diagnosis before but not trained - Worked in TB diagnosis facilities but not on TB - Trained in TB but never worked in TB diagnosis - Had experience and training in TB diagnosis
9. Opinion on LED use for routine testing	- More sensitive than ZN microscopy - Enhances staff performance in TB testing - Increases TB case finding - LED is higher maintenance than ZN - Staff not sufficiently trained in LED use - Staff not trained in LED maintenance/repair - LED spare parts not available locally - No increased sensitivity in LED and ZN - Increases workload (it takes 15 minutes per slide staining compared to 5 under ZN) - LED use is unclean and needs more resources to maintain
10. Perceptions towards LED use	- Better than direct light microscopy [ZN] - Enhances staff performance in TB testing - Increases TB case finding - It needs more maintenance than ZN - Staff not sufficiently trained in LED use - Staff not trained in LED maintenance and repair - LED spare parts not available in country - No difference between LED and direct light in testing quality - Increases workload (it takes 15 minutes per slide staining compared to 5 under ZN) - LED use is unclean and needs more resources to maintain
11. Deficiencies in resources at facility	- Resources are inadequate (human, financial and structural) - Lack of training in new technology use is a major barrier - Health system (laboratory) lacks infrastructural capacity to support - New technologies overwhelm an already weak system - Existing system cannot support LED introduction and use - Health system not sufficiently prepared to implement LED - Maintenance and spare parts of LED unavailable locally
12. Barriers to LED implementation	- Lack of training for staff in LED use - LED use takes more time in specimen examination - No increased sensitivity compared to ZN but more time for specimen examination - LED high maintenance/repair if broken
13. Formal education/training in TB care	- No formal training in TB care - No formal training in TB diagnosis

Table 5.1 ***Generated codes for emerging themes in responses to interview questions in HCWs' interviews (continued)***

Themes (Interview questions)	Initial codes
14. Perceptions of LED usefulness for TB testing	- Better than direct light microscopy (ZN) - Enhances staff performance in TB testing - Increases TB case finding - It needs more maintenance than ZN - Staff not sufficiently trained in LED use - Staff not trained in LED maintenance and repair - LED spare parts not available in country - No difference between LED and direct light in testing quality - Increases workload (it takes 15 minutes per slide staining compared to 5 under ZN) - LED use unclean and needs more resources to maintain
15. Perceived usefulness of LED use	- Received formal education in TB diagnosis - No formal education in TB diagnosis - Received formal training in TB diagnosis - No formal training in TB diagnosis - Adequate knowledge in TB diagnosis - Inadequate knowledge in TB diagnosis
16. LED acceptance among staff	- LED - Genexpert - Chest X-rays - Light Probe Assay - Digital X-rays
17. Things participants wish to see changed at a facility level	- Train staff in new technology use to improve access to quality diagnosis for all TB patients - Motivate staff to enhance the quality of care and consistency - Train staff in LED use, maintenance/repairs to reduce delayed diagnosis - Introduce proper recording and reporting protocols/systems for complete, accurate, standardised care for all TB patients - All diagnostic/treatment decisions should be made at facility
18. Tools used for routine testing at facility	- Adequate experience in TB diagnosis - Inadequate experience in TB diagnosis - Have the right skills for TB diagnosis - Does not have the right skills for TB diagnosis
19. Tools used for routine treatment decisions	- Inadequate training in LED use among staff - Guidelines not available for LED use at lab facilities - Staff technology preferences - Increased workload associated with LED routine use - LED use is more time-consuming compared to ZN - Few facilities introduced LED technology
20. Things participants wish to see changed at a regional level	- Effective leadership in disease control at facility, regional and national levels - Improve collaboration and streamline primary care services
21. Things participants wish to see changed at a national level	- Change in leadership, policy and strategic direction at MOH/Level - Policy and strategic focus on TB agenda needed at MOH/NTP) level - Increase funding for TB control locally (need to stop Nairobi model)

Table 5.1 ***Generated codes for emerging themes in responses to interview questions in HCWs' interviews (continued)***

Themes (interview questions)	Initial codes
22. How LED use influences diagnostic and treatment decisions	- LED is more sensitive and specific than ZN in TB testing - LED tests are more reliable and accurate than ZN - LED use enhances staff performance in TB testing - No difference between LED and ZN in testing quality - Increases workload (it takes 15 minutes per slide staining - compared to 5 under ZN)
23. Feasibility of LED for routine testing	- LED not feasible due to lack of staff training in its use - Guidelines for LED use not available at facility - Low literacy in use of diagnostic/treatment guidelines among staff - Low staff motivation due to lack of incentives (salaries) - System not sufficiently prepared for LED introduction and use - Lack of resources (financial, infrastructural)
24. Tools GPs base routine diagnostic/treatment decisions on	- Mostly on LED test results - No preferences for tools available for routine use - Prefer Genexpert over LED test results - Chest X-rays are reliable than LED - Other diagnostic tools - LED considered more reliable/suitable for routine - Staff trained in use of tools
25. Resource deficiencies at facilities	- Inadequate resources (human, financial and structural) - Lack of training in new technology use is a major barrier - Existing lab-system lacks infrastructural capacity to support new technologies - New technologies overwhelm an already weak system - Existing system cannot support LED introduction and use - Health system not sufficiently prepared to implement LED - Maintenance/spare parts for LED not available locally

Table 5.2 ***The thematic analysis of HCWs' responses to interview questions (all interview transcripts)***

Themes (Interview questions)	HCWs' responses to research questions)	Frequency of emerging themes in interview transcripts	n/N (%)
1. Current position at facility	- I'm lab tech-in-charge	04	04/25 (12.00)
	- Do routine lab work with no responsibilities	12	12/25 (48.00)
	- Work as an inventory lab technician	01	01/25 (04.00)
	- Lab technician responsible for infection control	01	01/25 (04.00)
	- Lab technician responsible for quality control (internal)	01	01/25 (04.00)
	- Work on triage at OPD	03	03/25 (12.00)
	- I'm a DOTS nurse	03	03/25 (12.00)
	- Counselling and flow-up nurse	03	03/25 (12.00)
	- Patient educator	03	03/25 (12.00)
	- Outreach nurse	03	03/25 (12.00)
	- General physician in TB care (facility-level)	04	04/25 (16.00)
	- Multi-drug resistant tuberculosis designates	02	02/25 (08.00)
2. Duration in current position at facility	- Worked at this centre for less than 1 year now	03	03/25 (12.00)
	- I have been working at this facility for 9 months	01	01/25 (04.00)
	- It's close to 2 years since I started working at this facility	02	02/25 (08.00)
	- I started working here 2 ½ years ago	02	02/25 (08.00)
	- Worked at this centre for over 3 years	03	03/25 (12.00)
	- Worked at this centre for 5 years	02	02/25 (08.00)
	- Worked for more than 6 years	03	03/25 (12.00)
	- Started working 7 years ago	02	02/25 (08.00)
	- Worked here close to 9 years	03	03/25 (12.00)
	- Worked here for 9 to 10 years	02	02/25 (08.00)
	- Worked here for more than 20 years	02	02/25 (08.00)

Table 5.2 ***The thematic analysis of HCWs' responses to interview questions (all interview transcripts) (continued)***

Themes (Interview questions)	HCWs' responses to research questions	Frequency of emerging themes in interview transcripts	n/N (%)
3. Previous experience/training in TB care (including diagnosis)	- No previous experience in TB diagnosis	20	20/25 (80.00)
	- No previous training in TB care (including diagnosis)	19	19/25 (76.00)
	- Had sufficient experience in TB diagnosis but no training	22	22/25 (88.00)
	- Worked in TB care (including diagnosis) prior to current job	02	02/25 (08.00)
	- Had experience and training in TB diagnosis	11	11/25 (05.00)
4. Types of tests performed at facility	- Smear microscopy performed at facility	23	23/25 (92.00)
	- Drug susceptibility performed at facility	23	23/25 (92.00)
	- Radiography imaging (chest X-rays – digital)	06	06/25 (24.00)
	- Conventional culture performed at facility	01	01/25 (04.00)
	- Helping with sputum collection process is part of my job	11	11/25 (44.00)
5. Tools used for routine testing at facility	- LED is used more frequently than other tools	24	24/25 (96.00)
	- Genexpert use is combined with LED for routine testing at facility	04	04/25 (16.00)
	- We combine LED, Genexpert and chest X-rays	03	03/25 (12.00)
	- Usually LED is used in parallel with Genexpert and culture	15	15/25 (60.00)
6. LED introduced at facility	- LED has been introduced at facility for 6 years now	15	15/25 (60.0)
	- LED introduced but not as intended due to lack of staff training	13	13/25 (52.00)
	- LED introduced but never used for routine testing	10	10/25 40.00)
	- LED introduced but not used due to lack of guidelines in its use	07	07/25 (28.00)
	- LED introduced at facility but stopped due to maintenance problems	01	01/25 (04.00)
	- LED not used for testing due to lack of reliable power supply	11	11/25 (44.00)

Table 5.2 ***The thematic analysis of HCWs' responses to interview questions (all interview transcripts) (continued)***

Themes (Interview questions)	HCW's responses to research questions	Frequency of emerging themes in interview transcripts	n/N (%)
7. LED implemented as initially intended	- LED implemented as intended	17	17/25 (68.00)
	- LED not implemented as intended due to system issues	03	03/25 (12.00)
	- LED implementation varies across facilities	04	04/25 (16.00)
	- No, LED has not been implemented as intended	13	13/25 (52.00)
	- Hard to tell	02	02/25 (08.00)
8. Reason (s) for LED not implemented as intended	- Existing lab infrastructures cannot support LED implementation	19	19/25 (76.00)
	- Lack of staff training in LED use affects implementation	22	22/25 (88.00)
	- Inadequate training in LED use among staff is very high	23	23/25 (92.00)
	- Routine/refresher training in use and maintenance for lab staff needed	18	18/25 (72.00)
	- Staff not trained in protocol use at facility	12	12/25 (48.00)
	- Face difficulties with LED maintenance/repair	15	15/25 (60.00)
	- No clear protocol provided for LED use at facility level	07	07/25 (28.00)
	- Guidelines not available for LED use at lab facilities	22	22/25 (88.00)
	- Staff preferences for LED technology use over ZN is a barrier	01	01/25 (04.00)
	- Increased workload associated with LED routine use	12	12/25 (48.00)
	- LED use is more time consuming compared to ZN	21	21/25 (84.00)
9. LED presently used for routine testing	- LED used for regular testing but not as anticipated	18	18/25 (72.00)
	- Not used due to lack of staff training in LED use	19	19/25 (76.00)
	- Guidelines not available for LED use at facility level	13	13/25 (52.00)
	- Low literacy in TB diagnosis/treatment guidelines affects routine LED use	17	17/25 (68.00)
	- Lack of or limited knowledge in LED use	22	22/25 (88.00)
	- Low staff motivation due to financial incentives	21	21/25 (84.00)
10. Perceptions towards LED use	- LED is perceived very useful for TB diagnosis	24	24/25 (96.00)
	- LED not perceived as useful, just more work	02	02/25 (08.00)
	- Perceived easy to use for routine testing	24	24/25 (96.00)
	- No preference for LED over ZN	01	01/25 (04.00)
	- More time consuming than ZN	15	15/25 (60.00)
	- Higher maintenance/repair than ZN	15	15/25 (60.00)
	- Inadequate training among staff in LED use	03	03/25 (12.00)
	- Perceived unsuitable for this environment	01	01/25 (04.00)
	- Increases lab workload because it takes more time to stain slides	12	12/25 (48.00)
	- LED use unclean/high maintenance	11	11/25 (44.00)
	- Facility not equipped to support LED use for routine testing	20	20/25 (80.00)
	- Perceived as unhealthy (causes cancer)	07	07/25 (28.00)
	- Guidelines unavailable at facility	16	16/25 (64.00)

Table 5.2 ***The thematic analysis of HCWs' responses to interview questions (all interview transcripts) (continued)***

Themes (Interview questions)	HCWs' responses to research questions	Frequency of emerging themes in interview transcripts	n/N (%)
11. Staff training in LED use	- Lab technicians received training in LED use for routine testing	10	10/25 (40.00)
	- Lab technicians received no training in LED use for routine testing	12	12/25 (48.00)
	- Lab technicians received training in LED use but not sufficient	15	15/25 (60.00)
	- Staff need for more refresher/routine training in LED use	20	20/25 (80.00)
	- Received formal education in TB diagnosis	01	01/25 (04.00)
	- No formal education in TB care including diagnosis	23	23/25 (92.00)
	- No formal training in TB diagnosis	22	22/25 (88.00)
	- Inadequate knowledge/experience in TB diagnosis	22	22/25 (88.00)
	- Need for routine/continued at all facilities	24	24/25 (96.00)
12. Deficiencies in staff training	- Lack of training in new technology use (i.e., LED) is a major deficiency	19	19/25 (76.00)
	- Laboratory facilities lack infrastructural capacity to support	15	15/25 (60.00)
	- New technologies overwhelm existing health system	10	10/25 (40.00)
	- Existing health system not fit for LED implementation	17	17/25 (68.00)
	- Inadequate knowledge/training in maintenance repair of LED	24	24/25 (96.00)
13. LED accepted among facility staff	- LED widely accepted among staff	23	23/25 (92.00)
	- LED accepted but not widely among staff	02	02/25 (08.00)
14. Barriers to LED acceptance	- Lack of training for staff for maintenance/repairs	24	24/25 (96.00)
	- Takes more time in specimen staining	13	13/25 (52.00)
	- More time for specimen examination than ZN	12	12/25 (48.00)
	- Staff lacks knowledge/experience in LED maintenance/repairs	23	23/25 (92.00)
15. Most reliable tools for TB testing	- LED is the most reliable of all diagnostic tools	13	13/25 (52.00)
	- Culture is the most reliable, and we use it as the reference standard for routine testing	10	10/25 (40.00)
	- None of the tools is reliable as we miss cases	11	11/25 (44.00)
	- Genexpert is the most reliable of all the tests	15	15/25 (60.00)
	- We use LED combined with Genexpert to increase reliability	24	24/25 (96.00)
	- Chest X-rays are used, mainly for children	04	06/25 (24.00)
	- Not sure any of the tools are reliable due to knowledge issues	05	05/25 (20.00)

Table 5.2 ***The thematic analysis of HCWs' responses to interview questions (all interview transcripts) (continued)***

Themes (Interview questions)	HCWs' responses to research questions	Frequency of emerging themes in interview transcripts	n/N (%)
16. LED use enhances staff performance	- Staff received no refresher training since LED introduction	20	20/25 (80.00)
	- Staff received feedback from managers in LED use	05	05/25 (20.00)
	- LED enhances staff performance in TB testing	11	11/25 (44.00)
	- Unclear if LED enhances staff performance in TB testing	07	07/25 (28.00)
	- Staff prefers LED use over ZN for routine TB testing	07	07/25 (28.00)
17. Challenges faced in LED use	- Existing system cannot support LED for routine use	21	21/25 (84.00)
	- Inadequate knowledge/experience in LED use among staff (all levels)	24	24/25 (96.00)
	- Don't have enough knowledge in LED maintenance	22	22/25 (88.00)
	- LED technology spare parts not available locally	25	25/25 (100.00)
	- System unfit to support LED implementation	18	18/25 (72.00)
18. Things participants wish to see changed at the facility level	- Train staff more in LED use for routine testing	24	24/25 (96.00)
	- Improve diagnostic service capacity to support LED routine use	17	17/25 (68.00)
	- Increase facility staff numbers	08	08/25 (32.00)
	- Introduce incentives for staff to improve performance in LED use	23	23/25 (92.00)
	- Reinforce lab diagnostic guidelines use at facility level	12	12/25 (48.00)
	- Introduce proper documentation of patients' tests/treatment outcomes	17	17/25 (68.00)
19. In TB care/diagnosis that participants wish to see changed at the regional level	- Clear and comprehensive TB control strategy at local levels	11	11(25 (44.00)
	- Improve access to quality diagnosis through coordinated TB care activities	13	13/25 (52.00)
	- Align TB control activities within and between facilities	10	10/25 (40.00)
	- The region should have an active role in TB control activities	09	09/25 (36.00)
	- Improve collaboration and streamline primary care services	05	05/25 (20.00)
Things participants wish to see changed at the national level	- Change in leadership, policy and strategic direction at MOH/Level	07	07/25 28.00)
	- Policy/strategic focus on TB control at MOH/NTP) level	04	04/25 (16.00)
	- Increase funding for TB control locally	02	02/25 (08.00)
	- More resources (financial and human) needed for TB control	03	03/25 (12.00)
	- Need for more private sector engagement	06	06/25 (24.00)

* A theme is defined as a pattern that captures something significant or interesting about the data and research. Themes are patterns across the data set that are important to the description of the attributes of the data related to a research subject[352].

Table 5.3 ***The summary of HCWs' responses to KAPs interview questions (N= 25)***

HCWs' responses to questions (all interview data)	Frequency of HCWs' responses (all documents)	Coded segments of all interview transcripts (%)	Number of documents feeding thematic analysis
- Smear microscopy performed	23/25	92.00	25
- Drug susceptibility test performed	18/25	72.00	25
- Conventional culture test performed	04/25	16.00	25
- Chest X-rays performed	04/25	16.00	25
- No previous training in TB care (including TB diagnosis)	16/25	64.00	25
- LED most commonly used technology for routine diagnosis	19/25	76.00	25
- Inadequate knowledge among staff in LED use/maintenance	20/25	80.00	25
- Used LED for routine testing (actual use)	12/25	48.00	25
- LED use enhances staff performance	18/25	72.00	25
- LED perceived high maintenance/repair than ZN	14/25	56.00	25
- LED perceived easy to use for routine testing	12/25	48.00	25
- LED perceived more useful for TB testing than ZN	09/25	36.00	25
- LED perceived more time consuming than ZN	06/25	24.00	25
- LED widely accepted among staff for routine use	11/25	44.00	25
- GPs base diagnostic/treatment decisions on Genexpert	19/25	76.00	25
- GPs prefer LED for diagnosis/treatment decisions	20/25	80.00	25
- LED introduced, but not implemented as initially intended	15/25	60.00	25

- LED implemented as initially intended	10/25	40.00	25
- LED enhances staff performance in TB testing	09/25	36.00	25
- No refresher training in LED use for routine testing	04/25	16.00	25
- Staff not formally trained in LED use	09/25	36.00	25
- Staff not formally trained in lab protocol use	19/25	76.00	25
- Inadequate resources (financial and human)	23/25	92.00	25
- Existing lab structures cannot support LED utilization	24/25	96.00	25
- Lack of infection control measures poses huge health risks to staff	20/25	80.00	25
- Need for region alignment of TB control activities across facilities	16/25	40.00	25
- Need for policy/strategic focus for TB care delivery at NTP/MOH level	13/25	52.00	25

Table 5.4 ***The frequency distribution of HCWs' responses to perception questions***

Health workers' responses to perception questions (N= 25)	**Nurses (n= 4) n/N (%)**	**Appendix E: Physicians (n= 6) n/N (%)**	**Lab techs (n= 15) n/N (%)**	**Total [n/N] (%)**
- Smear microscopy tests performed at TB care facilities	2 (50)	4 (67)	12 (80)	18/25 (72)
- DST (Genexpert) tests performed at TB care facilities	3 (75)	5 (84)	13 (87)	21/25 (84)
- GPs initiated diagnosis/treatments decisions on Genexpert tests	2 (50)	3 (50)	10 (67)	15/25 (60)
- GPs initiated diagnosis/treatments decisions on LED tests	2 (50)	3 (50)	5 (34)	10/25 (40)
- Genexpert preferred/most commonly used for testing	1 (25)	3 (50)	13 (87)	17/25 (68)
- LED implemented as intended	2 (50)	4 (67)	11 (74)	17/25 (68)
- LED not widely accepted	2 (50)	5 (84)	5 (34)	12/25 (48)
- LED widely accepted by HCWs	2 (50)	3 (50)	5 (34)	12/25 (48)
- LED perceived useful for TB diagnosis	3 (75)	2 (34)	4 (27)	9/25 (36)
- LED perceived not useful for TB diagnosis	3 (75)	3 (50)	9 (60)	15/25 (60)
- LED perceived more time consuming than ZN	1 (25)	5 (84)	11 (74)	17/25 (68)
- LED perceived higher maintenance than ZN	1 (25)	3 (50)	10 (67)	14/25 (56)
- LED enhances staff performance	3 (75)	3 (50)	12 (80)	18/25 (72)
- LED does not enhance staff performance	1 (25)	3 (50)	3 (20)	7/25 (28)
- Staff voiced unfavorable opinions on LED use/application	2 (25)	2 (34)	10 (67)	14/25 (56)
- GPs preferred Genexpert to LED for TB diagnosis	2 (25)	4 (67)	10 (67)	16/25 (64)
- Lack of information for use/maintenance of LED	3 (75)	5 (83)	12 (80)	20/25 (80)

APPENDIX TO CHAPTER 6

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews***

Themes (Interview questions)	**Initial codes**
1. Current role/responsibility	- Hospital manager
	- TB coordinator
	- NTP-TB Lab lead
	- TB manager
	- TB technical advisor
	- Monitoring/evaluation
	- Health information Officer
	- Data Manager
	- HIV/TB officer
	- Public health officer
	- Program director
	- Hospital director
	- TB advocacy officer
	- Public-private partnership officer
	- TB lab lead (WHO/WV/GF)
	- Other (please specify):
2. Number of organisation facilities managed	- None
	- 1-5 facilities
	- 6-10 facilities
	- Over 10 facilities

	- Responsible for all TB care facilities in country
	- Other (please specify):
3. Number of facilities that provide diagnostic/treatment services	- All facilities provide diagnostic/treatment services
	- Some but not all facilities
	- Our facilities provide diagnostic services only
	- Our facilities provide neither diagnostic nor treatment services
	- All facilities provide both diagnostic and treatment services
	- Other (please specify):

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
4. Types of test performed at facilities	- Smear microscopy
	- Drug susceptibility
	- Radiography (X-rays)
	- Culture
5. Routine use of LED at facilities	- LED used for routine testing
	- LED not used for routine testing
	- LED used for routine testing at a few facilities
6. Factors supporting LED-FM implementation	- Staff adequately trained in LED use
	- Need for more robust diagnostic tools
	- Staff preferences for LED use over ZN
	- LED use for routine testing is cleaner than ZN
	- LED is easy to use
	- LED is useful for TB diagnosis
7. Difficulties organization faced in LED implementation/use	- Staff uninformed about LED introduction
	- Maintenance/spare parts not available in country
	- Facilities not equipped for LED implementation/routine use
	- Organization not in TB diagnostic services
	- Insufficient staff training in LED use
	- Frequent disruption to LED reagents/supply chain
	- Guidelines for LED use unavailable at lab facilities
	- Staff prefer other tools to LED technology
	- LED more time-consuming than ZN
	- Limited technical expertise available in LED use (locally)
	- Purpose of LED use unclear to health teams (all levels)

	- Health workers in TB care unaware of LED usefulness
	- No clear policy or framework in LED use
	- Lack of supervision (all levels)
	- Lack of coordination of LED intervention activities
	- Staff motivation/moral issues
	- Lack of ownership

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
8. LED not implemented as intended (why)	- Guidelines not available for LED use at laboratory facilities
	- LED implemented as initially intended
	- Staff prefer use of old tools (ZN) to LED use
	- Increased workload associated with routine LED use
	- LED use is more time-consuming compared to ZN
	- Few facilities have introduced LED technology
	- Lack of partnership/network structures across stakeholders
	- Lack of functioning quality assurance/control/improvement systems
	- Inadequately trained health workforce across all laboratory sectors
	- Lack of programmatic/systematic readiness to adopt new tools
9. Facility staff training in LED use	- Lack of adequate training for staff in LED use
	- Training in general microscopy maintenance
	- Training in the use of guidelines for LED use at lab facilities
	- Lack of infection control at laboratory facilities
	- Lack of sufficient resources (financial)
10. Current gaps in LED implementation	- No clear/coherent policy/strategy for TB control
	- Program lacks ownership and is run by external entities
	- Single donor dependency problems
	- Lack of local government financial support
	- Lack of funding for different program functions
	- NTP/MOH role unclear in strategy/policy for TB control
	- Poor infrastructural capacity to support LED implementation
	- NTP lacks strong leadership in coordination of TB program activities
	- Laboratory structures are ill-equipped to support technology utilisation
	- Unclear standard operating guidelines for TB care service provision (all levels)
	- Existing lab facilities/network not aligned

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
11. LED acceptance among facility staff	- Widely accepted among staff for routine use
	- Not widely accepted at all facilities
	- Not accepted for routine use due to technical deficiencies
	- LED not implemented at all TB care facilities
12. Barriers to LED acceptability	- Inadequate training for health workers (all levels) in LED use
	- Limited technical expertise in LED use (at a country level)
	- Guidelines in LED use and maintenance not available in country
	- LED acceptance was influenced by staff training in LED use
	- Have no information on LED acceptance at facility level
	- Poor acceptance by facility staff due to a lack of training in its use
	- Purpose of LED use unclear to health teams (all levels)
	- Most of health workers are unaware of LED usefulness
	- No clear policy or framework for LED use
	- Inadequate resources (human, money, infrastructure)
	- Frequent interruption of supplies/reagents for LED use
	- Inadequate resources (financial, human, infrastructure)

13. Policies/guidelines for LED implementation	- Policies/guidelines in place for use but not utilised fully
	- Inadequate training in use of guidelines for staff
	- Guidelines not available for LED use at lab facilities
	- Staff resistance/reluctant to use guidelines

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
14. Procurement/supplies for LED	- Procurement/maintenance systems for LED in place
	- No systems for LED supplies procurement/maintenance
15. Body responsible for procurement/supplies/maintenance systems	- NTP/MOH Somaliland is responsible
	- The Global Fund is responsible
	- World Vision responsible
	- Joint responsibility of Global Fund/World Vision
	- WHO is responsible
	- Unclear who is responsible
16. Perceptions towards LED use	- Better than direct light microscopy [ZN]
	- Not useful for TB care
	- LED use consumes more resources than ZN
	- Suitable to local TB care needs
	- Enhances staff performance in TB testing
	- Increases TB case finding
	- LED is higher maintenance than ZN
	- Staff not adequately trained in LED use
	- Staff not trained in LED maintenance/repair
	- LED spare parts not available locally (in country)
	- No difference between LED and direct light in testing quality
	- Increases workload compared to ZN

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
17. Current challenges faced with LED implementation	- Lack of laboratory facilities' capability to support LED implementation
	- Unclear interoperability laboratory standards for technology utilisation
	- Severe funding cuts in TB program
	- Single donor funding dependency
	- Lacks adequate resources (human/financial)
	- Limited technical expertise in diagnosis at all levels in health system
	- Technology acceptance constrained due to a lack of protocols/guidelines
	- Logistical/operational challenges to support new technology utilisation
	- Poor fit for intended local needs (recipient)
	- Lacks funding for implementation/uptake/management of new technologies
	- Inadequacy of skilled/trained health workforce
	- Unclear lab regulatory protocols/SOPs for technology use/maintenance
	- Lacks political commitment/ownership from NTP/MOH
	- Poor governance/ownership of NTP impedes LED feasibility/acceptance
	- No procurement systems established at LED introduction locally
	- Lack of maintenance systems pose challenges to LED use
	- LED not yet utilised fully at facility level due to a lack of transparent protocols/process
	- Guidelines, protocols and manuals not made available to staff (at all levels)
	- Diagnostic services confused by unclear LED guidelines
	- Frequent disruptions to supplies/reagents for LED use at facility level
	- No clear strategy for implementation of new technologies

18. Solutions to overcome perceived challenges	- Adequate resource and structural means to support new technology implementation
	- Improve knowledge base among health workers in LED use
	- Harmonise TB diagnostic policy/guidelines/protocols for new technology use
	- Establish effective procurement/supply chain/maintenance systems (all levels)
	- Streamline performance-based/accountability mechanisms for TB diagnosis
	- Reform policy/strategy for TB care
	- Improve stakeholder engagement for new technology utilisation/outcome parameters
	- Develop mechanisms for resource mobilization to improve access and quality of TB care
	- Reclaim/take ownership of TB program
	- Integrate TB diagnostic services into primary care to reduce cost
	- Align new technologies/tools with local TB care needs

Table 6.1 ***Generated codes in HPs' responses to research questions in the interviews (continued)***

Themes (Interview questions)	Initial codes
19. Policy teams' perceptions of LED use	- Widely accepted among staff for routine use
	- Somewhat accepted
	- Not widely accepted for routine use
	- At some but not all facilities but all facilities
	- LED acceptance was influenced by staff training in LED use
	- Need for further training for staff in LED use
	- No increased sensitivity compared to ZN but more time for specimens
	- LED is no more effective than ZN in case finding (sensitivity)
	- Staff not trained in LED maintenance/repair
	- Useful for TB diagnosis
	- Suitable to local diagnostic needs
	- Lab techs tell me it's easier to use than ZN
	- Align diagnostic service policy/protocols for technology use (all levels)

20. Things HPs would like to see changed at a facility level	- Need a comprehensive program review and set clear priority for the TB program
	- Introduce/implement SOPs for TB care facilities (all levels)
	- Set clear SOPs bio-safety protocols/guidelines for all TB care facilities (lab/facility)
	- Transfer ownership to regional level
	- TB control should be locally led
21. Things HPs would like to see changed at a regional level	- Decentralise/align laboratory services/networks for TB care services
	- Establish decentralized specimen collection strategy at all laboratory facilities
	- Improve QC/QA/QI services at the facility level
	- Improve coordination for TB control activities across partners
	- Centralise laboratory diagnostic testing/validation system for new technology use
	- Ensure distribution of guidelines for introduction/implementation/use of new tools
	- Train staff in guidelines for new technology use
	- Develop regulatory policies for new technology use at TB care facilities
	- Reduce duplication in TB care
	- Mobilise more resources locally for TB control

	- Establish central supply chain locally
	- Improve staff motivation (all levels)
	- Build existing laboratory service capacity
	- Integrate all functions of TB program
	- Take ownership of program regionally
22. Things HPs would like to see changed at a national level	- Establish systems for reliable supply chain/procurement to reduce interruption
	- Prepare/improve system capacity to absorb new diagnostic technology
	- Innovation processes need to include end users and service innovations
	- Expand/harmonise local evidence-based diagnostic needs/guidelines/evaluation process
	- Local health authorities lead new diagnostic technology introduction
	- Local health authorities ensure applicability/feasibility of technology given resources
	- Seek technical expertise in technology use (train more staff)

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts***

Themes (Interview questions)	**HPs' responses to research questions (codes)**	**Frequency of codes in interview transcripts**	**n/N [%]**
1. Current role/responsibility	- Hospital manager	02	02/20 [10]
	- TB coordinator	06	06/20 [30]
	- NTP-TB Lab-lead	01	01/20 [05]
	- TB manager	03	03/20 [15]
	- TB technical advisor	01	01/20 [05]
	- Monitoring/evaluation	01	01/20 [05]
	- Health information Officer	01	01/20 [05]
	- Data manager	01	01/20 [05]
	- HIV/TB officer	01	01/20 [05]
	- Public health officer	00	00/20 [00]
	- Program director	02	02/20 [10]
	- Hospital director	02	02/20 [10]
	- TB advocacy officer	01	01/20 [10]
	- Public-private partnership officer	01	01/20 [10]
	- TB Lab-Lead (WHO/WV/GF)	01	01/20 [10]

	- Other (please specify):	00	00/20 [00]
2. Number of organization facilities managed	- None	00	00/20 [00]
	- 1-5 facilities	01	01/20 [05]
	- 6-10 facilities	07	07/20 [35]
	- Over 10 facilities	02	02/20 [10]
	- Responsible for all TB care facilities in country	09	09/20 [45]
	- Other (please specify):	00	00/20 [00]
3. Number of facilities that provide diagnostic/treatment services	- All facilities provide diagnostic/treatment services	20	20/20[100]
	- Some but not all facilities	00	00/20 [00]
	- Our facilities provide diagnosis services only	00	00/20 [00]
	- Our facilities provide neither diagnostic nor treatment services	00	00/20 [00]
	- Our facilities provide both diagnostic and treatment services	00	00/20 [00]
	- Other (please specify):	00	00/20 [00]

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts (continued)***

Theme (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
4. Types of test performed at facilities	- Smear microscopy	08	08/20 [40]
	- Drug susceptibility	03	03/20 [15]
	- Radiography (X-rays)	10	10/20 [50]
	- Culture	03	03/20 [15]
5. Routine use of LED at your facilities	- LED used for routine testing	14	14/20 [70]
	- LED not used for routine testing	00	00/20[00]
	- LED used for routine testing at few facilities	06	06/20 [30]
6. Factors supporting LED-FM implementation	- Staff adequately trained in LED use	01	01/20 [05]
	- Need for more robust diagnostic tools	19	19/20 [95]
	- Staff preferences for LED use over ZN	14	14/20 [70]
	- LED use for routine testing cleaner than ZN	12	12/20 [60]
	- LED is easy to use	18	18/20 [90]
	- LED is useful for TB diagnosis	17	17/20 [85]
7. Difficulties organization faced in LED implementation/use	- Staff uninformed about LED introduction	15	15/20 [75]
	- Maintenance/spare parts not available in country	13	13/20 [65]
	- Facilities not equipped for LED implementation/routine use	19	19/20 [95]

	- Organization not in TB diagnostic services	18	18/20 [90]
	- Insufficient staff training in LED use	16	16/20 [80]
	- Frequent disruption to LED reagents/supply chain	17	17/20 [85]
	- Guidelines for LED use unavailable at lab facilities	10	10/20 [50]
	- Staff prefer the use of other tools to LED technology	15	15/20 [75]
	- LED more time-consuming than ZN	12	12/20 [60]
	- Limited technical expertise available in LED use (locally)	11	11/20 [55]
	- Purpose for LED use unclear to health teams (all levels)	09	09/20 [45]
	- Health workers in TB care unaware of LED usefulness	15	15/20 [75]
	- No clear policy or framework in LED use	16	16/20 [80]
	- Lack of supervision (all levels)	13	13/20 [65]
	- Lack of coordination of LED intervention activities	11	11/20 [55]
	- Staff motivation/moral issues	17	17/20 [85]
	- Lack of ownership/leadership	18	18/20 [90]

Table 6.2 ***The frequency distribution of the HPs responses to interview questions for all transcripts (continues)***

Theme (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
8. LED not implemented as intended (why)	- Guidelines not available for LED use at laboratory facilities	11	11/20 [55]
	- LED implemented as initially intended	07	07/20 [35]
	- Staff prefer LED use	03	03/20 [15]
	- Increased workload associated with routine LED use	10	10/20 [50]
	- LED use is more time-consuming compared to ZN	04	04/20 [20]
	- Few facilities have introduced LED technology	14	14/20 [70]
	- Lack of partnership/network structures across stakeholders	15	15/20 [78]
	- Lack of functioning quality assurance/control/improvement systems	15	15/20 [79]
	- Inadequately trained health workforce across all laboratory sectors	18	18/20 [90]
	- Lack of programmatic/systematic readiness to adopt new tools	15	15/20 [75]
9. Facility staff training in LED use	- Lack of adequate training for staff in LED use	17	17/20 [85]
	- Training in general microscopy maintenance	14	14/20 [70]
	- Training in use of guidelines for LED use at lab facilities	18	18/20 [93]
	- Lack of infection control at laboratory facilities	19	19/20 [95]
	- Lack of sufficient resources (financial)	17	17/20 [88]

10. Current gaps in LED implementation	- No clear/coherent policy/strategy for TB control	17	17/20 [90]
	- Program lacks ownership or run by external entities	18	18/20 [90]
	- Single donor dependency problems	18	18/20 [90]
	- Lack of local government financial support	19	19/20 [95]
	- Lack of funding for different program functions	18	18/20 [60]
	- NTP/MOH role unclear in strategy/policy for TB control	15	15/20 [75]
	- Poor infrastructural capacity to support LED implementation	13	13/20 [65]
	- NTP lacks strong leadership in coordination of TB program activities	16	16/20 [80]
	- Laboratory structures are ill-equipped to support technology utilisation	14	14/20 [70]
	- Unclear guidelines/SOPs for TB care service provision (all levels)	17	17/20 [85]
	- Existing lab facilities/network not aligned	13	13/20 [65]

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts (continued)***

Themes (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
11. LED acceptance among facility staff	- Widely accepted among staff for routine use	07	07/20 [35]
	- Not widely accepted at all facilities	06	06/20 [30]
	- Not accepted for routine use due to technical deficiencies	02	02/20 [10]
	- LED not implemented at all TB care facilities	05	05/20 [25]
12. Barriers to LED acceptability	- Inadequate training for health workers (all levels) in LED use	19	19/20 [95]
	- Limited technical expertise in LED use (at a country level)	14	14/20 [70]
	- Guidelines in LED use and maintenance not available in country	15	15/20 [75]
	- LED acceptance was influenced by staff training in LED use	14	14/20 [70]
	- Have no information on LED acceptance at facility level	18	18/20 [90]
	- Acceptance among facility staff due to a lack of training in its use	15	15/20 [75]
	- Purpose for LED use unclear to health teams (all levels)	13	13/20 [65]
	- Most of health workers are unaware of LED usefulness	16	16/20 [80]
	- No clear policy or framework for LED use	13	13/20 [65]
	- Inadequate resources (human, money, infrastructure)	12	012/20 [60]
	- Frequent interruption of supplies/reagents for LED use	10	10/20 [50]
	- Inadequate resources (financial, human, infrastructure)	17	17/20 [85]
13. Policies/guidelines for LED implementation	- Policies/guidelines in place for use/but not utilized fully	13	13/20 [65]
	- Inadequate training in use of guidelines for staff	17	17/20 [85]
	- Guidelines not available for LED use at lab facilities	12	12/20 [60]
	- Staff resistance/reluctance to use guidelines	14	14/20 [70]

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts (continued)***

Theme (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
14. Procurement/supplies for LED	- Procurement/maintenance systems for LED in place	03	03/20 [15]
	- No systems for LED supplies procurement/maintenance	17	17/20 [85]
15. Body responsible for procurement/supplies/ maintenance systems	- NTP/MOH Somaliland is responsible	01	01/20 [05]
	- The Global Fund is responsible	19	19/20 [95]
	- World Vision responsible	00	0.00 [00]
	- Joint responsibility of Global Fund/World Vision	00	0.00 [00]
	- WHO is responsible	00	0.00 [00]
	- Unclear who is responsible	19	19/20 [95]
16. Perceptions towards LED use	- Better than direct light microscopy [ZN]	15	15/20 [75]
	- Not useful for TB care	12	12/20 [60]
	- LED use consumes more resources than ZN	13	13/20 [65]
	- Suitable to local TB care needs	16	16/20 [80]
	- Enhances staff performance in TB testing	07	07/20 [35]
	- Increases TB case finding	13	13/20 [65]
	- LED is higher maintenance than ZN	01	01/20 [05]
	- Staff not adequately trained in LED use	19	19/20 [95]
	- Staff not trained in LED maintenance/repair	15	15/20 [75]

	- LED spare parts not available locally (in country)	18	18/20 [90]
	- No difference between LED and direct light in testing quality	11	11/20 [55]
	- Increases workload compared to ZN	06	06/20 [30]

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts (continued)***

Themes (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
17. Current challenges faced with LED implementation	- Lack of laboratory facilities' capability to support LED implementation	10	10/20 [50]
	- Unclear interoperability laboratory standards for technology utilisation	15	15/20 [75]
	- Severe funding cuts in TB program	17	17/20 [85]
	- Single donor funding dependency	17	17/20 [85]
	- Lacks adequate resources (human/financial)	15	15/20 [75]
	- Limited technical expertise in diagnosis at all levels in health system	18	18/20 [90]
	- Technology acceptance constrained due to lack of protocols/guidelines	17	17/20 [85]
	- Logistical/operational challenges to support new technology utilisation	12	12/20 [60]
	- Poor fit for intended local needs (recipient)	11	11/20 [55]
	- Lacks funding for implementation/uptake/management of new technologies	19	19/20 [95]
	- Inadequacy of skilled/trained health workforce	17	17/20 [85]
	- Unclear lab regulatory protocols/SOPs for technology use/maintenance	13	13/20 [65]
	- Lacks political commitment/ownership from NTP/MOH	10	10/20 [50]
	- Poor governance/ownership of NTP impedes LED feasibility/acceptance	19	19/20 [95]
	- No procurement systems established at LED introduction locally	16	16/20 [80]
	- Lack of maintenance systems pose challenges to LED use	12	12/20 [60]

	- LED not yet utilized fully at facility level due to a lack of clear protocols/process	16	16/20 [80]
	- Guidelines, protocols and manuals not made available to staff (all levels)	14	14/20 [70]
	- Diagnostic services confused by unclear LED guidelines	18	18/20 [90]
	- Frequent disruptions to supplies/reagents for LED use at facility level	12	12/20 [60]
	- No clear strategy for implementation of new technologies	14	14/20 [72]
18. Solutions to overcome perceived challenges	- Need to improve resource and structural capacity to support use of new technology	16	16/20 [80]
	- Improve knowledge base among health workers in LED use	08	08/20 [40]
	- Harmonized TB diagnostic policy/guidelines/protocols for new technology use	14	14/20 [70]
	- Establish effective procurement/supply chain/maintenance systems (all levels)	12	12/20 [60]
	- Streamline performance-based/accountability mechanisms for TB diagnosis	15	15/20 [75]
	- Reform policy/strategy for TB care	10	10/20 [50]
	- Improve stakeholder engagement for new technology utilization/outcome parameters	09	09/20 [45]
	- Develop mechanisms for resource mobilization to support use of new technologies	15	15/20 [75]
	- Reclaim/take ownership of TB program	17	17/20 [85]
	- Integrate TB diagnostic services into primary care to reduce cost	15	15/20 [75]
	- Align new technologies/tools with local TB care needs	12	12/20 [60]

Table 6.2 ***The frequency distribution of the HPs' responses to interview questions – all transcripts (continued)***

Themes (Interview questions)	HP's responses to research questions (codes)	Frequency of themes in interview transcripts	n/N [%]
19. Policy teams' perceptions of LED	- Widely accepted among staff for routine use	10	10/20 [50]
	- Somewhat accepted	02	02/20 [10]
	- Not widely accepted for routine use	05	05/20 [25]
	- Accepted among staff at some but not all facilities	02	02/20 [10]
	- LED acceptance was influenced by staff training in LED use	12	12/20 [60]
	- Need for further training for staff in LED use	17	17/20 [85]
	- No increased sensitivity compared to ZN but more time for specimens	8	08/20 [40]
	- LED is no more effective than ZN in case finding (sensitivity)	16	16/20 [80]
	- Staff not trained in LED maintenance/repair	18	18/20 [90]
	- Useful for TB diagnosis	12	12/20 [60]
	- Suitable to local diagnostic needs	11	12/20 [55]
	- Lab techs tell me it's easier to use than ZN	13	13/20 [65]
20. Things HPs would like to see changed at a facility level	- Align all diagnostic service policy/protocols for technology use (all levels)	11	11/20 [65]
	- Need a comprehensive program review and set clear priority for the TB program	16	16/20 [80]
	- Introduce/implement SOPs for TB care facilities (all levels)	12	12/20 [60]

	- Set clear SOPs bio-safety protocols/guidelines for all TB care facilities (lab/facility)	18	18/20 [90]
	- Take ownership at regional level	17	17/20 [85]
	- TB control should be locally led	18	18/20 [90]
21. Things HPs would like to see changed at a regional level	- Decentralize/align laboratory services/networks for TB care services	15	15/20 [75]
	- Establish decentralized specimen collection strategy at all laboratory facilities	17	17/20 [85]
	- Improve QC/QA/QI services at facility level	14	14/20 [70]
	- Improve coordination for TB control activities across partners	17	17/20 [85]
	- Centralize laboratory diagnostic testing/validation system for new technology use	12	12/20 [60]
	- Ensure distribution of guidelines for introduction/implementation/use of new tools	14	14/20 [70]
	- Train staff in guidelines for new technology use	14	14/20 [70]
	- Develop regulatory policies for new technology use at TB care facilities	17	17/20 [85]
	- Reduce duplication in TB care	12	12/20 [60]
	- Mobilize more resources locally for TB control	16	16/20 [80]
	- Establish central supply chain locally	14	14/20 [70]
	- Improve staff motivation (all levels)	10	10/20 [50]
	- Build existing laboratory service capacity	18	18/20 [95]
	- Integrate all functions of TB program	14	14/20 [70]

	- Take ownership of program regionally	16	16/20 [80]
22. Things HPs would like to see changed at a national level	- Establish systems for reliable supply chain/procurement to reduce interruption	17	17/20 [85]
	- Prepare/improve system capacity to absorb new diagnostic technology	18	18/20 [90]
	- Innovation processes need to include end users and service innovations	15	15/20 [75]
	- Expand/harmonize local evidence-based diagnostic needs/guidelines/evaluation process	16	16/20/[80]
	- Local health authorities lead new diagnostic technology introduction	17	16/20 [85]
	- Local health authorities ensure applicability/feasibility of technology given resources	10	10/20 [50]
	- Seek technical expertise in technology use (train more staff)	17	17/20 [85]