GENEXPERT UTILIZATION AT A PUBLIC HOSPITAL LABORATORY IN NORTHERN MALAWI: A QUALITY IMPROVEMENT STUDY

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DECLARATION

I, Jonathan Majamanda, declare that this Research Report is my own, unaided work. It is being submitted for the degree of Master of Science in Epidemiology in the field of Implementation Science at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any university.

17th day of October 2019 in Johannesburg, South Africa.

DEDICATION

I humbly dedicate this degree to the Lord Almighty who has made it possible for me to come this far in education. A special feeling of gratitude to my loving fiancée, Alinafe C. Tauzi and many others for their words of encouragement and support during my study and research periods. My Father, my Mother, my brothers and sisters, you have never left my side and are very special to me. Through thick and thin, you have provided me all the support to make this level of my education come to pass.

I also dedicate this dissertation to my many friends who have supported me throughout the process. I will always appreciate all they have done.

ABSTRACT

Background

Tuberculosis (TB) is one of the major public health challenges in the world. New diagnostic measures have been developed as part of the fight against the pandemic. GeneXpert is a molecular TB diagnostic tool that detects the presence of TB and reports rifampicin resistance in two hours. However, there have been reports of underutilization of this diagnostic method in many settings, Malawi inclusive. Evidence from Mzuzu Central Hospital in Northern Malawi show low utilization of GeneXpert. Quality improvement, using the Model for Improvement (MFI) approach, has been shown to improve practice among healthcare providers and utilization of diagnostic platforms. This study therefore used the MFI to develop and implement change ideas for improvement of GeneXpert utilization at Mzuzu Central Hospital in Northern Malawi.

Methods

A quasi-experimental study comprising of pre-intervention, intervention and post-intervention phases with mixed methods study design was conducted to assess the baseline utilization of GeneXpert, conduct a root-cause analysis, develop and implement change ideas, and evaluate the impact of the change ideas. Record review was done to assess level of utilization before the intervention. The qualitative component was used to identify barriers to GeneXpert utilization and develop change ideas before the intervention, and assess level of improvement after the intervention. Key informants were purposively selected for in-depth interviews. A quality improvement team (QIT) was formed to develop and implement change ideas. Data were analyzed using STATA 14 SE and Nvivo12. Tables, bar graphs and run charts were used to present data.

Results

At baseline, the mean number of samples run per week was 11.0 (SD: 3.0). The weekly rejection rate was 8.2% (SD: 5.9). The mean weekly turnaround time was 80 hours (SD:15.6). After the intervention, the mean of samples run per week was 27 (145.6% increase), weekly rejection rate was 0.29% (96.5% improvement) and the turnaround time was 16 hours (80% improvement). These improvements were stable and sustained throughout the post-intervention study period.

Conclusion

The implemented small change ideas using the MFI approach improved GeneXpert utilization at Mzuzu Central Hospital. The improvements in all the three indicators were statistically significant. The barriers to utilization were technical (module failures, power interruptions and

stock outs), human resource (low doctor to patient ratio), financial (lack of donor support and GeneXpert expenses), motivational (lack of GeneXpert trainings) knowledge and information (lack of interdepartmental communication, incorrect completing of patient forms, insufficient sample production instructions to patients). Thus, it is important that the ministry of health and funding agencies tailor their funding towards increasing GeneXpert knowledge among health personnel and that the continuous professional developments on GeneXpert be encouraged in hospital departments.

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LIST OF ABBREVIATIONS (NOMENCLATURE)

ART	Anti-retroviral Therapy
ASSIST	Applying Science to Strengthen and Improve Systems
CMO	Chief medical officer
CNO	Chief nursing officer
CD4	Cluster of Differentiation 4 (immune cells)
CPD	Continuous Professional Development
LM	Laboratory manager
LT	Laboratory technician
MCPMEs	Massachusetts Coalition for the Prevention of Medical Errors
MDGs	Millennium Development Goals
MFI	Model for Improvement
MTB	Mycobacterium Tuberculosis
NGOs	Non-Governmental organizations
NIRN	National Implementation Research Network
OPD	Outpatient Department
PCR	Polymerase Chain Reaction
PDSA	Plan-Do-Study-Act
PI	Principal Investigator
PMTCT	Prevention of Mother-To-Child Transmission of HIV
PLHIV	People living with HIV
PTB	Pulmonary Tuberculosis
QI	Quality Improvement
QIT	Quality Improvement Team
RSA	Republic of South Africa
SDGs	Sustainable Development Goals
SES	Socio-economic Status
SORT IT	Structured Operational Research and Training Initiative
SSA	Sub-Saharan Africa
TAT	Turnaround time

TB	Tuberculosis
TDR	Tropical Disease Research
UNC	University of North Carolina at Chapel Hill
USD	United States dollar
USA	United Sates of America
WHA	World Health Assembly
WHO	World Health Organization
XDT	Extensive Drug Resistance
USAID	United States Agency for International Development

CHAPTER 1: INTRODUCTION

1.1 Background

Tuberculosis (TB) is an airborne contagious disease mainly caused by *Mycobacterium tuberculosis* which are mammalian tubercle bacilli. The bacilli usually attack the lungs, causing pulmonary TB (PTB), but can also attack other parts of the body such as the spine, lymph nodes, brain and kidneys; this is known as extra-pulmonary TB (EPTB) (1). Tuberculosis is the ninth leading cause of death worldwide (2). According to the 2018 WHO TB Report, TB is now the world's leading adult infectious killer, far surpassing HIV (3).

1.1.1 Global TB Burden

Although the global TB mortality rate shows a steady decline, the number of people affected globally is still huge. According to the World Health Organization (WHO) TB Report of 2017, there were 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an extra 374 000 deaths among HIV-positive people while 10.4 million people fell ill with TB in 2016. The WHO African Region accounted for one in every four TB cases (4). This is so due, among other factors, to HIV-TB co-infection.

HIV is the strongest risk factor for developing TB as it reduces the immune system's ability to fight infections (5, 6). Globally, HIV-infected persons accounted for 10% of the estimated 10.4 million TB cases in 2016 (4, 7). Approximately three quarters of the estimated HIV-associated TB cases (1.4 million in 2016) and deaths are in the WHO African Region, with eastern and southern African populations carrying most of the total global burden (2, 8). This makes the WHO African Region a TB hotspot. Antiretroviral therapy (ART) aims at boosting immunity and prolonging life of people living with HIV (PLHIV). Even with expansion of ART program, TB remains the leading cause of death amongst PLHIV accounting for approximately a third of HIV-related deaths (4). Furthermore, it is difficult to diagnose TB in PLHIV using microscopy since the bacterial count in their sputum is greatly reduced (9-11).

1.1.2 TB Burden in Malawi

Categorized among the high TB-HIV burdened countries (12), Malawi has an incidence rate of 193 new TB cases per 100,000 persons per year and an HIV prevalence of 9.1% (4, 13, 14). As HIV is a major risk factor for TB infection and TB is difficult to detect in PLWHIV, improving utilization of GeneXpert is, therefore, a necessity.

1.1.3 TB Interventions

Significant efforts to prevent and control TB have been jointly made by states and governments, Non-Governmental Organizations (NGOs) and private companies. For instance, the Structured Operational Research and Training Initiative (SORT IT), led by Tropical Disease Research (TDR) at WHO, was launched in 2012 to support operational research in TB and other public health programs like HIV and malaria (15). In 2014, the WHO End TB Strategy, a global effort aiming at 90% reduction in TB deaths and 80% reduction in TB incidence (new cases per year) by 2030, was adopted by the World Health Assembly (WHA). Part of the End TB Strategy was to diagnose at least 90% of all people with TB and treat them, diagnose at least 90% of key populations and achieve at least 90% treatment success on those diagnosed positive (90-(90)-90) by 2020 (4). The donors and partners in fight against TB, such as PEPFAR and Global Fund, have also been a great support in this fight (16).

In 2000, the Millennium Development Goals (MDGs) were developed with a bold TB target to have halted and begun to reverse the incidence of TB by 2015 (17, 18). In 2015 the United Nations General Assembly included the "ending the TB epidemic" as a target within the health related Sustainable Development Goals (SDG) 3, (7, 15). Although such global efforts have contributed to the decline in TB morbidity and mortality, TB control indicators of incidence, mortality and percentage of households that face huge costs due to TB disease still remain below international targets in many affected countries (4).

The burden of TB has been compounded by the advent of multi-drug resistant TB (MDR-TB) strains. In 2017, the WHO reported that 4.1% of new cases and 19% of previously treated cases had MDR-TB (4). MDR-TB is characterized by the failure of patients to respond to two most powerful anti-TB drugs,

rifampicin and isoniazid. In patients with extensively drug-resistant TB (XDR-TB), the mycobacteria are resistant to at least one fluoroquinolone and a second-line injectable drug (kanamycin, amikacin or capreomycin). The drug resistant type of TB are of public concern as treatment for these cases remains low, at 54% globally (4). Drug resistance has contributed to the failure to control and eliminate TB (19).

1.1.4 TB Diagnosis

Early diagnosis and adequate treatment of infectious patients are central in the fight against TB, and to ensure its elimination (20). Deficiencies of the diagnostic tools for TB have hampered efforts to fight TB. Conventional methods to diagnose TB including smear microscopy, chest X-ray and TB culture have seldom been efficient in this aspect. Microscopy has a low sensitivity of 36-43% meaning that it can only report 36-43% of TB cases as positive, leaving the rest undetected and denying them of the needed treatment. Chest X-ray is costly and hard to interpret implying that it cannot be installed in rural areas and will require elaborate expertise to interpret the results (20, 21).

The introduction of Computer Assisted Diagnosis (CAD) for TB may change how X-rays are interpreted in rural and resource limited settings (23). In settings where chest X-ray is already incorporated into TB diagnostic algorithms, use of CAD systems could eliminate problems of poor inter-reader reliability, and potential delays in interpretation if relying on human readers (22). Though it is the gold standard in TB diagnosis, TB culture has a long turn-around time (TAT) of 2 to 6 weeks, meaning the patient has a long window of infecting others before he/she starts treatment (21).

Turnaround time can be defined as “Period for completing a process-cycle”. For a laboratory personnel, and of course in this research report, TAT was defined as the time from receipt of sample in laboratory till report is generated (23). TB-culture diagnostic method is also prone to contamination with fast growing unwanted normal flora, and requires significant laboratory infrastructure which cannot be practically available in most rural settings (24) . This means TB culture is expensive and cumbersome and may not be widely available. Therefore, simplification of TB diagnosis is critical.

GeneXpert is an innovation that was introduced in 2010. It detects TB at a molecular level using the principle of recognizing a specific gene and amplifying it to detectable levels, called polymerase chain reaction (PCR). It is superior to the other diagnostic methods in that it gives the results within 2 hours,

and reports rifampicin resistance (25). The WHO recommends the replacement of the current GeneXpert cartridge with the new, next-generation Xpert® MTB/RIF Ultra (Xpert Ultra). This cartridge is more sensitive and is useful in detecting bacilli in specimens with low numbers, in paediatric specimens, tuberculous meningitis in HIV-infected adults, and possibly, has higher accuracy in the detection of rifampicin resistance (26-28).

1.2 Problem Statement

Poor utilization of GeneXpert is one of the major challenges in the fight against TB, leaving many TB patients undiagnosed, especially in countries where TB-HIV burden is high like Malawi (12). Recent studies have shown that there is underutilization of the GeneXpert diagnostic tool in Malawi and it has contributed to low TB case detection (12).

Malawi piloted the GeneXpert in 2011 in research laboratories only and rolled it out in 2013 through the National TB Control Program (NTP) with support from USAID/ PEPFAR (TB CARE II) and WHO (TB REACH) (29). Since the roll out of GeneXpert in Malawi, a strategy which was aimed to improve case notification and time to diagnosis, studies have shown an overall underutilization of the innovation in both referral and district laboratories (12). Data for the first and second quarters of 2017 revealed that, on average, the GeneXpert machine at Mzuzu Central Hospital Laboratory runs three samples per day although GeneXpert machine with four modules can run up to 16 samples each day (25, 30). This has likely led to low case detection and notification, and increased chances of transmitting the infection to more individuals. This also means more HIV-TB patients go without TB treatment. Studies in Africa, Malawi and observations at data from Mzuzu Central Hospital point to underutilization of GeneXpert as a possible cause of lack of improvement in the fight against TB (31-34).

1.3 Justification

With the huge burden of TB and HIV in Malawi (4, 7, 13, 14, 34, 35) we found it essential to improve the utilization of the GeneXpert. Several studies had shown that quality improvement using the Model for Improvement (MFI) can improve outcomes e.g. quality of care in surgery, management of adolescent diabetes, and utilization of GeneXpert (15, 36-38). To our knowledge, no quality improvement study had been conducted to investigate and address the underutilization of GeneXpert

for TB diagnosis in Malawi (4, 12, 34). With the negative impact TB has on health and economy, it is necessary to improve its utilization as a component of dealing with TB. Quality Improvement has been employed in Uganda to improve GeneXpert utilization and this inspired the use of QI in this study (39).

1.4 Research Question

Can small change ideas improve utilization of GeneXpert for TB detection at Mzuzu Central Hospital Laboratory in Malawi over a three-month period in 2018?

1.5 Research Aim

The main aim was to identify and implement small change ideas to improve GeneXpert utilization at Mzuzu Central Hospital Laboratory in Malawi over a three-month period in 2018.

1.6 Objectives

This objective was broken down to smaller achievable objectives as outlined below.

1. To identify factors affecting GeneXpert utilization at Mzuzu Central Hospital TB Laboratory in Malawi.
2. To develop, implement and document change ideas for improvement of GeneXpert utilization using the Model for Improvement at Mzuzu Central Hospital TB Laboratory in Malawi over a three-month period in 2018
3. To measure the impact of the change ideas on GeneXpert utilization at Mzuzu Central Hospital TB Laboratory in Malawi over a three-month period in 2018.

1.7 Literature Review

1.7.1 Superiority of GeneXpert

For the effective detection and control of the slow growing TB bacteria, highly sensitive and specific tools with a shorter turnaround time are fundamental (40). Owing to this remarkable feature, GeneXpert has received extensive applause for shortening turnaround time and thus has proved to be a very relevant technology for diagnosing TB in the past decade (41). It is an innovative molecular

diagnostic tool, for prompt detection of MTB and drug resistance. It detects the presence of MTB by amplifying its deoxyribonucleic acid (DNA) to detectable levels, and also detects the presence of resistant genes to rifampicin (11). Furthermore, this diagnostic tool that can be used at point of care with minimum risks and inconveniences (42). Its high sensitivity and specificity along with turnaround time of 2 hours facilitates timeous diagnosis and appropriate management of TB pleuritis and pericarditis (40).

Since the inception of GeneXpert in 2010, case detection and notification have greatly improved. Patients have stopped waiting for a week and more to get their results, and laboratory workers have been able to handle large volumes of samples in a short time, while doing other tasks (9, 10, 40) . Besides, GeneXpert has proved to work in both the high and low TB incidence settings (43). With GeneXpert, access to MDR-TB diagnosis has radically improved, with the number of MDR cases detected in adults and children rising by up to eight-fold, with a two-fold surge in the rate of bacteriologically confirmed TB (4). Grant Theron and colleagues, in their multi-centre randomized controlled trial comparing accuracy, and clinical effect of point-of-care between GeneXpert and microscopy, found that twice as many patients in the GeneXpert group had a same-day diagnosis and more received same-day treatment initiation compared to patients in the microscopy group (27). There were also more patients on treatment in the GeneXpert group due to reduced dropout as compared to microscopy group (more patients in GeneXpert group remained on treatment).

Using sputum culture as a reference standard test in as systematic review and meta-analysis, Detjen and colleagues found that GeneXpert has a pooled sensitivity of 86% (it detects 86% of true positive patients) and specificity of 98% (it can report 98% of patients without the disease as test negative). Comparatively, smear microscopy has sensitivity of 36-43% (45, 46). There are also remarkably significant post-diagnosis benefits of GeneXpert as compared to smear microscopy (47).

In a large randomized clinical trial evaluating the effect of replacing GeneXpert with smear microscopy on patient and program outcomes in South Africa, Churchyard and colleagues found that there was no difference between the GeneXpert and microscopy arms in terms of mortality, proportion starting tuberculosis treatment, and initial loss to follow up (36). However, they noted a 50% higher rate of people with bacteriological confirmation of TB in the GeneXpert group, thereby allowing a reduced time to treatment initiation (36).

In the same vein, a cluster randomized trial in Malawi revealed that screening using GeneXpert resulted in twice the rate of diagnosis when compared to microscopy. GeneXpert further resulted in a 50% reduction in mortality in patients with stage three or four HIV compared to microscopy (37). In the light of these advantages, the WHO in 2010 endorsed GeneXpert as the initial diagnostic test in people suspected of MDR-TB or HIV-associated TB, and as a follow-on test to microscopy, in settings where MDR and HIV related TB are not a major concern which Malawi adopted in 2012 (32).

All these are some of the benefits GeneXpert has over other tests, despite its shortcomings which include; its dependency on electricity making the common power outages in the developing countries a huge challenge, the reagent stock outs and its being a costly test to run as compared to smear microscopy. New technology has brought advancement in portable power batteries (UPS) that can run the machine for a considerable time during power cuts.

1.7.2 Utilization of GeneXpert

Despite these notable benefits already alluded to, and global efforts like the Sustainable Development Goals and End-TB strategies (SDGs) that aim at ending global TB epidemic, it still poses a great threat to lives globally. One of the factors enormously challenging efforts in the fight against TB is underutilization of diagnostic technologies like GeneXpert for rapid diagnosis (32). For instance, in 2015 alone, over 41% of new TB cases were undetected and unreported despite the presence of the GeneXpert diagnostic tool, according to WHO TB burden estimates of 2016 (35). Massive underutilization of this diagnostic tool has been reported in numerous countries (including DR Congo, Kenya, Moldova, Mozambique and Malawi) where, among others, the average turnaround time ranged from 0 to 7 days and lack of national test algorithms were rampant (12, 38).

Clouse et al. conducted a combined observational cohort study (patient level) and cross-sectional study (site-level GeneXpert availability) to evaluate implementation of GeneXpert among HIV-TB co-infected persons, availability, utilization and outcome. They found that although most health facilities had GeneXpert, only 4% of TB/HIV co-infected patients were tested using this diagnostic tool. Additionally, 54% of the patients who were not tested for TB were still being given TB treatment, despite availability of the GeneXpert on the site. In general terms, GeneXpert utilization was low despite the accessibility of the majority to the test (48).

1.7.3 Improvement Science (bridging the know-do gap)

There appears to be a huge gap between the knowledge that research has generates and the real-life application of such scientific knowledge. Onil Bhattacharyya, an authority in Implementation Science calls this chasm the know-do gap (49). In the fight against TB, this know-do gap could be leaving out many TB patients undiagnosed and increasing their infectivity. It could also be delaying the treatment and management of TB patients. Thanks to improvement science, there are empirical ways that the know-do gap can be bridged.

There is a growing interest of late in improvement science, a field which uses scientific methods to make systems and processes perform better. By critically examining the systems, improvement science identifies bottlenecks which could be improved for better performance. Drawing from the principle that a system will continue performing the way it does and achieving the same results until change is made, improvement science introduces changes in ways that allow systems to achieve improved outcomes (50). Since not every change translates to improvement, implemented ideas must be tested and monitored over time to assess if they have resulted in sustained, real or desired improvement (50, 51).

1.7.4 Improvement Models

Quality improvement (QI) aims to tackle problems within a system by identifying components of that system that can be changed to provide better outcomes (52, 53). The commonly used QI science tools include Lean, 6-Sigma and Model for Improvement (MFI) which are aimed to reduce waste, minimize errors in the system and improve systems performance respectively (54). Though each QI technique has a different philosophy, their overall goal is improving system performance. Originally designed for the manufacturing industry, the MFI has gained popularity in the health sector across the globe in the past decade, owing to its flexibility.

1.7.5 The Model for Improvement (MFI)

A change idea is an actionable, specific idea for changing a process, which Quality Improvement Teams test by running Plan-Do-Study-Act (PDSA) cycles in order to reach the aim and improve the system (55, 56). The MFI tests small change ideas on a small scale and for a shorter period and evaluate them in the Plan-Do-Study-Act (PDSA). Improvement ideas are then implemented on a large scale and the process begins again. It is a framework for fast-tracking improvement and it consists of two

main segments; the thinking and the doing segment. The thinking segment contains three vital questions leading to improvement, while the doing segment consists of the Plan-Do-Study-Act (PDSA) iterative cycles aimed at testing changes in real world settings. It is an iterative process of small tests of change of improvement actions. Each test cycle hypothesizes a change, implements it on a small scale, studies whether it works or not, and based on the results, decides what to try in the next cycle (54).

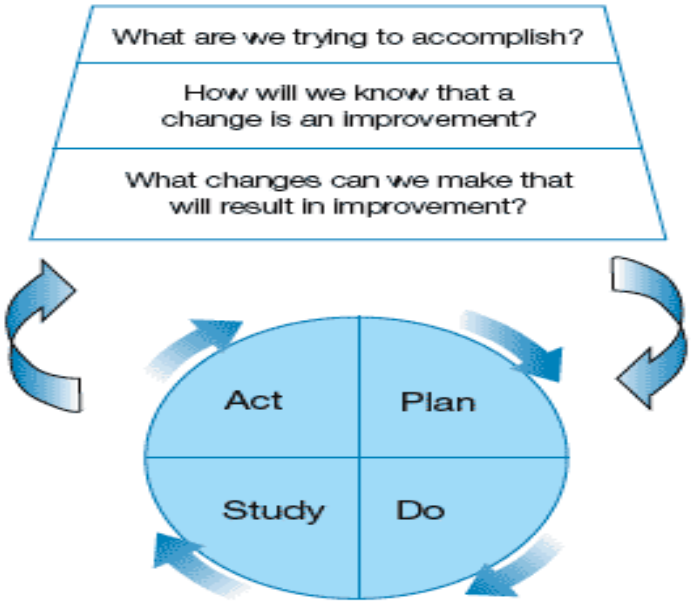


Figure1.1: The Model for Improvement (MFI)

1.7.6 Examples of MFI in Use

The past decade has seen a significant increase in the use of QI methods in the health sector (57-59). The Diabetes Quality Improvement Project (DQIP) which consisted of developing and implementing a set of national interventions for improving quality of diabetes outcomes led to improved quality of life and clinical outcomes for diabetic patients. It also helped in controlling diabetes epidemic in the United States of America (USA) (60). In Sweden ,Lean-6-Sigma (a combination of QI methods aimed at reducing waste and minimizing errors, respectively), and MFI were used to improve the quality of pediatric diabetes care, leading to a reduced possibility of late complications for children and teenagers with diabetes (61).

The Massachusetts Coalition for the Prevention of Medical Errors (MCPMEs) and the Institute for Healthcare Improvement (IHI) used this model to lower adverse drug events by identifying and implementing 16 best change ideas. Ultimately, time to blood anticoagulation for heparinized patients reduced, number of medical errors reduced, safety of patient-controlled analgesia improved, and time to therapeutic anticoagulation with heparin lowered as well (62). Equally, PDSA cycles improved clinical outcomes in a residency and fellowship curricula in medical intensive care in internal medicine at Harborview Medical Centre in the USA (63). The QI programs have also been implemented in Africa.

The Republic of South Africa (RSA) implemented a district-level Prevention of Mother-To-Child Transmission of HIV (PMTCT) QI program in KwaZulu Natal that considerably improved health outcome indicators in one year following intervention. The intervention was a participatory QI consisting of an initial assessment, workshops to assess results, identify weaknesses and set improvement targets and continuous monitoring to support changes. The coverage of Cluster of Differentiation 4 (CD4) immune cells testing increased from 40 to 97 (142.5% increase), uptake of maternal nevirapine increased from 57 to 96% (68.5% increase), uptake of infant nevirapine from 15 to 68% (353.3% increase) and Polymerase Chain Reaction (PCR) testing at six week in post-natal from 24 to 68% (183. 3% increase) (64).

In Tanzania, the MFI was used to improve performance outcomes in perioperative (surgical) care (65). The MFI has also been used to improve the quality of voluntary male medical circumcision in Uganda (66). USAID-ASSIST, in conjunction with the Ministry of Health in Uganda, conducted a project on increasing GeneXpert utilization in five laboratory hubs in Kampala. Using the MFI framework they identified problems of stock outs, power interruptions and conflicting test algorithms, and they implemented measures that raised the number of samples processed by 180% (from 91 to 164) in one month, though they did not assess sustainability (25, 30).

1.7.7 Concept of the Study

When doing QI projects using the MFI framework one of the most common designs for a test of change is the “before and after test” (pretest/posttest design) (67). In this design, a change is made and the circumstances after the change are compared to the circumstances before the change. The collection of data before the change provides the chronological understanding that is the core of the comparison.

Qualitative methods are often involved at the pretest stage (before the intervention) to have a deeper understanding of the system and challenges. Some have interviewed a single participant while others recommend a sample ranging from six to thirty (68). When considering the design of a PDSA test, a run chart that includes multiple measurements before and after the change is made, is easy to plot and offers excellent protection from misinterpreting the test results. (69). Appendix 8 details all the steps in a QI project using MFI.

These evidence-based interventions motivated our hypothesis that implementation of MFI could improve the utilization of GeneXpert in countries where it is underutilized. Though most of the approaches were tested at clinic level, we believe that results we could yield successful results at laboratory level as well.

CHAPTER 2: METHODS

This chapter, describes the methods that were used in this study. It discusses the study design, study context, study population, the intervention and data collection. This chapter also includes data, management and analysis plans, and concludes with an overview of ethical considerations.

2.1 Study Design

This is a quasi-experimental study comprising of pre-intervention, intervention and post-intervention phases with mixed methods study design. The quantitative component was used to measure utilization of GeneXpert pre-and-post-intervention. The qualitative component was used to identify barriers to GeneXpert utilization and develop change ideas before the intervention, and assess level of improvement after the intervention.

2.2 Study Site and Context

The Mzuzu Central Hospital laboratory was specifically chosen because it has one of the lowest GeneXpert utilization rates despite the high TB prevalence in the population which it serves. This is a referral level hospital laboratory in the Northern region of Malawi located at GPS11.4286° S, 33.9959° E. At the time of the study there was no district laboratory that referred GeneXpert samples to this laboratory and all GeneXpert test samples were received from the in-patient and out-patient departments in the hospital. The in-patient department comprises of the Male Medical Ward (MMW),

Female Medical Ward (FMW) and Paediatric Ward (PDW). The Male Medical Ward and the Female Medical Ward form clinicians form the inpatient TB department. The out-patient department comprises of the Antiretroviral Therapy (ART) Clinic and, the emergency and the general outpatient sections.

In the outpatient department, when a patient is suspected of having TB upon physical examination (complaining of persistent cough for 14 to 21 days, weight loss, having a TB history before or having visited a high MDR-TB prevalence area), they are given two bottles, one for on-spot sputum sample and another for a fresh morning sample. The instructions on how to produce a good sputum sample are given by the clinician to the patient. According to the algorithm, the samples from the outpatient department go for TB-microscopy test, unless the patient indicates that they come from a TB-pandemic area, they have recently travelled to TB-pandemic areas, they have once been treated of TB or they have a confirmed HIV positive test. In such cases, these patient samples go straight for GeneXpert test. In the inpatient department, all samples from admitted patients who have or are being suspected of having TB go for GeneXpert test. The rejection criterion for the laboratory was, all samples that have food particles, samples without request forms, samples with insufficient information on the request forms (e.g. no name, no HIV serostatus for admitted patients, insufficient sputum sample).

A QI intervention which followed the MFI framework was implemented and tested at Mzuzu central Hospital. This involved doing a baseline assessment to ascertain the level of GeneXpert utilization before the intervention as our comparator. To gain a deeper understanding of the gaps in utilization, in-depth interviews were conducted with experienced clinicians and laboratory technicians.

A Quality Improvement Team (QIT) was set which received a half-day training before the intervention on how to use the MFI to improve the level of GeneXpert utilization. This team comprised the departmental heads in the clinical departments (inpatient and outpatient departments), and the laboratory departments, headed by the researcher. The QIT was assessed to see it had understood how to apply the MFI. The training session was done in English, but Chichewa and Tumbuka languages were also used to help with explanations where matters were not clear since these two are the most spoken languages in the region. The use of integrated languages and involvement of the departmental heads helped to put the study and intervention into context and it was easy to have buy-in of the leadership (70, 71).

2.3 Study Population and Sampling

2.3.1 Quantitative Component

The study population for the quantitative study before the intervention was all the TB laboratory records, and we purposively selected only the records of tests done in the thirteen weeks before the study (from 1 November 2017 to 9 February 2018 for pre-intervention phase), two weeks of intervention (10 February to 24 February 2018 for the intervention phase) and thirteen weeks after the intervention (5 February to 31 may for the post intervention phase).

2.3.2 Qualitative Component

For the qualitative component, purposive sampling was employed to recruit eight key informants for the in-depth interviews. The inclusion criteria were all clinicians who had worked for five years or more in the TB department and had undergone GeneXpert training, and laboratory personnel working in TB laboratory who had undergone GeneXpert training. Since we wanted to an in-depth understanding of causes of the underutilization of GeneXpert, we purposively sampled the clinicians and laboratory technicians with experience rather than those with less experience to rule out responses to interview questions based on assumptions. Also, those with more experience would be more likely to be familiar with the pre-GeneXpert era and provide insights on evolution of laboratory practice. Of the eight, five were clinicians and two were laboratory personnel and one was a University Research Company (URC) laboratory support representative, an international non-governmental organization that offers technical support to medical laboratories. Of the eight, five were clinicians (all medical officers) and two were laboratory technicians and one was a University Research Company (URC) laboratory support representative. The URC is an international non-governmental organization that offers technical support to medical laboratories.

The QIT was recruited from the same study population (all clinicians and laboratory personnel). Purposive sampling was used to form the QIT which comprised of six departmental heads (two from the laboratory and four from the clinical departments). The researcher, who was the seventh member of the QIT, led the team. The departmental heads were selected to form the QIT to ease the process of implementation of the improvement ideas.

2.4 Overview of the Intervention

The intervention involved training the clinicians and laboratory technicians on the philosophy of the MFI and how to apply it in the context of Mzuzu Central Hospital. This was achieved by forming a QIT. The initial training took half day and, seven weeks later, there was a half day refresher training that served to perfect the skills obtained during the initial training. In-depth interviews were analysed and findings disseminated to QIT. Then the QIT developed strategies on how to improve utilization of GeneXpert after being informed by the findings from the pre-intervention phase and the in-depth interviews with key informants. The QIT meetings were mostly done on Saturdays and Sundays to avoid disturbing normal clinical and laboratory services. For the similar reason, the emergency meetings were always done over the lunch hour.

The training package also involved understanding the TB patient and sample flow from reception to the GeneXpert machine and back, to the time patient gets the results. Flow charts and well-illustrated diagrams were used. The Malawi national TB test algorithm (adopted from WHO) was also used.

As part of the intervention process, in-depth interviews were conducted with eight participants who had vast understanding of the GeneXpert diagnostic tool before the intervention to identify the implementation gaps within the context of Mzuzu Central Hospital. This helped in providing information that deepened the understanding of the barriers to GeneXpert utilization and contextualizing the intervention.

Prior to the intervention, the OPD patients with clinical presentation of TB were being asked to submit a sputum sample for smear microscopy. However, this changed during the intervention after seeing that the national test algorithm gave room to for clinicians to order a GeneXpert test for OPD patients based on their clinical judgment and justification for the test.

2.4.1 The Process of Implementation

The six steps that were taken in effecting the interventions (MFI) are detailed below.

Step one: Setting an aim

The researcher, guided by the baseline findings, came up with the aim statement, describing what the project wanted to achieve, by how much and within what time frame. It helped to answer the first question in the MFI; *what are we trying to accomplish?*

Step two: Creating the QIT

The QIT was set and members received half-day training on the MFI to build their skills on how to go about the improvement cycles.

Step three: Establishing improvement measures

Measures were identified to respond to the question; *how will we know that a change is resulting into an improvement?* The three types of measures that were used were: Outcome Measures which defined the ultimate goal that the entire improvement process wanted to achieve; the Process Measures which were specific metrics that helped in assessing whether the process was positively or negatively leading to the outcome metric. Process measures were useful because they provided an opportunity for corrective and adaptive feedback before the failure of the process; lastly, the Balancing Measures which were specific metrics that aimed at tracking any side effects resulting from improvement actions.

Step four: Developing change actions

Guided by the findings from pre-intervention data and their experience, the QIT developed the change ideas. A total of ten change ideas were initially suggested and were weighed on effort/impact table. Four change ideas emerged best. These four were ultimately merged into two.

Step Five: Testing change actions

The two change actions were tested using PDSA cycles, as explained below. Each PDSA is explained following the pattern outlined in Appendix 9.

2.4.2 First PDSA Cycle: First Change Idea

Improve completion of request forms, justification each test requested and provide patients with proper instructions for sputum production

Step One: Plan

During this stage, the QIT mainly sought to find a way of increasing the number of GeneXpert tests run daily. The main reasons for low GeneXpert utilization were incorrect completion of test request

forms, poor sputum production instructions to patients, and conflicting algorithms used in laboratory and the clinical departments. The QIT decided to train the clinicians and nurses on how to complete the forms and encourage them to justify the tests requested on the form and avoid delegating this task to students.

Step Two: Do

The QIT implemented the first change idea by reaching out to all the clinicians and nurses through morning meetings which are routinely held on Mondays, Wednesdays and Fridays. At each meeting the clinicians and nurses were reminded of this change idea. The QIT decided to collect data daily during the implementation phase (so that the improvement is easily seen) and weekly after the implementation. The researcher was assisted by one member of the QIT to clean weekly datasets, summarize and plot data points on the run charts. The team agreed to meet daily, right after data analysis to learn from the daily findings. The Chief Medical Officer and Chief Nursing Officer were tasked to repeat this communication to the clinicians and nurses for the whole week, in their respective subsequent meetings.

Step Three: Study

During the Study step, data were summarized and plotted on run charts for the week. The QIT members reviewed the quantitative data for the first week of intervention to learn from the findings and act by thinking about developing a new change action.

Step Four: Act

At this stage, the recommendation made in the study step was adopted and implemented in the second PDSA cycle.

2.4.3 Second PDSA Cycle: Second Change Idea

Introduce continuous professional development (CPDs) with nurses and clinicians on GeneXpert

Step One: Plan

During the first PDSA cycle, wrongly filled request forms and lack of interdepartmental communication were the leading cause of low GeneXpert utilization and resulted in a high mean TAT.

The QIT resolved to use the CPDs as a way of bringing all the clinicians and nurses together on the proper way of filling the request forms and how to communicate in time to other departments.

Step Two: Do

A common and spacious venue for the joint clinicians and nurses meeting was booked within the hospital premises. Nurses and clinicians were called the meeting where the researcher presented on: the importance of GeneXpert diagnostic tool, the superiority of GeneXpert over microscopy and x-ray, the problem of underutilization in the country and the hospital, the MFI (as a framework to improve GeneXpert use through the change actions) and how to fill forms and how to capture turnaround time. The questions were addressed by the researcher, the Chief Medical Officer, the Chief Nursing Officer and the hospital director, who took an active part in the whole project and whose interest was huge.

The following points were emphasized

1. Clinicians to justify their choice of test
2. Clinicians to offer proper instructions to patients on proper sputum production techniques
3. Clinicians and nurses to properly fill the test request forms (not to use students)
4. Nurses capture the turnaround time well
5. Use of internal lines to communicate with the requesting departments on missing information about the patient, or when results are out.

After this first CPD, it was suggested and agreed that similar presentations be made once every week during both clinicians and nurses morning meetings. One clinician who was also one of QIT members was tasked with organizing a suitable presentation for each week. One nurse volunteered to do the same for the nurses, working in collaboration with the clinician. The researcher was tasked with ensuring that every presentation was ready and relevant for each week

Step Three: Study

Daily data were summarized and data-points plotted on run charts. The overall aim was to look at what happened, observe the new patterns and compare with previous patterns.

Step Four: Act

The QIT met again to learn from the new findings. The team was concerned about whether the improvement would be sustained, and for how long.

2.5 Data Collection

Data collection was spread over 28 weeks and the weekly tasks were summarized in Table 2.2. Five data capturers were engaged to collect the quantitative data from the inpatient and outpatient departments mentioned in 2.2 above, and were on the following indicators: number of GeneXpert samples run, number of samples rejected, and weekly turnaround time. Data recorded for thirteen weeks, from 13th November 2017 – 10th February 2018, at Mzuzu Central Hospital were analysed as pre-intervention phase. This was followed two weeks of implementing the two PDSA cycles, from 11th to 24th February 2018 (analysed as intervention phase). Data recorded thirteen weeks post-intervention from 25th February to 19 May 2018 were analysed as the post-intervention phase. Data was collected on daily basis were summarized and analysed on weekly basis.

Questions in Appendix 1 were used by the researcher to conduct in-depth interviews (IDIs) with eight study participants between 7th and 8th February 2018. The IDIs were conducted in English and lasted for 17 to 42 minutes. The study participants' offices were arranged to ensure comfortability and convenience as well as privacy. Participants were allowed to speak freely even beyond the scope of the study questions. After the interviews, the recordings were transcribed by hired professional transcribers into computer files and proof-read by the researcher. The questionnaire was piloted before the study. Leading questions and probes were then identified and removed. The piloting was also to check understanding of questions and length of interviews.

Box 2.1: Data collection timeline

1. Phase One|: Pre-intervention
   Week 1
      Days 1 & 2: baseline quantitative data collection and analysis
                  identification of key informants
      Days 2 - 4: in-depth interviews with key informants
                  qualitative data analysis
      Day 5:   set up and meeting of the QIT

2. Phase Two: Intervention
   Week 2: first PDSA, first data point
   Week 3: second PDSA, second data point

3. Phase Three: Post-intervention
   Week 4: third data point
   Week 5 fourth data point
   Week 6: fifth data point & QIT review meeting
   Week 7: sixth data point
   Week 8: seventh data point
   Week 9: eighth data point
   Week 10: ninth data point
   Week 11: tenth data point
   Week 12: eleventh data point
   Week 13: twelfth data point
   Week 14: thirteenth data point
   Week 15: fourteenth data point
   Week 16: fifteenth data point
            second round of interviews with key informants and qualitative data analysis

2.6 Reflexivity: The Researcher's Role

At the onset, the researcher introduced himself as a Master of Epidemiology- Implementation Science candidate at the University of the Witwatersrand, School of Public Health. The researcher worked for three years with the Ministry of Health (Malawi) at Mzuzu Central Hospital as a Laboratory Technologist until 2017. The researcher had worked in different laboratory departments including the TB department, chemistry and haematology. He had also been part of the Laboratory Quality Assurance team. Part of his duties as a laboratory technologist, the researcher was involved in various TB trainings to nurses and clinicians on test algorithms, sample collection and transportation. The

Because the researcher identified himself as a former worker at this institution, the study participants were more confident in him and this helped them to truthfully answer the questions and supply the required information. The participants were also freer to express themselves because he could introduce himself in any of the three major languages (Tumbuka, Chewa and English) and allowed participants to switch to any of these languages. This allowed flexibility of the interviews and free expression of thoughts by the participants in any language they preferred. The TB laboratory is a section, is nested within the general laboratory. Rotational schedules had previously been introduced to ensure that every laboratory technician is acquainted with TB diagnostic methods, but delays in handling of samples resulted in continued prolonged TATs. Again, sending laboratory technicians who had no interest to work in TB laboratory never resulted in making them work in TB laboratory.

To reduce personal biases by the researcher's former experience at this institution, the interview-guide questionnaire used was piloted before the study. The professional qualitative data analyst from Mzuzu University was assisted in coding to minimize bias.

2.7 Data Management

2.7.1 Quantitative Data

Daily datasets were entered into Excel after collection. Data were double-checked for inconsistency, duplication and missing values. While filtering data, two repetitions were noted in data entry whereby two patients were captured twice, having same names, same age, same dates and same results. These were sorted immediately by removing the duplicate. Missing values were rectified immediately by checking with the hardcopy TB registers at both the laboratory and the wards. Then the Excel datasets were exported to Stata 14SE for analysis.

2.7.2 Qualitative Data

The interviews were transcribed by a hired professional transcriber, and were proof-read by the researcher. The transcribed interview files were uploaded onto Nvivo11 for coding and analysis.

2.8 Data Analysis

Objective 1: To identify factors affecting GeneXpert utilization at Mzuzu Central Hospital TB Laboratory in Malawi.

Since context specificity is critical in identification of implementation gaps for quality improvement projects, in-depth interviews were conducted with experienced clinicians and laboratory technicians prior to the intervention (72).

The grounded theory approach was used to analyse the data. The inductive themes were identified from the data. A good category system is said to have "arisen" from the data (68). Code validity was ensured by initially coding the first two transcripts and discussing with an expert in qualitative research from Mzuzu University. Afterwards, the codes that were agreed upon were used to code the rest of the interview transcripts. Only the themes that were relevant to the research question were reviewed and used. Ultimately, five themes emerged as factors affecting GeneXpert utilization at Mzuzu Central Hospital. These were: knowledge and information, motivational, financial, technical and human resource factors.

The fishbone was used to show how each factor resulted in low GeneXpert utilization. A fishbone diagram, also called a cause and effect diagram or Ishikawa diagram, is a visualization tool for categorizing the potential causes of a problem in order to identify its root causes. It is a visual way to look at cause and effect and helps in brainstorming to identify possible causes of a problem and in sorting ideas into useful categories(73).

Objective 2: To develop, implement and document change ideas for improvement of GeneXpert utilization using the Model for Improvement at Mzuzu Central Hospital TB Laboratory in Malawi.
The QIT developed eleven improvement ideas. These ideas were: Increase the number of CPDs on TB with more focus on GeneXpert, improve instructions given to patients on sputum collection, train clinicians on how to complete TB GeneXpert request forms, make the algorithm more accommodative than restrictive so that patients from OPD whose clinical presentation qualifies them for GeneXpert should be treated as such, motivate laboratory technicians to handle samples for GeneXpert in time, use rotational schedule for laboratory technicians to work on GeneXpert machine, increase the doctor : patient ratio and increase financial support for GeneXpert cartridges and reagents.

Given the limited time and resources that were available for the study, the QIT developed two improvement ideas that would give biggest impact with the least amount of effort, using the Effort/Impact analysis. These were;

1. Improve completion of request forms, justification each test requested and provide patients with proper instructions for sputum production
2. Introduce continuous professional development (CPDs) with nurses and clinicians on GeneXpert

Objective 3: To measure the impact of the change ideas on GeneXpert utilization at Mzuzu Central Hospital TB Laboratory in Malawi over a three-month period in 2018.

Run charts, which are graphs plotted over time which display the trend and pattern of a process, were plotted over the entire duration of the study (pre-intervention, intervention and post-intervention phases) to measure the effect of the implemented improvement ideas on utilization of GeneXpert (74). T-tests were run in Stata 14 SE to compare means before and after the intervention.

- Number of sputum samples run per week: sum of total sputum samples run in 5 work days
- Mean weekly TAT: sum of weekly TAT divided by 5
- Weekly rejection rates: $\frac{\text{Total number of samples rejected in a week} \times 100}{\text{Total number of samples received in a week}}$

2.9 Ethical Considerations

Ethical clearance and approval for the research was granted by the Human Research Ethics Committee (HREC) of the University of the Witwatersrand before commencement of any data collection (see appendix 4), Ethics clearance number M171193. Clearances from the Malawi National Health Sciences Research Committee (NHSRC) and the Mzuzu Central Hospital Research Committee were also given prior to kick starting data collection (see appendices 2 and 3). Study participants were given the information sheet a day before the interviews and informed consent forms were signed prior to commencing any interview (see Appendix 6). All interviews were audio recorded, with the permission of the respondent being interviewed (appendix6). Care was taken by the researcher to assure the respondents that they, and the place of their work, would not be identifiable in any subsequent report

by using a study code. Collected data were used strictly for the purposes of this study and were password-protected. Also, confidentiality and anonymity were ensured by using code numbers during data collection. Names and identifiable data of participants were not documented.

CHAPTER 3: RESULTS

This chapter reports the results obtained from the analysed data in all the three phases of the study.

3.1 Pre-intervention GeneXpert utilization

The results of the thirteen weeks' retrospective baseline assessment were summarized in tables and run charts. The mean number of samples run per week was 11.0 (SD: 3.0). The weekly rejection rate was 8.2% (SD: 5.9). The mean weekly turnaround time was 80 hours (SD:15.6) hours with a mean of 67.8 hours.

Table 3.1: Findings of indicators before the intervention

Indicator	Week												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Number of weekly samples run	13	8	14	12	15	8	15	11	10	7	8	10	9
Number of samples rejected	1	1	1	1	0	1	0	1	1	0	1	2	2
Rejection rate (%)	7.1	11.1	6.6	7.7	0	11.1	0	8.3	9.1	0	11.1	16.7	18.2
Mean TAT(hours)	86.8	39	77.4	46.5	90.0	192.0	102.0	80.0	86.4	72.0	51.0	46.0	104.0

3.1.2 Factors affecting GeneXpert utilization

Eight participants were interviewed in order to identify implementation gaps in GeneXpert utilization within the context of Mzuzu Central Hospital. Five male clinicians in total were interviewed. Two of these were from the in-patient department and three were from the out-patient department. Two laboratory technicians and one URC- laboratory technical support staff were interviewed. The mean age of the participants was 30 years (SD:3.0).

The full-details of the qualitative results are presented in Appendix 10. Five themes emerged from the interviews. These were knowledge and information, human resources, financial resources, technical and motivational factors. Motivational and knowledge/ information factors were related to the staff while the others were institutional factors. The themes are summarized in Figure 3.1

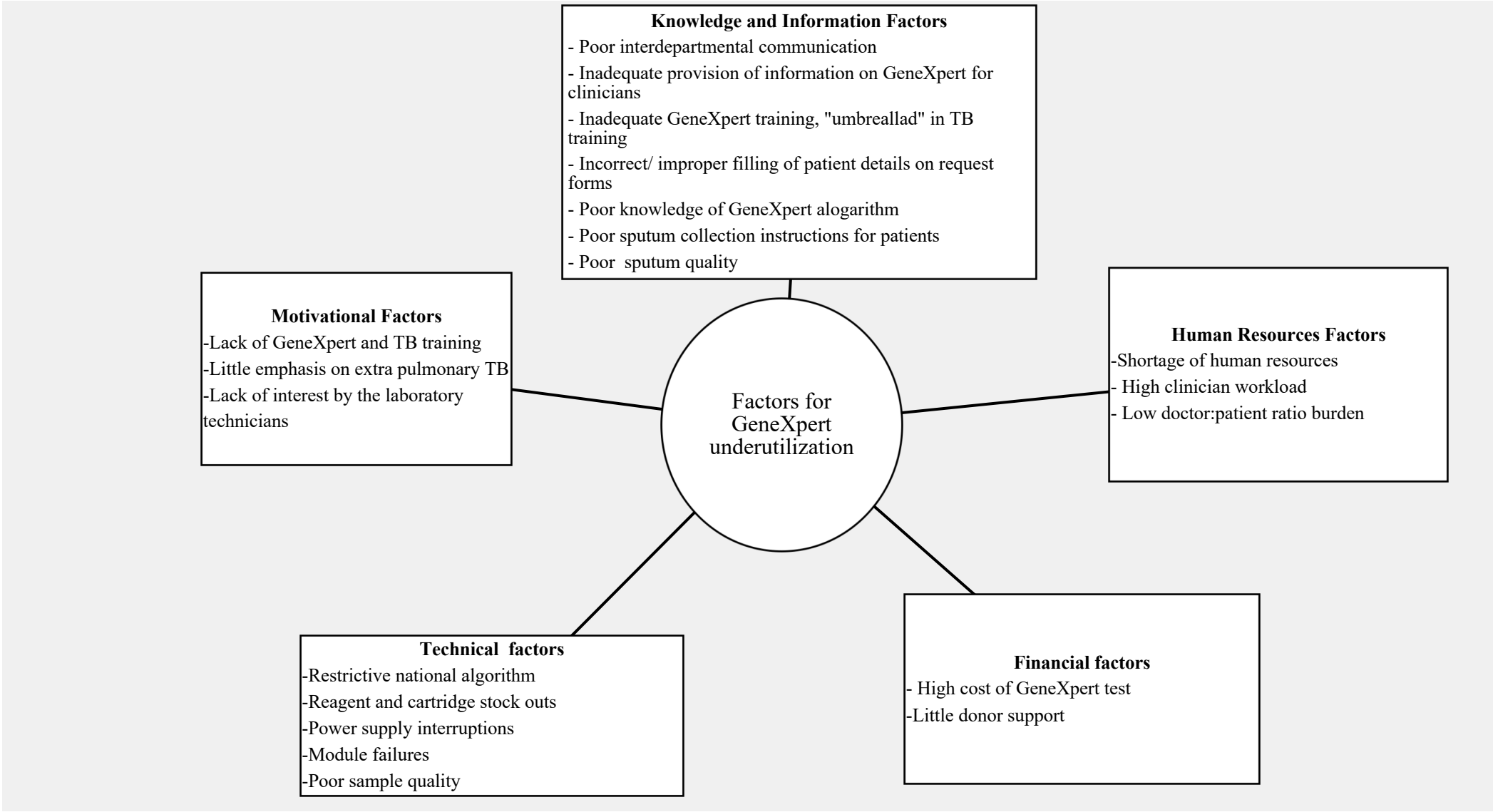


Figure 3.1: Factors contributing to GeneXpert underutilization at Mzuzu Central Hospital (Themes and sub-themes)

The factors for GeneXpert underutilization were summarized in table 3.2 according to how they affected each indicator. From the table, poor interdepartmental communication and incorrect/ improper filling of patient details on request forms appear to be one factors that affected all the indicators.

Table 3.2: Factors affecting each indicator

Indicator	Increased TAT	Increases rejection rate	Low number of samples run
Factors	▪ Poor interdepartmental communication ▪ Inadequate provision of information on GeneXpert for clinicians ▪ Incorrect/ improper filling of patient details on request forms ▪ Poor knowledge of GeneXpert algorithm ▪ Shortage of human resources ▪ Reagent and cartridge stock outs ▪ Power supply interruptions ▪ Module failures ▪ Lack of interest by the laboratory technicians	▪ Poor interdepartmental communication ▪ Incorrect/ improper filling of patient details on request forms ▪ Poor knowledge of GeneXpert algorithm ▪ Poor sputum collection instructions for patients ▪ Poor sputum quality (especially with food particles)	▪ Poor interdepartmental communication ▪ Inadequate provision of information on GeneXpert for clinicians ▪ Inadequate GeneXpert training, "umbrellaed" in TB training ▪ Incorrect/ improper filling of patient details on request forms ▪ Poor knowledge of GeneXpert algorithm ▪ Poor sputum collection instructions for patients ▪ Poor sputum quality ▪ Shortage of human resources ▪ High clinician workload ▪ Low doctor : patient ratio burden ▪ High cost of GeneXpert test ▪ Restrictive national algorithm ▪ Reagent and cartridge stock outs ▪ Power supply interruptions ▪ Module failures ▪ Lack of GeneXpert and TB training ▪ Little emphasis on extra pulmonary TB ▪ Lack of interest by the laboratory technicians

The QIT used information gathered in the pre-intervention phase to develop an aim statement. The overall aim was to increase the number of sputum samples, reduce turnaround times and eliminate rejection rates.

Box 3.1: Aim statement

The intervention aims
i. To increase the average number of sputum samples run per week at Mzuzu Central Hospital TB laboratory by 100% from baseline over the next thirteen week by implementing improvement ideas.
ii. To reduce the average weekly TAT of 80 hours by more than 50% to less than 40hrs.
iii. To reduce the average weekly rejection rate from 8.2% to 0% (elimination).

The QIT performed a root-cause analysis. This is a structured team process that helps to identify factors or causes of an unfavourable event (73). Possible change ideas that could be implemented to improve GeneXpert utilization according to their predicted level of effort and their perceived resultant impact are presented in Figure 3.2. Solutions with high impact and low effort and those with high impact and high effort were prioritized because of their ease of implementation.

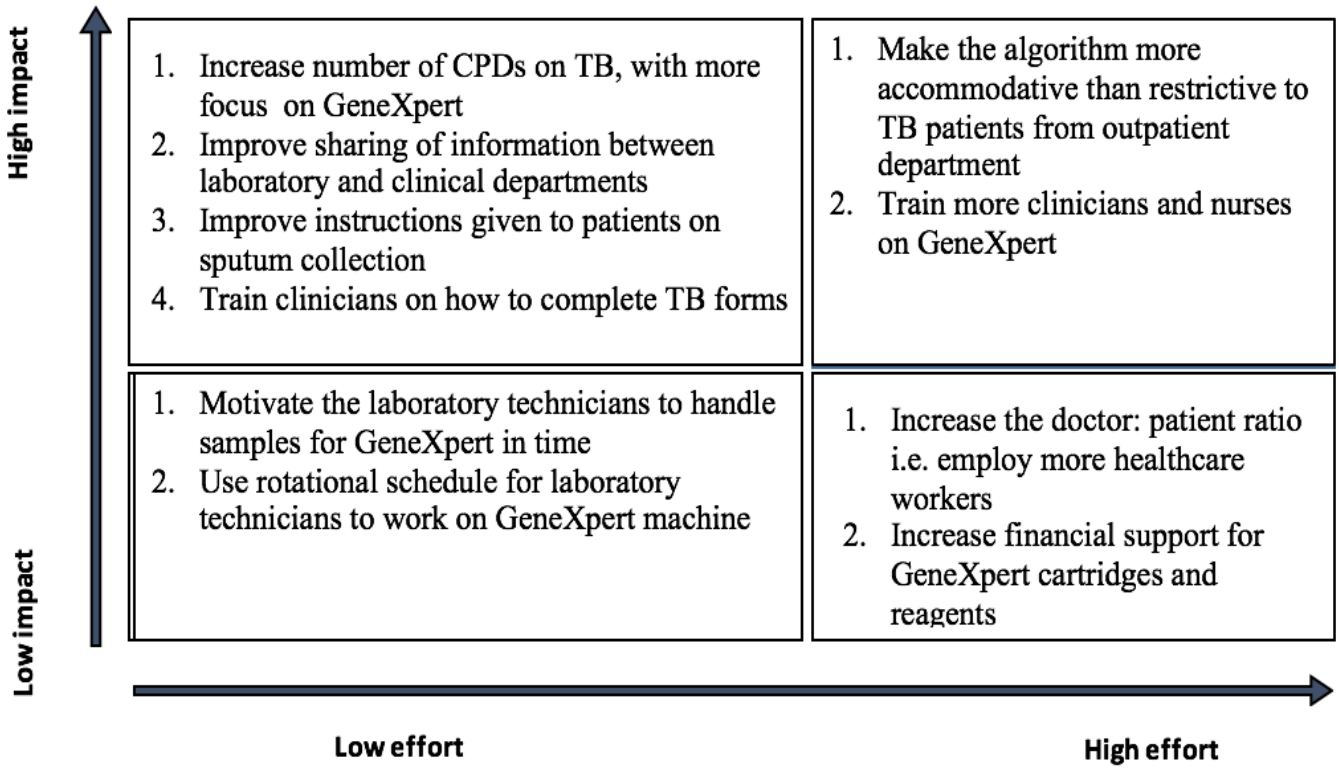


Figure 3.2: Effort/Impact analysis of suggested improvement ideas

Given the limited time and resources that were available for the study, the QIT developed and implemented two improvement ideas that would give biggest impact with the least amount of effort. These were;

1. Improve completion of request forms, justification each test requested and provide patients with proper instructions for sputum production
2. Introduce continuous professional development (CPDs) with nurses and clinicians on GeneXpert

The QIT also developed driver diagram utilization which helped to gain a concept of how each change concept would result in the desired improvement of the aim statement. A driver diagram is a visual representation of a theory of how things might be better, building upon knowledge gleaned from research, observation, and experience (75). The driver diagram showed diagrammatically the theory of how the aim statement was going to be achieved through change concepts that targeted increasing the clinicians, nurses and laboratory technicians' knowledge about GeneXpert and proper filling of test request forms.

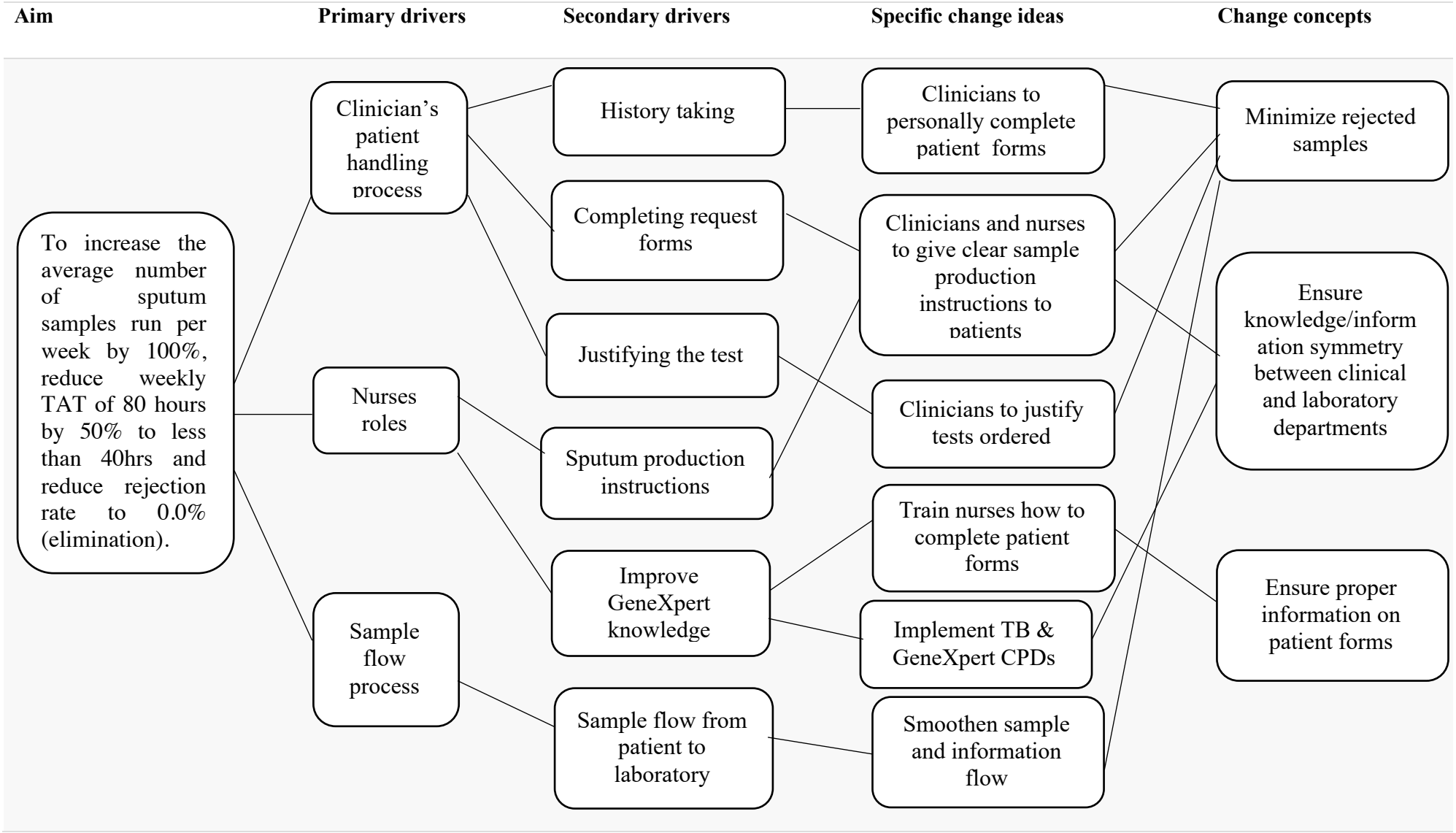


Figure 3.3: Driver diagram for improvement of GeneXpert utilization

3.2 The Intervention Phase

The two improvement ideas were sequentially implemented for two weeks, that is, first change idea was maintained when the second was introduced. Table 3.2 illustrates the changes that the two improvement ideas resulted in. The first PDSA resulted in increased number of samples per week, reduced turnaround times and reduced rejections. All the three indicators had significant changes. Further improvements were observed after implementation of second PDSA and all the indicators improved significantly. Overall improvement was: number of samples run per week increased by 73%, turnaround times reduced by 64% and rejection rate reduced by 70%.

Table 3.3: Summary of the findings of the intervention phase

Indicator	**Study phase (percent change)**			
	Before intervention	After first PDSA	After second PDSA	Combined effect
Mean number of samples run per week	11	18 (+63%)	20 (+10%)	19 (73%)
Mean TAT per week (hours)	80	39 (-51%)	34 (-13%)	36.5(-64%)
Mean rejection rate (%)	8.3	5 (-38%)	0 (-100%)	2.5 (-70%)

3.3 Post-intervention Phase

In the post intervention phase, the number of samples per week increased from 19 during intervention phase to 27 (71% increase). The turnaround times reduced from 36.5 hours during the intervention to 16 hours (56% reduction), while rejection rate reduced from 2.5% during intervention to 0.3% (88% reduction). Table 3.3 compares the findings of intervention and post intervention phases.

Table 3.4: Finding of intervention and post-intervention phases

Indicator	**Study phase (percent change)**	
	Intervention	After intervention
Mean number of samples run per week	19	27 (+71%)
Mean TAT per week (hours)	36.5	16.0 (-56%)
Mean rejection rate (%)	2.5	0.3 (-88%)

Overall, the number of samples run per week increased from 11 before the intervention to 27 after the intervention at 95% confidence interval $p < 0.001$ (see figure 3.4). The turnaround times dropped from

a weekly average of 80 hours before intervention to 16 hours after intervention at 95% confidence interval, p <0.001 (see figure 3.5). The rejection rate dropped significantly from 8.2% before the intervention to 0.29% after the intervention (p <0.001) (see figure 3.6). Up to 140 GeneXpert samples were run before the intervention (thirteen week period), 38 during the intervention (two weeks period) and 358 after intervention (thirteen weeks period).

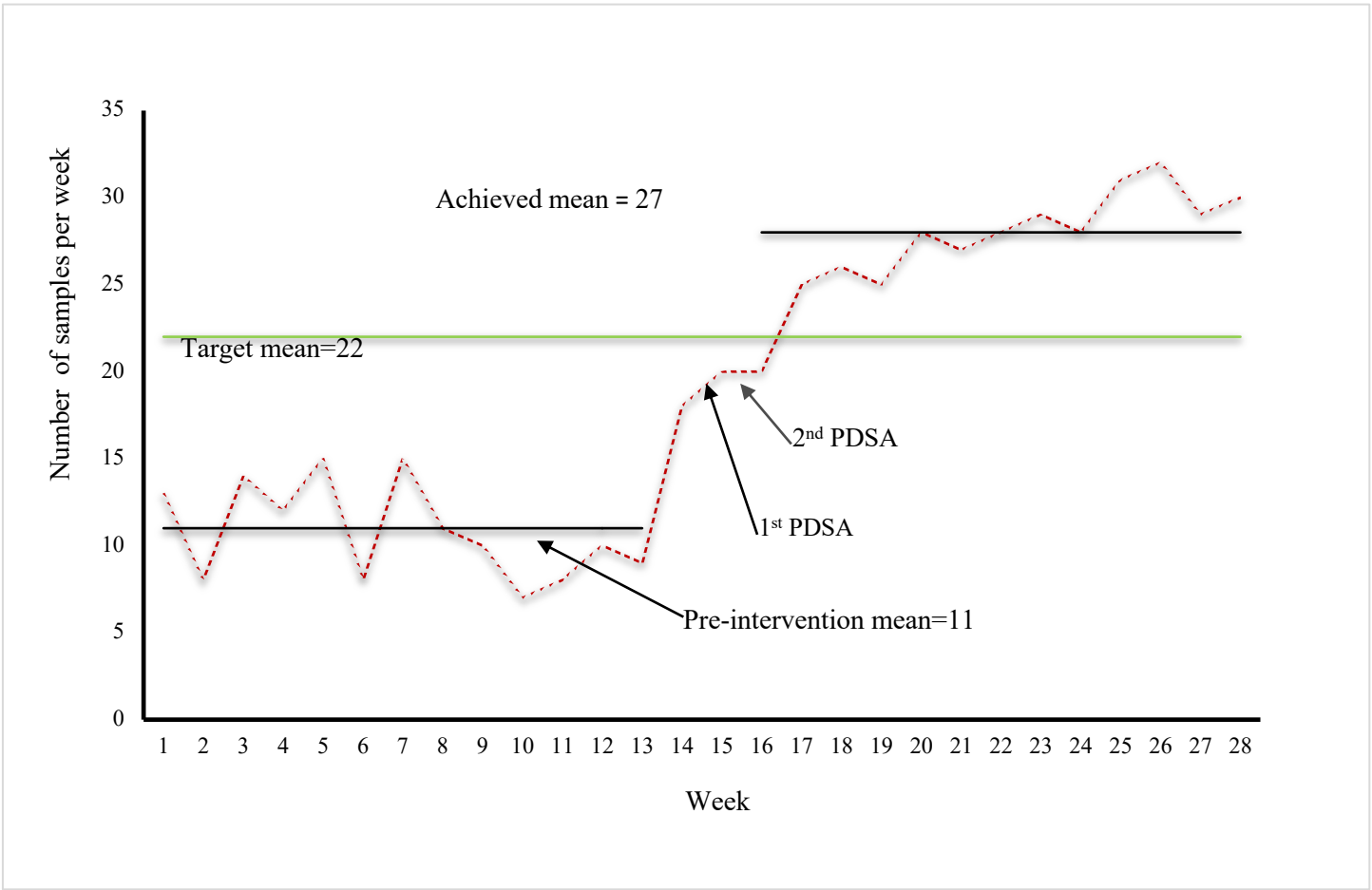


Figure 3.4: Number of weekly samples in the three study phases

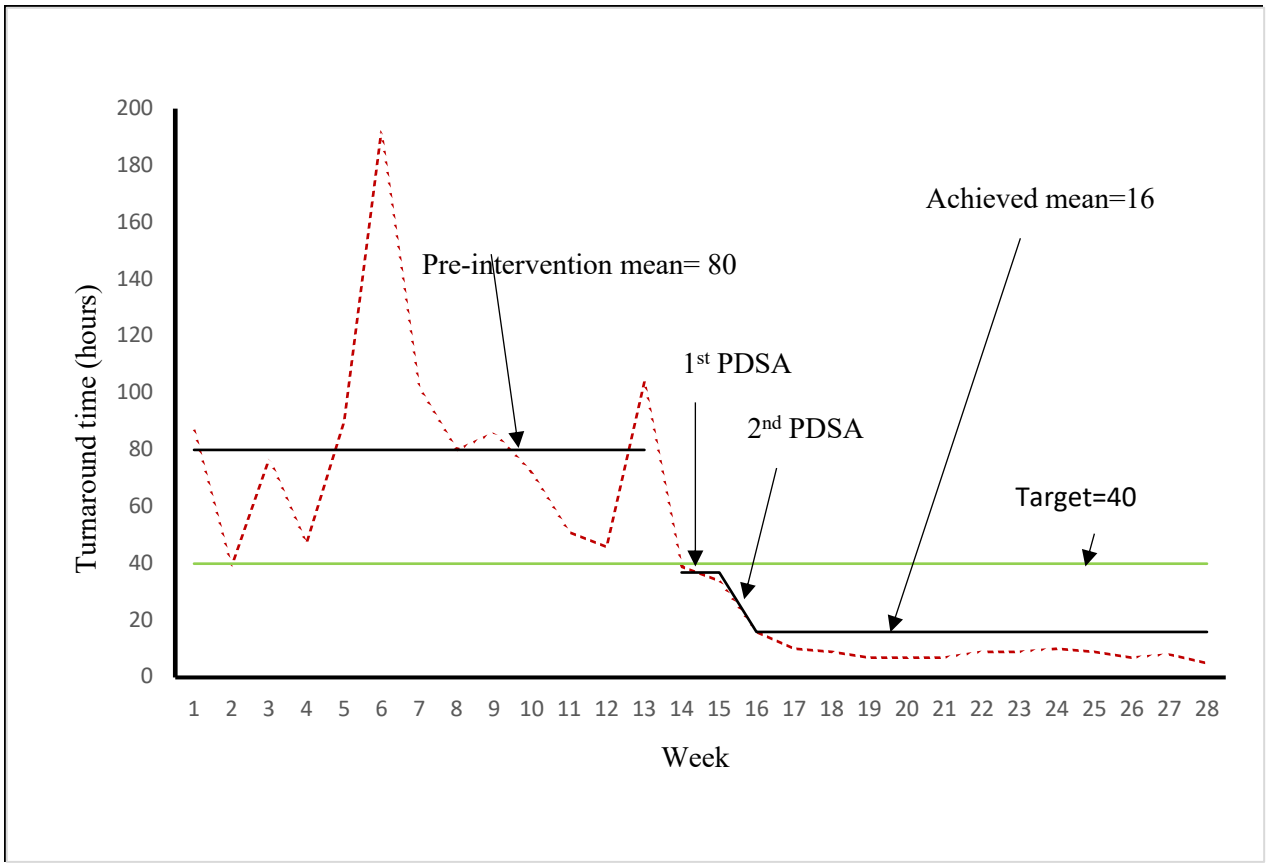


Figure 3.5: Turnaround time in the three study phases

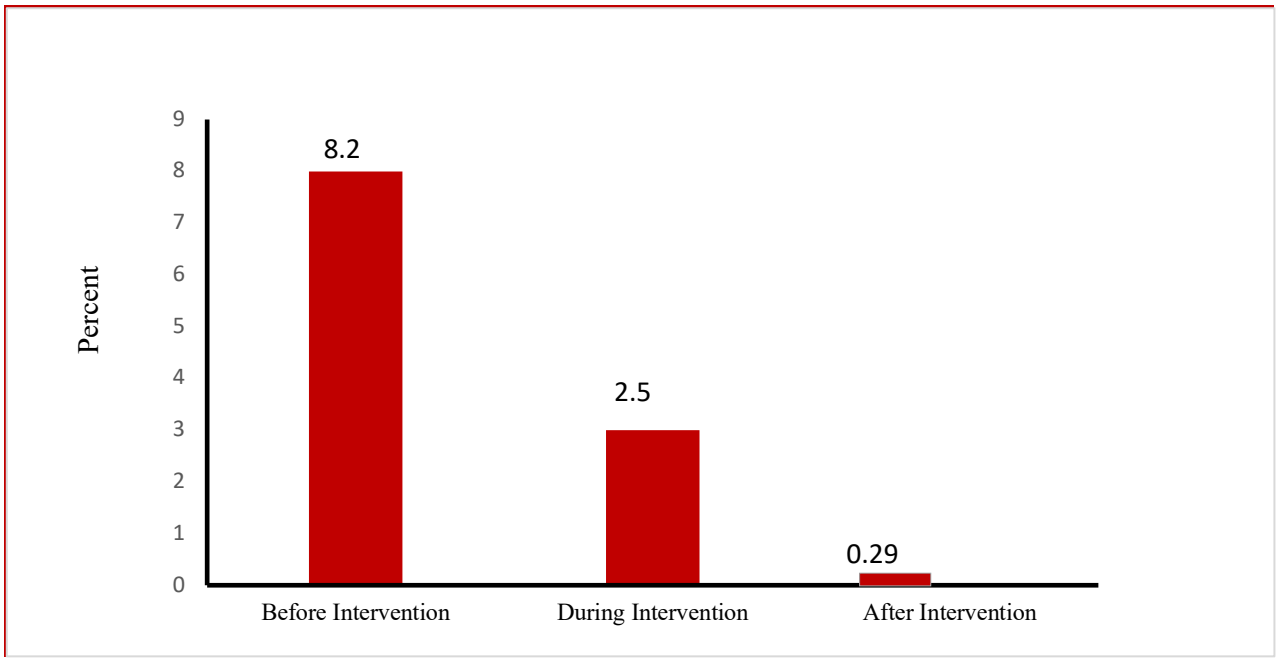


Figure 3.6: Average rejection rates in the three study phases

Table 3.4 gives a summary of all the indicators and the target values the achieved values. The table shows that the changes in the three indicators were all statistically significant, with p-values less than 0.001.

Table 3.5: Comparison of the indicators before and after intervention

Indicator	Baseline value	Target value	Achieved value	Achieved improvement	P-value
Mean of weekly samples run	11	22	27	145.5%	<0.001
Mean of weekly TAT (hours)	80	40	16	80%	<0.001
Mean rejection rate	8.20	0.00	0.29	96.5%	<0.001

In the second round of interviews in week thirteen after the study, the key informants stated that the number of samples had increased, sputum sample quality had improved, and rejection rates had decreased and forms were being properly completed. However, the key informants were quick to specify areas that needed attention to sustain the improvement. These included the continued organization of CPDs, continued improved communication between the laboratory and other hospital departments and the organization of formal GeneXpert trainings (see details in Appendix 11).

CHAPTER 4: DISCUSSION

In this study, small change ideas were developed and implemented using the Model for Improvement framework to improve GeneXpert utilization at Mzuzu Central Hospital in Malawi. Results from this study show that the intervention led to significant improvement which was sustained during the study period. There was an increase in the number of samples run per week and a decrease in turnaround time and rejection rates. These improvements may be attributed to the intervention.

4.1 Baseline Findings

At baseline, the number of samples run per week was low (11 samples per week) as compared to the volume of samples GeneXpert is built to handle (80 samples per week) (33). These findings are consistent with those found by Karamagi et al. (76) where five samples instead of 16 were being run per day. The results are further strengthened by the findings of Hanrahan et al. (33) where only one GeneXpert test was being run per day. Similarly, Creswell et al. (32) also noted low levels of utilization in nine countries in his study to evaluate results of early GeneXpert implementation. He found that the GeneXpert machine was only working four to five hours per day meaning that each machine processed only four to eight samples per day.

4.2 Factors that Resulted in Underutilization of GeneXpert

From the in-depth interviews, the factors that resulted in underutilization of GeneXpert were grouped into five themes.

Knowledge and information

Under this theme, the factors that emerged included lack of interdepartmental communication such that the laboratory and the clinical departments used different eligibility criteria (test algorithm) for samples to be tested using GeneXpert. In assessing the levels of knowledge among healthcare workers in Malawi, Banda et al. found that TB knowledge in terms of its pathophysiology and the algorithms among medical assistants was low, (77). To support this finding, Agonafir et al. also found that most healthcare workers (54.6%) had low knowledge about GeneXpert and its eligibility criterion (31).

Improperly completed forms were also a barrier to utilization in this study and it resulted in sample rejection or doing microscopy instead of GeneXpert. This also appeared as a barrier to GeneXpert utilization in a study conducted to improve GeneXpert utilization in Uganda (76). Another factor for underutilization was that doctors and nurses provided patients with poor sputum collection instructions because of workload burden as they had minimal time spent on each patient. This resulted in module failures due to blockage of the GeneXpert tubes by food particles in samples. These results are consistent with the findings of Meyer et al. which showed that quality of sample determine the results of the GeneXpert test i.e. blood stained sputum had low sensitivity and samples with food particles often produced indeterminate results due to blockage of tubes of the GeneXpert (78).

Human Resources Factors

This study found that there was a human resource shortage which resulted in a low doctor-patient ratio burden and huge clinician workload. This compromised the time given to each patient for history taking and physical examination, hence most signs of TB that would qualify a patient for GeneXpert were left unconsidered, creating a lot of missed opportunities. These results are consistent with the other findings which showed that most hospital settings in low and middle income countries have a low doctor-patient ratio, compromising the quality of health services rendered to patients (79). To fully realize the benefits of GeneXpert, there is need for funding agencies and governments to capitalize on strong patient-centered, staff and training programs (80) that are aimed to train more medical personnel so that the doctor to patient ratio burden is reduced and the quality of services rendered to patients improves. Dakito et al. in their study in Ethiopia found that the involvement of Health Extension Workers in sputum collection and treatment improved smear-positive case detection and treatment success rate due to improved service access (31). This could also be applied to improve GeneXpert utilization in areas with low health workers like Malawi.

Technical factors

Under this theme, factors of underutilization included reagent and cartridge stock outs, power supply interruptions and module failures. Since days would go without GeneXpert tests run, turnaround times were longer than normal and a lot of eligible patients went untested representing missed opportunities. These findings correlate with those of Karamagi et al. in Uganda, which is a low income country, that stock outs, module failures and power supply interruptions resulted in missed opportunities and long turnaround times (76). This study showed that stock outs were due to lack of a dedicated quality improvement staff member to make sure stocks were ordered in time, module failures were due to poor

sputum sample qualities especially those with food particles and power supply interruptions was a national problem.

Financial factors

Many studies including that of Menzies et al. and Andrews et al. have found that GeneXpert is a cost-effective test (82, 83). Vassal et al. though, found that GeneXpert was cost-neutral and highlighted the importance of considering implementation constraints when rolling out and evaluating the cost-effectiveness of a new diagnostic platform (84). In the face of little donor support for the Ministry of Health made hospital management opt for the less costly smear microscopy for TB diagnosis rather than the more costly GeneXpert. In a study evaluating the implementation of GeneXpert, it was indicated that the cost of GeneXpert is higher than that of smear microscopy (79).

The findings that most hospital management in middle and low income settings prefers smear microscopy since GeneXpert is expensive support these findings (33). However, there is need to do more research to further explore management dynamics and ideologies that might be leading to this situation. The implications of using microscopy instead of GeneXpert cannot be overemphasized since smear microscopy is less sensitive than GeneXpert, weakening the efforts in the fight against TB (85-87).

Motivational Factors

This study also found that there was lack of GeneXpert and TB training which acted as a disincentive and a de-motivator for clinicians to know about GeneXpert and for the laboratory technicians to use it routinely. This is consistent with the findings from Agonafir and colleagues (31) which indicated that GeneXpert training act as motivators for workers and are one of the best sources of information and knowledge about GeneXpert. Although Naidoo et al. in their study to evaluate changes in Healthcare Workers' knowledge about TB following a TB training found no significant clinical improvement (88), Agonafir et al. found it a great motivator for the healthcare workers (31).

With the limited time and resources available, this study intervened on knowledge and information, technical and motivational factors by using the two PDSA cycles.

4.3 Intervention Impact

One of the advantages the MFI has is that it offers a unique opportunity to learn from one PDSA cycle before implementing the next (89). As such, "single-bullet" interventions are likely not to produce the desired impact since interventions have to be multi-faceted and developed iteratively and adapt to local settings. This affords enough opportunity to respond to unforeseen obstacles and prevent unintended effects of the intervention.

According to the studies cited in this report the interventions were successful. For instance, in northern Uganda in 2016, the MFI was used to increase the number of GeneXpert tests run per month from 91 to 448 and the number of identified TB positives from 19 to 76 in five laboratory hubs (76).

In this study, the implementation of small change ideas coupled by a robust QIT and a multi-pronged study design led to significant improvement where an increase in the number of samples run per week and a decrease in TAT and rejection rates in the immediate post were observed. This finding is consistent with the findings of Kashmira et al. in their prospective study assessing the impact of GeneXpert detection of TB cases in the wards and initiation of TB treatment. They found that GeneXpert contributed minimally to overall TB diagnosis due to, among others, implementation challenges on sputum collection and care linkage between inpatient and outpatient departments (90), and recommended that these and other challenges should first be addressed for GeneXpert to start contributing substantially to patient care. Although the set target for rejection rate (zero percent) was not reached, the achieved value was close to the target and the trend was steady towards elimination. This may suggests that if the study had continued for a longer time, like Durlak suggests a one year, the target could have been reached (91).

These findings signify that implementation of small change ideas within the context of a health facility can greatly contribute positively to the fight against TB. The findings suggest that a similar approach might be successful in solving many health systems bottlenecks using the quality improvement models like the MFI in a contextualized manner.

4.4 Strength of the Study

The fact that this study was prospective, comparing pre-intervention with post-intervention findings is one of the strengths since it demonstrated empirical improvements in real life setting. The use of mixed methods is also another strength this study had. The in-depth interviews with key informants added strength to the quantitative data since they gave information on experiences and perceptions of those who actually did the work and therefore helped to tailor the intervention to meet the needs in this setting.

4.5 Study Limitations

This study took on a narrow scope of focusing on process indicators for outcomes. Future studies should consider facility or patient-level clinical outcomes and indicators that come as a result of improving GeneXpert utilization in order to satisfy more quality improvement aims of "patient-centeredness" (89). These include quarterly TB notification rates, proportions of microbiologically confirmed TB cases, proportions of newly diagnosed HIV-infected patients screened for TB, time to TB treatment initiation, and facility-level TB treatment success (as defined by WHO) (3, 92).

The study only focused on two of the five factors identified. However, the factors addressed were deemed most relevant by the QIT and were sufficient to improve performance to goal targets. Furthermore, time constraints and field realities made it difficult to continue with the intervention for longer than three months. Therefore, longer term assessment of sustainability was not possible.

Many researchers have hinted on the importance of motivating the health personnel to improve service delivery. The factors that have often emerged to motivate healthcare workers include type of hospital (whether it is primary, secondary of tertiary level hospital, with tertiary level having a highest motivation score), infrastructure development (e.g. staff houses), performance evaluation and management, staff development and promotion, availability of necessary resources (equipment and consumables) and access to formal training (93, 94). Although the participants in our study only hinted that staff development and promotion were issues, these factors were regarded as being high effort and high impact (looking at the scope of this study), hence we could not implement them. However, the government and other stakeholders should consider this aspect for general improvement of service delivery.

The interview-guide design was not based on an established implementation science framework such as the Consolidated Framework for Implementation Research (CFIR) (95). The CFIR has domains; intervention characteristics, inner setting, outer setting, characteristics of individuals involved, and the process of implementation. Within each domain are constructs (e.g. resources, leadership engagement, etc.) that further help specify and explain how and why interventions work in real-world settings. Future studies should consider applying the CFIR in designing the interview guide, structuring the presentation of the findings, and identifying areas for improvement using the IMF. Implementation outcomes (such as "reach" from the RE-AIM model) (96), could be considered and analysed over longer post intervention time horizon (6-12 months) to more fully measure the sustainability of the intervention . With more mentorship of laboratory and clinical personnel by the quality improvement champions and a longer study period, the results could be more generalizable.

Cascade-thinking is a model that helps to understand the steps that patients and TB service providers must negotiate to receive and deliver quality TB services (17-20). A logical "diagnostic and care pathway" for TB that describes several steps including how patients are identified for testing through screening, how testing is done, and how TB is diagnosed and results communicated to patients, has been presented by Perter Macpherson and colleagues (21). Application of this model, or other similar cascade-informed model, would help in designing and sustaining future quality improvement projects for GeneXpert utilization and systems harmonization between clinical and laboratory departments.

CHAPTER 5 - CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

In conclusion, the MFI was successfully used to identify change ideas that were easy to implement at low cost and with low effort. Even though only two of the five factors identified were addressed, the interventions were able to produce marked improvements in a short space of time. Although no intervention was developed for motivation, motivation was partially addressed by the interventions that were implemented since the CPDs that were introduced motivated the staff members. This

methodology is useful particularly in resource scarce environments as, once identified, changes can be made at little extra cost. There is also need for a "champion" to ensure continued implementation of change ideas.

The improvements were the result of choosing the right improvement model (MFI) coupled by effective implementation of the change ideas within an enabling context. The main challenges were categorized into information and knowledge, financial, motivational, human resource and technical. The challenges which were addressed in the study were fell mainly into knowledge and information, technical and motivational categories, using the two PDSA cycles. The fact that our study had a pretest and posttest aspect offers support to the evidence of the improvements arising from the intervention. This demonstrates that the implemented change ideas were predictive of the improvements in GeneXpert utilization in the post intervention phase of the study.

5.2 Recommendations

A key recommendation is the use of tools like MFI to identify areas for intervention. Therefore interventions tailored to needs of the facility/setting are more likely to succeed.

This study only observed the effects of the intervention for thirteen weeks, therefore, future studies and projects should be conducted for longer periods of time and with adequate financial support. The Ministry of Health (Malawi) and the funding agencies should also consider upscaling the intervention to other central hospitals (Kamuzu, Zomba and Queen Elizabeth). Since it is often difficult to sustain the changes that have been developed in improvement studies, the use of improvement "champions" to ensure continued practice of the implemented change ideas is key. Future studies should also consider implementing the change ideas that were suggested but not implemented in this study and using multiple tests of change (more than two PDSA cycles) since this has yielded desirable outcomes in many settings.

Since TB training that was not tailored for GeneXpert also contributed to low underutilization of GeneXpert, the Ministry of Health and the funding agencies should start tailoring their trainings to the GeneXpert and express it clearly even under TB training. Finally, we realize that the fight against TB is a cascade that begins with the clinician making assessment on the patient, recommending the right

diagnostic test, and the laboratory technician conducting that test within minimal time. There is need therefore, to strengthen all the steps in cascade using a systems approach improvement study to ensure reliable flow of samples and information. This can dramatically reduce time from ordering the test to releasing of the results and initiation of patient treatment.

The Malawi national TB guideline emphasizes case finding (29). Therefore, improving detection through having more samples sent for GeneXpert testing more cases will be detected and treated. Early diagnosis will mean more chances of successful treatment and reduce spread /transmission. This is a step in the right direction in the fight against TB.

APPENDICES

Appendix 1: Plagiarism declaration

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I JONATHAN GEOPHREY MAJAMANDA (Student number: 1661751) am a student registered for the degree of Masster of Epidemiology- Implementation Science in the academic year 2017/2018.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: Date: 29 March 2019

Appendix 2: Interview-guide questionnaire

GeneXpert Utilization at a Public Hospital Laboratory in Northern Malawi: a Quality Improvement Study

First Round Interview Guide Questionnaire for Quality Improvement

Study code : ……..Job title ……..…. ……..

Date…….

Checklist for Facilitator and Note taker

The In Depth Interview shall only progress once the following are confirmed;

- ✓ Study consent form has been signed and a copy given to the interviewee
- ✓ Interviewee has signed audio-recording consent form

Name of interviewer ……
Date……..

Questions

Note: start recording

1. Tell me about your position here at this facility
2. If there is a suspected TB case, how is it confirmed?
3. Could you tell me a little bit about the GeneXpert diagnostic tool
    a. How did you come to know about GeneXpert?
4. How do you use GeneXpert in this facility?
    a. What has been your experience in TB patient/sample management using GeneXpert?
    b. What are the procedures that you follow to ascertain a patient's eligibility for GeneXpert test?
5. Tell me about any challenges you experience using GeneXpert
6. What training have you received on using GeneXpert?
    a. Length of training?
    b. When?
7. How can GeneXpert be used optimally?
8. Is there anything else you would like to share on TB diagnosis in this facility?

Probes :

- Tell me more about that
- what eventually happens?
- Is this typical for you/ this hospital?
- Can you think of another example of this?
- "What else can you say about that?
- Give me more detail about that, please
- What exactly did you say?
- I'd like to hear more
- "Wow!
- Tell me more about that!"
- That is really interesting."

GeneXpert Utilization at a Public Hospital Laboratory in Northern Malawi: a Quality Improvement Study

Second Round Interview Guide Questionnaire for Quality Improvement

Study code : ……..Job title ……..…… ……..

Date……

Checklist for Facilitator and Note taker

The In Depth Interview shall only progress once the following are confirmed;

- ✓ Study consent form has been signed and a copy given to the interviewee
- ✓ Interviewee has signed audio-recording consent form

Name of interviewer ……
Date……..

Questions

Note: start recording

1. Since the last interview, how is GeneXpert being used?
    a. Have you seen any change in utilization of GeneXpert since the implementation of the change ideas?
2. Do you think the implemented changes should be continued?
    a. What modifications would they suggest?
3. Are there any other suggestions on how to optimize the utilization of GeneXpert?

Probes:

- Tell me more about that
- What eventually happens?
- Is this typical for you/ this hospital?
- Can you think of another example of this?
- "What else can you say about that?
- Give me more detail about that, please
- What exactly did you say?
- I'd like to hear more
- "Wow!
- Tell me more about that!"
- That is really interesting."

Thank you for participation in this study, your contributions are well appreciated.

Appendix 3: Authorization- Mzuzu Central Hospital

Telephone: 01 320 916 / 878
Fax: 320223/320973/270
directormch@malawi.net

In reply please quote No.....

The Hospital Director,
Mzuzu Central Hospital,
Private Bag 209,
Luwinga,
Mzuzu 2.

06 November 2017

Jonathan Majamanda
University of the Witwatersrand School of Public Health
27 St Andrews Road,
Parktown 2193
South Africa

Dear Sir,

PERMISSION TO CONDUCT RESEARCH STUDY AT MZUZU CENTRAL HOSPITAL

Refer to your letter Submitted on 26th October, 2017 in which you requested for permission to conduct a study titled ***"GeneXpert Utilization at Mzuzu central hospital laboratory in Malawi: a Quality Improvement Study"*** at our institution (Mzuzu Central Hospital). I am pleased to inform you that your request has been approved. You may use this letter as a "**Permission Letter"** to NHSRC.

When you are ready to collect data at our institution, you will be required to present the approval letter from National Health Science Research Committee (NHSRC) and this letter to the in-charge of the department you have selected before you can start your data collection.

Yours sincerely,

THE DIRECTOR
Mzuzu Central Hospital
06 NOV 2017
Private Bag 209, Luwinga
Mzuzu 2

Dr. F. Sinyiza
THE HOSPITAL DIRECTOR

Appendix 4: NHSRC Ethics Clearance – Malawi

Telephone: + 265 789 400
Facsimile: + 265 789 431

All Communications should be addressed to:

The Secretary for Health and Population

In reply please quote No.

.....

MINISTRY OF HEALTH AND POPULATION
P.O. BOX 30377
LILONGWE 3
MALAWI

16 November, 2017

Jonathan Majamanda
Mzuzu Central Hospital.

Dear Sir/Madam,

RE: Protocol 17/11/1920: GeneXpert Utilization at a Public Hospital Laboratory in Northern Malawi: A Quality Improvement Study.

Thank you for the above titled proposal that you submitted to the National Health Sciences Research Committee (NHSRC) for review. Please be advised that the NHSRC has **reviewed** and **approved** your application to **conduct** the above titled study.

- **APPROVAL NUMBER : 1920**
- The above details should be used on all correspondences, consent forms and documents as appropriate.
- **APPROVAL DATE : 16/11/2017**
- **EXPIRATION DATE**
  This approval expires on **15/11/2018**. After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the NHSRC Secretariat should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING:** All serious problems having to do with subject safety must be reported to the NHSRC within 10 working days using standard forms obtainable from the NHSRC Secretariat.
- **MODIFICATIONS**: Prior NHSRC approval using forms obtainable from the NHSRC Secretariat is required before implementing any changes in the protocol (including changes in the consent documents). You may not use any other consent documents besides those approved by the NHSRC.
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the NHSRC using standard forms obtainable from the NHSRC Secretariat.
- **QUESTIONS**: Please contact the NHSRC on phone number *+265 888 344 443* or by email on mohdoccentre@gmail.com.
- **OTHER**: Please be reminded to send in copies of your final research results for our records (Health Research Database).

Kind regards from the NHSRC Secretariat.

SECRETARY FOR HEALTH
2017 -11- 16
P.O BOX 30377, CAPITAL LILONGWE 3

.....
For: **CHAIRPERSON, NATIONAL HEALTH SCIENCES RESEARCH COMMITTEE**

Promoting Ethical Conduct of Research

Executive Committee: *Dr B. Chilima (Chairperson), Dr B. Ngwira (Vice-Chairperson)*
Registered with the USA Office for Human Research Protections (OHRP) as an International IRBIRB Number IRB00003905 FWA00005976

Appendix 5: Ethics Clearance- HREC

R14/49 Mr J Majamanda

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M171193

NAME: (Principal Investigator)	Mr J Majamanda
DEPARTMENT:	School of Public Health Medical School University
PROJECT TITLE:	GeneXpert utilization at a public hospital laboratory in northern Malawi: a quality improvement study
DATE CONSIDERED:	24/11/2017
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Drs N Ndlovu and M Hosseinipour
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	07/02/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature — Date: 12/02/2018

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 6: Participant's Informed Consent Form

Audio-recording consent form - In-depth interview

I hereby confirm that I have been informed by the study staff……about the nature, conduct, benefits and risks of study entitled GeneXpert Utilization at a Public Hospital Laboratory in Northern Malawi: a Quality Improvement Study.

- ✓ I have also received, read, and understood the above written information.
- ✓ The reason for audio-recording has been explained to me.
- ✓ I am aware that I may choose whether to participate or not to participate in the interview and to be recorded.
- ✓ I am aware that I may stop the interview at any point
- ✓ The researcher will take measures to make sure that the recording is kept confidential and safe
- ✓ Approvals from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand and National Health Sciences Research Committee (Malawi) have been sought
- ✓ My identity (interviewee) will never revealed to anyone but the researcher unless specific consent is obtained to do so. The information gathered does not my name but only a coded number so as to maintain anonymity.

PARTICIPANT:

_____

NAME SIGNATURE DATE AND TIME

I,_____ hereby confirm that the above participant has been fully informed about the nature and conduct of the above study.

SIGNATURE DATE AND TIME

Appendix 7: Stata outputs

```
. ttest numberrun, by (visit_2)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
1	13	10.76923	.7775194	2.803386	9.075161	12.4633
3	13	27.53846	.8594526	3.0988	25.66588	29.41105
combined	26	19.15385	1.770434	9.027479	15.50757	22.80012
diff		-16.76923	1.158963		-19.16121	-14.37725

```
    diff = mean(1) - mean(3)                                      t = -14.4692
Ho: diff = 0                                     degrees of freedom =       24

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.0000         Pr(|T| > |t|) = 0.0000          Pr(T > t) = 1.0000
```

```
. ttest rejectionrate, by (visit_2)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
1	13	8.239069	1.607241	5.79499	4.737191	11.74095
3	13	0	0	0	0	0
combined	26	4.119534	1.139647	5.811084	1.772387	6.466682
diff		8.239069	1.607241		4.921886	11.55625

```
    diff = mean(1) - mean(3)                                      t =   5.1262
Ho: diff = 0                                     degrees of freedom =       24

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 1.0000         Pr(|T| > |t|) = 0.0000          Pr(T > t) = 0.0000

.

. ttest tat2, by (visit)

Two-sample t test with equal variances
```

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
1	140	13.36429	.482181	5.705243	12.41093	14.31764
2	358	14.96089	.1850273	3.500881	14.59701	15.32477
combined	498	14.51205	.1923402	4.292248	14.13415	14.88995
diff		-1.596608	.4222408		-2.426209	-.767007

```
    diff = mean(1) - mean(2)                                      t =  -3.7813
Ho: diff = 0                                     degrees of freedom =      496

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.0001         Pr(|T| > |t|) = 0.0002          Pr(T > t) = 0.9999

.
```

Appendix 8: Detailed steps of the MFI

THE MODEL FOR IMPROVEMENT METHODOLOGY

Part 1: Three Fundamental Questions Leading to Improvement

i. **Setting an aim**: What are we trying to accomplish? The aim must be time-specific and measurable and must state the exact population that will be affected by the change.
ii. **Establishing measures**: How will we know a change is an improvement? The quality improvement team sets quantitative measures that will help to establish whether a specific change leads to improvement.
iii. **Identifying changes**: What change can we make that will result in improvement? Change ideas are identified by the quality improvement team, inspired by those who already work in the system or by experience from other successful improvements.

Part 2: The PDSA Cycles (Plan, Do, Study, Act)

This is a shorthand for testing a change in the real work setting by planning it, trying it, observing the results, and acting on what is learned.

i. **Plan**: in this step, the quality improvement team sets specific, measurable, attainable, realistic and timely objectives. The team clearly plans to carry out the change by responding to key questions such as "who?", "what?", "where?", and "when?", and develops the data collection plan.
ii. **Do**: at this step, the quality improvement team carries out the plan, monitors the process, and records data.
iii. **Study**: the team analyses data, compares results to objectives, and summarizes learned lessons (what did work? What did not work and why?)
iv. **Act**: from the learned lessons, the team identifies what next changes can improve the system better and the next PDSA cycle starts with new improvement strategies. The PDSA are "iterative", which means that the team tries several strategies, each PDSA cycle testing one set of strategies.

Six steps of the model for improvement

The six steps that an improvement team must go through when applying the Model for Improvement in a healthcare setting are:

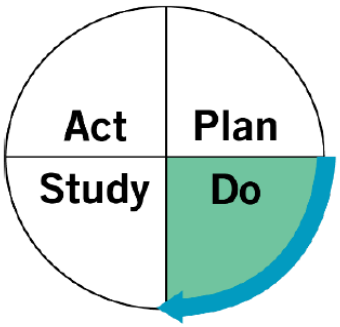
i. **Set an aim**. This is a general statement. The aim statement should be time-specific and measurable, stating exactly: "How good/much?" "By when?" and "For whom?"
ii. **Form a team**. Including the right people is critical when you are changing a complex system. The team should as much as possible include representatives of all processes affected by the aim of the improvement team.
iii. **Establish measures**. You need feedback to know if a specific change leads to an improvement, and quantitative measures often provide the best feedback.
iv. **Identify changes**. Where do new ideas come from, to achieve your aim? You can trigger creative thinking in various ways.
v. **Test changes**. This is PDSA cycle stage of the Model for Improvement. By planning a test of change, trying the plan, observing the results, and acting on what you learn, you will gradually move toward your aim.
vi. **Implement changes**. After you have a change that results in improvement under many conditions, the logical next step is to implement it – meaning, make the change the new standard process in one defined setting.

Source: Adapted from Implementation Research in Health- a Practical Guide.

Appendix 9: Summary of the PDSA pattern

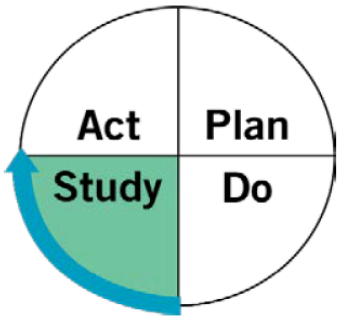
Plan: Plan the test, including a plan for collecting data.

- State the question you want to answer and make a prediction about what you think will happen.
- Develop a plan to test the change. (Who? What? When? Where?)
- Identify what data you will need to collect.



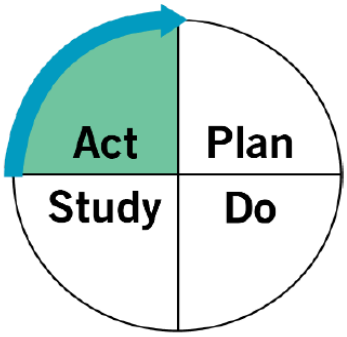
Do: Run the test on a small scale.

- Carry out the test.
- Document problems and unexpected observations.
- Collect and begin to analyze the data.



Study: Analyze the results and compare them to your predictions.

- Complete, as a team, if possible, your analysis of the da
- Compare the data to your prediction.
- Summarize and reflect on what you learned.



Act: Based on what you learned from the test, make a plan your next step.

- Adapt (make modifications and run another test), adop (test the change on a larger scale), or abandon (don't d another test on this change idea).
- Prepare a plan for the next PDSA.

Source: Institute for Healthcare Improvement (ihi.org)

Appendix 10: Results of first round interviews

Knowledge and information factors

While it is required of the laboratory technicians and clinicians to know patient eligibility criterion for GeneXpert test, there were indications that some did not know this criterion. As a result some eligible patients would be given microscopy other than GeneXpert test.

> "*Because most of the patients who have got TB sometimes we miss them because people don't know when it should be ordered, who should benefit from the GeneXpert, but when everyone has got that information, hopefully our patients will benefit from it*." *(Clinician-1)*

Participants also said lack of communication and sharing of information between the laboratory and the clinical departments, and that most test request forms were coming to the laboratory with insufficient patient information and wrongly filled.

> *"I think there is lack of communication and interaction. If the laboratory guys can link with us on GeneXpert, we can have the information they know and the information the clinicians know and there can't be these GeneXpert problems." (Clinician-2)*

Most of the participants reported that clinicians were not giving clear sputum production instructions to patients, leading not only to poor quality specimens which were usually laden with food particles and saliva, but also insufficient quantities of sputum supplied for testing. This was attributed to lack of trainings on GeneXpert and TB.

> *"There have been circumstances where we are all stranded we don't know what to do. What test we would carry on this particulars sample because the form isn't properly filled." (laboratory technician-2)*

> *"The main challenge is civic education. I think our clinicians and nurses are not well-trained on patient identification for sputum submission. I think that's the main challenge."(laboratory technician-3)*

Finance related factors

Though participants agreed that GeneXpert is a superior diagnostic tool than microscopy, most clinicians prefer to order smear microscopy instead, to redeem the government from the heavy costs of GeneXpert test in the face of low donor support. This, though, is done despite the knowledge of the low sensitivity smear microscopy has in comparison to GeneXpert.

> *"Yeah that's right coz there are some other circumstances that the GeneXpert is a best analysis tool compared to the AFB, so we look at the cost and that's why they bring up the format on how we can use the GeneXpert to only the patients who are HIV positive and those we are suspecting they have the MDR, MDR patients." (laboratory technician-2)*

When prompted on how low funding contributes to low utilization of GeneXpert, many participants mentioned that GeneXpert test is expensive, hence they opt to use it just for a critical few patients.

> *"...we know that the test is a bit expensive, so that's a challenge. So, we have a minimal people we can use the test for." (laboratory technician-3)*

Motivation related factors

A range of the younger participants both from the *laboratory* and clinical departments hinted that lack of trainings and workshops in the field of TB and GeneXpert, and lack of emphasis on extra-pulmonary TB demotivate them a lot to work in this department. This led to samples piling up in the TB *laboratory* without being attended to in time, hence long turnaround time.

> *"But also I look at aah, though there are a lot of people who have been trained on GeneXpert but you know TB a lot of people don't enjoy working with sputum, they may enjoy workshops but (laughs) on the ground they don't enjoy working with sputum. So, we have a lot of people who have been trained, but very few who are interested. So, you find the few who are interested the moment they are away the samples cannot be handled for GeneXpert. So that's the other key element which is lowering utilization and prolonging turnaround time.... I remember another time I was on holiday. I found samples two weeks they are just there.so you see how it feels." (laboratory technician-1)*

Technical factors

One theme that emerged from the study was that there were technical factors that were contributing to low GeneXpert utilization. In some instance the national test algorithm was being too restrictive, denying many patients a chance of being tested using GeneXpert. This translated to low numbers of GeneXpert tests. Another participant noted that the laboratory was using a different test algorithm from the one the clinicians were using, causing a lot of samples being rejected at the laboratory.

> *"Yeah there are several cases that have been undiagnosed because of the criteria we use on GeneXpert being that we are supposed to use it on patients who are HIV positive, those being suspected of having MDR TB, so the rest are left undiagnosed." (laboratory technician-3)*

Some participants stated how the cartridge and reagent stock outs, GeneXpert module failures, poor quality sputum samples, and power supply interruptions led to low levels of GeneXpert utilization. Sudden module failures resulted in samples taking long to be analyzed

> *"We have met with challenges like stock outs. I remember one time we spent the whole week without running samples because we didn't have the consumables." (laboratory technician-1)*

Some sputum samples would come with food particles and block the tubing inside the GeneXpert machine, resulting in sample processing errors and ultimately delaying processing of samples. Such samples were usually rejected :

"And again samples , some samples are poor in terms of sample collection, because we need the sample that does not have food particles, so we discover that some samples that are brought to the laboratory do have food particles... Later on, they block the machine and we can no more run samples" (laboratory technician-2)

There were mixed views on power supply as causing low GeneXpert utilization. Some laboratory technicians said power supply interruptions is not a problem since there are uninterruptible power source (UPS) batteries that are able to power the GeneXpert for 30 minutes in times of power interruptions. However, other laboratory technicians and clinicians admitted having been delayed receiving GeneXpert results due to power interruptions, though UPS batteries were available and functional.

"And another challenge is, you just don't know what has happened and you discover that the whole system is shut down. And basically, In most cases it has been due to power supply. And if this happens when our gen set has no fuel, the GeneXpert stops and all the sample analysis stops until electricity is back "(clinician-2)

Human resource related factors

The shortage of doctors leads to a limited time spent with each patient, which compromised history taking and leads to poor diagnosis. This vice leads some clinicians to missing certain signs that would lead to a proper TB diagnosis.

> *"Aah most of the times the ratio of clinicians to patients, usually, overwhelms us. So sometimes patient history itself may not be complete enough, and that contributes to the low use of GeneXpert." (clinician-1)*

Though at the time of this research, no primary and secondary hospitals were referring their TB patients and samples to Mzuzu, some participants indicated that being a referral hospital they receive a lot of referral samples increasing the workload and the TAT.

> *"Sometimes the results take more than a week because we are a central laboratory here in the Northern region so most of the sputum samples they come here so it's like a big work for us technicians." (laboratory technician-2)*

> *"So, with the lack of human resource that we have it's sometimes a challenge, the clinician can miss the diagnosis." (clinician-2)*

Appendix 11: Results of second round interviews

Level of utilization

Most participants noted an increase in the number of samples run per week though their estimations were inaccurate

> *"previously we were receiving generally less than 15 samples per week but now we are around 30, like double the number. This is a very good development and we have been puzzled that we have achieved it with very minimal cash involved." laboratory technician-2.*

Sputum sample quality and rejection rates

Comparing the rejection rates before and after the intervention, most respondents noted a remarkable improvement in rejection rates and quality of samples

> *"I have observed a change since the last interview after we discussed about the GeneXpert. Before that there were lots of samples rejected since clinicians could not justify well the reasons they ordered GeneXpert and us clinicians are able to justify the test, and the rejected samples have greatly reduced, I can say we have eliminated it." Clinician-2*

He also noted an improvement in the eligibility criterion as most samples were being given the needed tests and attention

> *"Obviously, there is great improvement in the utilization of the GeneXpert. Since the implementation of the new algorithm, most of the samples are going for GeneXpert especially those that have HIV, the children etc. Things have now improved." laboratory technician-3*

Filling of test request forms

Improper filling of forms was one of the major challenges before the intervention, and it contributed much to longer TATs

> *" there is proper information filled on request forms, and the TAT has greatly reduced… now everything is almost fine." laboratory technician-1*

One of the participants noted the importance of implementing these change ideas at the national level. Having seen the practicality of the project, he saw no impossibility of doing the same at the national level.

"Ohhh, I tell you (expressing awe and with emphasis) this type of project taken at national level will change the way we people think. There is going to be a great improvement nationwide on how we use GeneXpert and even other medical equipment. This is the way to go; simple methods, easy to implement and evaluate." laboratory technician-3

Areas of attention

The key informants also expressed areas that needed more vigilance to sustain the improvement and to improve even better. These included the continued organization of CPDs, continued improved communication between the laboratory and other hospital departments and the organization of formal GeneXpert trainings.

"I think we still have to keep doing civic education to clinicians because we keep receiving new clinicians who have no idea what we implemented." laboratory technician-1

"I can say there is a great improvement and this study has really helped us in this facility, and I think the clinicians, nurses and lab techs who took part in this research should continue teaching others so that this impact should not die." laboratory technician-2

" I feel we can do more by undergoing formal GeneXpert trainings, apart from the CPDs." Clinician-4

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