Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province

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TEN KEYWORDS

HIV diagnosis

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ABSTRACT

Introduction

A high burden of Human Immunodeficiency Virus (HIV) constitutes a key global public health concern. In South Africa, it is estimated that 260 000 children aged 0-14 years had HIV infection and only 63% of them were reported to have received HIV treatment in 2018. Without antiretroviral therapy (ART), HIV infection during infancy is associated with rapid disease progression where more than half of all infected children are expected to die before two years of age. Early infant diagnosis (EID) of HIV is therefore essential for accessing timely HIV treatment. However, preanalytical errors within the EID diagnostic cascade prevent optimal access to HIV polymerase chain reaction (PCR) results. The aim of this study was to describe the prevalence and contributing factors of preanalytical errors resulting in missed diagnostic opportunities for HIV among children below 18 months of age in Thabo Mofutsanyana (TM) district.

Methodology

The study was conducted using a descriptive cross-sectional study design and data was collected in two phases. Phase 1 involved obtaining the routine HIV PCR testing data set from the National Health Laboratory Services (NHLS) for all samples collected at TM public health facilities in 2018 and registered by NHLS. Phase 2 included a facility assessment checklist and semi structured questionnaire administered to 36 health care workers (HCWs) from 10 purposively selected health facilities. Data collected in phase 2 was analyzed to describe health facilities and HCW factors that might be contributing to the HIV PCR preanalytical errors.

Results

Phase 1. Of the 9318 samples included in the analysis, 49.6% were birth HIV PCRs whilst 42.1% and 8.3% were from 10 weeks and above 12 weeks age categories, respectively. A total of 745 (8%) samples were rejected because of the following preanalytical errors: insufficient specimen (84.3%), unsuitable sample (9.9%) and clerical error (5.8%).By age, the preanalytical errors were: birth (534), 10 weeks (170) and the above 12 weeks age category (41). Hospitals had the highest proportion of total preanalytical errors (58.1%). For PHCs the errors were: insufficient specimen (90%), unsuitable sample (5.5%) and clerical (4.8%).

Phase 2. The EID implementation levels for ten health facilities were determined by domain overall scores with interquartile ranges expressed as percentage of the highest possible score.

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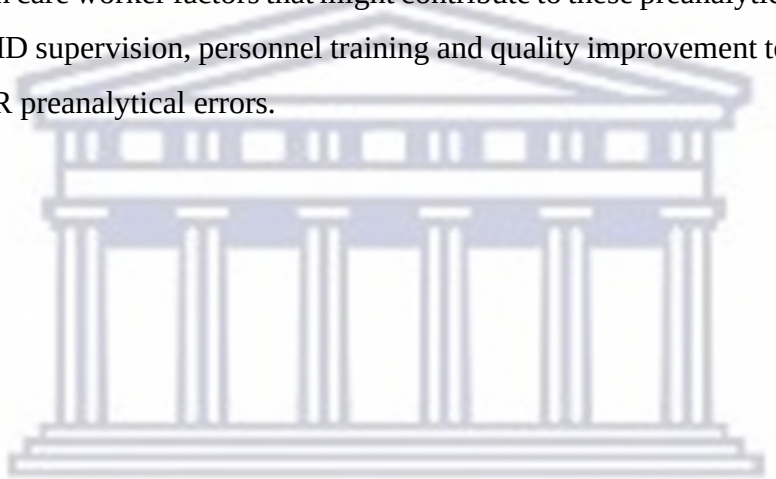
The highest possible overall score was 46. Overall percentage scores for facilities ranged from 47.8% to 91.3%. Facilities attained a median overall score of 29.5 (23.0-35.8) and median overall percentage score of 64.1% (50.0%-77.8%). Of the 6 domains assessed, physical facility domain had the highest percentage median score of 85.0 (80.0%-100.0%), followed by EID supplies and sample management at 80.0%. Supportive supervision and support had the lowest percentage median score of 20.0% (8.0%-35.0%), followed by personnel training at 50.0% (50.0%-50.0%).

Conclusion

The prevalence of insufficient HIV PCR specimen was reasonably high in TM district. Health facility and health care worker factors that might contribute to these preanalytical errors include deficiencies in EID supervision, personnel training and quality improvement tools and plans to address HIV PCR preanalytical errors.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DECLARATION

I declare that *Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province* is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Full name: Refuoe Cecilia Bulara Date: October 2021

Signature: _____

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LIST OF ABBREVIATIONS AND ACRONYMS

ANC .....Antenatal care

ANSUR .....Antenatal HIV Sentinel Surveillance

ART.....Antiretroviral therapy

CDW .....Cooperative Data Warehouse

CHC .....Community Health Centre

DBS.....Dry blood spot

DHIS .....District Health Information System

DNA.....Deoxyribonucleic acid

DOB .....Date of birth

DoH.....Department of Health

DRH .....Dihlabeng Regional Hospital

EDTA.....Ethylenediaminetetraacetic acid

EID.....Early infant diagnosis

EPI.....Expanded Program on Immunization

HCWs.....Health care workers

HEIs .....HIV exposed infants

HIV .....Human Immunodeficiency Virus

ICDM .....Integrated Chronic Disease Management

IMCI.....Management of Childhood Illnesses

IQR.....Interquartile range

IOS .....International Organization for Standards

LIS.....Laboratory Information System

LMICs .....Low-and middle-income countries

MCH .....Maternal and Child Health

MDOs.....Missed diagnosis opportunities

MISX.....Information does not match

MISXD.....Information does not match dry blood spot card

MMMRH .....Mofumahadi Monapo Mopeli Regional Hospital

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MTCT .....Mother to child transmission

NDNS.....Not done name or surname not indicated on the form

NDoH.....National Department of Health

NHLS .....National Health Laboratory Services

ODREG.....Duplicate registration

OPD.....Outpatient department

PCR.....Polymerase chain reaction

PHC.....Primary Health Care

PICT.....Provider-initiated HIV counselling and testing

PMTCT .....Prevention of mother to child transmission

PNC.....Postnatal care

PNs .....Professional nurses

POCT .....Point of care testing

QI .....Quality improvement

QIP .....Quality improvement plan

REDTA .....Require ethylenediaminetetraacetic acid sample

RfA.....Results for action

RNA .....Ribonucleic acid

RTHB.....Road to health booklet

RTHC.....Road to health card

SA .....South Africa

SA NDoH.....South African National Department of Health

SD .....Standard deviation

SNLAB .....Specimen not labelled

SOPs.....Standard operating procedures

SPSS.....Statistical Package for the Social Sciences

SDGs.....Sustainable Developmental Goals

TM.....Thabo Mofutsanyana

UCLT .....Unsuitable clotted

UCOMP .....Unsuitable dry blood spot card compromised

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UCONT.....Unsuitable contaminated

UEDTC .....Unsuitable ethylenediaminetetraacetic acid clotted

UESRC.....Unsuitable erythrocyte sedimentation rate tube received clotted

Us p24 Ag .....Ultra-sensitive p24 antigen

UNAIDS .....The Joint United Nations Programme on HIV/AIDS

UWC .....University of the Western Cape

WHO .....World Health Organization

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CHAPTER 1: INTRODUCTION AND PROBLEM STATEMENT

1.1 Introduction

HIV continues to be a major global public health issue, having claimed 36.3 million lives from the start of epidemic to 2020 (World Health Organization, 2021). Worldwide, 1.8 million children aged 0-14 years were estimated to be living with HIV in 2019 (UNAIDS, 2020). Mother to child transmission (MTCT) of HIV or vertical HIV transmission is responsible for more than 90% of HIV infections in children (Bwana, Frimpong, Simulundu, Mfinanga, Mboera & Michelo, 2016). The transmissions may occur during pregnancy, childbirth or during the breastfeeding period. The prevention of mother to child transmission of HIV (PMTCT) programme is therefore regarded as an efficient tool for preventing paediatric HIV infections globally (Inalegwu *et al*., 2016).

In South Africa, it is estimated that 260 000 children aged 0-14 years had HIV infection and only 63% of them were reported to have received treatment in 2018 (World Health Orgnization, 2019). In the same year, the final (at 18 months) mother to child HIV transmission rate including the breast feeding period was 5% (WHO, 2019). It is reported that without antiretroviral therapy (ART), HIV infection during infancy is associated with rapid disease progression where more than half of all infected children are expected to die before two years of age (Marinda *et al*., 2007). Fortunately, studies have shown dramatic survival benefits and mortality reduction for infants managed immediately after the confirmation of HIV diagnosis, thus highlighting the need for early infant diagnosis (EID) of HIV and fast-tracked linkage to care for those infected (Violari *et al*., 2008).

To ensure EID implementation, the WHO recommends virologic HIV testing using HIV deoxyribonucleic acid (DNA), HIV ribonucleic acid (RNA) and HIV ultra-sensitive p24 antigen (Us p24 Ag) assays for children below 18 months of age (World Health Organization, 2010). The virologic HIV testing is recommended because other serological assays suitable for antibody detection, are not reliable to definitively confirm HIV infection for this age group due to presence of maternal HIV antibodies that pass across the placenta in utero. The presence of maternal HIV antibodies in these children makes interpretation of a positive antibody result complicated (World Health Organization, 2007). South Africa has adopted the WHO recommendation on HIV DNA polymerase chain reaction (PCR) testing using dry blood spot (DBS) and whole blood in an ethylenediaminetetraacetic acid (EDTA) tube (National Health Laboratory Services, 2019), and from birth to 18 months, all HIV exposed children are

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expected to receive routine HIV testing. Routine birth testing for all HIV exposed infants (HEIs) was introduced into the national guidelines as a means of ensuring earlier detection of intrauterine infected infants (South African National Department of Health, 2015). Due to increasing numbers of children acquiring HIV infection during the post-natal period, the 2015 guidelines were revised in 2019 to accommodate a 6 months post-natal virological test together with guidance on the following: strengthening antenatal and postnatal care (PNC) for both HIV positive and negative mothers, introduction of a dolutegravir-based ART regimen which has been proven to reduce the risks of HIV transmission and promoting integrated management of the mother-baby pair by aligning PMTCT interventions with antenatal care (ANC) and Expanded Programme on Immunization (EPI) visits (South African National Department of Health, 2019).

With the advances in EID and the changing guidelines, the volume of samples submitted for HIV PCR testing in South Africa has increased from 13 069 in 2004 to 485 458 in 2015 (Mazanderani, Moyo & Sherman, 2017). Despite the increase, the registered HIV PCR samples that failed to yield either a positive or a negative HIV result proportionally decreased (expressed as the percentage of total errors) from 7.0% in 2010 to 4.4% in 2015. However, this is a different scenario with Thabo Mofutsanyana (TM) district, where there is increasing proportion (13.2 to 22.8% from June 2017 to January 2018 in accordance with Monthly Missed Diagnostic Opportunities per Facility-District-Thabo Mofutsanyana Summary) of these errors due to HIV PCR samples being rejected before they are analyzed, referred to as preanalytical errors.

Preanalytical errors may occur during the EID sample management process which includes sample handling, storage, transportation and preparation (Lippi *et al*., 2011). According to Mugauri *et al.* (2018), these errors are due to preventable reasons which require adherence to EID standard operating procedures (SOPs) by health care workers (HCWs). In the missed diagnostic opportunities (MDOs) within South African EID program 2010-2015 national study conducted by Mazanderani *et al*. (2017), preanalytical errors contributed 64.4% (49 581 samples) of the total HIV PCR testing errors (Appendix A). Documented HCWs errors include insufficient specimen, unsuitable sample and clerical errors (Inalegwu *et al*., 2016; Mazanderani *et al*., 2017). It is these three types of errors that is the focus of the study in the Thabo Mofutsanyana district.

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1.2 Problem statement

The South African Children with HIV Early ART trial demonstrated a 76% and 75% reduction in morbidity and mortality respectively, and the significant short cost reductions when children are initiated on ART before 3 months of age and before development of clinical HIV symptoms (Violari *et al*., 2008). However, the MDOs due to HIV PCR testing preanalytical errors delay HIV diagnosis in children and avert the opportunities to administer ART timely (Anoje *et al.*, 2012), thereby exposing pediatric HIV patients to more severe clinical manifestation of HIV. To address the HIV PCR preanalytical errors problem, National Health Laboratory Services (NHLS) continues to distribute HIV PCR results for action (RfA) reports to the different levels of Department of Health (DoH), conducts training on HIV PCR sample collection and sensitizes HCWs on laboratory request forms completion, patient preparation and sample management. Despite NHLS efforts to monitor and improve EID sample rejections through use of MDOs reports (National Health Laboratory Services, 2018a), districts like TM are still experiencing notable numbers of MDOs due to HIV PCR samples being rejected before analysis (National Health Laboratory Services, 2018b). Descriptive analysis of laboratory databases has been done and types of preanalytical errors established and measured at national level (Mazanderani *et al*., 2017). To further understand the problem, a similar analysis needs to be done at district level to inform facility level interventions to reduce the errors. The purpose of this study was to assess the prevalence and contributing factors of preanalytical errors in TM district.

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CHAPTER 2: LITERATURE REVIEW

This chapter provides a summary of HIV diagnosis in children younger than 18 months old, describes the EID programme, the existing evidence on MDOs which limit access to EID services and HIV PCR testing preanalytical errors as well as the documented strategies to minimize the MDOs.

2.1 HIV diagnosis in children below 18 months of age

Globally, HIV diagnostic testing came into existence around the early 1980s (Fearon, 2005). Since then a variety of sensitive diagnostic assays have been established with HIV-specific antibody (serological) testing being the most used method to identify HIV infection in adults and children above 18 months of age. The 18 months cut off age is linked to clearance of maternal HIV antibodies from a child's body (WHO, 2007). HIV diagnosis for HIV exposed children below 18 months of age is therefore complicated by the presence of maternal HIV antibodies in their serum (Ghadrshenas *et al*., 2013). This is because serological testing cannot differentiate between maternal HIV antibodies passively transferred to the infant during pregnancy and HIV antibodies produced by the infant. Antibody testing for children below 18 months of age is therefore not reliable for excluding HIV infection in this age group. Serological testing for this age group is only indicated for establishing HIV exposure when maternal HIV status is not known which is in line with WHO recommendation on the diagnosis of HIV infection in infants and children guideline (WHO, 2010). To definitively diagnose HIV infection in infants and children below 18 months of age, WHO recommended use of HIV virological testing which detects presence of viral nucleic acid (DNA or RNA) and viral particles such as p24 Ag. The recommended virological assays are inclusive of HIV DNA on DBS or whole blood specimen, HIV RNA on DBS, or plasma as well as Us p24 Ag on DBS or plasma.

According to Ciaranello, Park, Ramirez-Avila, Freedberg, Walensky and Leroy (2011), both DNA and RNA can be detected by PCR-based assays. PCR-based HIV DNA assay has been used for HIV diagnosis and WHO (2007), regarded it to be the standard method for diagnosing HIV in children below 18 months. HIV DNA assay is a qualitative assay since it only determines the presence or absence of nucleic acid without giving the amount of it in the sample being tested. DNA PCR is preferred over the other two tests because it needs whole blood which is easier to collect than the plasma needed by RNA and Us p24 tests (Ciaranello *et al*., 2011). Moreover, measuring HIV p24 Ag in blood is not sensitive enough to be used in early

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HIV diagnosis for infants and young children (Webber, Cotton & Stevens, 2001; Kebe *et al*., 2011). Lastly, studies have discouraged use of quantitative RNA PCR as a diagnostic tool, but rather for management and prognosis determination of ART patients because it provides additional information on virological status (McIntyre & Gray, 2000; Webber *et al*., 2001; Fearon, 2005).

As indicated earlier, DNA PCR can be performed on DBS or EDTA anticoagulated whole blood specimen, but DBS is favored over whole blood samples in EID. This is because the procedure does not require phlebotomy but use of a blood lancet to prick infants toe or heel, letting the blood to drip on to at least 3 circles of the DBS card and allowing the card to dry prior to packaging and sending it to a laboratory (Chiku *et al*., 2019). According to Ghadrshenas *et al.* (2013), this is possible because DBS storage does not need refrigerators at the sample collection facilities and samples can remain viable for weeks if they are kept at room temperature. Moreover, by their characteristic of being non-infectious and heat stable, DBS reduces sample transportation related expenses because they can be shipped by courier or mail (Ciaranello *et al*., 2011). Sauramba, Mushonga, Malunga, Shiripinda, Chikaka and Zhou (2018), thus regard DBS as one of the most effective strategies to increase EID uptake.

In South Africa, both DBS and whole blood in an EDTA tube are used for HIV DNA PCR testing (NHLS, 2019). To ensure accurate HIV diagnosis, both sample types need to be of good quality. Routine HIV PCR testing is offered to all HEIs at birth to identify intra-uterine HIV infection (SA NDoH, 2019). If the child tests HIV negative, the other repeat virological tests are conducted at 10 weeks, 6 months, or any time below 18 months if the child is symptomatic of HIV. Additional HIV PCR testing for a below 18 months child who initially tested negative is also conducted at 6 weeks post cessation of breast feeding. Since a conclusive HIV diagnosis for children younger than 18 months of age needs two positive virological results in SA, a first positive HIV PCR test is confirmed with another HIV PCR test, but ART is not delayed while waiting for confirmatory test results (SA NDoH, 2015; Mazanderani *et al.*, 2017). This early ART initiation is the goal of EID discussed below.

2.2 Early infant diagnosis (EID)

2.2.1 EID description

Routine diagnostic testing for all HEIs has made it possible to timely identify HIV infected children before they get sick. To achieve this, World Health Organization (2016), recommended EID which is defined as provision of a virological HIV test to all HEIs by two

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months of age. According to Bwana, Mfinanga, Simulundu, Mboera and Michelo (2018), EID is the component of Maternal and Child Health (MCH) services that has been integrated into the PMTCT programme since 2006 in the majority of Sub-Saharan African countries including South Africa. They further documented that EID is aimed at identifying HIV infection early and immediately linking all HIV infected infants to HIV care and treatment services. EID is achieved through following a sequence of key steps referred to as the EID cascade; identification of HEIs and acceptance of EID testing, proper sample collection and transportation, accurate testing that gives conclusive results with recommended turnaround times and reporting results to both HCWs and infants' parents as well as ART and cotrimoxazole prophylaxis initiation for eligible infants (Ciaranello *et al.*, 2011; Bobrow *et al*., 2016). According to Bobrow *et al.* (2016), opportunities to optimise infant outcomes and EID benefits can be lost at each step of the cascade.

2.2.2 Benefits of EID

According to Ciaranello *et al.* (2011), EID of HIV offers considerable benefits for the PMTCT programme, families, and infants (HIV exposed uninfected, HIV exposed infected as well as HIV unexposed, uninfected). EID assists with HIV diagnosis in children and therefore enables early ART initiation which eventually averts HIV related child morbidity and mortality (World Health Organization, 2008). Sauramba *et al*. (2018), also regarded EID as a critical step in facilitating ART provision and improving child survival which is one of the Sustainable Developmental Goals (SDGs). Izudi, Akot, Kisitu, Amuge and Kekitiinwa (2016), argued that early ART provision improves a child's quality of life by ensuring optimal HIV viral suppression and reducing the risk of opportunistic infections. In addition, EID supports decision making on infant feeding and assists in reducing provision of antibiotic prophylaxis for infants not infected with HIV (Bwana *et al*., 2018; Mugauri *et al*., 2018). Other benefits of EID include reduction of infant follow-up costs due to timely linking of HIV infected children to care and treatment, the opportunity to improve on HEIs follow-up, reduction of psychosocial distress for children not living with HIV, enabling of life planning for children infected with HIV and ability to monitor effectiveness of the PMTCT programme (Ghadrshenas *et al*., 2013; Bwana *et al*., 2018; Sauramba *et al*., 2018). In order to maximize these benefits, it is important to consider EID coverage and barriers to EID access.

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2.2.3 EID coverage

The WHO recommends EID testing coverage of >80% of HEIs for high HIV prevalence countries and >90% for low HIV prevalence countries (World Health Organization, 2017a). It is however, documented that in 2013, only 42% of HEIs from low-and middle-income countries (LMICs) received EID testing within two months of birth as recommended (Bobrow *et al*., 2016). For the same year, Bwana *et al*. (2016), also documented a 4% to 58% proportion of HEIs accessing EID testing in sub Saharan Africa. Similarly, studies have documented EID access ranging between 55% and 83% in South Africa (Chetty, Knight, Giddy, Crankshaw, Butler & Newell, 2012; Woldesenbet *et al*., 2015). The WHO (2019), has also documented 88.7% EID coverage for South Africa in 2018. According to Bwana (2016), institutional and individual factors have been shown to effect accessibility of EID services. These factors may lead to MDOs due to poor access to EID services.

2.3 Missed diagnosis opportunities (MDOs) for HIV

2.3.1 Definition of MDOs

As a result of local HIV testing guidelines, there are different definitions of MDOs for HIV adopted by different researchers. Chin, Hicks, Samsa, and McKellar (2013), defined MDOs for HIV as prior health care encounters occurring before the initial date of HIV testing. Generally, studies of missed opportunities for HIV diagnosis, have shown that patients with undiagnosed HIV often present to health settings numerous times before eventually receiving an HIV diagnosis (Rüütel, Lemsalu, Lätt & Epštein, 2019).

Specific to EID, Anaba *et al*. (2019), documented that MDOs are due to HEIs failing to present at a health facility for EID sampling, HEIs presenting at a health care setting without being sampled, HEIs presenting multiple times before EID samples are collected as well as getting sampled but results not being reported back. The first three causes of MDOs are associated with poor access to EID services while the latter may be a result of the samples being submitted for EID testing but failing to give either a negative or positive HIV result.

2.3.2 Health system bottlenecks contributing to MDOs for EID

A systematic review involving twenty seven studies by Bwana *et al.* (2016), has shown that in Sub-Saharan countries including South Africa, institutional factors impede EID provision. In their review, institutional factors that may result in MDOs included not documenting infant HIV status in the child road to health booklet (Woldesenbet *et al.*, 2015), insufficient training on HIV PCR test techniques among HCWs (Cherutich *et al*., 2008; Coulibaly *et al*., 2014;

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Chiku *et al*., 2019), low staffing levels (Coulibaly *et al*., 2014) and poor provision of provider-initiated counseling and testing services (PICT) for unknown, undocumented or undeclared HIV-exposed infants (Hassan *et al.*, 2012; Woldesenbet *et al.*, 2015). Woldesenbet *et al.* (2015), have also identified communication between antenatal and PNC units to be one institutional factor that can contribute to MDOs. Moreover, DBS test kit stock outs, and compromised quality of health care infrastructure identified by Coulibaly *et al*. (2014), can contribute to MDOs. Lastly, absence of national guidelines on HIV testing and algorithms for EID documented by Cherutich *et al*. (2008), can also contribute to MDOs.

Other institutional factors that can lead to MDOs include poor implementation of the Integrated Management of Childhood Illnesses (IMCI) programme. In order to improve child survival, South Africa adopted the IMCI strategy from 1997 (South African National Department of Health, 2011). Specific to HIV, IMCI HIV classification prompts HCWs (from Primary Health Care facilities) consulting under-five children to think of early symptomatic HIV infection (Sauramba *et al*., 2018), nonetheless the effective implementation of this strategy during routine care is dependent on HCWs willingness, skill and knowledge to detect HIV infected children (Feucht, Meyer, Thomas, Forsyth & Kruger, 2016). In a descriptive study to investigate missed opportunities in childhood HIV diagnosis leading to delayed ART initiation at Kalafong HIV services based in Gauteng province, 53% of the children who met IMCI clinical criteria (with documented HIV infection suggestive features) for HIV testing, were not correctly investigated, indicating less attention given to identification of children missed by PMTCT testing (Feucht *et al*., 2016).

Moreover, EID services tend to focus more on known HEIs which according to studies may also result in MDOs for more than half of all true HEIs (Sherman, Matsebula & Jones, 2005; Kellerman & Essajee, 2010; Ciaranello *et al*., 2011). According to Woldesenbet, Goga and Jackson (2012), if health care services continue to primarily focus on HEIs from the PMTCT programme, then there is a likelihood of failing to provide HIV testing for children missed by the PMTCT programme and children of mothers with undocumented HIV status. This means HIV testing needs for children are not likely to be achieved, and children missed by the PMTCT programme are at increased risk of being diagnosed at advanced stages of HIV infection.

A recent study conducted in rural North-Central Nigeria, concluded that although 85% of HEIs presented for HIV PCR testing, there were various MDOs that were a result of health system failures (Anaba *et al*. 2019). HEIs presenting multiple times before HIV PCR samples were collected and collecting HIV PCR samples without receipt of results were documented as part

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of system failures. Findings from the study have shown that 22% (n=58/257) of the samples collected did not have results returned to a health facility or infant. Similarly, a prospective study conducted in Ethiopia has documented that although median time (6.7 weeks) for HIV PCR sample collection after birth was acceptable, only 46.6% of results were retuned within 3 months from the collection date and 16% never received their results (Girma, Wendaferash, Shibru, Berhane, Hoelscher & Kroidl, 2017). If EID testing has been provided to HEIs but the HIV PCR samples are rejected prior to analysis at central laboratories, the rejections may lead to MDOs (Chiku *et al.*, 2019).

2.3.3 MDOs due to HIV PCR testing preanalytical errors.

Laboratory testing errors can occur across the path of laboratory workflow; in preanalytical, analytical and post analytical activities. Preanalytical errors are reported to predominate laboratory associated errors and range from 31.6% to 75% (Bonini, Plebani, Ceriotti & Rubboli, 2002). This is confirmed by Lippi *et al*. (2011), where preanalytical errors were found to account for nearly 60% to 70% of all errors occurring in laboratory diagnostics. According to Hammerling (2012), preanalytical errors can happen during the patient evaluation, patient identification, test order entry, request form completion, patient identification, sample collection, sample transportation, or during sample receipt in the laboratory. It is also indicated by Lippi *et al*. (2011), that most preanalytical errors are attributable to improper handling during collection procedures, handling and preparing or storing the samples.

HIV PCR testing preanalytical errors are established upon receipt of HIV PCR samples and accompanying laboratory request forms by laboratory clerks who examine the samples for quality and acceptability for HIV PCR testing. This process is guided by International Organization for Standards (IOS) mandate that clinical laboratories must develop the criteria for rejection or acceptance of the samples (Shiferaw, Yismaw & Getachew, 2018). HIV PCR samples that fail to meet the criteria are rejected for testing (Inalegwu *et al.*, 2016). DBS for HIV PCR rejection criteria defined in Chiku *et al*. (2019), is inclusive of incomplete identification on DBS cards or request forms, missing DBS card or request form, samples with evidence of contamination, DBS card with traces of blood clots, as well as DBS sample with less than 3 full circles (insufficient specimen). The DBS samples not meeting these criteria are rejected and consequently constitute MDOs due to preanalytical errors.

Mazanderani *et al*. (2017), classified the MDOS due to preanalytical errors into HCWs error and pre-analytical lab error. Both categories were further subdivided into several subcategories

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of errors based on Laboratory Information System (LIS) rejection codes. HCWs errors were insufficient specimen, clerical error, and unsuitable sample. These errors are inclusive of the following LIS rejection codes; insufficient sample volume, sample container empty and specimen not received or insufficient specimen; compromised DBS card, poor quality sample, sample hemolyzed, sample clotted, EDTA sample required, incorrect sample type, separate specimen required and out of range patient age for HIV PCR or unsuitable sample; labelling error, information does not match, specimen not labelled, incomplete form (no age, date of birth (DOB), patient name or patient surname) and duplicate registration for clerical error (Mazanderani *et al*., 2017; NHLS, 2018b).

With the efforts of making EID available to all HEIs as early as from birth, the volume of HIV PCR samples collected has increased and studies on the preanalytical errors discussed above have become gradually relevant since the more samples collected, the more the preanalytical errors (in terms of absolute numbers) are experienced (Inalegwu *et al*., 2016). To study the impact of rejections at different levels of health care in Nigeria, Inalegwu *et al.* (2016), conducted a cross-sectional descriptive study among HIV-exposed babies from 150 health facilities using prospectively collected data from January 2008 to December 2012. A sample rejection rate of 2.4% (n=786/32552) was established and the main reasons for rejections were improper sample collection, improper labelling and insufficient sample which contributed 14.8, 16.4 and 26.3% of total sample rejections, respectively. The study also provided evidence on contribution of different levels of health care facilities to total preanalytical errors where secondary health facilities have more likelihood of experiencing more numbers of rejected samples than clinics and tertiary hospitals. The secondary health facilities contributed 81.8% (n=643/786) of total errors as a result of collecting majority of the samples, 76.1% (n=24777/32552). The study concluded by recommending that programmes should monitor preanalytical errors and incorporate constant quality improvement (QI) activities to minimize errors linked to sample rejections.

Findings from a Zimbabwean national analytical cross-sectional study conducted by Chiku *et al*. (2019), have shown an EID sample rejection rate of 4% (n=1291/34950). They documented reasons for sample rejections (with the contributing percentage) as clotted sample: 1%, information mismatch: 4%, cross contamination: 6%, missing sample: 6%, missing laboratory request form: 11%, and insufficient specimen: 72%. Similarly, a study conducted at Mashonaland province in the same country, has documented insufficient specimen as the main contributor (77.9%) to EID preanalytical errors (Mugauri *et al*., 2018). In addition to

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determining EID sample rejection rates and rejection reasons, Chiku *et al*. (2019), established possible associations between the level of health care facility collecting samples and rejections. The results were that Primary Health Care (PHC) facilities experienced higher sample rejection rates. These results were comparable with a Nigerian study, where PHC facilities had the highest sample rejection rate of 4% (Inalegwu *et al*., 2016). Chiku *et al*. (2019), documented that the probable causes of the high sample rejection rates at PHC facilities were high demand for HIV PCR testing services, inadequate training for HCWs at rural facilities and lack of funds to support HCWs recruitments and procurement or maintenance of equipment at this kind of facilities.

To describe the reasons for the EID rejected samples and the two spot methods which is different from the standard method, Govender, Parboosing, Siyaca and Moodley (2016), conducted a descriptive analytic study at Albert Luthuli Central Hospital in KwaZulu Natal. In the study, 3.7% (n=3276/88481) of the DBS samples that were submitted to the laboratory were rejected because of preanalytical problems and 48.9% of preanalytical problems resulted from insufficient specimen volume. The study concluded that laboratory databases can be used to identify specific facilities for interventions like retraining of healthcare providers and they found no significant difference in rejections from 2 spot methods as opposed to standard (at least 3 spots) methods.

Using a laboratory database, the first South African national descriptive analysis on reasons for rejections was done by Mazanderani *et al*. (2017), using HIV PCR test data between January 2010 and December 2015 and it confirmed findings from the above discussed studies conducted at different locations. Preanalytical errors were at 64% (n=49581/76969 MDOs) where HCWs related errors contributed 85.1% of all preanalytical errors. HCWs related errors comprised insufficient specimen, unsuitable sample, and clerical errors which each contributed 27, 15.5 and 12.2% respectively. The remaining 14.9% of preanalytical errors were attributed to laboratory errors. Improved communication among health workers was considered a practical means for reducing the HIV PCR sample rejection rate in the study, which was also recommended by Lippi, Guidi, Mattiuzzi and Plebani (2006).

2.3.4 Strategies to minimize institutional MDOs due to EID inaccessibility and preanalytical errors

Bwana *et al.* (2016), described the following strategies to improve access to EID; documentation of HIV status in the health booklet, reduction of discrimination and stigma,

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improved privacy at immunization facilities, introduction of early infant HIV testing services at immunization services as well as ensuring offering of provider-initiated HIV counselling and testing (PICT) to infants.

Concerning reduction of preanalytical errors, policy formation on general sample management is key to prevention of these kind of errors. As a means to ensure that HCWs collecting samples have the required information and the samples are managed appropriately, sample management policies must be established and be reflected in the clinical laboratory handbooks (World Health Organization, 2011). It is further documented that the handbook should made available to all sample collection sites and address the six components of sample management. The components include information needed for requisitions; handling of urgent request; collection, labeling, preservation, and transport; safety practices; evaluating, processing and tracking samples; storage, retention and disposal.

Moreover, there is a comprehensive plan of interrelated steps advocated by Da Rin (2009), in a different resource setting in addition to what has been recommended to reduce preanalytical errors specifically associated with HIV PCR samples in sub-Saharan Africa (Lippi *et al*., 2006; Govender *et al.*, 2016; Inalegwu *et al*., 2016), discussed earlier. The steps incorporate development of clear procedures, automating functions (reducing error prone activities), monitoring quality indicators and improving communication among health care professionals, fostering interdependent co-operation and enhancement of health care professionals training. The suggested steps were also documented elsewhere by three different studies (Plebani & Bonini, 2002; Bates & Gawande, 2003; Lippi & Guidi, 2007).

From a study conducted by Nkengasong and colleagues, there is evidence showing that training HCWs on HIV PCR sample collection, handling and completion of sample request forms can lessen errors from 19.05 to 6.75% (Nkengasong *et al*., 2010 in Chiku *et at*., 2019). The enhancement of health care professionals training was also recommended by an analytical cross-sectional study conducted in Zimbabwe by Chiku *et al*. (2019) . They proposed a targeted (in areas experiencing high rejection rates) mentorship programme on HIV PCR sample collection, storage, as well as transportation. This is also in line with a Malawian qualitative analytical cross-sectional study participants' recommendation that extra training support on EID and routine supportive supervision for HCWs should be conducted in attempt to strengthen skills and knowledge (Bobrow *et al.*, 2016). Smit *et al*. (2014), made the similar recommendation that HCWs training and mentorship on HIV PCR sample collection, storage and transportation are vital in achieving improved collection of HIV PCR sample collection

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and standardized skills. In addition to HCWs training, considerations to minimise preanalytical errors could include continuous performance counselling of HCWs (Sauramba *et al*., 2018). They further indicated that training is to be extended to laboratory personnel who receive and process the samples since some rejections may be due to delay in processing samples because of limited laboratory personnel trained on receiving and analysing PCR samples. Identification of staff development needs on HIV PCR testing is dependent on consistent monitoring of HIV PCR sample rejections.

Chiku *et al*. (2019), have concluded that there is need for real time monitoring of HIV PCR rejection and health facility management notification to enable preventive and corrective actions. They further indicated that these corrective actions can be enhanced by institutional based pre-dispatch checking of quality of HIV PCR samples before they are sent to central laboratories for analysis. They claimed that pre-dispatch quality checking of the samples within health institutions can allow identification of gaps closer to the collection site and immediate corrective measures can be undertaken to minimize the impact of sample rejection on patient care.

According to Lippi and Guidi (2007), continuous monitoring of HIV PCR sample rejection and performance can assist with best practices recommendations. Additionally, they indicated that the monitoring is to be supported by in-depth problem analysis, reassessments, and reorganizations of quality requirements. The mentioned activities will subsequently inform continuous quality improvements and performance reviews documented to reduce preanalytical errors (Inalegwu *et al*., 2016; Izudi *et al.,* 2016; Shiferaw *et al*., 2018). Reports have shown that implementation of enhanced EID including point of care testing (POCT), is likely to address the HIV PCR sample rejection monitoring challenges experienced with conventional EID (Spooner *et al*., 2019).

POCT is defined as laboratory testing done at or near a site where clinical care is delivered (Lippi *et al.*, 2011). Through enabling onsite same day sample collection, analysis and reporting of results, POCT may help in cutting down the number of these steps involved in conventional EID and overcoming errors associated with these steps (Jani *et al*., 2014; Mwenda *et al*., 2018; Anaba *et al*., 2019). Similarly, World Health Organization (2017b), has documented that introduction of POCT EID technologies is the breakthrough which presents an opportunity for increased EID testing coverage by allowing same day test results and addressing the major challenges of traditional EID systems. Ghadrshenas *et al*. (2013), have also argued that POCT technologies present an opportunity to improve the EID programme by

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bringing EID testing out of the centralized laboratories. They further indicated that POCT technologies allow same visit results return, lessen the burden of handling, sample storage and transportation, do not require HCWs to have specialized laboratory skill to run the test, and expand EID testing to different healthcare entry points.

Lastly, patient follow-up and tracking is suggested to be integrated into the strategies to promote sample recollections when errors occur (Inalegwu *et al*., 2016). Their study findings revealed that only 8.8% (n=69/786) of rejected samples were repeated and that the infection rate for accepted samples against repeat samples was 9.9 and 15.9% respectively.

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CHAPTER 3: METHODOLOGY

This chapter focuses on the aim and objectives and methods used to conduct the study. The methods are inclusive of study design, population sampling, data collection, data analysis, ethics considerations and study validity.

3.1 Study aim and objectives

3.1.1 Aim

To describe the prevalence and contributing factors of preanalytical errors resulting in missed diagnostic opportunities for HIV among children below 18 months of age in Thabo Mofutsanyana district.

3.1.2 Objectives

1. To describe the prevalence of three types of preanalytical errors in EID PCR testing (insufficient specimen, unsuitable sample, clerical error) in TM district.
2. To describe health facility factors contributing to the EID preanalytical errors.
3. To describe health care worker factors contributing to the EID preanalytical errors.

3.2 Study design

This quantitative study was conducted using a descriptive cross-sectional study design. This design was the most appropriate design because it is suitable for measuring prevalence of health outcomes in a population (Bonita, Beaglehole & Kjellström, 2006). The design also allowed description of factors contributing to preanalytical errors without use of control groups.

3.3 Study setting

The study was conducted in the TM district public health facilities. TM is a category C municipality (DC19), located in the Eastern Free State province. As per the 2018/19-2020/21 TM District Health Plan, the District has a total population of 714 062 of which 81.9% (584 816) was uninsured for health care during the 2015/16 financial year. This means most of the population access health care from public health institutions which further necessitates the need for improved quality of health care provided at these institutions including HIV diagnosis and care of HIV exposed children. According to the South African National Department of Health (2017b), the 2015 antenatal HIV prevalence for TM district was 29.8%.

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TM district renders health care through 84 public health facilities: 72 Primary Health Care (PHC) clinics, 1 Community Health Centre (CHC), 9 District Hospitals and 2 Regional Hospitals. The District operates with 2 health laboratories (situated at Regional Hospitals), serving 75% of health facilities and the remaining health facilities (25%) are attended by a central laboratory in a neighboring district, which is around 197 kilometers from other health facilities. Samples including ones for HIV PCR are collected by a courier company daily and the HIV PCR results access is improved by NHLS-LABTRAK. The NHLS-LABTRAK is a system that allow registered user to have a web results access. This system assists in cases where NHLS or courier company delays sending printed HIV PCR results to a facility, when the printed results are misplaced at a health facility or when the child is seeking health care at another facility where the HIV PCR test was not initially performed at.

On average, TM district records 523 (birth and 10 weeks tests) HIV PCR samples per month (District Health Information System, 2018), through 84 public health facilities. The number of HIV PCR samples is estimated to be higher than the one reported since there are HIV PCR tests which according to South African National Department of Health (2017a), are not reported on the District Health Information System (DIHS). Age-appropriate HIV PCR testing six weeks post cessation of breast feeding, 6 months HIV PCR and testing of symptomatic HEIs are some of the tests not being reported in the DHIS. All facilities providing HIV PCR testing receive hard copies of their HIV PCR results through the same courier company collecting the samples.

In addition to individualized paper-based HIV PCR reports that are couriered to all the TM health facilities and the online NHLS LABTRACK access by some of the health facilities, rejected HIV PCR samples feedback with patient identifying information is shared with health facilities and other Cooperative Data Warehouse (CDW) registered stake holders in managing EID programme on weekly basis using HIV PCR RfA report. The HIV PCR RfA report is intended to facilitate fast-tracking linkage to HIV care for children who tested HIV positive and retesting of the children with the rejected HIV PCR samples (NHLS, 2018b). TM District Management team responsible for the PMTCT Programme also receives monthly facility MDO reports from NHLS CDW. This is an aggregated data report which according to NHLS (2018b), helps to monitor HIV PCR sample rejections and assists in prioritizing training interventions.

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3.4 Study population and sampling

The study was conducted in two phases. Phase 1 addressed objective 1, while phase 2 addressed objectives 2 and 3 of the study. Based on prevalence and types of HIV PCR testing preanalytical errors in phase 1, phase 2 involved purposive selection of health facilities based on their proportion of total preanalytical errors experienced to total number of samples they collected. Total preanalytical errors are inclusive of three preanalytical errors i.e. insufficient specimen, unsuitable sample, and clerical error. For feasibility purposes, five worst performing and the five best performing facilities (in terms of HIV PCR preanalytical errors) meeting inclusion criteria were identified and approached for participation in the study.

Phase 1

The study population was all HIV PCR samples for children below 18 months collected in the TM district public health facilities between 1st January 2018 and 31st December 2018 and registered by NHLS. The study population was initially estimated to be more than 6276 based on monthly number of HIV PCR samples for birth and 10 weeks testing reported on DHIS by the TM district. This is because HIV PCR tests done outside birth and 10 weeks data elements definition are not reported on DHIS, although it was the only accessible system to the researcher that could be used to estimate the number of HIV PCR samples collected by the TM district.

Inclusion criteria

- HIV PCR samples collected between 1st January 2018 and 31st December 2018 regardless of them being initial, repeat, or confirmatory tests.

Exclusion criteria

- HIV PCR samples collected between 1st January 2018 and 31st December 2018 and tested by a laboratory but missing any of the key fields; date of birth, date sample taken or HIV PCR result.

The initial sample size was calculated to be 376 HIV PCR samples but there was no population sampling as the researcher made use of all HIV PCR samples meeting inclusion criteria which were 9673. The inclusive sample was utilized because the researcher used an existing routine EID data set from NHLS to describe preanalytical errors which made it feasible to study the entire study population.

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Phase 2

Five best performing and five worst performing facilities were selected for this phase based on prevalence of HIV PCR preanalytical errors.

Inclusion criteria

- A public health facility offering EID testing and having collected HIV PCR samples through the year of 2018.

Exclusion criteria

- The health facilities that were not operational during the time of data collection.

Seventeen health facilities did not experience HIV PCR sample rejections for the whole year of 2018 and were considered as best performing. All the 17 were arranged in order of the number of HIV PCR tests conducted in 2018, the two highest volume, one at the middle and the two lowest volumes for sample collection were selected for participation in the study. This was done because the already selected worst performing facilities included both high, middle, and low volume PCR test health facilities. The selected best performing facilities were of similar characteristics with the worst performing ones in terms of the subdistricts they are located, the health laboratory they send their samples to, and the volume of EID samples collected. Facilities experienced preanalytical errors were ranked in terms of proportion of total preanalytical errors experienced in the same period and the 5 with highest proportion formed the sample of worst performing health facilities.

Health care worker participants

For HCWs participants, the study population was all HCWs who are involved with collection of EID PCR testing based at the 10 participating public health facilities.

Inclusion criteria

- HCWs who have been working/based at the facility for at least 1 year prior to data collection.
- HCWs who have collected HIV PCR samples in the year preceding data collection, 2019.

Exclusion criteria

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- HCWs temporarily placed/relieving at participating health facilities at the time of data collection.

The sample size was not known during planning of the study, and it was estimated to be 30 to 70 HCWs based on known minimum number of HCWs performing HIV PCR testing at PHC facilities and maximum of ten HCWs to be recruited at each facility having high numbers of HCWs performing EID testing. The initial proposal was that, for each participating facility, a maximum of 10 participants will be recruited through proportional stratified sampling. However, after the selection of 10 participating facilities, none had more than 10 HCWs meeting criteria to participate in the study. Thirty-six HCWs participated in the study.

3.5 Data collection and management.

Data collection was in two phases. Phase 1 involved requesting TM EID database from NHLS to achieve objective 1 of the study and inform phase 2 data collection. Phase 2 data collection was done using semi structured questionnaires (Appendix B) and a facility assessment checklist (Appendix C).

Phase 1

The routine EID electronic data set was requested from NHLS Cooperative Data Warehouse using a CDW Data Request Form_FM10069 (Appendix D). Requested retrospective data was the EID PCR samples (de-identified) collected at TM public health facilities between 1st January and 31st December 2018 and registered by NHLS. The decision to request and use 2018 data was informed by the finding that EID preanalytical errors for TM district increased between July 2017 and January 2018.

Since CDW is the central repository of all test-sets within NHLS, the request was specific to EID HIV PCR data set. The EID data set with 9771 sample records was received in excel format. The description of data elements on the excel spread sheet included the following: district code, district name, subdistrict code, subdistrict, facility code, facility name, ward code, DOB, age tested in years, age tested in months, age tested in days, gender, specimen type, date specimen taken, date specimen tested, rejection reason code and HIV PCR result. The date specimen tested and HIV PCR result for the rejected samples were documented as null. The researcher used routine laboratory data because according to Sherman, Lilian, Bhardwaj, Candy and Barron (2014), it represents a reliable and relatively low-cost method of monitoring the PMTCT programme and improving patient care as opposed to costly and labor-intensive

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surveillance studies. They further documented that there is evidence that the NHLS data set is in line with findings in the population as a whole, based on the 2010 South African PMTCT Evaluation (SAPMTCTE) study.

Phase 2

This phase of data collection involved simultaneous data collection on health facility and HCWs factors contributing to the preanalytical errors to address objective 2 and 3 of the study. Both the facility assessment check list and questionnaire were administered by the researcher in August and September 2020.

Facility assessment checklist

A facility check list adapted from Nsibande *et al*. (2019), was used to collect heath facility data to determine if the required supplies and physical infrastructure for EID PCR testing were present at 10 health facilities participating in the study. Facility/Unit Managers provided written informed consent before administering the assessment checklist.

The checklist had two sections; section A and B. Section A collected data on health facility profile while section B on six domains; personnel, physical facility, supplies, sample management, testing phase as well as supervision and support. Data for section B of the assessment checklist was gathered by inspecting areas of the facilities where data was collected from and by interviewing Facility Managers or facility staff members most familiar with EID testing identified by Facility/Unit Managers.

On section B, responses were checked yes, partial, and no and scored 2, 1 and 0, respectively. For the yes responses, elements being assessed should have all been present or fully implemented, or not applicable to the facility. Partial response or observation was marked when not all elements were met or if there was yes response with no supporting evidence or unsatisfactory documentation. Lastly the no response was marked if all required elements were not there or not met. Comments were also documented for each partial or no responses. The facility scoring was performed during data collection and overall total scores for all domains was 46.

Semi-structured questionnaire

A semi-structured questionnaire was used by the researcher to collect data through interviewing 36 HCWs who perform HIV PCR tests at the same health facilities where the facility check list

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was administered. The questionnaire collected data on EID training, EID supervision, HIV PCR supplies, HIV PCR sample collection processes, HIV PCR results management including feedback on preanalytical sample rejections and challenges HCWs were experiencing with HIV PCR sample collection.

The list of HCWs performing EID testing in participating health facilities were obtained from Facility/Unit Managers. In order to determine if indeed the HCWs met criteria to participate in the study, they were asked when last they collected HIV PCR samples and how long they have been working at the participating facility before the questionnaire was administered.

3.6 Data analysis

For both phases of analysis, data in an excel sheet was imported and analysed using Statistical Package for the Social Sciences (SPSS) version 27 software. Descriptive analysis using means with standard deviations (SD) and medians with interquartile ranges (IQR) were employed to describe continuous variables while frequencies and percentages were used for categorical variables. A 95% confidence interval and 5% confidence limits were used in determining the significance level of the study results. Since it was not possible to link the preanalytical errors with the individual HCW who took the sample, a plausibility approach to analysis was adopted at the level of a facility to understand factors contributing to the errors.

Phase 1

The EID data set containing 9673 records was analyzed. Prior to analysis, the spreadsheet contained three variables on age tested; age tested in years, age tested in months and age tested in days and in cases where a sample was rejected, the age tested was zero. To have one variable for age tested in days which also caters for ages of children with rejected PCR samples, a new variable was created. The variable was age sample taken, which was computed using the difference between the date sample taken and DOB variables. Moreover, the analysis excluded the EID sample type (DBS or whole blood in EDTA tube) as 94% (9116/9673) records had blank EID sample types.

The analysis involved simple descriptive analysis with prevalence of the three error types stratified by subdistrict, type of facility (PHC, CHC and hospital), volume of samples collected, child age at testing and sex of the child using frequency tables.

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Phase 2

Facility assessment checklist

Data collected using the facility assessment checklist was captured in excel, imported, and analyzed using SPSS. For section A of the checklist, descriptive statistics were used to determine distribution of health facilities (in terms of their preanalytical errors) by facility type, subdistrict, locality, number of EID testers, HIV PCR sample type utilized at the facility, frequency of sending HIV PCR samples to the laboratory, health laboratory testing the samples, monthly average number of samples sent to the laboratory, frequency of ordering EID test kits and participation in the Antenatal HIV Sentinel Surveillance (ANSUR).

Analysis of Section B of the checklist involved facility scoring description by domain, overall data set and by best performing versus poor performing facility in terms of total preanalytical errors experienced. The median and IQR of overall scores for best performing and worst performing facilities were calculated and compared. Total percentage scores for all domains were used to determine EID testing implementation level for each facility adapted from Nsibande *et al.* (2019). The EID testing implementation level total percentage scores were categorised into 5 levels summarised in table 1.

Table 1: EID testing implementation levels

Levels	**Total percentage scores**	**Interpretation**
0	<40%	needs improvement in all areas and immediate remediation
1	40-59%	needs improvement in specific areas
2	60-79%	facility partially ready for site certification
3	80-89%	facility close to site certification
4	>=90%	eligible for site certification

HCWs questionnaire

Descriptive analysis using median with IQR was employed to describe numeric variables while frequencies and percentages were used for categorical variables. Findings were compared for participants from best performing and worst performing facilities, stratified by personnel

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training, support and supervision, knowledge on EID supplies management, blood sampling as well as receipt of EID results.

3.7 Validity and reliability

In phase 1 the study population was clearly defined with inclusion and exclusion criteria and random error at selection as defined by Joubert and Ehrlich (2007), was prevented by using the inclusive sample of EID PCR samples for an entire year of 2018. Participating health facilities were selected through purposive sampling; a non-probability sampling that relies on the researcher's judgment (Lærd, 2012). To minimize the researcher's bias in the study, the judgment of the researcher was based on clear criteria of selecting the participating health facilities guided by phase 1 data analysis on number of rejected HIV PCR samples experienced by each health facility.

The questionnaire was adapted from validated questions used in other studies (Chatterjee *et al*., 2011; Bölenius, Brulin, Grankvist, Lindkvist & Söderberg, 2012) and modified to the local context. Similarly, the facility checklist was adapted from Nsibande *et al*. (2019) in which questions were validated. The checklist was also modified to a local and EID context. Instrument standardization was achieved through pretesting of both the questionnaire and facility checklist at two public health facilities (from one subdistrict not participating in phase 2 of the study data collection) prior to phase 2 data collection of the main study. Pretesting of the tools was also undertaken to estimate time required to collect data for each tool. Problems and discrepancies identified during the pretesting of the tools were noted and rectified. The revised versions of the questionnaire and facility checklist were used in phase 2 data collection of the main study. The researcher privately administered the questionnaire to participants at their workplace to improve the response rate.

As recommended by Robson and McCartan (2016), the researcher checked collected data for errors by identifying missing or strange values and a decision on whether to correct or exclude it from analysis was made during the data cleaning process. HIV PCR samples with error codes not adequately defined by NHLS were excluded from analysis since the data was collected retrospectively. During data entry, information captured was double checked to ensure that correct data had been captured.

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3.8 Ethics considerations

The study was approved by University of the Western Cape (UWC) Biomedical Research Ethics Committee (Appendix E) and Free State Health Research and Ethics Committee (Appendix F). Prior to data collection, written and verbal approvals were obtained from the TM District Manager (Appendix G) and Managers of the participating health facilities, respectively. The researcher also obtained the authority to access de-identified the EID PCR data set from NHLS for the study purpose and the spreadsheet was password protected.

The study did not induce any harm to participants. To ensure informed consent, participants and participating institutions were provided with clear information regarding their participation in the research. The potential participants were given the study information sheets (Appendix H and I) detailing the study purpose, risks, benefits, and methods. The implementation of informed consent process clearly specified the voluntary nature of research participation. The participating HCWs were informed that if at any point in time, they decide to terminate their participation or refuse to provide information or need clarity on the study, their right would be respected. They were additionally guaranteed anonymity and confidentiality in that the researcher would privately administer the questionnaire to one participant at the time, no participant identifying information (on consent forms) would be kept together with data collecting tools in which unique identifiers were used and the researcher would be responsible to secure data records which would be retained under locked instrument and accessed by the researcher and research supervisors. Consent forms (Appendix J and K) were thereafter issued to all participants for authorization before participating in the study. Both consent forms and the information sheets were not translated due to English language based professional training of HCWs.

Information acquired from the study was kept securely during data collection and analysis processes. Electronic data was encrypted with password and stored in a password protected computer while hard copies of data records were kept in a locked cabinet. The study findings are reported anonymously with health facility allocated a 4-digit code. Data generated from the study will be retained for the period of 5 years. The hard copies of the data records were sealed in a box and kept in a locked cabinet.

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CHAPTER 4: RESULTS

This chapter presents results from data collected from phase 1 and 2 of the study.

4.1 Phase 1 results

There were 9412 EID samples collected in TM district and registered by NHLS from January to December 2018. During the analysis, 94 (1%) samples were excluded due to not meeting inclusion criteria. The excluded samples were analyzed by NHLS but were missing date of birth and the HIV PCR results. HIV PCR results for 9318 samples included in the analysis are summarized in figure 1.

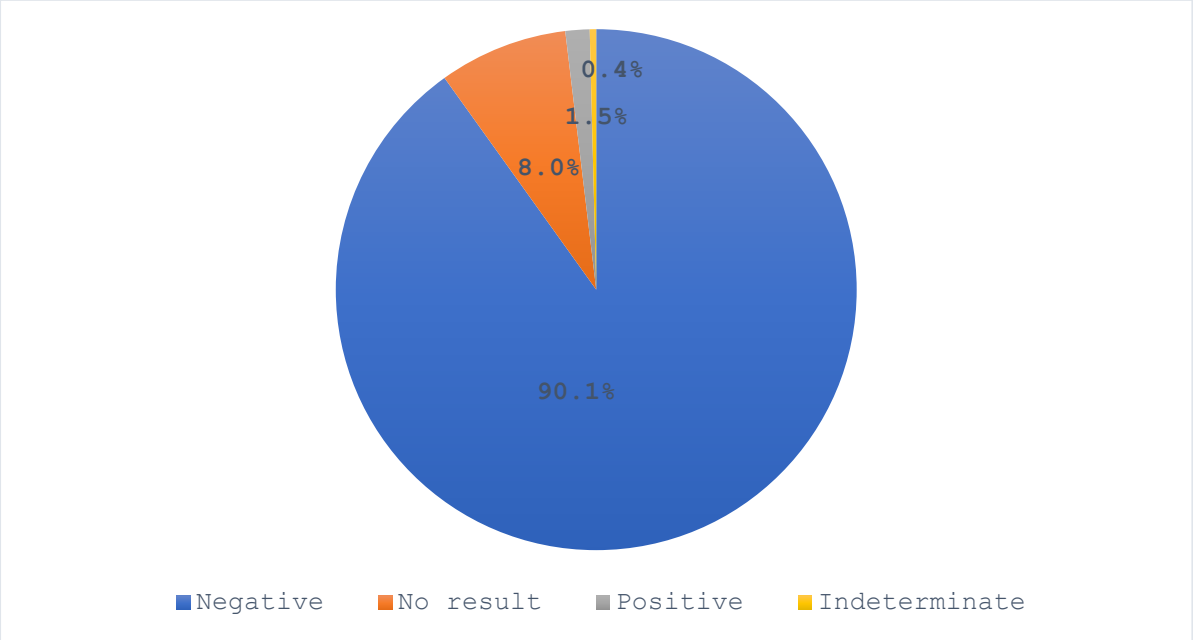

Figure 1: HIV PCR test results summary, (n=9318)

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Of the 9318 samples included in the analysis, 750 (8%) did not yield an HIV PCR result. Amongst the 750 samples not having an HIV PCR result, there were 3 lost in transit, 1 cancelled by the doctor and 1 which gave an invalid result (analytical error). The remaining 745 (8%) samples were rejected because of the following pre analytical errors: insufficient specimen, clerical error, and unsuitable sample. Figure 2 shows prevalence of the 3 types of pre analytical errors.

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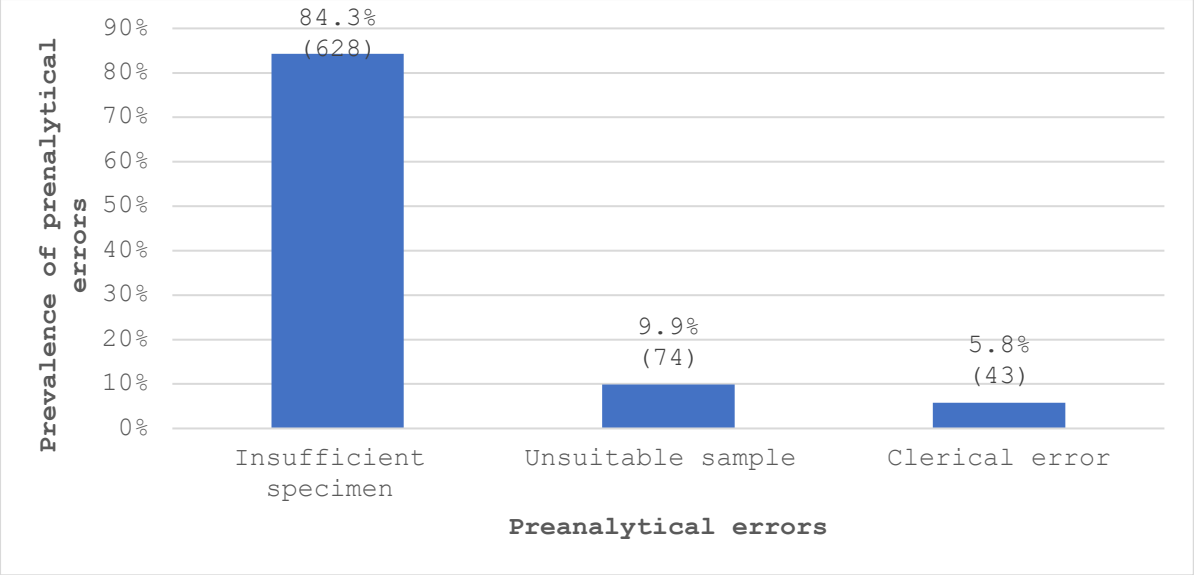

Figure 2: Prevalence of preanalytical errors, (n=745)

The prevalence of insufficient specimen, unsuitable sample and clerical error were 84.3%, 9.9% and 5.8% respectively. The prevalence of the three error types was further stratified by subdistrict, type of facility, child age at sample collection and sex in table 2.

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Table 2: Prevalence of the three HCW related preanalytical errors stratified by subdistrict, type of facility, child age at testing and gender, (n=9318)

	Collected HIV PCR samples n (%)	HCW related pre-analytical errors n (%)			
		Total	Insufficient specimen	Unsuitable sample	Clerical error
Subdistrict					
MAP	4160 (44.6)	416	372 (89.4%)	25 (6.0%)	19 (4.6%)
Dihlabeng	2458 (26.4)	137	90 (65.7%)	30 (7.2%)	17 (4.1%)
Setsoto	1139 (12.2)	103	93 (90.3%)	7 (6.8%)	3 (2.9%)
Nketwana	603 (6.5)	38	32 (84.2%)	4 (10.5%)	2 (5.3%)
Mantsopa	502 (5.4)	25	19 (76.0%)	4 (16.0%)	2 (8.0%)
Phumelela	456 (4.9)	26	22 (84.6%)	4 (15.4%)	0 (0%)
Total	9318 (100)	745	628 (84.3)	74 (9.9%)	43 (5.8%)
Type of facility					
PHC	5101 (54.7)	310	278 (89.7)	17 (5.5%)	15 (4.8%)
CHC	125 (1.3)	2	2 (100%)	0 (0%)	0 (0%)
Hospital	4092 (43.9)	433	348 (80.4%)	57 (13.1%)	28 (6.5%)
Total	9318 (100)	745	628 (84.3)	74 (9.9%)	43 (5.8%)
Child age at testing					
Birth (0-42 days)	4617 (49.6)	534	466 (87.3%)	45 (8.4%)	23 (4.3%)
10 wks. (43-144 days)	3927 (42.1)	170	132 (77.7%)	23 (13.5%)	15 (8.8%)
Above 12 wks-18 months (145-547)	774 (8.3)	41	30 (73.2%)	6 (14.6%)	5 (12.2%)
Total	9318 (100)	745	628 (84.3%)	74 (9.9%)	43 (5.8%
Child gender					
Female	4770 (51.2)	369	309 (83.7%)	34 (9.2%)	26 (7.1%)
Male	4548 (48.8)	376	319 (84.8%)	40 (10.6%)	17 (4.5%)
Total	9318 (100)	745	628 (84.3%)	74 (9.9%)	43 (5.8%)

NB: CHC= Community Health Centre, HIV= Human Immunodeficiency Virus, MAP= Maluti-a-Phofung, n= number of samples, PCR= Polymerase chain reaction, PHC= Primary Health Care, and wks.= weeks.

Maluti-A-Phofung (MAP) subdistrict collected the highest number of samples; 4160 (44.6% of total samples), while Phumelela subdistrict collected the least samples; 456 (4.9%).

On facility type, there is only one CHC facility in the district and it contributed 1.3% of the total samples collected in the District. PHC facilities collected just over half of all the samples (54.7% of total samples) and the hospitals collected 43.9% of total samples. However, hospitals had the highest number of total preanalytical errors of 433 out of 745 samples (58.1%). Ninety

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percent of PHC errors were insufficient specimen, followed by 5.5% and 4.8% of unsuitable sample and clerical errors, respectively. CHCs only experienced insufficient specimen errors.

The birth HIV PCR samples contributed 49.6% to total samples collected, 42.1% was from 10 weeks and 8.3% from above 12 weeks age category. Birth HIV PCR had more preanalytical errors (534), followed by 10 weeks (170) and the above 12 weeks age category (41).

Almost a similar proportion of females and males were offered HIV PCR testing. Female samples contributed 51.2% (4770/9318) and males (4548/9318) 48.8% of total samples collected. A total of 376 males' samples were rejected and the females' samples rejected were 369 (the percentages are 7.7 and 8.2). Both females and males' samples contributed almost equally to insufficient specimen error; 49.2% and 50.8%. The prevalence of unsuitable sample was slightly higher for males, 54.1% (40/74). For clerical error, females had higher prevalence of 60.5% (26/43 samples) compared to their male counter parts.

HCWs errors laboratory information system (LIS) rejection codes

Insufficient specimen

There were 628 samples rejected due insufficient specimen. Of the 628 samples that were rejected, 99% of them had insufficient specimen LIS rejection code and 1% (8/628) had specimen not received LIS rejection code. In all subdistricts, insufficient specimen had the highest prevalence of HCWs preanalytical errors. MAP contributed 372 samples (59.2%) of the district insufficient specimen error while Mantsopa contributed least to the error by 19 samples (3.0%), see figure 3.

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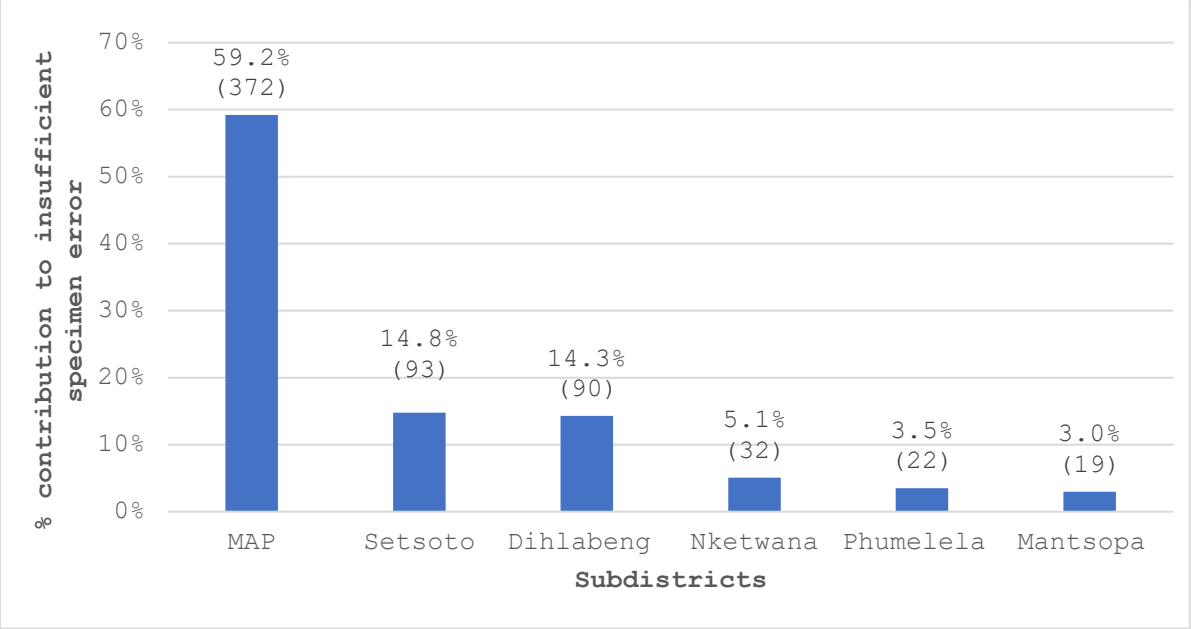

Figure 3: Subdistricts contribution to insufficient specimen error, (n=628)

Setsoto subdistrict contributed almost the same number of insufficient specimens as Dihlabeng subdistrict, although the later collected approximately double the number of samples as Setsoto.

Amongst the insufficient specimen errors, 2/628 (0.3%) occurred at CHC, 278/628 (44.3%) at PHC and 348/628 (55.4%) at hospitals. Hospitals had less samples collected than PHC facilities, but they contributed a larger portion of 55.4% to the total insufficient specimen error. Of the 628 insufficient specimens, 466 (74%) were birth tests. Lastly, insufficient specimen prevalence was 50.8% for males and 49.2% for females.

Unsuitable sample

There were 74 HIV PCR samples rejected due to unsuitable sample error. Unsuitable sample prevalence for the different subdistricts was between 6% and 16.0% (table 2). Dihlabeng subdistrict had the highest percentage of unsuitable sample 40.5% (30/74) although it collected a smaller number of samples than MAP. Mantsopa, Nketwana and Phumelela subdistricts contributed equal percentage of 5.4% (4/74).

Amongst the 74 unsuitable sample, 57 were from hospitals, 17 from PHCs and none from CHCs (table 2). The unsuitable sample error for hospitals was constituted by all seven LIS codes for unsuitable sample summarised in table 3, while at PHC facilities the same error was

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only due to compromised DBS card LIS code. The majority of unsuitable samples were from birth testing 45/74.

Table 3: LIS rejection codes related to unsuitable sample error, (n=74)

Rejection reasons	LIS rejection codes for unsuitable sample	Type of facility affected	Number of samples	Percentage contribution to unsuitable sample error
Require EDTA sample	REDTA	Hospital	4	5.4%
Unsuitable clotted	UCLT	Hospital	24	32.4%
Unsuitable DBS compromised	UCOMP	Hospital and PHC	24	32.4%
Unsuitable contaminated	UCONT	Hospital and PHC	2	2.7%
Unsuitable EDTA clotted	UEDTC	Hospital	18	24.3%
Unsuitable ESR* tube received clotted	UESRC	Hospital	1	1.4%
Unsuitable hemolyzed	UHAEM	Hospital	1	1.4%

NB: * Erythrocyte sedimentation rate

Both the UCLT and UCOMP LIS rejection codes contributed 32.4% of the unsuitable sample error. The hospitals and PHC facilities respectively contributed 33.3% (8/24 samples) and 66.7% (16/24 samples) to UCOMP LIS rejection code.

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Clerical errors

There were 43 samples rejected due to clerical errors. Compared to the other two HCWs preanalytical errors, clerical error had the lowest prevalence of 5.8% (table 2). Mantsopa and Nketwana subdistricts had equal contribution of 4.7% (2/43) to the total clerical error. Phumelela subdistrict did not experience sample rejection due to clerical errors. MAP and Dihlabeng subdistricts contributed most to the clerical errors.

Clerical error prevalence for hospitals was 65.1% (28/43) and 34.9% (15/43) for the PHC facilities. Five LIS rejection codes contributed to the 43 samples rejected due to clerical error. These included duplicate registration (ODREG), information does not match (MISX), information does not match DBS card (MISXD), specimen not labelled (SNLAB) and name or

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surname not indicated on the form (NDNS). The most common error was MISXD. Birth tests contributed over half of clerical errors. Table 4 shows how each of these LIS rejection codes contributed to the total number of samples rejected before analysis due to clerical error stratified by subdistrict, facility type and child age at testing.

Table 4: Clerical error LIS rejection codes, (n=43)

	Number of samples rejected due to clerical error LIS code	**LIS rection codes for clerical error**				
Subdistrict		**0DREG**	**MISX**	**MISXD**	**NDNS**	**SNLAB**
MAP	19	4	2	8	0	5
Dihlabeng	17	4	8	2	1	2
Setsoto	3	1	1	1	0	0
Nketwana	2	0	0	1	0	1
Mantsopa	2	0	0	2	0	0
Phumelela	0	0	0	0	0	0
Total	43	9	11	14	1	8
Type of facility						
PHC	15	5	2	7	0	1
CHC	0	0	0	0	0	0
Hospital	28	4	9	7	1	7
Total	43	9	11	14	1	8
Child age at testing						
Birth (0-42 days)	23	4	9	7	0	3
10 wks. (43-144 days)	15	3	2	5	1	4
Above 12 wks.-18 months (145-547)	5	2	0	2	0	1
Total	43	9	11	14	1	8

4.2 Phase 2 results

4.2.1 Facility assessments checklist results

Description of facilities included in the study

Table 5 shows the profiles of facilities that participated in phase 2 of the study. Of the 10 health facilities that participated, 9 were PHC facilities and 1 was a hospital. Half of the participating facilities were from MAP subdistrict, 30% from Dihlabeng and 20% from Nketwana subdistricts. The location of 80% of the facilities was described as rural and 20% as urban.

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Table 5: Profile of facilities that participated in the study, (n=10)

Facility code	Performance category	Facility type	Subdistrict name	Setting	ANSUR site	Number of HIV PCR collectors
TM01	worst	PHC	MAP	rural	no	3
TM02	worst	hospital	MAP	rural	no	13
TM03	worst	PHC	MAP	rural	yes	3
TM04	worst	PHC	Dihlabeng	rural	yes	4
TM05	worst	PHC	Nketwana	rural	yes	2
TM06	best	PHC	Dihlabeng	urban	yes	5
TM07	best	PHC	Dihlabeng	urban	yes	7
TM08	best	PHC	MAP	rural	yes	4
TM09	best	PHC	MAP	rural	no	2
TM10	best	PHC	Nketwana	rural	no	3

HIV PCR samples from Dihlabeng and Nketwana subdistricts are sent to Dihlabeng Regional Hospital (DRH) NHLS for processing, while the ones for MAP subdistrict are sent to Mofumahadi Monapo Mopeli Regional Hospital (MMMRH) NHLS. In all participating health facilities, DBS was used to collect HIV PCR samples and samples were sent to laboratory daily for processing. Sixty percent of facilities were ANSUR sites. The total number of HIV PCR sample collectors for participating facilities ranged from 2 to 13 professional nurses (PNs). But of the 13, only 8 PNs met the study inclusion criteria. Facilities had different frequencies for ordering EID supplies (see figure 4). Half of the facilities ordered supplies weekly.

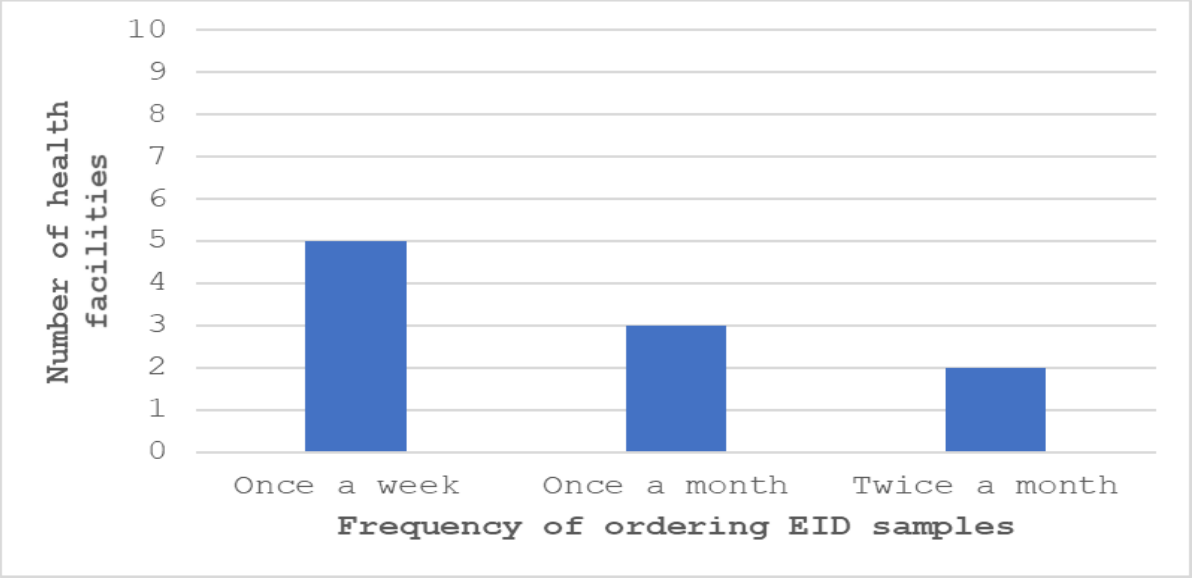

Figure 4: Frequency of ordering EID supplies from NHLS, (n=10)

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The total number of HIV PCR samples recorded to have been collected by the participating facilities 3 months prior to the study data collection is shown in figure 5. The highest number of samples was collected by TM02 (83 samples, the hospital), and the least was 2. The average number of samples for the PHC facilities was 13.

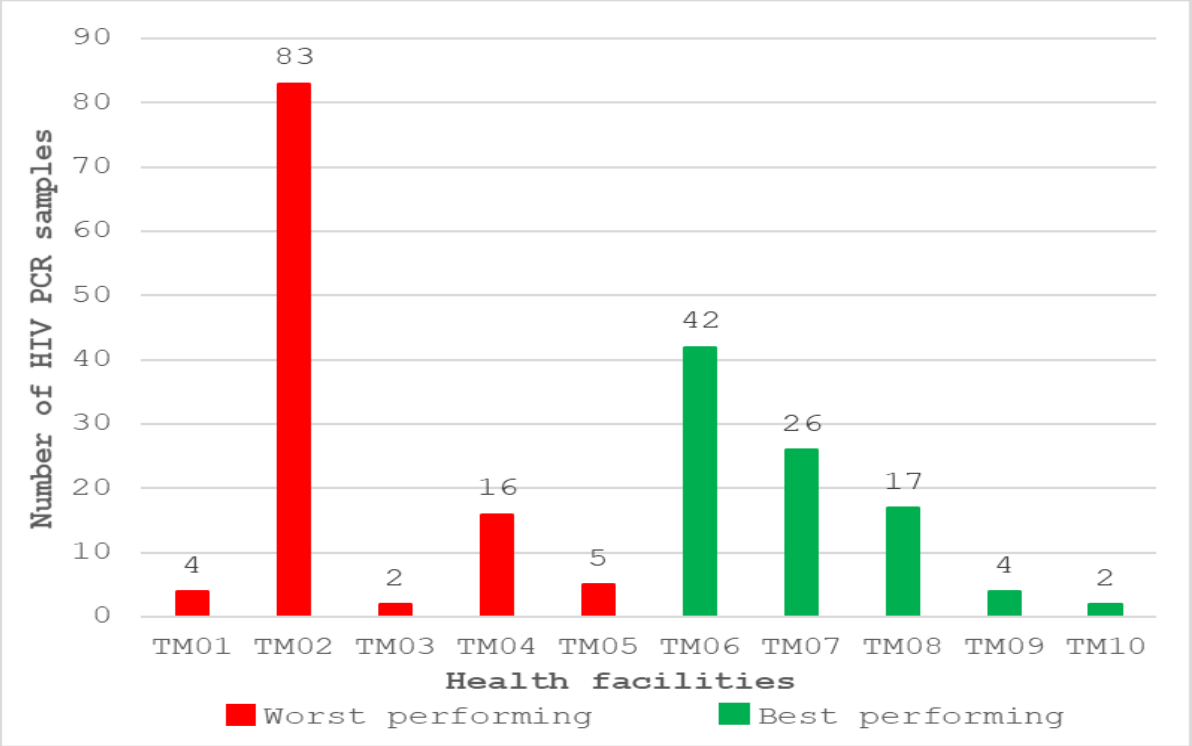

Figure 5: Number of HIV PCR samples collected by health facilities in the previous 3 months, (n=10)

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Facility implementation level

Table 6 shows the overall domain score for facilities and their implementation levels. The facility implementation levels were determined by domain overall scores expressed as percentage of the highest possible score. The highest possible overall score was 46. Overall percentage scores ranged from 47.8% (for facility TM02) to 91.3% (for facility TM06) Facilities attained a median overall score of 29.5 (23.0-35.8) and median overall percentage score of 64.1% (50.0%-77.8%).

Four facilities were on implementation level 1, another four on level 2, one on level 3 and the last one on level 4 (table 7). This means 4 of the assessed facilities needed improvement in a specific area and 10% in all areas immediately. Facility implementation levels were further stratified by facilities performance category in table 7.

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Table 6: Facilities overall domain score and implementation levels, (n=10)

Facility Performance category	Facility	Overall domain score for facility	Percentage of highest possible score (46)	Implementation level
	TM01	23	50.0%	1
	TM02	22	47.8%	1
	TM03	29	63.0%	2
	TM04	27	58.7%	1
Worst	TM05	23	50.0%	1
	TM06	42	91.3%	4
	TM07	38	82.6%	3
	TM08	35	76.1%	2
	TM09	32	69.6%	2
Best	TM10	30	65.2%	2

NB:

Level 0: a score of less than 40%, facility needs improvement in all areas and immediate remediation.

Level 1: a score of 40%-59% and facility needs improvement in specific areas.

Level 2: a score of 60%-79% and is partially ready for national site certification.

Level 3: a score of 80%-89% and is close to national site certification.

Level 4: a score of 90% or higher and is eligible for national site certification.

Table 7: Distribution of implementation levels by facility performance category

Performance category	Number of facilities	Level 0 (<40%) Number	Level 1 (40-59%) Number	Level 2 (60-79%) Number	Level 3 (80-89%) Number	Level 4 (>=90%) Number
Worst	5	0	4	1	0	0
Best	5	0	0	3	1	1

A higher number (4) of low performing facilities were on implementation level 1, while the higher number (3) of best performing facilities were on implementation level 2. The worst performing facilities were on implementation level 2 and below, whereas best performing facilities were on implementation level 2 and above.

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Domains scores

There were six domains assessed using the facility check list and each domain had a maximum possible score. Table 8 shows different domains that were assessed. Median scores with IQR were calculated for each domain. In order to make domain median comparisons, individual domain scores were expressed as the percentages of highest possible domain scores.

Table 8: Domains assessed and their median scores

Domains	**Total possible domain score**	**Median domain score (IQR)**	**Median score as a % of possible domain score (IQR)**
Personnel training	2	1.0 (1.0-1.0)	50.0% (50.0%-50.0%)
Physical facility (Testing area/room or physical infrastructure)	10	8.5(8.0-10.0)	85.0% (80.0%-100.0%)
EID supplies	10	8.0 (6.0-9.3)	80.0% (60.0%-93.0%)
EID sample management	10	8.0 (5.0-10.0)	80.0% (50.0-100.0%)
EID testing phase	4	3.0 (2.0-3.3)	75.0% (50.0%-82.5%
Supervision and support	10	2.0 (0.8-3.5)	20.0% (8.0%-35.0%)
Total	**46**	**29.5(23.0-35.8)**	**64.1% (50.0%-77.8%)**

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Physical facility domain had the highest percentage median score of 85.0 (80.0%-100.0%), followed by EID supplies and sample management at 80.0%. Supportive supervision and support had lowest percentage median score of 20% (8.0%-35.0%).

Domain median scores were further stratified by worst and best performing facilities in which median comparisons were made using independent median test and findings are illustrated in figure 6. Domain median score for best performing facilities was 35.0 (31.0-40.0) and 23.0 (22.5-28.0) for worst performing facilities. The domains median score for worst performing facilities was lower than the median score for best performing facilities and they were significantly different (*p*-value 0.008 from independent-sample median test).

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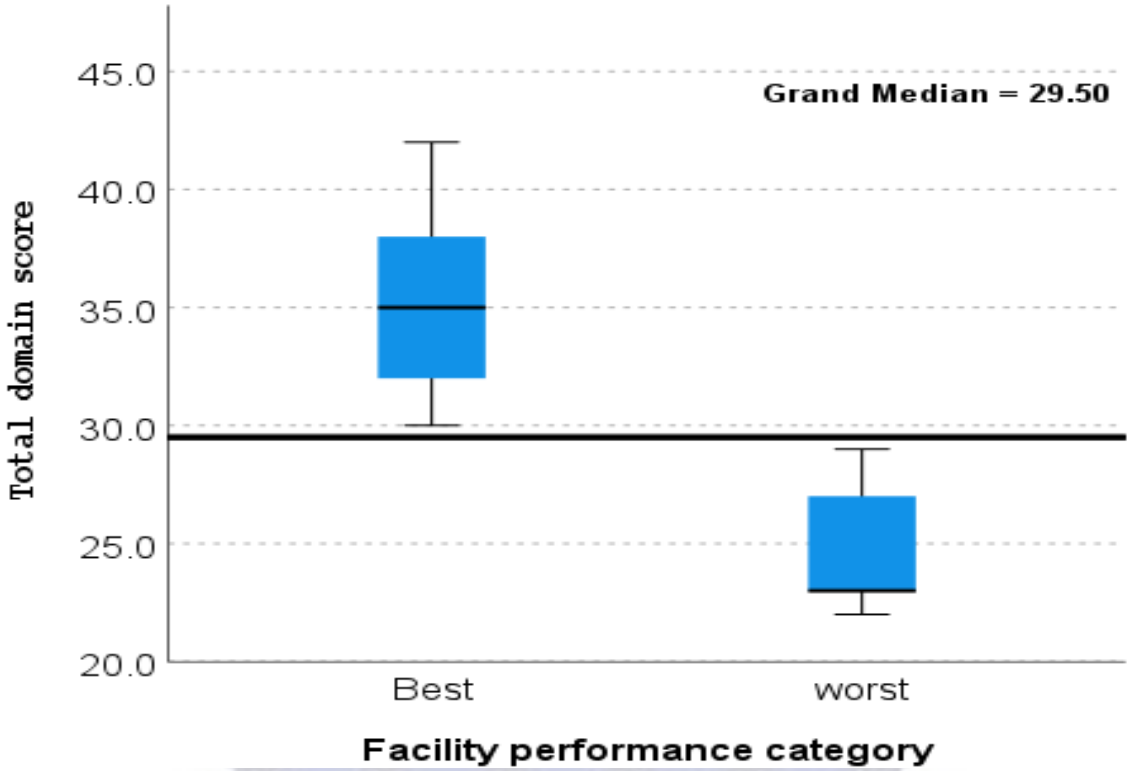

Figure 6: Median scores comparisons for best and worst performing facilities using independent-samples median test

Table 9: Domain median scores stratified by worst and best performing facilities

Domains	**Best performing facilities**		**Worst performing facilities**	
	Median score (IQR)	**Median score as a % of total possible domain score (IQR)**	**Median score**	**Median score as a % of total possible domain score (IQR)**
Personnel Training	1.0 (1.0-1.0)	50% (50%-50%)	1.0 (1.0-1.0)	50% (50%-50%)
Physical facility	10.0 (8.5-10.0)	100% (85%-100%)	8.0 (7.5-9.0)	80% (75%-90%)
EID supplies	8.0 (7.0-10.0)	80% (70%-100%)	6.0 (5.5-8.5)	60% (55%-85%)
EID sample management	10.0 (10.0-10.0)	100% (100%-100%)	5.0 (4.0-6.0)	50% (40%-60%)
EID testing phase	3.0 (3.0-4.0)	75% (75%-100%)	2.0 (2.0-3.0)	50% (50%-75%)
Supervision and support	2.0 (1.0-6.0)	20% (10%-60%)	1.0 (0.5-2.5)	10% (5%-25%)

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During data collection notes were taken for facilities that scored partial or no on elements that were being assessed. These comments are integrated into the findings for each domain assessed.

Personnel training

Median scores for both facility categories were similar. All facilities assessed got a partial score on this assessed element since they were all not having training records for staff reported to have been trained on EID.

Physical facility (Testing area/room or physical infrastructure)

Elements assessed in this domain were the presence of a designated consultation room for EID testing, if the designated area was clean and organised for EID testing, sufficient lighting, and EID test kit storage. Facilities performed quite well on the domain as both the best and worst performing health facilities had highest median percentage score of 100% and 80% respectively. The worst performing facilities did not have a full score due to the following; 3 (60%) facilities were conducting HIV PCR testing in any consultation room and as a result 2 facilities further lost points on the question "is everything needed for testing there, accessible, and available in the testing area?'' At facility TM02, DBS kits were not kept in the testing room to control missing stock problem.

EID supplies

Elements assessed in this domain were HIV PCR stock availability on the day of assessment, if DBS kits were within the expiry date, availability of stock cards and if they were up to date. The best performing facilities had percentage median score of 80% while the worst performing facilities had 60%. Eighty percent (8/10) facilities lost points on EID stock card availability and updating. Out of the 10 assessed facilities, 4 (40%) facilities (2 from best performing and 2 from worst performing facilities) did not have stock cards or a similar system to track supply of HIV PCR test kits and as a result they automatically lost additional points on stock card updating on receipt and issuing of test kits. Four facilities (1 best performing and 3 worst performing) did have EID stock cards but they were not updated. Lastly, facility TM01 (one of the worst performing facilities) had 1 DBS card within expiry date (not enough stock) and 1 expired DBS card on the day of assessment.

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EID sample management

Elements assessed included HIV PCR sample storage SOP's availability, following of sample storage SOP, availability of HIV PCR sample acceptability evaluation SOP, facility notification of rejected HIV PCR samples and availability of quality improvement plans (QIPs) to address sample rejections. The best performing facilities had percentage median score of 100% while the worst performing facilities had 50%. This domain had the highest percentage median score difference between best and worst performing health facilities.

There were several factors identified at worst performing facilities which made them to score less and contributed to the observed difference. Firstly, 60% of facilities were not following the SOP for sample storage prior to packaging. At facility TM01, there was no DBS drying rack and samples were kept on plain paper to dry. At facility TM02, there was no drying rack in one area and HIV PCR samples were reported to be packed immediately after collection. At facility TM01, drying rack with samples were kept at the foot of the examination bed, which was too close to the floor of a very small consultation room. Secondly, 60% percent (3/5) of the worst performing facilities were not having a designated area for PCR testing under (physical facility domain) and offering HIV PCR tests in different areas which all did not have sample management SOPs for each area resulting in partial score on SOPs being in place for HIV PCR samples storage and evaluating them for acceptability. Lastly, 100% of the worst performing facilities never had documented nor reported QIP addressing HIV PCR sample rejections.

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Regarding facility notification of rejected HIV PCR samples, all 10 facilities were receiving hard copies of HIV PCR results from which they identify rejected samples. At facility TM02, the results were received but were not signed off like in all other 9 facilities, although it did not impact on its score.

EID testing phase

Elements assessed were availability of laboratory handbook and SOPs for HIV PCR sample collection and their posting. The best performing facilities had percentage median score of 75% while the worst performing facilities had 50%. All assessed facilities had a laboratory handbook, although facility TM03 and TM05 had 2015 versions and TM01 had one with a description matching the 2020 version locked in the Facility Managers office who was not at the facility on the day of assessment.

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Ninety percent of assessed facilities had SOPs for HIV PCR sample collection and facility TM05 (wort performing) did not have. Two (facility TM06 and TM08) of the best performing facilities had their SOPs posted and 3 did not, which made them to have partial scores on the element. All 4 worst performing facilities had their HIV PCR sample collection SOPs not posted.

Supervision and support

In general, facilities performed poorly on this domain achieving lowest percentage median score of 20% (10%-60%) and 10% (5%-25%) for best and worst performing facilities, respectively. Figure 7 illustrates responses to 5 assessment questions for the domain. Assessment questions were.

- 6.1 Does the person in charge/person responsible for EID program at the testing facility/unit review EID PCR samples before being dispatched to Laboratory?
- 6.2 Does testing facility receive periodic EID supervisory visits?
- 6.3 Is feedback provided during supervisory visit and documented?
- 6.4 Does facility receive implementing partners support?
- 6.5 Does facility receive QI support?

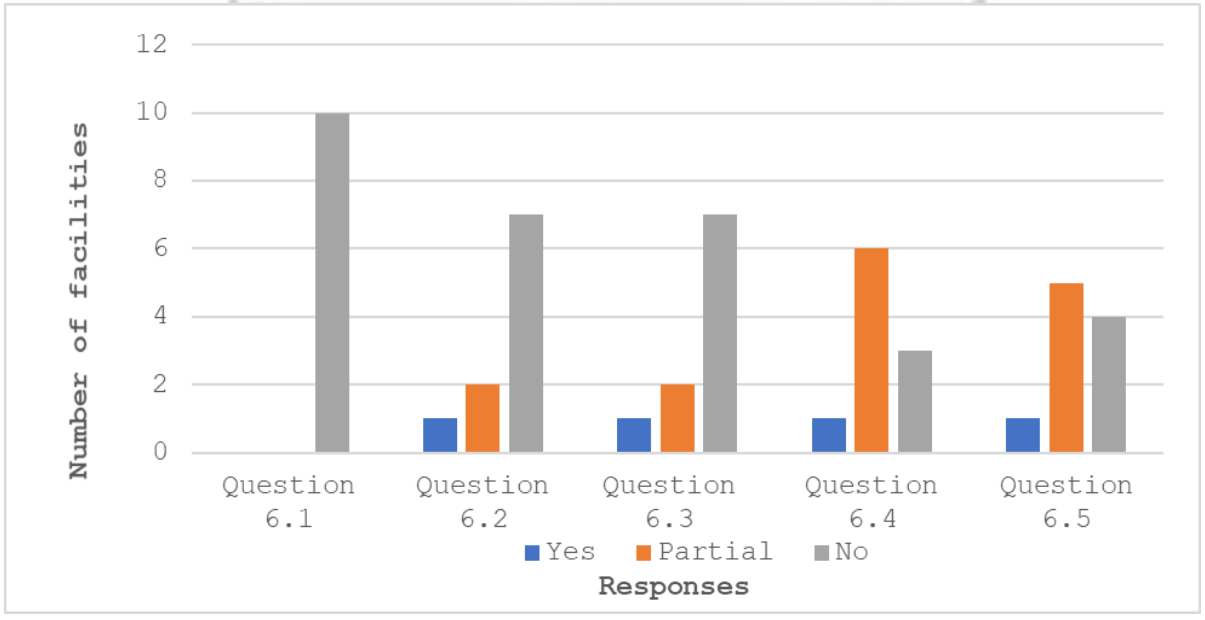

Figure 7: Responses to supervision and support domain assessment questions

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In all facilities, EID PCR samples were not being reviewed by the person in charge before they were being dispatched to NHLS. Seventy percent (4 from worst performing and 3 from best performing) of facilities responded no to the question on receipt of supervisory visits, while 20% responded partial (equal contribution from both facility performance categories) and one facility responded yes, and it was one of the best performing facilities: facility TM06. Similar percentage of responses were observed regarding supervisory visits feedback. For receipt of supporting partners support question, 60% of facilities responded partial (equal contribution of both facility performance categories), 30% responded no (2 from worst performing and 1 from best performing), and 10% (facility TM07 under best performing) responded yes. Lastly for receipt of quality improvement support question, 50% of facilities obtained partial score (3 best performing and 2 worst performing), 40% did not obtain score (3 worst performing and 1 best performing), and one (facility TM06 under best performing) obtained a full score.

4.2.2 Health care worker interviews

Study participants description

Thirty-six PNs participated in the study, 8 from the hospital and 28 from PHC facilities. Seventeen (47.2%) were from worst performing facilities and 19 (52.8%) from best performing facilities. Median age for participants was 52 years (IQR 41.3-56.0) while their median years of experience was 21.5 years (IQR 9.0-29.0). Table 10 shows participants distribution by characteristics and facility performance category.

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Table 10: Distribution of participants

Variables	Totals	Worst performing facilities	Best performing facilities
Gender			
Female	32	17	15
Male	4	0	4
Age			
Median age (IQR)	52.0 (41.3-56.0)	52.0 (43.5-56.0)	52.0 (36.0-56.0)
Years of experience			
Median years of experience (IQR)	21.5 (9.0-29.0)	25.0 (11.5-29.0)	20.0 (9.0-30.0)
Main responsibility at the facility			
Operational management	7	3	4
Patient care	29	14	15
EID sample type collected			
DBS	36	17	19
Whole blood in EDTA tube	0	0	0
Age from which participants perform EID sample collection			
At Birth	12	7	5
At 10 weeks	23	9	14
Other*	1	1	0

NB: *Any time HIV PCR is prescribed for children.

Thirty-two nurses were females and 4 were males. All 4 males were from best performing facilities. Seven (19.4%) participants were Facility/Unit Managers and 29 (80.6%) were PNs responsible for patient care. Median age for participants from worst and best performing facilities was 52 years. Median years of experience for participants from worst performing and best performing facilities was 25.0 (11.5-29.0) and 20.0 (9.0-30.0) respectively. All participants were using DBS to collect EID samples.

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Majority (71.9%) of participants were collecting EID samples from 10 weeks and they were all from PHCs. Twelve (33.3%) participants were collecting EID samples from birth (7 from hospital and 5 from two best performing facilities). One participant from the hospital was collecting EID samples at any age below 18 months when prescribed for the child.

EID training for professional nurses

Thirty-four participants were trained on EID, 16 (47.1%) received formal training and 18 (52.9%) on the job training. The two (both from one worst performing facility) that were performing EID but not trained have been able to collect HIV PCR samples through ward demonstrations that were conducted in their presence. Table 11 summarises participants distribution by type of training received and their facility performance category.

Table 11: Distribution of participants by training elements and facility performance category

Training elements	**Total No of participants**	**No of participants from worst performing**	**No of participants from best performing**
Type of training received			
Formal	16	9	7
On the job	18	6	12
None	2	2	0
Total	**36**	**17**	**19**
Declared competent			
Formal	12	7	5
On the job	9	3	6
Total	**21**	**10**	**11**
Refresher training received			
Formal	3	1	2
On the job	2	0	2
None	26	12	14
Total	**31**	**13**	**18**

Sixty-two percent (21/34) of participants trained on EID were declared competent to collect HIV PCR samples after receiving the training and there was almost equal contribution of participants from best and worst performing facilities.

Of the participants trained on EID, 3 received training within the past 2 years and were therefore not eligible for refresher training. Thirty-one participants were due for refresher

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training at the time of the study data collection, however 5 (16.1%) received refresher training in the past two years.

Regarding when participants were trained, 13 (38.2%) could not remember the year they received EID training since it was a long time ago. Seven were from worst performing facilities and 6 from best performing facilities. The remaining 21 were trained between 2005 and 2018 and Figure 8 illustrates different years participants received EID training (formal and on the job) grouped by facility performance category where the participants were from.

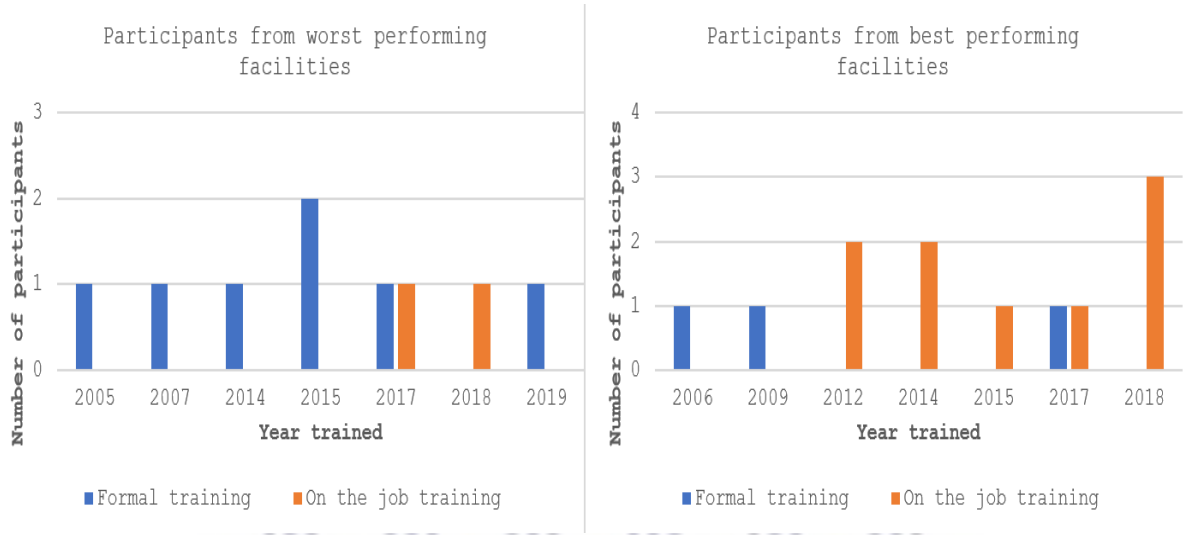

Figure 8: Years when participants received EID training

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Between 2005 and 2009, participants received formal training and from 2012 to 2019 there was a combination of both formal and on the job, trainings received by participants. Seven participants received formal training from worst performing facilities and 3 from best performing facilities. Majority (9/12) of participants from best performing facilities received on the job training which was between 2012 and 2018 while few (2/9) participants from worst performing facilities received same training in 2017 and 2018.

Support and supervision on EID

Participants were asked whom they consult when they have questions about EID and were allowed to choose more than one answer in order of preference. Four participants (1 from worst performing and 3 from best performing facilities) indicated that they never ask or consult. Thirty-two (remaining from 36) mentioned different sources to ask or consult and table 12 summarises different sources which received first preference from the participants.

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Table 12: Sources of support or information on EID, (n=32)

Sources consulted	Totals	Number of participants from worst performing	Number of participants from worst performing
Another nurse in this Facility	14	8	6
Guidelines	10	3	7
Facility/Unit Manager	2	1	1
The Doctor	2	1	1
PMTCT Coordinator	2	1	1
District Specialist	0	0	0
NHLS	2	1	1
Totals	**32**	**15**	**17**

Fourteen participants (8 from worst performing and 6 from best performing facilities) mentioned another nurse in their facility as their first preference and 10 (3 from worst performing and 7 from best performing facilities) mentioned guidelines as their first preference.

In addition, highest number (20) of participants responses had asking a nurse in their facility, followed by 16 participants who mentioned consulting the guidelines in the responses. Few participants (2) mentioned asking the Facility/Unit Manager. None of the participants mentioned NHLS trainer nor District Specialists though they were part of the options to choose from. Participants were further asked how often they receive support/supervision/mentoring on EID and their responses are summarised in figure 9.

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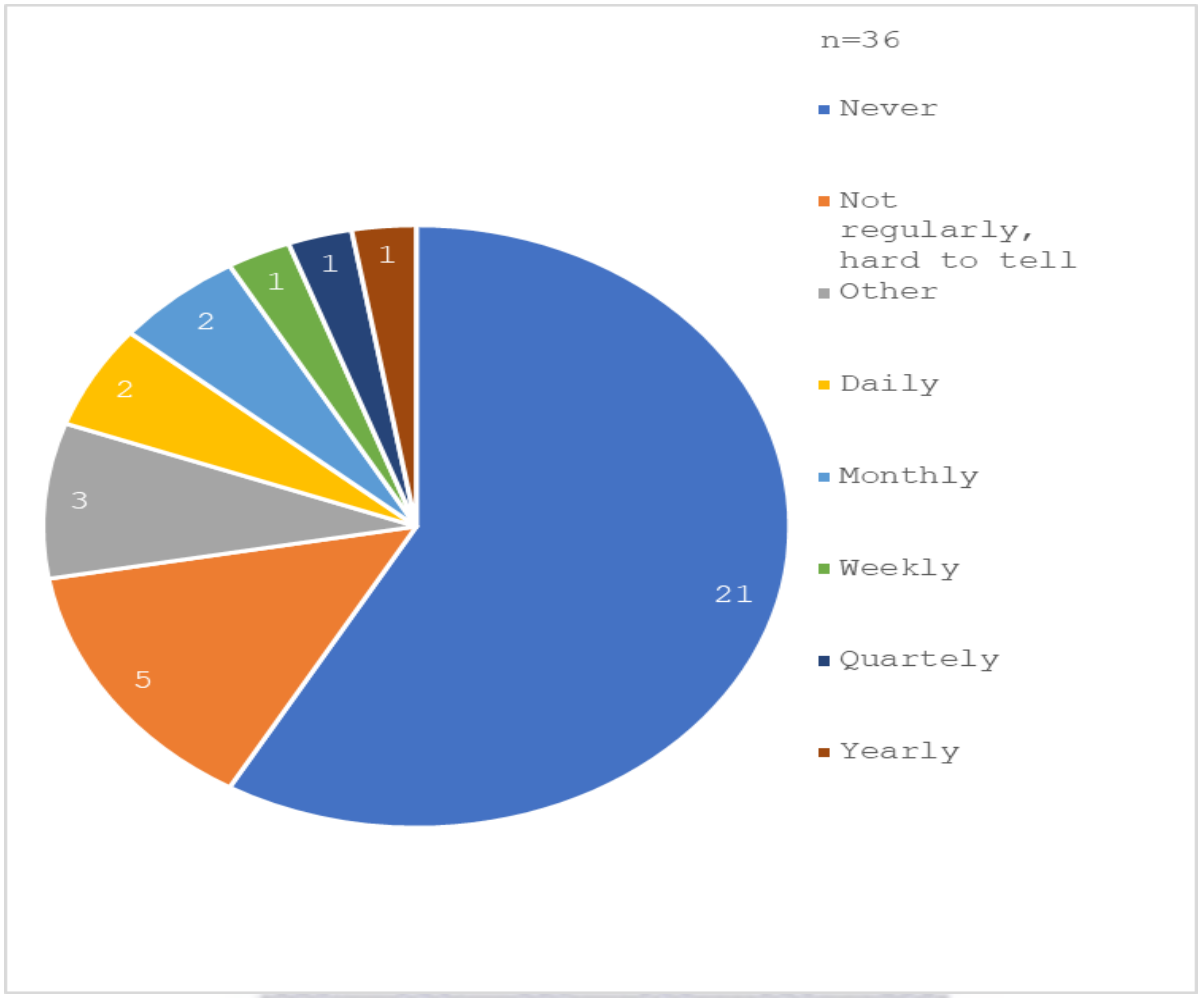

Figure 9: Frequency of receiving EID support/supervision/mentoring by participants

NB: Other included 2 participants who responded, 'when there is need' and 'when relieving in IMCI unit'.

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Majority (21/36) of the participants never received EID supervision and 5 indicated that it was hard to tell, since supervision was not provided regularly. Of the 21 participants who never received supervision, 10 were from best performing facilities and 11 were from worst performing facilities. Different providers of EID supervision and mentorship to the participants are summarized in table 13.

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Table 13: EID supervision and mentorship providers stratified by number of participants and facility performance category

Supervision/mentoring providers	No of participants	No of participants from worst performing	No of participants from best performing
Facility/Unit Manger	5	4	1
Supporting partner	2	0	2
Another nurse in this facility	2	0	2
Facility PMTCT representative	1	0	1
PMTCT Coordinator	1	1	0
Local Area Manager	1	1	0
IMCI Coordinator	1	0	1
Facility/Unit Manager and another nurse at this facility	1	0	1
PMTCT Coordinator and District Specialist	1	0	1
Totals	**15**	**6**	**9**

Participants were to mention all people providing support on EID, that is more than one response was allowed. Thirteen participants received support from a single provider. Five participants received support from Facility/Unit Manager and most (4/5) contribution was from worst performing facilities participants. Two participants received EID support from more than one provider, and both were from best performing facilities.

Responding to if they need to be trained on EID sample collection during the support visit, were they being trained, 11 participants responded yes and 4 responded no. Of the 4 who indicated that they were not trained, 3 were from best performing (were provided support by Facility/Unit Manager) and 1 was from worst performing (was provided support by Facility/Unit Manager).

EID Supplies

Thirty-five participants were aware of where they order EID supplies, 17 were ordering from DRH NHLS and 18 from MMMRH NHLS. One participant who did not know where the EID supplies were ordered from and how, was from Facility TM02. All the 35 participants were also aware of the different request forms used for their facilities which were DRH NHLS order forms, PHC order book: materials for specimen collection (N3) and specimen collection forms for hospitals only. None of the participant reported EID supplies stock out in the past month.

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Test requisition by participants.

Table 14 shows participants responses on how often they performed tasks that could prevent clerical errors during test requisition. Generally, there were almost similar responses from participants from worst and best performing facilities. Similar findings were observed on responses for the sample labelling summarised in table 15.

Table 14: Participants responses on performing tasks that could prevent clerical errors

How often do you perform the following tasks?	**No of participants from worst performing**					**No of participants from best performing**				
	Always	**Often**	**Seldom**	**Never**	**N/A**	**Always**	**Often**	**Seldom**	**Never**	**N/A**
Compare the patient's names with the information on the test request form.	16	0	1	0	0	16	1	2	0	0
Use the test request form that somebody else has filled in.	0	0	2	15	0	0	0	4	15	0
Sign the test request form filled by somebody else.	0	1	2	14	0	0	0	3	16	0
Check the information on the test request form if somebody else has completed it for you (N/A if responded *).	1	1	0	1	14	3	1	1	0	14
Check that the test request form and EDTA tube/DBS card identification (barcode) match before delivery to the laboratory.	16	0	0	1	0	17	0	1	1	0

NB: * Never use the test request form that somebody else has filled in.

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Sample labelling by participants

Table 15**:** Participants responses on timing of sample labelling, (n=36)

When do you label the DBS card/EDTA test tube?	**No of participants from worst performing**				**No of participants from best performing**			
	Always	**Often**	**Seldom**	**Never**	**Always**	**Often**	**Seldom**	**Never**
Before I approach the patient.	1	0	2	14	4	2	1	12
Alongside patient before sampling.	13	2	0	2	12	3	1	3
Alongside patient after sampling.	1	2	0	14	2	2	1	14
At a later occasion.	0	1	0	16	1	0	2	16
Somebody else has labelled DBS card/EDTA tube in advance.	0	0	1	16	0	1	1	17
Somebody else has labelled DBS card/EDTA tube after sampling	0	0	0	17	0	1	2	16

Sample condition checking

Thirty-four participants were always checking EID sample condition. One (from worst performing) was never checking and another one (from best performing) seldomly checked the sample condition.

Checking of sample volume and appropriate test request received similar number of responses from participants and from same facility performance categories. Thirty-four participants responded always, 1 never (from worst performing facility) and the other one seldom (from best performing facility).

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Sample preparation and transportation

Responding to the question asking where they store EID samples in the facility before they are being packed, 26 participants indicated that they are stored in the room in which they are taken, and the participants were from 8 facilities. The other remaining 10 participants from two facilities (worst performing) indicated other as their response and specified the areas which were the utility room (7), specimen room (2) and being packed immediately after collection (1).

Table 16 shows the summary of participants responses on where they store packed EID samples in the facility while awaiting collection.

Table 16: Places of storing EID samples before being dispatched to NHLS

Place where samples are stored prior to collection	**No of participants from worst performing**	**No of participants from best performing**
Room in which they were taken	0	2
Facility pharmacy	3	0
Facility/Unit manager's office	0	10
Outpatient Department (OPD)	7	0
Nurse's station	1	0
Blood collection room	2	0
Labour ward	2	0
Specimen room	2	2
Observation room	0	5
Total	**17**	**19**

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Participants for each facility were keeping samples at one place, except one from worst performing facility (facility TM02) who was keeping samples at nurses' station while other colleagues were keeping them at OPD while they are awaiting collection by NHLS. Majority (10/19) of the participants from best performing facilities were keeping the samples in Facility/Unit manager's office while ones from worst performing facilities were keeping them in OPD.

All participants reported to be sending HIV PCR samples to laboratory daily and that there was no minimum number of samples that they were allowed to send at a time.

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Test result feedback to participants

Thirty-two (88.9%) participants had access to EID test results and the 4 who did not have access were from one worst performing facility. Participants were accessing EID test results through calling the laboratory using the unique bar code on the infant's road to health card (RTHC), using NHLS LAB TRACK and receiving EID results hard copies which were delivered at their facilities. All 32 participants reported to be using a combination of methods to access HIV PCR results and a common method from all participants was that hard copies of the HIV PCR results were delivered at the facility. Half (16/32) of the participants were accessing results through the combination of receiving hard copies from the laboratory and using NHLS LAB TRACK.

Thirty-one participants reported to have no samples rejected in the past month and as a result reasons for sample rejections, challenges experienced that might have contributed to the sample rejections, as well as how the challenges can be addressed could not be established.

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CHAPTER 5: DISCUSSION

This chapter presents the interpretation of the phase 1 and 2 key study findings in terms of their comparability to existing literature, researcher's interpretations as well as their implications. It also includes the limitations of the study.

5.1 Prevalence of the three types of preanalytical errors in EID PCR testing

The study found that the prevalence of insufficient specimen, unsuitable sample and clerical error were 84.3%, 9.9% and 5.8% respectively. Insufficient specimen was the most prevalent reason for preanalytical sample rejections in the TM district, followed by unsuitable sample and clerical error. Similar findings were documented in a study in Mashonaland West province (Zimbabwe) where 77.9% of HIV PCR samples were rejected because of insufficient specimen, 12.1% rejected because of unsuitable sample and 10.7% rejected because of the clerical error (Mugauri *et al*., 2018). The findings of the study are also comparable to a South African study in which 49.5% of HIV PCR samples were rejected due to insufficient specimen, 28.3% due to unsuitable sample and 22.2% due to clerical error (Mazanderani *et al*., 2017). The latter study however, had significantly fewer samples rejected due to insufficient specimen and a higher proportion of samples rejected due to unsuitable sample and clerical error than the current study.

This notable difference from the Mazanderani *et al*. (2017) national study probably relates to the fact that they used 2010 to 2015 HIV PCR data in which 36% of the HIV PCR samples did not yield valid results and were not coded because of the unstandardised LIS used by NHLS while the current study used 2018 HIV PCR data in which almost all sample rejection reasons were coded because of the single LIS that is now being used by NHLS. They also documented that it was not possible to accurately describe pre-analytical rejection trends from 2010 to 2015 because of the large number of non-coded reasons for rejections, where HIV PCR samples were rejected but the rejection reasons were either not provided or could not be obtained from the LIS. Moreover, their study findings might have shifted focus from insufficient specimen to unsuitable sample and clerical error in the districts including TM post 2015. This might be the case because their study was a national one, conducted in SA and showed a reduction in the number of rejections due to insufficient specimen but a simultaneous increase in unsuitable samples and clerical errors from 2010 to 2015.

The finding that insufficient specimen is the most prevalent reason for sample rejection in the current study was in contrary to a Nigerian study where 26.3% of samples were rejected due to

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improper sample collection, followed by 16.4% for improper labelling and 10.8% for insufficient specimen (Inalegwu *et al*., 2016). This difference could have been influenced by different LIS rejection code categories used by SA NHLS and Nigerian National Health Laboratory. For example, with Nigerian NHLS there is rejection reason 'improper collection', which could constitute either insufficient specimen or unsuitable sample if classified by SA NHLS. The other possible factor for the difference is that their study only used DBS samples while the current study phase 1 analysis used both HIV PCR sample types: DBS and EDTA anticoagulated whole blood. Additionally, their data analysis included rejected samples for children above 18 months and unknown sample rejection reasons which in total contributed 14.1% of total samples rejected and the current study analysis did not include these 2 elements during data analysis. Lastly in their study, samples for children less 6 weeks of age were rejected while in the current study this is not one of the sample rejections reasons since SA guidelines allow sample collection from birth.

Hospitals were also found to have contributed a larger portion of total rejected HIV PCR samples than PHCs although hospitals collected 43.9% of the total HIV PCR samples collected by the District. Hospitals contributed 55.4% to total insufficient specimen, 77% to unsuitable sample and 65.1% to clerical error. The findings are however not consistent with those reported in other studies where the bulk of the rejected samples came from facilities with the highest number of patients presenting for EID testing (Inalegwu *et al*., 2016; Chiku *et al.*, 2019). In Chiku and colleagues study, HIV PCR samples collected at PHCs were five times more likely to be rejected (Chiku *et al*., 2019). The possible explanation for the different findings is that Inalegwu *et al.* study collected data during the time of the PMTCT program decentralization to PHCs and accelerated scale-up process where Community Health Extension Workers were part of HIV PCR sample collectors while in the current study, the HIV PCR samples were only collected by PNs at PHC facilities. The other possible explanation could be that in the current study District, the HIV programme inclusive of EID is comparatively getting more support (including trainings and mentorship) from Implementing Partners and the programme is more mature at PHC facilities than at hospitals since HIV patients remain in HIV care at PHCs, not at hospitals.

NHLS (2019), recommends use of both DBS and EDTA anticoagulated whole blood samples for HIV PCR testing in SA. However, DBS sample is preferred over EDTA anticoagulated whole blood samples for HIV PCR testing because it allows testing even in facilities with inadequate resources for collection, storage and transportation of blood samples (Inalegwu *et*

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al., 2016). In the current study, the unsuitable sample error codes (require EDTA sample, unsuitable clotted, unsuitable EDTA clotted unsuitable haemolyzed), observed only at hospitals (in table 3) indicated use of both HIV PCR sample types at hospitals which might have contributed to high sample rejection rates observed at hospitals where they have inadequate doctors to take HIV PCR samples.

The study showed Setsoto subdistrict to have the highest proportion (90.3%) of samples rejected due to insufficient specimen. Again, Setsoto subdistrict collected almost half of the samples collected by Dihlabeng subdistrict (see table 2), but they both have almost equal number of samples rejected due to insufficient specimen. This was an unexcepted finding which needs further investigation.

The preanalytical sample rejections observed in the TM district are associated with missed diagnostic opportunity for children infected with HIV, and thus compromise quality of care rendered to the HIV exposed children. These rejections highlight the need for innovative interventions such as POCT and eLAB in EID testing. Lastly, the study did not look at look at if children affected by preanalytical errors are tracked for HIV PCR retesting which is another area that needs studying.

5.2 Health facility and health care worker factors contributing to EID preanalytical errors.

The study found that the best performing facilities had better EID implementation levels compared to worst performing facilities. The worst performing facilities were observed to be on EID implementation level 2 and less which indicates inadequate implementation of EID quality assurance which can negatively impact quality of HIV PCR samples collected from these facilities. EID data used to select participating facilities was collected in 2018 and the facility assessment was conducted in 2020. This time difference might have allowed some facilities to maintain, lose or improve their EID implementation status.

The study found major gaps in EID supervision and support which were uniform at both worst and best performing facilities in the facility assessment. Overall median percentage score for supervision and support was 20.0% (IQR 8.0%-35.0%). In addition, supervision and support median percentage score for worst and best performing facilities were 10% (IQR 5.0%-25%) and 20% (IQR 10%-60%) respectively. The results were confirmed by the study finding from PNs interviews that majority (21) of participants were not receiving EID supervision and

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support (from either within the facility or externally). There was almost equal contribution of participants from both worst and best performing facilities.

Lack of EID supervision and support might be contributing to the HIV PCR preanalytical error due to sample rejection that are observed at TM facilities since staff support through onsite-based EID training and mentoring activities can prevent HIV PCR specimen rejection rates (Inalegwu *et al*., 2016; Sauramba *et al*., 2018). Deficiencies in supervision and support observed at the facilities may be a result of limited supervisory teams due to having one Coordinator responsible for the PMTCT programme for the whole district and not having clinic supervisors in TM district.

Lastly on supervision, the study found that there was no dedicated person at all facilities to review quality of DBS samples collected before being dispatched to the laboratory for testing. The checking could have prevented collection of suboptimal DBS sample collections and might have facilitated the recollection of another DBS sample before affected children were discharged from hospital.

Personnel training was another area which was found to be lacking in terms of available EID training records at facilities and the actual training of PNs collecting HIV PCR samples for EID. The study found an overall training median percentage score of 50% (IQR 50%-50%) which was similar for both worst and best performing facilities. In addition to this finding, staff interviews showed that 34 participants were trained on EID and two from the worst performing facility were not trained but they were collecting HIV PCR samples for HEIs. Lack of EID training together with other factors might be contributing to sample rejections, as insufficient training on HIV PCR test techniques among HCWs is documented to contribute to preanalytical errors (Cherutich *et al*., 2008; Coulibaly *et al*., 2014; Chiku *et al*., 2019).

It was also found that 62% of participants (almost equal number of participants from best and worst performing facilities) were not declared competent after EID training and 26 participants were due for EID refresher training. Lack of training seems to be a contributing factor to HIV PCR sample rejection at both facility types. Thirty-four participants could not remember the year they were trained but the finding from the 21 that could remember was, 7 from worst performing facilities received formal training and 9 from best performing received on the job training. This finding is inconsistent with the argument made by Smit *et al*. (2014), that in-service training cascading model is not effective since its quality seems to be poorer. From the study finding, it is difficult to determine whether on the job training improved HIV PCR sample

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rejection rates at best performing facilities or formal training was not improving HIV PCR sample rejection at worst performing facilities.

According to SA NDoH (2017b), all HIV PCR tests performed between birth and 6 weeks are regarded as birth HIV PCR. Again, the number of reported birth PCR tests done at delivering health facilities is often less than the number of live births from mothers living with HIV in TM district. HEIs presenting at PHC at 3 days PNC visit or 6 weeks visits are to be offered HIV PCR testing if they were not tested at birth. The study found that 71.9% of the PHC PNs reported to be collecting HIV PCR samples from 10 weeks and only 5 participants from best performing PHC facilities (not delivering) were collecting samples from birth. The finding indicates deviation from PMTCT guidelines which might have a negative impact on EID coverage and lead to repeat MDOs for infants who were not offered PCR testing at birth.

Regarding EID supplies, none of the participating facilities experienced EID supplies stockout despite 8 of them not complying with EID stock management in terms stock card availability and updating. This might have been a result of bundled EID commodities which according to Ghadrshenas *et al*. (2013), streamlines the supply chain and decreases the likelihood of stockouts and reappropriations.

The study demonstrated that there was no notable deviation from the HIV PCR test requisition process and timing of sample labelling that could result in clerical error; sample condition checking; sample preparation and transportation by participants from worst and best performing facilities. The finding was not expected as facilities were experiencing HIV PCR sample rejections attributable to labelling errors, incorrect sample types, and submission of insufficient and unsuitable samples for testing. This is because according to Mugauri *et al*. (2018), these preanalytical errors are due to preventable factors which reflect noncompliance with the minimum requirements of the SOP for HIV PCR sample collection. The finding could have been influenced by the fact that generally the sampling process is guided by the same SOPs when it comes to sample requisition, labelling and checking for testing suitability and participants could have applied the same knowledge when responding to questions specific to HIV PCR sample requisition, labelling and suitability checking since they were not observed when they perform reported tasks.

Despite paper-based HIV PCR results being made available to health facilities by NHLS and other means of getting HIV PCR results, 4 participants from worst performing facilities were not accessing HIV PCR results. Participants might not be accessing results because care and

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results follow-up of HEIs is done at PHC facilities after the mother-baby pair is discharged from delivering facilities (if it is not a PHC). Moreover, none of the participants reported to have experienced sample rejection within a month prior to study data collection. This means there is limited chance for corrective actions or QI interventions to improve sample rejections if HIV PCR sample collectors are not aware of the sample rejections.

It is documented that sample rejection rates can be significantly reduced by applying QI tools and continuous QI interventions that seek to identify and correct system defects (Inalegwu *et al.,* 2016). In the current study, all worst performing facilities were not having QI plans to address HIV PCR sample rejection rates. The study also discovered that 3 of the worst performing facilities were not following HIV PCR sample management prior to packaging and were not having a designated area or room for HIV PCR testing in which HIV PCR sample management SOPs are displayed. The findings demonstrate noncompliance to Integrated Chronic Disease Management (ICDM) recommendation that services including EID testing are to be provided at Maternal and Child Health patients stream or consultation room. The findings also suggest need for an EID quality assurance tool to identify systems defects affecting EID services. There are several important limitations to consider regarding the study.

5.3 Limitations of the study

The requested EID data set from NHLS excluded EID samples for children above 18 months of age yet the unsuitable age or out of range patient age for HIV PCR is one of the commonest errors in the TM district. This kind of error may be due to clerical error where HCWs working at delivering health facilities may mistakenly write mothers date of birth when requesting the HIV PCR test for the child. Again, the study focus was on missed opportunities for HIV diagnosis related to preanalytical errors and the analytical errors like invalid and indeterminate results were not considered during phase 1 analysis even though these errors were experienced by facilities. In addition, use of secondary data made it impossible to establish which sample type (DBS or EDTA anticoagulated whole blood) had more sample rejections as sample type was excluded during phase 1 data analysis due to missing data. Furthermore, phase 2 data collection happened immediately post the Covid-19 first surge during which health facilities headcounts dropped together with number of HIV PCR samples collected at participating facilities and as a result, there were fewer sample rejections experienced signifying a potential for a very low number of HCWs to share challenges with HIV PCR sample collection. Additionally, none of the HCWs reported to have had sample rejections even at health facilities

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which had HIV PCR sample rejections and challenges HCWs were experiencing on HIV PCR sample collection could not be established. Moreover, there could have been social desirability bias in HCWs interviews since they may say that they do things ‘always’ in during sampling when actually they do just to please the interviewer. Lastly, phase 2 of the study focused on DBS sample type since participating facilities and HCWs were only collecting DBS samples for HIV PCR testing.

In terms of study design limitations, we cannot infer direct association between prevalence of preanalytical errors and explanatory health system variables because of the descriptive cross-sectional nature of the study. Another key limitation of the study was the long delay between phase 1 and 2 due to the preapproval processes and Covid-19 restrictions which delayed phase 2 data collection.

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CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

This chapter presents the conclusions drawn from the study results and recommendations for further research, policy, and practice**.**

6.1 Conclusions

Eight percent of samples did not yield a PCR result. The prevalence of preanalytical errors insufficient specimen, unsuitable sample and clerical error were 84.3%, 9.9% and 5.8% respectively. The prevalence of insufficient specimen was reasonably high in TM district. Hospitals contributed more (58.1%) preanalytical errors than PHC facilities, although they collected a smaller number of PCR samples than PHC facilities. Birth HIV PCR had more preanalytical errors.

Health facility and health care workers factors that might contribute to these preanalytical errors include deficiencies in EID supervision, personnel training, quality improvement tools such as using EID SOPs as well as quality improvement plans to address preanalytical errors.

6.2 Recommendations

6.2.1 Further research

The study has highlighted a number of areas for further research that could be pursued further by stakeholders involved in EID testing. Further studies could be conducted to establish which sample type (DBS or EDTA anticoagulated whole blood) have more sample rejections as the current study could not. Moreover, further studies might look at why hospitals have contributed more sample rejections than PHCs where more samples were collected and the factors that might contribute to high proportion of samples rejected due to insufficient specimen in Setsoto subdistrict. In addition, further research is needed to look at actions taken by health facilities to facilitate HIV PCR retesting of affected children after receiving rejected sample rejection notifications. Lastly, reported non-deviation from EID sampling procedure by professional nurses in facilities experiencing EID sample rejections is another area that would merit to be investigated further.

6.2.2 Policy and practice

- Allocate additional resources to training (especially training related to birth testing since that had the most errors), support and supervision of staff involved in HIV PCR sample collection. This will increase the pool of trained, competent, and supervised

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HIV PCR sample collectors which might subsequently decrease the number HIV PCR samples rejected due to preanalytical errors.

- Nominate facility based supervisory staff to assess the quality of EID samples before they are being sent to NHLS. This may prevent suboptimal EID samples being sent to NHLS only to be rejected. Again, the process may assist in identifying sample collectors needing support on HIV PCR sample collection which can prevent future collection of suboptimal samples.
- Include sample rejection rates in monthly data or performance review meetings at all levels of health care. This might raise alert and promote development of QIPs to address EID sample rejection rates.
- Strengthen Integrated Chronic Disease Management (ICDM) implementation at PHC facilities which recommends different streams for patient management if facility structure allows. This can be achieved by ensuring that there is designated consulting room for EID testing within maternal and child stream in which EID SOPs and commodities are placed. In addition, this will ensure that nurses relieving in Maternal and Child Health stream provide EID testing within the same stream.
- Introduce a quality assurance assessment tool for EID testing in addition to NHLS support to facilities with high numbers of HIV PCR results for action. The tool could assist in identifying preventable health facility factors that may lead to EID sample rejections. The current SPI RT assessment can be adopted and modified to suit EID testing evaluation.
- Expand eLAB project to include EID testing at both PHCs and hospitals. eLAB is the mhealth digital system currently designed to improve viral load monitoring through electronic patient result delivery from NHLS to health facilities. eLAB may improve EID results reading since it uses mobile devices to send alerts for VL results for action and can track if such results have been read by heath facilities.
- Consider national implementation of Point of Care Testing (POCT) for EID. POCT testing could improve EID sample rejections by cutting down the number of steps involved in conventional EID testing and overcoming errors associated with these steps.

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APPENDICES

Appendix A: Missed diagnostic opportunities within South African EID program 2010-2015

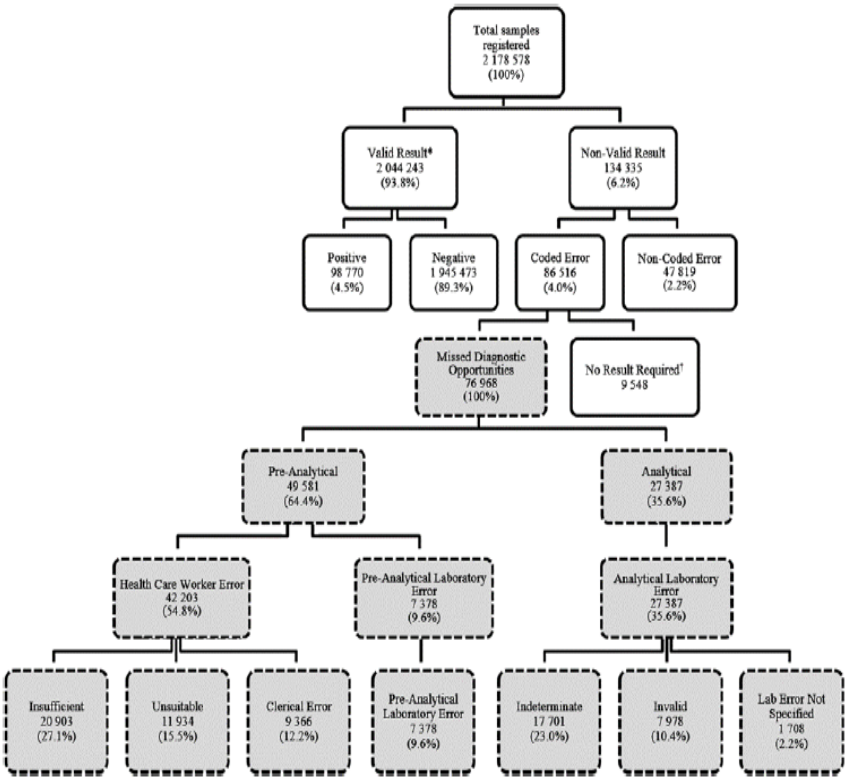

Figure 1: Diagram showing HIV PCR samples registered between 2010 and 2015 and the missed diagnostic opportunities adapted from Mazanderani *et al.* (2017)

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Appendix B: Semi-structured questionnaire for health facility staff

SEMI-STRUCTURED QUESTIONNAIRE FOR HEALTH FACILITY STAFF

Unique identifier

Date of Interview: ___ ___/___ ___/___ ___
Day/Month/Year (e.g. 22/01/2020)

Facility Name: _____ Researcher's Name _____

Participant has signed written consent. Yes No ☐ ☐

Introduction:
I would like to ask you about early infant diagnosis (EID). Please remember, you do not have to answer question you do not wish to answer. May we begin?

Instruction Please allocate participant a unique identifier using the last two letters of their first names followed by the last two letters of their surnames and the day of the month. E.g. Tom Smith interviewed on the 22nd, would be OMTH22. Please document the unique identifier on all pages		
Question number	**Questions**	**Responses**
1.	Gender	[1] Female [2] Male
2.	Qualification	1=MBChB 2=Nursing degree 3=Nursing diploma 4=Other Specify_____
3.	Years of experience	_____
4.	Main responsibility in the facility	_____
5.	Date of birth	_ _/_ _/ _ _ _ d d/ m m/y y y y
6.	From what age of children do you perform EID sample collection?	1=Birth 2=10 weeks 3=6 months 3=Between 7 and 18 months 4=Other (specify) _____
7.	Which EID sample type do you collect?	[1] DBS [2] Whole blood in EDTA tube
TRAINING		
8.	Have you received training on EID?	[1] Yes [2] No If yes skip to Q10, if no, attend Q9 only and the move to Q14
9.	How have been performing EID testing without being trained? _____ _____	
10.	What kind of training did you receive?	_____
11.	When were you trained?	_ _ _ _ y y y y
12.	Were you declared competent to collect EID samples?	[1] Yes [2] No
13.	Have you received a refresher training on EID within the last two years?	[1] Yes [2] No [3] N/a if trained within 2 yrs.

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SUPPORT AND SUPERVISION		
14.	If you have a question about EID, who do you ask? **More than 1 answer allowed and write the number in order of preference**	1=Facility/Unit manager 2=Another nurse in this facility 3=A nurse in another facility 4=The doctor 5=PMTCT Coordinator 6=District specialist 7=NHLS trainer 8=Guidelines 9=Other (specify) _____.
15.	How often do you receive support/supervision/mentoring on EID?	1=Daily 2=Weekly 3=Every 2 weeks 4=Monthly 5=Quarterly 6=Yearly 7=Never **(if chosen, skip to Q18)** 8=Not regularly, hard to tell when 9=Other (specify) _____.
16.	Who provides this support/supervision/mentoring on EID? **More than 1 answer allowed, write the numbers in order of preference**	1=Facility/Unit manager 2=Another nurse in this clinic 3=A nurse in another clinic 4=The doctor 5=Clinical Mentor 6=PMTCT Coordinator 7=District specialist 8=NHLS trainer 9=Other (specify) _____.
17.	If you need to be retrained on EID sample collection, are you being retrained during the support/supervision/mentoring visit?	[1] Yes [2] No
SUPPLIES		
18.	Where do you order additional EID supplies?	_____
19.	How do you order additional EID supplies?	_____ _____
20.	Have you had stock-outs of any EID consumables in the past month?	[1] Yes [2] No If yes, for how long (days) 1= gloves _____ 2= filter paper _____ 3= lancets _____ 4= packing envelopes _____ 5= desiccant packs _____ 6= humidity cards _____ 7= 0ther specify _____

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TEST REQUESITION

21. How often do you perform the following tasks?

	Never	Seldom	Often	Always
1. Compare the patient's names with the information on the test request form.	☐	☐	☐	☐
2. Use test requests form that somebody else has filled in.	☐	☐	☐	☐
3. Sign the test request form filled by somebody else.	☐	☐	☐	☐
4. Check the information on the test request form if somebody else has completed it for you. (N/A if 2 above is never).	☐	☐	☐	☐
5. Check that the test request form and EDTA tube/DBS card identification (barcode) numbers match, before delivery to the laboratory.	☐	☐	☐	☐

SAMPLE LABLING

22. When do you label the DBS card/EDTA test tube?

	Never	Seldom	Often	Always
1. Before I approach the patient	☐	☐	☐	☐
2. Alongside the patient before sampling	☐	☐	☐	☐
3. Alongside the patient after sampling	☐	☐	☐	☐
4. At a later occasion	☐	☐	☐	☐
5. Somebody else has labelled DBS card/EDTA tube in advance.	☐	☐	☐	☐
6. Somebody else labels the DBS card/EDTA tube after sampling	☐	☐	☐	☐

SAMPLE CONDITION

23. How often do you check EID sample condition?

	Never	Seldom	Often	Always
1. Adequate sample volume	☐	☐	☐	☐
2. Appropriate test request	☐	☐	☐	☐
3. EDTA tube/DBS card contamination	☐	☐	☐	☐

SAMPLE PREPARATION AND TRANSPORTATION

24.	Where do you store infant EID samples in the facility before they are packed?	1=Room in which they were taken 2=Facility pharmacy 3=Facility/Unit Manager's office 4=Facility's staff tearoom 5=Facility fridge 6=Other (specify) _____.
25.	Where do you store packed infant EID samples in the facility while awaiting collection?	1=Room in which they were taken 2=Facility pharmacy 3=Facility/Unit Manager's office 4=Facility's staff tearoom 5=Facility fridge 6=Other (specify) _____.
26.	How frequently are these EID samples sent to laboratory for testing? **Only one response**.	1=Daily 2=On certain standardized day/days of the week 3=Once a week (no standardized day, i.e. adhoc whenever there are enough specimens to send)

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		4=Ad hoc basis – sometimes once a week, sometimes fortnightly 5=Not sent to the lab 6=Other (specify) _____
27.	Is there a minimum number of EID samples you can send at a time?	1=Yes 2=No If No, skip to Q28. If yes, how many: _____
TEST RESULTS FEEDBACK		
28.	Do you access EID test results?	[1] Yes [2] No **(if No, end the interview)**
29.	How do you access EID test results? **(More than one response acceptable)**	1. Calling the laboratory and using the unique barcode on the infants RTHB [1] Yes [2] No 2. Calling the place of birth [1] Yes [2] No 3. It is delivered at the facility [1] Yes [2] No 4. SMS printer [1] Yes [2] No 5. Using NHLS LAB TRACK [1] Yes [2] No 6. Other (specify)_____
30.	Roughly how many samples have you had that were rejected (before being analyzed by laboratory) in the past 3 months?	_____ samples **(if none/not aware end the interview)**
31.	What were the reasons for EID sample rejection? _____ _____ **(If it was due sample lost during transit, laboratory error or analytical error end the interview).**	
32.	What challenges have you experienced in EID testing that might have contributed to sample rejections? _____ _____	
33.	How do you think each of the challenges can be addressed? _____ _____	

Thank you for taking time to answer these questions today. Please remember that your identity is and will be completely protected.

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Appendix C: Facility assessment checklist

FACILITY ASSESSMENT CHECK LIST

INSTRUCTIONS: Please complete this form with one designated staff member, designated by the Facility/Unit Manager.

NB: checklist to be completed by the Researcher and is based on seeing the tools/equipment/supplies available. It does not capture reported availability.

PART A This section collects characteristics of the facility being assessed	
SITE INFORMATION	
Today's date	_ _ / _ _ / _ _ _ _ (m m /d d /y y y y)
Researcher's name	
Facility name	
Facility type	☐PHC Clinic ☐CHC ☐District Hospital ☐Regional Hospital
Subdistrict	
Setting as defined by the Facility/Unit Manager	☐ Urban ☐ Rural ☐ Peri-urban

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Number of EID PCR testers facility has	_____ Nurses _____ Doctors _____ Other specify _____
Sample type utilized by facility for EID PCR testing	☐ DBS ☐ Whole blood in EDTA tube
Frequency of sending EID PCR samples to laboratory for testing	☐Daily ☐Twice a week ☐Once a week ☐Twice a month ☐Monthly ☐Other (Specify)_____
Laboratory testing facility EID samples	_____
Total number of EID PCR samples collected from HEI below 18 months of age. ***Use NHLS reports. Review previous 3 months and give total.***	_____/_____ samples collected/rejected (month 1) _____/_____ samples collected/rejected (month 2) _____/_____ samples collected/rejected (month 3) _____/_____ samples collected/rejected (Total)
Frequency of ordering EID PCR stock	☐ Daily ☐ Once a week ☐ Twice a week ☐ Twice a month ☐ Monthly ☐ Other (Specify)_____
Antenatal HIV Sentinel Surveillance (ANSUR) site	☐ Yes ☐ No

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PART B

Stepwise Process for improving the quality of EID HIV PCR testing. Please check **Yes, Partial or No**, where applicable. Indicate "**Yes**" only when all elements are satisfactorily present or not applicable. Provide comments for each "**Partial**" or **"No"** response.

Scoring: Yes=Complete and fully implemented = 2 points, **Partial** = Evidence of some elements in place = 1 point, No = No evidence = 0 point

1.0	**PERSONNEL**	**YES**	**PARTIAL**	**NO**	**COMMENTS**	**SCORE/2**
1.1	Have all testers received EID HIV PCR training? *Partial if yes but there no training records*					
1.0	**PERSONNEL Total:**					
2.0	**PHYSICAL FACILITY** **(Testing area/room or physical infrastructure)**					**SCORE/10**
2.1	Is there a designated room for EID HIV PCR testing? *Partial if the room is used for other things as well.*					

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2.2	Is the testing area clean for EID HIV PCR testing? *Clean- is everything sterile and disinfected not just things thrown away*					
2.3	Is the testing area organized for HIV PCR testing? *Organised-is everything needed for the testing there, accessible, and available*					
2.4	Is enough lighting available in the designated testing area? *Observe and record, do not ask*					
2.5	Are the DBS test kits kept in a temperature-controlled environment based on the manufacturer's instructions? *Area well ventilated and cool, shielded from direct sunlight.* ***Environment conditions + temperature=Yes. Partial if only one is met explain in comments. No if neither is met.***					

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2.0	**PHYSICAL FACILITY Total:**					
3.0	**EID SUPPLIES**	**YES**	**PARTIAL**	**NO**	**COMMENTS**	**SCORE/10**
3.1	Are HIV PCR test kits in stock today? *Ask to see the kits*					
3.2	Are all within the expiry date? *Ask to see the kits*					
3.3	Does facility have stock cards (or a similar system) to track supplies of PCR test kits?.....					
3.4	Are stock cards updated on a transactional basis?					
3.5	Are the EID supplies distributed as standardized bundles to this site's testing points? *Standard bundle for HIV PCR DBS kit. Roche DBS bundle include a collection card, 2 alcohol swabs, gauze, and lancet*					

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3.0	**SUPPLIES Total:**					
4.0	**SAMPLE MANAGEMENT**	**YES**	**PARTIAL**	**NO**	**COMMENTS**	**SCORE/10**
4.1	Are SOPs in place for HIV PCR sample storage? *Only tick yes if seen*					
4.2	Are SOPs for sample storage followed?					
4.3	Are SOPs in place for evaluating PCR sample acceptability?					
4.4	Is facility notified (by laboratory) of rejected PCR samples if it has? *Check yes for N/A, where facility has never received HIV PCR sample rejections for the past year.*				If YES by: ☐ Phone ☐ Email ☐Others, specify _____	
4.5	Is quality improvement plan available to address HIV PCR sample rejections? *Partial if yes but there is no documentation. Check yes for N/A; where facilities did not have PCR sample rejections in the past 3 months.*					

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4.0	**SAMPLE MANAGEMENT Total:**					
5	**TESTING PHASE**	**YES**	**PARTIAL**	**NO**	**COMMENTS**	**SCORE/4**
5.1	Is Laboratory handbook available at testing point? *Check to see which year is being used*					
5.2	Are SOPs for HIV PCR sample collection available and posted? *Both conditions met=Yes* *Some/one condition(s) met=Partial* *Neither conditions met=No*					
5.0	**TESTING PHASE ..... Total**					
6	**SUPERVISION/SUPPORT**	**YES**	**PARTIAL**	**NO**	**COMMENTS**	**SCORE/10**
6.1	Does the person in charge/person responsible for the EID program at the testing facility review EID PCR samples before being dispatched to Laboratory?					

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6.2	Does the testing facility receive periodic EID supervisory visits? *Check supervisory documents*					
6.3	Is feedback provided during supervisory visit and documented? *Check the supervisory documents* *If no in 6.2, check no*					
6.4	Does facility receive Implementing Partners support on EID? *Check the documents- you can get* *documents from the Facility/Unit Managers.*				If yes, list them	
6.5	Does facility receive quality improvement (QI) support? *Check the documents- you can get* *documents from the Facility/Unit Managers.*				If yes, specify QI providers	
6.0	**SUPERVISION/SUPPORT Total**					
PART C: SUMMARY						
	Section	**Total possible score**	**Points given**	**Percentage**		

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1	PERSONNEL	2		
2	PHYSICAL FACILITY	10		
3	SUPPLIES	10		
4	SAMPLE MANAGEMENT	10		
5	TESTING PHASE	4		
6	SUPERVISION/SUPPORT	10		
Total score		46		

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Appendix D: NHLS data request and approval letter

NATIONAL HEALTH LABORATORY SERVICE

Academic Affairs and Research
Modderfontein Road, Sandringham, 2031
Tel: +27 (0)11 386 6142
Fax: +27 (0)11 386 6296
Email: babatyi.kgokong@nhls.ac.za
Web: www.nhls.ac.za

26 February 2020

Applicant: Refuoe Cecilia Bulara
Institution: University of Western Cape
Department: School of Public Health
Email: 3812911@myuwc.ac.za
Cell: 083 341 2560

Re: Approval to access National Health Laboratory Service (NHLS) Data

Your application to undertake a research project **"Missed opportunities for HIV in children below 18 months in Thabo Mofutsanyana District Free State Province"** using data from the NHLS database has been reviewed. This letter serves to advise that the application has been approved and the required data will be made available to you ***without patient names*** to conduct the proposed study as outlined in the submitted application. Submissions should be made annually on the AARMS system – https://aarms.nhls.ac.za.

Please note that approval is granted on your compliance with the NHLS conditions of service and that the study can only be undertaken provided that the following conditions have been met.

- Processes are discussed with the relevant NHLS departments (i.e. Information Management Unit and Operations Office) and are agreed upon.
- Confidentiality is maintained at participant and institutional level and there is no disclosure of personal information or confidential information as described by the NHLS policy.
- NHLS Data cannot be used to track patients as no pre-approval/consent is obtained from Patients.
- CDW form is to be completed for the request with clear indications of the data required.
- All data requested should be in accordance with the research protocol submitted and approved by the relevant Ethics Committee.
- Request for the inclusion of the NHLS as a source of data in the original protocol to be approved by Ethics as NHLS does not have a Human Research Ethics Committee.
- A final report of the research study and any published paper resulting from this study are submitted and addressed to the NHLS Academic Affairs and Research office and the NHLS has been acknowledged appropriately.

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. Any data related queries may be directed to NHLS Corporate Data Warehouse, contact number: 011 386 6074 email: zarina.sabat@nhls.ac.za

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research

http://etd.uwc.ac.za/

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel: (011) 386-6125/6/7/9 Fax: (011) 386-6308 email: helpdesk6@nhls.ac.za

ACCESS TO DATA FROM CDW FMI0069

Each application will be approved or rejected subject to the ability to extract this data and the availability of the data, and subject to the intended usage of the requested data. Applications that are incomplete and/or do not contain supporting documentation, will be rejected.

APPLICANT DETAILS			
Applicant's Name and Surname	Refuoe Cecilia Bulara	**Telephone Number**	(+27)83 341 2560
Email Address	3812911@myuwc.ac.za	**Cell Phone Number**	(+27)83 341 2560
Business Role / Designation	Program Coordinator	**Laboratory/ Department/ Branch / Region or External Organisation**	Right to Care Free State
Supervisor Name	Prof Tanya Doherty	**Telephone Number**	(+27)21 9380693
Supervisor Designation	Chief Specialist Scientist : Health Sytsems Reserch Unit at SA Medical Resech Coucil	**Email Address**	Tanya.Doherty@mrc.ac.za

TERMS AND CONDITIONS

- **Data / Information is not to be used in contravention of Sections 14, 15, 16 and 17 of the National Health Act 61 of 2004 and the Promotions of Access to information Act 2 of 2000.**
- **The applicant undertakes to ensure that the data supplied to it by the NHLS is used ethically and solely for the purposes for which it is provided as detailed in this application, and further acknowledges that it shall remain liable for any breaches of this clause by the end user.**
- **If the purpose for the data requested in this application is for research, or if patient identity linked data is required, ethics approval and the full protocol must be attached to this application form. It is the responsibility of the applicant to ensure that their institutions' Human Ethics approval includes explicit authorisation to access the requested NHLS data.**
- **The applicant undertakes to store the NHLS data in a confidential manner by separating patient identifying details from laboratory data and storing the master list that links patient identifying details to study patient identifiers in a separate, secure location.**
- **The information is for the private use of the applicant only, unless further approval is obtained from the NHLS. In the event of this, the applicant shall give due credit, including affiliation, of the participation of the NHLS in any such publications or presentations.**
- **The applicant undertakes to provide the Manager: Academic Affairs and Research at the NHLS with a copy of any report, presentation or publication emanating from the use of this data, if for research purposes.**

ACCEPTANCE OF CONDITIONS

By signing this document we accept the conditions as stated above.

Applicant Signature		**Date**	**16/01/20**

http://etd.uwc.ac.za/

NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel: (011) 386-6125/6/7/9 Fax: (011) 386-6308 email: helpdesk6@nhls.ac.za

ACCESS TO DATA FROM CDW FMI0069

Supervisor Signature		Date	16/01/20

Note: All fields in this section must be completed

DATA REQUEST DETAILS					
Request Type (Tick)	☒ New ☐ Modify (Provide previous request details)	**Data Format (Tick)**	☒ Excel ☐ CSV	**Data Delivery (Tick)**	☐ CD / DVD ☒ Email
Frequency of Extract (Tick)	☒ Once ☐ Repeat	**If Repeat, specify frequency (Tick)**	☐ Daily ☐ Weekly		☐ Monthly ☐ Annually

DESCRIPTION OF REQUIRED DATA EXTRACT	
Details of Data required	**De-identified Database of all HIV PCR samples collected between 1st January 2018 and 31st December 2018.**
Region (For data extract, e.g. Province, Laboratory or Facility etc)	**Thabo Mofutsanayana District**
Date range of extract (Period for which data is required)	**1st January 2018 to 31st Decebember 2018**
Fields required (e.g. Patient name, Date of Birth, etc)	**District, Subdistrict, Facility, Ward, Sex, Patient age, Sex, Date HIV PCR sample collected, Sample type (DBS or EDTA), Date PCR sample reviewed, HIV PCR result. If HIV PCR test is not resulted (e.g. is not negative, positive or indeterminate), please provide rejection reason.**

ADDITIONAL INFORMATION
Definitions of Test results Text for rejected samples. For example the diffrence between there test result text "unsuit clotted" and "unsuit EDTA clotted" appearing on MDOs report.

DESCRIPTION OF INTENDED USE OF DATA EXTRACT (e.g. research, epidemiology study, cost analysis of service, drug effectiveness, disease surveillance
Research

LIST WHO WILL HAVE ACCESS TO THIS DATA
Refuoe Bulara , Prof Tanya Doherty and Dr Witness Chirinda (Co- Supervisor).

In the event of a dispute concerning this document, the electronic version stored on Q-Pulse will be deemed to be the correct version

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NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel: (011) 386-6125/6/7/9 Fax: (011) 386-6308 email: helpdesk6@nhls.ac.za

ACCESS TO DATA FROM CDW FMI0069

PROJECT NAME AND REGISTRATION NUMBER (If data is required for a registered research project. Please attach the Ethics Approval and full Protocol.)
Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province. Reference number BM19/9/8

NHLS RESPONSIBILITIES
The NHLS will: • Ascertain if it is possible to extract the required data. • Register the application and issue a registration number. • Only release the requested data to the applicant whose name is specified on this application form.
After this application has been completed and approved, please raise a service request with the NHLS IT Service Desk (Contact Number: (011) 386-6125/6/7/9): • Send an email to helpdesk6@nhls.ac.za, • Scan this application form and attach it to the email, or fax it to (011) 386-6308.

FOR OFFICE USE					
APPROVAL BY RESEARCH OFFICE (Research data requests only)					
Check List	☐ Signed by Supervisor ☐ Ethics Approval attached ☐ Research Protocol attached				
EXECUTIVE Manager: Academic Affairs and Research + DA	PROF M.P. MLISANA	Signature		Date	27/02/2020
CEO APPROVAL (Only for non-research data requests requiring sensitive data)					
Chief Executive Officer	Dr K.S. Chetty	Signature		Date	2/3/2020
CDW APPROVAL					
CDW Manager		Signature		Date	/ /20

APPROVED

Name: Dr Babatyl Malope-Kgokong

National Manager: Academic Affairs and Research

Date: 27/02/20 Sign: .....

In the event of a dispute concerning this document, the electronic version stored on Q-Pulse will be deemed to be the correct version

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NATIONAL HEALTH LABORATORY SERVICE HELPDESK
Tel: (011) 386-6125/6/7/9 Fax: (011) 386-6308 email: helpdesk6@nhls.ac.za

ACCESS TO DATA FROM CDW FMI0069

In the event of a dispute concerning this document, the electronic version stored on Q-Pulse will be deemed to be the correct version

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Appendix E: UWC ethical clearance

UNIVERSITY of the WESTERN CAPE

OFFICE OF THE DIRECTOR: RESEARCH
RESEARCH AND INNOVATION DIVISION

Private Bag X17, Bellville 7535
South Africa
T: +27 21 959 4111/2948
F: +27 21 959 3170
E: research-ethics@uwc.ac.za
www.uwc.ac.za

19 November 2019

Ms RC Bulara
School of Public Health
Faculty of Community Health Sciences

Ethics Reference Number: BM19/9/8

Project Title: Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province.

Approval Period: 31 October 2019 – 31 October 2020

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

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Appendix F: Free State Department of Health ethical clearance

health
Department of Health
FREE STATE PROVINCE

20 January 2020

Ms. RC Bulara
School of Public Health
Faculy of Community Health Science
UWC

Dear Ms RC Bulara

Subject: Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province.

- Please ensure that you read the whole document, Permission is hereby granted for the above – mentioned research on the following conditions:
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of **Thabo Mofutsanyana District Facilities** nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of the University of the Western Cape and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of the University of the Western Cape and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** sebeelats@fshealth.gov.za / makenamr@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- **Please discuss your study with Institution Manager on commencement for logistical arrangements see 2nd page for contact details.**
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- **As part of feedback you will be required to present your study findings/results at the Free State Provincial health research day**

Trust you find the above in order.

Kind Regards

Dr D Motau
HEAD: HEALTH
Date: 20/01/2020

Head : Health
PO Box 227, Bloemfotein, 9300
4th Floor, Executive Suite, Bophelo House, cnr Maitland and, Harvey Road, Bloemfotein
Tel: (051) 408 1646 Fax: (051) 408 1556 e-mail:khusemj@fshealth.gov.za@fshealth.gov.za/chikobvup@fshealth.gov.za
www.fs.gov.za

http://etd.uwc.ac.za/

health
Department of Health
FREE STATE PROVINCE

20 January 2020

Ms. RC Bulara
School of Public Health
UWC

Dear Ms. RC Bulara

Subject: Missed opportunities for HIV diagnosis in children below 18 Months in Thabo Mofutsanyana District , Free State.

Please find below the contact details of the District Managers for Thabo Mofutsanyane District for logistical arrangements.

Thabo Mofutsanyane District		
Name: Mr. DS Ntsutle **Email**: ntsutleds@fshealth.gov.za **Tel**: 058 713 0232	**PA**: Me Zodwa **Email**: mosiapn@fshealth.gov.za	
Bakenpark Clinic Bethlehem Clinic Blue Gum Bush Clinic Bohlokong Clinic Boiketlo Clinic Boitumelo (Senekal) Clinic Bolata Clinic Bophelong (Vrede) Clinic Clocolan Clinic Dihlabeng Hospital Dinkweng Clinic Elizabeth Ross Hospital Eva Mota Clinic Fateng Tse Ntsho Clinic Harrismith Clinic Highway Junction Clinic Hlohlolwane Clinic Intabazwe Clinic Itemoheng Hospital Itumeleng (Clarens) Clinic John Daniel Newberry Hospital Kokelong Clinic Kopanong Clinic Leratswana Clinic Lesedi Clinic Leseding Clinic	Lindley Clinic Ma-haig Clinic Makeneng Clinic Makhalaneng Clinic Makoane Clinic Malesaona Clinic Mamello CHC Marakong Clinic Masebabatso Clinic Matsieng Clinic Matwabeng Clinic Memel Clinic Meqheleng Clinic Mofumahadi Manapo Mopeli Hospital Monontsha Clinic Mphatlalatsane Clinic Mphohadi Clinic Namahali Clinic Nketoana Hospital Nothnagel Clinic Nthabiseng Clinic Paballong Clinic Paul Roux Clinic Petsana Clinic Phuthuloha Hospital	Phekolong Hospital Phomolong (Ficksburg) Clinic Phumelela Hospital Phuthaditjhaba Clinic Qholaqhwe Clinic Rearabetswe Clinic Reitumetse Clinic Reitz Clinic Relebohile (Rosendal) Clinic Riverside Clinic Sekamotho Mota Clinic Senekal Clinic Soetwater Clinic Tebang Clinic Thaba Bosiu Clinic Thabang Clinic Thebe Hospital Thusa Bophelo Clinic Tina Moloi Clinic Tseki Clinic Tshiame B Clinic Tshirela Clinic Vrede Clinic Zamani Clinic

Trust you find the above in order.

Kind Regards

Head : Health
PO Box 227, Bloemfotein, 9300
4th Floor, Executive Suite, Bophelo House, cnr Maitland and, Harvey Road, Bloemfotein
Tel: (051) 408 1646 Fax: (051) 408 1556 e-mail khusemi@fshealth.gov.za/chikobvup@fshealth.gov.za
www.fs.gov.za

http://etd.uwc.ac.za/

Appendix G: Thabo Mofutsanyana District Health Manager study approval letter

health
Department of Health
FREE STATE PROVINCE

Dear Ms R. Bulara

PERMISSION TO CONDUCT RESEARCH IN THE THABO MOFUTSANYANA DISTRICT HEALTH FACILITIES

I have received your request communicating your intention to collect data through Health Worker interviews at the Health Facilities in Thabo Mofutsanyana District. Permission is hereby granted by the Free State Head of Department and the ethics approval granted University of the Western Cape Health Science Research Ethics Committee.

You are hereby released to arrange visit(s) with the respective Facility Managers and CEOs at the following Health Facilities:

- Paballong Clinic
- Elizabeth Ross District Hospital
- Leseding Clinic
- Thaba Bosiu Clinic
- Reitumetse Clinic
- Bohlokong Clinic
- Bethlehem Clinic
- Tseki Clinic
- Eve Mota Clinic
- Leratswana Clinic

Please ensure that the recruitment of the participant respects Patient Rights and does not interfere with other Health Care obligations of the participants.

I reiterate that you are encouraged to present your study findings at the Free State Department of Health Research Day.

Yours Sincerely

D.S Ntsutle
District Director
Thabo Mofutsanyana Health District

Ntsutle D.S
District Director
Thabo Mofutsanyana
Health District

Date: 12 · 08 · 2010

Mr DS Ntsutle
District Director
Thabo Mofutsanyana Health District
Tel: 058 713 0232
E-Mail: ntsutleds@fshealth.gov.za

www.fs.gov.za

http://etd.uwc.ac.za/

Appendix H: Health Facility/Unit Manager information sheet

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21 959 2809 Fax: 27 21 959 2872

E-mail: soph-comm@uwc.ac.za

INFORMATION SHEET: HEALTH FACILITY/UNIT MANAGER

Project Title: Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province.

What is this study about?

This is a research project being conducted by Refuoe Cecilia Bulara, Prof Tanya Doherty and Dr Witness Chirinda at the University of the Western Cape. We are inviting your facility to participate in this research project because it is a public health facility collecting HIV PCR samples for children below 18 months born from mothers living with HIV and it has been enrolled under the study. The purpose of this research project is to describe the impact of three types of preanalytical errors (errors that cause the specimens to be rejected before laboratory analysis) in HIV PCR testing and the contributing factors in the Thabo Mofutsanyana district.

What will I be asked to do if I agree to facility participation?

You will be asked to sign the consent form as a prerequisite for facility participation in the study. The researcher will double check with you that you fully understand the research, your role as FM in the study and any implication the research has for your facility. You will then be required to nominate the staff member who will assist researcher in completing the facility assessment checklist. The estimated time to complete the checklist is 30-45 minutes. The checklist is to determine if the required supplies and physical infrastructure for HIV PCR testing are present at your facility. Kindly note that the checklist will not capture reported availability, but it is based on seeing the tools, equipment and supplies available to support EID in your facility.

http://etd.uwc.ac.za/

Would my facility participation in this study be kept confidential?

To ensure confidentiality in the study, researchers will keep research information in locked instruments which are accessible to researchers only. Instruments like computers will be password protected.

If we write a report or article about this research project, your facility identity will be protected since we are committed to extend confidentiality beyond data collection phase of the study.

What are the risks of this research?

Based on the nature of the study, researchers are not aware of anticipated risk that may result from your facility participation in the study. If there is risk involved, an appropriate referral will be made to a suitable professional for further assistance or intervention.

What are the benefits of this research?

This research is not designed to help your individual facility, but the results may help the district to learn more about missed opportunities for HIV diagnosis in children below 18 months of age in the district (Thabo Mofutsanyana) and describe factors contributing to HIV PCR samples that are rejected before laboratory analysis. We hope that, in the future, other people might benefit from this study through improved understanding of HIV PCR sample rejection magnitude and the contributing factors.

Findings from the study are anticipated to inform district quality improvement plans on managing HIV PCR rejection rates which is hoped to ultimately improve HIV care offered to children born from mothers living with HIV.

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Does my facility have to be in this research, and may I stop its participation at any time?

Your facility participation in this research is completely voluntary. You may choose not to give permission to conduct the study in your facility. If you have granted permission to conducting study in your facility, you may withdraw the decision at any time without any consequences.

What if I have questions?

This research is being conducted by Refuoe Bulara (principal investigator) from School of Public Health at the University of the Western Cape. If you have any questions about the research study itself, please contact Refuoe Cecilia Bulara at: 55 Prinsloo Street Ladybrand 9745, +278 33412560, 3812911@myuwc.ac.za. Should you have any questions regarding this

http://etd.uwc.ac.za/

study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Prof Uta Lehmann

Head of Department: School of Public Health

University of the Western Cape

Private Bag X17

Bellville 7535

ulehmann@uwc.ac.za

Prof Anthea Rhoda

Dean: Faculty of Community and Health Sciences

University of the Western Cape

Private Bag X17

Bellville 7535

chs-deansoffice@uwc.ac.za

UNIVERSITY of the
WESTERN CAPE

This research has been approved by the University of the Western Cape's Biomedical Research Ethics Committee.

Biomedical Research Ethics Committee

University of the Western Cape

Private Bag X17

Bellville

7535

Tel: 021 959 4111

http://etd.uwc.ac.za/

e-mail: research-ethics@uwc.ac.za

REFERENCE NUMBER: BM19/9/8

http://etd.uwc.ac.za/

Appendix I: Health Care Worker information sheet

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Tel: +27 21 959 2809 Fax: 27 21 959 2872

E-mail: soph-comm@uwc.ac.za

INFORMATION SHEET: HEALTH CARE WORKER

Project Title: Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province.

What is this study about?

This is a research project being conducted by Refuoe Cecilia Bulara, Prof Tanya Doherty and Dr Witness Chirinda at the University of the Western Cape. We are inviting you to participate in this research project because you are health care worker involved in collecting HIV PCR samples for children below 18 months born from mothers living with HIV, in a public health facility enrolled under the study. The purpose of this research project is to describe the impact of three types of preanalytical errors (errors that cause the specimens to be rejected before laboratory analysis) in HIV PCR testing and the contributing factors in the Thabo Mofutsanyana district.

What will I be asked to do if I agree to participate?

You will be asked to sign the consent form as a prerequisite for your participation in the study taking placing at your health facility. The researcher will double check with you that you fully understand the research, your role in the study and any implication the research has for you. You will then be interviewed using a questionnaire designed to collect information on your demographic data, training on HIV PCR testing, EID supervision, PCR supplies, PCR sample collection processes, PCR results management including feedback on preanalytical sample rejection and challenges HCWs are experiencing on HIV PCR sample collection. The estimated time to complete the questionnaire is 30-45 minutes.

http://etd.uwc.ac.za/

Would my participation in this study be kept confidential?

The researchers undertake to protect your identity and the nature of your contribution. To ensure your anonymity, researchers will use code identifiers on the questionnaires and the linking information will stored separately from the completed questionnaires. Moreover, research data will be kept under lock and will only be accessible to researchers.

To ensure your confidentiality, researchers will keep research information in locked instruments which are accessible to researchers only. Instruments like computers will be password protected.

If we write a report or article about this research project, your identity will be protected since we are committed to extend confidentiality beyond data collection phase of the study.

What are the risks of this research?

Based on the nature of the study, researchers are not aware of anticipated physical, financial, and legal risk that may result from participating in the study. However, there may be some emotional and psychological risks from participating in this research study because all human interactions and talking about self or others carry some amount of risks. We will nevertheless minimise such risks and act promptly to assist you if you experience any discomfort, psychological or otherwise during the process of your participation in this study. Where necessary, an appropriate referral will be made to a suitable professional for further assistance or intervention.

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What are the benefits of this research?

This research is not designed to help you personally, but the results may help the district to learn more about missed opportunities for HIV diagnosis in children below 18 months of age in the district (Thabo Mofutsanyana) and describe factors contributing to HIV PCR samples that are rejected before laboratory analysis. We hope that, in the future, other people might benefit from this study through improved understanding of HIV PCR sample rejection magnitude and the contributing factors.

Findings from the study are anticipated to inform district quality improvement plans on managing HIV PCR rejection rates which is hoped to ultimately improve HIV care offered to children born from mothers living with HIV.

http://etd.uwc.ac.za/

Do I have to be in this research, and may I stop participating at any time?

Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time without any consequences.

What if I have questions?

This research is being conducted by Refuoe Bulara (principal investigator) from School of Public Health at the University of the Western Cape. If you have any questions about the research study itself, please contact Refuoe Cecilia Bulara at: 55 Prinsloo Street Ladybrand 9745, +278 33412560, 3812911@myuwc.ac.za. Should you have any questions regarding this study and your rights as a research participant or if you wish to report any problems you have experienced related to the study, please contact:

Prof Uta Lehmann

Head of Department: School of Public Health

University of the Western Cape

Private Bag X17

Bellville 7535

ulehmann@uwc.ac.za

Prof Anthea Rhoda

Dean: Faculty of Community and Health Sciences

University of the Western Cape

Private Bag X17

Bellville 7535

chs-deansoffice@uwc.ac.za

This research has been approved by the University of the Western Cape's Biomedical Research Ethics Committee.

UNIVERSITY of the WESTERN CAPE

http://etd.uwc.ac.za/

Biomedical Research Ethics Committee

University of the Western Cape

Private Bag X17

Bellville

7535

Tel: 021 959 4111

e-mail: research-ethics@uwc.ac.za

REFERENCE NUMBER: BM19/9/8

http://etd.uwc.ac.za/

Appendix J: Facility/Unit Manager consent form

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535,

South Africa*Tel: +27 21-959 2809, Fax: 27 21-959 2872*

E-mail: soph-comm@uwc.ac.za

CONSENT FORM: HEALTH FACILITY/UNIT MANAGER

Title of Research Project: Missed opportunities for HIV diagnosis in children below 18months in Thabo Mofutsanyana District, Free State Province.

The study has been described to me in language that I understand. My questions about the study have been answered. I understand what facility participation will involve, and I agree to have facility assessed and the decision is out of free will. I understand that facility identity will not be disclosed in the study report. I understand that facility may be withdrawn from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.

Facility/Unit Manager's name……....

Facility/Unit Manager's signature…….

Date……

Biomedical Research Ethics Committee

University of the Western Cape

Private Bag X17.....

Bellville

7535

Tel: 021 959 4111

E-mail: research-ethics@uwc.ac.za

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Appendix K: Health Care Worker consent form

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CONSENT FORM: HEALTH CARE WORKER

Title of Research Project: Missed opportunities for HIV diagnosis in children below 18 months in Thabo Mofutsanyana District, Free State Province.

The study has been described to me in language that I understand. My questions about the study have been answered. I understand what my participation will involve, and I agree to participate of my own choice and free will. I understand that my identity will not be disclosed to anyone. I understand that I may withdraw from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.

Participant's name…….……

Participant's signature…….

Date……...

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University of the Western Cape

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