

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



LSHTM Research Online

Gumede, S; (2019) Evaluating Implementation of revised (post 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using Routinely Collected Data in Zambia. PhD (research paper style) thesis, London School of Hygiene & Tropical Medicine. DOI: <https://doi.org/10.17037/PUBS.04652894>

Downloaded from: <http://researchonline.lshtm.ac.uk/4652894/>

DOI: <https://doi.org/10.17037/PUBS.04652894>

Usage Guidelines:

Please refer to usage guidelines at <https://researchonline.lshtm.ac.uk/policies.html> or alternatively contact researchonline@lshtm.ac.uk.

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

<https://researchonline.lshtm.ac.uk>

LONDON
SCHOOL *of*
HYGIENE
& TROPICAL
MEDICINE



**Evaluating Implementation of revised (post 2010)
World Health Organisation Guidelines on Prevention
of Mother to Child Transmission of HIV using
Routinely Collected Data in Zambia.**

SEHLULEKILE GUMEDE

**Thesis submitted in accordance with the requirements
for the degree of Doctor of Philosophy of the
University of London
December 2018**

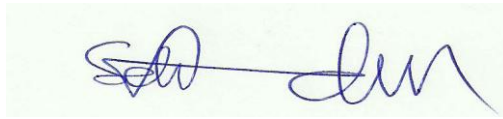
**Faculty of Epidemiology and Population Health
Department of Population Health**

The work contained in this thesis was supported by a project
funded from Bill and Melinda Gates Foundation

Declaration of work

I, Sehlulekile Gumede-Moyo confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature:

A handwritten signature in blue ink, appearing to read 'Sehlulekile Gumede-Moyo', is displayed on a light green rectangular background.

Date: 6 December 2018

Abstract

The Joint United Nations Program on HIV/AIDS (UNAIDS) over the past two decades has documented the heavy burden and impact of HIV on mothers and infants living in resource-limited settings. The sub-Saharan Africa (SSA) region still faces a challenge of significant numbers of pregnant women who acquire HIV infection during pregnancy or postpartum but who are not diagnosed and offered antiretroviral medicines. The achievement of the UNAIDS goal relies on a successful implementation of a set of prevention of mother-to-child transmission (PMTCT) of HIV interventions called the PMTCT cascade. The goal of elimination of new paediatric infections has not been met, so there is a need to investigate why some programs are not effective. Routinely collected clinic data can provide much needed information on the prevalence of HIV among pregnant women and the uptake of services for PMTCT of HIV. In Zambia there is a substantial amount of data that has been collected through the SmartCare electronic health record system over the years, but the database has never been used to analyse the implementation of PMTCT programs.

A mixed method study design was used which included a systematic review of literature, quantitative and qualitative methods. A systematic review of literature was conducted to identify, evaluate and summarise the findings from analysis of quantitative retrospective and prospective cohort studies that utilised routinely collected data with a focus on provision and utilisation of post 2010 PMTCT services in SSA. The quantitative analysis of SmartCare routinely collected data provided an overview of PMTCT coverage and the performance of early infant diagnosis (EID) services. Qualitative data was collected using in-depth interviews, observations and focus groups discussions (FGD) to understand the implementation procedures of SmartCare.

The findings from the systematic review of literature showed a decrease in the mother to child transmission (MTCT) rate but poor quality routinely collected data. The quantitative analysis of 104, 155 pregnant women seeking antenatal care (ANC) services in 886 health facilities indicated an increase from 2010 to 2015 in the proportion of HIV- infected women who were already on treatment. The analysis of data comprising 32, 593 HIV-infected infants born in the pre (2006-2009) and post (2010-2016) Option B+ periods revealed that there has been progress in the EID program implementation. The results from the two quantitative studies were characterised by missing data which introduced bias and affected the external validity of the findings. The findings from SmartCare data analysis were triangulated with the Health

Management Information System (HMIS), which further confirmed the conclusion drawn. The SmartCare database has structural challenges which can be traced to its development and in addition it has faced a lot of implementation challenges which include funding gaps, lack of feedback from the system and the absence of uniform data collection and verification procedures.

The thesis is the first study to have attempted to evaluate the implementation of PMTCT guidelines using routinely collected data from the SmartCare electronic health record (EHR) system database. Recommendations arising from the thesis include upgrading of SmartCare into a networked Open Medical Record System. The Zambia MoH with its partners could also implement a SmartCare performance-based financing initiative in order to improve the implementation of EHR system. Further studies are needed to investigate the impact of implementing PMTCT guidelines particularly on the retention in care and adherence to treatment and EID.

Acknowledgements

This PhD has been a life changing experience. I am still amazed and grateful to the Almighty God for bringing all things together. It all worked according to His plan. I have been privileged to work with diverse and wonderful characters from whom I have been transformed academically and socially. Above all, I have rediscovered myself, grown personally, learnt to be patient, reach out for help, and exercise self-discipline.

I have been blessed with incredible supervisors, who made this journey a very worthwhile ride by giving me an opportunity to learn from them and explore my research ideas.

Professor Suzanne Filteau, I am deeply appreciative of your support and your meticulous standards. Your consistent constructive reviews in shaping this thesis have been invaluable.

I have learnt from the best and very grateful. Jim Todd, thank you for enabling funding of my studies by the Bill and Melinda Gates Foundation. I feel incredibly privileged to have been part of the SEARCH team. You have given me an exposure to a world of Digital Health Informatics, which I taken a keen interest in.

I am grateful to Paul Mee for being a wonderful member of my advisory committee, for his statistical advice, and for providing constructive feedback. Ab Schaap, thank you for the time you spent understanding the SmartCare data, assistance in cleaning it and excellent statistical support. Virginia Bond I am grateful for imparting me with your qualitative data management skills. Jasleen Singh, you were a great student within a student.

This work would not have been possible without the support of the Ministry of Health ICT, Strategic Information and Monitoring and Evaluation departments. I specifically acknowledge Dr Crispin Moyo for grasping my research ideas and Liswaniso Liswaniso for his assistance in data extraction which was mainly outside his day to day duties- May God Bless you! To the secretaries of the directors under the Ministry of Health departments who always welcomed me with warm hearts and channelled all my requests, I am truly grateful.

I am greatly indebted to the SmartCare Implementing partners for giving an opportunity to learn from their experience and their valuable time.

To my wonderful siblings, thank you for cheering me on. You are such a blessing and I always consider myself lucky to have been born among you.

My sincere gratitude goes to my dear parents who laid a good education foundation and gave me opportunities that they never had. You worked so hard and sacrificed so much to give me the best for my education. I am proud to be your daughter!

This work is dedicated to my lovely family – Nkosilathi, Fezile Jessica and Zoleka Joanna Moyo. You are my source of pride, strength and resilience. Thank you for letting me be me and being part of this work. I know I must have been boring with my study demands, but you put up with me. I love you unreservedly.

Table of Contents

Declaration of work	2
Abstract.....	3
Acknowledgements.....	5
Table of Contents.....	7
Table of Figures and Tables.....	12
LIST OF ABBREVIATIONS.....	13
Chapter 1: Introduction.....	15
1.1 Rationale of the Study.....	15
1.2 Study Aim and Objectives	16
1.4 Conceptualisation and Disciplinary Approach	18
1.5 Role of the Candidate.....	19
Chapter 2: Background	21
2.1 Global Commitment to eliminate new paediatric HIV infections	21
2.2 Timing of mother to child transmission.....	22
2.3. Origins of PMTCT.....	23
2.4 post 2010 World Health Organisation PMTCT guidelines.....	25
2.4.1 Evolution of the PMTCT Cascade.....	28
2.4.2 Efficacy and Effectiveness of PMTCT Options	29
2.4.3 Cost effectiveness of PMTCT Options	30
2.5. Early Infant Diagnosis	31
2.6 Adherence to PMTCT options	32
2.7 Routinely collected data.....	32
2.8 Conclusion	34
Chapter 3: Overview of Methods.....	35
3.0 Introduction.....	35
3.1 Study location	35
3.1.1 PMTCT Program in Zambia	36
3.1.2 EID program in Zambia.....	37
3.2 Study Setting.....	38
3.2.1 The SEARCH Project	38

3.2.1 SmartCare Electronic Health System.....	38
3.3 Study design.....	41
3.3.1 Sequence of study design implementation.....	45
3.4 Quantitative Data Extraction and Cleaning	45
3.4.1 Data Access.....	45
3.4.2 ANC Data extraction.....	45
3.4.3 ANC Outcomes of Interest.....	46
3.4.4 ANC Data cleaning	46
3.4.5 EID Data extraction	47
3.4.6 EID data cleaning.....	47
3.5. Data management.....	47
3.6 Research ethics.....	47
Chapter 4: Systematic Literature Review Paper	49
4.1 Introduction.....	53
4.2 Methods.....	54
4.3 Summary of Results	55
4.4 Discussion	60
4.5 Conclusion	63
4.6 References.....	65
4.7 Table and Figure Legends.....	70
Chapter 5: Quantitative paper using ANC services data set	81
5.1 Introduction.....	85
5.2 Method	86
5.2.1 Study Design.....	86
5.2.2 Data Sources	86
5.2.3 Data Extraction	87
5.2.4 Statistical Analysis.....	88
5.2.5 Ethics.....	88
5.3 Results.....	88
5.3.1 Demographics	88
5.3.2 HIV test results	88
5.3.3 ART initiation	89
5.4 Discussion.....	89

5.5 Conclusion	92
5.6 References	94
Chapter 6: Quantitative paper using data set of HIV- infected infants	102
6.1 Background	106
6.2 Methods	106
6.2.1 Study design	106
6.2.2 Statistical methods	107
6.3 Results	107
6.3.1 Age of diagnosis	108
6.3.2 Time to ART initiation	108
6.4 Discussion	109
6.5 Conclusions	112
6.6 Declarations	114
6.7 References	115
6.8 Figure legends	120
Chapter 7: Qualitative paper on implementation challenges of the SmartCare electronic health record system	127
7.1 Introduction	131
7.2 Methods	132
7.2.1 Study design	132
7.2.2 Study Setting	132
7.2.3 Sampling	133
7.2.4 Data sources	134
7.2.5 Data Management and Analysis	135
7.3 Research ethics	135
7.4 Results	136
7.4.1 Database Development and Ownership	136
7.4.2 Funding and staffing	137
7.4.3 Data Collection Process	138
7.4.4 Health Facility setup	141
7.5 Discussion	142
7.6 Conclusion	144
7.7 References	146

Chapter 8: Health Management Information System (HMIS) Data	151
8.1 Introduction.....	151
8.2 Method.....	152
8.2.1 Data collection	152
8.2.2 Outcomes of interest:	152
8.3 Data Analysis	153
8.4 Results.....	153
8.4. 1 HMIS Data	153
8.4.2 SmartCare data.....	154
8.4.3 Cohort of HIV-infected women	155
8.4.2 ART Initiation.....	157
8.5 Discussion.....	158
8.6 Conclusion	159
Chapter 9: Discussion	160
9.1 Introduction.....	160
9.2 Summary of Findings.....	160
9.2.1 Decrease in MTCT rates in SSA, but poor quality routinely collected data.....	160
9.2.2 Increase in the proportion of HIV infected women already on treatment	162
9.2.3 Progress in the EID	164
9.2.4 Missing Data	165
9.3 Study limitations	167
9. 4 Conclusion	168
9.5 Recommendations.....	168
9.6 PhD Contribution.....	169
10. References.....	170
Appendices.....	183
Appendix 1: PhD Timelines.....	183
Appendix 2: Data Collection Flow Process	184
Appendix 3: LSHTM Ethical Clearance.....	185
Appendix 4: Ministry of Health Permission Letter.....	187
Appendix 5: Zambia SEARCH Project Ethical Clearance	188
Appendix 6: LSHTM SEARCH Project Ethical Clearance.....	189
Appendix 7: Qualitative Amendment Clearance	190

Appendix 8: FDG Written Informed Consent Waiver.....	191
Appendix 9: Informed Consent Forms	192
9.1 Informed Consent – In-depth Interviews	192
9.2 Informed Consent – Focus Group Discussions.....	195
Appendix 10: Chapter 5 Additional Results	198
10.1 Time to ART initiation per province in months.....	198
Appendix 11: Chapter 6 Additional Results	199
11.2 Univariable and multivariable analysis for age at HIV test.....	199
Appendix 11.2: Univariable and multivariable analysis for time from diagnosis to ART initiation	202
Appendix 12: Chapter 8 Additional Results	204
Appendix 12.1: HMIS data Summary	204
Appendix 12.2: Proportion of pregnant women across provinces.....	205
Appendix 13: Qualitative Questionnaires	206
13.1 Leadership Level Interview Guide.....	206
13.2. Operational Level Interview Guide	210
13.3 Data Entry Level Interview Guide.....	214
13.4 SmartCare Facility Managers Interview Guide	218
13.5 Focus Group Discussions Interview Guide - English.....	222
13.6 Bemba Focus Group Discussions Interview Guide	227
13.7 Nyanja Focus Group Discussions Interview Guide	232
13.8 Tonga Focus Group Discussions Interview Guide	237
Appendix 14: Published Papers	241
Appendix 14.1: Chapter 4.....	241
Appendix 14.2: Chapter 6.....	253

Table of Figures and Tables

Figure 2.1: Origins of PMTCT Guidelines	26
Figure 2.2: PMTCT Cascade	27
Table 3.1: Smart Care Module Groups	40
Figure 3.3: SmartCare Model Structure	40
Table 3.2: Overview of Objectives and Methods	44
Figure 4. 1: PRISMA Chart	71
Figure 4. 2: Comparison of MTCT Rate and PMTCT Option	72
Table 4.1: Uptake of PMTCT services and Infant outcomes.....	73
Table 4.2: Retention rate, Adherence and Magnitude of Loss to follow up (LTFU)	78
Table 5.1: Demographic Characteristics.....	97
Table 5.2: HIV test Result	98
Figure 5.1: Sample size data flow	99
Figure 5.2: Distribution of HIV positive women.....	100
Figure 5.3: Time to ART initiation.....	101
Table 6.1: Univariable analysis results for sex, season, province and year of birth.....	121
Figure 6.1: Mean age at HIV test and time from diagnosis to treatment initiation by year of birth.....	125
Figure 6.2: Percentage of HIV tests performed within 2 months of births by province in 2010 and 2015.....	126
Table 7.1: Breakdown of In-depth Interviews and Focus Group Discussions Participants...	148
Figure 7.1 - Breakdown of In-depth interviews key informants.....	149
Figure 7.2: SmartCare Data flow	149
Table 8.1: Number of pregnant women who attended ANC services using HMIS data for 2013-16	154
Table 8.2: Number of pregnant women who attended ANC services using SmartCare data.	155
Figure 8.1: Distribution of HIV-infected pregnant women (2013-16)	156
Figure 8.2: Distribution of HIV-infected pregnant women by province (2013-16)	157
Figure 8.3 Proportion of pregnant women on treatment (2013-16).....	158

LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal Care
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT	Zidovudine
CDC	Centre of Disease and Control
DBS	Dry Blood Spots
DHS	Demographic and Health Survey
EBF	Exclusive breastfeeding
EHR	Electronic Health Records
EID	Early infant diagnosis
FGD	Focus group discussions
HAART	Highly active antiretroviral therapy
HMIS	Health Management Information System
HIV	Human immunodeficiency virus
LSHTM	London School of Tropical Medicine and Hygiene
M& E	Monitoring and evaluation
MOH	Ministry of Health
MCH	Mother and child health
MRS	Medical Record System
MTCT	Mother-to-child transmission of HIV
NVP	Nevirapine
PEP	Post Exposure Prophylaxis
PEPFAR	United States President's Emergency Plan for AIDS Relief
PMTCT	Prevention of mother-to-child transmission of HIV
PTS	Patient tracking system
Sd-NVP	Single dose of Nevirapine
UNAIDS	Joint United Nations Program on AIDS
UNFPA	United Nations Population Found
UNICEF	United Nations International Children's Emergency Fund
ZDV	Zidovudine
VCT	Voluntary counselling and testing

WHO
3TC

World Health Organisation
Lamivudine

Chapter 1: Introduction

The Joint United Nations Program on HIV/AIDS (UNAIDS) over the past two decades has documented the heavy burden and impact of HIV on mothers and infants living in resource-limited settings. Globally, AIDS-related illnesses are the leading cause of death among 15–49-year-old females who are in their reproductive stage(1). The sub-Saharan Africa (SSA) region still faces a challenge of significant numbers of pregnant women who acquire HIV infection during pregnancy or postpartum but who are not diagnosed and offered antiretroviral medicines (2). The 2011 Global Plan towards the elimination of new HIV infections among children and keeping mothers alive aimed to reduce new childhood infections by 90% and HIV-related maternal death by 50% by 2015(3). The drive to eliminate mother-to-child transmission of HIV continues to yield results, with 93% of pregnant women living with HIV in the eastern and southern African region receiving antiretroviral prophylaxis in 2017(2). The target of elimination of new paediatric infections has not been met, so there is a need to investigate why some programs are not effective.

A commonly used surrogate marker for program effectiveness is program coverage. For prevention of mother-child-transmission of HIV (PMTCT) this would be the proportion of HIV-infected women and exposed infants in a population who access the different components of the PMTCT programmatic cascade(4). Estimates of coverage with PMTCT services among all HIV-infected pregnant women are vital to monitor progress relative to targets (5).

1.1 Rationale of the Study

Routinely collected clinic data can provide much needed information on the prevalence of HIV among pregnant women and the uptake of services for PMTCT of HIV(5). The use of routinely collected data can be timely and cost-efficient for decision making as data are already available for analysis (6). However in Zambia there is underutilization of routinely collected data in the HIV programs (7). An important component of this study is to investigate how routine program data can be used for assessing the outcome of a PMTCT program and by doing so, help adjust or fine-tune program implementation in an evidence-informed way.

1.2 Study Aim and Objectives

Zambia has been using ‘SmartCare’, an electronic health records (EHR) system for the routine collection of HIV data since 2004, and currently most facilities wishing to dispense ART are required to use this system. This means there is a substantial amount of data that has been collected over the years, but the database has never been used to analyse the effectiveness of implementing PMTCT programs. The study aimed to use routinely collected data to give an overview of the effectiveness of post 2010 World Health Organisation (WHO) PMTCT guidelines implementation and improve decision making in the Zambia health care system. The main objectives were:

1. To synthesise and evaluate the impact of implementing post-2010 WHO PMTCT guidelines on attainment of PMTCT targets in Sub-Saharan Africa through a systematic review of literature.
2. To describe trends in the coverage of PMTCT services from 2010 to 2015 using the SmartCare database of routine clinical information collected in Zambia.
3. To evaluate the performance of Zambia’s early infant diagnosis services using routinely collected data of HIV-infected infants in the SmartCare database for the period January 2006 to December 2016.
4. To use qualitative research to understand the implementation procedures of the SmartCare system.

1.3 Structure of the Thesis

This thesis is presented in nine chapters and follows the format of the “research paper style” dissertation. It is made up of manuscripts that have been published, or under review together with introductory, methods, triangulation and discussion chapters. Each of the four manuscripts, written in the format of the journals where they are published or intended to be published, establishes an independent chapter. Each chapter that contains a journal manuscript is prefaced by the required LSHTM cover sheet. The references for each of the published papers are presented at the end of each chapter whilst the references for the unpublished sections are presented at the end of the thesis. The outline of the chapters is as follows:

Chapter 1- Introduction

This chapter presents an overview of the research through a brief description of the knowledge gap, study rationale and the research aims and objectives. The roles of the candidate in the research are also outlined.

Chapter 2 – Background

The chapter gives the background of the global commitment to elimination of new paediatric infections through the use of antiretroviral therapy (ART). The post-2010 WHO PMTCT guidelines are also described. A particular focus was made to the literature from Sub-Saharan Africa and the 22 priority countries, including Zambia, with a high burden of HIV.

Chapter 3 – Methods

The chapter highlights the methods used for the study and includes overall study design, study location and the ethical considerations during the conduct of the study.

Chapter 4 - Systematic Literature Review Paper

The chapter is a published article in the Journal of Medicine and is titled **Implementation Effectiveness of Revised (post- 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using routinely collected Data in sub-Saharan Africa: A Systematic Literature Review.**

Chapter 5: Quantitative paper using antenatal services data set

This paper is an analysis of a dataset of pregnant woman seeking antenatal (ANC) services in health facilities using the SmartCare electronic health record system. The article is under review with the Frontiers in Public Health journal. The manuscript is titled: **Evidence that an Increasing Proportion of HIV-infected Pregnant Zambian Women attending ANC are already on ART: Analysis using Routinely Collected Data (2010-2015).**

Chapter 6: Quantitative paper using data set of HIV- infected infants

The manuscript outlines the progress of the early infant diagnosis program in Zambia using the data of HIV-infected infants extracted from the SmartCare database. The paper was first

authored by an MSc student, Jasleen Singh, who analysed the dataset under my supervision for her summer project. The manuscript was published by the BMC Public Health journal and is titled **Progress in the performance of HIV Early Infant Diagnosis services in Zambia using routinely collected data from 2006 to 2016.**

Chapter 7 – Qualitative paper on implementation challenges of the SmartCare electronic health record system

The chapter is a qualitative manuscript under review with the Health Informatics Journal. The paper presents the findings from investigating the implementing procedures of SmartCare and unearths the reasons for missing data in the two quantitative papers presented above. It is titled **A Qualitative Inquiry into Implementing an Electronic Health Record System (SmartCare) for Prevention of Mother-to-Child Transmission data in Zambia.**

Chapter 8: Health Management Information System (HMIS) Data

The purpose of this chapter was to present aggregate HMIS data and triangulate findings from the SmartCare database on outcomes similar to those discussed in Chapter 5.

Chapter 9 - Discussion

The implications of the study findings from the four papers and triangulating findings are outlined as well as the strengths and limitations of this work. Conclusions and recommendations are also drawn.

1.4 Conceptualisation and Disciplinary Approach

The purpose of this research was to inform practice; hence the candidate adopted a pragmatic approach with an aim to guide the delivery of PMTCT health services from the lessons learnt in the study. The candidate has training in international public health and is a public health practitioner with more than 15 years experience in strategic management of research operations and population-based surveys, designing and implementing research operations system. The candidate has also extensive research exposure through working with donors, government entities and the private sector. Through this work she had noted that there is a lot of data that is collected but not adequately analysed specifically for maternal and child health programs, which she has great interest in. The candidate would have included in her research

the infant feeding practices of HIV-exposed infants; however, it seemed that data in this area are not adequately collected. During the last three years, the candidate has worked for the School of Public Health, University of Zambia as a research fellow in a project whose aim was to support the utilisation of routinely-collected data for strengthening services and transparency in delivering services to people living with HIV.

The candidate had the ambition to develop her quantitative research skills in analysing big data. In addition, the qualitative segment was added as a result of the initial analysis of the routinely collected data which had a lot of missing data requiring explanation regarding to the completeness, accuracy and representativeness of the findings. It was therefore crucial to have a mixed method study which provided added value to the candidate. The systematic literature review skills ensured the candidate justification for further research as this identified gaps in utilisation of routinely collected data for evaluation PMTCT programs.

This research was built on the realisation that there is a dearth of evidence on implementing electronic health systems in developing countries. The results show the value of using these data, which give a potential for a greater role in understanding patient health. The routine health information systems are often overlooked in the African health systems and the candidate now aspires to venture into further research in health informatics.

1.5 Role of the Candidate

I conceived the ideas, designed the studies and developed them further with my supervisors, Professor Suzanne Filteau and Mr Jim Todd, together with Dr Paul Mee the advisory committee member. Mrs Tendai Munthali and Dr Patrick Musonda appraised the quality of a portion of the included studies for the systematic review of literature study. I extracted all the data from the SmartCare database with the assistance of Ministry of Health ICT department. I cleaned and analysed the data with the assistance from the two supervisors and advice from Mr Ab Schaap and Dr Paul Mee for the quantitative studies. I supervised Dr Jasleen Singh for her MSc Summer project to analyse the EID data set which I had already extracted, from the SmartCare database and cleaned, in preparation for analysis. I also assisted her to draft the early infant diagnosis paper. I conducted all the in-depth interviews and observations for the qualitative study. The focus group discussions with women seeking PMTCT services were moderated by a trained field assistant who was fluent in the local languages (Bemba and

Nyanja). Dr. Virginia Bond assisted in analysis of the qualitative data and the construction of the manuscript. I am also the corresponding author for all the manuscripts presented in this thesis.

Chapter 2: Background

2.1 Global Commitment to eliminate new paediatric HIV infections

The use of ART by HIV-positive pregnant and breastfeeding women is the cornerstone of the strategy to PMTCT (8, 9) of HIV. The global community in June 2011 committed to accelerate progress for PMTCT through an initiative whose goals were to eliminate new paediatric HIV infections by 2015 and improve maternal, new-born and child health and survival in the context of HIV(3). The Global Plan emphasized the expansion of comprehensive, integrated, and efficacious interventions for PMTCT within a maternal and child health (MCH) framework, to achieve targets by 2015 (3, 10). Subsequently the 2016 United Nations General Assembly Political Declaration on ending the AIDS epidemic by 2030 committed, among other things, to reduce the number of children newly infected with HIV annually to less than 40 000, and to reach and sustain 95% of pregnant women living with HIV with lifelong HIV treatment by 2018 (11).

The achievement of high coverage and uptake of services along the PMTCT cascade is crucial for national and international mother-to-child transmission (MTCT) elimination goals (3). Twenty-two countries in sub-Saharan Africa with a high burden of MTCT were identified as priority countries for intensified support to achieve the UNAIDS HIV elimination goal (3, 12). These countries are Botswana, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, Kenya, Lesotho, Malawi, Mali, Mozambique, Namibia, Nigeria, South Africa, South Sudan, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe (13). As of October 2016, the WHO recommendation for lifelong ART for all pregnant and lactating women (Option B+) was being nationally implemented in the 22 priority countries (14). In 2017, the global coverage of pregnant women living with HIV had access to ARV medicines to prevent transmission of HIV to their babies was 80% [61–95%] (15).

As a result of increased coverage and improved regimens, rates of HIV transmission from mothers to infants during pregnancy and breastfeeding have decreased around the world (8). The largest decline was in eastern and southern Africa, where it fell from 18% of infants born to mothers living with HIV in 2010 to 6% in 2015(16). In 2017, 210 000 new infections were averted due to PMTCT(15). Some countries in the SSA like South Africa are approaching the very low MTCT rates achieved in high- income countries, but several others such as Zambia, Angola, DRC, Nigeria, Lesotho and Kenya lag far behind at the moment (17). In Zambia

coverage of pregnant women living with HIV accessing antiretroviral medicines was 92% [78 - >95] in 2017, a decrease from 95% in 2015(15).

Although the use of antiretroviral therapy (ART) for the prevention of mother-to-child transmission (PMTCT) is essential, effective programmes to achieve early infant diagnosis (EID) are critical when that prevention fails (18). There is strong evidence that the early initiation of ART in HIV-infected children can substantially reduce HIV-related morbidity and mortality (19). To ensure timely HIV diagnosis and access to ART, the WHO recommends that HIV-exposed children are regularly followed-up, tested for HIV and initiated on ART (20). However EID coverage in Zambia was 46 % in 2017 (15), which is far below the target although new HIV infections among children reduced from over 10 000 in 2010 to 8 900 in 2016 (21).

2.2 Timing of mother to child transmission

MTCT occurs as a continuum across three time periods; in-utero, perinatal and postnatally through breastfeeding (22). Without intervention, the risk of mother-to-child transmission of HIV (MTCT) can be as high as 45%, however successful implementation of PMTCT programs can reduce this risk to around 2% in non-breastfeeding populations and less than 5% in breastfeeding populations (10, 23). Maternal risk factors for in utero transmission include high plasma HIV viral load, low CD4 count and late stage of HIV disease. The risk of transmission ranges from 1% with plasma viral load of less than 400copies / μ l. to 32% with plasma viral load of 100,000copies / μ l. At delivery risk factors include: mode of delivery, premature delivery, long duration of membrane rupture, and infection in the birth canal. Post-natal risk factors include mixed feeding, recent maternal HIV infection and mastitis (24). Interventions for PMTCT can either take a programmatic or individualised approach (25).

Preventive interventions need to be considered within the context of the environment of the mother-infant pair. Lack of any breastfeeding or termination of breastfeeding before 6 months of age increases the risk of gastro-enteritis, and mortality as well as increasing the risk of malnutrition in the absence of safe and nutritious feeding alternatives. Hence, in usually resource-poor countries, risks of gastroenteritis and malnutrition outweigh the risk of transmission of HIV (26). Randomised controlled studies have demonstrated the low risk of breast milk transmission where the mother is on ART, or the infant is on pre-exposure prophylaxis (23). Therefore in African settings PMTCT programs should be designed around

breastfeeding together with provision of ART (26). The combined effect of maternal ART and infant post-exposure prophylaxis has been adopted into programs in Africa to reduce MTCT, and so, despite breastfeeding, the risk of transmission is $\leq 5\%$; this compares to the UK where the risk of transmission is as low as 0.1% with maternal ART and formula feeding (27).

An estimated 3.3 million children are infected with HIV globally, with 90% of them residing in sub-Saharan Africa (28). Children aged 0-4 are among the most vulnerable to HIV, facing the highest risk of AIDS-related deaths compared to any other age group (29). New paediatric infections declined by 66% between 2010 and 2015(8), in 2017 210, 000 new infections were averted due to PMTCT(15). Without treatment approximately 50% of HIV-infected infants die before the age of two (30). One of the main factors for low coverage among children is the large number of infants who remain undiagnosed but would be eligible for treatment under current treatment guidelines (31). In Zambia the estimated percentage of children (aged 0–14 years) living with HIV receiving ART, in 2015 was 61%, 3% lower than the adult coverage (8). Therefore, there is an urgent need to address the important programmatic

2.3. Origins of PMTCT

In 1982 United States of America reported the first case of paediatric HIV (32), 18 months after the first report of HIV in adults (33). Parental risk for HIV transmission to child was identified in 1983, confirming that most paediatric HIV infections occurred via transmission from mother-to-child and that one in four HIV-infected mothers transmitted HIV to their infants (32). No specific prevention interventions existed at that time other than identification of HIV status and, if infected, to avoid pregnancy. By 1985, the first guidance on paediatric HIV in the United States recommended that pregnant women in high-risk groups be offered counselling and voluntary HIV testing, and that HIV-infected women should avoid breastfeeding (33). In 1987, the approval of AZT for adults was subsequently proposed as a MTCT preventive strategy. The 67% reduction in MTCT in the '076 AZT trial' was the first demonstration of 'treatment as prevention'. Unfortunately, these interventions were too complex to administer (e.g., the protocol required both oral and intravenous AZT, the need for a sustainable infrastructure, and sustained attendance of women to ANC, which was not the norm) and, therefore, not feasible for most deliveries in LMICs at that time. Subsequent researches focused on simpler options to achieve similar results were initiated (34). Between 1997 and 1999, the HIVNET 012 randomised trial conducted in Uganda concluded that

Nevirapine lowered the risk of HIV-1 transmission during the first 14-16 weeks of life by nearly 50% in a breastfeeding population (34).

Recommendations expanded from selective testing of high-risk pregnant women in February 1995, to HIV education and voluntary routine testing for all pregnant women in the United States, leading to the universal routine ‘opt-out’ antenatal HIV testing with patient notification.

By the late 1990s, enhanced affordability of AZT enabled Botswana to launch Africa’s first PMTCT program with short-course AZT while new research added a simple, sdNVP for enhanced efficiency, nearly halving transmission risk (35). In 1997, the recommendation to stop breastfeeding as soon as replacement feeds were available was the first programmatic acknowledgement that HIV transmission extends into the breastfeeding period. This recommendation became problematic in LMICs, as adequate supplies of safe infant formula could not be assured. The realization that the risk of transmission must be balanced against optimal feeding practices became important in PMTCT programs, and growing consideration was given to infant survival beyond the risk of transmission (36)

In 2000, a 5-year NVP donation to developing countries expanded the availability of PMTCT for most LMICs. Additional research indicated that combining AZT and sdNVP was highly effective and capable of reducing MTCT to rates seen with triple ARV in resource-rich countries, which became the global standard for PMTCT. However, delays in program implementation, in part due to supply chain management problems of AZT and sdNVP, resulted in the majority of HIV-infected pregnant women in LMICs never receiving prophylaxis.

Further, emerging concerns about rapidly developing resistance from sdNVP were becoming clear. Recognition of breastfeeding as the cornerstone of infant survival in LMICs spurred research on safe breastfeeding (37, 38). In 2003, the concept of rapid weaning of breastfeeding with targeted testing to minimize transmission risks during breastfeeding was introduced. Subsequently, calls for exclusive breastfeeding for 6 months with gradual weaning and an increased emphasis on ARV prophylaxis during breastfeeding were expanded in 2006. Although this represented a clear progression in thinking, correct programmatic implementation and messaging around this strategy was mired in confusion. Only when normative bodies began incorporating not only HIV, but also child survival into consideration

of reducing risks did this issue progress. By 2008, clinical trials examined varying prophylactic approaches of expanded ARV during breastfeeding and led to implementation of such programs by 2010 (39-41)

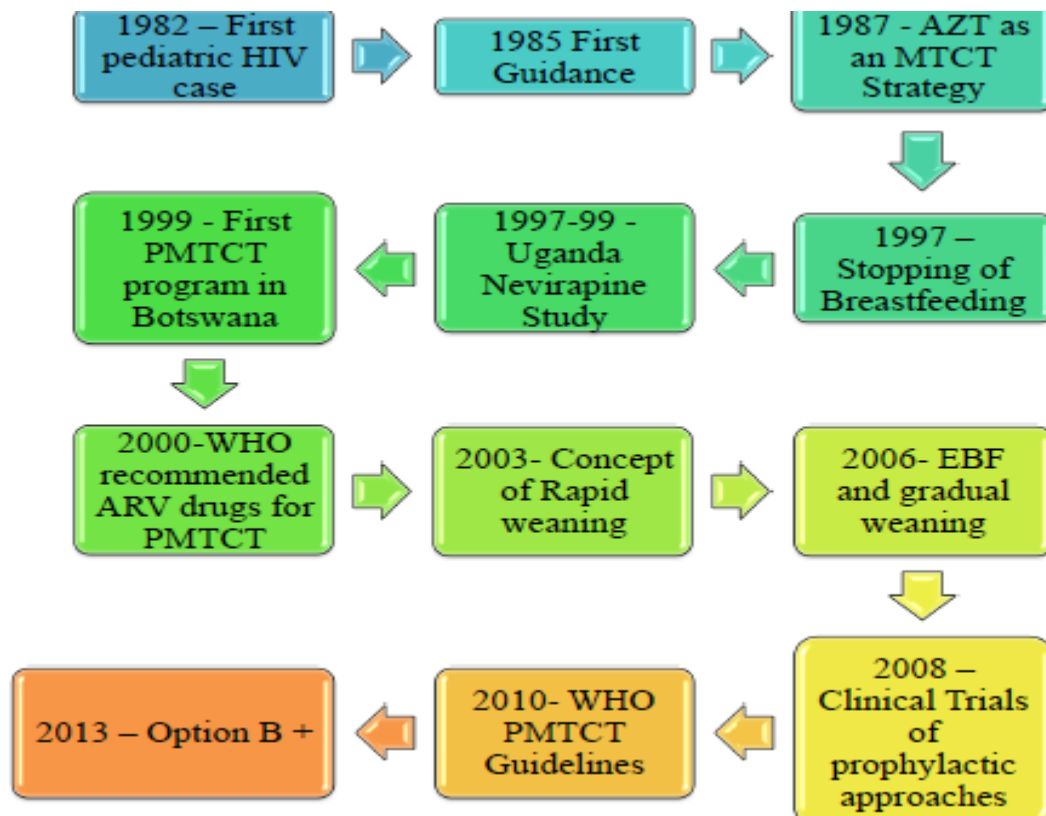
The 2010 WHO PMTCT guidelines recommended eliminating the use of single-drug regimens, favouring longer duration of ARVs during pregnancy and breastfeeding, including ART for ineligible pregnant/breastfeeding women under Option B, in resource-limited settings (42).

The 2010 guidelines also recommended extending ARV coverage through duration of breastfeeding exposure, now recommended for at least 12 months. In 2011, 'Option B+, or lifelong ART for all HIV-positive pregnant/ breastfeeding women regardless of CD4 cell count, was adopted by Malawi in response to difficulties implementing CD4 cell testing. Preliminary data from Malawi's B+ programs reported a rapid increase in the number of pregnant and breastfeeding women on ART (43). More so, MTCT rates have decreased considerably in many resource-limited areas (44, 45).

2.4 post 2010 World Health Organisation PMTCT guidelines

Global PMTCT guidelines have evolved from short-course antiretroviral (ARV) prophylaxis for mothers and infants to prevent HIV transmission, towards longer and more potent ARV regimens with the potential to improve maternal health (46-49) (*Figure 2.1*). WHO in 2010 revised its PMTCT guidelines (48). This was in an effort to achieve the goal of reducing mother-to-child transmission to less than 5% by 2015 (50). These guidelines offered two options: Option A and Option B. Under Option A, pregnant women with a $CD4 \geq 350$ cells/ μ L receive ART prophylaxis including daily Zidovudine from 14 weeks gestation through one week postpartum, single-dose Nevirapine at delivery, and daily Lamivudine from delivery through one week postpartum. Their infants receive daily Nevirapine from birth through one week after the cessation of breastfeeding. Women with $CD4 \leq 350$ cells/ μ L or WHO clinical stage 3 or 4 disease are put permanently on triple-drug ART regardless of symptoms. Under Option B, all women receive triple-drug ART from 14 weeks gestation through the cessation of breastfeeding, and infants receive a daily Nevirapine or Zidovudine dose from birth to 4–6 weeks. (49). This recommendation replaced earlier guidelines that endorsed combination ART for women who met criteria for treatment based on CD4 cell count or disease stage (47).

Figure 2.1: Origins of PMTCT



Refer to section 2.3 on PMTCT origins

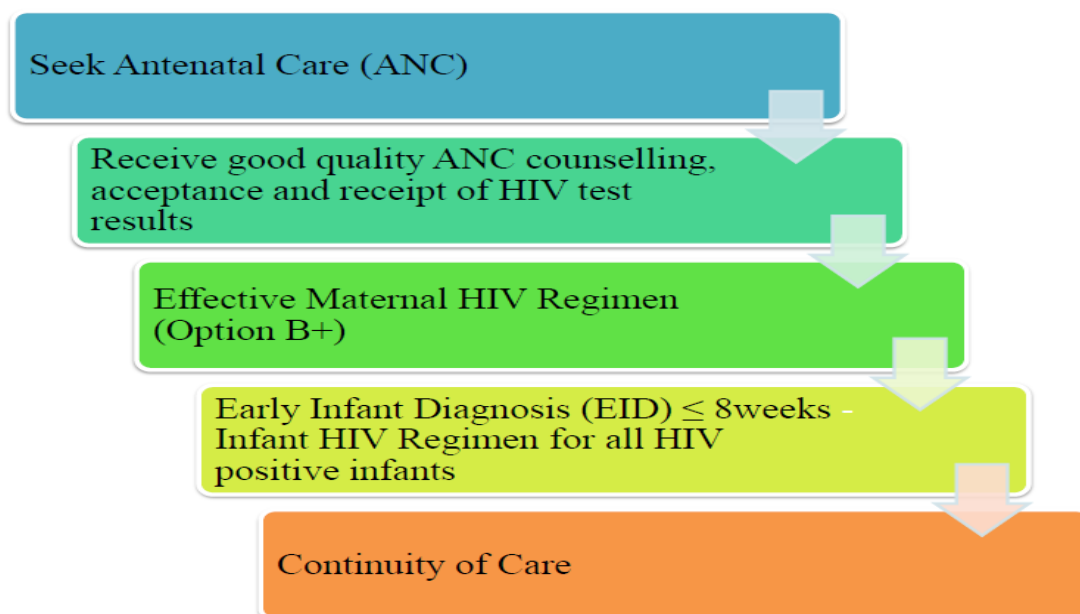
In 2013, WHO revised its guidelines for the treatment and prevention of HIV and recommended that all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should continue ART for life known as "Option B+" whilst their infants receive daily Nevirapine or Zidovudine from birth to 4–6 weeks. Among women on ART prior to pregnancy, early MTCT in Malawi's Option B+ programme compares favourably to transmission rates observed in developed countries (51).

Zambia revised its national PMTCT guidelines in 2010 in accordance with the new WHO guidelines and, along with many other developing countries, adopted Option A(52). In 2013, after more than two years implementing Option A, Zambia announced that it would revise its PMTCT guidelines again and adopt Option B+(53).

Effective PMTCT programs require women and their infants to receive a cascade of interventions (**Figure 2.2**) including uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, appropriate infant feeding, uptake of infant HIV testing and other post-natal health care services (54). Several factors

could influence uptake of the PMTCT cascade services including health system factors that affect service uptake, user-related or individual factors and broader socio-cultural factors (55-57). Health system or structural issues such as staffing level, availability and cost of ART, capacity of health personnel to prescribe appropriate regimens; shortage of supplies in facilities, failure to follow up mothers' or infants' status, and giving wrong information or suboptimal quality of counselling could lead to loss or dropout from the PMTCT cascade (57-62). Individual factors such as mothers' knowledge of PMTCT, socioeconomic and demographic characteristics, pregnancy history, as well as broader socio-cultural factors such as fear of stigma, lack of interest, cultural, family and social barriers are factors that influence successful completion of the PMTCT cascade services (63-65). There is evidence that performance based financing (an incentive scheme directed to health providers) has improved the quality and quantity of antenatal care interventions in Rwanda (66) and Mozambique (67). Other SSA countries could explore financing initiative in order to improve the implementation the implementation of PMTCT guidelines

Figure 2.2: PMTCT Cascade



Zambia adapted the implementation of Option B+ based on a health outcome and cost implication analytic model on the national health system perspective (68) rather than based on participant consultation. In Tanzania where the acceptability of Option B+ was explored, women's views on Option B+ were divided and those in favour of B+ were highly determined to prolong life for their own sake and were concerned for the welfare of their children. Others

questioned their own ability to adhere to life-long ART, thinking that they would be less motivated to take drugs after protecting their child, and fearing the drug side effects and the challenges of chronic daily medication (69). In addition preliminary data from Malawi the first country to introduce Option B+, a nation-wide cohort of women on Option B+ showed that 17% of Option B+ clients were lost to follow-up within 6 months after delivery (70).

Acceptability and adherence to Option B+ has not been investigated in Zambia. However Kamuyango et al (71) and Ngarina et al (72) reported that default and incomplete adherence were more common in the Option B+ cohort compared to the pre-Option B cohort in Malawi and Tanzania respectively. In a recent Swaziland study, on challenges and successes in the implementation of Option B+, the risk of attrition was higher among women initiated on ART during the later enrolment phase which had a higher proportion of same-day ART initiations (73). Adherence to PMTCT options especially to Option B+ will therefore need massive public education as women are particularly vulnerable to disruptions in adherence during pregnancy and breastfeeding.

2.4.1 Evolution of the PMTCT Cascade

The PMTCT cascade (*Figure 2.2*) is a series of key stepwise activities that constitute a critical pathway to successful PMTCT that begins with all pregnant women and ends with the detection of a final HIV status in HIV-exposed infants (HEIs) (74). The PMTCT cascade, with defined indicators to measure each step, has evolved over time with each advance in the science of PMTCT and the release of revised World Health Organization (WHO) guidelines (*Figure 1*). Model-based analyses suggest that reaching elimination of MTCT targets is feasible, but only with dedicated efforts to support medication adherence and retention in care for women and infants throughout the PMTCT cascade, as well as interventions targeting maternal-child health care and safer breastfeeding practices (75).

Before the use of antiretroviral medicines for PMTCT, early WHO guidelines focused on counselling, offering and acceptance of HIV testing, and receiving HIV antibody test results for pregnant women and HEIs at 18 months of age (47). Steps along the cascade expanded as interventions to prevent transmission were introduced and access to antiretroviral therapy improved. Indicators changed as recommendations evolved from single-dose Nevirapine prophylaxis to initiation of lifelong antiretroviral therapy for all pregnant and lactating women (Option B+) (48, 76, 77). Also, development of early infant diagnosis (EID) capacity led to the addition of HIV testing at 6 weeks to the cascade (78). The final HIV outcome in

children cannot be determined until the end of exposure through breastfeeding. The antenatal and early infant follow-up (6–8 weeks) steps of the cascade have received more attention than the later postnatal period (74).

2.4.2 Efficacy and Effectiveness of PMTCT Options

Options A and B have to date not been directly compared in a trial, though indirect evidence from Chasela et al, suggests similar efficacy (37). The only head-to-head comparison thus far has been of the postpartum components in the BAN study, where no differences in proportions of HIV transmission were noted between maternal and infant prophylaxis regimens at 28 weeks of life (2.9% vs. 1.7%; $p=0.10$)(37). Across multiple sites in South Africa, Kenya, and Burkina Faso, the Kesho Bora study showed lower rates of HIV transmission at 12 months when combination maternal regimens (antenatal, intrapartum, postpartum through 6 months of breastfeeding) were compared to antenatal ZDV and peripartum NVP (5.4% vs. 9.5%; log-rank $p=0.029$). Interestingly, the transmission rates between the two arms were comparable at birth (1.8% vs. 2.5%), suggesting similar efficacy between the antenatal components of Option A and Option B among women who are not eligible for ART (38). In their comparison of three combination antiretroviral regimens, Shapiro and colleagues demonstrated high rates of virologic suppression (defined as < 400 copies/mL) at delivery and throughout the breastfeeding period ($>92\%$). Only 8 of 709 (1.1%; 95% CI: 0.5–2.2) of infants were infected - among the lowest transmission rates ever reported in breastfeeding infants, with the majority acquiring HIV in utero (79).

Although efficacy of Options A and B is believed to be similar, there are limited data on effectiveness outside clinical trials. Low early (4–8 weeks) MTCT rates have been reported for the South African national program under Option A conditions suggesting good overall effectiveness in a relatively well-resourced health system (57). However, several observational studies under Option A have reported paradoxically lower early MTCT rates among ART-eligible pregnant women receiving ART compared with non-eligible women receiving short-course Zidovudine (AZT) prophylaxis (62, 80). Several studies have demonstrated that the lowest rates of transmission occur among women on ART at the time of conception (62, 80, 81). Therefore, particularly in settings with high rates of unplanned pregnancies and poor penetration of family planning, B+ is likely to be superior to A and B for PMTCT in subsequent pregnancies. Our systematic review of literature (Chapter 4 and (45)), showed a continued decline in the incidence of HIV among children, as indicated by

low MTCT rates, and an average rate of mother-to-child transmission of approximately 9.9% was achieved in East and Southern Africa in 2017 (2).

Research data have suggested that Options A, B, or B+ may be associated with important adverse outcomes, including drug resistance, congenital anomalies, preterm delivery, and impaired infant growth (82-86). The results from a recent systematic review of literature on use of ARVs during pregnancy and adverse birth outcomes among women living with HIV-1 in low and middle income countries (LMICs) revealed mixed evidence suggesting both potential harm and potential benefit for most regimens (87). The harmful or protective effects of certain regimens varies depending on the drug backbone (87). Women who received Zidovudine-based ART (Zidovudine, Lamivudine, and Lopinavir/Ritonavir) had the lowest HIV-1 MTCT prevalence of 0.5% and the highest low birth weight prevalence of 20%, whereas, women who received Zidovudine plus single-dose NVP had the highest HIV-1 MTCT prevalence of 2% and the lowest low birth weight prevalence of 9% (88). The most recent regimens based on Option B+ and Test and Treat policies are more likely to be effective at reducing MTCT rates but are associated with likelihood of increased low birth weight and preterm birth.

2.4.3 Cost effectiveness of PMTCT Options

Cost-effectiveness is a formal methodology to assess value for money. Two discrete outcomes: 1) healthcare costs, in dollars or other currency, and 2) health benefits, in life-years saved (LYS), quality-adjusted life-years (QALYs), or disability-adjusted life-years (DALYs) are calculated (89, 90). Several studies have evaluated Options A, B, or B+, with wide variations in the costs and outcomes considered, as well as the choice of comparator strategies. The greatest number of recent reports have examined Option B, and found it to be either cost-saving or very cost-effective when compared to no PMTCT, single dose of Nevirapine (sdNVP), or dual antenatal ARV prophylaxis. (89, 91-97). A Zimbabwean study comparing Options A and B indicated that Option B led to greater life-years gained for both mothers and infants, and was also less expensive (92).

Fasawe *et al* (93) in Malawi examined maternal and infant outcomes for Options A, B and B+ separately and concluded that, if implemented as recommended, Options A, B and B+ are equivalent in preventing new infant infections, yielding cost effectiveness ratios between USD 37 and USD 69 per disability adjusted life year averted in children. However, Option

B+ also yielded favourable incremental cost effectiveness ratios (ICER) of USD455 per life year gained over the current practice.(93). A study that examined health outcomes and cost impact of the shift to WHO 2013 recommendations in Zambia, suggested that the shift from 2010 Option A to the 2013 guidelines (Option B+) would result in a 33% reduction of the risk of HIV transmission among exposed infants (68). The risk of transmission to sero-discordant partners for a period of 24 months would be reduced by 72% with ARVs during pregnancy and breastfeeding and further reduced by 15% with lifelong ART. The probability of HIV-infected pregnant women initiating ART would increase by 80%. It was also suggested that while the shift would generate higher PMTCT costs, it would be cost-saving in the long term as it spares future treatment costs by preventing infections in infants and partners (68).

2.5. Early Infant Diagnosis

EID of HIV is a critical step in ensuring infant survival. The landmark CHER (Children with HIV Early Antiretroviral Therapy) study in South Africa demonstrated that starting ART before 12 weeks of age reduced mortality by 76% and disease progression by 75% in HIV-infected infants as compared to delayed ART (98). As a result of this trial and a growing body of evidence, in 2008 the WHO updated its paediatric HIV guidelines to recommend immediate ART for all HIV-infected infants under 12 months, irrespective of clinical or immune status (48). In 2013 this was extended to all HIV-infected children under 5 years (49). An effective EID service should achieve the following: identify all HIV-exposed infants, provide HIV testing and ensure return of results in a timely manner; retain HIV-exposed infants and their mothers in care; and identify all HIV-infected infants and link them to treatment services to ensure timely initiation of ART (99). A recent study in Malawi revealed that children born to women who received ART are less likely to be lost to follow-up and more likely to be tested for HIV (100).

In our review of literature (Chapter 4 (45)), the uptake of EID (less than 2 months) ranged from less than 60% in Nigeria (101) and Zambia (62) to 100% in 2012 according to South African national data where it increased from 87% in 2010 (102). The age at which polymerase chain reaction (PCR) test for HIV was done ranged from 4 weeks to 18 months. In South Africa, 80% of exposed infants had PCR results at 6 weeks (103), whereas in Malawi 52% underwent testing at 6–12 weeks and 28% tested at 12 months(104).

Age at first PCR had an impact on the MTCT of HIV-exposed infants (45). In Tanzania, the proportion of HIV-infected infants was higher among infants who appeared later for HIV testing (18% at 3–6 months) than among those who presented earlier (6.4% at 1–2 months) under Option A implementation (105). An Ethiopian study reported that late enrolment to the exposed infant follow-up clinic was significantly and independently associated with increased MTCT of HIV (AOR= 2.89, 95% CI: 1.35, 6.21) (106).

2.6 Adherence to PMTCT options

Adherence to ART is essential for maximal suppression of viral replication and avoidance of drug resistance (107, 108) As such, good adherence is believed to be a critical determinant of long-term survival among HIV-infected individuals (109). In a systematic review and meta-analysis from over 20 countries, adequate adherence (>80%) was shown to drop from 75% (CI 71.5-79.7) during pregnancy to 53% (CI 32.8-72.7) postpartum among women on ART (109). Tracing women on Option B+ who default in Uganda, Malawi and Zimbabwe was recently reported to be difficult as women implicitly choose not to be traced by providing a false address at enrolment (110). In addition, the need to begin treatment is not yet urgent for less seriously ill women with more recent Option B+ and Test and Treat policies as they consider themselves “healthy” without treatment (111).

In Zambia (112), self reported adherence rate to Option A was 82.5 % during pregnancy, 84.2 % at one week postpartum, 81.5 % at six weeks postpartum, and 70.5 % at 24 weeks postpartum, whilst in Ethiopia self reported adherence rate to Option B+ was 87% during pregnancy (113). The quality of counselling was indicated as a predictor of adherence as mothers who were counselled on the correct intake of ARV medications had 4.7 (95% CI) 1.98 – 11.36) times’ higher odds of adherence than those who were not counselled properly.

2.7 Routinely collected data

Routinely collected health data (RCD) are data collected for purposes other than research or without specific a priori research questions developed before collection (114). It includes clinical information from electronic health records, health administrative data, disease registries and epidemiologic surveillance systems. Data quality from RCD systems remain in question (115), as research and evaluation have traditionally been termed ‘secondary’ uses of these data, because the data are used for purposes other than those for which they were

originally collected (116). The perceived advantages of RCD should be viewed cautiously, because of the inevitable biases of observational research and specific biases due to the nature of these data (117).

Extensive resources have been invested in the field of routinely collected data: these include the set-up of disease registries and clinical databases at regional, national or international levels; the promotion of the use of electronic health records; and making use of wearable devices for the collection of health data (117-119). However, in resource-limited settings with the limited resources and capacities, most of the electronic systems are still side by side to the paper documentation (120-123). RCD in electronic form can be linked over time, and across data sources, to create longitudinal records for individuals and multilevel data structures (116).

In spite of the demands for quality data, routine health information systems in many resource-limited settings continue to perform below expectations. Often the systems are unable to be used for their intended purposes of generating accurate and reliable data. Where data is collected and generated, the information is often not used for planning and management (124, 125). Other reasons for poor quality data include design/structural issues relating to inappropriate data collection tools and procedures (125, 126), poor recording due to inadequate skills(125, 127, 128) inadequate resources(125, 127) leading to poor capturing and reporting of data (129, 130), elements, staff attrition (127-129) and lack of use of already generated data, which may hinder constructive feedback to data producers (125, 127, 128, 130).

Recent studies which have attempted to use routinely collected data have recommended the importance of evaluating the availability, quality and completeness of data from routine ANC data systems before recommending that these data be used to replace data collected in ANC surveillance surveys (131-135). Hence there is a need to optimize quality systems to ensure robust routine HIV testing for programmatic and surveillance purposes.

Routine data can either be patient or aggregate data. Patient data is data relating to a single patient, such as his/her diagnosis, name, age, earlier medical history etc. Patient based data is important when you want to track longitudinally the progress of a patient over time. On the other hand, aggregated data is the consolidation of data relating to, multiple patients, and

therefore cannot be traced back to a specific patient. Aggregate data cannot provide the type of detailed information which patient level data can, but is crucial for planning and guidance of the performance of health systems. Patient data is highly confidential and therefore must be protected, whereas security concerns for aggregated data are not as crucial as for patient data, as it is usually impossible to identify a particular person to an aggregate statistic. Routinely collected data is should not be distributed without adequate data dissemination policies in place as it misused and misinterpreted.

2.8 Conclusion

The global initiative to eliminate new paediatric HIV infection by 2015 and improve maternal, newborn and child health and survival in the context of HIV has resulted in increase in the PMTCT coverage and reduction in HIV infections among children. However, the targets set have not been reached in most of the 22 priority countries with a high burden of HIV, which also includes Zambia. The PMTCT cascade has evolved in line with the introduction of various post 2010 WHO PMCT of guidelines. My research intended to use the PMTCT cascade points as a framework for analysis specifically in ART initiation points for both HIV-infected mothers and infants.

Chapter 3: Overview of Methods

3.0 Introduction

This chapter presents the methods used in this study which included: the systematic review of literature, quantitative analysis of routinely collected data and qualitative data collection and handling. The ethical considerations are also outlined.

3.1 Study location

Zambia is a landlocked country in south-central Africa, neighbouring the Democratic Republic of the Congo to the north, Tanzania to the north-east, Malawi to the east, Mozambique, Zimbabwe, Botswana and Namibia to the south, and Angola to the west (*Figure 3.1*). As of 1 January 2018, the population of Zambia was estimated to be 17,470,471 people (136). Zambia is classified as a lower middle income country.

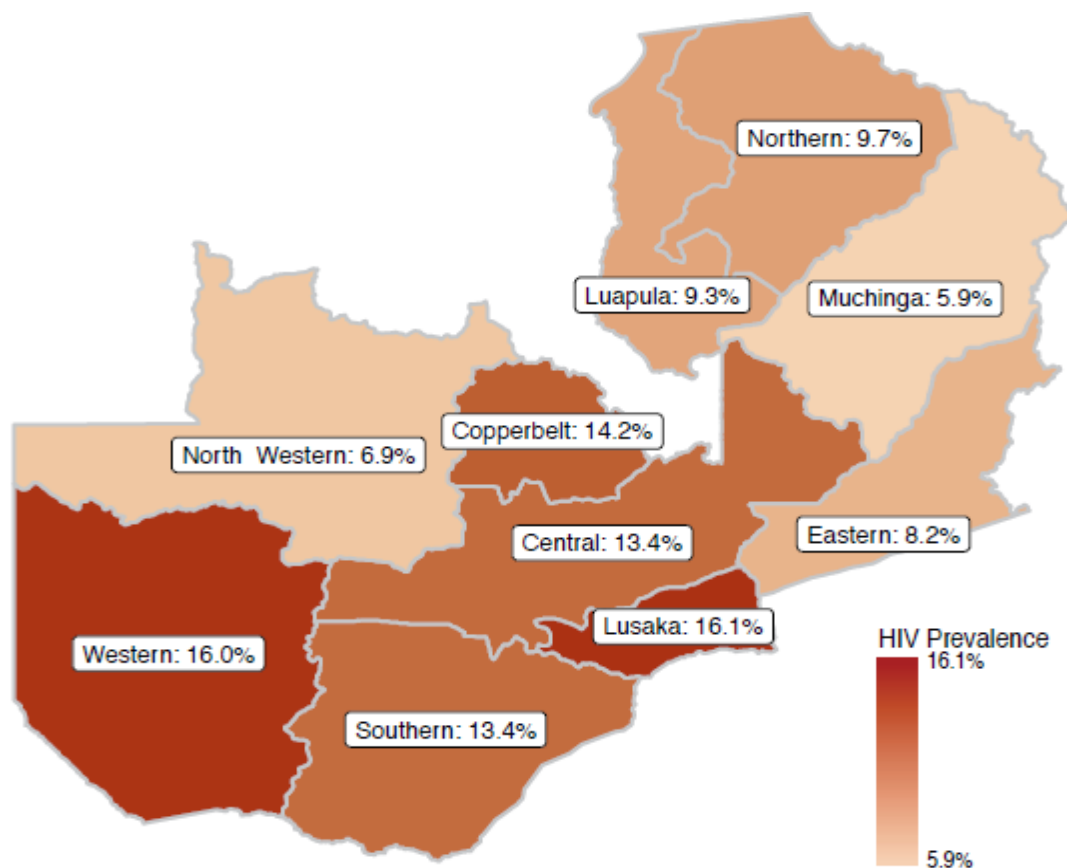
Figure 3.1: Location of Zambia in Africa



Zambia is experiencing a generalized and mature HIV/AIDS epidemic, with a national HIV prevalence rate of 11.6 percent among adults ages 15 to 49 in 2016 (137). The primary modes of HIV transmission are through heterosexual sex and mother-to-child transmission (138). The prevalence of HIV among females aged 15 to 49 years in Zambia is 14.5 % higher than in their male counterparts which is 8.6% (139). The HIV prevalence in the 15-49 years age group varies geographically across Zambia, ranging from 5.9 percent in Muchinga Province to 16.0 percent in Western Province and 16.1 percent in Lusaka (*Figure 3.2*). (139) .

Infection rates are highest in cities and towns along major transportation routes and lower in rural areas with low population density (138). In 2016, Zambia adopted the WHO guidelines on offering all people living with HIV antiretroviral therapy regardless of their CD4 count(140). Of the estimated 1.2 million people living with HIV in Zambia, only 67% know their status as of 2016 (8, 141). Among people living with HIV (PLHIV) ages 15-59, who know their status 85.4% self-report current use of ART: 84.9 percent of HIV-positive females and 86.2 percent of HIV-positive males.

Figure 3.2: HIV Prevalence among adults by province



Adapted from the Zambia Population-based HIV Impact Assessment (2015-16)(139)

3.1.1 PMTCT Program in Zambia

Zambia has been implementing a rigorous PMTCT program which has seen the percentage of children born HIV-positive drop by 51% between 2011 and 2012, a decline from 19,000 to 9,500 (142). In 2015, 87% of pregnant women living with HIV were receiving effective antiretroviral treatment, just under universal health targets of 90% (8), by end of 2017 the coverage percentage was 92%(15). The SmartCare database includes a dedicated module for

collecting the PMTCT data, and is designed to be used in all health facilities providing the PMTCT services.

Zambia launched its PMTCT initiative as a three-year pilot program in 1999. In 2003, the first national PMTCT of HIV program was initiated. In 2007, an updated version was published, followed by another in 2008 and another in 2010. There has been a remarkable expansion in the release of prophylactic medication regimens to mothers and infants between the years 1999 and 2010. The current policy (2013) recommends that all pregnant women living with HIV who are Zambian citizens are provided with free ARV drugs for life, regardless of their CD4 count (53). It also guides health care workers to follow a family-centred approach in testing and counselling for HIV, as well as in care and treatment.

Zambia also adopted a provider-initiated HIV testing and counselling model in 2006. New ANC clients are informed about PMTCT during group pre-test counselling. Unless a client opts out, providers perform a rapid HIV test that produces results within one hour. Individual post-test counselling is offered as part of the standard package of ANC and delivery services (143). Ninety-six percent of mothers received antenatal care from a skilled provider and 91% of women had an HIV test either during antenatal care or during labour for their most recent birth and received the test results (144).

3.1.2 EID program in Zambia

The latest 2016 Zambian MoH guidelines, in line with WHO guidelines, recommend HIV PCR testing for HIV-exposed infants by 6 weeks of age and again at 6 months (145). In Zambia only 3 public-sector laboratories currently perform HIV early infant diagnosis, with two of them located in the capital Lusaka, so rural areas face significant delays in receiving results (146). The cost of infant PCR assays (which are more expensive than antibody tests) is another limiting factor, as well as the need to repeat PCRs in infants who are breastfed (147).

HIV-infected women and their exposed infants receive HIV counselling from clinic staff and are advised to have infants tested by HIV PCR at 6 weeks and 6 months of age. Blood is collected from infants by heel stick and stored as dried blood spots (DBS) in the laboratory at the HIV clinic. Batches of specimens are transported by road to the central laboratories for testing by PCR. If the HIV PCR test is negative or invalid at 6 months of age, the infant is recommended to return at 12 and 18 months of age or 6 weeks after cessation of breastfeeding. If the results are available and the infant is HIV PCR positive, the caregiver is

counselled to have their child begin ART and another DBS specimen is collected for confirmatory testing (145).

Project Mwana was an innovative health initiative implemented by the Zambian Ministry of Health with the support of UNICEF and its collaborating partners: the Zambia Centre for Applied Health Research and Development (ZCHAR), a Boston University affiliate; the Zambia Prevention, Care and Treatment Partnership (ZPCT); and the Clinton Health Access Initiative (CHAI). Through the use of RapidSMS mobile technology, the project delivers test results for diagnosis of HIV in infants in real time to rural clinics and facilitates communications between clinics and community health workers communities(148). The community health workers then inform mothers that the results are ready for their collection. The project begun as a pilot in 13 districts of Zambia in June 2010, and is now being implemented across all 10 provinces of Zambia across a total of 1,030 health facilities.

3.2 Study Setting

3.2.1 The SEARCH Project

The PhD research was nested in the project called SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) whose aim was to support the utilisation of routinely-collected HIV data for strengthening services, and provide transparency about the benefits and equity in delivering services to people living with HIV. The Bill & Melinda Gates Foundation funded the collaboration between the London School of Hygiene & Tropical Medicine and the Ministries of Health in Tanzania and Zambia. The SmartCare Database was the source of routinely collected data in Zambia.

3.2.1 SmartCare Electronic Health System

SmartCare is one of the largest electronic patient monitoring systems in Africa. It is a Zambian Ministry of Health led project funded from the United States Centre for Disease Control and Prevention (CDC). Its implementing partners include Jhpiego, U.S. Agency for International Development; the Centre for Infectious Disease Research in Zambia; Zambia HIV/AIDS Prevention, Care and Treatment Partnership; Zambia National AIDS Network; the Elizabeth Glaser Paediatric AIDS Foundation (EGPAF); John Snow International (JSI)/DELIVER; Aids Relief/Catholic Relief Services; the Zambia Defence Force (ZDF) Medical Services; the Zambia Police Medical Services; the Churches Health Association of Zambia and Chreso ministries.

SmartCare was developed to improve continuity of care and provide timely data on maternal and child health, HIV/AIDS, tuberculosis and malaria interventions for public health purposes, including Health Management Information System (HMIS) trend reporting and analysis for health officials and clinicians (149). SmartCare is now also required for any facility in Zambia desiring accreditation to dispense ARV drugs for HIV clients. Since 2005, SmartCare has been deployed in over 800 facilities (Western Province - 72; Southern Province - 153; North-western Province – 38; Lusaka Province - 106; Central Province – 65; Copper belt Province – 151; Eastern Province – 113; Northern Province – 26; Luapula Province - 39 and, Muchinga – 71) in 94 districts and has an enrolment of more than 900,000 HIV positive patients. Approximately 61% of those enrolled are female. Although this represents only 40% of all clinics in Zambia, these include the biggest and busiest clinics. The MoH does not have precise records of the specific numbers of facilities implementing SmartCare per year owing to inadequate resources to enable close monitoring and documentation of the implementation.

3.2.1.1 SmartCare Model Structure

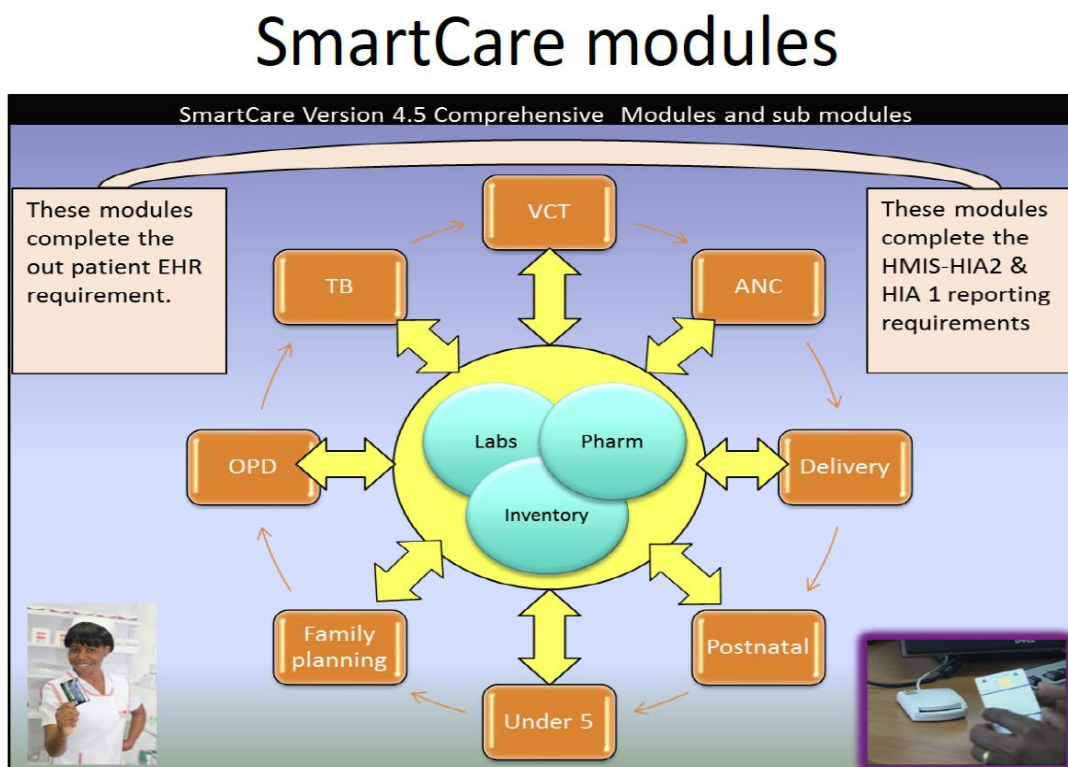
SmartCare is organised into comprehensive modules and sub-modules (*Figure 3.3*). This was mainly influenced by its funders depending on the information they wanted at that particular time. The main module groups (*Table 3.1*) are: clinical group comprising the following modules – ANC, Delivery, Postnatal, ART, Paediatric ART, PMTCT follow up, Under 5 among others – (these are mainly of interest for this research); logistic group which constitute information on drug dispensing and orders; monitoring and evaluation groups which includes health management information system reports, graphing, data analysis, data merge from facilities for MOH; and the continuity of care group which had data from across facilities and within facilities. Through the data merge the SmartCare information can be used to obtain data for the monthly reports to MOH, including the HMIS-HIA report.

Table 3.1: Smart Care Module Groups

SN	Module Group	Components
1	Clinical	Includes the following modules – ANC, Delivery, Postnatal, ART, Paediatric ART, PMTCT follow up, Under 5 among others – (these are mainly of interest for this research)
2	Logistic	Consists of information on drug dispersion and orders
3	Monitoring and Evaluation	Includes health management information system reports, graphing, data analysis, data merge from facilities for MOH
4	Continuity of Care	Data from across facilities and within facilities

All patients in SmartCare have a unique identity (ID) number, and information from various modules is linked through the unique ID number (149). Infants are registered as separate individuals with unique numbers different from their mothers. Thus it proved impossible to link mother-infant pairs for the present study.

Figure 3.3: SmartCare Model Structure



Adapted from Ministry Health HMIS workshop Presentation

3.2.1.2 Data capturing process

Data is captured under a number of ‘modules’ across a range of health issues. Records are updated at every point of clinical service. SmartCare enables the capture of all patient data into one centralised database that can be accessed from any supported health facility. Patients enrolled in the system can have their records accessed at whichever SmartCare-supported facility they present to in the country. Patients are issued with Smartcards at their initial consultation which contains all their clinical information and treatment details. When they present at another facility the health worker simply plugs the Smartcard into the online system and can access all the patients’ details (*Appendix 2*).

Data on a range of HIV and pregnancy related outcomes are collected during the patient consultation with the clinician, who records the information on paper forms in facilities that are paper-based and directly on the computer in the few facilities which are computer-based. These forms are then entered into the SmartCare database by data entry clerks who have been trained in using the SmartCare database. Data is collected from each facility on a monthly basis and submitted to a District Health Information Officer, who aggregates and sends the data to the province level Senior Health Information Officers. From here the data are wired to a national server at MoH headquarters.

3.3 Study design

In order to achieve the stated aim and objectives, a mixed-methods approach was used. The quantitative and qualitative methods were chosen to complement each other in addressing the objectives (*Table 3.2*). Through the use of systematic review of literature, the researcher was able to review evidence available on the implementation of the post 2010 WHO PMTCT guidelines in Sub Saharan Africa. The quantitative routinely collected data from the SmartCare Database provided an overview of coverage of PMTCT and performance of EID services. An inquiry of implementation procedures of SmartCare was carried out using qualitative methods. The research methods employed under the objective to which they contributed are outlined below and details are provided in the individual chapters.

Objective 1: *To synthesise and evaluate the impact of implementing post-2010 World Health Organisation (WHO) prevention of mother-to-child transmission (PMTCT) guidelines on attainment of PMTCT targets in Sub Saharan Africa through a systematic review of literature.*

Systematic reviews aim to identify, evaluate, and summarize the findings of all relevant individual studies over a health-related issue, thereby making the available evidence more accessible to decision makers (150). The systematic review involved analysis of quantitative retrospective and prospective cohort study designs that utilised routinely collected data with a focus on provision and utilisation of the cascade of PMTCT services, and evaluated implementation of post 2010 PMTCT guidelines. The systematic review provided justification for further research, in addressing the overall aim of the study as it identified gaps in the use of utilisation of routinely collected data for evaluation PMTCT programs. The detailed systematic review methods are presented in Journal of Medicine manuscript format in Chapter 4.

Objective 2: *To describe trends in the coverage of PMTCT services from 2010 to 2015 using the SMART Care database of routine clinical information collected in Zambia.*

Quantitative methods were used to analyse routinely collected data from the Ministry of Health electronic SmartCare database for a cohort of all pregnant women attending antenatal care (ANC) from January 2010 to December 2015 in health facilities. Descriptive analysis was employed to quantify the proportion of HIV-positive pregnant women attending ANC, percentage of HIV pregnant women initiated on ART and time from diagnosis to treatment initiation. Further details are presented in Chapter 5 of the thesis in the Frontiers in Public journal manuscript format.

Objective 3: *To evaluate the performance of Zambia's early infant diagnosis services routinely collected data from the SmartCare database was performed for the period January 2006 to December 2016.*

Similar to objective 2, quantitative methods were used to analyse routinely collected data from the Ministry of Health electronic SmartCare database for a cohort of HIV-infected infants from January 2006 to December 2016. Univariable logistic regression was conducted

to identify factors associated with later infant testing and treatment initiation. A detailed presentation of analysis is in Chapter 6 in the BMC Public Health manuscript format.

Objective 4: *To understand the implementation procedures of SmartCare*

Qualitative methods were used to understand the implementation procedures of SmartCare. Data was collected using in-depth interviews, observations and focus groups discussions (FGD) between September and November 2016. Seventeen in-depth interviews were held with a range of key informants from the Ministry of Health and local and international organisations implementing SmartCare. Four data entry observations and three FGDs with 22 pregnant and lactating women seeking PMTCT services were conducted. Data was analysed using a thematic content approach. A detailed report of the study is presented in Chapter 7 of the thesis.

Table 3.2: Overview of Objectives and Methods

Where Results are presented	Objective	Study Design	Main Outcome	Analysis
Paper 1 (Chapter 4)	To synthesise and evaluate the impact of implementing post-2010 World Health Organisation (WHO) prevention of mother-to-child transmission (PMTCT) guidelines on attainment of PMTCT targets in Sub Saharan Africa.	Systematic review of literature	Quantitative retrospective and prospective cohort study designs that utilised routinely collected data with a focus on provision and utilisation of the cascade of PMTCT services, and evaluated implementation of post 2010 PMTCT guidelines.	Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA)
Paper 2 (Chapter 5)	To describe trends in the coverage of PMTCT services from 2010 to 2015 using the SMART Care database of routine clinical information collected in Zambia.	Retrospective cohort study	Proportion of HIV-positive pregnant women attending ANC, percentage of HIV pregnant women initiated on ART and time from diagnosis to treatment initiation	Descriptive analysis
Paper 3 (Chapter 6)	To evaluate the performance of Zambia's early infant diagnosis services routinely collected data from the SmartCare database was performed for the period January 2006 to December 2016	Retrospective cohort study	Age at infant HIV test and time from diagnosis to treatment initiation.	Univariable and multivariable logistic regression
Paper 4 (Chapter 7)	To understand the implementation procedures of SmartCare	Qualitative study using in-depth interviews, observations and focus groups discussions (FGD) between September and November 2016.	Challenges in implementing a Zambian EHR system labelled 'SmartCare' in order to improve PMTCT data	Thematic content analysis
Chapter 8	To triangulate data from an independent source with findings from Chapter 5	Retrospective analysis of ANC HMIS data from 2013 to 2016	Routine aggregate surveillance ANC data from the HMIS	Descriptive analysis

3.3.1 Sequence of study design implementation

The components of a mixed methods study can be undertaken at the same time or sequentially with either the quantitative study undertaken first followed by the qualitative study or vice versa (151). The mixed methods of this study were undertaken in a sequential manner. The systematic review of literature was done first. The systematic review of literature allowed for further research as it indicated underutilisation of routinely collected for PMTCT programs (45). This was then followed by data extraction, cleaning and quantitative analysis of routinely collected data from the SmartCare data. The quantitative data from a cohort of pregnant women attending ANC and HIV-positive infants were cleaned and analysed separately.

The findings from the two quantitative studies required extracting surveillance data from a Zambian EHR system, SmartCare. The work highlighted some deficiencies including large amounts of missing data, especially in more recent years, and variable performance across the country. This confirmed the need for a qualitative study to understand the implementation procedures of SmartCare. Thematic content analysis was carried out to give an account of challenges in implementing the SmartCare Electronic health system and recommendations drawn to improve PMTCT data.

The findings of these studies were presented in individual paper for publications in various journals. The summaries of findings were then triangulated for interpretation in order to draw conclusions and recommendations. Timelines for the study are presented in (*Appendix 1*).

3.4 Quantitative Data Extraction and Cleaning

3.4.1 Data Access

To access the MOH SmartCare data, an access agreement with the Policy Directorate in MoH was developed with the support of SEARCH management team. Removal of personal information of the recipients was done by the MoH ICT team and the unique identifier for the data was the SmartCare ID number. The individual level data from the ANC and EID datasets were extracted and cleaned separately. The extraction and cleaning of the data for all modules was undertaken by the candidate in 2017, prior to combining the data for analysis.

3.4.2 ANC Data extraction

Data from the ANC module was linked to the HIV Client Summary module and the ARV Eligibility Interaction Module to identify HIV-positive women. Data from the Obstetric

History Module was then used to segregate PMTCT clients from general ART clients. The oldest date of HIV testing and ANC visit date were used to determine whether women had known their HIV status before the ANC visit.

3.4.3 ANC Outcomes of Interest

1. Proportion of HIV positive pregnant women (*i.e.* the number of pregnant women with a new HIV test result documented in ANC clinic plus pregnant women with known status but not on ART and pregnant women who are already on ART / the total number of pregnant women presenting to ANC clinic per calendar
2. Proportion of women on ART was calculated from the number of HIV-infected pregnant women receiving combination ART during ANC and those already on ART (*i.e.* the number of HIV-infected pregnant women documented to have received combination ART during ANC or ART clinic / the total number of pregnant women enrolled in ANC clinic with either newly documented HIV infection or known prior.

3.4.4 ANC Data cleaning

These following steps were taken to ensure the data which was analysed was clean:

- Removing of duplicate visits – this was done for every individual woman, with the same gravida and parity as this was assumed that it was the same pregnancy.
- Removal of implausible parity and gravida mothers *i.e.* mother who had very odd gravida and parity for their age.
- Parity profile by age groups histograms were also plotted in Stata 14 to determine whether they were normal distributed. The age groups were in five year intervals.
- Removal of any records of mothers whose age was not within the reproductive age using the WHO standard of 15-49 year distribution. During this exercise, they were also enough mothers in the dataset that were highly implausible as they were a lot mothers under the age of 12 with more than 5 children and mothers above 50 years of age. It was also difficult otherwise to distinguish garbage data and therefore, the use the WHO standard was opted. The final sample age distribution profiles of mothers were similar to the Demographic Health Survey (DHS) data.
- The final data set were inspected on a year by year basis, and 2016 was excluded for analysis as number of mothers recorded during the year dropped to 2500, from above 10, 000 of the previous years.

3.4.5 EID Data extraction

The EID dataset was extracted from Under 5 Registration module and the Paediatric ART module. The following variables were extracted for all infants on ART: sex, date of birth, year of birth, province where infant was registered to start ART, date of HIV positive test, age at HIV test, date of ART initiation, year of ART initiation.

The main outcomes of interest were age at first infant HIV test (which was determined from infant date of birth and age at HIV test) and time from diagnosis to treatment initiation (determined from date of HIV positive and date of ART initiation)

3.4.6 EID data cleaning

- Removal of 1,648 entries for infants born before 2006, as these were not in our targeted sample.
- For the outcome 'age at infant HIV testing', 317 entries were erroneously entered as having age at testing < 0 months of age and were excluded from the analysis.
- For the outcome 'time from diagnosis to ART initiation', a total of 21,712 (66.62%) entries had missing data as there was no date of HIV test for most infants.

3.5. Data management

The data was stored separately on the LSHTM computer, personal laptop and H drive. The data were organised in files and folders on these devices. All the devices were secured with a password. Since the data were for educational purposes, they were shared with LSHTM supervisors and the SEARCH project team members. After completion of studies the data will be held in the LSHTM Research Data Repository and retrieved as needed for academic and publishing purposes.

Throughout the qualitative data collection period the researcher kept a field diary, where she documented areas she needed to explore further during the interview or interesting. She also documented any new ideas and insights coming out of interviews held that required additional exploration in subsequent interviews.

3.6 Research ethics

Permission to use SmartCare data was granted by the Zambia Ministry of Health. Permission to collect data from the health facilities was granted by the MoH district offices (*Appendix 4*). The study was approved by the Zambia Biomedical Ethical Board (Ref 101-04-16) (*Appendix 5*) and the LSHTM Research Ethics Committee (Ref 12086) (*Appendix 6*). An Amendment to

add the qualitative component was also approved when the initial quantitative analysis showed a lot of missing data (*Appendix 7*). The researcher met the costs associated with travel and refreshments for the FDGs.

Written informed consent was obtained from all in-depth interview participants including their consent to record the interviews and publish anonymous quotations. Verbal consent was sought for FGD participant upon receipt for a waiver from the Zambia Biomedical Ethical Board (*Appendix 8*). Participation in the study was entirely voluntary and participant anonymity was maintained throughout the processes of interview transcription, data analysis and presentation by using pseudonyms.

Chapter 4: Systematic Literature Review Paper

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646
F: +44 (0)20 7299 4656
www.lshtm.ac.uk

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1405741	Title	Mrs
First Name(s)	Sehlulekile		
Surname/Family Name	Gumede-Moyo		
Thesis Title	Evaluating Implementation of revised (post 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using Routinely Collected Data in Zambia.		
Primary Supervisor	Suzanne Filteau		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Journal of Medicine		
When was the work published?	October 2017		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

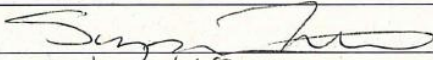
Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

SECTION D – Multi-authored work

<p>For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)</p>	<p>I conceived the idea, carried out the review and wrote the manuscript.</p>
---	---

SECTION E

Student Signature	S Gumede-Moyo
Date	December 2018

Supervisor Signature	
Date	4/12/18

Implementation effectiveness of revised (post- 2010) World Health Organisation guidelines on prevention of mother to child transmission of HIV using routinely collected data in sub-Saharan Africa: A systematic literature review.

Sehlulekile Gumede-Moyo^{1,2} MPH, MBA, BSc; **Suzanne Filteau**¹ PhD, MSc, BSc; **Tendai Munthali**^{2,3} MSc, BA; **Jim Todd**¹ MA, MSc; and **Patrick Musonda**² PhD, MSc.

Corresponding author: Sehlulekile Gumede-Moyo, Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. (sehlulekile.gumede@lshtm.ac.uk).

Abstract

Objective: To synthesise and evaluate the impact of implementing post-2010 World Health Organisation (WHO) prevention of mother-to-child transmission (PMTCT) guidelines on attainment of PMTCT targets.

Methods: Retrospective and prospective cohort study designs that utilised routinely collected data with a focus on provision and utilisation of the cascade of PMTCT services were included. The outcomes included the proportion of pregnant women who were tested during their antenatal clinic (ANC) visits; mother-to-child transmission (MTCT) rate; adherence; retention rate; and loss to follow-up (LTFU).

Results: Of the 1210 references screened, 45 met the inclusion criteria. The studies originated from 14 countries in sub-Saharan Africa. The highest number of studies originated from Malawi (10) followed by Nigeria and South Africa with 7 studies each. More than half of the studies were on Option A whilst the majority of Option B+ studies were conducted in Malawi. These studies indicated a high uptake of HIV testing ranging from 75% in Nigeria to over 96% in Zimbabwe and South Africa. High proportions of CD4 count testing were

¹*Department of Population Health, Faculty of Epidemiology and Population Health, London school of Hygiene and Tropical Medicine, London, UK*

²*School of Public Health, University of Zambia, Lusaka, Zambia*

³*Ministry of Health, Lusaka, Zambia*

reported in studies only from South Africa despite that in most of the countries CD4 testing was a prerequisite to access treatment. MTCT rate ranged from 1.1% to 15.1% and it was higher in studies where data was collected in the early days of the WHO 2010 PMTCT guidelines. During the postpartum period, adherence and retention rate decreased, and LTFU increased for both HIV-positive mothers and exposed infants.

Conclusion: Irrespective of which Option was followed, uptake of antenatal HIV testing was high but there was a large drop off along later points in the PMTCT cascade. More research is needed on how to improve later components of the PMTCT cascade, especially of Option B+ which is now the norm throughout Sub-Saharan Africa.

LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ANC	Ante Natal Care
ART	Antiretroviral therapy
ARV	Antiretroviral
DRC	Democratic Republic of Congo
EID	Early Infant Diagnosis
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
LTFU	Lost to Follow-up
MTCT	Mother-to-child transmission of HIV
NVP	Nevirapine
PMTCT	Prevention of mother-to-child transmission of HIV
UNAIDS	Joint United Nations Program on AIDS
UNFPA	United Nations Population Found
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organisation

4.1 Introduction

The Joint United Nations Program on HIV/AIDS (UNAIDS) over the past two decades has documented the heavy burden and impact of HIV on mothers and infants living in resource-limited settings. Among the 260,000 new paediatric infections of HIV worldwide in 2012, 90% of new cases occurred in Sub-Saharan Africa [1]. The use of antiretroviral therapy (ART) by HIV-positive mothers is the cornerstone of strategies to prevent mother-to-child transmission (PMTCT) during the ante-partum and peri-partum periods and for the duration of breastfeeding [2].

The World Health Organization (WHO) in 2010 revised guidelines and offered two options: Option A and Option B. Under Option A, pregnant women with a $CD4 \geq 350$ cells/ μ L receive ART prophylaxis from 14 weeks gestation through one week postpartum, single-dose Nevirapine at delivery, and daily Lamivudine from delivery through one week postpartum. Their infants receive daily Nevirapine from birth through one week after the cessation of breastfeeding. Women with $CD4 \leq 350$ cells/ μ L or WHO clinical stage 3 or 4 disease are put permanently on triple-drug ART. Under Option B, all women receive triple-drug ART from 14 weeks gestation through the cessation of breastfeeding, and infants receive a daily Nevirapine or Zidovudine dose from birth to 4–6 weeks [2]. In 2013, WHO revised its guidelines for the treatment and prevention of HIV and recommended that all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should continue ART for life known as "Option B+" whilst their infants receive daily Nevirapine or Zidovudine from birth to 4–6 weeks [3]. Option B+ is now a norm in Sub-Saharan Africa, with all the 21 Global Plan countries implementing it except for Nigeria as of October 2015 [4].

Effective PMTCT programmes require women and their infants to receive a cascade of interventions including uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, safe child birth practices and appropriate infant feeding uptake, with infant prophylaxis, HIV testing and other postnatal health care services following delivery [5]. The global community committed to accelerate progress for PMTCT through an initiative whose goals were to eliminate new paediatric HIV infection by 2015 and improve maternal, newborn and child health and survival in the context of HIV [6]. Elimination of new paediatric infections has not been met, so there is a need to investigate why some programs are not effective. This systematic review of the literature was performed to evaluate the impact of implementing the WHO post-2010 PMTCT guidelines in order to inform practices which could help reach PMTCT targets.

4.2 Methods

Data Sources: The following databases were searched for articles published from January 2010 to October 2016: Africa Wide Information, Medline, Embase; and reference lists from publications provided additional articles. The search was limited to English language journals for studies in sub-Saharan Africa. The following search terms and their variations were combined: prevention of mother to child transmission of HIV; PMTCT cascade; PMTCT options; effectiveness of PMTCT; PMTCT Option A; PMTCT Option B; PMTCT Option B+; antiretroviral treatment; ART; antenatal care; Human Immunodeficiency Virus; HIV-exposed infants' health outcomes; infant feeding; early infant diagnosis, adherence; retention in care; loss to follow-up (LTFU).

Study Selection: The searched results were exported using reference management software Endnote 7.3 and duplicates were removed. The titles, abstracts and full texts of potentially relevant studies were reviewed for eligibility. An adapted Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) flow chart was drawn (Flow Diagram). The selected studies had to include data collected post the WHO 2010 PMTCT guidelines. The inclusion criteria were: retrospective and prospective cohort study designs that utilised routinely collected data with a focus on provision and utilisation of the cascade of PMTCT services; studies with particular interest in WHO Option A, B or B+ implementation; studies from countries which had adopted WHO post-2010 PMTCT guidelines during the data collection period, and studies which evaluated implementation of post 2010 PMTCT guidelines. Qualitative studies, randomized controlled trials, reviews, commentaries, editorials and modelling studies were excluded. Two independent reviewers (SGM and TM) reviewed the full text articles for inclusion, exclusion and extracted data on outlined outcomes. Ethical approval was granted from London School of Tropical Medicine and Hygiene Research Ethics Committee (Ref: 12086).

Data Extraction: Data was extracted using a standardised data extraction form which summarised key information from relevant studies. The following information was extracted: proportion of pregnant women who were tested during their antenatal clinic (ANC) visits; proportion of women who tested HIV-positive; proportion of women who were already on ART before pregnancy; proportion of women who received their HIV test results; proportion of women tested for CD4 cell count; type of PMTCT option for mothers and their infants; adherence of women to ART; infant feeding methods; infant age when polymerase chain reaction (PCR) was done; MTCT rate; proportion of infants reported to die or be LTFU as

missing three consecutive clinic visits; and retention rate which is the continuous engagement from diagnosis in a package of prevention, treatment, support and care services. In case of studies where data collection began before 2010 only post 2010 data was extracted.

4.3 Summary of Results

Study Characteristics: A total of 944 potentially eligible full text articles out of 2913 studies based on titles and abstracts were identified. Forty-five met the inclusion criteria (Flow Diagram – Figure 4.1) and they originated from 14 countries in sub-Saharan Africa, (Table 4.1). The highest number of studies originated from Malawi (10) followed by Nigeria and South Africa with 7 studies each. The period of data collection was from 2010 to April 2015. The sample sizes for the selected studies ranged from 113 to 2, 215, 090 participants; the largest sample sizes were from the studies that utilized national data from South Africa and Ghana.

Uptake of ANC services: The data on HIV testing during ANC visits was extracted from 8 studies (Table 4.1) conducted in Malawi [7-9], Nigeria [10, 11], Ghana [12], Zimbabwe [13] and South Africa [14]. These studies indicated a high uptake of HIV testing ranging from 75% in Nigeria to over 96% in Zimbabwe and South Africa. The high uptake of HIV testing could have been attributable to policy changes in integrating HIV testing in ANC and shifting from opt-in to opt-out testing

The proportion of women who were already on ART prior to ANC visits, was reported in six studies, from Malawi [7-9], Zimbabwe [13], Kenya [15] and Zambia [16]. In Zimbabwe only 7% of the women were already on ART during their ANC visits whilst in Malawi, implementation of option B+, resulted in an increase of women who were already on ART before pregnancy [7-9] from 30% before Option B+ to 48% after Option B+ adaptation. In a matched cohort study of Option A and B, in four sites receiving external technical support for the provision of PMTCT-related care in Zambia, 48% of women were already on ART prior to their first ANC visit [16]. Findings are not representative of PMTCT service delivery in Zambia as a whole, since the sites receive technical support for the provision of PMTCT-related care from the Boston University PMTCT Integration Project through the President's Emergency Plan for AIDS Relief (PEPFAR). External support can also influence health facility characteristics and operational aspects of a facility such as capacity, location, staffing and services provided.

Four out of the seven studies that had information on CD4 count testing were from South Africa [17-20] and the rest from Kenya [15], Zambia [16] and Mozambique [21]. The proportion of women who had CD4 testing during ANC visits from Kenya, Zambia and Mozambique was below 60% despite that over the data collection period of these studies, CD4 testing was supposed to be a prerequisite to access care. In South Africa the proportion of women tested for CD4 count increased from 66% in 2010 to 76% in 2012 according to a study that utilised national data. [19]

Exposure to PMTCT options: Thirty-five (78%) studies reported on Option A (Tables 1 and 2) and they were from the 14 representative countries with South Africa contributing seven studies [14, 17-19, 22-24]. Implementation of Option B+ was investigated in Nigeria [25, 26], Malawi [7-9, 27-32], Mozambique [33], Zimbabwe [34] and Ethiopia [35, 36] in 16 studies which were synthesised. The two studies which reported on all three Options (A, B and B+) were conducted in Malawi [29] and Nigeria [25] where the data collection covered a longer period.

Infant outcomes: The MTCT rate was reported in 29 studies (Table 1) and ranged from 1.1% to 15.1%. MTCT rate was high (above 10%) mainly in studies where data was collected in the early days [37-42] of the WHO 2010 PMTCT guidelines although South Africa reported a low MTCT rate of 2% during the same period [20]. In Zambia there was a reduction in MTCT rate from 12% in 2010 [37] to 3% in a retrospective study conducted from 2011 to 2014 [43]. The lowest MTCT rate of 1.1% was reported from Nigeria [26]; however, the author indicated that the study involved HIV-positive women who booked for antenatal care in a tertiary institution, and were likely to be wealthier and more educated than the general population and perhaps more likely to adhere to ART and other PMTCT interventions

Exposure to PMTCT options and MTCT rate: In a study from Cameroon, under option A, the MTCT rate was 3.7% for infant mother pairs who both received prophylaxis; 16.2% when only the mothers received prophylaxis; 12% for mothers without prophylaxis whose infants received Nevirapine, and 31.3% when neither mother or infant received prophylaxis [44]. In Zambia, lower rates of MTCT were associated with both mother and infant receiving prophylaxis: 4.2% compared to 20.1% in a no intervention group at 0-6 weeks [37]. In South Africa, in-utero transmission rate was highest among women who required ART but did not

initiate treatment (8.5%) compared to 2.7% and 0.4% among women who received ART and women who were not eligible for ART and received prophylaxis under option A [14].

In Ethiopia, absence of maternal ART was significantly and independently associated with maternal to child transmission of HIV (AOR = 5.02, 95% CI: 2.43, 10.4) [45].

Results from two studies that compared option A and B+ from Ethiopia [36] and Malawi[8], both confirmed supremacy of option B+ over A in terms of MTCT rate. In Ethiopia, none of the infants whose mothers received option B+ had a positive PCR result whilst the MTCT rate for those under option A was 3.9% [36]. In Malawi the MTCT rate was 2.9% under Option A, 1.9% under Option B+, and 1.1% for infants whose mothers received ART for their own health [8].

Figure 4.2 shows MTCT rates at the end of data collection year and according to which option was used; only studies showing overall MTCT rates, not rates at younger ages when HIV transmission may have been ongoing in a breastfeeding population, are shown. Option A had higher MTCT rates in most of the studies under review; however, most Option A studies preceded the Option B+ studies. The general functions of the PMTCT programs have been improving over time with studies carried out after 2013 showing lower MTCT rates even under Option A.

Timing of ART initiation and MTCT: In Kenya where an MTCT rate of 8.9% was reported, lack of maternal use of ART at the time of delivery was associated with increased risk of MTCT for infants of women who were on Option A and B [15]. In Nigeria MTCT (0.4%) was lower among women on ART before pregnancy compared to women who started ART during pregnancy or delivery which was at 2% [46].

Impact of infant feeding on MTCT: The impact of infant feeding mode was not explored in the analysis of most studies under this review with only 13 studies providing results (Table 4.2). Exclusive breastfeeding is commonly measured through household surveys by asking mothers/caregivers of sample infants less than 6 months of age regarding intake in the previous day and night. However there is a lack of uniformity of methods used for collecting exclusive breastfeeding data in the countries under review. Infant feeding methods were reported in studies from Zambia [37] Malawi [7], DRC [40], Ethiopia [36, 45], Cameroon

[42, 47], Nigeria [26, 46, 48, 49], South Africa [18] and Tanzania[39]. High levels of exclusive breastfeeding were reported, with Malawi reporting that 99% of HIV-exposed infants exclusively breastfed in the first 6 months.

MTCT of HIV was significantly higher with mixed feeding (adjusted odds ratio (aOR): 6.7, 95% CI 1.6-28.3; p=0.009) in Cameroon under Option A exposure [42]. Similarly in Nigeria MTCT was higher for mixed fed infants at 14.2%, compared to 3.73% for exclusively breastfed infant and 2.43% for exclusively formula-fed infants at 18 months [49]. This was consistent with a study in Ethiopia where mixed infant feeding practices were significantly and independently associated with MTCT of HIV (AOR = 4.18, 95% CI: 1.59, 10.99) [45]. Lower rates of MTCT were found in children who never breastfed in Zambia at 2.5% at 0-6 weeks compared to 6.5% those who had been breastfed under Option A exposure [37].

Early Infant diagnosis: Early Infant diagnosis (EID) of HIV by PCR was reported in 20 studies from 8 countries (Table 4.). The uptake of EID ranged from less than 60% in Nigeria [25] and Zambia [37] to 100% in 2012 according to South African national data where it increased from 87% in 2010 [19]. The age at which PCR was done ranged from 4 weeks to 18 months. In South Africa, 80% of exposed infants had PCR results at 6 weeks [24], whereas in Malawi 52% underwent testing at 6–12 weeks and 28% tested at 12 months[31].

Impact of age at first PCR on MTCT: Age at first PCR had an impact on the MTCT of HIV-exposed infants. In Tanzania, the proportion of HIV-infected infants was higher among infants who appeared later for HIV testing (18% at 3–6 months) than among those who presented earlier (6.4% at 1–2 months) under Option A implementation [39]. The Tanzanian observations were in agreement with the Ethiopian study which reported that late enrolment to the exposed infant follow-up clinic was significantly and independently associated with MTCT of HIV (AOR= 2.89, 95% CI: 1.35, 6.21) [45].

ART initiation of HIV-positive infants: ART initiation of HIV-positive infants is a key stage of the PMTCT cascade. In this review it was reported in three studies from DRC[40], Zambia[41] and Nigeria[11]. Among HIV-infected infants in DRC, 97% enrolled in 2011-2012 were initiated on ART; this was an increase from 61% for infants enrolled in 2007-2008 [40]. Lower rates were reported in Zambia where 67% of infants who tested positive started

ART by the end of the study[41] and Nigeria where 75% of HIV-positive infants were initiated on ART[11].

Retention in care: Retention in routine maternal-infant HIV care of HIV exposed infants was explored in three studies from Zambia, Malawi and Rwanda. In Zambia the retention rate of HIV-exposed infants under Option A, at 6 months after delivery was 62% compared to 30% of HIV-unexposed infants under the same ongoing routine care conditions [16]. In Malawi 72% of HIV-exposed infants remained in care after 12 months under Option B+[31], whereas in Rwanda under Option B, infants' 12-month retention was 81% (95% CI: 76%, 86%) [50].

In Malawi, the retention in HIV care of women initiated on Option B+ was 85%, compared to 93% after 2 years among those initiated on ART because of clinical or CD4 cell count criteria [29]. These results were consistent with the findings from Rwanda where mothers eligible for ART for their own health were better retained across all the time periods, 66% (CI: 59%, 73%), compared with those not eligible and receiving ART solely for PMTCT, 47% (CI: 37%, 57%), at 12 months, $p < 0.001$ [50]. Another Malawian study highlighted that initiation of ART on the same day as HIV diagnosis was independently associated with reduced retention in the first 6 months (aOR 2.27; 95% CI: 1.34–3.85; $p = 0.002$) under Option B+ [9].

In a retrospective record review of women presenting to antenatal care or maternal and child health services at 34 health facilities in rural Zimbabwe, retention in ART care after 6 months of Option B+ initiation was 83% [34]. In contrast, retention for Rwandan mothers exposed to option B was 68% at 6 weeks post-delivery, decreasing to 58% by 12 months [50].

Lost to follow up: Data on the magnitude of LTFU (missing three consecutive clinic visits) along the PMTCT cascade was reported in nine studies (Table 4.2) from Malawi [27, 28, 51], Tanzania [38], Kenya [15], Nigeria [10, 25] and Ethiopia [35, 36]. In the studies from Malawi and Ethiopia this was explored in the context of Option B+ whilst in the other countries it was explored under Option A.

In Tanzania [38], 61% of infants receiving treatment were lost to follow up at the time of review, despite the high proportion of guardians and parents who returned for PCR results (92% in 2010 and 98% in 2011). The results were consistent with a study from Malawi where 48% of the HIV-exposed infants were declared LTFU in the database although 96% of the them in the cohort had their PCR test done at 24 months [52]. However, Nigeria reported low rates of LTFU for HIV-infected infants of less than 15% [11, 46] despite that the studies

evaluated different PMTCT options. In Kenya LTFU increased with the age of infants with 9.6 % of enrolled infants not returning for any follow-up care, 26.4 % dropping out by 9 months and 39 % by 18 months of age [15].

In Ethiopia under option B+ implementation, the cumulative proportions of women LTFU at 6, 12 and 24 months were 12%, 15% and 23%, respectively [35]. Similar results were reported in Malawi where cumulative incidence of LTFU by year 2 was 24.5% (95%CI, 23.2%–25.8%) among women who started ART during pregnancy, 20.2% (95% CI, 18.3%–22.2%) among those who started ART while breastfeeding, and 17.0% (95% CI, 15.2%–18.8%) among those who were neither pregnant nor breastfeeding when they started treatment [30].

The independent risk factors for LTFU were younger maternal age at ART initiation, missing CD4 cell count at ART initiation, ART initiation on the same day of diagnosis, and starting ART at hospital [35]. The risk of being LTFU was higher in ‘B+ pregnant’ (adjusted hazard ratio [asHR]: 2.77; 95% CI: 2.18–3.50; $P < 0.001$) and ‘B+ lactating’ (asHR: 1.94; 95% CI: 1.37–2.74; $P < 0.001$) compared to women on ART for their own health in Mozambique [33].

Adherence: Adherence to ART drugs for PMTCT by the mothers, was reported in two studies (Table 4.2) from Malawi [51] and Zambia [43]. Adherence during the postpartum period in Zambia [43] ranged from 71% to 84% at different times postpartum. The results of the study were consistent with the Malawian study where 70% of women exposed to option B+, who started ART during pregnancy and breastfeeding adhered adequately during the first 2 years of ART [30]. However, default and incomplete adherence were more common in the option B+ compared to the Option A in Malawi [51], where 4% of women in the option B+ cohort had less than 95% adherence compared to 2% for the-option A cohort.

4.4 Discussion

The Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive prioritized 21 countries in Sub-Saharan Africa. The studies in the review originated from 14 of the priority countries. The studies show a continued decline in the incidence of HIV among children, as indicated by low MTCT rates, but the target of a 90% reduction by 2015 was not met, reduction in incidence being only 76% in the 21 priority countries (54). South Africa reported low MTCT rates under Option A implementation[24] even from the results of the facility-based cross-sectional study conducted in 2010 [53]. This

could have been as a result of their health system which is better resourced than most of the countries under review.

Many of the studies on the impact of infant feeding methods and exposure to various ART regimens were conducted before the 2010 WHO PMTCT [54, 55]. Although infant feeding results were available from only a minority of studies in this review, the results of the review are in agreement with the findings which led to the current guidelines. In the countries under review breastfeeding is very common, and breastfed infants have an increased risk of MTCT of HIV [56]. Mixed feeding is also a common practice in Sub-Saharan Africa and is an additional risk for postnatal HIV transmission [57]. As revealed by the studies from Tanzania [39] and Ethiopia [45], where there was increase in MTCT over time, continued breastfeeding in the face of low adherence to ART treatment, is a risk.

Option B+ which initiates lifelong ART to all pregnant and breastfeeding women is now widespread in Sub-Saharan Africa, with all the 22 Global Plan countries implementing it except for Nigeria. As of October 2015, Option B+ was being nationally implemented in 14 (Angola, Burundi, Cameroun, Chad, Ethiopia, Kenya, Lesotho, Malawi, South Africa, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe) out of the 21 Countries in Sub-Saharan Africa, and scale-up continues in 6 countries (Botswana, Cote d'Ivoire, DRC, Ghana, Mozambique and Namibia) [4]. In this review, Implementation of Option B+ was investigated in Nigeria [25, 26] , Malawi [7-9, 27-32], Mozambique [33], Zimbabwe [34] and Ethiopia [35, 36]. Most studies came from Malawi since they were the pioneers of this option; hence there is a need to explore the impact of implementing the Option B+ guidelines and identifying missed opportunities along the PMTCT cascade in other countries which have adopted it.

The implementation of Option B+ in Malawi resulted in a five-fold increase in the numbers of pregnant women being enrolled on ART. Nonetheless, default and incomplete adherence were more common in Option B+ implementation [43, 51]. These results were consistent with a qualitative study conducted in Tanzania among mothers who were put on Option B+ during pregnancy who indicated various reasons for poor adherence to ART, which included lack of motivation to continue ART after weaning the child and protecting the child from becoming infected, stigma and poverty [58]. There is also a need to adjust operational practices related to quality of counselling as it has been indicated to be a predictor of adherence to

treatment[59]. Moreover a recent study suggested that retention in all postnatal programs, including those outside the context of HIV is poor globally, elaborating the need for evidence based intervention strategies and further research on the drivers of disengagement.[60]

The retention in care of HIV-infected and lactating mothers under Option B+ was poor and driven by early losses [9, 27-29, 34, 50]. Hence implementation of Option B+ requires that policy makers rethink ways of ensuring optimal adherence to ART for maximal suppression of viral replication and avoidance of drug resistance. One possibility is to explore the use of cell phone SMS which has been found to be useful in Africa for improving the quality of care and follow-up of people with HIV/AIDS [61, 62].

The consolidated guidelines recommend that HIV-exposed infants be tested for HIV between 6-8 weeks, at the end of breastfeeding, and at any point they present with illness[3]. However in the studies under review the retention rate tended to decrease during the post-partum period [16, 27-29, 32]. This reduction in post-partum retention rate implies that HIV-exposed infants will be detached from the health system, thus missing opportunities for PCR testing. A systematic review of mostly Sub-Saharan countries found that about a third of HIV-exposed children in standard PMTCT programs fall out of care in 3 months after delivery and a further 45% stop care after their first HIV test [63]. Furthermore, low rates of infected infants are initiated on ART despite being PCR-tested [32, 38], raising concerns on the benefits of EID and the referral to care and treatment of these infected infants. Similar results were reported by Chatterjee et al, in their descriptive analysis of national EID programs in four countries where only 22% to 38% of infected infants were initiated on ART[64]. There is a need for strategic and technical developments for ensuring that drop-out rates along the PMTCT cascade are minimal.

Limitations of the study

The major limitation of the review is that the results of most of the study findings may not be representative of the general health care systems in the countries reviewed as only two studies from Ghana and South Africa used national data for analysis. There are also profound variations in the implementation of PMTCT programs across countries. For instance, in Nigeria MTCT was reported to be 1.1% [26] which was largely attributed to the study population which comprised wealthier and more educated women than the general

population. There is a research gap of evaluating PMTCT interventions using large cohorts that can be generalizable to the whole population.

The limitations of the data sources of this review are mainly due to the retrospective nature posing problems of incomplete recordings. Moreover, the data used in these studies was originally collected for different purposes from this review and therefore hard to compare data when a lot of time points differ because of different timings of key outcomes. However, the advantage of using routinely collected data is that research will be conducted in a timely and cost-efficient manner as data are already collected and available for analysis [65].

All the studies reported challenges in the documentation of routine services, linkage of HIV diagnosis to care and active follow-up of those enrolled in care. The data collection systems often lack immediacy as many are paper-based with records completed at each facility and collated centrally. This is likely to be a challenge in most Sub-Saharan countries and therefore there is a need to improve management of health information systems through the use of modern technology.

4.5 Conclusion

Irrespective of which Option was followed, uptake of antenatal HIV testing was high but there was a large drop off along later points in the PMTCT cascade. More research is needed on how to improve later components of the PMTCT cascade, especially of Option B+ which is now the norm throughout Sub-Saharan Africa.

There is research gap for studies that investigated the full cascade of interventions that include uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, appropriate infant feeding, uptake of infant HIV testing and other post-natal health care services in the context of the PMTCT Option B+ interventions. In view of the gap there is a need for implementation research evaluating real world effectiveness of the 2010 WHO PMTCT guidelines specifically Option B+.

Authors' affiliations

1. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, United Kingdom;
2. School of Public Health, University of Zambia, Lusaka, Zambia;
3. Ministry of Health, Lusaka, Zambia.

Competing interests

None declared.

Authors' contributions

SGM conceived the idea, carried out the review, and wrote the manuscript. TM and PM appraised the quality of a portion of the included studies for quality control. SF and JT critically reviewed drafts and approved the final manuscript.

Acknowledgements

The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472.

4.6 References

1. UNAIDS. *Global plan towards the elimination of New HIV infections among children by 2015 and keeping their mothers alive*. 2011.
http://www.unaids.org/sites/default/files/media_asset/20110609_JC2137_Global-Plan-Elimination-HIV-Children_en_1.pdf. Accessed on 17 August 2015
2. UNAIDS. *Global HIV/AIDS response epidemic update and health sector progress towards universal access*. 2011.
http://www.unaids.org/sites/default/files/media_asset/20111130_UA_Report_en_1.pdf. Accessed on 17 August 2015
3. UNAIDS. *Countdown to Zero: Global Plan Towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011-2015*. Geneva: 2011.
http://www.unaids.org/sites/default/files/media_asset/20110609_JC2137_Global-Plan-Elimination-HIV-Children_en_1.pdf. Accessed on 17 August 2015.
4. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaC. *Option B+ countries and PMTCT regimen 2015* [cited 2016 17 August 2016]. Available from: <http://emtct-iatt.org/b-countries-and-pmtct-regimen/>
5. Padian, N.S., et al., *HIV prevention transformed: the new prevention research agenda*. Lancet, 2011. **378**(9787): p. 269-78.
6. UNAIDS, *Countdown to Zero: Global Plan Towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011-2015*. 2011: Geneva.
http://www.unaids.org/sites/default/files/media_asset/20121211_Women_Out_Loud_en_1.pdf. Accessed on 22 December 2015.
7. Price, A.J., et al., *Uptake of prevention of mother-to-child-transmission using Option B+ in northern rural Malawi: a retrospective cohort study*. Sexually Transmitted Infections. **90**(4): p. 309-14.
8. Kim Maria H. ; Ahmed Saeed ; Hosseinipour Mina C.; Yu, X.N.C.C., Frank; Paul Mary E.; Kazembe Peter N; Abrams, Elaine J., *The Impact of Option B+ on the Antenatal PMTCT Cascade in Lilongwe, Malawi*. Journal of Acquired Immune Deficiency Syndromes: JAIDS, 2015. **68**(5): p. 77.
9. Chan, A.K., et al., *Same day HIV diagnosis and antiretroviral therapy initiation affects retention in Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi*. J Int AIDS Soc, 2016. **19**(1): p. 20672.
10. Okusanya BO, A.A., Aigere EO, Salawu SE, Hassan R., *Scaling Up Prevention of PMTCT of HIV infection to primary health centres in Nigeria: Findings from two primary health centres in North West Nigeria*. African Journal of Reproductive Health 2013. **17**(4): p. 130-7.
11. Pharr, J.R., et al., *Linkage to Care, Early Infant Diagnosis, and Perinatal Transmission Among Infants Born to HIV-Infected Nigerian Mothers: Evidence From the Healthy Beginning Initiative*. J Acquir Immune Defic Syndr, 2016. **72 Suppl 2**: p. S154-60.
12. P. Dako-Gyeke, B.D., S. Ayisi Addo, M. Atuahene, N. A. Addo, and A. E. Yawson, *Towards elimination of mother-to-child transmission of HIV in Ghana: an analysis of national programme data*. BMC International Journal for Equity in Health, 2016. **15**(5): DOI 10.1186/s12939-016-0300-5.
13. Gonese, E., et al., *Is Zimbabwe ready to transition from anonymous unlinked sero-surveillance to using prevention of mother to child transmission of HIV (PMTCT)*

- program data for HIV surveillance?: results of PMTCT utility study, 2012.* BMC Infect Dis, 2016. **16** (97): DOI 10.1186/s12879-016-1425-2.
14. Akthar Hussain, D.M., Sudhindra Naidoo, Tonya M. Esterhuizen *Pregnant Women's Access to PMTCT and ART Services in South Africa and Implications for Universal Antiretroviral Treatment.* PLoS Med, 2011. **6**(12): p. e27907.
 15. Nduati, E.W., et al., *Outcomes of prevention of mother to child transmission of the human immunodeficiency virus-1 in rural Kenya-a cohort study.* BMC Public Health, 2015. **15**(1): p. 1008.
 16. Scott, C.A., et al., *Uptake, outcomes, and costs of antenatal, well-baby, and prevention of mother-to-child transmission of HIV services under routine care conditions in Zambia.* PLoS One, 2013. **8**(8): p. e72444.
 17. Schnippel K, M.C., Long LC, Larson BA., *Delays, interruptions, and losses from prevention of mother-to child transmission of HIV services during antenatal care in Johannesburg, South Africa: a cohort analysis.* BMC Infect Dis 2015 **6**(15).
 18. Technau, K.G., et al., *Timing of maternal HIV testing and uptake of prevention of mother-to-child transmission interventions among women and their infected infants in Johannesburg, South Africa.* J Acquir Immune Defic Syndr, 2014. **65**(5): p. e170-8.
 19. S Bhardwaj , P.B., Y Pillay , L Treger-Slavin, P Robinson, A Goga, G Sherman, *Elimination of mother-to-child transmission of HIV in South Africa: Rapid scale-up using quality improvement.* South African Medical Journal, 2014. **104**(3).
 20. Hussain, A., et al., *Pregnant women's access to PMTCT and ART services in South Africa and implications for universal antiretroviral treatment.* PLoS One, 2011. **6**(12): p. e27907.
 21. Gimbel, S., et al., *What does high and low have to do with it? Performance classification to identify health system factors associated with effective prevention of mother-to-child transmission of HIV delivery in Mozambique.* J Int AIDS Soc, 2014. **17**: p. 18828.
 22. Moodley, P., R. Parboosing, and D. Moodley, *Reduction in perinatal HIV infections in KwaZulu-Natal, South Africa, in the era of more effective prevention of mother to child transmission interventions (2004-2012).* J Acquir Immune Defic Syndr, 2013. **63**(3): p. 410-5.
 23. Sherman, G.G., et al., *Laboratory information system data demonstrate successful implementation of the prevention of mother-to-child transmission programme in South Africa.* S Afr Med J, 2014. **104**(3 Suppl 1): p. 235-8.
 24. M Ibeto, J.G., V Cox, *Closing the gaps: Steps towards elimination of mother-to-child transmission of HIV.* Southern African Journal of HIV Medicine, 2014. **15**(3): p.107-109.
 25. Rawizza, H.E., et al., *Loss to Follow-Up within the Prevention of Mother-to-Child Transmission Care Cascade in a Large ART Program in Nigeria.* Curr HIV Res, 2015. **13**(3): p. 201-9.
 26. II Okafor, E.U., SN Obi, and BU Odugu, *Virtual Elimination of Mother-to-Child Transmission of Human Immunodeficiency Virus in Mothers on Highly Active Antiretroviral Therapy in Enugu, South-Eastern Nigeria.* Annal of Medicinal Health Sciences Research, 2014. **4**(4): p. 615-618.
 27. Tweya, H., et al., *Understanding factors, outcomes and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi.* Trop Med Int Health, 2014. **19**(11): p. 1360-6.
 28. Tenthani, L., et al., *Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ('Option B+') in Malawi.* Aids, 2014. **28**(4): p. 589-98.

29. Koole, O., et al., *Improved retention of patients starting antiretroviral treatment in Karonga District, northern Malawi, 2005-2012*. J Acquir Immune Defic Syndr, 2014. **67**(1): p. e27-33.
30. Andreas D. Haas, M.T.M., Matthias Egger, Lyson Tenthani, Hannock Tweya, Andreas Jahn, Oliver J. Gadabu, Kali Tal, Luisa Salazar-Vizcaya, Janne Estill, Adrian Spoerri, Nozgechi Phiri, Frank Chimbandira, Joep J. van Oosterhout, and Olivia Keiser, *Adherence to Antiretroviral Therapy During and After Pregnancy: Cohort Study on Women Receiving Care in Malawi's Option B+ Program*. Clinical Infections, 2016. **63**(9): p. 1227-1235.
31. G. Martínez Pérez, C.M., D. Garone, R. Coulborn, A. D. Harries, B. Hedt-Gauthier, M. Murowa, G. S. Mwenelupembe, R. Van den Bergh, and L. Triviño Durán, *HIV testing and retention in care of infants born to HIV- infected women enrolled in 'Option B+' , Thyolo, Malawi*. Public Health Action. , 2014. **4**(2): p. 102-104.
32. Ng'ambi, W.F., et al., *Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012-2014*. Trop Med Int Health, 2016. **21**(8): p. 995-1002.
33. Llenas-Garcia, J., et al., *Retention in care of HIV-infected pregnant and lactating women starting ART under Option B+ in rural Mozambique*. Trop Med Int Health, 2016. **21**(8): p. 1003-1012.
34. Dzangare, J., et al., *HIV testing uptake and retention in care of HIV-infected pregnant and breastfeeding women initiated on 'Option B+' in rural Zimbabwe*. Trop Med Int Health, 2016. **21**(2): p. 202-9.
35. Mitiku, I., et al., *Factors associated with loss to follow-up among women in Option B+ PMTCT programme in northeast Ethiopia: a retrospective cohort study*. J Int AIDS Soc, 2016. **19**(1): p. 20662.
36. Tolessa Olana, T.B., Walelign Worku and Birkneh Tilahun Tadess, *Early infant diagnosis of HIV infection using DNA-PCR at a referral center: an 8 years retrospective analysis* BMC AIDS Research and Therapy 2016. **13**(29).
37. Torpey, K., et al., *Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia*. PLoS One, 2012. **7**(8): p. e42859.
38. Mercy G Chiduo, B.P.M., Zahra P Theilgaard, C Bygbjerg, Jan Gerstoft, Martha Lemnge and Terese L Katzenstein *Early infant diagnosis of HIV in three regions in Tanzania; successes and challenges*. BMC Public Health 2013. **13**(910).
39. Mwendu, E.M., et al., *Effectiveness of prevention of mother-to-child HIV transmission programmes in Kilimanjaro region, northern Tanzania*. Trop Med Int Health, 2014. **19**(3): p. 267-74.
40. Feinstein L, E.A., Chalachala JL, Okitolonda V, Lusiana J, Van Rie A, Chi BH, Cole SR, Behets F., *Temporal changes in the outcomes of HIV-exposed infants in Kinshasa, Democratic Republic of Congo during a period of rapidly evolving guidelines for care (2007-2013)*. AIDS, 2014. **28**(3): p. 301-11.
41. Catherine G. Sutcliffe , J.H.v.D., Francis Hamangaba, Felix Mayani, William J. Moss, *Turnaround Time for Early Infant HIV Diagnosis in Rural Zambia: A Chart Review*. PLoS ONE 2014. **9**(1): p. e87028.
42. Jean Jacques N Noubiap, A.B., Sylvie Agokeng, *Mother-to-child transmission of HIV: findings from an Early Infant Diagnosis program in Bertoua, Eastern Cameroon*. The Pan African Medical Journal, 2013. **15**(65).
43. Sumiyo Okawa, M.C., Naoko Ishikawa, Henry Kapyata, Charles Yekha Msiska, Gardner Syakantu, Shinsuke Miyano, Kenichi Komada, Masamine Jimba and Junko Yasuoka, *Longitudinal adherence to ART drugs for PMTCT of HIV in Zambia*. BMC Pregnancy and Child Birth, 2015. **15**(1).

44. Saounde Temgoua, E.M., et al., *HIV-1 Early Infant Diagnosis is an Effective Indicator of the Prevention of Mother-to-Child Transmission Program Performance: Experience from Cameroon*. *Curr HIV Res*, 2015. **13**(4): p. 286-91.
45. Koye, D.N. and B.M. Zeleke, *Mother-to-child transmission of HIV and its predictors among HIV-exposed infants at a PMTCT clinic in northwest Ethiopia*. *BMC Public Health*, 2013. **13**: p. 398.
46. Sagay, A.S., et al., *Mother-to-Child Transmission Outcomes of HIV-Exposed Infants Followed Up in Jos North-Central Nigeria*. *Curr HIV Res*, 2015. **13**(3): p. 193-200.
47. Edith Michele Saounde Temgoua, C.N.N., Anne Cecile Zoung-Kanyi Bissek, Joseph Fokam, Serge Clotaire Billong, Samuel Martin Sosso, Charlotte Tangipumdu, Elise Lobe Elong, Irene Domkan and Vittorio Colizzi, *HIV-1 Early Infant Diagnosis is an Effective Indicator of the Prevention of Mother-to-Child Transmission Program Performance: Experience from Cameroon*. *Current HIV Research* 2016. **13**(4): p. 286 - 291.
48. SB Banwat, N.O., A Auta, S Omale, *Anti retroviral drug prophylaxis in prevention of mother-to-child transmission of HIV infection in a treatment centre in Jos, Nigeria*. *Journal of Pharmacy and Bioresources*, 2015. **11**(2): p. 93-100.
49. Anigilaje, E.A., et al., *HIV-free survival according to the early infant-feeding practices; a retrospective study in an anti-retroviral therapy programme in Makurdi, Nigeria*. *BMC Infect Dis*, 2015. **15**: p. 132.
50. Woelk G.B., N.D., Behan S., Mukaminega M., Nyirabahizi E., Hoffman H.J., Mugwaneza P., Ribakare M., Amzel A., Ryan Phelps B, *Retention of mothers and infants in the prevention of mother-to-child transmission of HIV programme is associated with individual and facility-level factors in Rwanda*. . Woelk G.B., Ndatimana D., Behan S., Mukaminega M., Nyirabahizi E., Hoffman H.J., Mugwaneza P., Ribakare M., Amzel A., Ryan Phelps B, 2016. **19**.
51. Kamuyango, A.A., et al., *One-year outcomes of women started on antiretroviral therapy during pregnancy before and after the implementation of Option B+ in Malawi: A retrospective chart review*. *World J AIDS*, 2014. **4**(3): p. 332-337.
52. Wingston F. Ng'ambi, S.A., Anthony D. Harries, Dalitso Midiani, Philip Owiti, Kudakwashe C.Takarinda, Salem Gugsa and Sam Phiri, *Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012–2014*. *Tropical Medicine and International Health*, 2016. **21**(8): p. 995–1002 august 2016.
53. Goga, A.E., et al., *First population-level effectiveness evaluation of a national programme to prevent HIV transmission from mother to child, South Africa*. *J Epidemiol Community Health*, 2015. **69**(3): p. 240-8.
54. World Health Organization. *New data on the prevention of mother-to-child transmission of HIV and their policy implications: conclusions and recommendations. Technical Consultation on behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV*. Geneva: WHO, 2001. http://apps.who.int/iris/bitstream/10665/66851/1/WHO_RHR_01.28.pdf. Accessed on 20 September 2015.
55. Little, K.M., et al., *A review of evidence for transmission of HIV from children to breastfeeding women and implications for prevention*. *Pediatr Infect Dis J*, 2012. **31**(9): p. 938-42.
56. Coutsooudis, A., et al., *Late postnatal transmission of HIV-1 in breast-fed children: an individual patient data meta-analysis*. *J Infect Dis*, 2004. **189**(12): p. 2154-66.
57. Iliff, P.J., et al., *Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival*. *Aids*, 2005. **19**(7): p. 699-708.

58. Ngarina, M., et al., *Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania*. BMC Public Health, 2013. **13**: p. 450.
59. Haftamu Ebuy, H.Y., Mussie Alemayehu, *Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, Northern Ethiopia* International Journal of Infectious Diseases 2015. **33**: p. 123-129.
60. Myer, L. and T.K. Phillips, *Beyond "Option B+": Understanding Antiretroviral Therapy (ART) Adherence, Retention in Care and Engagement in ART Services Among Pregnant and Postpartum Women Initiating Therapy in Sub-Saharan Africa*. J Acquir Immune Defic Syndr, 2017. **75 Suppl 2**: p. S115-S122.
61. Mark J. Siedner, D.S., Alexander J. Lankowski, Michael Kanyesigye, Mwebesa B. Bwana, Jessica E. Haberer and David R. Bangsberg, *A combination SMS and transportation reimbursement intervention to improve HIV care following abnormal CD4 test results in rural Uganda: a prospective observational cohort study*. BMC Medicine for Global Health 2015. **13**(160): p. DOI 10.1186/s12916-015-0397-1.
62. Larry W Chang, V.N.-C., Sheila Kalenge, Jack F Kelly, Robert C Bollinger, and Stella Alamo-Talisuna, *Perceptions and acceptability of mHealth interventions for improving patient care at a community-based HIV/AIDS clinic in Uganda: a mixed methods study*. AIDS Care, 2014. **25**(7): p. 874–880.
63. Sibanda, E.L., et al., *The magnitude of loss to follow-up of HIV-exposed infants along the prevention of mother-to-child HIV transmission continuum of care: a systematic review and meta-analysis*. AIDS, 2013. **27**(17): p. 2787-97.
64. Chatterjee, A., et al., *Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries*. BMC Public Health, 2011. **11**: p. 553.
65. Grzeskowiak, L.E., A.L. Gilbert, and J.L. Morrison, *Methodological challenges in using routinely collected health data to investigate long-term effects of medication use during pregnancy*. Therapeutic advances in drug safety, 2012: 4(1): p. 27-37.
66. Bannink-Mbazzi F, L.-Z.M., Ojom L, Kabasomi SV, Esiru G, Homsy J., *High PMTCT program Uptake and coverage of mother , their partners, and babies in Northern Uganda: achievements and lesson learnt over 10 years of implementation (2002-2011)*. Journal of Acquired Immune Deficiency Syndromes, 2013. **62**(5): p. 138-45.
67. Julie N. Mugerwa, Z.N., Adeodata Kekitiinwa, Albert Maganda, Racheal Ayanga, Ayoub Kakande, Joyce Matovu, Josaphat Byamugisha, Godfrey Esiru, Mary G. Fowler *PMTCT, Makerere University-Johns Hopkins Research Collaboration *Early Infection Among Ugandan HIV-Exposed Infants Whose Mothers Received Option B+ vs Option A*, in *International Antiviral Society -USA*. 2014: March 3-6, 2014 | Boston, Massachusetts.

4.7 Table and Figure Legends

Table 4.1

Abbreviations used: ANC = antenatal clinic; EID = early infant diagnosis; MTCT = mother to child HIV transmission; LTFU = lost to follow-up

Option A - pregnant women with a $CD4 \geq 350$ cells/ μ L receive ART prophylaxis including daily Zidovudine from 14 weeks gestation through one week postpartum, single-dose Nevirapine at delivery, and daily Lamivudine from delivery through one week postpartum. Their infants receive daily Nevirapine from birth through one week after the cessation of breastfeeding. Women with women with $CD4 \leq 350$ cells/ μ L or WHO clinical stage 3 or 4 disease are put permanently on triple-drug ART regardless of symptoms.

Option B- all women receive triple-drug ART from 14 weeks gestation through the cessation of breastfeeding, and infants receive a daily Nevirapine or Zidovudine dose from birth to 4–6 weeks.

Option B+ - all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should continue ART for life.

Table 4.2

Abbreviations used: ART=antiretroviral therapy; LTFU=lost to follow-up

Retention rate - the continuous engagement from diagnosis in a package of prevention, treatment, support and care services;

Lost to follow-up - missing three consecutive clinic visits;

Figure 4.1

Abbreviations used; MTCT = mother to child HIV transmission;

Key – The numbers in brackets are study references and the points are the MTCT rate.

Figure 4. 1: PRISMA Chart

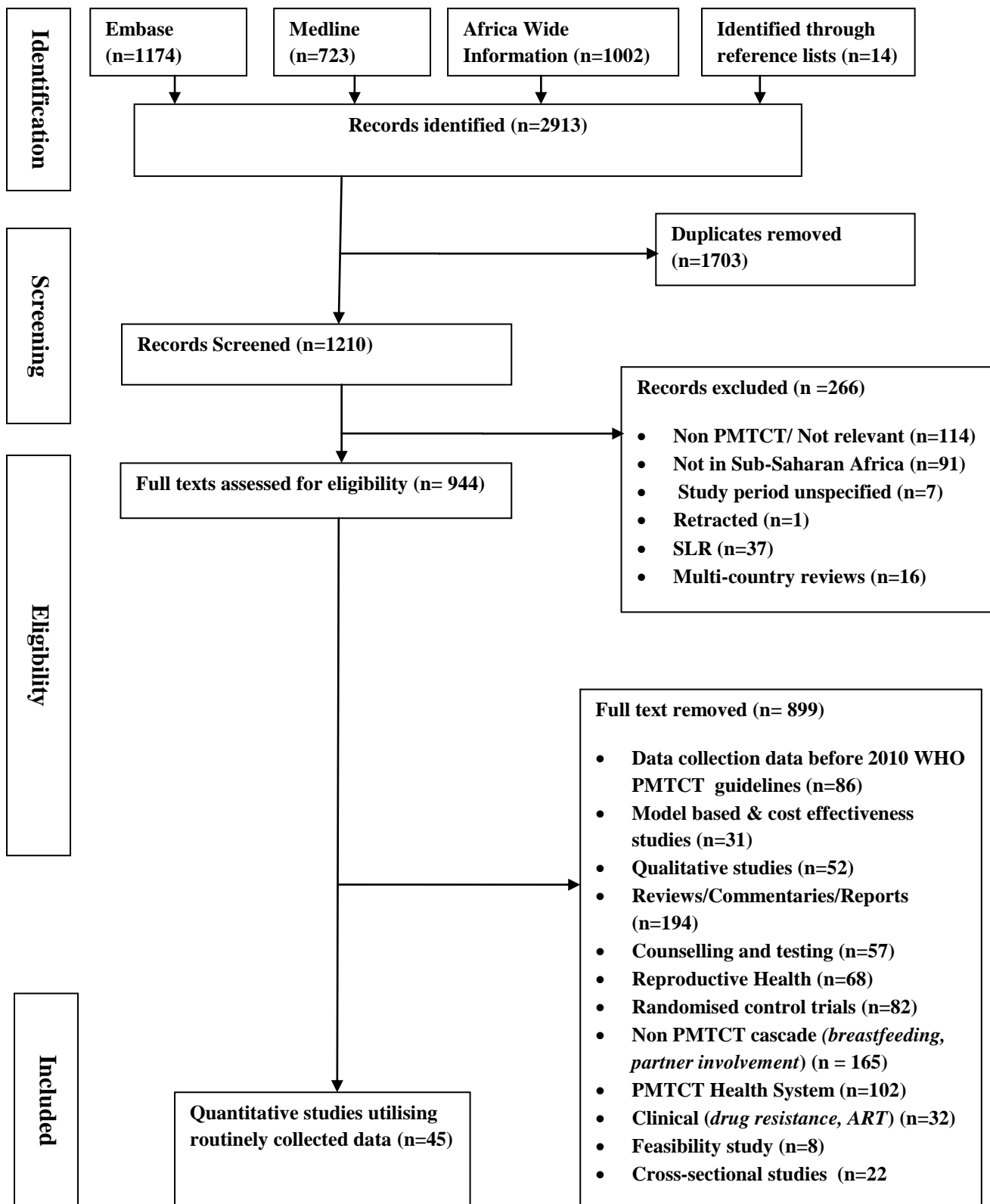
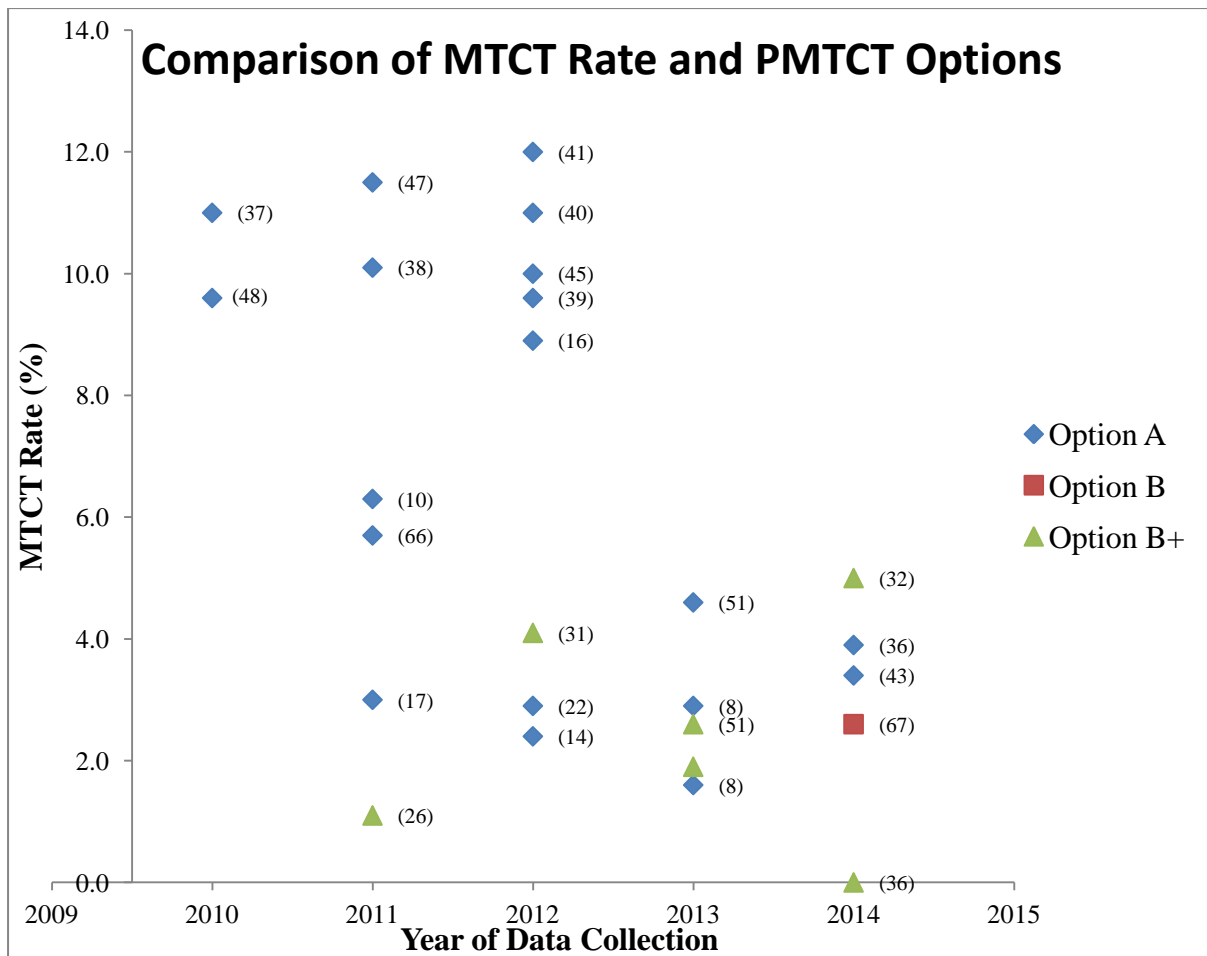


Figure 4. 2: Comparison of MTCT Rate and PMTCT Option



Key – The numbers in brackets are study references and the points are the MTCT rate across different time periods. The country of study origin of the studies are indicated in Table 4.1

NB// some of the studies such as reference 8 and 36 reported MTCT rates of more than 1 PMTCT options

Table 4.1: Uptake of PMTCT services and Infant outcomes¹

Author	Data collection Period	Country	Tested for HIV during ANC Visit	Infant Feeding methods	Early Infant Diagnosis (EID)	Infant outcomes
Option A Studies						
Temgoua et al [47]	2010-2011	Cameroon	23%	31.9% were exclusively breastfed, 35.9% were formula fed, 14.4% were mixed fed.	12.6% at ≤6 weeks, 61.1% at >6 weeks -6 months, 26.3% at >6 months,	Overall MTCT rate was 11.5% MTCT rate was 3.7% for infant mother pairs who received prophylaxis; 16.2% for mothers who received prophylaxis and baby without ART; 12% for mother without prophylaxis and infant with Nevirapine and 31.3% for mother baby pair without prophylaxis and Nevirapine
Noubiap et al [42]	2010	Cameroon		44.6% were exclusively breastfed, 33% were formula fed, 22.4% were mixed fed.	71.4% at ≤ 6 months 28.8 % at >6 months.	Overall MTCT rate 11.6%. MTCT increased with mixed feeding (aOR: 6.7, 95% CI 1.6-28.3; p=0.009 MTCT increased if EID at > 6 months compared with ≤6 months (aOR: 6.5, 95% CI 1.4-29.3; p=0.014).
Feinstein et al [40]	2007-2012	DRC		94.4% were exclusively breastfed in 2011-2012	63% by 2 months in 2011–2012	MTCT rate 11%. 3% dead by 18 months. Among HIV-infected infants, 97% were initiated on ART.
Dako-Gyeke et al [12]	2011-2013	Ghana	2011 - 83% 2012 - 76% 2013 - 75%			
Banwat, et al [48]	2009 - 2010	Nigeria		80.3% were exclusively breastfed		MTCT rate 9.6%.
Okusanya et al [10]	2010 - 2011	Nigeria	97.3%			MTCT rate 6.3%.
Anigilaje et al [49]	2008 - 2011	Nigeria		24.5% were exclusively breastfed, 67.9% were formula fed, 7.6 % were mixed fed		MTCT rates at 18 months were 3.73% for exclusively breastfed infants, 2.43% for exclusively formula fed infants and 14.2% for mixed fed and MF respectively.

Author	Data collection Period	Country	Tested for HIV during ANC Visit	Infant Feeding methods	Early Infant Diagnosis (EID)	Infant outcomes
Moodley et al [22]	2004 - 2012	South Africa			97.4% at 4-8 weeks	MTCT rate was 2.9% by 2012
Bhardwaj et al [19]	2010 - 2012	South Africa			87% in 2010, 93% in 2011, 100% in 2012.	
Hussain et al [14]	2010	South Africa	99.2%		58.9% at birth	MTCT rate 2.4% in-utero transmission rate was highest among women who required ART but did not initiate treatment (8.5%) compared to 2.7% and 0.4% among women who received ART and women who were not eligible for ART and received PMTCT
Schnippel et al [17]	2012 - 2013	South Africa				
Technau et al [18]	2011	South Africa	92%	51% were exclusively breastfed; 13% were formula fed 36% were mixed fed		
Sherman et al [23]	2003 - 2012	South Africa			73% at 6 weeks	MTCT rate was 2.4%
Ibeto et al [24]	2012 - 2013	South Africa			80% at 6 weeks	MTCT rate was 1.6%
Chiduo et al [38]	2009-2011	Tanzania			91.5% in 2010, 97.8% in 2011	MTCT rate of 9.21 % in 2010 and 10.1% in 2011
Mwendo et al [39]	2009- 2012	Tanzania		88.6% were exclusively breastfed; 7.1% were formula fed 3.9% were mixed fed	77.7% at 1-2months, 16.8% at 3-6 months, 5% at 7-12 months,	Overall MTCT rate 9.6% The proportion of HIV-infected infants was higher among infants who appeared later for HIV testing (18% at 3–6 months) than among those who presented earlier (6.4% at 1–2 months).
Bannik- Mbazzi et al [66]	2002 - 2011	Uganda	2010 - 95.5% 2011 - 96%			MTCT rate of 5.7% in 2010, and 6.1% 2011
Scott et al [16]	2011	Zambia				MTCT rate was 3%

Author	Data collection Period	Country	Tested for HIV during ANC Visit	Infant Feeding methods	Early Infant Diagnosis (EID)	Infant outcomes
Torpey et al [37]	2007- 2010	Zambia		86.4% were ever breastfed; 56.8% were exclusively breastfed; 22% were mixed fed	22.4% between 0-6 weeks, 59.1% between 6 weeks- 6months, 59.1% between 6 12months.	MTCT rate was 11% in 2010 Lower rates of positive PCR results were associated with 1) both mother and infant receiving prophylaxis, 2) children never breastfed and 3) mother being 30 years old or greater
Gonese et al [13]	2012	Zimbabwe	96%			
Option A and B Studies						
Koye and Zeleke [45]	2012	Ethiopia		78.8% were exclusively breastfed; 13.3% were formula fed; 7.9% were mixed fed		MTCT rate was 10 % Late enrolment to the exposed infant follow up clinic (AOR = 2.89), rural residence (AOR = 5.05), home delivery (AOR = 2.82), absence of maternal ART(AOR = 5.02) and mixed infant feeding practices (AOR = 4.18, 95) were significantly and independently associated with maternal to child transmission of HIV
Nduati et al [15]	2006 - 2012	Kenya				MTCT rate was 8.9 % in 2012 Age at enrolment, nutritional status, residential distance from the hospital and mothers' HAART status at the time of delivery were independently associated with MTCT of HIV infection.
Sutcliffe et al [41]	2010 - 2012	Zambia			98% of the infants	MTCT rate 12%
Okawa et al [43]	2011 - 2014	Zambia			80.4 % of infants	MTCT rate of 3.4 %
Option A, B and B+ Studies						
Rawizza et al [25]	2004 - 2014	Nigeria			Median age - 1.6 months; was available for 53% of their infants	MTCT for infants whose mothers received any antenatal and/or delivery care was 2.8% versus 20.0% if their mother received none.
Option A and B+ Studies						

Author	Data collection Period	Country	Tested for HIV during ANC Visit	Infant Feeding methods	Early Infant Diagnosis (EID)	Infant outcomes
Olana et al[36]	2006 - 2014	Ethiopia		79% were exclusively breastfed 14.6% exclusive replacement 4.7 % were mixed fed	Done for 66.7%	Overall MTCT rate of 4.3% MTCT rate for infants who received Option B+ - 0 % MTCT rate for mother and infant receiving prophylaxis was 3.9%.
Kamuyango et al [51]	2009 - 2013	Malawi	94%		82 % at 7.6 weeks under Option A; Under Option B+, 86.5 % at 6.9 weeks	MTCT rate was 4.6 % under Option A, and 2.6 % under Option B+.
Kim et al [8]	2010 - 2013	Malawi				MTCT rate under Option A - 2.9, 1.9% in infants born to mothers who received Option B+ and 1.1% for infants with mothers received ART for their own health.
Option B Studies						
Mugerwa et al [67]	2010 - 2014	Uganda		73.4% exclusively breastfed; 26.6% exclusive replacement		MTCT rate of 2.6%; MTCT was lower among women on ART before pregnancy compared to women who started ART during pregnancy or delivery
Option B+ Studies						
Price et al [7]	2011 - 2013	Malawi	90%	98.8% were breastfed	6.4% at 6-8 weeks; 9.5% of at 9 weeks; Not done for 73% of the infants and unknown for 11.1%	
Chan et al [9]	2011- 2012	Malawi	81%			
Martínez Pérez et al [31]	2011 - 2012	Malawi			80.3% underwent 52.0% at 6–12 weeks, 28.1% at 12 months	MTCT rate was 4.1% and all had been started on ART by the age of 12 months
Ngambi et al [32]	2012-2014	Malawi		43% were exclusively breastfed; 50% were mixed fed;	89% at 6 weeks, and 96% at 24 months	MTCT rate was 5% for tested at 6 weeks and 8% for those tested at 24 months

Author	Data collection Period	Country	Tested for HIV during ANC Visit	Infant Feeding methods	Early Infant Diagnosis (EID)	Infant outcomes
				4% stopped breastfeeding before registration		
Okafor et al (24)	2009-2011	Nigeria		91.8% were exclusively breastfed; 5.5% were mixed fed; 2.7% formula fed		MTCT rate of 1.1% at 18 months
Pharr et al [11]	2013	Nigeria	75%		Done for 71% of infants	
Dzangare et al [34]	2014.	Zimbabwe	95%			

¹ Abbreviations used: ANC, antenatal clinic; EID, early infant diagnosis; MTCT, mother to child HIV transmission; LTFU, lost to follow-up

Table 4.2: Retention rate, Adherence and Magnitude of Loss to follow up (LTFU) ^{1,2}

Author	Data collection Period	Country	Retention Rate	Loss to Follow Up (LTFU)	Adherence to ART
Option A Studies					
Okusanya et al [10]	2010 – 2011	Nigeria		30% of HIV infected mothers and 25% of exposed infants LTFU	
Chiduo et al [38]	2009-2011	Tanzania		61% of infants LTFU	
Scott et al [16]	2011	Zambia	62% of HIV exposed were retained in care compared to 30% of comparison unexposed		
Option A and B Studies					
Nduati et al [15]	2006 – 2012	Kenya		9.6 % of enrolled infants did not return for any follow-up care, 39.0% were lost to follow-up before 18 months of age; 26.4% LTFU at 9 months, 39% at 18 months	
Sutcliffe et al [41]	2010 – 2012	Zambia	86% of caregivers returned for results and 67% of infants who tested positive started ART by the end of the study		
Okawa et al [43]	2011 – 2014	Zambia			ART adherence 82.5 % during pregnancy, 84.2 % at 1 week postpartum, 81.5 % at 6 weeks, and 70.5 % at 24 weeks.
Option A, B and B+ Studies					
Koole et al [29]	2005 – 2012	Malawi	Women who started ART because of Option B+ had retention rate of 85% compared to 93% among women of child bearing age initiated on ART because of clinical or CD4 cell count criteria.		

Author	Data collection Period	Country	Retention Rate	Loss to Follow Up (LTFU)	Adherence to ART
Rawizza et al [25]	2004-2014	Nigeria	66% of the women completed the entire cascade of services including antenatal, delivery and at least one infant follow up visit.	21% prior to delivery care with a further 16% lost prior to first infant visit.	
Option A and B+ Studies					
Kamuyango et al [51]	2009 – 2013	Malawi		Pregnant women were likely to be lost to follow up compared to non pregnant women initiating therapy for disease stage or CD4 count	Default and incomplete adherence were more common in the Option B+ cohort than under Option A
Kim et al [8]	2010 – 2013	Malawi		High LTFU rate at 6-8weeks; 22% were lost to follow-up care and treatment.	
Option B Studies					
Sagay et al [46]	2009 - 2011	Nigeria		14.1% of the HIV exposed infants were LTFU between birth and 18 months	
Woelk et al [50]	2010 – 2012	Rwanda	Women 58% (95% CI: 52%, 64%) were retained 12 months post-delivery, Infants' 12-month retention was 81% (95% CI: 76%, 86%).	Overall, the majority of loss to retention was observed in the 30 days after antenatal registration.	
Option B+ Studies					
Mitiku et al [35]	2013-2015	Ethiopia		The cumulative proportion of patients LTFU at 6, 12 and 24 months after ART initiation was 11.9% (95% CI: 8.9, 16.0%), 15.7% (95% CI: 12.0, 20.4%) and 22.5% (95%CI: 17.3, 29.2%), respectively. Overall 16.5% were LTFU	
Tenthani et al [28]	2011- 2012	Malawi	82.2 % at 6 months postnatal	17.1% LTFU, Six months after initiation 23.9 % in all Option B+ patients who started ART while pregnant	
Chan et al [9]	2011- 2012	Malawi	Initiation of ART on the same day as HIV diagnosis was independently associated with reduced retention in the first six months (aOR 2.27; 95% CI: 1.34–3.85; $p=0.002$).		

Author	Data collection Period	Country	Retention Rate	Loss to Follow Up (LTFU)	Adherence to ART
Haas et al [30]	2011 – 2013	Malawi		The cumulative incidence of LTF by year 2 was 24.5% (95% CI, 23.2%–25.8%) among women who started ART during pregnancy, 20.2% (95% CI, 18.3%–22.2%) among those who started ART while breastfeeding, and 17.0% (95% CI, 15.2%–18.8%) among those who were neither pregnant nor breastfeeding when they started treatment.	70% of women who started ART during pregnancy and breastfeeding adhered adequately during the first 2 years of ART
Tweya et al [27]	2011 – 2013	Malawi	85% at 3mths; 82% at 6mths; 79% at 12mths	20% of these 47% collected ARVs and did not return; 12% collected at 2 visits; 9% at 3 visits and 32% at 4 or more visits	
Martínez Pérez et al [31]	2011 – 2012	Malawi	71.7% of the exposed infants remained in care at 12 months.		
Ngambi et al [32]	2012-2014	Malawi		Overall, 48% of HIV-exposed infants were declared lost-to-follow-up in the database.	
Llenas-García et al [33]	2013 – 2014	Mozambique		48.5% of Option B+ women were LTFU. The risk of being lost to follow-up was higher in pregnant' (adjusted sub hazard ratio [asHR]: 2.77; 95% CI: 2.18–3.50; P < 0.001) and lactating' (asHR:1.94; 95% CI: 1.37–2.74; P < 0.001	
Pharr et al [11]	2013	Nigeria		13% of the enrolled infants were LTFU	
Dzangare et al [34]	2014	Zimbabwe	Retention in ART care after 6 months of Option B+ initiation was 82.6%		

¹ definitions: retention rate - the continuous engagement from diagnosis in a package of prevention, treatment, support and care services; lost to follow-up - missing three consecutive clinic visits;

1 ART=antiretroviral therapy; LTFU=lost to follow-up.

Chapter 5: Quantitative paper using ANC services data set



London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646
F: +44 (0)20 7299 4656
www.lshtm.ac.uk

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1405741	Title	Mrs
First Name(s)	Sehlulekile		
Surname/Family Name	Gumede-Moyo		
Thesis Title	Evaluating Implementation of revised (post 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using Routinely Collected Data in Zambia.		
Primary Supervisor	Suzanne Filteau		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	Frontiers in Public Health
Please list the paper's authors in the intended authorship order:	Sehlulekile Gumede-Moyo; Jim Todd; Ab Schaap; Paul Mee; and Suzanne Filteau
Stage of publication	Submitted

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I extracted, analysed the data and wrote the initial draft of the manuscript with guidance from supervisors.
--	--

SECTION E

Student Signature	S Gumede-Moyo
Date	December 2018

Supervisor Signature	
Date	4/12/18

Evidence that an increasing proportion of HIV-infected pregnant Zambian women attending ANC are already on ART: Analysis using routinely collected data (2010-2015)

Sehlulekile Gumede-Moyo (MPH, MBA, BSc)^{1,2§}; **Jim Todd** (MA, MSc)¹; **Ab Schaap** (MSc, MA)^{1,3} **Paul Mee** (PhD, MSc, BSc)¹ and **Suzanne Filteau** (PhD, MSc, BSc)¹

1. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK
2. School of Public Health, University of Zambia, Lusaka, Zambia
3. ZAMBART, University of Zambia, School of Medicine

[§]Corresponding author: Sehlulekile Gumede-Moyo. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. (sehlulekile.gumede@lshtm.ac.uk).

Email addresses of authors:

SGM: sehlulekile.gumede@lshtm.ac.uk

JT: jim.todd@lshtm.ac.uk

AB: ab.schaap@lshtm.ac.uk

PM: paul.mee@lshtm.ac.uk

SF: suzanne.filteau@lshtm.ac.uk

Key words: ANC, PMTCT, ART, pregnant, HIV- infected, coverage,

Abstract

Introduction: Accurate estimates of coverage of prevention of mother-to-child (PMTCT) services among HIV-infected pregnant women are vital for monitoring progress towards HIV elimination targets. The achievement of high coverage and uptake of services along the PMTCT cascade is crucial for national and international mother-to child transmission (MTCT) elimination goals. In eastern and southern Africa, MTCT rate fell from 18% of infants born to mothers living with HIV in 2010 to 6% in 2015. This paper describes the degree to which World Health Organization (WHO) guidelines for PMTCT services were implemented in Zambia between 2010 and 2015.

Method: The study used routinely collected data from all pregnant women attending antenatal clinics (ANC) in SmartCare health facilities from January 2010 to December 2015. Categorical variables were summarized using proportions while continuous variables were summarized using medians and interquartile ranges.

Results: There were 104,155 pregnant women who attended ANC services in SmartCare facilities during the study period. Of these, 9% tested HIV-positive during ANC visits whilst 43% had missing HIV test result records. Almost half (47%) of pregnant women who tested HIV-positive in their ANC visit were recorded in 2010. Among HIV-positive women, there was an increase in those already on ART at first ANC visit from 9% in 2011 to 74% in 2015. The overall mean time lag between starting ANC care and ART initiation was 7 months, over the six year period, but there were notable variations between provinces and years.

Conclusion: The implementation of the WHO post 2010 PMTCT guidelines has resulted in an increase in the proportion of HIV-infected pregnant women attending ANC who are already on ART. However, the variability in HIV infection rates, missing data, and time to initiation of ART suggests there are some underlying health service or database issues which require attention.

(296 words)

5.1 Introduction

The use of antiretroviral therapy (ART) by HIV-positive pregnant and breastfeeding women is the cornerstone of the strategy to prevent mother-to-child HIV transmission (PMTCT) (1, 2). Global PMTCT guidelines have evolved from short-course antiretroviral (ARV) prophylaxis for mothers and infants to prevent HIV transmission, towards longer and more potent ARV regimens with the potential to improve maternal health (3-6). The World Health Organization (WHO) recommendation for lifelong ART for all pregnant and lactating women (Option B+) is nearly universally adopted in the 22 priority countries with a high burden of HIV and moving towards full implementation (7). In 2017, the global coverage of pregnant women living with HIV had access to ARV medicines to prevent transmission of HIV to their babies was 80% [61–95%] and 210 000 new infections were averted due to PMTCT(8)

Effective PMTCT programmes require women and their infants to receive a cascade of interventions including uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, safe child birth practices, appropriate infant feeding, infant prophylaxis, and HIV testing and other postnatal health care services (9). As the WHO PMTCT guidelines have been evolving over time, the key indicators included in the PMTCT cascade have also changed (3-6). The steps along the cascade expanded as new interventions to prevent HIV transmission were introduced and access to ART improved (10).

A commonly used surrogate marker for programme effectiveness is programme coverage. For PMTCT this would be the proportion of HIV-infected women and exposed infants in a population that access the different components of the PMTCT programmatic cascade (11). Estimates of coverage with PMTCT services among all HIV-infected pregnant women are vital to monitor progress relative to targets, and to secure donor funding for PMTCT programmes (12). With the endorsement of the new infant HIV infection elimination goal, countries target to increase coverage of PMTCT services to $\geq 95\%$ (13).

Zambia revised its national PMTCT guidelines in 2010 in accordance with the new WHO guidelines and, along with many other developing countries, adopted Option A (14). Under Option A, HIV-positive pregnant women with a CD4 count ≥ 350 cells/ μL received ART prophylaxis to prevent transmission of HIV to their baby. This consisted of daily Zidovudine from 14 weeks gestation through to one week postpartum, single-dose Nevirapine at delivery, and daily Lamivudine from delivery through to one week postpartum. Their infants received daily Nevirapine from birth through to one week after the cessation of breastfeeding. Women

with CD4 \leq 350 cells/ μ L or WHO clinical stage 3 or 4 disease were initiated onto lifelong triple-drug ART, regardless of symptoms (5). In 2013, after more than two years implementing Option A, Zambia announced that it would revise its PMTCT guidelines again and adopt Option B+(15). Option B+ recommends that all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should start and continue ART for life whilst their infants receive daily Nevirapine or Zidovudine from birth to 4–6 weeks (6).

This paper describes trends in the coverage of PMTCT services from 2010 to 2015 using the SmartCare database of routine clinical information collected in Zambia. This is the first study to have evaluated the effectiveness of implementing post 2010 PMTCT interventions nationwide using SmartCare routine data.

5.2 Method

5.2.1 Study Design

This was a retrospective cohort study using routinely collected data. The study population was all pregnant women attending antenatal care (ANC) from January 2010 to December 2015 in health facilities using the SmartCare database.

In Zambia over 90% of pregnant women attend ANC services at least once during their pregnancy, but only 47% deliver at health facilities (16). Thus it is difficult to ensure that eligible pregnant women receive the complete treatment to prevent transmission of HIV to their babies. Although more than 75% of the ANC facilities currently provide PMTCT services, the majority of these facilities are along the country's main rail line and in urban centres, resulting in geographical inequity (16).

5.2.2 Data Sources

The study retrospectively analysed the Ministry of Health electronic SmartCare database, using routinely collected data from all pregnant women attending ANC from January 2010 to December 2015. SmartCare is a Zambian Ministry of Health-led project funded from the United States Centre for Disease Control and Prevention (CDC) (17). The SmartCare database was developed to improve continuity of care and provide timely data on maternal and child health, HIV/AIDS, tuberculosis and malaria interventions for public health purposes. Since 2005, the SmartCare database has been deployed in over 800 health facilities,

which represents 40% of all facilities in Zambia, including the biggest and busiest health facilities. These results come from 886 health facilities from all provinces in Zambia. The Southern province had the most number of facilities (254/886) represented in the dataset, followed by the Copperbelt (187/886), and Eastern (166/886) provinces. Muchinga and Northern provinces had the least number of facilities, 10 and 26, in the analysed dataset.

5.2.3 Data Extraction

The data was extracted into Excel, without names, but with the unique identity (ID) number, and then transferred to Stata 13 for cleaning and analysis. All women enrolled in a facility using SmartCare have an electronic health record about their ANC visits which includes information collected in each visit. Records are updated at every point of clinical service. SmartCare is organised into comprehensive modules and sub-modules. The information from various modules is linked through the unique ID number. For this study, the ANC data was linked to the HIV Client Summary module and the ARV Eligibility Interaction Module to identify HIV-positive women. Data from the Obstetric History Module was then used to segregate PMTCT clients from general ART clients. The oldest date of HIV testing and ANC visit date were used to determine whether women had known their HIV status before the ANC visit. The final data were stratified by province using the geography file from the Central Statistical Office (CSO) which has a list of all the districts and provinces.

The first step in data cleaning was to remove duplicate data for repeat visits in the same pregnancy (based on parity and gravid status). This was done by keeping the first visit date of each pregnancy then populating any empty fields with information captured at later visits in the same pregnancy. Records for all the mothers less than 15 years and those above 49 years of age were dropped from the sample making our target group to be those between 15-49 years (reproductive age group). Age groups were categorised as 15-24, 25-34, and 35-49 years. Marital status was grouped into single, married, divorced, widowed and missing. The education status groups were no education, primary education, junior secondary, secondary, and tertiary education.

5.2.4 Statistical Analysis

The data were used to estimate the proportion of HIV-positive pregnant women attending ANC by province and year. The study population was divided into three strata: pregnant women with a new HIV test result documented in ANC clinic, pregnant women with known status but not on ART, and pregnant women who were already on ART. Among the total number of pregnant women presenting to ANC clinic in each calendar year; the percentages in each group were calculated.

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were used to conduct and report on the findings of this study (18).

5.2.5 Ethics

Ethical approval was granted from Zambia Biomedical Research Ethic Committee (Ref 101-04-16) and the LSHTM Research Ethics Committee (Ref 12086). Permission to use SmartCare data was granted by the Zambia Ministry of Health. The Ethics Committees that approved the study waived the need for written informed consent to be obtained as this was a secondary analysis of previously collected data and the authors had access only to de-identifiable information.

5.3 Results

5.3.1 Demographics

A total of 105,373 pregnant women attended ANC services in SmartCare facilities from January 2010 to December 2015 (Figure 5.1). After removal of those aged 14 years or less and those above 49 years, there were 104,155 in the final study sample (Table 5.1) with 33% recorded in 2010. Most women were from Copperbelt (27%), Southern (21%) and Eastern (21%) provinces whilst the fewest were from Luapula and North-western provinces. The majority (51%) were between 15 to 24 years and 82% were married. A high proportion had attained primary level (34%) and secondary level (39%) education, however educational level attainment data was missing for 20% of pregnant women.

5.3.2 HIV test results

Overall during the study period 9% of pregnant women tested HIV-positive (Table 5.2) at ANC visits whilst 43% had missing HIV test result records. In addition, 34% of the missing HIV test results were in 2014, whereas only 2% were in 2011. More so, over 60% of HIV test results were missing in Lusaka and Muchinga provinces.

The overall percentage of HIV-positive pregnant women, who tested for the first time at the ANC decreased from 13% in 2010 to 5% in 2013 and then to 0.15% in 2015. The percentage with missing HIV test results increased from 11% in 2010 to 65% in 2013 and then to 98.8% in 2015 (Table 5.2).

5.3.3 ART initiation

Almost half (47%) of the pregnant women who tested HIV-positive in their ANC visit were recorded in 2010 (Figure 5.2). More women knew their HIV-positive status in 2015 (30%) than in 2011 (9%). There was a large increase in the proportion of HIV-positive women who were already on ART from 9% of the HIV-positive women seen in 2011 to 74% of the HIV-positive women seen in 2015.

The overall mean time difference between HIV-positive diagnosis at the first ANC visit and ART initiation was 7 months. If a woman was diagnosed at 14 weeks the analysis suggests that most women were not started on ART until after delivery (7-9 months). However, there are notable variations between visit years (Figure 5.3). There were also large differences between provinces; for example, in 2010 pregnant women in Luapula province took an average of 37 months from diagnosis to treatment whereas in the Copperbelt it took less than 1 month.

5.4 Discussion

Zambia initiated the PMTCT programme in 1999 to address the burden of vertical transmission of HIV and to integrate PMTCT in all maternal, newborn and child health services throughout the country (14). The results of this study show that, although there is a high rate of engagement with PMTCT services, the variability in HIV infection rates, missing data and time to initiation of ART suggests there are some underlying health service or database issues which require attention.

Our results indicate a progressive increase in the proportion of women HIV-infected who were already on ART before registering for ANC in their visit year (from 3% in 2010 to 74% in 2015). This is likely to be attributable to the introduction of Option B+ for those women with repeat pregnancies and adoption in 2013 of WHO Test and Treat guidelines that recommend anyone who tests positive for HIV should be started on treatment, regardless of their CD4 count. However, the UNAIDS Prevention Gap report indicated a decline in

pregnant women living with HIV who received effective ART from 96% in 2013 to 87% in 2015 (1). In a systematic review of literature on the effectiveness of implementing post 2010 PMTCT guidelines, we concluded that many HIV-infected women who are engaged in care during pregnancy are lost to follow-up during the postpartum period (19).

The increased volume of patients initiating ART due to test-and-treat and Option B+ could have threatened programme performance and negatively affected the HIV continuum of care for all HIV-infected patients (20). Mathematical modelling using the Lifelong ART tool indicated that the probability of HIV-infected pregnant women initiating ART would increase by 80%. It was also suggested that while the shift would generate higher PMTCT costs, it would be cost-saving in the long term as it spares future treatment costs by preventing infections in infants and partners (21).

Other studies from Africa have shown that the uptake of PMTCT services could be influenced by health system or structural issues such as staffing level, availability and cost of ART, capacity of health personnel to prescribe appropriate regimens, shortage of supplies in facilities, failure to follow up mothers' or infants' status, and giving wrong information or suboptimal quality of counselling leading to loss or dropout from the PMTCT cascade (22-27). In Zambia lack of human resources remains a serious impediment to addressing HIV, so that even when physical resources are available, there is often not the healthcare personnel to administer them (28). However, knowledge around PMTCT is high: the Zambia Demographic Health Survey (ZDHS) 2013-14, reported that 82% of women and 66% of men were aware of the risk of MTCT and that it can be reduced by taking special drugs during pregnancy (29).

In our study 65% (983/1501) of the women who were initiated on ART after testing HIV-positive during their ANC were documented after the adoption of Option B+ (2013-15). However, increasing ART initiation coverage does not always translate to programme effectiveness: for example, in a surveillance exercise conducted in Lusaka in 2003, 32% of HIV-infected women reported not to actually ingest the NVP tablet given to them in ANC (30). In addition, the risk of being lost to follow up was higher in 'B+ pregnant' compared to women on ART for their own health in Mozambique (31). In Malawi where Option B+ was first piloted, default and incomplete adherence were more common with Option B+ than with

Option A (32). Hence more efforts must be directed to postnatal programs that ensure retention in care so that women who are initiated on ART do not disengage.

The SmartCare database offers real time data which can enable the Zambian health policy makers to act on urgent PMTCT interventions and improve health care quality and outcomes of mothers and their infants. SmartCare is a facility-based approach which is unable to account for individuals who do not access ANC services; hence it's possible that we might overestimate PMTCT effectiveness (11). The ANC SmartCare database sample was likely to be biased towards the generally better outcomes of those who receive ANC services. However, with over 90% pregnant women attending ANC services at least once during their pregnancy (29), the results could be a good indicator of program performance.

These results come from more than 800 health facilities from all provinces in Zambia, and hence representative of the population of pregnant women in Zambia, although some provinces, such as Lusaka, may be under represented due to data quality. The level of missing data on HIV test results indicate that this data must be viewed with caution and hence prevents us making meaningful conclusions in the later years (2014-15) where the missing data HIV test results is almost 99%. This was despite the efforts of PEPFAR and the Ministry of Community Development, Mother and Child Health to strengthen the Health Management Information Systems (HMIS) and linkages with the national electronic health record system (33). The main efforts were supposed to be directed towards supporting partners to utilize the capability of SmartCare to electronically populate the HMIS. In contrast, our study found that the SmartCare database has not been mined and data quality has been deteriorating due to the lack of utilization of the data and its findings. We are conducting qualitative research to investigate the problems with using the SmartCare system and how to improve them.

Our study shows that there are major problems in both the completeness of the collection and reporting of data that tracks PMTCT service delivery. The data quality challenges were similar to other studies from the region using routinely collected data (12, 20, 34, 35). Despite tremendous progress and many country-driven successes achieved during the Global Plan, operational challenges in data use, monitoring, and evaluation for PMTCT persist. Collecting longitudinal data on mother–baby pairs throughout the PMTCT cascade is challenging but necessary to optimize maternal and infant outcomes. However the Global

Plan priority countries (which include Zambia) health records are not properly completed, hence the need to scale up electronic data systems (36) such as the SmartCare.

Limitations

SmartCare data collection is implemented parallel to the main line Ministry of Health HMIS, which also collects HIV test results. This has caused high levels of missing HIV test results data in the SmartCare as clinicians prefer to enter the information in the HMIS forms compared to SmartCare forms which are longer (5-6 pages per interaction).

Due to data security and confidentiality from data custodians, we were not able to get the exact date of birth and the national identity numbers for individuals in the SmartCare database. As a result we could not match records of the same individuals in cases where they are double registered through change of name, or facility. A commonly used surrogate marker for programme effectiveness is programme coverage, i.e. the proportion of HIV-infected/exposed mother/infant pairs in a population that receive a PMTCT intervention (11). In our study the infant-mother pairs could not be linked as infants are registered as separate individuals with unique numbers.

The decrease in the number of records for over 30,000 in 2010 to 10,000 in 2015 is likely to have introduced bias and hence affects the external validity of our study. The findings could have been triangulated against HMIS data as this could provide an opportunity to identify omissions and errors in the dataset.

The data was mainly collected for administrative purposes without research intentions; for example, breastfeeding is part of the PMTCT cascade but the database contains no infant feeding information.

5.5 Conclusion

The implementation of the WHO post 2010 PMTCT guidelines has resulted in an increase in the proportion of HIV-infected pregnant women attending ANC who are already on ART. The SmartCare database could enable Zambian health policy makers to act on urgent PMTCT interventions and improve health care quality and outcomes of mothers and their infants. However, there is a need first to improve procedures for data collection and entry. The missing data observations indicated the need for further qualitative research to determine why it was such a problem.

(2969 words)

Authors' contributions

SGM analysed the data and wrote the initial draft of the manuscript with guidance from SF and JT. AB PM and JT provided advice on cohort datasets and statistical analyses. All authors contributed to subsequent drafts of the manuscript and approved the final version.

Availability of Data

No additional data available.

Competing interests

None declared.

Acknowledgements

The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472. We also thank the Ministry of Health, Department of Policy and Planning for granting us permission to access the SmartCare database.

5.6 References

1. UNAIDS. *Prevention Gap Report*. 2016. https://unaids.org.br/wp-content/uploads/2016/07/2016-prevention-gap-report_en.pdf. Accessed on 10 December 2017
2. UNAIDS. *HIV/AIDS Fact Sheet*. 2017. http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf. Accessed on 15 December 2017
3. World Health Organisation. *New data on the prevention of mother-to-child transmission of HIV and their policy implications: conclusions and recommendations. Technical Consultation on behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV*. Geneva: WHO, 2001. http://www.who.int/reproductive-health/publications/new_data_prevention_mtct_hiv/index.html. Accessed on 18 December 2017
4. World Health Organisation. *Antiretroviral drugs for antiretroviral drugs for treating pregnant women and preventing hiv infection in infants: towards universal access towards universal access Recommendations for a public health approach*. Geneva, Switzerland: 2006. http://www.who.int/hiv/pub/mtct/arv_guidelines_mtct.pdf?ua=1 . Accessed on 17 December 2017
5. World Health Organisation. *WHO Guidelines on HIV and infant feeding 2010: Principles and recommendations for infant feeding in the context of HIV and a summary of evidence*. Geneva, Switzerland: World Health Organization Departments of Child and Adolescent Health and Development and HIV, in collaboration with UNAIDS, UNFPA and UNICEF, 2010. http://apps.who.int/iris/bitstream/10665/44345/1/9789241599535_eng.pdf. Accessed on 13 December 2017.
6. World Health Organisation. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing hiv infection recommendations for a public health approach*. Geneva, Switzerland WHO, 2013 June 2013. http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf. Accessed on 13 December 2017
7. World Health Organisation. *HIV TREATMENT AND CARE FACT SHEET Treat All: Policy Adoption And Implementation Status In Countries*. 2017. <http://41.77.4.165:6510/apps.who.int/iris/bitstream/10665/258538/1/WHO-HIV-2017.35-eng.pdf> . Accessed on 12 January 2018
8. UNAIDS. AIDSInfo: UNAIDS; 2018 . Available from: <http://aidsinfo.unaids.org/>. Accessed on 20 September 2018
9. Padian NS, McCoy SI, Karim SS, Hasen N, Kim J, Bartos M, et al. *HIV prevention transformed: the new prevention research agenda*. *Lancet*. 2011;378(9787):269-78.
10. Hamilton E, Bossiky B, Ditekemena J, Esiru G, Fwamba F, Goga AE, et al. *Using the PMTCT Cascade to Accelerate Achievement of the Global Plan Goals*. *Journal of acquired immune deficiency syndromes*. 2017;75 Suppl 1:S27-S35.
11. Stringer E.M. CBH, Chintu N., Creek T.L., Ekouevi D. K., Coetzee D., Tih P., Boulle A., Dabis F., Shaffer N., Wilfert C.M., and Stringer J.S.A. *Monitoring effectiveness of programmes to prevent mother-to-child HIV transmission in lower-income countries*. *Bulletin of the World Health Organisation*. 2008;86(1):57-62.
12. Gourlay A, Wringe A, Todd J, Michael D, Reniers G, Urassa M. *Challenges with routine data sources for PMTCT programme monitoring in East Africa: insights from Tanzania*. *Global health action*. 2015;8.

13. Ciaranello AL, Perez F, Keatinge J, Park JE, Engelsmann B, Maruva M, et al. *What will it take to eliminate pediatric HIV? Reaching WHO target rates of mother-to-child HIV transmission in Zimbabwe: a model-based analysis*. PLoS medicine. 2012;9(1):e1001156.
14. Zambia Ministry of Health. *Zambia National PMTCT Protocol Guidelines Lusaka Zambia*: 2010.
15. Government of the Republic of Zambia MoH. *Lifelong antiretroviral drugs (ARV's) for all HIV positive pregnant women in Zambia: Policy guidelines for health facilities in Zambia*. Lusaka, Zambia: 2013.
16. UNICEF. *UNICEF Zambia Fact Sheet* [10 December 2017]. Available from: https://www.unicef.org/zambia/5109_8456.html.
17. Muyunda G.. *Zambia leads the way in SmartCare electronic health records system, a benefit to both providers and patients 2011* [cited 2016 5 June 2016]. Available from: <https://www.jhpiego.org/success-story/zambia-leads-the-way-in-SmartCare-electronic-health-records-system-a-benefit-to-both-providers-and-patients/>. Accessed on 10 Decenver 2017
18. Benchimol EI, Smeeth L, Guttman A, Harron K, Hemkens LG, Moher D, et al. [*The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement*]. Z Evid Fortbild Qual Gesundhwes. 2016;115-116:33-48.
19. Gumede-Moyo S., Filteau S., Munthali T., Todd J., Musonda P, . *Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa: A Systematic Literature Review*. Medicine. 2017;96(40).
20. Chung N.C. B-MC, Chilengi R, Kasaro M. P., Stringer J. S. A and Benjamin H. Chi B. H. *Patient engagement in HIV care and treatment in Zambia, 2004–2014*. Tropical Medicine and International Health. 2017.
21. Ishikawa N ST, Miyano S, Sikazwe I, Mwango A, Ghidinelli M. N, Syakantu G,. *Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia*. PloS one. 2014;9(3):e90991.
22. Urban M, Chersich M. *Acceptability and utilisation of voluntary HIV testing and nevirapine to reduce mother-to-child transmission of HIV-1 integrated into routine clinical care*. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2004;94(5):362-6.
23. Kinuthia J, Kiarie JN, Farquhar C, Richardson BA, Nduati R, Mbori-Ngacha D, et al. *Uptake of prevention of mother to child transmission interventions in Kenya: health systems are more influential than stigma*. Journal of the International AIDS Society. 2011;14:61.
24. Uwimana J, Zarowsky C, Hausler H, Jackson D. *Engagement of non-government organisations and community care workers in collaborative TB/HIV activities including prevention of mother to child transmission in South Africa: opportunities and challenges*. BMC health services research. 2012;12:233.
25. Peltzer K, Mlambo G. *Factors determining HIV viral testing of infants in the context of mother-to-child transmission*. Acta paediatrica (Oslo, Norway : 1992). 2010;99(4):590-6.
26. Woldesenbet S, Jackson D, Lombard C, Dinh TH, Puren A, Sherman G, et al. *Missed Opportunities along the Prevention of Mother-to-Child Transmission Services Cascade in South Africa: Uptake, Determinants, and Attributable Risk (the SAPMTCTE)*. PloS one. 2015;10(7):e0132425.
27. Torpey K, Mandala J, Kasonde P, Bryan-Mofya G, Bweupe M, Mukundu J, et al. *Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia*. PloS one. 2012;7(8):e42859.
28. Zambia National AIDS Council . *GARPR Zambia Country Report 2013*. 2014.
29. Central Statistical Office. *Zambia Demographic and health survey - 2013-14*. Lusaka, Zambia: 2014.

30. Stringer JS, Sinkala M, Maclean CC, Levy J, Kankasa C, Degroot A, et al. *Effectiveness of a city-wide program to prevent mother-to-child HIV transmission in Lusaka, Zambia*. AIDS (London, England). 2005;19(12):1309-15.
31. Llenas-Garcia J, Wikman-Jorgensen P, Hobbins M, Mussa MA, Ehmer J, Keiser O, et al. *Retention in care of HIV-infected pregnant and lactating women starting ART under Option B+ in rural Mozambique*. Tropical medicine & international health : TM & IH. 2016;21(8):1003-12.
32. Kamuyango AA, Hirschhorn LR, Wang W, Jansen P, Hoffman RM. *One-year outcomes of women started on antiretroviral therapy during pregnancy before and after the implementation of Option B+ in Malawi: A retrospective chart review*. World journal of AIDS. 2014;4(3):332-7.
33. PEPFAR. *Zambia Country Operational Plan FY 2014 2015*.
34. Mate KS, Bennett B, Mphatswe W, Barker P, Rollins N. *Challenges for routine health system data management in a large public programme to prevent mother-to-child HIV transmission in South Africa*. PloS one. 2009;4(5):e5483.
35. Annabelle Gourlay AW, Jim Todd, Caoimhe Cawley, Denna Michael, Richard Machedemba, Benjamin Clark, Clemens Masesa, Milly Marston, Mark Urassa and Basia Zaba. *Uptake of services for prevention of mother-to-child transmission of HIV in a community cohort in rural Tanzania from 2005 to 2012*. BMC health services research. 2016;16(4):1249-5.
36. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaCI, editor B+ Monitoring & Evaluation Framework Dissemination and Country Consultation: Technical Synthesis. 2015; Kampala, Uganda.

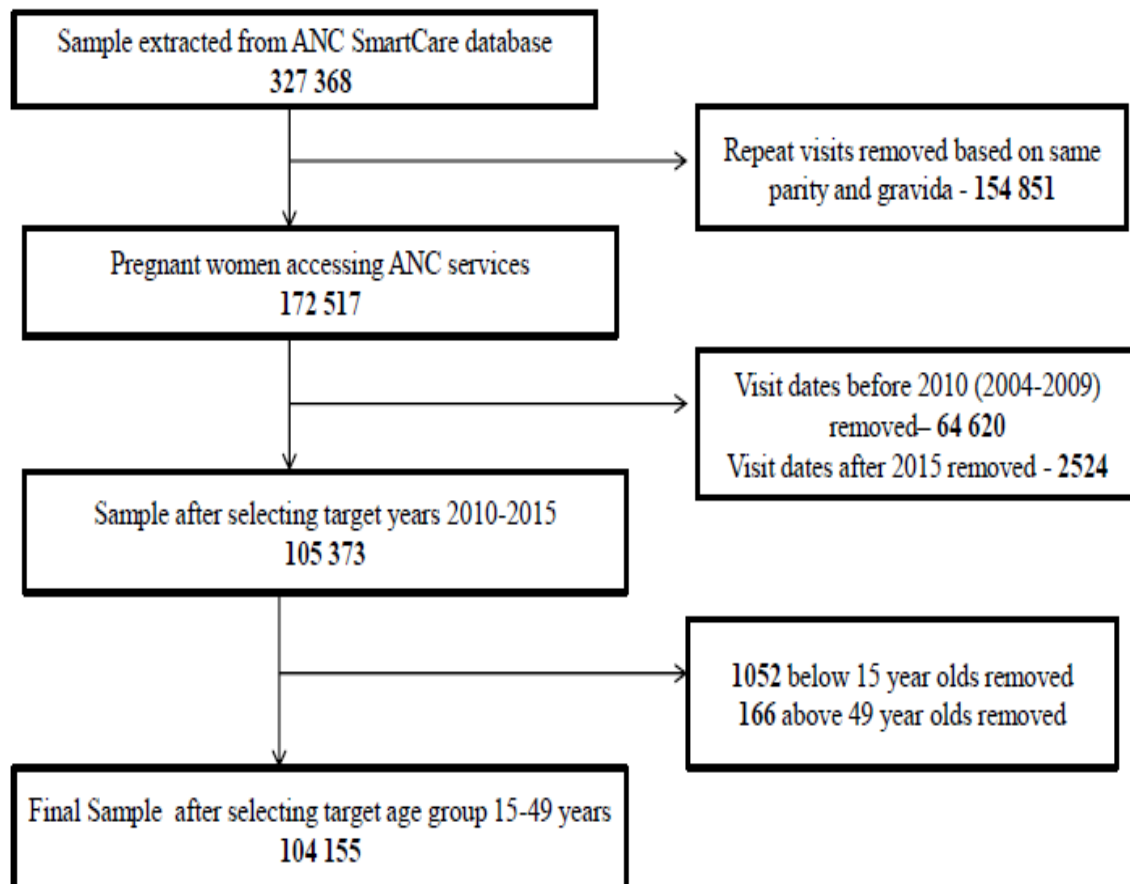
Table 5.1: Demographic Characteristics

			Year of Visit							
			2010	2011	2012	2013	2014	2015	Total	
Age Categories	15 to 24 yrs	N	16,518	7,124	8,181	8,069	8,224	5,382	53,498	
		%	51	51	51	51	53	52	51	
	25 to 34 yrs	N	12,486	5,439	6,162	5,873	5,644	3,881	39,485	
		%	38	39	39	37	36	37	38	
	35 to 49 yrs	N	3,494	1,424	1,610	1,750	1,716	1,178	11,172	
		%	11	10	10	11	11	11	11	
Marital Status	Single	N	3,125	1,291	1,393	800	783	1,135	8,527	
		%	10	9	9	5	5	11	8	
	Married	N	27,139	11,774	13,124	12,940	12,727	7,569	85,273	
		%	84	84	82	82	82	72	82	
	Divorced	N	149	61	70	52	48	68	448	
		%	0.5	0.4	0.4	0.3	0.3	0.7	0.4	
	Widowed	N	100	69	59	43	52	50	373	
		%	0.3	0.5	0.0	0.0	0.0	0.5	0.4	
	Missing	N	1,985	792	1,307	1,857	1,974	1,619	9,534	
		%	6	6	8	12	13	16	9	
	Education Level Attained	No Education	N	1,593	474	1,134	676	657	363	4,897
			%	5	3	7	4	4	3	5
Primary Level		N	12,309	4,580	5,631	5,441	4,384	3,026	35,371	
		%	38	33	35	35	28	29	34	
Secondary Level		N	12,770	6,098	6,372	5,291	5,057	4,558	40,146	
		%	39	44	40	38	32	44	39	
Tertiary		N	646	533	434	434	348	392	2,787	
		%	2	4	3	3	2	4	3	
Missing		N	5,180	2,302	2,382	3,850	5,138	2,102	20,954	
		%	16	16	15	25	33	20	20	
Total			32,498	13,987	15,953	15,692	15,584	10,441	104,155	

Table 5.2: HIV test Result

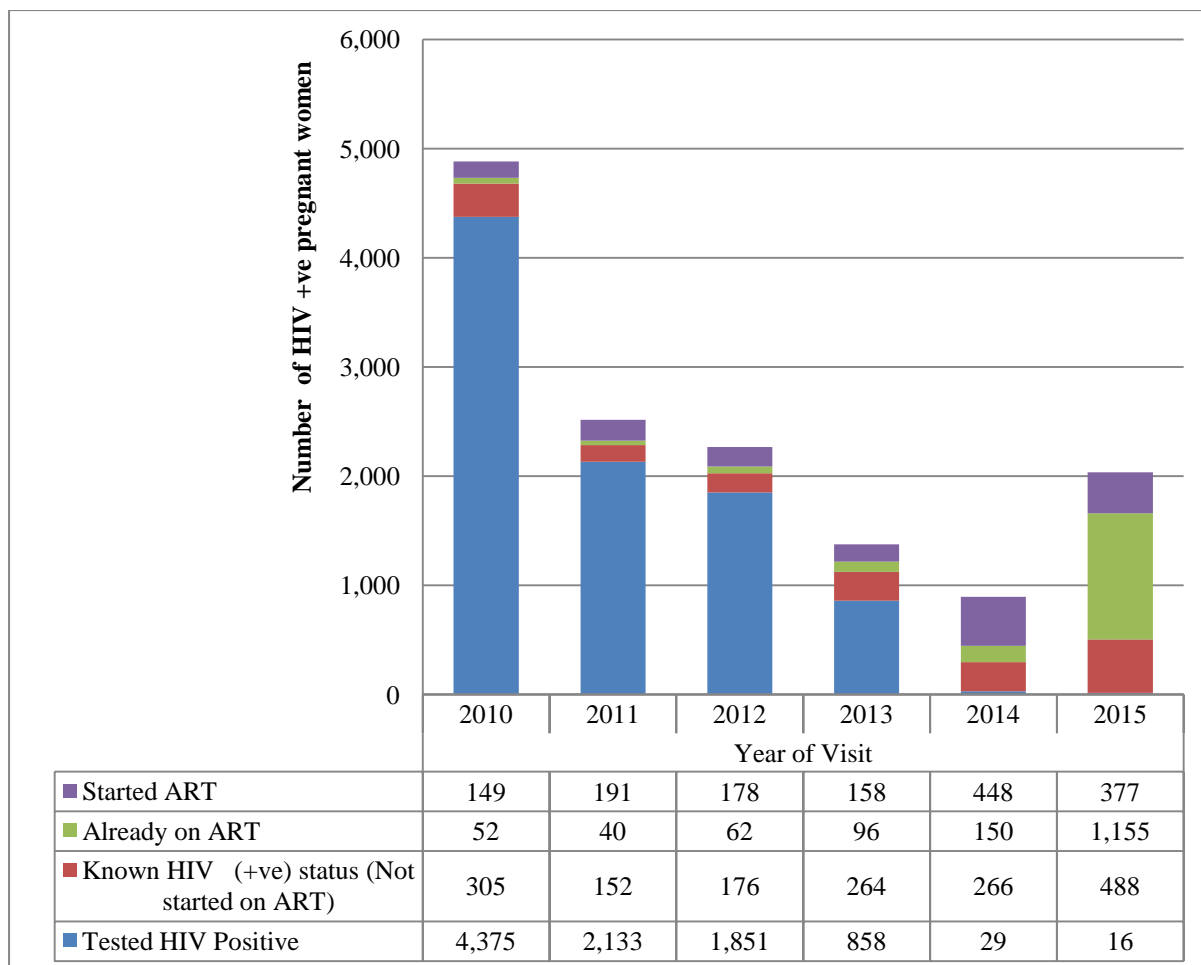
Result of HIV Test	Year of Visit						
	2010	2011	2012	2013	2014	2015	Total
Negative (N)	24,411	10,773	10,209	4,533	348	106	50,380
(%)	75	77	64	29	2	1	48
Positive (N)	4,375	2,133	1,851	858	29	16	9,262
(%)	13	15	12	5	0.3	0.2	9
Not Clear (N)	81	16	15	14	0	0	126
(%)	0.3	0.1	0.1	0.1	0.0	0.0	0.1
Missing (N)	3,631	1,065	3,878	10,287	15,207	10,319	44,387
(%)	11	8	24	66	98	99	43
Total N	32,498	13,987	15,953	15,692	15,584	10,441	104,155

Figure 5.1: Sample size data flow



The Data Flow chart represents the flow chart of participants eligible for inclusion in the analysis

Figure 5.2: Distribution of HIV positive women by year of visit



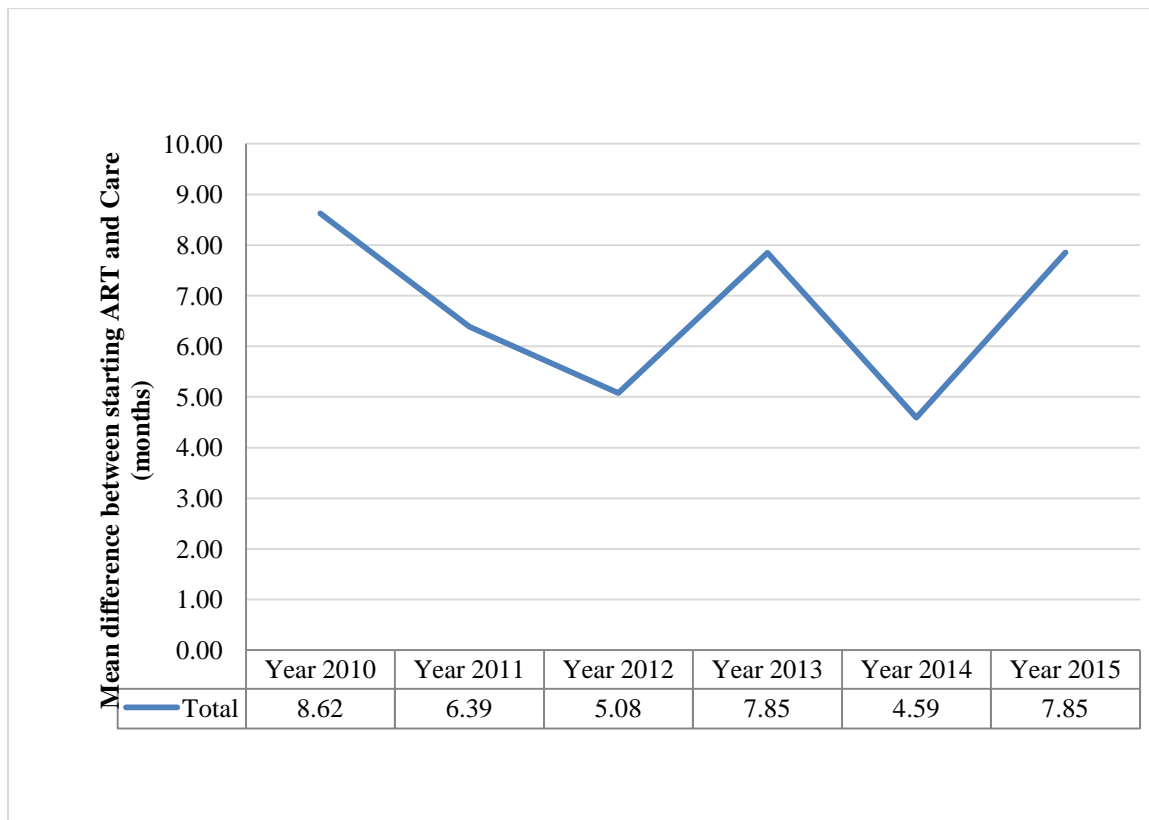
Started ART refers to women who first tested positive during ANC for this pregnancy and were started on ART.

HIV-positive not started on ART refers to women who first tested HIV-positive in this pregnancy but were not started on ART because they were pregnant when Option A was in place.

Already on ART refers to pregnant women who were already on ART before seeking ANC services for this pregnancy.

Known HIV-positive status refers to women with known HIV-positive status before ANC for this pregnancy so were not tested again but were not started on ART because they were on Option A.

Figure 5.3: Overall time to ART initiation in months



Time to ART initiation is the number of months calculated from the time a woman was diagnosed HIV positive to the time they were initiated on ART.

Chapter 6: Quantitative paper using data set of HIV- infected infants

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646

F: +44 (0)20 7299 4656

www.lshtm.ac.uk

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1405741	Title	Mrs
First Name(s)	Sehlulekile		
Surname/Family Name	Gumede-Moyo		
Thesis Title	Evaluating Implementation of revised (post 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using Routinely Collected Data in Zambia.		
Primary Supervisor	Suzanne Filteau		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	BMC Public Health		
When was the work published?	November 2018		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes.

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	Choose an item.

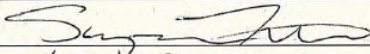
SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)

I conducted the data extraction and cleaning from the SmartCare database. I supervised Jasleen Singh, who was an MSc student to analyse the dataset and write up the manuscript. I was also the corresponding author for the publication process.

SECTION E

Student Signature	S Gumede-Moyo
Date	December 2017

Supervisor Signature	
Date	4/12/18

Progress in the performance of HIV early infant diagnosis services in Zambia using routinely collected data from 2006 to 2016

Jasleen Singh¹, Suzanne Filteau¹, Jim Todd¹ and Sehlulekile Gumede-Moyo^{1,2§}

1. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

2. School of Public Health, University of Zambia, Lusaka, Zambia

§Corresponding author: Sehlulekile Gumede-Moyo. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. (sehlulekile.gumede@lshtm.ac.uk).

Email addresses of authors:

JS: jasleen.singh1@alumni.lshtm.ac.uk

SF: suzanne.filteau@lshtm.ac.uk

JT: jim.todd@lshtm.ac.uk

SGM: sehlulekile.gumede@lshtm.ac.uk

Abstract

Background

Early diagnosis and treatment initiation of HIV-infected infants can greatly reduce the risk of infant mortality. The WHO recommends testing HIV-exposed infants at 6 weeks of age and immediate initiation of antiretroviral therapy if positive. This study aimed to determine the feasibility of using an electronic health records system to evaluate the performance of Zambia's HIV Early Infant Diagnosis services.

Methods

A retrospective analysis of routinely collected data from the *Zambian SmartCare* database was performed for the period January 2006 to December 2016. The study population includes all HIV-infected infants (n=32,593) registered during this period on treatment for HIV. Univariable logistic regression was conducted to identify factors associated with later infant testing and treatment initiation.

Results

The mean age at infant HIV test decreased from 10.10 months in 2006 to 3.49 months in 2016. Infants born in 2015 were almost 4 times more likely to be tested under 2 months of age compared to infants born in 2006 (OR: 3.72, p-value: <0.001). The mean time from diagnosis to treatment initiation decreased from 220 days in 2006 to 9 days in 2015. There was substantial regional variability with infants in the provinces of Copperbelt, Luapula and Southern performing best in outcomes and Eastern, Lusaka and Western performing the worst.

Conclusions

HIV-exposed infants born more recently have significantly better outcomes than infants born a decade ago in Zambia, which could be as a result of increased attention and funding for HIV programmes.

Keywords: Early infant diagnosis, HIV, PMTCT

6.1 Background

Early diagnosis and treatment initiation of HIV-infected infants with antiretroviral therapy (ART) can reduce the risk of early infant mortality by 76% [1]. However, treatment for HIV-infected children lags considerably behind adult treatment and without treatment approximately 50% of HIV-infected infants die before the age of two [2]. The World Health Organisation (WHO) recommends testing HIV-exposed infants by 6 weeks of age and immediate initiation of ART if positive. Despite these recommendations infants are lost at every step of the early infant diagnosis cascade [3].

Zambia has been using the electronic health records system SmartCare for the routine collection of HIV data since 2004. SmartCare was developed to improve continuity of care and provide timely data on maternal and child health HIV interventions for public health purposes. To date no analysis of the paediatric HIV data has been performed. This study was a retrospective analysis of routinely collected data from the SmartCare database over the period 2006 to 2016, to determine if infants are being tested and initiated on treatment in the correct timeframe. This information can be used to inform decisions on improving the provision of early infant diagnosis services in Zambia.

6.2 Methods

6.2.1 Study design

This retrospective analysis of routinely collected data was conducted as part of the SEARCH (Sustainable Evaluation through the Analysis of Routinely Collected HIV data) project which aims to support the utilisation of routinely collected HIV data. The SEARCH project is collaboration between the London School of Hygiene and Tropical Medicine and the Ministries of Health in Zambia and Tanzania. The data source was SmartCare, one of the largest electronic patient monitoring systems in Africa. Introduced as a pilot project in 2004 by the Zambian Ministry of Health with funding from the US Centers for Disease Control (CDC), it has now been rolled out across all ten provinces of Zambia and is used to monitor and plan improvements in the country's HIV services. All facilities in Zambia wishing to dispense ART are required to use SmartCare. Since 2005 SmartCare has been deployed to over 800 facilities in 94 districts, with an enrolment above 900,000 patients. This represents approximately 40% of all clinics in Zambia; these are the largest and busiest ART clinics and the requirement to join SmartCare if clinics wish to prescribe ART means that most Zambian patients on ART care captured in SmartCare database [4].

Data was extracted by a SEARCH team member from the Zambian SmartCare database modules, Paediatric ART and Under 5 Registration, between the years 2006 and 2016 using a standardised data extraction form. The study population includes all HIV-infected infants registered during this period on treatment for HIV. Age at infant HIV test was determined by linking the Under 5 Registration module (which has infant date of birth) and Paediatric ART module (which has date of infant HIV test). Infants are registered as independent patients from their mothers and the system does not have a link between the mother and infant pairs; therefore, information could not be collected on the mother's treatment, on the proportion of HIV-exposed infants who tested HIV-negative, or on HIV-exposed infants who missed both testing and provision of ART. For this reason, we are focusing this analysis solely on HIV-infected infants born between January 2006 and December 2016 who have received ART.

6.2.2 Statistical methods

Categorical variables were summarised by frequencies and percentages and continuous variables by histograms. Univariable and multivariable logistic regression were conducted with “age at HIV test” and “time from diagnosis to treatment initiation” as the dependent variables and the following independent variables: infant sex, province, year of birth, and season of birth. Season were defined as early dry (June to August); late dry (September to November); early rainy (December to February) and late rainy (March to May).

Odds ratios with 95% confidence intervals were calculated to identify risk factors for age at test under 2 months and time from diagnosis to treatment under 2 weeks. For the variable ‘province’ Lusaka was chosen as the reference group because it is the most populous province, and it contains the capital city where the SmartCare project was first rolled out so has the largest number of registered infants. Although multivariable analysis was also conducted for all variables to display adjusted odds ratios, the results showed little difference and so only the univariable analysis results are included in this paper. All analysis was performed using STATA 14 and graphics were produced using STATA and Microsoft Excel.

6.3 Results

A total of 32,593 HIV-infected infants on ART in Zambia were identified from SmartCare over the period 2006 to 2016. The number of infants in the database on ART increased from 1,761 in 2006 to peak at 3,720 in 2009 and then steadily decreased to 108 in 2016. Main

comparisons over time used 2015 since there were too few infants listed in 2016 for age at testing and none for time to treatment initiation.

6.3.1 Age of diagnosis

For the outcome ‘age at infant HIV testing’, 20,260 (62.16%) infants had complete data recorded. Looking at the country as a whole, the mean age at HIV testing has steadily decreased from 10.10 months for infants born in 2006 to 3.49 months in 2016 (Fig.6.1). Infants born in 2015 were more likely to be tested under 2 months of age compared to infants born in 2006 (OR: 3.72, p-value: <0.001). For infants born in 2016 an even greater association was found (OR: 5.62, p-value: <0.001), but this result must be viewed with some caution as there were far fewer infants in the database for the year 2016 (n=108) than 2015 (n=386).

Considering all years together, infants in all provinces, especially Western province (OR: 0.21, p-value: <0.001) were less likely to be tested under 2 months of age as compared to infants in Lusaka; an exception was Southern province which had an increased odds (OR: 1.83, p-value: 0.001). Fig. 2 shows the percentage of HIV tests performed within 2 months of birth in the years 2010 and 2015 by province. All provinces show an overall improvement, particularly Copperbelt, Luapula and Southern. The years 2010 to 2015 were chosen for the comparison to coincide with the changes in prevention of mother-to-child transmission (PMTCT) guidelines in Zambia over this period, as discussed below.

Infants born in the late dry season were more likely to be tested within 2 months than infants born in the early dry season (OR 1.39; p value: <0.001) (Table 6.1). There was no association found for sex.

6.3.2 Time to ART initiation

For the outcome ‘time from diagnosis to ART initiation’, 10,881 (33.38%) infants had complete data recorded. At the country level the mean time from diagnosis to starting treatment has decreased significantly from 220 days for infants born in 2006 to 9 days in 2015 (Fig.6.1). Infants born in 2015 were more likely to start treatment in under 2 weeks compared to infants born in 2006 (OR 2.29; p value: <0.001).

Infants in all provinces had an increased likelihood of starting treatment within 2 weeks as compared to Lusaka, despite being less likely to be tested under 2 months. Luapula showed the biggest difference (OR: 3.83, p-value: <0.001). The provinces showing the most

improvement from 2006 to 2015 were Copperbelt, Central and Northern. Female infants were slightly more likely to start treatment in under 2 weeks compared to males (OR: 1.10; p value: 0.004). Season showed no significant association.

6.4 Discussion

In Zambia the age at infant HIV test has shown a steady decline, with the exception of the period 2010 to 2013 which showed a slight increase. This period coincides with the implementation of new WHO treatment guidelines for PMTCT. Changes in WHO recommendations over the past decade on when to initiate ART in pregnant women have had major implications for the delivery of HIV services, and help explain the trends in service delivery. From 2010 Zambia adopted Option A, a complex guideline consisting of different maternal treatment regimens during pregnancy, labour and postpartum as well as infant prophylaxis [5]. This complexity of regimen changes, combined with the need for regular clinic visits in early infancy, led to high attrition rates and infants receiving improper doses of daily Nevirapine [6]. Option B+ which was adapted in 2013 [7] this barrier by recommending treating all pregnant women with lifelong ART regardless of CD4 count. By simplifying the process considerably, in Malawi (where it was first trialled), switching to Option B+ led to a five-fold increase in the number of pregnant women enrolled on ART in the first quarter of implementation [8]. When Zambia announced its policy for universal ART in 2015, there was an increase in the volume of patients initiating on ART [9]. Zambia has made progress towards elimination of HIV mother-to-child transmission with a reduction in new HIV infections among children from 10,000 in 2010 to 8,900 in 2016. This could be as result of improved coverage of pregnant women living with HIV accessing antiretroviral medicines to 86% [10]. In our study we were not able to calculate the MTCT rate because the SmartCare database does not have information on the HIV exposed infants who are not on ART.

All provinces showed a subsequent reduction in age at test between 2013 and 2015 with the implementation of Option B+, in which all pregnant women with HIV are offered lifelong ART regardless of CD4 count [11]. The progress could also be attributed to Option B+ as previous studies have concluded that children born to women who received ART are less likely to be lost to follow-up and more likely to be tested for HIV [12-14]. This suggests that under Option B+ mothers and their infants are more likely to be attached to the health care system. Therefore efforts have to be made to ensure that the infants who are tested and initiated are retained in care. In Tanzania, 61% of infants receiving treatment were lost to

follow up at the time of review, despite the high proportion of guardians and parents who returned for PCR results (92% in 2010 and 98% in 2011) [15]. The results were consistent with a study from Malawi where 48% of the HIV-exposed infants were declared lost to follow up (LTFU) in the database although 96% of the them in the cohort had their PCR test done at 24 months [16]. Hence despite the reduction in the age of testing the progress of EID must be enhanced by ensuring continuity in care. In Zambia the estimated percentage of children (aged 0–14 years) living with HIV receiving ART, in 2015 was 61% [17], 3% lower than the adult coverage.

An effective EID service should achieve the following: identify all HIV-exposed infants, provide HIV testing and ensure return of results in a timely manner; retain HIV-exposed infants and their mothers in care; and identify all HIV-infected infants and link them to treatment services to ensure timely initiation of ART [18]. Our data set could not allow us to effectively analyse all these steps hence our conclusion of the progress of EID could have been overestimated as only 33.38% infants had complete data recorded. The poor data quality might have an effect on the external validity of the study. Hence the reasons for poor data quality have been qualitatively explored (*Gumede-Moyo et al submitted*). It is also likely that poor data entry over these years has impacted the results; SmartCare has evolved from a system solely used to track patients into an extensive database of all patients receiving ART in the country. This has resulted in a large amount of data being collected for each patient which is very time consuming for the clinician, who often omits collecting data for certain fields they deem irrelevant to their patient's care. In addition, power outages in remote areas of Zambia are a major problem and can occur for prolonged periods of time during the day, limiting the time that data can be entered into the system. This means that data collection is often not up to date and this could contribute to the apparently poor performance of Western province.

Our study is the first to attempt to analyse the progress of EID using the SmartCare database as a source for exposed infants on ART dataset. A more comprehensive dataset of the HIV status of all exposed infants could have been obtained from the ANC and Under 5 paper registers. However, the majority of studies using paper based routine data have also acknowledged the common problem of missing data [19]. This could be assumed to be one of the causes of under-utilisation of routinely collected data which was observed by Munthali et al [20].

The best performing provinces in 2015 (Figure 2) for ‘percentage of tests performed within 2 months of birth’ were Luapula, Southern and Copperbelt; surprisingly Lusaka was the second worst performing province after Western. Of the nine provinces of Zambia (excluding Muchinga province which was created in 2011 and not included in this database), Lusaka and Copperbelt are predominantly urban whereas the remaining are predominantly rural [21]. Previous studies have shown that the burden of HIV is highest in Zambia’s ‘urban poor’ [22, 23], and indeed data from the latest Zambian 2013-14 DHS showed that Lusaka and Copperbelt have the highest adult HIV prevalence, at 16.3% and 18.2% respectively [24]. Despite the similar HIV prevalence and population sizes, Copperbelt saw a more dramatic improvement in age at infant testing between 2013 and 2015 than Lusaka. The stark difference between the performance of Copperbelt and Lusaka is also seen in the percentage of infants tested under 2 months of age, which was amongst the highest in Copperbelt in 2015 compared to 2010, but rose much less in Lusaka during the same period. This regional variability seen could be attributed to the concentration of donor funded programmes in the various provinces. Despite Zambia’s classification as a lower-middle income country, it remains heavily dependent on external donors to finance its national HIV response. PEPFAR and the Global Fund account for 95% of donor funding for HIV care [25]. Given external aid makes up the bulk of HIV funding in Zambia, it is possible that decisions on which areas of the country to target may influence the trends in HIV outcomes we have seen at a provincial level.

Infants born in the early dry season tended to be tested earlier compared to infants born in the late dry season, although there was no association found between dry and rainy seasons. Season was chosen as a variable of interest because previous studies in Sub-Saharan Africa have shown an association between being born in the rainy season and poorer outcomes for HIV-exposed infants [26, 27]. Reasons suggested for the higher mortality experienced by infants born in the rainy season include a more contaminated water supply from the rains and food scarcity in the period preceding the harvest [28, 29].

Study Limitations

This research has shown that routinely collected data offers a valuable opportunity for the near real-time surveillance of large quantities of data. The SmartCare database of registered infants receiving ART represents a robust sample of the population under study over the stated time period, although we recognise there was a steady decrease in the numbers of

infants registered onto SmartCare from 2009 onwards. The large amounts of missing data did not only introduce bias but also compromised the statistical power of a study. Other limitations with using this database are that the database was designed for practical use by healthcare workers and not research so the variables collected are limited to those deemed most useful for the clinical care of patients. In addition, mother-infant pairs are not linked within SmartCare, and so the analysis was restricted to HIV-infected infants on ART and we were not able to analyse outcomes for HIV-exposed uninfected infants. This would be valuable information for any future assessment of mother-to-child HIV transmission prevention and control programs in Zambia.

6.5 Conclusions

Early infant diagnosis of HIV is essential to achieve prompt treatment initiation and reduce infant mortality. Infants born more recently have better clinical HIV care than infants born a decade ago in Zambia, which could be as a result of more inclusive treatment eligibility guidelines. Provincial variability in the performance of early infant diagnosis services is substantial. Further research is needed on the reasons for such stark regional disparities in HIV service provision in Zambia, and on addressing missed opportunities for infant testing.

List of abbreviations

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
CD4	T-lymphocyte cell bearing CD4 receptor
CDC	Centres for Disease Control and Prevention
DHS	Demographic and Health Survey
EID	Early infant diagnosis
HIV	Human immunodeficiency virus
LTFU	Lost to follow up
LSHTM	London School of Hygiene and Tropical Medicine
MTCT	Mother-to-child transmission
PEPFAR	President's Emergency Plan for AIDS Relief
PMTCT	Prevention of mother-to-child transmission of HIV
SEARCH	Sustainable Evaluation through the Analysis of Routinely Collected HIV data
UNAIDS	Joint United Nations Program on AIDS
WHO	World Health Organisation

6.6 Declarations

Ethics approval and consent to participate

The study used secondary data, and hence there was no direct contact with the patients whose individual data was stripped of unique identifiers. Permission to use the data was obtained from the Zambia Ministry of Health and ethical clearance was obtained from the London School of Hygiene and Tropical Medicine (Ref 8410-01) and the University of Zambia Biomedical Research Ethics Committee (Ref 101-04-16).

Availability of data and materials

The data collected through the SmartCare database belongs to the Zambian Ministry of Health; however any further information pertaining to the database can be addressed by corresponding author sehlulekile.gumede@lshtm.ac.uk

Consent for publication

Not applicable

Competing interests

None declared

Funding

The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472.

Authors' contributions

JS conducted the statistical analysis and drafted the manuscript. SGM conducted the data extraction and cleaning from the SmartCare database. SF and SGM supervised the study and JT, as SEARCH project principal investigator, obtained ethical and regulatory approvals and advised on data analysis. All authors have read, commented on and approved the final manuscript.

Acknowledgements

We would like to acknowledge the support of the SEARCH team and the Ministry of Health in Zambia.

6.7 References

1. Violari A, Cotton M. F, Gibb D. M, Babiker A. G, Steyn J, Madhi S. A, et al. (2008) Early antiretroviral therapy and mortality among HIV-infected infants. *The New England Journal of Medicine*, 359(21), 2233–2244. <https://doi.org/10.1056/NEJMoa0800971>
2. Newell L, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, & Dabis F. (2004) Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: A pooled analysis. *Lancet*, 364(9441), 1236–1243. [https://doi.org/10.1016/S0140-6736\(04\)17140-7](https://doi.org/10.1016/S0140-6736(04)17140-7)
3. UNAIDS. ‘On the Fast-track to an AIDS-Free Generation’. 2016. [Cited 2017 July 13]. Available from: http://www.unaids.org/sites/default/files/media_asset/GlobalPlan2016_en.pdf
4. Muyunda G. ‘Zambia leads the way in SmartCare electronic health records system, a benefit to both providers and patients 2011’. [Cited 2018 September 11]. Available from: <https://www.jhpiego.org/success-story/zambia-leads-the-way-in-smartcare-electronic-health-records-system-a-benefit-to-both-providers-and-patients/>.
5. Ishikawa N, Shimbo T, Miyano S, Sikazwe I, Mwango A, Ghidinelli N, Syakantu G. (2014) Health outcomes and cost impact of the new WHO 2013 Guidelines on prevention of mother-to-child transmission of HIV in Zambia. *PLoS ONE*, 9(3). <https://doi.org/10.1371/journal.pone.0090991>
6. Chi H, Stringer A, Moodley D. (2013) Antiretroviral drug regimens to prevent mother-to-child transmission of HIV: A review of scientific, program, and policy advances for sub-Saharan Africa. *Current HIV/AIDS Reports*, 10(2), 124–133.

7. Government of the Republic of Zambia Ministry of Health. 'Lifelong antiretroviral drugs (ARV's) for all HIV positive pregnant women in Zambia: Policy guidelines for health facilities in Zambia'. 2013. [Cited 2018 September 11]. Available from: <http://catalogue.safaids.net/sites/default/files/publications/Policy-guidelines-for-eMTCT-Option-B+ Zambia-2013.pdf>
8. Kieffer M. P, Mattingly M, Giphart A, van de Ven R, Chouraya C, Walakira M, Simonds R. J. (2014) Lessons Learned From Early Implementation of Option B+. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 67, S188–S194. <https://doi.org/10.1097/QAI.0000000000000372>
9. Chung N.C. B-MC, Chilengi R, Kasaro M. P., Stringer J. S. A and Benjamin H. Chi B. H. Patient engagement in HIV care and treatment in Zambia, 2004–2014. *Tropical Medicine and International Health*. 2017;22(3):332-9.
10. UNAIDS. UNAIDS Global AIDS Update Data Book. Geneva; 2017. [Cited 2018 September 11]. Available from: http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS_Global_AIDS_Update_2017_Data_book_2017_en.pdf
11. UNICEF. 'Options B and B+: Key considerations for countries to implement an equity-focused approach'. 2012 [Cited 2017 July 7]. Available from: https://www.unicef.org/aids/files/hiv_Key_considerations_options_B.pdf
12. Haas A, van Oosterhout J, Tenthani L, Jahn A, Zwahlen M, Msukwa MT et al. (2017) HIV transmission and retention in care among HIV-exposed children enrolled in Malawi's

prevention of mother-to-child transmission programme. *Journal of the International AIDS Society*. 2017;20(1):21947.

13. Cromwell A, Dow A, Low D, Chirambo C, Heyderman R, Dube Q et al. (2015) Barriers to successful early infant diagnosis of HIV infection at primary care level in Malawi. *The Pediatric Infectious Disease Journal*. 2015;34(3):273-5.

14. Feinstein L, Chalachala J, Okitolonda V, Lusiana J, Van Rie A, Chi B, Cole S, Behets F. (2014) Temporal changes in the outcomes of HIV-exposed infants in Kinshasa, Democratic Republic of Congo during a period of rapidly evolving guidelines for care (2007-2013). *AIDS* (London, England). 2014;28(3):301-11.

15. Mercy G, Chiduo B, Zahra P, Bygbjerg C, Jan G, Martha L, Terese K. (2013) Early infant diagnosis of HIV in three regions in Tanzania; successes and challenges. *BMC Public Health*. 2013;13(910).

16. Wingston F, Ng'ambi S, Anthony H, Dalitso M, Philip O, Kudakwashe T, Salem G, Sam P. (2016) Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012–2014. *Tropical Medicine and International Health*. 2016;21(8):995–1002

17. UNAIDS. 'Prevention Gap Report'. 2016. [Cited 2018 September 11]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf

18. Sugandhi N, Rodrigues J, Kim M, Ahmed S, Amzel A, Tolle M, et al. (2013) HIV-exposed infants: rethinking care for a lifelong condition. *AIDS* (London, England). 2013;27 Suppl 2:S187-95.

19. Gumede-Moyo S, Filteau S, Munthali T, Todd J, Musonda P. Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa: A systematic literature review. *Medicine* (Baltimore). 2017;96(40):e8055.
20. Munthali T. MP, Mee P, Gumede S, Schaap A, Mwinga A, Phiri C, Kapata N, Michelo C, Todd J. (2017) Underutilisation of routinely collected data in the HIV programme in Zambia: A review of quantitatively analysed peer-reviewed articles. *BMC Research Policy and Systems*. 2017;15(51).
21. UNAIDS. ‘GARPR Zambia country report’. 2015. [Cited 2017 August 8]. Available from: http://www.unaids.org/sites/default/files/country/documents/ZMB_narrative_report_2015.pdf
22. Chanda-Kapata P, Kapata N, Klinkenberg E, William N, Mazyanga L, Musukwa K, Mwaba P. (2016) The adult prevalence of HIV in Zambia: results from a population based mobile testing survey conducted in 2013–2014. *AIDS Research and Therapy*, 13(1), 4. <https://doi.org/10.1186/s12981-015-0088-1>
23. Kandala N.B, Ji C, Cappuccio P. F, & Stones, R. W. (2008) The epidemiology of HIV infection in Zambia. *AIDS Care*, 20(7), 812–819. <https://doi.org/10.1080/09540120701742292>
24. Central Statistical Office, Zambia; Ministry of Health, Zambia; ICF International. ‘Zambia Demographic and Health Survey 2013-14’. 2014. [Cited 2017 August 9]. Available from: <https://www.dhsprogram.com/pubs/pdf/FR304/FR304.pdf>

25. Health Policy Project. ‘Sustainable HIV Financing in Zambia: Baseline analysis and prospects for new domestic resource mobilization’. 2015. [Cited 2017 August 20]. Available from: https://www.healthpolicyproject.com/pubs/2876_ZambiaHIVFinancingFeb.pdf
26. Kourtis A. P, Wiener J, Kayira D, Chasela C, Ellington S. R, Hyde L, Jamieson D.J. (2013) Health outcomes of HIV-exposed uninfected African infants. *AIDS*, 27(5), 749–759. <https://doi.org/10.1097/QAD.0b013e32835ca29f>
27. Zash R, Souda S, Leidner J, Ribaud H, Binda K, Moyo S, Shapiro R. (2016) HIV-exposed children account for more than half of 24-month mortality in Botswana. *BMC Pediatrics*, 16(1), 103. <https://doi.org/10.1186/s12887-016-0635-5>
28. Lilian R.R, Kalk E, Bhowan K, Berrie L, Carmona S, Technau K, Sherman G. G. (2012) Early diagnosis of in utero and intrapartum HIV infection in infants prior to 6 weeks of age. *Journal of Clinical Microbiology*, 50(7), 2373–2377. <https://doi.org/10.1128/JCM.00431-12>
29. Francke J.A, Penazzato M, Hou T, Abrams E.J, Maclean R.L, Myer L, Ciaranello A. (2016) Clinical Impact and Cost-effectiveness of Diagnosing HIV Infection during Early Infancy in South Africa: Test Timing and Frequency. *Journal of Infectious Diseases*, 214(9), 1319–1328. <https://doi.org/10.1093/infdis/jiw379>

6.8 Figure legends

Figure 6.1:

Figure Name: Mean age at HIV test and time from diagnosis to treatment initiation by year of birth

Description of Figure:

Blue line is Age at HIV Test and the Red line is the Time from diagnosis to treatment initiation.

Figure 6.2

Figure Name: Percentage of HIV tests performed within 2 months of birth by province in 2010 and 2015

Description of Figure:

The percentages represent the proportion of infants who were tested within 2 months of birth by province in 2010 and 2015

NB//There was no 2015 data for North-Western province. The other missing province is Muchinga province which was newly created in 2011 and is not included in this database.

Table 6.1: Univariable analysis results for sex, season, province and year of birth

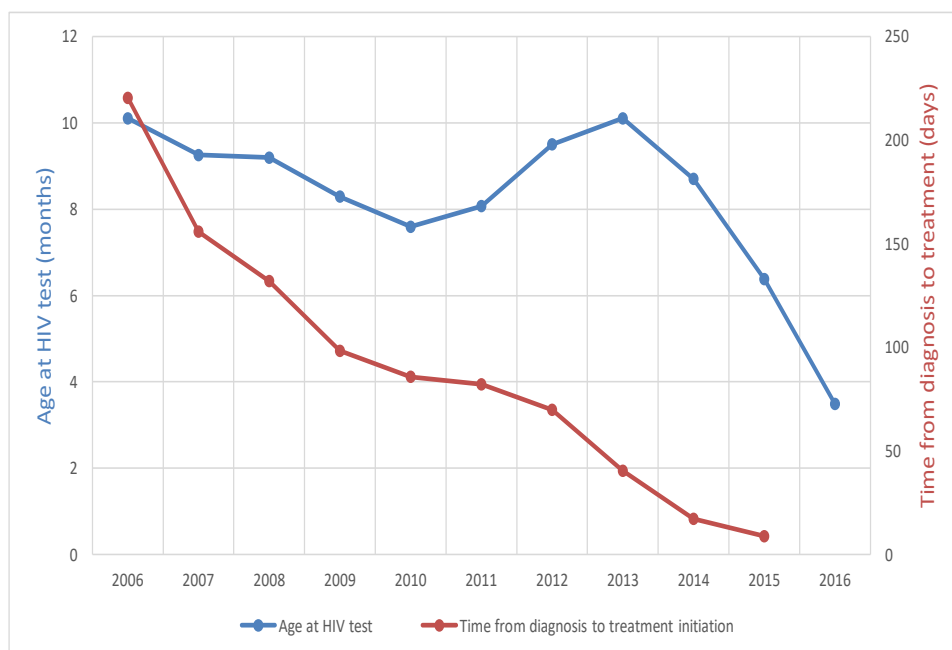
Variable	Age at test		Time from diagnosis to ART		Logistic regression for testing at < 2 months			Logistic regression for time from diagnosis to ART < 2 weeks		
	<2 months	n (%)	<2 weeks	n (%)	OR	95% CI	P-value	OR	95% CI	P-value
<i>Sex</i>										
Male	550/10,537	(5.2)	2,249/10,537	(21.3)	1.00	-	-	1.00	-	-
Female	603/11,185	(5.4)	2,568/11,158	(23.0)	1.03	0.92, 1.17	0.573	1.10	1.03, 1.17	0.004
<i>Season</i>										
Early dry	914/5,254	(17.4)	1,478/5,254	(28.1)	1.00	-	-	1.00	-	-
Late dry	946/4,168	(22.7)	1,135/4,168	(27.2)	1.39	1.26, 1.54	<0.001	0.96	0.87, 1.05	0.333
Early rainy	926/5,364	(17.3)	1,509/5,364	(28.1)	0.99	0.90, 1.10	0.856	1.00	0.92, 1.09	0.999
Late rainy	912/5,474	(16.7)	1,611/5,474	(29.4)	0.95	0.86, 1.05	0.311	1.07	0.98, 1.16	0.137

Variable	Age at test		Time from diagnosis to ART		Logistic regression for testing at < 2 months			Logistic regression for time from diagnosis to ART < 2 weeks		
	<2 months	n (%)	<2 weeks	n (%)	OR	95% CI	P-value	OR	95% CI	P-value
<i>Province</i>										
Lusaka	365/5,394	(6.8)	822/5,394	(15.2)	1.00	-	-	1.00	-	-
Central	94/2,288	(4.1)	688/2,288	(30.1)	0.59	0.47, 0.74	<0.001	2.39	2.13, 2.69	<0.001
Copperbelt	294/4,778	(6.2)	1,648/4,778	(34.5)	0.90	0.77, 1.06	0.210	2.93	2.66, 3.22	<0.001
Eastern	59/2,072	(2.8)	431/2,072	(20.8)	0.40	0.31, 0.53	<0.001	1.46	1.28, 1.66	<0.001
Luapula	56/1,341	(4.2)	547/1,341	(40.8)	0.60	0.45, 0.80	0.001	3.83	3.36, 4.37	<0.001
Northern	57/983	(5.8)	350/983	(35.6)	0.85	0.64, 1.13	0.262	3.08	2.65, 3.57	<0.001
North-Western	25/883	(2.8)	244/883	(27.6)	0.40	0.27, 0.61	<0.001	2.12	1.80, 2.50	<0.001
Southern	394/3,366	(11.7)	718/3,366	(21.3)	1.83	1.57, 2.12	<0.001	1.51	1.35, 1.69	<0.001

Variable	Age at test		Time from diagnosis to ART		Logistic regression for testing at < 2 months			Logistic regression for time from diagnosis to ART < 2 weeks		
	<2 months	n (%)	<2 weeks	n (%)	OR	95% CI	P-value	OR	95% CI	P-value
Western	24/1,577	(1.5)	285/1,577	(18.1)	0.21	0.14, 0.32	<0.001	1.27	1.06, 1.42	0.007
<i>Year of birth</i>										
2006	220/1,709	(12.9)	340/1,709	(19.9)	1.00	-	-	1.00	-	-
2007	412/2,619	(15.7)	547/2,619	(20.9)	1.26	1.06, 1.51	0.009	1.06	0.91, 1.24	0.430
2008	528/3,475	(15.2)	790/3,475	(22.7)	1.21	1.02, 1.44	0.025	1.18	1.03, 1.37	0.020
2009	683/3,678	(18.6)	861/3,678	(23.4)	1.54	1.31, 1.82	<0.001	1.23	1.07, 1.42	0.004
2010	675/2,718	(24.8)	726/2,718	(26.7)	2.24	1.89, 2.65	<0.001	1.47	1.27, 1.70	<0.001
2011	446/1,812	(24.6)	612/1,812	(33.8)	2.21	1.85, 2.64	<0.001	2.05	1.76, 2.40	<0.001

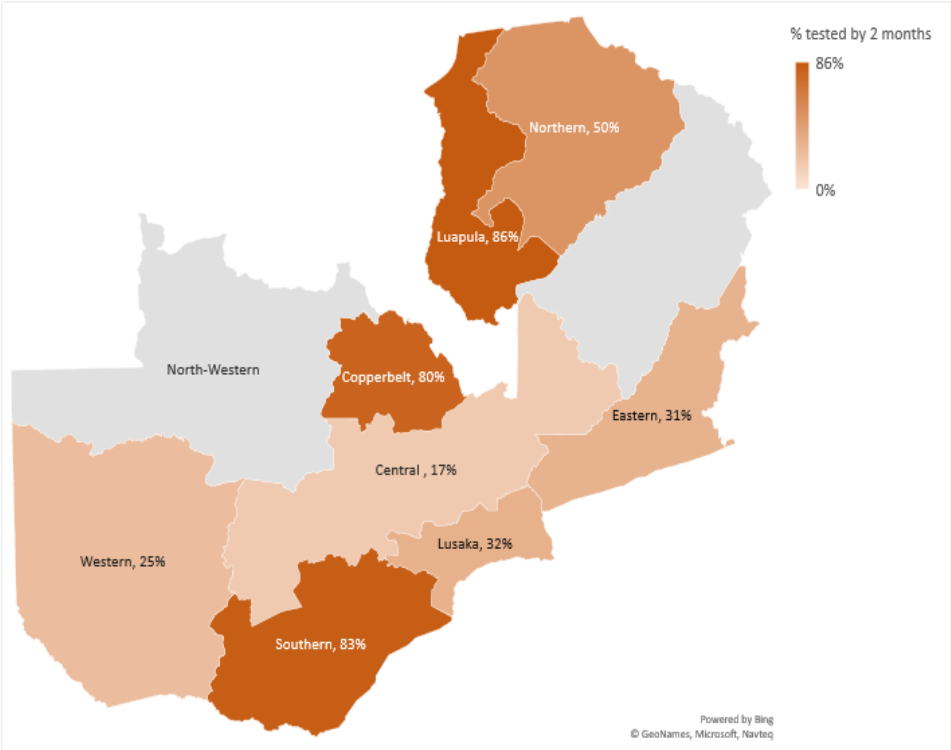
Variable	Age at test		Time from diagnosis to ART		Logistic regression for testing at < 2 months			Logistic regression for time from diagnosis to ART < 2 weeks		
	<2 months	n (%)	<2 weeks	n (%)	OR	95% CI	P-value	OR	95% CI	P-value
2012	191/1,384	(13.8)	564/1,384	(40.8)	1.08	0.88, 1.33	0.450	2.77	2.35, 3.26	<0.001
2013	186/1,352	(13.8)	605/1,352	(44.7)	1.08	0.88, 1.33	0.474	3.26	2.76, 3.85	<0.001
2014	171/1,019	(16.8)	548/1,019	(53.8)	1.36	1.10, 1.70	0.005	4.68	3.90, 5.62	<0.001
2015	137/386	(35.5)	140/386	(36.3)	3.72	2.87, 4.83	<0.001	2.29	1.80, 2.92	<0.001
2016	49/108	(45.4)	0/108	(0.0)	5.62	3.71, 8.51	<0.001	-	-	-

Fig. 6.1: Mean age at HIV test and time from diagnosis to treatment initiation by year of birth

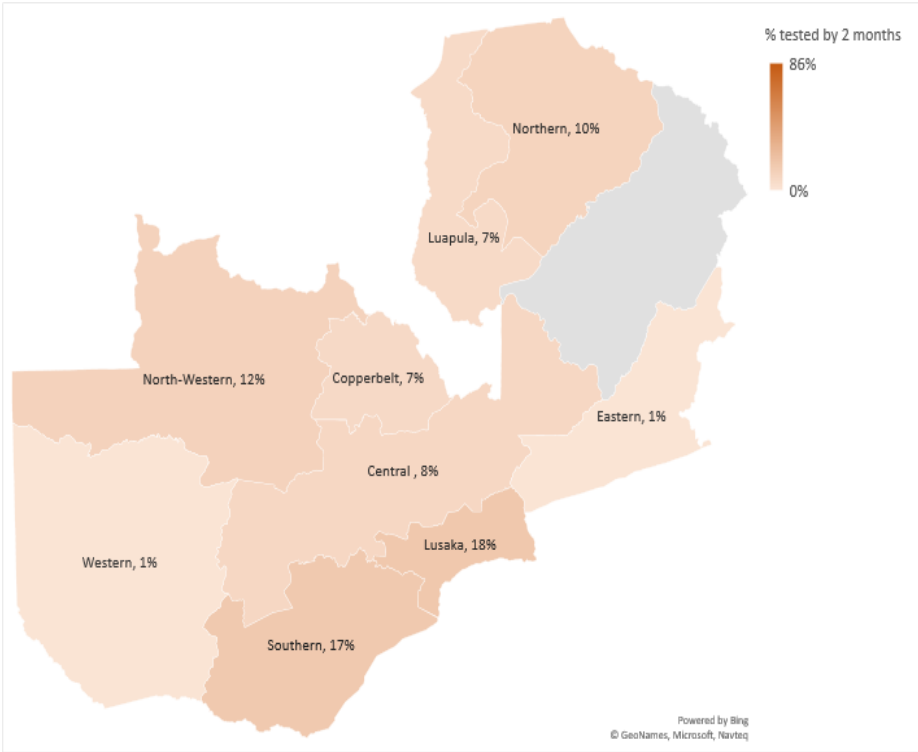


The blue line is Age at HIV testing is in months
The red line is Time from diagnosis to treatment in days

Figure 6.2: Percentage of HIV tests performed within 2 months of births by province in 2010 and 2015



2010



2015

Chapter 7: Qualitative paper on implementation challenges of the SmartCare electronic health record system

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

T: +44 (0)20 7299 4646

F: +44 (0)20 7299 4656

www.lshtm.ac.uk

RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1405741	Title	Mrs
First Name(s)	Sehlulekile		
Surname/Family Name	Gumede-Moyo		
Thesis Title	Evaluating Implementation of revised (post 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using Routinely Collected Data in Zambia.		
Primary Supervisor	Suzanne Filteau		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	International Journal of Health Informatics
Please list the paper's authors in the intended authorship order:	Sehlulekile Gumede-Moyo (BSc, MPH, MBA,) Jim Todd (MA, MSc) ; Virginia Bond (MSc, MA) Paul Mee (BSc, MSc, PhD) and Suzanne Filteau (BSc, MSc, PhD)
Stage of publication	Submitted

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)

I conceived the study and conducted all the interviews and observations. I conducted the analysis and drafted the manuscript

SECTION E

Student Signature	S Gumede-Moyo
Date	December 2018

Supervisor Signature	
Date	4/12/18

A Qualitative Inquiry into Implementing an Electronic Health Record System (SmartCare) for Prevention of Mother-to-Child Transmission data in Zambia

Sehlulekile Gumede-Moyo (BSc, MPH, MBA,)^{1,2§}; Jim Todd (MA, MSc)¹ ; Virginia Bond (MSc, PhD)^{1,3} Paul Mee (BSc, MSc, PhD)¹ and Suzanne Filteau (BSc, MSc, PhD)¹

. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

2. School of Public Health, University of Zambia, Lusaka, Zambia

3. ZAMBART, University of Zambia, School of Medicine

§Corresponding author: Sehlulekile Gumede-Moyo. Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. (sehlulekile.gumede@lshtm.ac.uk)

Email addresses of authors:

SGM: sehlulekile.gumede@lshtm.ac.uk

JT: jim.todd@lshtm.ac.uk

VB: virginia.bond@lshtm.ac.uk

PM: paul.mee@lshtm.ac.uk

SF: suzanne.filteau@lshtm.ac.uk

Key words: PMTCT, routinely collected data, electronic health records, implementation.

Abstract

Introduction: Routinely collected clinic data can provide information for surveillance of program implementation and impact. In services for the prevention of mother-to-child transmission (PMTCT) of HIV among pregnant women in Sub-Saharan Africa, the data collection systems often lack immediacy as paper-based records are completed at each facility and aggregate data are collated centrally. Electronic Health Records (EHR) could present an opportunity to improve accuracy, timeliness and scope of surveillance data. This study aimed to investigate the challenges in implementing a Zambian EHR system labelled ‘SmartCare’ in order to improve PMTCT data.

Method: Data was collected using in-depth interviews, observations and focus groups discussions (FGD) between September and November 2016. Seventeen in-depth interviews were held with a range of key informants from the Ministry of Health and local and international organisations implementing SmartCare. Four data entry observations and three FGDs with 22 pregnant and lactating women seeking PMTCT services were conducted. Data was analysed using a thematic content approach.

Results: The SmartCare system has evolved from various patient tracking systems into a multifunctional system. Funding challenges impede data collection due to manpower constraints and shortages of data collection supplies. Challenges associated with data collection depend on whether a paper- or computer-based system is utilised. There is no uniformity in the data quality verification and submission strategies employed by various implementing partners. There isn’t much feedback from the EHR system at health facility level, which has led to disengagement as stakeholders do not see the importance of the system.

Conclusion: SmartCare has structural challenges which can be traced from its development. Funding gaps have resulted in staffing and data collection disparities within implementing partners. The lack of feedback from the system has also led to complacency in operational level which has resulted in poor data quality in later years.

(297 words)

7.1 Introduction

Routinely collected clinic data can provide much needed information on the prevalence of HIV among pregnant women and the uptake of services for prevention of mother-to-child transmission (PMTCT) of HIV(1). The use of routinely collected data can be timely and cost-efficient for decision making as data are already available for analysis (2). Collection of high-quality routine data on these services and outcomes for HIV-positive mothers and HIV-exposed infants is essential for monitoring and evaluation of PMTCT programmes, for clinical management of patients, and for managing stocks of HIV test kits and drugs (1) For both the clinic staff and health system managers, having access to reliable data that reflects the processes of care and clinical outcomes is the first step to ensuring effective delivery of an intervention within a health care system(3, 4). However in Zambia there is underutilization of routinely collected data in the HIV programmes (5).

In our systematic review of literature of previous work we noted that the data collection systems for PMTCT programs in Africa often lack immediacy as many are paper-based with records completed at each facility, and with individual level data that are inaccessible to central planners(6). Electronic health records (EHRs) could present an opportunity to supplement current sources of routinely collected surveillance data (7). EHRs are real-time, patient-centered records that make information available instantly and securely to authorized users (8). While an EHR does contain the medical and treatment histories of patients, an EHR system is built to go beyond standard clinical data collected in a provider's office and can include a broader view of a patient's care (9).

Various EHR systems are implemented globally (10-12). A systematic of review of literature about the effect of EHR systems in resource-constrained settings recommended that it is urgent to evaluate barriers to implementation (13). Our own research on extracting surveillance data from a Zambian EHR system, SmartCare, has highlighted some deficiencies including large amounts of missing data, especially in more recent years, and variable performance across the country (14, 15). The overall goal of our study is to improve the implementation of an EHR system in Zambia labelled 'SmartCare' and address the fundamental need for timely and high-quality data.

7.2 Methods

7.2.1 Study design

This qualitative study included in-depth interviews, observations and focus groups discussions (FGDs) conducted between September and November 2016.

7.2.2 Study Setting

SmartCare is a Zambian Ministry of Health (MoH)-led project funded by the United States Centre for Disease Control and Prevention (CDC). SmartCare was developed to improve continuity of care and provide timely data on maternal and child health, HIV/AIDS, tuberculosis and malaria interventions for public health purposes, including Health Management Information System (HMIS) trend reporting and analysis for health officials and clinicians (16).

The SmartCare database is a derivative of the PTS (patient tracking system) which was developed in 2004, based on a health facility-centred EHR system. In 2010, it became a national medical health program and was then rolled out throughout the country. It is implemented by government, and both international and local organisations primarily for patient management. Most of the international organisations were involved in the database development, and the local organisations became involved when implementation was rolled out throughout the country (after 2009).

SmartCare is organised into comprehensive modules and sub-modules (*Figure 7.1*). This was mainly influenced by its funders depending on the information they wanted at that particular time. The main module groups are: clinical group comprising the following modules – ANC, Delivery, Postnatal, ART, Paediatric ART, PMTCT follow up, Under 5 among others – (these are mainly of interest for this research); logistic group which constitute information on drug dispensing and orders; monitoring and evaluation groups which includes health management information system reports, graphing, data analysis, data merge from facilities for MOH; and the continuity of care group which had data from across facilities and within facilities. Through the data merge the SmartCare information can be used to obtain data for the monthly reports to MOH.

Data is captured under a number of ‘modules’ across a range of health issues. Records are updated at every point of clinical service. SmartCare enables the capture of all patient data into one centralised database that can be accessed from any supported health facility. Patients

enrolled in the system can have their records accessed at whichever SmartCare-supported facility they present to in the country. Patients are issued with Smartcards at their initial consultation which contains all their clinical information and treatment details. When they present at another facility the health worker simply plugs the Smartcard into the system and can access all the patients' details.

Data on a range of HIV and pregnancy related outcomes are collected during the patient consultation with the clinician, who records the information on paper forms in facilities that are paper-based and directly on the computer in the few facilities which are computer-based. The paper forms are then entered into the SmartCare database by data entry clerks who have been trained in using the SmartCare database. Data is collected from each facility on a monthly basis and submitted to a District Health Information Officer, who aggregates and sends the data to the province level Senior Health Information Officers. From here the data are wired to a national server at MoH headquarters (*Figure 7.3*)

For the purposes of this study, routine data is defined as data that are routinely generated through antenatal care (ANC) and PMTCT service delivery, and routinely recorded in standard SmartCare data tools.

7.2.3 Sampling

The implementing partners (IPs) were purposively sampled in consultation with the MoH to identify diverse organizations. These included both well-resourced international organizations and less well-resourced local and government-owned organizations. Within each of the selected IPs, a diverse range of interviewees were purposively recruited in order to give the broadest range of perspectives (17, 18). The approaches to recruitment of participants were flexible, being negotiated with key contacts and recommendations from managers who were also considered for in-depth interviews. The FGDs were conducted at maternal and child health (MCH) departments in health facilities among consenting pregnant and lactating HIV-positive women on ART.

Six health facilities from the representative IPs were also purposively selected based on local considerations which included, among these facilities: those best performing versus struggling; those which are paper- or computer-based; and facilities which had already transitioned to 'test and treat' for general population HIV care. Most of the facilities sampled were in Lusaka City, and only one was peri-urban. The choice of Lusaka was based on the

following considerations: 1) logistics, 2) facilities in Lusaka are busy and have the highest case loads, 3) our previous work has shown that facilities in Lusaka show a wide range of successes and failures, and 4) overall Lusaka performs poorly compared to the rest of the country and therefore it was important to investigate the working of SmartCare in Lusaka city.

7.2.4 Data sources

Data were generated from 17 in-depth semi-structured interviews, four data entry observations and three FGDs with 22 pregnant and lactating women seeking PMTCT services from three health facilities (Table 7.1). The face-to-face semi-structured interviews were held with a range of key informants from MOH, and local and international organisations SmartCare IPs. IP informants were from leadership, operational and implementation levels (*Figure 7.2*). The key informants for implementation levels were based in the 6 sampled health facilities, whilst in-depth interviews with leadership and implementation level participants were carried out in their work places. For leadership staff and some senior operational level staff the interviews were carried out in their individual offices. For the operational level participants who were in shared office space, interviews were carried in boardrooms.

Interviews with key informants were conducted by the first author in English. They lasted 30 to 60 minutes and consisted of a series of open-ended questions with follow-up question probes. The interview guides were specific to the hierarchical levels of operation, namely: leadership level (persons involved in the strategic direction of SmartCare); operational level (Data Managers and Monitoring and Evaluation personnel); and implementation level (Data entry clerks and MCH in-charge clinicians). The interview guides were designed to capture information on SmartCare development, implementation procedures, data quality management and linkage between SmartCare and PMTCT services. The FGD sessions were conducted by the first author and a co-moderator who was fluent in the local languages (Bemba and Nyanja). These discussions were guided by an interview guide containing open-ended questions and lasted for 60 to 90 minutes. The interview guide was designed to capture the general knowledge and experience of the PMTCT programme and SmartCare operations. Two FGDs were carried out in different Lusaka health facilities, and one in the peri-urban area.

The observations were conducted to familiarise the researcher with the realities of the SmartCare data collection and entry environments. These were planned to be conducted in 6 health facilities through interaction with study participants and relevant actors as well as personal reactions to the related events without the use of a specific tool. However in 2 health facilities data entry was not taking place on the scheduled visit days due to power outage, hence only in-depth interviews were conducted with implementing level staff.

7.2.5 Data Management and Analysis

The in-depth interviews and FGDs were tape-recorded and subsequently transcribed verbatim. FGDs were then translated into English. Data was collected aiming to get sufficient data from relevant actors/perspectives to ensure it was qualitatively representative (19). Detailed field notes were taken on the sites following the observations for analysis.

Data were collected and analysed without a constraining overarching framework, which enabled us to capture the diversity of experiences of the SmartCare implementation efforts. A thematic content approach was conducted; this was done by reading the transcribed material systematically, line by line, in order to identify the meaning units. Meaning units were defined as strings of the text expressing a single coherent thought, up to the point at which the coherent thought changed. Thereafter, the meaning units were marked by a code, describing what the text unit was about. Coding was done without any pre-conceived ideas.

The codes were defined and organised so that those referring to the same subject were grouped into categories. The interview guide was used as a starting point for grouping the information, but during the analysis new categories were developed. When this happened, we re-coded. The data was managed manually in Excel sheets. The underlying meanings of the categories were formulated into a theme. The original data was re-assessed by an assistant (MSc Student) after analysis in order to detect any concepts or information that would have been missed. The first author discussed the results with SF, JT and the MSc student.

7.3 Research ethics

Written informed consent was obtained from all in-depth interviews participants including their consent to record the interviews and publish anonymous quotations. Verbal consent was sought for FGD participants. Participation in the study was entirely voluntary and participant anonymity was maintained throughout the processes of interview transcription, data analysis and presentation by using pseudonyms. Permission to collect data from the health facilities

was granted by the MoH district offices. The study was approved by the Zambia Biomedical Ethical Board (Ref 101-04-16) and the LSHTM Research Ethics Committee (Ref 12086).

7.4 Results

The comments from key informants, observations and the focus group discussions enabled us to characterise four fundamental issues that are key in the implementation of SmartCare: database development and ownership, funding and staffing, the data collection process, and health facility set up.

7.4.1 Database Development and Ownership

The development of SmartCare was mainly CDC-led, with the government of Zambia through the MoH supporting the process. Multiple stakeholders using various patient tracking software were brought together to form SmartCare. Reflecting on the history of SmartCare, two IP informants identified the leading role of CDC and the subsequent collaboration with a broader group of partners.

'The initial development was by the American-funded institutions and a few people from the MoH because they had gone into partnership. They were developers at MoH and also at CDC, the rest of the institutions like us were only required to use the software.'

Implementing partner leader.

'There were other systems that were used by other partners throughout the country e.g., there was a system called the CareWare which was similar to SmartCare but it was just a patient summary. Then there was another system which was used in the private sector which I can't remember the name. Lessons were drawn from all these systems and brought into one and this is how SmartCare was born.'

Implementing partner leader.

There was a consensus among the leaders of the SmartCare implementation that the database has also evolved from a system to track patients to its current form as a mixture of a patient tracking tool, a clinical care tool, a reporting tool, and a surveillance tool. This was as a result of different stakeholders who had different data needs which took the form of added modules. The changes have however, made it difficult to classify and use the database because it now tries to address multiple issues simultaneously.

'I wanted my things as well and partly I wanted things that PEPFAR (The United States President's Emergency Plan for AIDS Relief) wanted because our money comes from them. If I can't report on PEPFAR indicators, I don't get more money' –Implementing partner leader.

'...it was just a mixture of ideas which were clinically required but each person had different needs for information, some needed it for research purposes, I needed it for patient follow up, another person needed it for forecasting and quantification' - Implementing partner leader

The resulting SmartCare forms are 6-7 pages for a normal interaction per visit because of requirements from its various stakeholders. In addition, a lot of data has been entered into the system making it bulky. This has caused the system to become very slow, and in the mornings it takes a very long time to reboot as narrated by operational and implementing level participants. Data entry is often interrupted as the system also hangs up because it is so bulky. Hence a lot of backlogs are experienced which results in a lot of data not being entered.

'Because the system is slow they have to wait instead of entering 100 files per day they are only able to enter 60 or so.' - Database Manager.

'Last year it had serious faults and we were not using it for a while' – Data Entry Clerk.

Although there is a SmartCare technical working group, chaired by the MoH where operations are discussed, it is not clear who is guiding the process, and what should be added into the database to make it work better.

7.4.2 Funding and staffing

The database operations are managed by the monitoring and evaluation (M&E) departments of the IPs. The structures of the M&E departments differ across the IPs, with international organisations having much bigger and better resourced departments. The local IPs have much leaner structure, rely mostly on volunteers, and run into problems due to financial constraints. This was elaborated by the leadership and implementing level participants.

'The positions of data entry clerks in the facilities are actually paid for by the donor. It's not sustainable because the moment the donor says we are pulling out, there will not be any data entry personnel in these facilities.' - Implementing partner leader.

Mostly the people who enter data in the health facilities where we operate are employed by us. Apart from that we also provide support through volunteers; in most cases we also provide peers and counsellors. –Data Base Manager.

The manpower constraint in the local partners has resulted in the loss of data during long grant negotiations. Data is lost as data entry staff are laid off between funding cycles since their salaries are dependent on grants. In addition, these partners have designated personnel who enter general ART data whilst PMTCT data is mainly entered when the data entry personnel have specific interest or have trained temporary volunteer staff.

The funding of operations also affects the supplies required for the day to day operations as narrated by both operations and implementing personnel.

‘We normally run out of forms, especially when funding is out. When we don't have funding the facilities also have challenges in printing the forms because toner is expensive.’ - Data Entry Clerk.

‘...when the computers are down because of the virus, data entry doesn't happen.’ - M &E Officer.

In some small facilities where the MoH is solely responsible for data collection and entry, there are no data entry clerks and hence clinicians enter the data on the computer after hours. This is usually done only by staff that are passionate and so give it time according to a MoH leader.

‘In the government facilities there is no designated person to manage ART data for SmartCare; its health workers who just do that on their own. - ‘Implementing partner leader.’

7.4.3 Data Collection Process

7.4.3.1 Data entry

The SmartCare data is collected either directly onto a computer or using a paper-based method. When using the computer-based data collection and entry method, clinicians have to enter data directly in the computer; this method is still being piloted in a few facilities mainly in the Southern and Lusaka provinces. For the paper-based data method, client information is documented in the SmartCare care forms. The papers are then taken to the data entry room where the information is entered into the computer. In some facilities which are deep rural

(where there is no electricity at all) they are using paper only and the forms are then transferred to a location where there are computers and entered into the database.

With both the computer and the paper-based methods the greatest challenge is incomplete forms which translate to missing data in the database. In some facilities which are computer-based, the data entry clerks noticed that there are also some clinicians who still prefer entering data on paper and handing over to the data entry clerks to enter on the computer.

'In as much as data is supposed to be entered at each service point, some people prefer entering the data on paper and they hand over the data to me.' - Data Entry Clerk

According to implementing level staff, with the paper-based method, once the client leaves the facility it is a challenge to follow up on the missing data on the forms.

'There are usually many gaps in the forms; the forms are not fully completed more than half of the time.' - Data Entry Clerk.

'When the forms are not complete I return them to whoever was supposed to be entering the data at that service point but the challenge is that they will tell you the person has gone and that can't follow them up and even so in the next visit they will not even bother correcting the information' - Data Entry Clerk.

One of the MoH participants explained that the incomplete data forms could be a result of the competing demands to physically attend to clients and fill out the forms in the high volume facilities.

'... It takes 20-30 minutes just to enter the data for one interaction. In clinics where there are many patients, how many patients are you going to see in a day?' – Implementing partner leader.

The implementation challenges of the SmartCare database depend on the data collection and entry method used. Power outages were the greatest challenge: under the computer-based method, client information is not collected, as some clinicians will be reluctant to use the alternative method, whereas with the paper-based method there will be a backlog of work.

Some well-funded partners have installed solar power systems in the health facilities, and this enables them to enter data without interruptions. Despite having good power supply, there is

a challenge in these facilities of some clinicians who are not computer literate. Furthermore, because of other competing health facility priorities, the power is rarely used for data entry.

'.....would you want to power theatre activities or you want to power computers for data entry? Theatre is life saving and data can be entered anytime.' – Implementing partner leader.

7.4.3.2 Data quality verification

Verification of data quality is specific to each implementing partner. The verification process involves comparing the patient information on the paper forms and registers against the information in the database. The international partners also have verification procedures imbedded in the Monitoring and Evaluation strategies as narrated by one of their participants.

'We are doing double data entry for 10% of our files.' – Data Manager.

On the other hand, verification is rarely done by the local organisation due to manpower constraints as indicated by an operational level participant.

'When I get time, I check what is in the system versus what is in the registers. However it's rare that I get that time because I always have files to enter into the system. In that case I wait for the Quality Control people from Head Office to come and do random verifications for me.' - Data entry clerk

All the partners reported that there are some instances where they can't find patient files, making it difficult for them to verify the data that is in the computer with the raw data.

'There are certain instances where we can't find patient files'. – M&E Officer.

The patient files will tell me that a facility has 200 clients whilst SmartCare has 300 clients; this is because some of these files are kept somewhere, could be files of staff members or people with prominent positions in that particular area'. – Database Manager

The SmartCare Database system has reports that are built in the application. However all the partners alluded that these reports are very inconsistent and incorrect.

'In some cases it will show a large number of people who would have been initiated in a day more than what we would have actually done.' – MCH Nurse in Charge.

7.4.3.3. Submission of data to the main database

There is also no uniformity in submission of the data to the main database, although according to the MOH the data is supposed to flow from the facility to the district, province and then to the main database at head office (Figure 7.2). Some partners wait for MoH to request data whilst some submit their data to CDC.

'They sometimes come to the facilities and collect the data on their own since they are the ones who own these facilities as well' – M & E officer

'We do not follow that procedure as per say because we collect data directly from the sites and aggregate it from here and submit to CDC. If MOH requests it, we submit to them but we are not that consistent' - Database Manager

7.4.3.4 Feedback from Database

There is no standardised procedure for reporting data that is collected by IPs. The partners normally use the information internally as well as sharing with the donors supporting them.

'We also have special reports that we do in a monthly basis such as the PEPFAR report' – M & E Coordinator.

In contrast, the nurses-in-charge in some of the facilities reported that they have never received feedback from the system.

'We have not received anything; they don't give us any reports. We would, however, want to receive reports so that we would know how we are fairing.' – MCH Nurse in Charge.

As viewed by one of the leaders who participated in the study, the lack of feedback from the system has led to disengagement and some stakeholders not seeing the importance of documenting client information in the SmartCare Database.

'A lot of the staff collecting this data do not understand how and why they are collecting this data and they are frustrated by it as it also takes lots of their time entering this data' – Implementing partner leader.

7.4.4 Health Facility setup

The set up in some health facilities is in such a way that the PMTCT services are offered in the ANC department whereas ART services are offered in places designated solely for ART.

The nurses in charge in such health facilities narrated that the facility setup could be a great challenge in ensuring that the PMTCT data is entered in an efficient manner.

‘Probably if it was housed within the ART department, you could have the same person entering the PMTCT data into the SmartCare’ – MCH nurse in charge.

In addition, the MCH nurses-in-charge indicated that client files sometimes go missing between the MCH and the data room.

‘I am sure when they are sending the files; some are lost during transfer in different departments.’ – MCH nurse-in-charge.

Overall, women seeking PMTCT services did not have concerns on the implementation of SmartCare, as according to them the healthcare workers will be doing their job.

‘The person who is supposed to enter the data does so because he was trained anyway’- PMTCT FGD Mothers.

‘We just carry our cards and leave them to do their job’- PMTCT FGD Mothers.

‘We are here for our lives and that of our babies, we have to comply and be patient’- PMTCT FGD Mothers

7.5 Discussion

The study has provided evidence on the SmartCare implementation challenges. It has also provided insights as to how to improve implementation, and data quality. The main points were to collect less, but better data, to engage the clinic staff by providing regular feedback, and to improve the software. Fortunately, PMTCT clients appear already satisfied with the system.

The design of EMR systems does not always get attention due to pressures related to their functionality requirements(10). SmartCare was exposed to pressures as its data model evolved from a patient tracking system into a multi-functional system due to demands of various stakeholders. In an effort to shape the SmartCare database into a manageable tool that can be used for public health purposes, CDC and MOH could streamline the process for including and excluding information that is collected. There is a need to cut down on the number of fields collected so that less data of high-quality is collected. This could improve

the system by: reducing the amount of data so that it takes less time to collect and people might more readily do it; and having a less bulky database which will be less likely to be affected by computer crashes and faster to use.

SmartCare could be developed into an Open Medical Record System (MRS), which has been reported to be successful in other developing countries like Rwanda, and Kenya (20). The system could also be upgraded such that: data can be accessible and be shared in multiple sites; multiple users can enter data simultaneously; data can be backed up automatically at more than one site; information can be communicated between multiple locations; data are accessible and shared at multiple sites and the system can be debugged and upgraded over the internet without visiting remote sites (10, 21).

In Ethiopia the quality of data was reported to be affected by dual documentation where both paper based and electronic systems were used (22). Learning from the Ethiopian experience, it is important that there is uniformity in the implementation of SmartCare throughout the country so that everyone will be on the same level. This will allow for comparisons across geographic regions and longitudinal analyses.

In our findings workload affected the documentation, as evidenced by poor data quality in the quantitative analysis of SmartCare PMTCT data (14, 15). In low –resource countries there is a shortage of a qualified work- force and most health care institutions do not have dedicated IT staff for their EMR systems (23). The results of our study are consistent with a systematic review of literature on the role of EHR systems in developing countries which pointed to the lack of financial and human resources as major challenges in implementing EMR systems (24). Therefore, there is a great need for strong commitment from both the government and the donors to invest in improving the implementation of the system.

There was a notable lack of appreciation of the system, and a need to train and support end users of the system such as the clinicians who are directly involved in the data collection process. For both the clinic staff and health system managers, having access to reliable data that reflects the processes of care and clinical outcomes is the first step to ensuring effective delivery of an intervention within a health care system(4). Hence, there should be better buy-in of the staff at the facilities in order to make sure that they fill in the forms regularly and accurately. The data from the database should be presented to facility staff as an advocacy tool which is needed in their facilities, so that they would appreciate the need for it (25, 26).

Similarly, in their description of the rationale and experience in scaling up EMR in Malawi, Douglas and colleagues concluded that health workers will not adopt a system if they do not find sufficient value in it (27).

Strengths and Limitations of the study

We obtained a rich and nuanced appreciation of the implementation of the SmartCare as we sampled from a range of IPs, health facilities, stakeholders and implementation systems. The depth of the inquiry enabled us to consider a range of explanatory factors. Most of these factors were related to the EHR system and its implementation. We also considered the factors encountered by the PMTCT clients but these did not emerge as major concerns.

There are several limitations of the study, such as the restriction to health facilities in and around Lusaka. Lusaka is the capital city of Zambia and therefore the health facilities selected could be receiving financial and technical support of an order that is unlikely to be offered in remote facilities even by the same IP. However, our previous work on the quantitative analysis of PMTCT data does not support this argument as several provinces had better data quality than Lusaka (14, 15).

7.6 Conclusion

The SmartCare system has structural challenges which can be traced from its development. Funding gaps have resulted in staffing and data collection disparities within implementing partners. The lack of feedback from the system has also led to complacency in operational level which has resulted in poor data quality in later years. The data from the database, if appropriately understood, could be used by health facility staff as an advocacy tool, as well as in monitoring the impact of PMTCT programs. Our research could aid other countries wanting to develop their own EHR systems.

Summary

What is known

- Electronic Health Records (EHR) could present an opportunity to improve accuracy, timeliness and scope of surveillance data
- Data collection systems for PMTCT programs in Africa often lack immediacy as many are paper-based with records completed at each facility, and with individual level data that are inaccessible to central planners.

What this study adds on

- There is need to invest in EHR systems for them to be implemented in a very efficient manner.
- It is important that there is uniformity in the implementation of EHR.
- Feedback from the system must be presented to stakeholders.

Authors' contributions

SGM conceived the study and conducted all the interviews and observations under the supervision of SF, and JT. Analysis was conducted by SGM with the input from SF, JT and VB. The manuscript was drafted by SGM with contributions from all the authors. All authors read and approved the final manuscript.

Availability of Data

No additional data available.

Competing interests

None declared.

Acknowledgements

The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472. We also thank the Ministry of Health, Department of Policy and Planning for granting us permission to access the SmartCare database. The authors thank all the participants who contributed their time and effort to the study and Jasleen Singh (MSc student) for going through the transcripts and assessing the initial analysis.

7.7 References

1. Gourlay A, Wringe A, Todd J, Michael D, Reniers G, Urassa M, et al. Challenges with routine data sources for PMTCT programme monitoring in East Africa: insights from Tanzania. *Global health action*. 2015;8:29987.
2. Grzeskowiak LE, Gilbert AL, Morrison JL. Methodological challenges in using routinely collected health data to investigate long-term effects of medication use during pregnancy. *Ther Adv Drug Saf*. 2013;4(1):27-37.
3. Shaw V. Health information system reform in South Africa: developing an essential data set. *Bulletin of the World Health Organization*. 2005;83(8):632–6.
4. Mate KS, Bennett B, Mphatswe W, Barker P, Rollins N. Challenges for routine health system data management in a large public programme to prevent mother-to-child HIV transmission in South Africa. *PloS one*. 2009;4(5):e5483.
5. Munthali T. MP, Mee P., Gumede S., Schaap A, Mwinga A., Phiri C., Kapata N., Michelo C., and Todd J. Underutilisation of routinely collected data in the HIV programme in Zambia: A review of quantitatively analysed peer-reviewed articles. *BMC Research Policy and Systems*. 2017;15(51).
6. Gumede-Moyo S, Filteau S, Munthali T, Todd J, Musonda P. Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa: A systematic literature review. *Medicine (Baltimore)*. 2017;96(40):e8055.
7. Russell A, Hellawell G. The future of electronic health records. *Br J Hosp Med (Lond)*. 2013;74(11):604-5.
8. Namulanda G, Qualters J, Vaidyanathan A, Roberts E, Richardson M, Fraser A, et al. Electronic health record case studies to advance environmental public health tracking. *J Biomed Inform*. 2018;79:98-104.
9. Cifuentes M, Davis M, Fernald D, Gunn R, Dickinson P, Cohen DJ. Electronic Health Record Challenges, Workarounds, and Solutions Observed in Practices Integrating Behavioral Health and Primary Care. *J Am Board Fam Med*. 2015;28 Suppl 1:S63-72.
10. Fraser HS, Biondich P, Moodley D, Choi S, Mamlin BW, Szolovits P. Implementing electronic medical record systems in developing countries. *Inform Prim Care*. 2005;13(2):83-95.
11. Allen C, Jazayeri D, Miranda J, Biondich PG, Mamlin BW, Wolfe BA, et al. Experience in implementing the OpenMRS medical record system to support HIV treatment in Rwanda. *Stud Health Technol Inform*. 2007;129(Pt 1):382-6.
12. Siika AM, Rotich JK, Simiyu CJ, Kigotho EM, Smith FE, Sidle JE, et al. An electronic medical record system for ambulatory care of HIV-infected patients in Kenya. *Int J Med Inform*. 2005;74(5):345-55.
13. Oluoch T, Santas X, Kwaro D, Were M, Biondich P, Bailey C, et al. The effect of electronic medical record-based clinical decision support on HIV care in resource-constrained settings: a systematic review. *Int J Med Inform*. 2012;81(10):e83-92.
14. Singh J, Filteau S, Todd J, Gumede-Moyo S. Progress in the performance of HIV early infant diagnosis services in Zambia using routinely collected data from 2006 to 2016. *BMC public health*. 2018;18(1):1297.
15. Gumede-Moyo S, Todd J, Schaap A, Mee P, Filteau S. Effect of prevention of mother-to-child transmission strategies on antiretroviral therapy coverage in pregnant women in Zambia: analysis using routinely collected data (2010–15). *Lancet Global Health*. 2019;7(Supplement 1):S25.
16. Muyunda G. Zambia leads the way in SmartCare electronic health records system, a benefit to both providers and patients 2011 [Available from:

<https://www.jhpiego.org/success-story/zambia-leads-the-way-in-smartcare-electronic-health-records-system-a-benefit-to-both-providers-and-patients/>.

17. Lincoln NKDYS. Handbook of Qualitative Research 2nd ed. London: Sage Publications; 2000.
18. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nurs Health Sci*. 2013;15(3):398-405.
19. Graneheim U.H. LB. Qualitative Content Analysis in Nursing Research: Concepts, Procedures and Measures to Achieve Trustworthiness. *Nurse Education Today* 2004;24:105-12.
20. Mamlin BW, Biondich PG. AMPATH Medical Record System (AMRS): collaborating toward an EMR for developing countries. *AMIA Annu Symp Proc*. 2005:490-4.
21. Della Mea V. Internet electronic mail: a tool for low-cost telemedicine. *J Telemed Telecare*. 1999;5(2):84-9.
22. Abiy R, Gashu K, Asemaw T, Mitiku M, Fekadie B, Abebaw Z, et al. A Comparison of Electronic Medical Record Data to Paper Records in Antiretroviral Therapy Clinic in Ethiopia: What is affecting the Quality of the Data? *Online journal of public health informatics*. 2018;10(2):e212.
23. Fritz F, Tilahun B, Dugas M. Success criteria for electronic medical record implementations in low-resource settings: a systematic review. *J Am Med Inform Assoc*. 2015;22(2):479-88.
24. Williams F, Boren SA. The role of the electronic medical record (EMR) in care delivery development in developing countries: a systematic review. *Inform Prim Care*. 2008;16(2):139-45.
25. Ivers NM, Sales A, Colquhoun H, Michie S, Foy R, Francis JJ, et al. No more 'business as usual' with audit and feedback interventions: towards an agenda for a reinvigorated intervention. *Implementation science : IS*. 2014;9:14.
26. Hemler JR, Hall JD, Cholan RA, Crabtree BF, Damschroder LJ, Solberg LI, et al. Practice Facilitator Strategies for Addressing Electronic Health Record Data Challenges for Quality Improvement: EvidenceNOW. *J Am Board Fam Med*. 2018;31(3):398-409.
27. Douglas GP, Gadabu OJ, Joukes S, Mumba S, McKay MV, Ben-Smith A, et al. Using touchscreen electronic medical record systems to support and monitor national scale-up of antiretroviral therapy in Malawi. *PLoS medicine*. 2010;7(8).

Table 7.1: Breakdown of In-depth Interviews and Focus Group Discussions Participants

Type of respondents	Number of respondents	Method
Leadership	3	In-depth interviews
Database Management	6	
Data Entry Clerks	5	
MCH- Nurse-in charge	3	
Total	17	
Pregnant Mothers	(>20 years) 2	Focus Group Discussions
	(20-25years) 3	
	(26-30 years) 4	
	(31-35 years) 2	
	(36-40 years) 1	
	Total 12	
Lactating Mothers	(>20 years) 1	Focus Group Discussions
	(20-25years) 2	
	(26-30 years) 2	
	(31-35 years) 3	
	(36-40 years) 2	
	Total 10	

Figure 7.1: SmartCare Model Structure

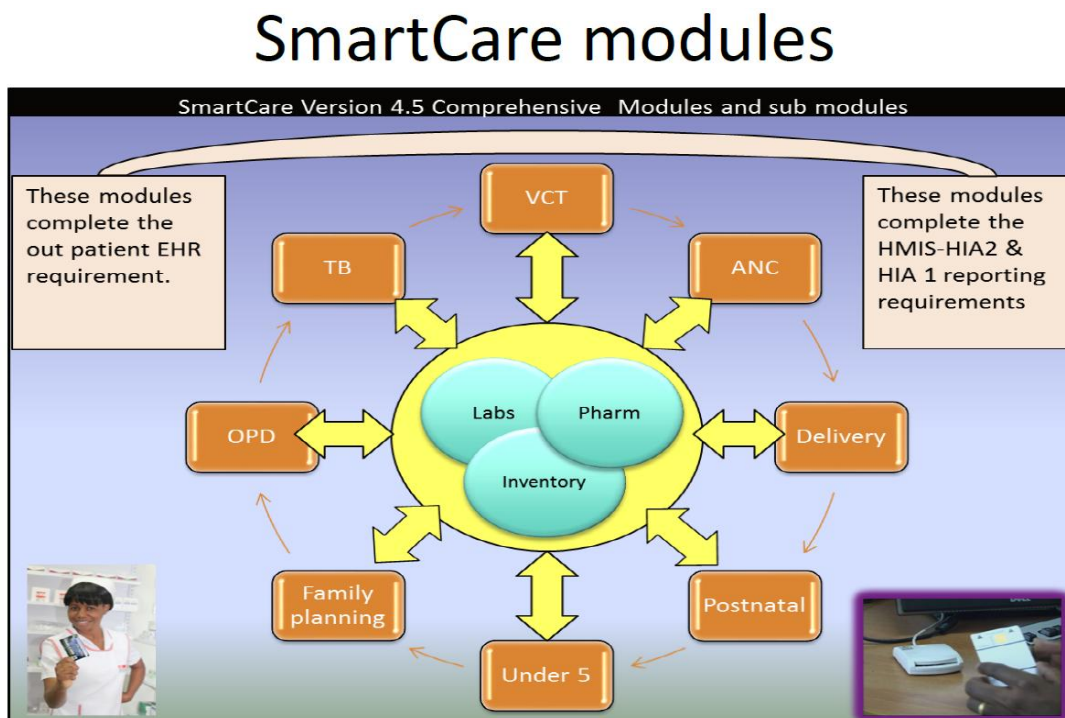
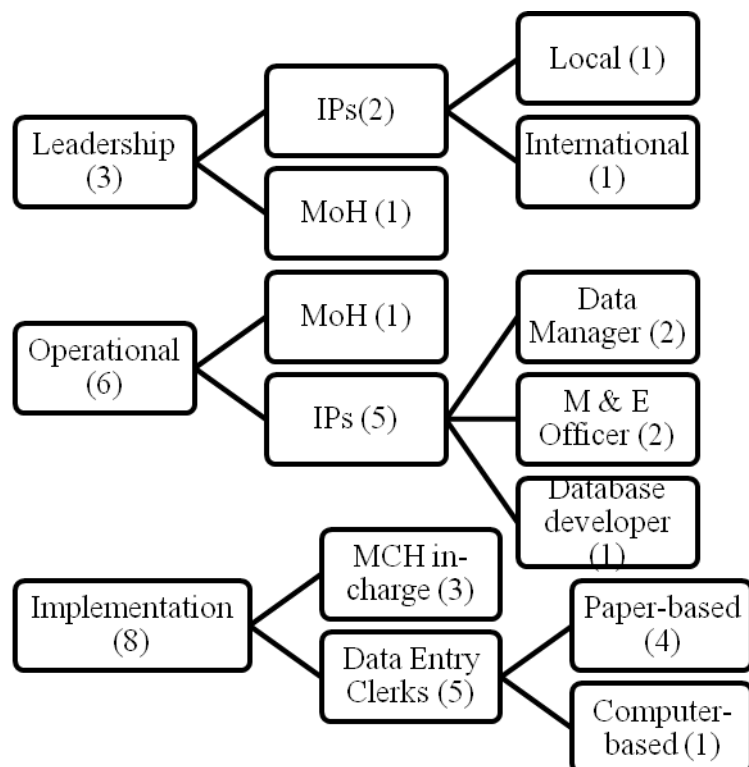
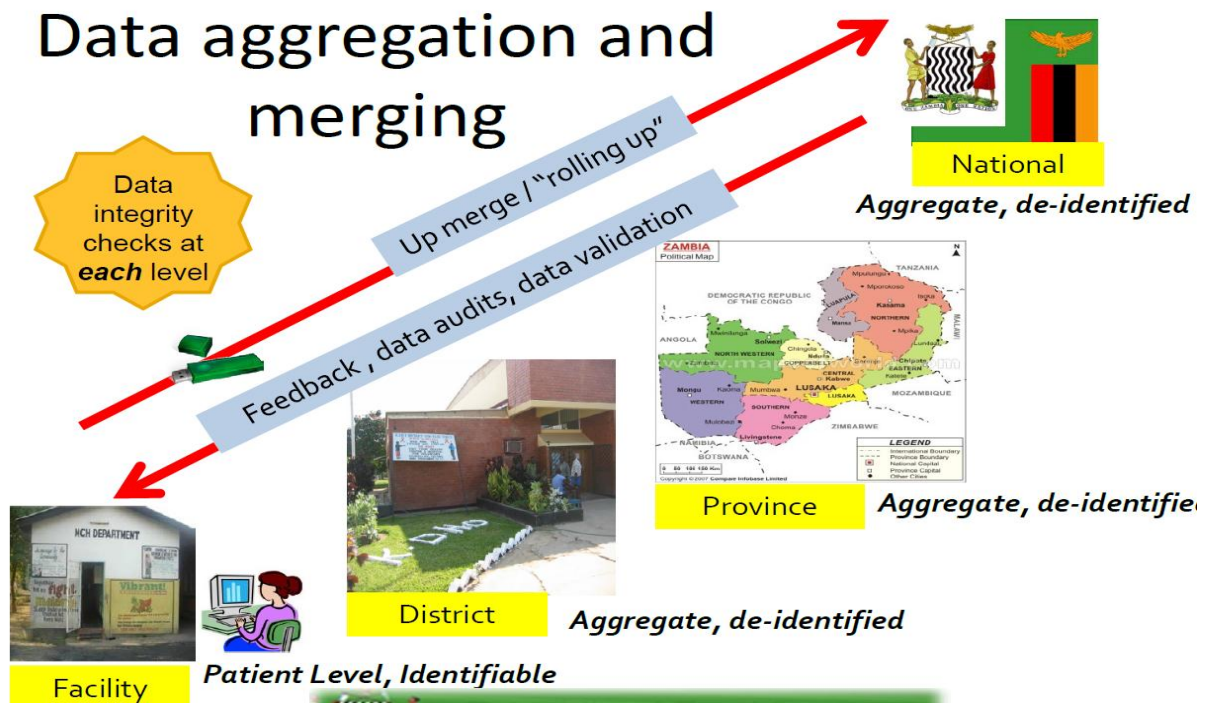


Figure 7.2 - Breakdown of In-depth interviews key informants



Figures in brackets are for the number of people interviewed for that designated level.

Figure 7.3: SmartCare Data flow



Chapter 8: Health Management Information System (HMIS) Data

8.1 Introduction

The main objective of the chapter is to present data from an independent source, the Health Management Information System (HMIS), on outcomes similar to those discussed in Chapters 5 for the purpose of triangulating findings from the SmartCare data. The HMIS data are aggregated by health facilities and submitted monthly through districts to the national MoH. As such the data differ from SmartCare (which records individual level data from the patients) and provides specific information about key health conditions in a regular format.

A well-functioning health information system is one that ensures the production, analysis, dissemination and use of reliable and timely information on health determinants, health system performance and health status (152). An HMIS is only successful to the extent to which it facilitates the production, analysis, dissemination and use of information reliably and in a timely fashion (153). Researchers may also draw upon it to answer critical health system questions pertaining to effectiveness or efficiency of health programs (154).

Zambia has developed a well-integrated health information system providing information for evidence-based planning. The HMIS was designed in 1996 under the context of health sector reforms in order to provide efficient and effective support to the planning, monitoring and evaluation of health care services (155). The HMIS underwent a revision in 2008, which enabled the incorporation of facility indicators to monitor progress of health targets, and as a result of this, a new web based software, District Health Information System (DHIS-2) was developed (156). The DHIS-2, which is supported by WHO, has enhanced capabilities in terms of the number of data elements that can be captured, analyses that can be performed and reports that can be generated.

The quality of HMIS data which influences the use of the data generated from HMIS and factors affecting its use have been assessed in various settings in Africa (124, 157-161). In Zambia before DHIS was developed; there was limited coverage and under-utilisation of the HMIS in respect to timeliness, completeness of reports, data usage, and accessibility (155, 162).

In the National Health Strategic Plan 2017 – 2021, the MoH admitted that there has been a perception of poor data quality from HMIS due to inconsistent primary sources of data associated mainly with poor coverage and completeness (156). As a result they committed to

incorporate and standardize the monitoring and evaluation (M&E) framework across all levels of the health care delivery system and use of data at all levels of decision-making to facilitate research.

8.2 Method

The study design was a retrospective analysis of routine aggregate surveillance data from the HMIS database from 2013 to 2016. These years were selected to correspond with SmartCare data except that HMIS data prior to 2013 was unavailable.

8.2.1 Data collection

The HMIS activities are overseen by the Department of Policy and Planning. The District HMIS Officer is responsible for all district data collection and reporting activities. All districts and central levels reporting is done through a web-based, open source information system (District Health Information System - DHIS 2). However most facilities are still using paper forms and report at district level where the data is entered on a computer.

All pregnant women who register for antenatal (ANC) services are given a personalised card where all interventions pertaining to their maternal history are entered. Women keep these cards and they can access maternal services in any health clinic in the country. When determining the number of women seeking ANC care, only the first visit is considered to avoid repeat counts. Deliveries are recorded at the time they occur even though the original ANC visit when the card was given may have come from the previous year.

The MoH ANC aggregate data was collected on Excel sheets which were designed by the candidate. The data elements of interest were: total number of women seeking ANC services; number of pregnant women already on antiretroviral treatment (ART); number of women who tested HIV-positive on their ANC visit; and number of women who were initiated on ART.

8.2.2 Outcomes of interest:

- 1) The proportion of HIV-positive pregnant women was calculated from the total number of all HIV-positive women (i.e., the number of women who first tested HIV-positive during ANC visit for that particular year, plus women who were already on ART before seeking ANC services) / the total number of pregnant women seeking ANC services.

- 2) The total proportion of women on ART was calculated from the number of HIV-infected pregnant women on ART (*i.e.* the number of HIV-infected pregnant women documented to have received ART during ANC (initiated on visit plus already on ART prior to visit) / the total number of pregnant women enrolled in ANC clinic with either newly documented HIV infection or known prior HIV infection);
- 3) The proportion of women already on ART was calculated from the number of women who were already on ART before seeking ANC services for this pregnancy/ the total number of pregnant women enrolled in ANC clinic with either newly documented HIV infection or known prior HIV infection.
- 4) The proportion of women who were initiated on ART upon testing HIV-positive was calculated from the number of women who were initiated on ART on testing HIV-positive during their ANC visit / the number of women who tested HIV-positive on their ANC visit.

8.3 Data Analysis

The quantitative data was analyzed using Microsoft Office Excel in proportions. The results were presented in tables and graphs.

8.4 Results

8.4. 1 HMIS Data

From the HMIS data, a total of 2,537,785 pregnant women were registered for ANC services from 2013 to 2016 across the 10 provinces in Zambia (Table 8.1). The majority of the women were from Lusaka (16%); Eastern and Copperbelt (13%); and Central and Southern at 11% each. The least number of women were from Muchinga and Northern Provinces at 6% each. The total number of women seeking ANC services increased gradually from 2013 to 2016 according to the HMIS data.

Table 8.1: Number of pregnant women who attended ANC services using HMIS data

Province		Year of Visit				Total
		2013	2014	2015	2016	
Central	N	61,868	72,932	74,101	74,091	282,992
	%	11%	11%	11%	11%	11%
Copperbelt	N	69,582	82,245	83,279	83,400	318,506
	%	13%	13%	13%	12%	13%
Eastern	N	80,671	85,556	84,073	85,046	335,346
	%	15%	13%	13%	13%	13%
Luapula	N	43,743	56,092	54,523	53,826	208,184
	%	7.9%	8.6%	8.2%	8.0%	8.2%
Lusaka	N	82,881	94,041	102,023	118,035	396,980
	%	15%	14%	15%	17%	16%
Muchinga	N	31,439	36,313	37,061	35,920	140,733
	%	5.7%	5.6%	5.6%	5.3%	5.5%
North-Western	N	49,552	59,658	59,552	56,837	225,599
	%	9%	9%	9%	8%	9%
Northern	N	34,120	41,679	43,502	43,116	162,417
	%	6%	6%	7%	6%	6%
Southern	N	57,808	73,398	76,069	77,862	285,137
	%	10.5%	11.3%	11.5%	11.5%	11.2%
Western	N	38,742	48,296	47,964	46,889	181,891
	%	7.0%	7.4%	7.2%	6.9%	7.2%
Total		550,406	650,210	662,147	675,022	2,537,785

8.4.2 SmartCare data

The SmartCare database showed a decrease over time in the number of records of pregnant women who were captured in the electronic health record system (Table 8.2). The 2016 SmartCare figure was very low, and this resulted in the data for that year being excluded from the Chapter 5 analysis. In contrast, in the HMIS dataset 2016 had the highest number of women who were registered for ANC services. Despite that SmartCare is representative of approximately 40% of the healthcare facilities in Zambia, a comparison of the sample sizes indicate that SmartCare only captured 2% of women testing for HIV in ANC from 2013-2016. Partly this is due to the fact that women already known HIV-positive were not recorded in the SmartCare dataset, which suffer from the implementation challenges discussed in Chapter 7.

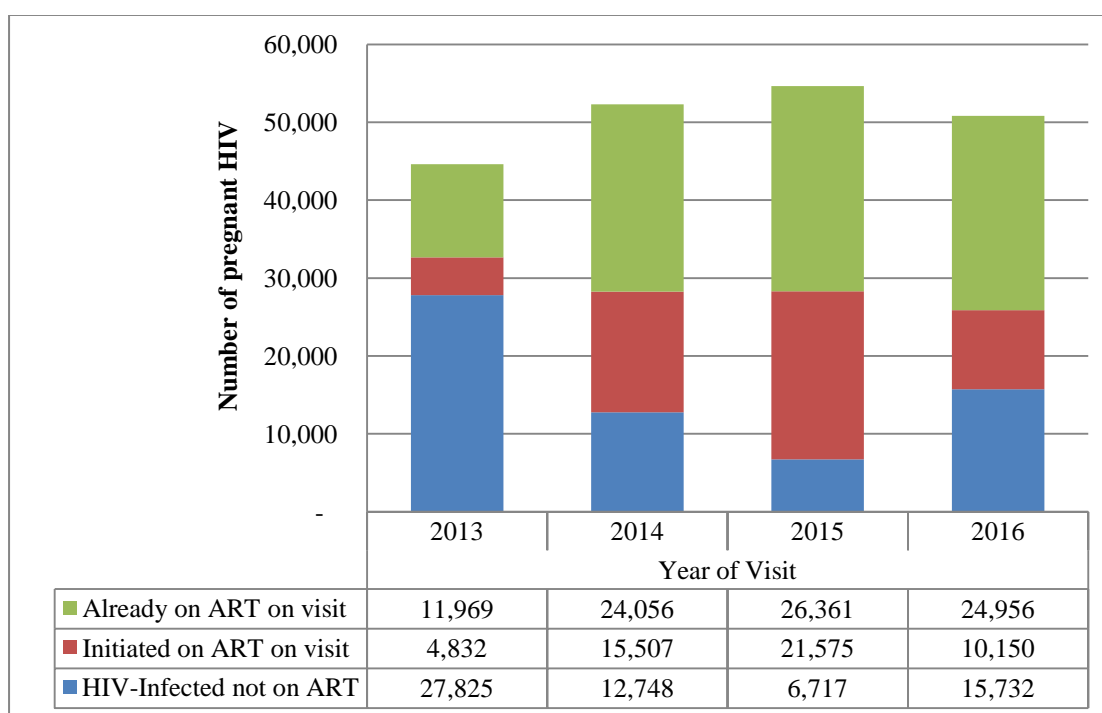
Table 8.2: Number of pregnant women who attended ANC services using SmartCare

Province		Year of Visit				Total
		2013	2014	2015	2016	
Central	N	1,938	1,471	310	79	3,798
	%	12%	9%	3%	3%	9%
Copperbelt	N	3,390	3,610	2,763	110	9,873
	%	22%	23%	27%	4%	22%
Eastern	N	5,448	4,881	1,148	404	11,881
	%	35%	31%	11%	16%	27%
Luapula	N	218	110	124	28	480
	%	1.4%	0.7%	1.2%	1.1%	1.1%
Lusaka	N	979	1,037	1,801	781	4,598
	%	6%	7%	17%	31%	10%
North-Western	N	78	242	401	8	729
	%	0.5%	1.5%	3.9%	0.3%	1.6%
Northern	N	755	758	550	175	2,238
	%	5%	5%	5%	7%	5%
Southern	N	2,463	3,330	3,045	891	9,729
	%	16%	21%	29%	35%	22%
Western	N	290	71	74	14	449
	%	1.9%	0.5%	0.7%	0.6%	1.0%
Muchinga	N	108	105	199	52	464
	%	0.7%	0.7%	1.9%	2.0%	1.0%
Total		15,667	15,615	10,415	2,542	44,239

8.4.3 Cohort of HIV-infected women

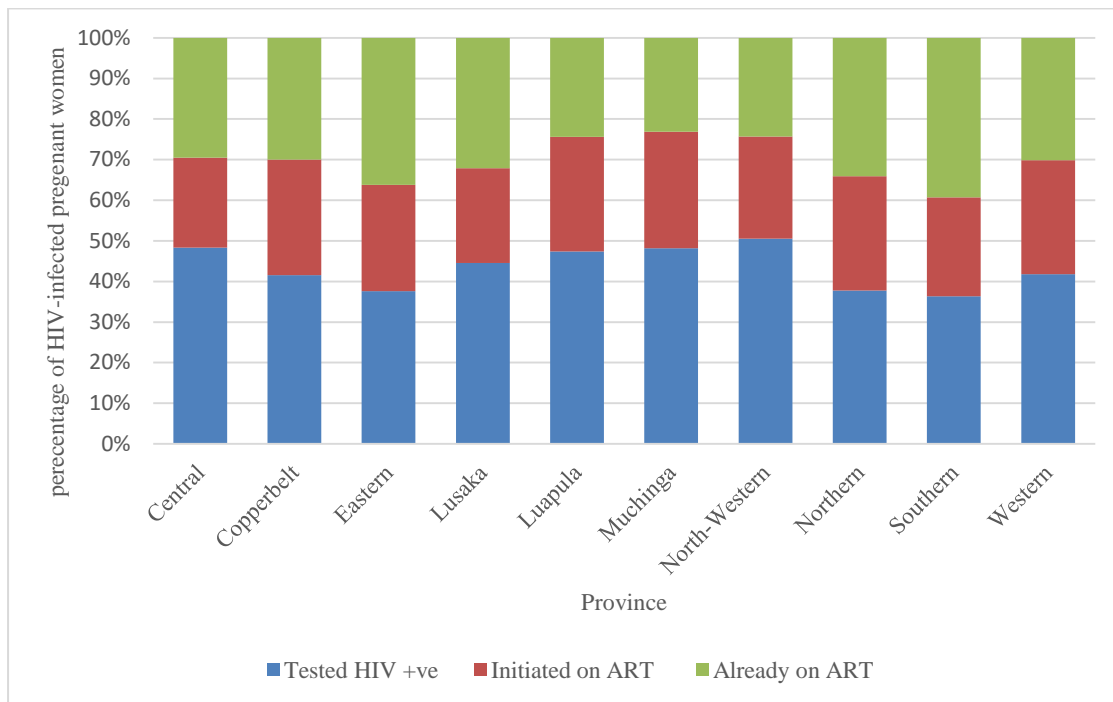
A total of 115,086 pregnant women tested HIV-positive during their ANC registration; 25% of these women were from Lusaka and 20% were from the Copperbelt. Muchinga and North Western provinces had the lowest numbers at 3% and 4 % respectively. During the 4-year period of analysis, 87,342 pregnant women seeking ANC services were already on ART (Figure 8.1), with 30% of them registered in 2015. The majority of these were from Lusaka (25%) and Copperbelt (19%). Over the same period in the SmartCare data set approximately 98% of the HIV test results were missing, and this was across all the provinces as outlined in Chapter 5.

Figure 8.1 Distribution of HIV-infected pregnant women using HMIS data (2013-16)



There were notable disparities in the implementation of the PMTCT services across the provinces. The percentages of women who tested HIV-positive during their ANC visit ranged from 36.3% in Southern province to 50.6% in North-Western province (Figure 8.2). Among HIV-infected women, 48.3% tested HIV-positive in Central province compared to 36.3% in Southern which had almost the same number of women who were registered for ANC services (Table 8.1). The proportion of women who were initiated on ART was almost uniform across the provinces ranging from 22% in Central province to 28% in Copperbelt, Luapula, Muchinga, Northern and Western provinces. The Southern and Eastern provinces had the highest proportion of women who were already on ART at 39% and 36% respectively. Muchinga and North-Western provinces registered the lowest percentages at 23% and 24% of women who were already on ART. The similar disparities were also reported Chapter 5 results.

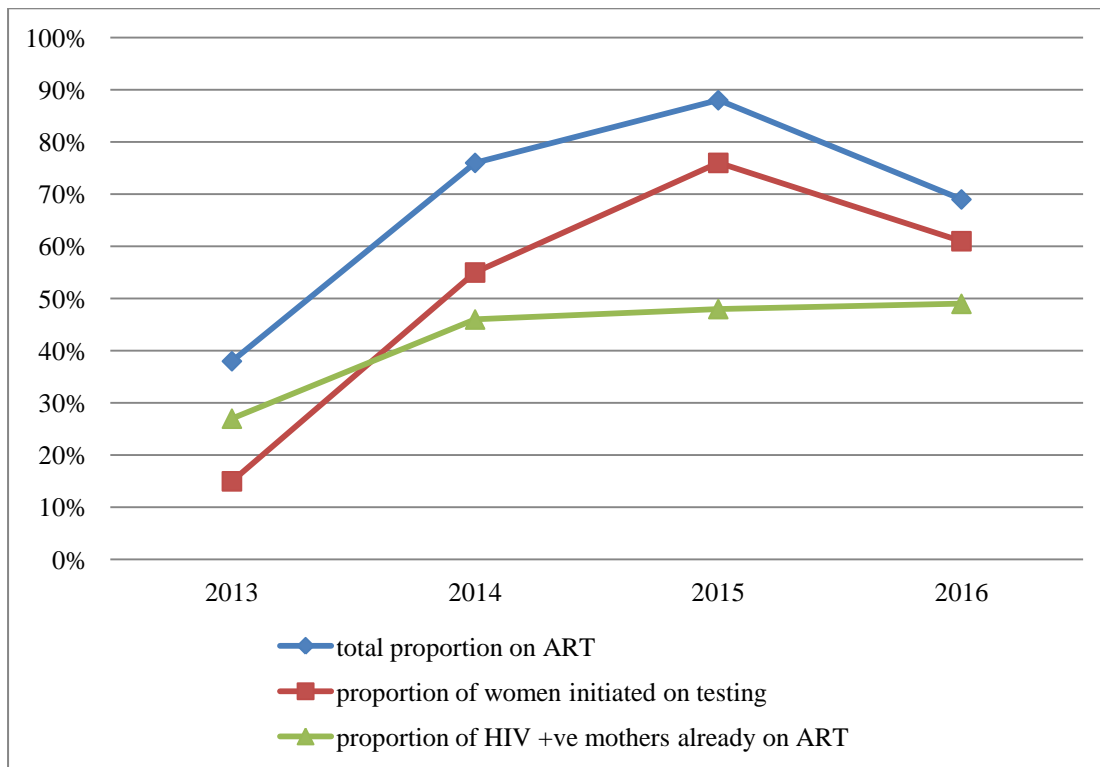
Figure 8.2 Distribution of HIV-infected women by province (2013-2016) using HMIS data



8.4.2 ART Initiation

There was a sharp increase in the percentage of HIV-infected women who were on treatment between 2013 and 2014 (38% to 76%) illustrated in Figure 8.3. The increase was proportional to the increase in the percentage of women who were initiated on ART on testing which increased more than 3 times from 15% to 55% over the same period. Similarly, women who were already on ART at their initial ANC pregnancy registration almost doubled moving from 27% in 2013 to 46% in 2014. Overall during the period under review, Lusaka province had the highest proportion (25%) of women who were already on treatment upon ANC registration followed by Copperbelt at 19%. However, the Copperbelt province had the overall highest percentage (23%) of women initiated on ART on testing HIV-positive, whereas Lusaka was 22% despite that it had the largest number of women who tested HIV-positive.

Figure 8.3 Proportion of pregnant women on treatment (2013-2016)



8.5 Discussion

The HMIS data confirms the conclusion from analysis of SmartCare data that there has been an increase in the proportion of pregnant HIV-infected women seeking ANC services who are already on treatment. HMIS data analysis complements the findings of SmartCare data analysis which was compromised by the poor data quality as elaborated in Chapter 5 & 6.

The HIMS records aggregate data from every health facility whether it has electronic patient records (SmartCare), or not. As such the data represents the whole country, big facilities and small facilities, and all provinces. The data show numbers that are comparable with the national census, with more patients in larger provinces as the data have a national focus, then the results are generalizable to the whole population.

The sharp increase in the proportion of HIV-infected pregnant women on HIV treatment coincided with the adoption of Option B+, an approach which recommends treating all pregnant and breastfeeding women with lifelong ART regardless of CD4 count. The WHO Test and Treat guidelines that recommend anyone who tests positive for HIV should be started on treatment, regardless of their CD4 count was also introduced, during the same

period (163). A surge in the number women initiated on ART has also been reported in other studies from the region (15, 87, 100, 164). However the implementation of Option B + was not immediate and could have been slowed by existing health infrastructure constraints (165). The findings of this analysis also indicated a decline in the proportion of pregnant women on treatment from 2015 to 2016 (163). It is postulated that Option B+ could have threatened programme performance and negatively affected the HIV continuum of care for all HIV–infected patients (166) as a result of the surge in the number of HIV-infected individuals enrolled for HIV treatment. .

The quality of HMIS data was not assessed, and hence its accuracy, completeness and timeliness cannot be fully confirmed. This is also against the background that the MoH admitted that the HMIS could be affected by poor data quality (156). It is therefore recommended that for future use the HMIS data quality should be assessed. This could be done through 1) cross- checking of selected registers and client/patients’ cards to investigate deviations between reported patient statistics and those in the appropriate registers; and 2) conducting key informant interviews with the health facility managers and data management officers on factors influencing the observed data quality.

8.6 Conclusion

The HMIS data complemented the SmartCare data analysis and confirmed that there has been an increase in the proportion of pregnant HIV-infected women seeking ANC services who are already on treatment.

Chapter 9: Discussion

9.1 Introduction

This chapter aims to synthesize the findings of the studies in the 4 chapters presented as papers and the triangulation chapter. A view of what has been achieved and a discussion on how the research questions were addressed are highlighted. The chapter finally discusses the policy implications of the findings, and proposes recommendations and suggestions for future research.

9.2 Summary of Findings

The study aimed at evaluating the implementation of the post 2010 WHO PMTCT guidelines using routinely collected data. The research gaps in the use of routinely collected data for evaluation of PMTCT programs were identified following a systematic review of literature. The implementation effectiveness of WHO PMTCT guidelines was evaluated by analysing data from a cohort of 104,155 pregnant woman seeking ANC services in 886 health facilities throughout the 10 provinces in Zambia. Among these pregnant women a subset of HIV-infected women were followed down the PMTCT cascade. The results from the ANC dataset were triangulated against the HMIS data from 2013 to 2016. These years had a drastic decrease in the SmartCare records of women seeking ANC services and an increase in missing HIV test results. The progress of early infant diagnosis was analysed using a dataset of 32,593 HIV-infected infants born pre- and post- the 2010 guidelines. The implementation challenges of the SmartCare EHR system, which was the source of data, was also investigated to address the fundamental need for timely, complete, high-quality data.

The critical findings of this research are: 1) decrease in MTCT rates in SSA, but poor quality routinely collected data; 2) an increase in the proportion of HIV-infected pregnant women attending ANC in Zambia who know their status, and are already on ART; 3) HIV-exposed infants born more recently have significantly better care and treatment than infants born a decade ago; 4) The SmartCare database has large amounts of missing data and 5) SmartCare implementation is affected by structural challenges, funding gaps, and lack of feedback from the system.

9.2.1 Decrease in MTCT rates in SSA, but poor quality routinely collected data

The systematic review of literature (chapter 4), showed a continued decline in the incidence of HIV among children, as indicated by low MTCT rates. However, very few studies investigated the implementation of Option B+, which is now fully implemented in the 22

priority countries with a high burden of HIV(14). South African studies reported low MTCT rates under Option A implementation, which further suggests that Options A and B have similar efficacy (37). The argument should however take into consideration that the South African health system is better resourced than in most countries in Sub-Saharan Africa. Furthermore, there is a need to investigate the impact of implementing Option B+, on these poorly resourced health systems. In Malawi Option B+ programs reported a rapid increase in the number of pregnant and breastfeeding women on ART (43). Hence an investigation is needed of how these countries could be coping with the surge in coverage percentages, likely to be exerting pressure. Chung et al postulated that in Zambia Option B+ could have threatened program performance and negatively affected the HIV continuum of care for all HIV–infected patients (166).

The early studies on retention and adherence of Option B + also revealed that retention in care of HIV-infected and lactating mothers is poor and driven by early losses (70, 167-171). Similarly, default and incomplete adherence were more common in the Option B+ cohort compared to the pre-Option B cohort (71) and also tended to decrease during the postpartum period (112). For the PMTCT guidelines to be effective there is a need to rethink ways of ensuring optimal adherence to ART for maximal suppression of viral replication and avoidance of drug resistance. In addition there is also need to adjust operational practices related to quality of counselling as it has been indicated to be a predictor of adherence to treatment(113). Following women who are lost to follow up (LTFU) is a great challenge in SSA as women may implicitly choose not to be traced by providing a false address at enrolment(110).

The major challenge with the data collection systems for PMTCT programs of the studies that were included in the analysis was that they often lacked immediacy with considerable data quality concerns. This could be as a result of absence of processes such as data-quality checks and data-analysis in health facilities. In most Sub-Saharan countries there seems to be an absence of a culture of information use, as a result of lack of trust in the data, and the inability of program and facility managers to analyse, interpret and use information (125, 128). In spite of the demands for quality data, routine health information systems in many resource-limited settings continue to perform below expectations, and are often not used for their intended purposes of generating accurate and reliable data; where data is generated, the information is not sufficiently used for planning and management (124, 125).

9.2.2 Increase in the proportion of HIV infected women already on treatment

The results from both the SmartCare and the HMIS data bases indicated a progressive increase in the proportion of women who were already on ART before registering for ANC in their visit year. This increase demonstrates that Zambia has made progress towards the UNAIDS 90–90–90 Targets (90% of people living with HIV who know their status, 90% who receive ART, and 90% who have suppressed viral loads)(163). Zambia has also managed to increase the proportion of pregnant women living with HIV who received effective antiretroviral medicines to prevent the mother-to-child transmission of HIV to 92% in 2017(2).

Despite that there has been an increase in the proportion of women already on ART from our findings; there has also been a decrease in the number of women in the SmartCare database between 2010 and 2015. The decrease in the numbers and increase in the missing data could have introduced bias in later years of analysis as the data that was analysed was not representative. It could also represent problems with the way that SmartCare data are recorded, as indicated in the qualitative research (Chapter 7). However, these results could be a good indicator of program performance since 40% of Zambian health facilities are part of SmartCare, and these are the largest and busiest ART clinics. The requirement to join SmartCare if clinics wish to prescribe ART means that most Zambian patients on ART should be captured in SmartCare database (149). The trend of gaps in the data quality in using data from routine PMTCT programs have also been recently reported in Ethiopia (172). The results of this study were also consistent with mathematical modelling using the lifelong ART tool that indicated that the probability of HIV-infected pregnant women initiating ART would increase by 80% (68). Triangulation of the dataset with nation-wide HMIS aggregate data which is more representative also confirmed these findings as the trends followed the same patterns.

The system in Zambia is such that pregnant and lactating women are given ‘VIP’ treatment which allows them to be served faster under the ANC department compared to those under General ART. In 2014, the General ART program was observed to have had a surge in numbers owing to the Test and Treat policy (140) with some clients taking over 6 hours waiting to get their medication. Most of the women were not confident on their own ability to adhere to life-long ART after weaning their infants or when the infant turns 18 months owing

to the long waiting time it takes for those on general ART to get their medication. These findings were themes from the qualitative research which were not in the paper but they permit better understanding of the overall situation. This was consistent with the Tanzanian study where women on Option B+ indicated that they might not adhere to treatment thinking that they would be less motivated to take drugs after protecting their child, and fearing the drug side effects and the challenges of chronic daily medication (69). Some of the younger women even indicated that they would plan having more babies so that they continue to be under the PMTCT ‘VIP’ treatment. Therefore there is a need to continuously explore strategies to ensure that women on Option B+ are not LTFU once their infants reach 18 months. Their counterparts from Uganda, Malawi and Zimbabwe reported that beginning treatment is not yet urgent as they are less seriously ill and considered themselves “healthy” without treatment (110).

Although our results show a significant increase in the proportion of mothers who were already on treatment during pregnancy, Zambian mothers are presenting to antenatal care late in their pregnancy(173) and only 47% deliver at health facilities (138). In Southern Ethiopia, home deliveries were seen as an excuse to avoid the stigma and risk of marital break-down associated with disclosure of an HIV-positive status by pregnant women(174). This is likely to be a similar possibility in the Zambian women, as MCH – in charge interviewed during the qualitative study (Chapter 7) also pointed that they still have cases of women who prefer not to disclose their HIV status to their partners. Some of the lactating women on PMTCT who were interviewed during focus group discussions mentioned that their greatest fears were to disclose the HIV-positive status of their infants to their partners as they were likely to be blamed for it. Evidence from my qualitative study revealed that some of the pregnant women also go to the extent of hiding their SmartCare cards and even collect and take their ARVs without knowledge of their partners or relatives. The pregnant women seem to be keen to protect their unborn infants but, after weaning the infant, may not be willing to continue taking their medication in secret. Male partner participation in ANC/PMTCT is low in SAA in general SSA (175-179) and may be even lower in Zambia compared to the other countries in the region (180). Pregnant women are encouraged to bring their partners but the initiative is not heavily enforced. Many women in these countries fear violence and divorce if tested positive (175, 176) and MTCT is regarded as only the mother’s responsibility (181).

The barriers to uptake of ANC have to be addressed, in the context of PMTCT as this is important for the success of Option B+ and ‘treat all’ initiatives. In Zambia lack of human resources remains a serious impediment to addressing HIV, so that even when physical resources are available, there is often not the healthcare personnel to administer them (142). The SmartCare forms are 5-6 pages per interaction, which is likely to have created a burden on the healthcare personnel and resulted in data gaps. The clinicians, who are responsible for collecting SmartCare data either on paper or computer, have to prioritise their duties of serving patients to carefully completing the data forms. This further exacerbated by lack of feedback from the EHR system.

Due to inconsistent data collection and entry, this study did not distinguish the analysis of the different post 2010 PMTCT options. These were also rolled out at different times throughout the country. The coverage analysis of the different PMTCT options could have been key in view of the evolving guidelines. As posited by Nicol et al, the changes in PMTCT guidelines are often not aligned with data-collection tools such as registers and tally sheets, and there may be inadequate mentoring and supervisory support systems to facilitate the use of information at facility level (124).

9.2.3 Progress in the EID

The consolidated guidelines recommend that HIV-exposed infants be tested for HIV between 6-8 weeks, at the end of breastfeeding, and at any point they present with illness (3). Our results showed the mean age at HIV testing has steadily decreased and the proportion tested under 2 months of age increased between 2006 and 2016. The findings are an indication of the progress of implementing the revised PMTCT guidelines. In this study it was not possible to determine the MTCT rate, because we could not link the infants to their mothers.

These results have to be viewed with caution as a commonly used surrogate marker for program effectiveness is program coverage, i.e. the proportion of HIV-infected/exposed mother/infant pairs in a population that receive a PMTCT intervention (4). The analysis was restricted to HIV-infected infants on ART as this was what was available. The infants who are registered are mainly those who are HIV-positive as these are usually brought to health facilities for their medication and are captured under the pharmacy module. When women deliver in maternity wards; their records are not automatically taken to SmartCare data rooms as these are often located apart.

HIV-positive mothers usually bring their infants to be tested at prescribed times (6 weeks, 6 and 18) months and get messages of their infant test results through Project Mwana. HIV test results are transmitted to the caregivers through an SMS-based system which automatically notifies caregivers with access to mobile phones that their infants' test results are ready to be picked (18). However Project Mwana, and SmartCare are not linked, hence the information for test results of infants who are not initiated on ART is not entered directly into SmartCare. These records seem not to flow to SmartCare data room and, as earlier mentioned, the health personnel could also be burdened with their workloads and end up not prioritising recording these results. In some cases in the database there are also records of infants on ART but their test dates or test results are not indicated.

They are also some mothers who deliberately reported that they register their infants in different health facilities from the ones that they usually use for confidentiality reasons as they would like to protect their children from stigma. Hence implementing a system that is directly linked for both programs is challenging and requires significant human and financial resources. The other foreseen challenge is that even after testing HIV-exposed infants, a significant proportion of caregivers do not return for the results. In a study that intended to determine turnaround time for EID in rural Zambian HIV clinic, only 86% of caregivers returned for results and 67% of infants who tested positive started ART by the end of the study (146). A more comprehensive dataset of the HIV status of all exposed infants could have been obtained from the ANC and Under 5 registers. However, the majority of studies using paper based routine data have also acknowledged the common problem of missing data as discussed in Chapter 4(45). This could be assumed to be one of the causes of under utilisation of routinely collected data which was observed by Munthali et al (7).

9.2.4 Missing Data

Our study shows that there are major problems in both the completeness of the collection of data that tracks PMTCT service delivery. The data quality from SmartCare seemed to be deteriorating over years. For instance in the ANC dataset, the percentage with missing HIV test results increased from 11% in 2010 to 65% in 2013 and then to 98.8% in 2015. The poor data quality aspect has an effect on the external validity of this study. The missing data could have been attributable to the fact that SmartCare data collection is implemented parallel to the main line Ministry of Health HMIS which also collects HIV test results. This could have

caused high levels of missing HIV test results data in the SmartCare as clinicians prefer to enter the information in the HMIS forms compared to SmartCare forms which are longer (5-6 pages per interaction) and clinicians may omit certain fields they deem irrelevant to their patient's care. Presentation of HMIS data supported this hypothesis as the dataset had HIV test results of pregnant women seeking ANC services. The qualitative study also revealed that the evolution of the EHR system from various patient tracking systems into a multifunctional system has created implementation challenges associated with the model structure of the EHR system.

Among other reasons, the lack of feedback from the system mentioned by the implementing partner personnel during qualitative data collection has also exacerbated the high levels of missing data as shown by the number of infants in the paediatric data set which increased from 1,761 in 2006 to peak at 3,720 in 2009 and then steadily decreased to 108 in 2016. Main comparisons over time of the study used 2015 since there were too few infants listed in 2016 for age at testing and none for time to treatment initiation. The proportions of infants missing data on either age at testing or time of starting ART was high (34%) but did not differ by province or year. In addition, power outages in most areas of Zambia are a major problem and can occur for prolonged periods of time during the day, limiting the time that data can be entered into the system. This means that data collection is often not up to date and this could contribute to the apparently poor data quality.

The data quality challenges were similar to other studies from the region using routinely collected data (5, 166, 182, 183). Despite tremendous progress and many country-driven successes achieved during the Global Plan, operational challenges in data use, monitoring, and evaluation for PMTCT persist. Collecting longitudinal data on mother–baby pairs throughout the PMTCT cascade is challenging but necessary to optimize maternal and infant outcomes. However the Global Plan priority countries (which include Zambia) health records are not properly completed, hence the need to scale up electronic data systems (184) such as the SmartCare when improved.

The lack of standardised implementation procedures by various SmartCare partners which was evident in the qualitative study is a cause of concern which also fuels poor data quality. There is no uniformity in the data quality verification and submission strategies employed by

various implementing partners. These strategies are largely determined by the funding which also differs across an array of implementing organisations.

9.3 Study limitations

The limitations of this PhD research stem from the use of secondary data. The analysis of the overall mean time to ART initiation from diagnosis by year of visit showed huge interprovincial variations over time. It was therefore difficult to determine whether there has been a decrease with time due to increase in the missing HIV test results specifically in the later years. It is also possible that facilities in provinces that have missing data are the ones which are performing well. In addition with increase in the missing HIV test data overtime it was difficult to determine the time from diagnosis to ART initiation as very few records were available. High statistical power is associated with large sample sizes as it makes it easier to establish even the smallest of statistically significant differences. The analysis of HMIS data also showed that Lusaka had highest proportion of women who were initiated on ART. Missing data was similar across all provinces although our quantitative analysis showed that Lusaka province was most likely to have missing. Since Lusaka has one of the highest HIV prevalence rates, this could have also introduced bias into our study and have a negative effect on the external validity of the study.

The Smartcare data examined was from all the 10 provinces across the countries. By using the whole country dataset, despite its poor data quality, the candidate was able to show that routine data collection systems are vulnerable to other factors in the health care system. If the analysis was done for a sample of the data, the candidate was likely to have chosen from best performing facilities, from implementing partners which are also well funded and have data quality management strategies; however it was not going to be very representative of what was happening in the country.

In the EID study the candidate intended to show variability between provinces and over time. If it was possible to have data for all HIV-exposed infants, the MTCT rates at various points such as 6 weeks, 6 months, and after weaning could have been calculated. The association between the MTCT rates at various points and the mothers' characteristics such as age, education level and marital status could also have been analysed if there was linkage of mother-infant pairs. In addition the association between MTCT rates and infant feeding methods could also have been analysed, however the under 5 module which is supposed to have infant feeding data was not populated.

Given that data security and confidentiality are two important issues associated with the use of routinely collected health data. The MOH should come up with a way of scrambling national ID numbers to correspond with the unique SmartCare identifiers, so that researchers willing to analyse the data are able to identify individuals who register in different facilities.

9.4 Conclusion

The implementation of the WHO post 2010 PMTCT guidelines has resulted in an increase in the proportion of HIV-infected pregnant women attending ANC who are already on ART. Infants born more recently have better clinical HIV care than infants born a decade ago in Zambia. The time between HIV diagnosis and ART initiation has greatly reduced however there is substantive provincial variability in the performance of PMTCT service.

The SmartCare system has structural challenges which can be traced from its development. Funding gaps have resulted in staffing and data collection disparities within implementing partners. The lack of feedback from the system has also led to complacency at the operational level which has resulted in poor data quality in later years. The SmartCare database could enable Zambian health policy makers to act on urgent PMTCT interventions and improve health care quality and outcomes of mothers and their infants.

9.5 Recommendations

- For SmartCare to be used to evaluate national PMTCT health outcomes and present comparison across provinces, districts and facilities, the following issues need to be addressed:
 1. SmartCare must be able to link data of mother–infant pairs, so that the data can be used to evaluate the impact of PMTCT program using MTCT rates across different time periods.
 2. The operation procedures of data collection and quality management should be standardised across implementation partners.
 3. The database outputs should be made available at facility, district and provincial levels so that the implementers could have a better understanding of what happens at each level of implementation.
 4. The system could also be upgraded into a such that: multiple users can enter data simultaneously; data can be backed up automatically at more than one site; information can be communicated between multiple locations; data are

accessible and shared at multiple sites and the system can be debugged and upgraded over the internet without visiting remote sites (185, 186).

9.6 PhD Contribution

1. This is the first study to have evaluated the implementation post 2010 PMTCT interventions nationwide using SmartCare EHR system routine data. There is underutilisation of routinely collected PMTCT data in Zambia whereas the SmartCare database could present an opportunity to supplement current sources of routinely collected surveillance data. The Stata do files generated for data cleaning and analysis will be shared with the Ministry Health for their own internal uses. Since SmartCare is being implemented across the whole country, the results of this study can be generalizable to the whole population.
2. The qualitative paper is also the first document to exhaustively investigate the implementation of SmartCare since its inception in 2004. Through the qualitative research I obtained a rich and nuanced appreciation of the implementation of the SmartCare as we sampled from a range of IPs, health facilities, stakeholders and implementation systems. The depth of the inquiry enabled us to consider a range of explanatory factors. The findings will be shared with the policy makers in order to help them to improve the implementation of the EHR system.
3. Electronic health record systems can have a transformative effect in the health systems, however their full potential has not been realised in developing countries. The insights from this PhD could aid other countries wanting to develop their own EHR systems.

10. References

- UNAIDS. Women and Girls and HIV. Geneva, Switzerland; 2018.
http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS_Women_and_girls_and_HIV_2018.pdf. Accessed on 1 August 2018.
2. UNAIDS. UNAIDS DATA 2018. Geneva; 2018.
http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf. Accessed on 1 August 2018.
3. UNAIDS. Countdown to Zero: Global Plan Towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011-2015. Geneva, Switzerland; 2011.
http://www.unaids.org/sites/default/files/media_asset/20110609_JC2137_Global-Plan-Elimination-HIV-Children_en_1.pdf. Accessed on 15 August 2018.
4. Stringer E.M, CBH, Chintu N., Creek T.L., Ekouevi D. K., Coetzee D., Tih P., Boule A., Dabis F., Shaffer N., Wilfert C.M., and Stringer J.S.A. Monitoring effectiveness of programmes to prevent mother-to-child HIV transmission in lower-income countries. *Bulletin of the World Health Organisation*. 2008;86(1):57-62.
5. Gourlay A, Wringe A, Todd J, Michael D, Reniers G, Urassa M. Challenges with routine data sources for PMTCT programme monitoring in East Africa: insights from Tanzania. *Global health action*. 2015;8.
6. Grzeskowiak LE, Gilbert AL, Morrison JL. Methodological challenges in using routinely collected health data to investigate long-term effects of medication use during pregnancy. *Ther Adv Drug Saf*. 2013;4(1):27-37.
7. Munthali T. MP, Mee P., Gumede S., Schaap A, Mwinga A., Phiri C., Kapata N., Michelo C., and Todd J. Underutilisation of routinely collected data in the HIV programme in Zambia: A review of quantitatively analysed peer-reviewed articles. *BMC Research Policy and Systems*. 2017;15(51).
8. UNAIDS. Prevention Gap Report. 2016.
http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS-2016-prevention-gap-report_en.pdf. Accessed on 4 August 2018
9. UNAIDS. HIV/AIDS Fact Sheet. 2017.
http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf. Accessed on 16 August 2018
10. World Health Organisation. PMTCT Strategic Vision 2010- 2015: Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Geneva, Switzerland; 2010.
http://www.who.int/hiv/pub/mtct/strategic_vision.pdf?ua=1. Accessed on 5 August
11. UNAIDS. Political Declaration on HIV and AIDS: On the Fast Track to Accelerating the Fight against HIV and to Ending the AIDS Epidemic by 2030. Geneva; 2016. .
http://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf. Accessed on 2 September 2018.
12. UNAIDS. Global HIV/AIDS response epidemic update and health sector progress towards universal access. 2011
http://apps.who.int/iris/bitstream/handle/10665/44787/9789241502986_eng.pdf?sequence=1
Accessed on 2 September 2018.
13. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaC. Option B+ countries and PMTCT regimen 2015 [Available from: <http://emtct-iatt.org/b-countries-and-pmtct-regimen/>].
14. World Health Organisation. Progress Report 2016 Prevents HIV, Test and Treat All: WHO Support for Country Impact. Geneva: WHO; 2016.

- <http://apps.who.int/iris/bitstream/handle/10665/251713/WHO-HIV-2016.24-eng.pdf?sequence=1>. Accessed on 2 August 2018.
15. UNAIDS. AIDSInfo: UNAIDS; 2018 [cited 2018 20 September]. Available from: <http://aidsinfo.unaids.org/>.
 16. UNAIDS. UNAIDS Data 2017. 2017. http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS_Global_AIDS_Update_2017_Data_book_2017_en.pdf. Accessed on 4 August 2018
 17. World Health Organisation. Focus on Innovations in Africa Executive Summary of the Report on the Global Health Sector Response to HIV, 2000-2015. 2015. http://apps.who.int/iris/bitstream/handle/10665/198148/WHO_HIV_2015.40_eng.pdf?sequence=1 Accessed on 17 August 2018
 18. Seidenberg P, Nicholson S, Schaefer M, Semrau K, Bweupe M, Masese N, et al. Early infant diagnosis of HIV infection in Zambia through mobile phone texting of blood test results. *Bulletin of the World Health Organization*. 2012;90(5):348-56.
 19. Edmonds A, Yotebieng M, Lusiana J, Matumona Y, Kitetele F, Napravnik S, et al. The effect of highly active antiretroviral therapy on the survival of HIV-infected children in a resource-deprived setting: a cohort study. *PLoS medicine*. 2011;8(6):e1001044.
 20. World Health Organisation. World Health Organization. Consolidated Guidelines on the Use of Anti-retroviral Drugs for Treating and Preventing HIV Infection Recommendations for a Public Health Approach Geneva: WHO; 2016. http://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf;jsessionid=16E6F682F14DD912FE7AC00B0A3551B5?sequence=1 Accessed on 20 September 2018
 21. UNAIDS. UNAIDS Global AIDS Update Data Book. Geneva; 2017. http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS_Global_AIDS_Update_2017_Data_book_2017_en.pdf Accessed on 20 August 2018
 22. Joint United Nations Programme on HIV/AIDS, et al. Women Out Loud: How Women Living with HIV will help the World End AIDS. 2012. <http://www.unaids.org/en/resources/presscentre/featurestories/2012/december/20121211wom-enoutloudv> Accessed on 20 August 2018.
 23. Taylor GP, Clayden P, Dhar J, Gandhi K, Gilleece Y, Harding K, et al. British HIV Association guidelines for the management of HIV infection in pregnant women 2012. *HIV medicine*. 2012;13 Suppl 2:87-157.
 24. Cooper ER, Charurat M, Burns DN, Blattner W, Hoff R. Trends in antiretroviral therapy and mother-infant transmission of HIV. The Women and Infants Transmission Study Group. *Journal of acquired immune deficiency syndromes (1999)*. 2000;24(1):45-7.
 25. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS (London, England)*. 2008;22(8):973-81.
 26. McIntyre J. Use of antiretrovirals during pregnancy and breastfeeding in low-income and middle-income countries. *Current opinion in HIV and AIDS*. 2010;5(1):48-53.
 27. Stevens J, Lyall H. Mother to child transmission of HIV: what works and how much is enough? *The Journal of infection*. 2014;69 Suppl 1:S56-62.
 28. World, Health, Organisation. Global Update on the Health Sector Response to HIV. Geneva; 2014. <http://www.who.int/hiv/pub/global-update.pdf> Accessed on 4 August 2018.
 29. UNICEF. For Every Child, End AIDS: Seventh Stocktaking Report. New York, USA; 2016. https://www.unicef.org/publications/index_93427.html Accessed on 4 September 2018.
 30. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*. 2004;364(9441):1236-43.

31. Sutcliffe CG, Thuma PE, van Dijk JH, Sinywimaanzi K, Mweetwa S, Hamahuwa M, et al. Use of mobile phones and text messaging to decrease the turnaround time for early infant HIV diagnosis and notification in rural Zambia: an observational study. *BMC pediatrics*. 2017;17(1):66.
32. Ammann AJ. Is there an acquired immune deficiency syndrome in infants and children? *Pediatrics*. 1983;72(3):430-2.
33. Centers for Disease C. Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired immunodeficiency syndrome. *MMWR Morbidity and mortality weekly report*. 1985;34(48):721-6, 31-2.
34. Guay LA, Musoke P, Fleming T, Bagenda D, Allen M, Nakabiito C, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *Lancet*. 1999;354(9181):795-802.
35. Eshleman SH, Becker-Pergola G, Desevye M, Guay LA, Mracna M, Fleming T, et al. Impact of human immunodeficiency virus type 1 (hiv-1) subtype on women receiving single-dose nevirapine prophylaxis to prevent hiv-1 vertical transmission (hiv network for prevention trials 012 study). *The Journal of infectious diseases*. 2001;184(7):914-7.
36. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. *Lancet*. 2000;355(9202):451-5.
37. Chasela CS, Hudgens MG, Jamieson DJ, Kayira D, Hosseinipour MC, Kourtis AP, et al. Maternal or infant antiretroviral drugs to reduce HIV-1 transmission. *The New England journal of medicine*. 2010;362(24):2271-81.
38. Kesho Bora Study G, de Vincenzi I. Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomised controlled trial. *The Lancet Infectious diseases*. 2011;11(3):171-80.
39. Thomas TK, Masaba R, Borkowf CB, Ndivo R, Zeh C, Misore A, et al. Triple-antiretroviral prophylaxis to prevent mother-to-child HIV transmission through breastfeeding--the Kisumu Breastfeeding Study, Kenya: a clinical trial. *PLoS medicine*. 2011;8(3):e1001015.
40. Taha TE, Kumwenda J, Cole SR, Hoover DR, Kafulafula G, Fowler MG, et al. Postnatal HIV-1 transmission after cessation of infant extended antiretroviral prophylaxis and effect of maternal highly active antiretroviral therapy. *The Journal of infectious diseases*. 2009;200(10):1490-7.
41. Mofenson LM. Prevention in neglected subpopulations: prevention of mother-to-child transmission of HIV infection. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2010;50 Suppl 3:S130-48.
42. World, Health, Organization. WHO Recommendations on the Diagnosis of HIV Infection in Infants and Children. Geneva, Switzerland: Geneva, Switzerland; 2010. http://apps.who.int/iris/bitstream/handle/10665/44275/9789241599085_eng.pdf?sequence=1 Accessed on 1 September 2018
43. Centers for Disease, Control, Prevention. Impact of an innovative approach to prevent mother-to-child transmission of HIV--Malawi, July 2011-September 2012. *MMWR Morbidity and mortality weekly report*. 2013;62(8):148-51.
44. Dryden-Peterson S, Lockman S, Zash R, Lei Q, Chen JY, Souda S, et al. Initial programmatic implementation of WHO option B in Botswana associated with increased projected MTCT. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*. 2015;68(3):245-9.

45. Gumede-Moyo S, Filteau S, Munthali T, Todd J, Musonda P. Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa: A systematic literature review. *Medicine (Baltimore)*. 2017;96(40):e8055.
46. World Health Organisation. New data on the prevention of mother-to-child transmission of HIV and their policy implications: conclusions and recommendations. Technical Consultation on behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV. . Geneva: WHO; 2001. www.who.int/reproductive-health/publications/new_data_prevention_mtct_hiv/index.html. Accessed on 18 August 2018.
47. World Health Organisation. Antiretroviral Drugs for Antiretroviral Drugs for Treating Pregnant Women and Treating Pregnant Women and Preventing HIV Infection in Infants: Preventing HIV Infection in Infants: Towards Universal Access Towards Universal Access. Recommendations for a public health approach. Geneva, Switzerland; 2006. http://www.who.int/hiv/pub/mtct/arv_guidelines_mtct.pdf?ua=1 . Accessed on 17 August 2018
48. World Health Organisation. WHO Guidelines on HIV and infant feeding 2010: Principles and recommendations for infant feeding in the context of HIV and a summary of evidence. Geneva, Switzerland: World Health Organization Departments of Child and Adolescent Health and Development and HIV, in collaboration with UNAIDS, UNFPA and UNICEF; 2010. http://apps.who.int/iris/bitstream/10665/44345/1/9789241599535_eng.pdf. Accessed on 17 August 2018.
49. World Health Organisation. Consolidated Guidelines on the use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach. Geneva, Switzerland WHO; 2013 June 2013. http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf. Accessed on 17 August 2018
50. UNAIDS. Global Plan towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011–2015. 2011. http://www.unaids.org/sites/default/files/media_asset/20110609_JC2137_Global-Plan-Elimination-HIV-Children_en_1.pdf. Accessed on 4 August 2018
51. Leach-Lemens C. Option B+ cuts mother-to-child HIV transmission dramatically in Malawi 2016 [cited 2018 10 October]. Available from: <http://www.aidsmap.com/Option-B-cuts-mother-to-child-HIV-transmission-dramatically-in-Malawi/page/3038713/>.
52. Zambia MoH. Zambia National PMTCT Protocol Guidelines Lusaka Zambia; 2010.
53. Government of the Republic of Zambia MoH. Lifelong antiretroviral drugs (ARV's) for all HIV positive pregnant women in Zambia: Policy guidelines for health facilities in Zambia. Lusaka, Zambia; 2013.
54. Padian NS, McCoy SI, Karim SS, Hasen N, Kim J, Bartos M, et al. HIV prevention transformed: the new prevention research agenda. *Lancet*. 2011;378(9787):269-78.
55. Tudor Car L, van-Velthoven MH, Brusamento S, Elmoniry H, Car J, Majeed A, et al. Integrating prevention of mother-to-child HIV transmission (PMTCT) programmes with other health services for preventing HIV infection and improving HIV outcomes in developing countries. *The Cochrane database of systematic reviews*. 2011(6):Cd008741.
56. Wettstein C, Mugglin C, Egger M, Blaser N, Vizcaya LS, Estill J, et al. Missed opportunities to prevent mother-to-child-transmission: systematic review and meta-analysis. *AIDS (London, England)*. 2012;26(18):2361-73.
57. Woldesenbet S, Jackson D, Lombard C, Dinh TH, Puren A, Sherman G, et al. Missed Opportunities along the Prevention of Mother-to-Child Transmission Services Cascade in

- South Africa: Uptake, Determinants, and Attributable Risk (the SAPMTCTE). *PloS one*. 2015;10(7):e0132425.
58. Urban M, Chersich M. Acceptability and utilisation of voluntary HIV testing and nevirapine to reduce mother-to-child transmission of HIV-1 integrated into routine clinical care. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 2004;94(5):362-6.
 59. Kinuthia J, Kiarie JN, Farquhar C, Richardson BA, Nduati R, Mbori-Ngacha D, et al. Uptake of prevention of mother to child transmission interventions in Kenya: health systems are more influential than stigma. *Journal of the International AIDS Society*. 2011;14:61.
 60. Uwimana J, Zarowsky C, Hausler H, Jackson D. Engagement of non-government organisations and community care workers in collaborative TB/HIV activities including prevention of mother to child transmission in South Africa: opportunities and challenges. *BMC health services research*. 2012;12:233.
 61. Peltzer K, Mlambo G. Factors determining HIV viral testing of infants in the context of mother-to-child transmission. *Acta paediatrica (Oslo, Norway : 1992)*. 2010;99(4):590-6.
 62. Torpey K, Mandala J, Kasonde P, Bryan-Mofya G, Bweupe M, Mukundu J, et al. Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia. *PloS one*. 2012;7(8):e42859.
 63. Kohler PK OK, Mills LA, Okanda J, Kinuthia J, Olilo G, Odhiambo F, Laserson KF, Zierler B, Voss J, John-Stewart G. Shame, guilt, and stress: Community perceptions of barriers to engaging in prevention of mother to child transmission (PMTCT) programs in western Kenya. *AIDS patient care and STDs*. 2014;28(12):643-51.
 64. Madiba S, Letsoalo R. HIV disclosure to partners and family among women enrolled in prevention of mother to child transmission of HIV program: implications for infant feeding in poor resourced communities in South Africa. *Global journal of health science*. 2013;5(4):1-13.
 65. Gourlay A, Birdthistle I, Mburu G, Iorpenda K, Wringe A. Barriers and facilitating factors to the uptake of antiretroviral drugs for prevention of mother-to-child transmission of HIV in sub-Saharan Africa: a systematic review. *Journal of the International AIDS Society*. 2013;16:18588.
 66. de Walque D, Gertler PJ, Bautista-Arredondo S, Kwan A, Vermeersch C, de Dieu Bizimana J, et al. Using provider performance incentives to increase HIV testing and counseling services in Rwanda. *Journal of health economics*. 2015;40:1-9.
 67. Schuster RC, de Sousa O, Reme AK, Vopelak C, Pelletier DL, Johnson LM, et al. Performance-Based Financing Empowers Health Workers Delivering Prevention of Vertical Transmission of HIV Services and Decreases Desire to Leave in Mozambique. *International journal of health policy and management*. 2018;7(7):630-44.
 68. Ishikawa N ST, Miyano S, Sikazwe I, Mwangi A, Ghidinelli M. N, Syakantu G,. Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia. *PloS one*. 2014;9(3):e90991.
 69. Ngarina M, Tarimo EA, Naburi H, Kilewo C, Mwanyika-Sando M, Chalamilla G, et al. Women's preferences regarding infant or maternal antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV during breastfeeding and their views on Option B+ in Dar es Salaam, Tanzania. *PloS one*. 2014;9(1):e85310.
 70. Tweya H, Gugsa S, Hosseinipour M, Speight C, Ng'ambi W, Bokosi M, et al. Understanding factors, outcomes and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi. *Tropical medicine & international health : TM & IH*. 2014;19(11):1360-6.
 71. Kamuyango AA, Hirschhorn LR, Wang W, Jansen P, Hoffman RM. One-year outcomes of women started on antiretroviral therapy during pregnancy before and after the

implementation of Option B+ in Malawi: A retrospective chart review. *World journal of AIDS*. 2014;4(3):332-7.

72. Ngarina M, Popenoe R, Kilewo C, Biberfeld G, Ekstrom AM. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. *BMC public health*. 2013;13:450.

73. Etoori D, Kerschberger B, Staderini N, Ndlangamandla M, Nhlabatsi B, Jobanputra K, et al. Challenges and successes in the implementation of option B+ to prevent mother-to-child transmission of HIV in southern Swaziland. *BMC public health*. 2018;18(1):374.

74. Hamilton E, Bossiky B, Ditekemena J, Esiru G, Fwamba F, Goga AE, et al. Using the PMTCT Cascade to Accelerate Achievement of the Global Plan Goals. *Journal of acquired immune deficiency syndromes (1999)*. 2017;75 Suppl 1:S27-S35.

75. Doherty K, Ciaranello A. What is needed to eliminate new pediatric HIV infections: the contribution of model-based analyses. *Current opinion in HIV and AIDS*. 2013;8(5):457-66.

76. World, Health, Organisation. Consolidated ARV guidelines: What's the Evidence. Geneva, Switzerland; 2013.

77. World, Health, Organisation. WHO Guidelines Approved by the Guidelines Review Committee. Geneva: World Health Organization Copyright (c) World Health Organization 2015.; 2015. http://apps.who.int/iris/handle/10665/186275?search-result=true&query=Guideline+on+When+to+Start+Antiretroviral+Therapy+and+on+Pre-Exposure+Prophylaxis+for+HIV&scope=%2F&filtertype_0=dateIssued&filter_relational_operator_0>equals&filter_0=%5B2000+TO+2018%5D&rpp=10&sort_by=score&order=desc
Accessed on 17 August 2018

78. World, Health, Organization. WHO Recommendations on the Diagnosis of HIV Infection in Infants and Children. Geneva, Switzerland: Geneva, Switzerland; 2010. http://apps.who.int/iris/bitstream/handle/10665/44275/9789241599085_eng.pdf?sequence=1
Accessed on 1 September 2018.

79. Shapiro RL, Hughes MD, Ogwu A, Kitch D, Lockman S, Moffat C, et al. Antiretroviral regimens in pregnancy and breast-feeding in Botswana. *The New England journal of medicine*. 2010;362(24):2282-94.

80. Kim MH, Ahmed S, Buck WC, Preidis GA, Hosseinipour MC, Bhalakia A, et al. The Tingathe programme: a pilot intervention using community health workers to create a continuum of care in the prevention of mother to child transmission of HIV (PMTCT) cascade of services in Malawi. *Journal of the International AIDS Society*. 2012;15 Suppl 2:17389.

81. Kim MH, Ahmed S, Hosseinipour MC, Giordano TP, Chiao EY, Yu X, et al. Implementation and operational research: the impact of option B+ on the antenatal PMTCT cascade in Lilongwe, Malawi. *Journal of acquired immune deficiency syndromes (1999)*. 2015;68(5):e77-83.

82. Powis KM, Kitch D, Ogwu A, Hughes MD, Lockman S, Leidner J, et al. Increased risk of preterm delivery among HIV-infected women randomized to protease versus nucleoside reverse transcriptase inhibitor-based HAART during pregnancy. *The Journal of infectious diseases*. 2011;204(4):506-14.

83. Siberry GK, Williams PL, Mendez H, Seage GR, 3rd, Jacobson DL, Hazra R, et al. Safety of tenofovir use during pregnancy: early growth outcomes in HIV-exposed uninfected infants. *AIDS (London, England)*. 2012;26(9):1151-9.

84. Ford N CA, Mofenson L. Safety of efavirenz in the first trimester of pregnancy: an updated systematic review and meta-analysis. *AIDS (London, England)*. 2011(25):2301-4.

85. Powis KM, Smeaton L, Ogwu A, Lockman S, Dryden-Peterson S, van Widenfelt E, et al. Effects of in utero antiretroviral exposure on longitudinal growth of HIV-exposed uninfected infants in Botswana. *Journal of acquired immune deficiency syndromes (1999)*. 2011;56(2):131-8.
86. Persaud D BA, Ziemniak C, . Slower clearance of nevirapine resistant virus in infants failing extended nevirapine prophylaxis for prevention of mother-to-child HIV transmission. *AIDS research and human retroviruses*. 2011(27):823-9.
87. Saleska JL, Turner AN, Maierhofer C, Clark J, Kwiek JJ. Use of Antiretroviral Therapy During Pregnancy and Adverse Birth Outcomes Among Women Living With HIV-1 in Low- and Middle-Income Countries: A Systematic Review. *Journal of acquired immune deficiency syndromes (1999)*. 2018;79(1):1-9.
88. Fowler MG, Qin M, Fiscus SA, Currier JS, Flynn PM, Chipato T, et al. Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention. *The New England journal of medicine*. 2016;375(18):1726-37.
89. Kuznik A LM, Hermans S, Castelnuro B, Auerbach B, Semeere A, Sempa M, Ssewankambo F, Manabe Y. Evaluating the cost-effectiveness of combination antiretroviral therapy for the prevention of mother-to-child transmission of HIV in Uganda. *Bull World Health Organ*. 2012(90):595-603.
90. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. *Jama*. 1996;276(15):1253-8.
91. Binagwaho A, Pegurri E, Drobac PC, Mugwaneza P, Stulac SN, Wagner CM, et al. Prevention of mother-to-child transmission of HIV: cost-effectiveness of antiretroviral regimens and feeding options in Rwanda. *PloS one*. 2013;8(2):e54180.
92. Ciaranello AL, Perez F, Engelsmann B, Walensky RP, Mushavi A, Rusibamayila A, et al. Cost-effectiveness of World Health Organization 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe. *Clinical Infectious Diseases*.56(3):430-46.
93. Fasawe O, Avila C, Shaffer N, Schouten E, Chimbwandira F, Hoos D, et al. Cost-effectiveness analysis of Option B+ for HIV prevention and treatment of mothers and children in Malawi. *PloS one*. 2013;8(3):e57778.
94. Orlando S MM, Mancinelli S, Loitta G, Giglio P, Alumendo E, Ziegler I, Palombi L, Shawa M. Cost-effectiveness of using HAART in prevention of mother-to-child transmission in the DREAM-Project Malawi. *Journal of acquired immune deficiency syndromes (1999)*. 2010(55):631-4.
95. Robberstad B E-OB. Preventing mother to child transmission of HIV with highly active antiretroviral treatment in Tanzania--a prospective cost-effectiveness study. *Journal of acquired immune deficiency syndromes (1999)*. 2010(55):397-403.
96. Shah M JB, Abimiku A, Walker DG. . Cost-effectiveness of new WHO recommendations for prevention of mother-to-child transmission of HIV in a resource-limited setting. *AIDS and HIV Research*. 2011(25):1093-102.
97. Schmidt NC R-PJ, Fernandez AD, . Costs and benefits of multidrug, multidose antiretroviral therapy for prevention of mother-to-child transmission of HIV in the Dominican Republic. . *Int J Gynaecol Obstet* 2012. 2012(116):219-22.
98. Kourtis AP, Bulterys M, Nesheim SR, Lee FK. Understanding the timing of HIV transmission from mother to infant. *Jama*. 2001;285(6):709-12.
99. Sugandhi N, Rodrigues J, Kim M, Ahmed S, Amzel A, Tolle M, et al. HIV-exposed infants: rethinking care for a lifelong condition. *AIDS (London, England)*. 2013;27 Suppl 2:S187-95.
100. Haas AD, van Oosterhout JJ, Tenthani L, Jahn A, Zwahlen M, Msukwa MT, et al. HIV transmission and retention in care among HIV-exposed children enrolled in Malawi's

- prevention of mother-to-child transmission programme. *Journal of the International AIDS Society*. 2017;20(1):21947.
101. Rawizza HE, Chang CA, Chaplin B, Ahmed IA, Meloni ST, Oyeboode T, et al. Loss to Follow-Up within the Prevention of Mother-to-Child Transmission Care Cascade in a Large ART Program in Nigeria. *Current HIV research*. 2015;13(3):201-9.
 102. S Bhardwaj PB, Y Pillay , L Treger-Slavin, P Robinson, A Goga, G Sherman. Elimination of mother-to-child transmission of HIV in South Africa: Rapid scale-up using quality improvement. *South African Medical Journal*. 2014;104(3).
 103. M Ibeto JG, V Cox. Closing the gaps: Steps towards elimination of mother-to-child transmission of HIV. *Southern African Journal of HIV Medicine*. 2014;15(3).
 104. G. Martínez Pérez CM, D. Garone, R. Coulborn, A. D. Harries, B. Hedt-Gauthier, M. Murowa, G. S. Mwenelupembe, R. Van den Bergh, and L. Triviño Durán. HIV testing and retention in care of infants born to HIV- infected women enrolled in ‘Option B+’, Thyolo, Malawi. *Public Health Action* 2014;4(2):102-4.
 105. Mwendo EM, Mtuy TB, Renju J, Rutherford GW, Nondi J, Sichalwe AW, et al. Effectiveness of prevention of mother-to-child HIV transmission programmes in Kilimanjaro region, northern Tanzania. *Tropical medicine & international health : TM & IH*. 2014;19(3):267-74.
 106. Koye DN, Zeleke BM. Mother-to-child transmission of HIV and its predictors among HIV-exposed infants at a PMTCT clinic in northwest Ethiopia. *BMC public health*. 2013;13:398.
 107. Sethi AK CD, Gange SJ, Moore RD, Gallant JE. . Association between adherence to antiretro- viral therapy and human immunodeficiency virus drug resistance. . *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2003(37):1112–18.
 108. Nieuwkerk PT SM, Burger DM Limited patient adherence to highly active antiretroviral therapy for HIV-1 infection in an observational cohort study. *Arch Intern Med* 2001(161):1962-68.
 109. Nachega JB, Uthman OA, Anderson J, Peltzer K, Wampold S, Cotton MF, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *AIDS (London, England)*. 2012;26(16):2039-52.
 110. Cataldo F., Seeley J., Nkhata M.J., Mupambireyi Z., Tumwesige E., M. GD. She Knows That She Will not Come Back: Tracing Patients and New Thresholds of Collective Surveillance in PMTCT Option B+. *BMC health services research*. 2018;76(18).
 111. Kawuma R., Seeley J., Mupambireyi Z., Cowan F., Bernays S. “Treatment is not yet necessary”: delays in seeking access to HIV treatment in Uganda and Zimbabwe. *African Journal of AIDS Research*. 2018.
 112. Sumiyo Okawa MC, Naoko Ishikawa, Henry Kapyata, Charles Yekha Msiska, Gardner Syakantu, Shinsuke Miyano, Kenichi Komada, Masamine Jimba and Junko Yasuoka. Longitudinal adherence to ART drugs for PMTCT of HIV in Zambia. *BMC Pregnancy and Child Birth*. 2015;15(1).
 113. Haftamu Ebuy HY, Mussie Alemayehu. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, Northern Ethiopia *International Journal of Infectious Diseases* 2015;33:123-9.
 114. Benchimol EI, Smeeth L, Guttman A, Harron K, Hemkens LG, Moher D, et al. [The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement]. *Z Evid Fortbild Qual Gesundhwes*. 2016;115-116:33-48.

115. Nicholls SG, Langan SM, Benchimol EI. Routinely collected data: the importance of high-quality diagnostic coding to research. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2017;189(33):E1054-e5.
116. Jorm L. Routinely collected data as a strategic resource for research: priorities for methods and workforce. *Public health research & practice*. 2015;25(4):e2541540.
117. Hemkens LG, Contopoulos-Ioannidis DG, Ioannidis JP. Routinely collected data and comparative effectiveness evidence: promises and limitations. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2016;188(8):E158-64.
118. World, Health, Organization. National eHealth strategy toolkit: International Telecommunication Union Who.int. ; 2012 [cited 2019 8 February].
119. World, Health, Organisation. Electronic health records: manual for developing countries: Wpro.who.int; 2006 [cited 2019 8 February].
120. Abiy R, Gashu K, Asemaw T, Mitiku M, Fekadie B, Abebaw Z, et al. A Comparison of Electronic Medical Record Data to Paper Records in Antiretroviral Therapy Clinic in Ethiopia: What is affecting the Quality of the Data? *Online journal of public health informatics*. 2018;10(2):e212.
121. Fraser HS, Blaya J. Implementing medical information systems in developing countries, what works and what doesn't. *AMIA Annu Symp Proc*. 2010;2010:232-6.
122. Saczynski JS, McManus DD, Goldberg RJ. Commonly used data-collection approaches in clinical research. *The American journal of medicine*. 2013;126(11):946-50.
123. Akanbi MO, Ocheke AN, Agaba PA, Daniyam CA, Agaba EI, Okeke EN, et al. Use of Electronic Health Records in sub-Saharan Africa: Progress and challenges. *Journal of medicine in the tropics*. 2012;14(1):1-6.
124. Nicol E, Dudley L, Bradshaw D. Assessing the quality of routine data for the prevention of mother-to-child transmission of HIV: An analytical observational study in two health districts with high HIV prevalence in South Africa. *Int J Med Inform*. 2016;95:60-70.
125. Chen H, Yu P, Hailey D, Wang N. Methods for assessing the quality of data in public health information systems: a critical review. *Stud Health Technol Inform*. 2014;204:13-8.
126. Ferguson L, Grant AD, Ong'ech JO, Vusha S, Watson-Jones D, Ross DA. Prevention of mother-to-child transmission of HIV: assessing the accuracy of routinely collected data on maternal antiretroviral prophylaxis coverage in Kenya. *Sexually transmitted infections*. 2012;88(2):120-4.
127. Hotchkiss DR, Aqil A, Lippeveld T, Mukooyo E. Evaluation of the Performance of Routine Information System Management (PRISM) framework: evidence from Uganda. *BMC health services research*. 2010;10:188.
128. Nicol E, Bradshaw D, Phillips T, Dudley L. Human factors affecting the quality of routinely collected data in South Africa. *Stud Health Technol Inform*. 2013;192:788-92.
129. Hotchkiss DR, Diana ML, Foreit KG. How can routine health information systems improve health systems functioning in low- and middle-income countries? Assessing the evidence base. *Advances in health care management*. 2012;12:25-58.
130. Aqil A, Lippeveld T, Hozumi D. PRISM framework: a paradigm shift for designing, strengthening and evaluating routine health information systems. *Health policy and planning*. 2009;24(3):217-28.
131. Girma M, Wendaferash R, Shibru H, Berhane Y, Hoelscher M, Kroidl A. Uptake and performance of prevention of mother-to-child transmission and early infant diagnosis in pregnant HIV-infected women and their exposed infants at seven health centres in Addis Ababa, Ethiopia. *Tropical medicine & international health : TM & IH*. 2017;22(6):765-75.
132. Billong SC, Dee J, Fokam J, Nguefack-Tsague G, Ekali GL, Fodjo R, et al. Feasibility Study of HIV Sentinel Surveillance using PMTCT data in Cameroon: from Scientific Success to Programmatic Failure. *BMC infectious diseases*. 2017;17(1):3.

133. Sirengo M, Rutherford GW, Otieno-Nyunya B, Kellogg TA, Kimanga D, Muraguri N, et al. Evaluation of Kenya's readiness to transition from sentinel surveillance to routine HIV testing for antenatal clinic-based HIV surveillance. *BMC infectious diseases*. 2016;16:113.
134. Young PW, Mahomed M, Horth RZ, Shiraiishi RW, Jani IV. Routine data from prevention of mother-to-child transmission (PMTCT) HIV testing not yet ready for HIV surveillance in Mozambique: a retrospective analysis of matched test results. *BMC infectious diseases*. 2013;13:96.
135. Gonese E, Mushavi A, Mungati M, Mhangara M, Dzangare J, Mugurungi O, et al. Is Zimbabwe ready to transition from anonymous unlinked sero-surveillance to using prevention of mother to child transmission of HIV (PMTCT) program data for HIV surveillance?: results of PMTCT utility study, 2012. *BMC infectious diseases*. 2016;16(97):DOI 10.1186/s12879-016-1425-2.
136. Countrymeters. Zambia Information 2018 [8 August 2018]. Available from: <http://countrymeters.info/en/Zambia/>.
137. LusakaTimes.Com. Zambian HIV rate prevalence rate reduces- Dr Chilufya. Lusaka Times. 2017 23 February 2017.
138. UNICEF. UNICEF Zambia Fact Sheet [Available from: https://www.unicef.org/zambia/5109_8456.html].
139. ZAMPHIA. Zambia Population-Based HIV Impact Assessment 2015–2016. 2016.
140. Zambia, Ministry, of, Health. Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection. Lusaka, Zambia: Directorate of Clinical Care and Diagnostic Service; 2016 2 December 2017.
141. UNAIDS. Update:Zambia offering antiretroviral therapy regardless of CD4 count 2018 [8 August 2018]. Available from: http://www.unaids.org/en/resources/presscentre/featurestories/2017/august/20170818_zambia.
142. Zambia, National, AIDS, Council. GARPR Zambia Country Report 2013. 2014.
143. Touré H AM, Dabis F: . To what extent could performance-based schemes help increase the effectiveness of prevention of mother-to-child transmission of HIV (PMTCT) programs in resource-limited settings? A summary of the published evidence. . *BMC public health*. 2010(10).
144. Central Statistical Office. Zambia Demographic and health survey - 2013-14. Lusaka, Zambia; 2014.
145. Republic, of, Zambia, Ministry, of, Health. Zambia Consolidated Guidelines for Treatment and Prevention of HIV infection. Zambia; 2016.
146. Sutcliffe CG, van Dijk JH, Hamangaba F, Mayani F, Moss WJ. Turnaround time for early infant HIV diagnosis in rural Zambia: a chart review. *PloS one*. 2014;9(1):e87028.
147. Kellerman S, Essajee S. HIV testing for children in resource-limited settings: what are we waiting for? *PLoS medicine*. 2010;7(7):e1000285.
148. UNICEF, Zambia. 'Project Mwana: Using mobile technology to improve early infant diagnosis of HIV' 2012 [8 August 2018]. Available from: https://www.unicef.org/partners/Partnership_profile_2012_Mwana_Zambia_V2_approved.pdf.
149. Muyunda G. Zambia leads the way in SmartCare electronic health records system, a benefit to both providers and patients 2011 [Available from: <https://www.jhpiego.org/success-story/zambia-leads-the-way-in-smartcare-electronic-health-records-system-a-benefit-to-both-providers-and-patients/>].

150. Gopalakrishnan S, Ganeshkumar P. Systematic Reviews and Meta-analysis: Understanding the Best Evidence in Primary Healthcare. *Journal of family medicine and primary care*. 2013;2(1):9-14.
151. Creswell J. *Research design: Qualitative, quantitative, and mixed method approaches*. 2nd ed: Sage; 2003.
152. World, Health, Organisation. *Everybody Business: Strengthening Health Systems To Improve Health Outcomes: WHO's Framework For Action*. Geneva: WHO Library; 2007.
153. World, Health, Organisation. *Monitoring the Building Blocks of Health Systems: A Handbook of Indicators and their Measurement Strategies*. Geneva: WHO; 2010.
154. Sharma A, Rana SK, Prinja S, Kumar R. Quality of Health Management Information System for Maternal & Child Health Care in Haryana State, India. *PloS one*. 2016;11(2):e0148449.
155. Republic, of, Zambia. *National Health Strategic Plan 2011-2015*. Lusaka, Zambia2011.
156. Republic, of, Zambia, Ministry, of, Health. *Zambia National Health Strategic Plan 2017 – 2021*. Lusaka, Zambia2017.
157. Karengera I, Onzima RAD, Simon-Peter K, Govule K. Quality and Use of Routine Healthcare Data in Selected Districts of Eastern Province of Rwanda *International Journal of Public Health Research*. 2016;4(2):5-13.
158. Hong TT, Phuong Hoa N, Walker SM, Hill PS, Rao C. Completeness and reliability of mortality data in Viet Nam: Implications for the national routine health management information system. *PloS one*. 2018;13(1):e0190755.
159. Kasambara A, Kumwenda S, Kalulu K, Lungu K, Beattie T, Masangwi S, et al. Assessment of implementation of the health management information system at the district level in southern Malawi. *Malawi medical journal : the journal of Medical Association of Malawi*. 2017;29(3):240-6.
160. O'Hagan R, Marx MA, Finnegan KE, Naphini P, Ng'ambi K, Laija K, et al. National Assessment of Data Quality and Associated Systems-Level Factors in Malawi. *Global health, science and practice*. 2017;5(3):367-81.
161. Nisingizwe MP, Iyer HS, Gashayija M, Hirschhorn LR, Amoroso C, Wilson R, et al. Toward utilization of data for program management and evaluation: quality assessment of five years of health management information system data in Rwanda. *Global health action*. 2014;7:25829.
162. Mutemwa RI. HMIS and decision-making in Zambia: re-thinking information solutions for district health management in decentralized health systems. *Health policy and planning*. 2006;21(1):40-52.
163. World, Health, Organisation. *WHO Guidelines Approved by the Guidelines Review Committee*. Geneva: World Health Organization. Copyright (c) World Health Organization 2016.; 2016.
http://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf?sequence=1
Accessed on 5 August
164. Shaffer N, Abrams EJ, Becquet R. Option B+ for prevention of mother-to-child transmission of HIV in resource-constrained settings: great promise but some early caution. *AIDS (London, England)*. 2014;28(4):599-601.
165. Chi BH, Mutale W, Winston J, Phiri W, Price JT, Mwiche A, et al. Infant Human Immunodeficiency Virus-free Survival in the Era of Universal Antiretroviral Therapy for Pregnant and Breastfeeding Women: A Community-based Cohort Study From Rural Zambia. *The Pediatric infectious disease journal*. 2018;37(11):1137-41.

166. Chung N.C. B-MC, Chilengi R, Kasaro M. P., Stringer J. S. A and Benjamin H. Chi B. H. Patient engagement in HIV care and treatment in Zambia, 2004–2014. *Tropical Medicine and International Health*. 2017;22(3):332-9.
167. Tenthani L, Haas AD, Tweya H, Jahn A, van Oosterhout JJ, Chimbwandira F, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ('Option B+') in Malawi. *AIDS (London, England)*. 2014;28(4):589-98.
168. Koole O, Houben RM, Mzembe T, Van Boeckel TP, Kayange M, Jahn A, et al. Improved retention of patients starting antiretroviral treatment in Karonga District, northern Malawi, 2005-2012. *Journal of acquired immune deficiency syndromes (1999)*. 2014;67(1):e27-33.
169. Woelk G.B. ND, Behan S., Mukaminega M., Nyirabahizi E., Hoffman H.J., Mugwaneza P., Ribakare M., Amzel A., Ryan Phelps B. Retention of mothers and infants in the prevention of mother-to-child transmission of HIV programme is associated with individual and facility-level factors in Rwanda. . Woelk GB, Ndatimana D, Behan S, Mukaminega M, Nyirabahizi E, Hoffman HJ, Mugwaneza P, Ribakare M, Amzel A, Ryan Phelps B. 2016;19.
170. Chan AK, Kanike E, Bedell R, Mayuni I, Manyera R, Mlotha W, et al. Same day HIV diagnosis and antiretroviral therapy initiation affects retention in Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi. *Journal of the International AIDS Society*. 2016;19(1):20672.
171. Dzangare J, Takarinda KC, Harries AD, Tayler-Smith K, Mhangara M, Apollo TM, et al. HIV testing uptake and retention in care of HIV-infected pregnant and breastfeeding women initiated on 'Option B+' in rural Zimbabwe. *Tropical medicine & international health : TM & IH*. 2016;21(2):202-9.
172. Mirkuzie AH. Implementation and outcomes of guideline revisions for the prevention of mother-to-child HIV transmission in Mother Support Programme, Addis Ababa, Ethiopia. *PloS one*. 2018;13(6):e0198438.
173. Scott CA, Iyer HS, Lembela Bwalya D, Bweupe M, Rosen SB, Scott N, et al. Uptake, outcomes, and costs of antenatal, well-baby, and prevention of mother-to-child transmission of HIV services under routine care conditions in Zambia. *PloS one*. 2013;8(8):e72444.
174. Merdekios B, Adedimeji AA. Effectiveness of interventions to prevent mother-to-child transmission of HIV in Southern Ethiopia. *International journal of women's health*. 2011;3:359-66.
175. Haile F, Brhan Y. Male partner involvements in PMTCT: a cross sectional study, Mekelle, Northern Ethiopia. *BMC pregnancy and childbirth*. 2014;14:65.
176. Elias M, Mmbaga EJ, Mohamed AA, Kishimba RS. Male partner involvement in the prevention of mother to child transmission of HIV infection in Mwanza Region, Tanzania. *The Pan African medical journal*. 2017;27:90.
177. Amano A, Musa A. Male involvement in PMTCT and associated factors among men whom their wives had ANC visit 12 months prior to the study in Gondar town, North west Ethiopia, December, 2014. *The Pan African medical journal*. 2016;24:239.
178. Morfaw F, Mbuagbaw L, Thabane L, Rodrigues C, Wunderlich AP, Nana P, et al. Male involvement in prevention programs of mother to child transmission of HIV: a systematic review to identify barriers and facilitators. *Systematic reviews*. 2013;2:5.
179. Manjate Cuco RM, Munguambe K, Bique Osman N, Degomme O, Temmerman M, Sidat MM. Male partners' involvement in prevention of mother-to-child HIV transmission in sub-Saharan Africa: A systematic review. *SAHARA J : journal of Social Aspects of HIV/AIDS Research Alliance / SAHARA , Human Sciences Research Council*. 2015;12:87-105.

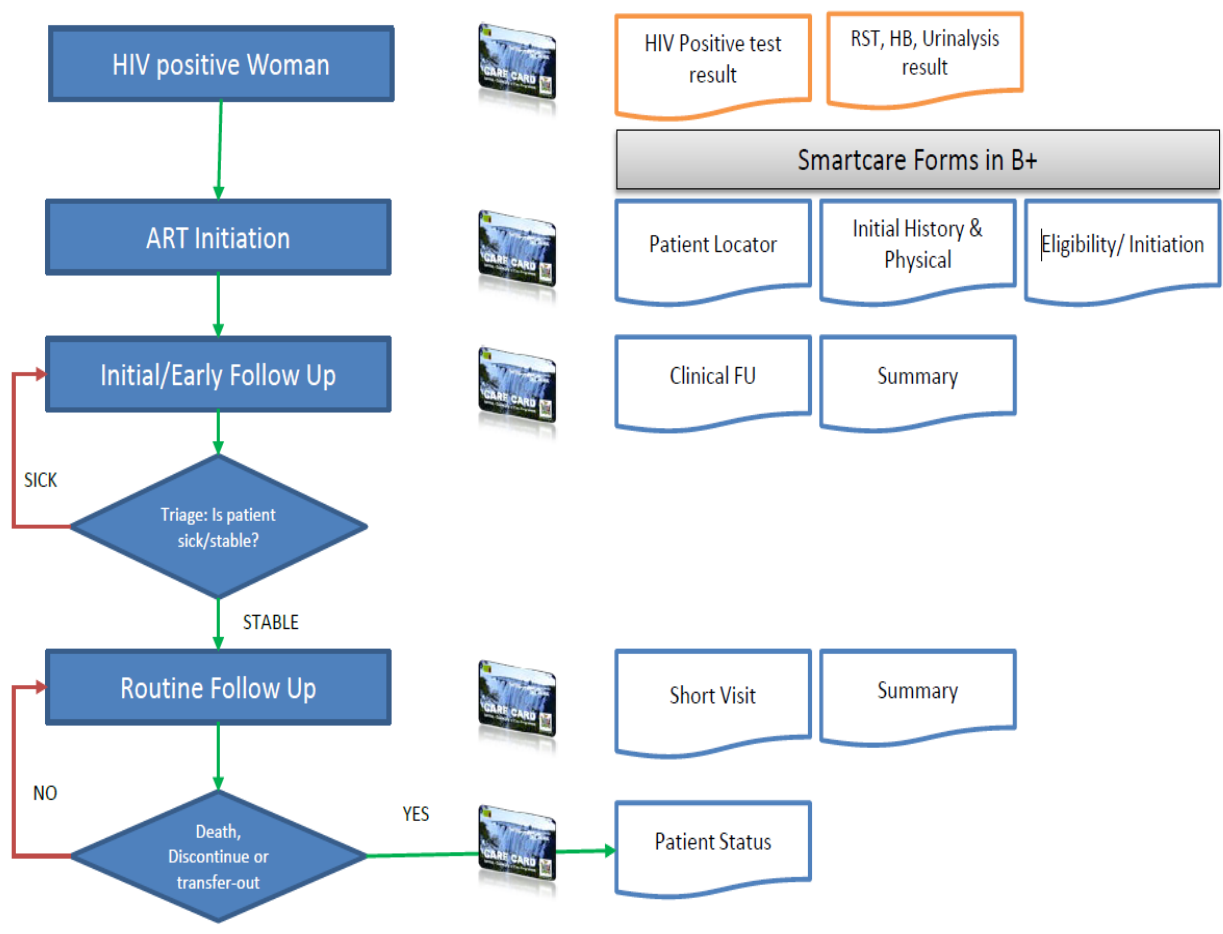
180. Kashitala J, Nyambe N, Mwalo S, Musamba J, Chishinga N, Kasonde P, et al. Is Male Involvement in ANC and PMTCT Associated with Increased Facility-Based Obstetric Delivery in Pregnant Women? *African journal of reproductive health*. 2015;19(2):117-24.
181. Koo K, Makin JD, Forsyth BW. Where are the men? Targeting male partners in preventing mother-to-child HIV transmission. *AIDS care*. 2013;25(1):43-8.
182. Mate KS, Bennett B, Mphatswe W, Barker P, Rollins N. Challenges for routine health system data management in a large public programme to prevent mother-to-child HIV transmission in South Africa. *PloS one*. 2009;4(5):e5483.
183. Annabelle Gourlay AW, Jim Todd, Caoimhe Cawley, Denna Michael, Richard Mchemba, Benjamin Clark, Clemens Masesa, Milly Marston, Mark Urassa and Basia Zaba. Uptake of services for prevention of mother-to-child transmission of HIV in a community cohort in rural Tanzania from 2005 to 2012. *BMC health services research*. 2016;16(4):1249-5.
184. The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaCI, editor B+ Monitoring & Evaluation Framework Dissemination and Country Consultation: Technical Synthesis. 2015; Kampala, Uganda.
185. Fraser HS, Biondich P, Moodley D, Choi S, Mamlin BW, Szolovits P. Implementing electronic medical record systems in developing countries. *Inform Prim Care*. 2005;13(2):83-95.
186. Della Mea V. Internet electronic mail: a tool for low-cost telemedicine. *J Telemed Telecare*. 1999;5(2):84-9.

Appendices

Appendix 1: PhD Timelines

PhD Year	YEAR 1 - 2015					Year 2 - 2016					Year 3 - 2017					Year 4 - 2018					Year 5 - 2019																		
Months	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	
Topic Development	■	■																																					
Smart Care Data Access/ Preparations		■	■																																				
Systematic Literature Review				■	■	■	■																																
Smart Care Data Extraction								■	■	■	■	■	■	■																									
Quantitative Data analysis															■	■	■	■	■																				
PhD Upgrading																																							
1st Publication																																							
Qualitative Data collection																																							
Qualitative Data Analysis																																							
2nd Publication																																							
3rd Publication																																							
4th Publication																																							
Thesis writing																																							
1st Thesis Submission																																							
Viva																																							
Time At LSHTM	■	■		■	■																																		

Data capture process



Appendix 3: LSHTM Ethical Clearance

London School of Hygiene & Tropical Medicine

Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

www.lshtm.ac.uk

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Observational / Interventions Research Ethics Committee

Ms. Sehulekile Gumedé
LSHTM

21 March 2017

Dear Sehulekile,

Study Title: Implementation Effectiveness of Revised (post- 2010) World Health Organisation Guidelines on Prevention of Mother to Child Transmission of HIV using routinely collected Data in Zambia

LSHTM Ethics Ref: 12086

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Investigator CV	Seh Gumedé- Moyo CV	31/01/2015	1
Local Approval	LSHTM_Ethics Approval Letter	08/02/2016	1
Local Approval	Search Zambia Ethics Approval	30/04/2016	1
Protocol / Proposal	Upgrading doc 270516	27/05/2016	1
Local Approval	MOH National Health Research	30/05/2016	1
Protocol / Proposal	Informed Consent FDG	16/09/2016	3
Protocol / Proposal	Informed Consent Indepth interviews	16/09/2016	2
Local Approval	MOH Permission letter	22/09/2016	1
Local Approval	UNZA BREC Qualitative	21/10/2016	1
Local Approval	Ethical Clearance UNZABREC	22/10/2016	1
Protocol / Proposal	Protol LEO 100117	10/01/2017	2
Covering Letter	12086 Ethics Clarification-2	28/02/2017	2
Protocol / Proposal	UNZA BREC Qualitative	20/10/2017	1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: <http://leo.lshtm.ac.uk>
Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,



Professor John DH Porter
Chair

ethics@lshtm.ac.uk
<http://www.lshtm.ac.uk/ethics/>


Improving health worldwide

Appendix 4: Ministry of Health Permission Letter

All correspondence should be addressed to the District Medical Officer

In reply please write
No. _____

Tel: +260-211-258854
Fax: +260-211290429



REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH

LUSAKA DISTRICT HEALTH OFFICE
P.O. BOX 30827
LUSAKA

Tuesday, September 27, 2016.

Ms. Sehlulekete Gumede-Moyo
London School of Hygiene and Tropical Medicine
Keppel Street
LONDON
U.K. WC1E 7HT.

Dear Ms. Sehlulekete,


RE: REQUEST FOR PERMISSION TO CARRY OUT RESEARCH IN YOUR ORGANISATION.

I refer to your letter dated 20th September, 2016, with the above captioned subject.

Lusaka District Medical Officer has no objection to your request provided:

1. The normal operations of the Health facilities are not disturbed
2. My office is fully apprised on progress of the research
3. That the final study results/report is shared with my office.

Yours sincerely,



Dr. Gideon Zulu
District Medical Officer
LUSAKA DISTRICT HEALTH OFFICE.

C.C.: HEALTH CENTRE IN-CHARGES.

Appendix 5: Zambia SEARCH Project Ethical Clearance



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALIJ ZA 44370
Fax: + 260-1-250753
E-mail: unzacc@unza.zm
Assurance No. FWA0000338
IRB00001131 of IORG0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

19th October, 2016.

Your Ref: 010-04-16.

Prof. James J. Todd,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London,
UK WC1E 7HT.

Dear Prof. Todd,

**RE: SUBMISSION AMENDED PROTOCOL ENTITLED: "SUSTAINABLE
EVALUATION THROUGH ANALYSIS OF ROUTINELY COLLECTED HIV
DATA (SEARCH) PROJECT" (REF. No. 010-04-16)**

Your application to amend the study protocol to include a qualitative study has been approved.
The approval is for the same period for the initial one granted.

Yours sincerely,

Dr. S.H Nzala
VICE-CHAIRPERSON

Appendix 6: LSHTM SEARCH Project Ethical Clearance

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636
www.lshtm.ac.uk



Observational / Interventions Research Ethics Committee

Mr. Jim Todd
DPH / EPH
LSHTM

18 August 2014

Dear Mr. Todd,

Study Title: Sustainable Evaluation through Analysis of Routinely Collected HIV data

LSHTM ethics ref: 8410

Thank you for your application of 17 July 2014 for the above research, which has now been considered by the Observational Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Protocol / Proposal	Routine data proposal_revised_Oct2013_4.doc	16/10/2013	Oct2013_4

After ethical review

Any subsequent changes to the application must be submitted to the Committee via an Amendment form on the ethics online applications website. All studies are also required to notify the ethics committee of any serious adverse events which occur during the project via an Adverse Event form on the ethics online applications website. At the end of the study, please notify the committee via an End of Study form on the ethics online applications website. Ethics online applications website link: <http://leo.lshtm.ac.uk>

Yours sincerely,

A handwritten signature in black ink, appearing to read 'John Porter'.

Professor John DH Porter
Chair

ethics@lshtm.ac.uk
<http://www.lshtm.ac.uk/ethics/>

Appendix 7: Qualitative Amendment Clearance



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@unza.zm
Assurance No. FWA00000338
IRB00001131 of IORG0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

19th October, 2016.

Your Ref: 010-04-16.

Prof. James J. Todd,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London,
UK WC1E 7HT.

Dear Prof. Todd,


RE: **SUBMISSION AMENDED PROTOCOL ENTITLED: "SUSTAINABLE
EVALUATION THROUGH ANALYSIS OF ROUTINELY COLLECTED HIV
DATA (SEARCH) PROJECT" (REF. No. 010-04-16)**

Your application to amend the study protocol to include a qualitative study has been approved.
The approval is for the same period for the initial one granted.

Yours sincerely,

Dr. S.H Nzala
VICE-CHAIRPERSON

Appendix 8: FDG Written Informed Consent Waiver


THE UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax : 260-1-250753
E-mail: unzareo@unza.zm
Assurance No. FWA00000338
REGISTRATION NO. OF ETHICS 0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

28th November, 2016.

Your Ref: 010-04-16.


Prof. James J. Todd,
London School of Hygiene and Tropical Medicine,
Keppel Street,
London,
UK WC1E 7HT.

Dear Prof. Todd,

RE: REQUEST FOR FOCUS GROUP DISCUSSION WRITTEN CONSENT WAIVER
FOR: "SUSTAINABLE EVALUATION THROUGH ANALYSIS OF ROUTINELY
COLLECTED HIV DATA (SEARCH) PROJECT" (REF. No. 010-04-16)

We acknowledge receipt of notification of getting verbal consent instead of written. This is in order and acceptable to do so.

Yours sincerely,



Dr. S.H Nzala
VICE-CHAIRPERSON

Appendix 9: Informed Consent Forms

9.1 Informed Consent – In-depth Interviews



Study purpose

The study aims to use routinely collected data to give an overview of the effectiveness of post 2010 WHO PMTCT guidelines implementation and improve decision making in the Zambia health care system. The SmartCare Database is the source of routinely collected data

Procedures and duration

If you agree to take part in the study, we will talk on a one on one basis. The one on one discussion will take approximately 30 minutes to 1 hour. You will then be asked questions about specific issues related to SmartCare and PMTCT Implementation. The information will be audio recorded and then written down on a computer. Nothing you say will be directly attributable to you.

Confidentiality

We will use a participant identification number instead of actual names on the study information. The information we collect may be shared with other researchers who are involved in this study but if shared, it will be anonymously. These ideas will be published in order to improve the understanding of the scientific community about these issues. It will not be possible to link any information published in this way to the individuals who told their stories. The information may be stored for many years at the LSHTM in London and University of Zambia.

Risks

The risks of participating in this study are small. It is possible that you may feel uncomfortable with some of the questions that are asked in which case you do not need to answer them. You can withdraw from the study at any time.

Benefits

You are unlikely to benefit directly from participating in this study. However the information that we collect could be used by policy makers to plan and prioritize strategies to address identified gaps in implementation of SmartCare and PMTCT programs.

Voluntary participation

We hope that you will take part in this study. However, you do not have to take part in this study if you do not want them to. If you decide that you should take part but then change your mind you may withdraw at any time without having to give a reason.

Offer to answer questions

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

For any other questions that you may have about this study, please contact the person in charge of the study: **Mrs Sehlulekile Moyo on this phone number: 09777 61451**

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant or research-related injuries; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact:

University of Zambia

Biomedical Research Ethics Committee

Ridgeway Campus

Box 50110

Lusaka, Zambia

Phone: +260 – 1 - 256067

AUTHORIZATION

You are making a decision whether you should participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

STATEMENT OF CONSENT TO BE AUDIO-TAPED

I understand that audio recordings will be taken during the study. (Mark either “Yes” or “No”)

I agree to be audio recorded

Yes

No

Name (please print)

Date

Signature

9.2 Informed Consent – Focus Group Discussions

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Study purpose

The study aims to use routinely collected data to give an overview of the effectiveness of post 2010 WHO PMTCT guidelines implementation and improve decision making in the Zambia health care system. The SmartCare Database is the source of routinely collected data

Procedures and duration

If you agree to take part in the study, we will talk to you in group of 8 to 12 women. The focus group discussion will take approximately 2 hours. You will then be asked questions about specific issues related to SmartCare and PMTCT Implementation. The information will be audio recorded and then written down on a computer. Nothing you say will be directly attributable to you.

Confidentiality

We will use a participant identification number instead of actual names on the study information. The information we collect may be shared with other researchers who are involved in this study but if shared, it will be anonymously. These ideas will be published in order to improve the understanding of the scientific community about these issues. It will not be possible to link any information published in this way to the individuals who told their stories. The information may be stored for many years at the LSHTM in London and University of Zambia.

Risks

The risks of participating in this study are small. It is possible that you may feel uncomfortable with some of the questions that are asked in which case you do not need to answer them. You can withdraw from the study at any time.

Benefits

You are unlikely to benefit directly from participating in this study. However the information that we collect could be used by policy makers to plan and prioritize strategies to address identified gaps in implementation of SmartCare and PMTCT programs.

Voluntary participation

We hope that you will take part in this study. However, you do not have to take part in this study if you do not want them to. If you decide that you should take part but then change your mind you may withdraw at any time without having to give a reason.

Offer to answer questions

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

For any other questions that you may have about this study, please contact the person in charge of the study: **Mrs Sehlulekile Moyo on this phone number: 09777 61451**

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant or research-related injuries; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact:

University of Zambia

Biomedical Research Ethics Committee

Ridgeway Campus

Box 50110

Lusaka, Zambia

Phone: +260 – 1 - 256067

AUTHORIZATION

You are making a decision whether you should participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

STATEMENT OF CONSENT TO BE AUDIO-TAPED

I understand that audio recordings will be taken during the study. (Mark either “Yes” or “No”)

I agree to be audio recorded

Yes

No

Name (please print)

Date

Signature

Appendix 10: Chapter 5 Additional Results

10.1 Time to ART initiation per province in months

Province	Year 2010	Year 2011	Year 2012	Year 2013	Year 2014	Year 2015	Mean
Central	9.5	0.4	3.2	6.4	3.8	3.1	4.4
Copperbelt	0.0	0.4	9.4	9.3	3.7	4.3	4.5
Eastern	11.6	0.0	10.3	14.7	4.8	4.3	7.6
Luapula	37.1	33.7	15.1	23.0	0.4	20.0	21.5
Lusaka	16.2	32.5	6.1	7.7	8.8	14.1	14.2
North-Western	17.9	0.3	0.1	3.2	1.8	19.0	7.0
Northern	7.0		1.2	10.0	4.4	1.4	4.0
Southern	6.0	6.0	3.7	3.6	3.7	6.3	4.9
Western	10.1	9.5	7.2	19.0	9.7	2.8	9.7
Total	8.6	6.4	5.1	7.8	4.6	7.9	6.7

Appendix 11: Chapter 6 Additional Results

11.2 Univariable and multivariable analysis for age at HIV test

Variable	Age at test		Univariable analysis			Multivariable analysis				
	<2 months (%)	n	>2 months (%)	n	OR	95% CI	P value	aOR*	95% CI	P value
<i>Sex</i>										
Male	550 (5.22)		9,987 (94.78)		1.00	-	-	1.00	-	-
Female	603 (5.39)		10,582 (94.61)		1.03	0.92, 1.17	0.573	0.97	0.85, 1.11	0.665
<i>Province</i>										
Lusaka	365 (6.77)		5,029 (93.23)		1.00	-	-	1.00	-	-
Central	94 (4.11)		2,194 (95.89)		0.59	0.47, 0.74	<0.001	0.46	0.35, 0.59	<0.001
Copperbelt	294 (6.15)		4,484 (93.85)		0.90	0.77, 1.06	0.210	0.69	0.58, 0.83	<0.001
Eastern	59 (2.85)		2,013 (97.15)		0.40	0.31, 0.53	<0.001	0.27	0.20, 0.37	<0.001
Luapula	56 (4.18)		1,285 (95.82)		0.60	0.45, 0.80	0.001	0.44	0.31, 0.61	<0.001
Northern	57 (5.80)		926 (94.20)		0.85	0.64, 1.13	0.262	0.69	0.50, 0.96	0.029
North-Western	25 (2.83)		858 (97.17)		0.40	0.27, 0.61	<0.001	0.25	0.15, 0.40	<0.001
Southern	394 (11.71)		2,972 (88.29)		1.83	1.57, 2.12	<0.001	1.36	1.13, 1.63	0.001
Western	24 (1.52)		1,553 (98.48)		0.21	0.14, 0.32	<0.001	0.14	0.08, 0.23	<0.001
<i>Year of birth</i>										
2006	220 (12.87)		1,489 (87.13)		1.00	-	-	1.00	-	-

Variable	Age at test		Univariable analysis			Multivariable analysis		
	<2 months n (%)	>2 months n (%)	OR	95% CI	P value	aOR*	95% CI	P value
2007	412 (15.73)	2,207 (84.27)	1.26	1.06, 1.51	0.009	0.80	0.49, 1.30	0.365
2008	528 (15.19)	2,947 (84.81)	1.21	1.02, 1.44	0.025	0.70	0.46, 1.08	0.106
2009	683 (18.57)	2,995 (81.43)	1.54	1.31, 1.82	<0.001	1.11	0.74, 1.65	0.623
2010	675 (24.83)	2,043 (75.17)	2.24	1.89, 2.65	<0.001	1.31	0.87, 1.96	0.191
2011	446 (24.61)	1,366 (75.39)	2.21	1.85, 2.64	<0.001	2.24	1.50, 3.34	<0.001
2012	191 (13.80)	1,193 (86.20)	1.08	0.88, 1.33	0.450	1.63	1.08, 2.46	0.020
2013	186 (13.76)	1,166 (86.24)	1.08	0.88, 1.33	0.474	2.27	1.51, 3.40	<0.001
2014	171 (16.78)	848 (83.22)	1.36	1.10, 1.70	0.005	2.79	1.85, 4.21	<0.001
2015	137 (35.49)	249 (64.51)	3.72	2.87, 4.83	<0.001	27.03	16.43, 44.49	<0.001
2016	49 (45.37)	59 (54.63)	5.62	3.71, 8.51	<0.001	-	-	-
<i>Birth quarter</i>								
Jan – March	919 (15.13)	5,154 (84.87)	1.00	-	-	1.00	-	-
April – June	968 (16.60)	4,865 (83.40)	1.12	1.01, 1.23	0.029	1.29	1.07, 1.56	0.009
July – Sept	869 (19.37)	3,618 (80.63)	1.35	1.22, 1.49	<0.001	1.94	1.60, 2.35	<0.001
Oct – Dec	942 (24.36)	2,925 (75.64)	1.81	1.63, 1.99	<0.001	2.90	2.40, 3.50	<0.001

Variable	Age at test				Univariable analysis			Multivariable analysis		
	<2 months (%)	n	>2 months (%)	n	OR	95% CI	P value	aOR*	95% CI	P value
					2.00					

Appendix 11.2: Univariable and multivariable analysis for time from diagnosis to ART initiation

Variable	Time from diagnosis to ART				Univariable analysis			Multivariable analysis		
	<2 weeks	n (%)	>2 weeks	n (%)	OR	95% CI	P value	aOR*	95% CI	P value
Sex										
Male	2,249	(21.34)	8,288	(78.66)	1.00	-	-	1.00	-	-
Female	2,568	(22.96)	8,617	(77.04)	1.10	1.03, 1.17	0.004	1.06	0.97, 1.16	0.165
Province										
Lusaka	822	(15.24)	4,572	(84.76)	1.00	-	-	1.00	-	-
Central	688	(30.07)	1,600	(69.93)	2.39	2.13, 2.69	<0.001	3.10	2.65, 3.64	<0.001
Copperbelt	1,648	(34.49)	3,130	(65.51)	2.93	2.66, 3.22	<0.001	5.05	4.42, 5.78	<0.001
Eastern	431	(20.80)	1,641	(79.20)	1.46	1.28, 1.66	<0.001	1.21	1.02, 1.43	0.026
Luapula	547	(40.79)	794	(59.21)	3.83	3.36, 4.37	<0.001	8.69	6.83, 11.05	<0.001
Northern	350	(35.61)	633	(64.39)	3.08	2.65, 3.57	<0.001	5.03	3.98, 6.37	<0.001
North-Western	244	(27.63)	639	(72.37)	2.12	1.80, 2.50	<0.001	2.46	1.96, 3.09	<0.001
Southern	718	(21.33)	2,648	(78.67)	1.51	1.35, 1.69	<0.001	1.35	1.16, 1.56	<0.001
Western	285	(18.07)	1,292	(81.93)	1.27	1.06, 1.42	0.007	1.25	1.04, 1.51	0.018
Year of birth										
2006	340	(19.89)	1,369	(80.11)	1.00	-	-	1.00	-	-
2007	547	(20.89)	2,072	(79.11)	1.06	0.91, 1.24	0.430	1.10	0.82, 1.48	0.531
2008	790	(22.73)	2,685	(77.27)	1.18	1.03, 1.37	0.020	1.60	1.23, 2.07	<0.001
2009	861	(23.41)	2,817	(76.59)	1.23	1.07, 1.42	0.004	2.32	1.81, 2.98	<0.001
2010	726	(26.71)	1,992	(73.29)	1.47	1.27, 1.70	<0.001	2.56	1.99, 3.30	<0.001
2011	612	(33.77)	1,200	(66.23)	2.05	1.76, 2.40	<0.001	2.65	2.04, 3.43	<0.001
2012	564	(40.75)	820	(59.25)	2.77	2.35, 3.26	<0.001	3.23	2.47, 4.21	<0.001
2013	605	(44.75)	747	(55.25)	3.26	2.76, 3.85	<0.001	3.70	2.84, 4.82	<0.001

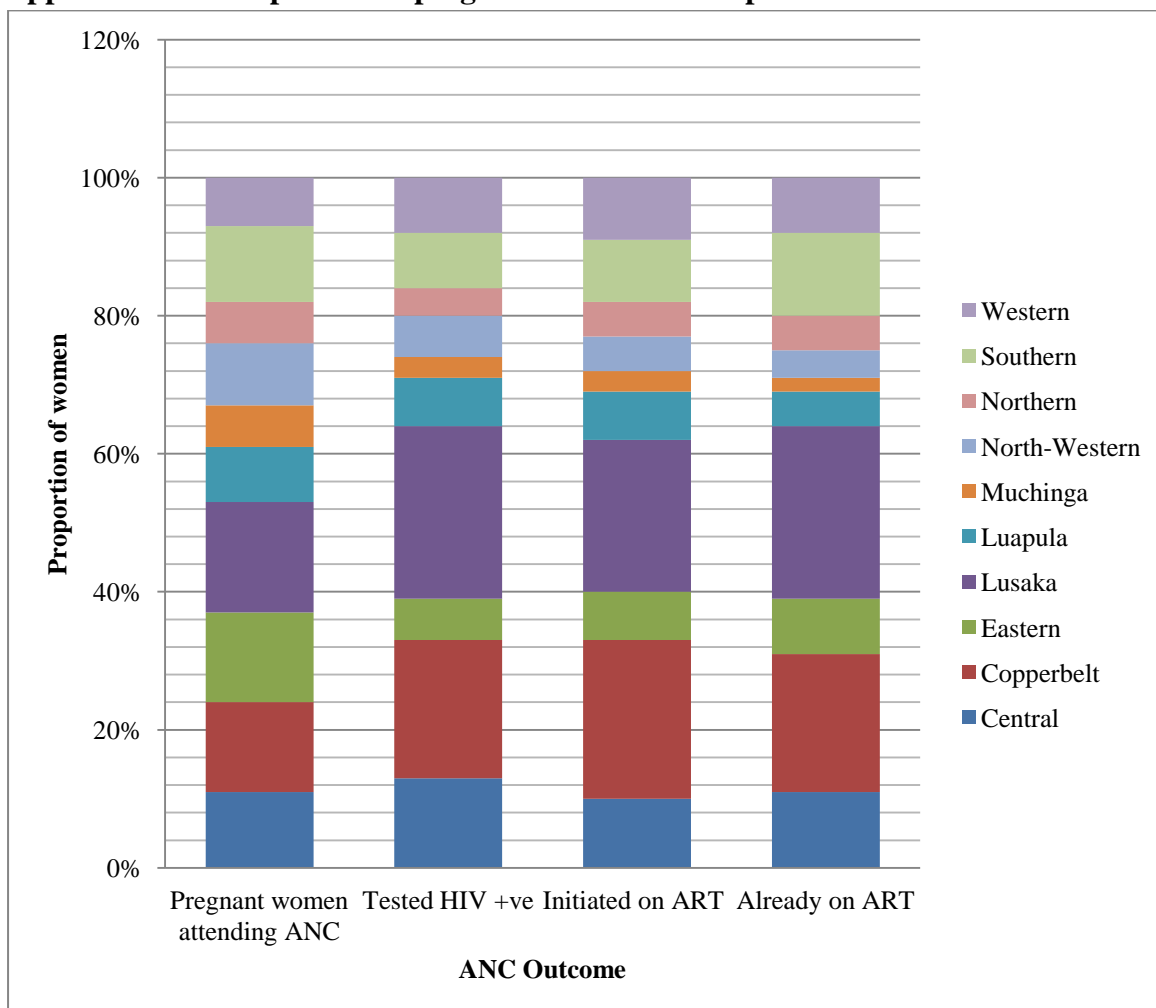
Variable	Time from diagnosis to ART				Univariable analysis			Multivariable analysis		
	<2 weeks	n (%)	>2 weeks	n (%)	OR	95% CI	P value	aOR*	95% CI	P value
2014	548 (53.78)		471 (46.22)		4.68	3.90, 5.62	<0.001	7.78	5.83, 10.38	<0.001
2015	140 (36.27)		246 (63.73)		2.29	1.80, 2.92	<0.001	15.48	9.44, 25.40	<0.001
2016	0 (0)		108 (100)		0.00	-	<0.001	-	-	-
<i>Birth quarter</i>										
Jan - March	1,759 (28.96)		4,314 (71.04)		1.00	-	-	1.00	-	-
April - June	1,654 (28.36)		4,179 (71.64)		0.97	0.90, 1.05	0.463	0.92	0.82, 1.04	0.179
July - Sept	1,296 (28.88)		3,191 (71.12)		0.10	0.91, 1.08	0.928	1.03	0.91, 1.16	0.659
Oct - Dec	1,024 (26.48)		2,843 (73.52)		0.88	0.81, 0.97	0.007	1.02	0.89, 1.16	0.791

Appendix 12: Chapter 8 Additional Results

Appendix 12.1: HMIS data Summary

Province name	2013				2014				2015				2015				2016			
	ANC Visits	Tested HIV +ve	Initiated on ART	Already on ART	ANC Visits	Tested HIV +ve	Initiated on ART	Already on ART	ANC Visits	Tested HIV +ve	Initiated on ART	Already on ART	ANC Visits	Tested HIV +ve	Initiated on ART	Already on ART	ANC Visits	Tested HIV +ve	Initiated on ART	Already on ART
Central	61868	3730	325	1183	72932	3269	1201	2567	74101	3093	2767	2715	74101	3093	2767	2715	74091	4981	882	2856
Copperbelt	69582	7185	1505	2357	82245	6862	3552	4766	83279	6125	4466	5098	83279	6125	4466	5098	83400	2958	2295	4722
Eastern	80671	2284	424	956	85556	1899	993	2161	84073	1787	1523	2416	84073	1787	1523	2416	85046	607	494	1633
Lusaka	82881	7565	1188	2570	94041	6734	3853	6152	102023	7607	4539	6343	102023	7607	4539	6343	118035	7176	2105	6942
Luapula	43743	2250	213	699	56092	1361	1136	1150	54523	1443	1684	1521	54523	1443	1684	1521	53826	1069	778	1325
Muchinga	31439	584	103	226	36313	604	422	622	37061	762	694	599	37061	762	694	599	35920	2064	289	571
North-Western	49552	1605	167	647	59658	1191	818	663	59552	1227	1133	774	59552	1227	1133	774	56837	2932	569	1059
Northern	34120	1368	379	875	41679	998	608	966	43502	1152	942	1300	43502	1152	942	1300	43116	1385	442	1026
Southern	57808	3113	389	1317	73398	2832	1590	3127	76069	2684	1791	3531	76069	2684	1791	3531	77862	1065	890	2874
Western	38742	2973	139	1139	48296	2505	1334	1882	47964	2412	2036	2064	47964	2412	2036	2064	46889	1645	1406	1948
Total	550406	32657	4832	11969	650210	28255	15507	24056	662147	28292	21575	26361	662147	28292	21575	26361	675022	25882	10150	24956

Appendix 12.2: Proportion of pregnant women across provinces



Appendix 13: Qualitative Questionnaires

13.1 Leadership Level Interview Guide

Participants were leaders who have been involved in the SmartCare implementing from CDC, Ministry of Health and Implementing partners

1.0 Basic information

1. Date of interview:
2. Interview Participant Unique ID Number:

2.0 Introduction

- Self-introduction and welcoming of participant.
- Explanation of the general purpose of the interview discussion and why the participant was chosen.
- Explanation of the presence and purpose of recording equipment.
- Addressing the issue of confidentiality.
- Signing of the informed consent form.

3.0 Interview

SmartCare Development

1. Can you tell me about the process for the development of the SmartCare Database?

Probe

- Who 'drove' the process? (Name, institution, role)
- What was your personal role (or the role of your department/institution process?)
- Who else was involved (service providers, service users etc.)?
- How was this participation organized?

2. Is this process documented anywhere?

Probe:

E.g. Minutes of meetings – are these publicly accessible?

3. What were the most contentious issues that were discussed during the development process?

Probe:

- How these issues were resolved?

4. Were there any perspectives not represented that you think it might have been useful to include?
5. Was there anything that could have been improved in this process?
6. Was there any opportunity for implementing partners to comment on the database development?

SmartCare Implementation

1. How are SmartCare facilities chosen?
Probe:
 - What type of support do facilities get on inception?
2. How are facilities allocated to implementing partners?
3. How are people aware of SmartCare at health facility level?

Probe

- How are people made aware of SmartCare?
 - How are people working at different levels of the same health facility made aware?
4. There is often a difference between how SmartCare implementation guidelines look on paper and how they are implemented?

Probe

- To what extent is it different for each implementing partner group (international/ local /government owned)
 - Mention some key points relevant to implementation
5. What are the most contentious issues in SmartCare implementation?

Probe

- Obstacles that have arisen?
6. What do you think are the needs of implementing partners to facilitate data quality of SmartCare?
 7. What steps are needed to improve data quality?

Data Quality Assessment

1. How often do you verify the data that is collected from SmartCare Facilities?
Probe

- Who is responsible for the verification process?
 - Is there a standard verification process tool?
 - What are the challenges?
2. How often is the data collected from facilities submitted to district offices/provincial/head office?
- Probe:
- Who is responsible for the submission process?
 - Is there a standard data submission procedure that you need to follow?
 - What are the challenges of the submission process?
3. Do facilities always have supplies that you need for data collection and entry?
4. How often do you hold implementation review sessions with IPs/ operational level staff?
- Probe
- Training / Frequency?
 - How long are training sessions?
5. Is the program delivered in the same manner by all partners?
- Probe
- Staffing levels for IPs?
 - Capacity of staff for different IPs?
 - Availability of infrastructure?
 - Support services?

PMTCT Services and SmartCare

1. Can you tell me a bit about PMTCT services offered in SmartCare facilities?
- Probe:
- What is the purpose of offering the services?
 - Do women have a choice of being part of the services?
 - How have the PMTCT services affected your work?
 - Your relationship with clients?
 - For facilities with test and treat policy – probe how this has affected the services offered?
2. What's the process for offering PMTCT services in these facilities?
- Probe:

- HIV Testing & Counselling?
 - ART Eligibility/Initiation?
 - Early Infant diagnosis ?
3. What do you think are the main barriers within facilities that make it difficult for pregnant women to access PMTCT services if they need them?
- Probe:
- Availability of some services limited to certain days?
 - Waiting times?
4. Can you describe to me the current system of linkage between PMTCT and SmartCare services?
- Probe:
- HIV Testing & Counselling?
 - ART Eligibility/Initiation?
 - HIV Prevention?
 - Early Infant diagnosis?
5. What happens to women once they are registered for SmartCare?
- Probe:
- Who is responsible to ensure that she is registered for SmartCare
 - How do you ensure that they are registered for SmartCare?
 - What do you do if a woman says that she does not want to be enrolled for SmartCare?
6. What do you think are the main barriers within this facility that make it difficult for the linkage between PMTCT and SmartCare?
- Probe
- Linkages between mothers and infants?
 - Infant Diagnosis test results?
7. What do you think can be done to improve linkage between PMTCT and SmartCare?

Closing

Closing remarks: That's all the questions I have. Is there anything else that you would like to tell me or ask me about?

Thank you for participating in this discussion.

13.2. Operational Level Interview Guide

Participants were operational level staff – M& E Managers, Database Managers

I. Basic Data

1. Date of interview:
2. Implementing Partner Name:
3. Facility Name / Code:
4. Facility Location:

II. Introduction

- Welcome participant and introduce yourself.
- Explain the general purpose of the interview discussion and why the participant was chosen.
- Explain the presence and purpose of recording equipment.
- Address the issue of confidentiality.
- Read the information sheet to the participant
- Go through informed consent procedures

Let's start with a few general questions about you

1. How long have you worked here?
2. What's your current position?
3. What has been your involvement with SmartCare?
4. What training have you had on SmartCare related issues?

Probe:

- How long was the training?
- Who offered training

5. Are you adequately-prepared to work on issues around Smart Care in general?

Probe:

When was the last time you received SmartCare - related training?

Let's talk a little bit about the work that you do relating to PMTCT services

8. Can you tell me a bit about PMTCT services offered in this facility?

Probe:

- What is the purpose of offering the services?
- Do women have a choice of being part of the services?
- How have the PMTCT services affected your work?
- Your relationship with clients?
- For facilities with test and treat policy – probe how this has affected the services offered?

9. What's the process for offering PMTCT services in this facility?

Probe

- PMTCT Cascade?

10. How do you manage your time when there are many clients in this facility?

11. Do you always have supplies that you need for PMTCT services?

12. Is there anything that you think can be done to improve PMTCT services in this facility?

Let's talk about SmartCare

13. When did this facility start implementing SmartCare?

Probe:

- How was the facility selected?
- What type of support did this facility get during inception?
- Is the SmartCare for this facility Paper based or Computer based?
- Why does this clinic use this method for data collection?
- Will this change?
- What are the problems with the current system?
- Is it the same system for all clinics and clients in the facility?
- What happens if a client comes in from another health facility?

- Can their records be accessed and managed?
- How are their data entered?

14. How often do you verify the data that is collected in this facility?

Probe

- Who is responsible for the verification process?
- Is there a standard verification process tool?
- What are the challenges?

15. How often do you submit data that is collected in this facility to district offices/provincial/head office?

Probe:

- Who is responsible for the submission process?
- Is there a standard data submission procedure that you need to follow?
- What are the challenges of the submission process?

16. Do you always have supplies that you need for data collection and entry?

17. What do you think are the main barriers within this facility that make data collection and entry difficult?

18. What do you think can be done within the health care system to improve data collection and entry under SmartCare?

Probe:

- What difference do you think this would make for you? For patients?

Let's talk about link between PMTCT services and SmartCare

19. Can you describe to me the current system of linkage between PMTCT and SmartCare services?

Probe:

- HIV Testing & Counselling?
- ART Eligibility/Initiation?
- Early Infant diagnosis?

20. What happens to her once she registers for SmartCare?

Probe:

- Who is responsible to ensure that she is registered for SmartCare?
- How do you ensure that they are registered for SmartCare?
- What do you do if a woman says that she does not want to be enrolled for SmartCare?

21. Can you tell me about a particularly difficult case, mentioning no woman's or staff's names, that you've had where it was hard for you to link an HIV positive woman to SmartCare services?

Probe:

- How would you do things differently if you were in that situation again?

22. Are there any aspects of SmartCare service provision that you think could be improved? Probe:

- What difference do you think this would make for you?
- For patients?

23. What do you think are the main barriers within this facility that make it difficult for the linkage between PMTCT and SmartCare?

24. Is there anything else that you think could be done by other people within the health system to help facilitate this linkage into SmartCare?

25. Are there things about being a health worker at this facility that you would like to improve?

Probe:

- What makes your job easier?
- What makes it harder?

What difference do you think this would make for you? For patients?

Closing remarks: That's all the questions I have. Is there anything else that you would like to tell me?

Thank you for participating in this discussion.

13.3 Data Entry Level Interview Guide

- A. Basic Data
- B. Date of interview:
- C. Implementing Partner Name:
- D. Facility Name / Code:
- E. Facility Location:
- F. Time interview started:
- G. Time interview ended:

B. Introduction

- Welcome participant and introduce yourself.
- Explain the general purpose of the interview discussion and why the participant was chosen.
- Explain the presence and purpose of recording equipment.
- Address the issue of confidentiality.
- Read the information sheet to the participant
- Go through informed consent procedures

Let's start with a few general questions about you

1. How long have you worked here?
2. What's your current position?

Probe:

What do you do on a typical day at work?

3. What training have you had on SmartCare related issues?

Probe:

- How long was the training?
 - Who offered training
4. Are you adequately-prepared to work on issues around Smart Care in general?

Probe:

When was the last time you received SmartCare - related training?

Let's talk about Data entry and collection

5. When did this facility start implementing SmartCare?

Probe:

- How was the facility selected?
- What type of support do they get during inception?

6. Can you explain to me the data collection and entry process for SmartCare?

Probe

- Paper based or Computer based.

7. How do you manage your time when there are many clients in this facility?

8. What do you think are the main barriers within this facility that make data collection and entry difficult?

9. Are there any aspects of SmartCare data entry that you think could be improved?

Probe:

- What difference do you think this would make for you? For patients?

10. How often do you verify the data that is collected in this facility?

Probe

- Who is responsible for the verification process?
- Is there a standard verification process tool?
- What are the challenges?

11. How often do you submit data that is collected in this facility to district offices/provincial/head office?

Probe:

- Who is responsible for the submission process?

12. Is there a standard data submission procedure that you need to follow?

Probe:

- What are the challenges?

13. Do you always have supplies that you need for data collection and entry?

14. What are the challenges of data collection and entry?

15. What do you think can be done within the health care system to improve data collection and entry under SmartCare?

Let's talk a little bit about the work that you do relating to PMTCT services

16. Can you tell me a bit about PMTCT services offered in this facility?

Probe:

- What is the purpose of offering the services?
- Do women have a choice of being part of the services?
- How have the PMTCT services affected your work?
- Your relationship with clients?
- For facilities with test and treat policy – probe how this has affected the services offered?

17. What's the process for offering PMTCT services in this facility?

18. How do you manage your time when there are many clients in this facility?

Probe:

Do you spend less time on some of the PMTCT Cascade steps?

19. What do you think are the main barriers within this facility that make it difficult for pregnant women to access PMTCT services if they need them?

Probe:

- Distance to facilities
- Availability of some services limited to certain days?
- Waiting times?

Let's talk about link between PMTCT services and SmartCare

20. Can you describe to me the current system of linkage between PMTCT and SmartCare services?

Probe:

- HIV Testing & Counselling?
- ART Eligibility/Initiation?
- HIV Prevention?
- Early Infant diagnosis?

21. What happens to her once she registers for SmartCare?

Probe:

- Who is responsible to ensure that she is registered for SmartCare?
- How do you ensure that they are registered for SmartCare?
- What do you do if a woman says that she does not want to be enrolled for SmartCare?

22. Can you tell me about a particularly difficult case that you've had where it was hard for you to link an HIV positive woman to SmartCare services?

Probe:

How would you do things differently if you were in that situation again?

23. What do you think are the main barriers within this facility that make it difficult for the linkage between PMTCT and SmartCare?

24. Are there any aspects of PMTCT SmartCare linkage service provision that you think could be improved? Probe:

What difference do you think this would make for you? For patients?

25. Are there things about being a health worker at this facility that you would like to improve?

Probe:

- What makes your job easier?
- What makes it harder?

If necessary, provide examples: need more staff because patient load is high, need training, salaries should be paid on time etc.

13.4 SmartCare Facility Managers Interview Guide

I. Basic Data

- Date of interview:
- Implementing Partner Name
- Facility Name / Code
- Facility Location:
- Time interview started
- Time interview ended

II. Introduction

- Welcome participant and introduce yourself.
- Explain the general purpose of the interview discussion and why the participant was chosen.
- Explain the presence and purpose of recording equipment.
- Address the issue of confidentiality.
- Read the information sheet to the participant
- Go through informed consent procedures

Let's start with a few general questions about you

1. How long have you worked here?
2. What's your current position?

Probe:

What do you do on a typical day at work?

Let's talk a little bit about the work that you do relating to PMTCT services

3. Can you tell me a bit about PMTCT services offered in this facility?

Probe:

- What is the purpose of offering the services?
 - Do women have a choice of being part of the services?
 - How have the PMTCT services affected your work?
 - Your relationship with clients?
 - For facilities with test and treat policy – probe how this has affected the services offered?
4. What's the process for offering PMTCT services in this facility?

Probe

- PMTCT Cascade?
5. How do you manage your time when there are many clients in this facility?

Probe:

- Do you spend less time on some of the PMTCT Cascade steps?
6. Do you always have supplies that you need for PMTCT services?
7. What do you think are the main barriers within this facility that make it difficult for pregnant women to access PMTCT services if they need them?

Probe:

- Distance to facilities
 - Availability of some services limited to certain days?
 - Waiting times?
8. Is there anything that you think can be done to improve PMTCT services in this facility?

Let's talk about SmartCare

9. When did this facility start implementing SmartCare?

Probe:

- How was the facility selected?
 - What type of support did this facility get during inception?
10. What has been your involvement with SmartCare?
11. What training have you had on SmartCare related issues?
12. Are you adequately-prepared to work on issues around Smart Care in general?

Probe:

- When was the last time you received SmartCare - related training?
13. Who is responsible for verifying the data collected in this facility?

Probe:

- Roles of those responsible?
- Frequency of verifications?

14. Do you always have supplies that you need for SmartCare services?

15. Is there anything that you think can be done to improve SmartCare services in this facility?

Let's talk about link between PMTCT services and SmartCare

16. Can you describe to me the current system of linkage between PMTCT and SmartCare services?

Probe:

- HIV Testing & Counselling?
- ART Eligibility/Initiation?
- Early Infant diagnosis?

17. What happens to her once she registers for SmartCare?

Probe:

- Who is responsible to ensure that she is registered for SmartCare?
- How do you ensure that they are registered for SmartCare?
- What do you do if a woman says that she does not want to be enrolled for SmartCare?

18. Can you tell me about a particularly difficult case that you've had where it was hard for you to link an HIV positive woman to SmartCare services?

Probe:

- How would you do things differently if you were in that situation again?
19. Are there any aspects of SmartCare service provision that you think could be improved? Probe:

- What difference do you think this would make for you?
- For patients?

20. Are there things about being a health worker at this facility that you would like to improve?

Probe:

- What makes your job easier?
- What makes it harder?

If necessary, provide examples: need more staff because patient load is high, need training, salaries should be paid on time etc.

Probe:

What difference do you think this would make for you? For patients?

21. What do you think are the main barriers within this facility that make it difficult for the linkage between PMTCT and SmartCare?
22. Is there anything else that you think could be done by other people within the health system to help facilitate this linkage into SmartCare?

Closing remarks: That's all the questions I have. Is there anything else that you would like to tell me?

Thank you for participating in this discussion

13.5 Focus Group Discussions Interview Guide - English

- Date of interview:
- Implementing Partner Name:
- Facility Name / Code:
- Facility Location:

Objectives:

- Share different experiences (good and bad) related to the use of SmartCare for PMTCT services.
- Identify the major barriers and facilitating factors that affect women's Uptake of PMTCT services

Materials:

Flip chart paper and pens

Pens for participants to fill out informed consent and demographic information

- Read and have participants sign consent forms. (5 minutes)
- Have participants' complete information form. (5 minutes)
- Explain focus group process. (5 minutes)

As explained in the consent form, everything you say here is confidential. Everything you say in this discussion will be kept private. It is important to us that you give us your honest opinions. We will be tape-recording your comments. The tape will be kept confidential, and names will not be used in any quotations that might be included in written reports.

Our discussion will last about two hours. To cover everything and end on time, I may sometimes move the discussion on, but everyone will have an opportunity to speak. Please speak clearly, one at a time, and share your opinions. There are no right or wrong answers. We are interested in your opinions and you do not have to agree with one another - we are interested in hearing different opinions.

INTRODUCTIONS (5 minutes): Get participants interacting, and prepare for introductions and expectations. Introductions: Ask participants to turn to their neighbour and ask them a few things about themselves so that each pair can introduce each other to the larger group. Explain that if people don't want to use their real names they can choose a fake name. Ask each person to introduce her partner and two things about them. As part of these

introductions, introduce yourself and the note-taker (and anyone else from the research team who is in the room).

OBJECTIVE (5 minutes): Explain the objectives for the workshop e.g. through this discussion, our objective is to find out more about the SmartCare and PMTCT Services. We will listen and learn from you to get a better understanding of the services and your ideas on how to improve them.

GROUND RULES (5 minutes): Say “We would like to hear everyone’s ideas and have a good meeting. What rules should we use in working together today?” Give an example of one rule (e.g. listen to and respect one another’s views), and then ask for other rules. Record suggestions.

If the group doesn’t mention **CONFIDENTIALITY**, add it to the list and explain “You might want to share personal stories during this discussion, but your stories should NOT be shared with anyone else after our discussion is over.”

Examples of Meeting Rules:

- Encourage everyone to participate to the extent that they feel comfortable.
- Listen to one another and respect one another’s views
- Don’t interrupt when a person is speaking
- Keep things confidential
- Turn off cell phones

Once the list is completed, say “These will be our rules for this discussion so that we can all be comfortable.

1. Can you describe the process from when the health worker first talked to you about PMTCT?

Probe

- How did the health worker tell you?
- What did you talk about?
- Then what happened?

2. What do you remember about the health worker?

Probe:

- Can you remember any good things about the interaction with her?
- And any bad things? No need to mention any staff names.

3. When were you enrolled under SmartCare?

PROBE:

- Where / Which Facility?
- Who did you talk to?
- Do they have a SmartCare card?

4. Did the health worker take you to the SmartCare Department?

Probe:

- Can you tell me about your experience at the SmartCare Department on that day?
- What happened when you first arrived? And then what?
- What services were you given?

5. What did they tell you about SmartCare services?

Probe:

- What did s/he say to you about it?

6. Did you tell anyone that you are enrolled under SmartCare?

Probe:

- Who did you tell?
- When did this happen?
- How did they react when you told them?

(Deal with each person to whom they have disclosed individually)

- Did they understand?
- Has this changed over time?

7. Can you describe people's attitude towards SmartCare?

Probe

- Did they show anyone their SmartCare cards?

8. How often do you come to this facility?

Probe

- Reasons?

9. Is this facility accessible?

Probe

- Mode of transport?
- Distance travelled?

(Deal with each person to whom they have disclosed individually)

10. How long do you usually take at the facility?

Probe

- Waiting time?
- Waiting area?
- Privacy?
- Is it longer for people on SmartCare compared to other general patients?

(Deal with each person to whom they have disclosed individually)

11. Do you think that pregnant women who test HIV-positive want to access to PMTCT services?

Probe:

- Type of services?
- Why?
- Why not?

(Services along the PMTCT Cascade)

12. Do most women who access PMTCT services disclose their HIV status to their partners? And families?

Probe:

- Why?
- Why Not.

13. Does stigma persist as an issue affecting decisions to access PMTCT related services?

Probe:

- In what ways?
- How do some women overcome this?
-

14. Do you think that people's partners and families are generally supportive of pregnant women accessing PMTCT services if they need them?

Probe:

- Why? Why not?
- What kind of support do they provide?
- In what ways are they unsupportive?
- How about the community?

15. What are the things that have helped you overcome some of the barriers that we've talked about and helped you come to access PMTCT services at this facility?

16. What do you think can be done to make it easier for pregnant women to access PMTCT services?

WRAP-UP (5 mins):

Thank you very much. We've now gone through all of our questions for this discussion group and we just have a few minutes left. Is there anything else that any of you would like to add or to ask?

Thank you very much for taking part. There is a drink and snack for each of you here and please see to collect your compensation for taking part.

Interviewer Notes

- Comments about respondents
- Comments on specific questions
- Any other comments

13.6 Bemba Focus Group Discussions Interview Guide

- Date of interview:
- Implementing Partner Name:
- Facility Name / Code:
- Facility Location:

Efyotulefyawa

- Ukulanda ifintu ifingi ifyapusanapusana (ifisuma ne fibi) ifikatishanya nobubomfyi bwa SmartCare aya PMTCT
- Ukumona inshila ishikulu ishilenga bana mayo ukukana poka amafwilisho aya PMTCT

Ifilefyauka:

Ama pepala ayakulembapo ayakulu naba bopeni

Amabopeni yabantu abalesendako ulubali ukubomfya ukulembela pafipepala ifyakusuminisha nefyo bekala nefyo bakwata.

- Belenga elyo uleke abalesendako ulubali uku saina ifipepala ifyakusuminisha. (5 minutes)
- Leka abalesendako ulubali bapwishe ukulemba ichipepa ichilanda pafyo bekala (5 minutes)
- Londolola inshila iyaku kulandishanya uku. (5 minutes)

Kwati efyo twalondolola mwipepala yakusuminisha fyonse efyo twalalanda pano fyalaba efya nkama.Fyonse efyo mwalalanda mukulandishanya uku fikasungwa mu nkama.Chikankala sana kuli ifwe ikutupelaamatontokanyo yenu ayachine.Tukala mi senda amashiwi yenu.Iyi Tape ukasungwa munkama elyo amashina yenu tayakabonfyewepo mukulanda ukulikonse pakubomfya mukulemba report.

Ukulandishanya kwesu kwalasenda inshita iyalakumako kuma hola yabili.Kuti tupwishe fyonse munshita,munshita shimbi kuti nasenda ukulandishanya oku,mwisakamana bonse mwalapelwa inshita yakulanda.Ndelomba mulelandisha,umuntu umo panshita imo nokulanda amatontokanyo yenu.Takuli ubwasuko ububi nangula ubusuma.ifwe tulefyaya fye ama tontontokanyo yenu eyo tamufwile ukusuminishanya-tulefwaya ukumfwa amatontontokanyo ayapusanapusana.

- Pakwamba: Leka abalesenda ulubali bale landishanya elyo upekanye ukuishibisha nefyo balechetekela.Ukuishibisha: eba abalesendamo ulubali uku lolesha kuli ba

nebba babo elyo bepushane ifintu ifinono pali bene pakuti abantu babili babili baishibishe kwibumba ilikulu.

- Eba umuntu nomuntu eshibishe abantu pamunaknwe pafintu fibili pali ena. Londolola ukuti nga abantu tabalefwaya ukubomfya amashina yabo ayachine kuti basala ukupanga amashina nga inshila yaku ishibisha. Ishibishe na ba kukwafwa ukulemba (elyo nomuntu onse owo mulebomba nankwe fya kufwailikisha mumuputule uyu.)
- Efyo tulefyaya: Londolola ichikulu cha workshop, kwati ukupitila mukulandishanya uku, efyotulefywaya kusanga ifingi pamafwilisho ya SmartCare na PMTCT. Twala umfwa nokusambilila kuli imwe pakuti tusende ukumfwikisha ukusuma pa ma fwilisho elyo nama tontokanyo yenu efyo tunga twala pantanshi amafwilisho aya.
- Amafunde Yakukonka: Landa tulefwaya ukumfwa amatontokanyo yamuntu onse elyo nokukwata meeting isuma. Mafundeshi twalabomfwa pakuti tubombele chapamo lelo. Pela ichishibisho cha funde chimo (Kwati. Ukumfwila nokupela umuchinsi amatontokanyo yamuntu ulionse) Elyo wipushe yambi amafunde. Lemba efyo balelanda.
- Inga ibumba talilandile INKAMA, lundapo kufyo balandile nokulondolola ukweba ati kuti bafwaya ukulanda amashiwi ayakuminefye bena pakulandishanya uku, koma aya amashiwi tayafwile ukusabankanyishiwa kumuntu ulionse ngatwapwisha ukulandishanya uku.

Ifishibisho fya mafunde aya meeting:

- Bakoseleshe bonse ukusendako ulubali pakweba ati bayumfweko ukukakuluka.
- Ukumfwilana noku pela umuchinshi kutontokanyo lyamunenu
- Takuli ukuputukisha umuntu inga alelanda
- Sungeni ifintu fyonse munkama.
- Shimyeni ama lanya.

Inga babwisha fyonse ukulanda, Landa ati aya eyalaba amafunde yesu mukulandishana uku pakweba ati bonse tube abakakuluka.

1. Ndongololweniko inshila ukwamba elyo mwalandile na babomfi bafyabumi akakwambililapo pali PMTCT.

Ipukisha

- Bamwebeleshani ababomfi ba fyabumi?

- Finshi mwalandilepo?
- Elyo ninshi ichachitike?
- Finshi mwibukishapo paba bomfi babumi?

Ipukisha

Kuti mwaibukishako ichintu ichisuma mukulanda kwenu mwakwete nabena?

Inga ichintu ichibi? Tachilefwaika ukulanda amashima yaba bomfi.

2. Mwailembeshe lwisa ku SmartCare?

Ipukisha

- Kwisa/Inchende isa?
- Mwalandile nabanani?
- Mwalikwata Kadi iya SmartCare?

3. Bushe ababomfi ba fyabumi balimitwala kuchipao cha SmartCare?

Ipukisha

- Njebeniko eflyo mwwaumfwile elyomwali kuchipao cha SmartCare bulya bushiku?
- Finshi fwachitike elyo mwafikilefye pakwamba?Elyo finshi fwakonkelepo?
- Mafwilisho nshi eyo bamipele?

4. Finshi bamwebele pama fwilisho ya SmartCare?

Ipukisha

- Finshi balandile kuli imwe pali ifi?

5. Bushe mwali ebapo umuntu ulionse ukweba ati mwali ilembesha ku SmartCare?

Ipukisha

- Nabanani mwaebele?
- Nilisa fyachitike ifi?
- Bachitile shani elyo mwabebele pali ifi?

(bomba nomuntu uwo baebele umoumo)

Bali umfwikisha?

Bushe fwalichinja nenshita ipitilepo?

6. Ndondololweniko imitontokanyishishe yabantu pali SmartCare?

Ipukisha

- Bushe balelanga ama kadi yabo aya SmartCare?

7. Mwisa imiku inga kunchende eyi?

Ipukisha

- Umulandu wanshi?

8. Bushe iyi nche ilifye apasuma?

Ipukisha

- Mubomfya transipoti yashani?
- Inga Ubutali mukwenda?

(bomba nomuntu uwo baebele umoumo)

9. Musende inshita itali shani panchende apa?

Ipukisha

- Inshita yakulolela?
- Panchende yakulolelela?
- umwafisamikwa?
- Bushe chilasenda inshita itali kulibalya ababa pa SmartCare nga mwalinganya na balwele bambi?

(bomba nomuntu uwo baebele umoumo)

10. Bushe muletokanya ati banamayo abamafumo abobasanga notushishi twa HIV balafwaya uku sendako amafwilisho aya PMTCT?

Ipukisha

Mitundu yama fwilisho?

Ninshi?

Ninshi pantu?

11. Bushe bana mayo abengi abasenda amafwilisho aya PMTCT balanda efiyo babasanga kubyena mwabo?naba lupwa?

Ipukisha

Ninshi?

Ninshi pantu?

12. Bushe ukwimwenamo echintu ichilenga ukukana ukupoka amafwilisho ubukumine PMTCT?

Ipukisha

- Munshila nshi?
- Inga bambi bana mayo bachita shani pali ichi?

13. Bushe muletonkanya ukweba ati abena mwabo naba lupwa mukumonafye balafwa banamayo abamafumo mukusenda amafwilisho aya PMTCT inga balefwaya?

Ipukisha

- Ninshi?ninshi pantu?
- Babapela ubwafwilisho bwashani?
- Munshilanshi esho tabafwila?
- Inga abantu?

14. Fintu nshi efyamyafwile ukupitapo ifintu ifikanya eflyo twachilalandapo elyo nokumyafwa ukusendako amafwilisho pa nchende eyi?

15. Finshi muletonkanya ati kuti fya afwako banamayo abamafumoukusendako amafwilisho aya PMTCT?

Pwisha

Twatotela sana.Natupitamo amepusho yonse aya kulandishanya kwesu mwibumba eli elyo tushele fye nakashita akanono.kuliko chiimbi echo mulefwaya ukulundapo nagula ukwipusha?

Interviewer Notes

- Comments about respondents
- Comments on specific questions
- Any other comments

13.7 Nyanja Focus Group Discussions Interview Guide

- Date of interview:
- Implementing Partner Name:
- Facility Name / Code:
- Facility Location:

Chimenetifuna

- Ku uzana vintu vosiyanasiyana (vabwino na voipa) mukugwilizana ndikusebenzesa ma masamaliloyabwino yama tandizo ya PMTCT.
- Kuona njila zikulu zamene zimalesa azimai kutengako matandizo ya PMTCT

Zofunikila:

Mapepala yolembapo yakulu ndi ma bolopeni

Ma bolopeni niya otengakombali kuti basebenzese kulembela zintu zovomeleza kutengako mbali ndi mwamene bankalila

- Belenga ndiku ona kuti otenga mbali ba saina vipepalo vovomeleza, (5 minutes)
- Onakuti otengambalai basiliza kulemba pa pepala la nkani (5 minutes)
- Fotokoza njila yo kambilana uku (5 minutes).

Monga mwamene tafotokozela mupepala lovomeleza vonse vamene muzakamba kuno vizankala vachisinsi. Vonse vamene muzakamba visungidwa mobisika. Nicholinga ngako kuti mutipase maganizo yanu ya zoona. Tiza kutengani mau mu tape mayanko yanu, Iyi Tape izasungidwa mwachisinsi ndipo mazina yanu siyazakasebenzesewa olo kuikidwa mu report yomwe tizalemba.

Uku kukambilana kwatu kuzatenga ma hola yabili. Kuti tisilize vonse pa ntawi, ntawizina ningatenge kukambilana kwatu, koma aliyense azapasiwa mupata okamba. Nipemba muzikamba konveka, umozi pantawi, ndi kukamba maganizo yanu. Kulibe yanko yachendi ndi yanko ya boza. Ise tifuna chabe maganizo yanu ndipo simuyenekela kuvomelezana tifuna kunvela maganizo yosiyana siyana.

CHOYAMBILILA: (ma mineti 5) Ona kuti otenga mbali bakambisana ndi kukonzekela kuzifotokoza ndi zamene balindilila kuona. Kuzifotokoza: Uza otenga mbali kuti aliyense ayanga nebba wake ndikumufunsa zintu zing'ono pali beve kuti bantu babilibabili bazifotokoze ku gulu likulu. Funsa muntu aliyense afotokoze munzake ndikukamba zintu zibile palimunzake. Bauze kuti ngati bantu sibafuna kusebenzesa mazina yao yazo ona banga

sanke kusebenzesa mazina yozipangila munga mbali yo zifotokoza,zikambe iwe ndi kalembela(ndipo na aliyense alimu gulu yanu yo fufuza ali mu chipinda umu)

Chofunikila (maminati 5): Bauze chamene mwachitila iyiworkshop, munga kupitila mu kukambisana kwatu uku, tifuna kuzibilapo vambili pali SmartCare ndi matandizo ya PMTC.Tizanvelela ndikupunzila kuchokela kuli imwe munga mwamene tingapelekele pasogolo matandizo aya

Malamulo (maminati 5): Kamba ‘Tifuna kunvela maganizo yamuntu aliyense ndipo nilinamalamulo yamene yiyenekela kusebenzesa pamozi lelo?Pasa chisanzo cha lamulo limozi (munga, nvelela ndikupasa ulemu ganizo yamunzako), ndipo funsa malamuloyenangu ndikulemba zizakambidwa.

Ngati gulu sizakamba CHISINSI, ifakepo pa mundandanda ndiku bauza kuti munga fune kukamba chntu chanu chabe pakukambilana uku koma ichisichiyenekela ku uziwa kumuntu aliyense tikasiliza kukambilana uku.

Zisanzo za Malamulo ya meeting:

- Ona kuti bonse batengako mbali kufikila kuti bazinvela kumasuka.
- Nvelelani muntu umozi ndikupasa ulemu maganizo yamunzanu
- Osajubisa muntu ngati akamba
- Sungani vintu mwachisinsi
- Zimyani ma lanya.

Mukasiliza mundandanda oyu, Kamba ‘aya ndiye yazankala malamulo yatu pakukambilana kwatu kuti tonse tinkale omasuka.

1. Ni fotokozele njila kuyambila pamene banchito ba zaumoyo banakamba naimwe pali PMTCT koyamba?

Funsisisa

- Banaku uzani bwanji banchito ba zaumoyo?
 - Muna kambisana chani?
 - Manje nichani chinachitika?
2. Nichani chamene mukumbukila pa banchito bazaumoyo?

Funsisisa

- Mungakumbukileko chintu chilichonse chabwino pakukambisilana kwanu ndibeve?
- Nga vintu voipa? Kulibe chofunikila kukamba na zina yaba nchito aba.
- Munalembesa liti kunkala pa SmartCare?

Funsisisa

- Kuti/dela liti?
- Munakamba nabandani?
- Kodi muli nakadi ya SmartCare?

3. Kodi banchito zaumoyo banakupelekani ku chigao cha SmartCare?

Funsisisa

- Mungani uze mwamene munakunvelela ku chigao cha
- Nichani china chitika pamene munayambilila kufika? Manje chinakonkapo?
- Munapasiwa tandizo yabwanji?

4. Bana ku uzana chani pa matandizo ya SmartCare?

Funsisisa

- Bana ku uzani chani pali ichi?

5. Muna uzako aliyense kuti ndimwe bolembesewa ku SmartCare?

Funsisisa

- Muna Uza Ndani?
- Ichi chinachitika liti?
- Bana oneka pamene muna bauza?

(Sebenza na muntu aliyense wamene bana uza umozindiumozi)

- Chinvela?
Kodi ichi chachinja pa ntawi yapita?

6. Mungafotokozani maganizo yabantu pali SmartCare?

Funsisisa

- Benzo langiza aliyense ma SmartCare cards yao?

7. Muma bwela kangati kudela ili?

Funsisisa

- Zifukwa?

8. Ili dela lili pafufi nakwanu?

Funsisisa

Muma sebenzesa transipoti yabwanji?

Nipatali bwanji kuyenda?

(Sebenza na muntu aliyense wamene bana uza umozindiumozi)

9. Mumankala ntawi itali bwanji kupadela?

Funsisisa

- Ntawi yo lindilila?
- Pa nchende yo lindilila
- Kubbisika?
- Kodi chitenga ntawi ku bantu baja balipa SmartCare kulinganiza nabantu bodwala benangu chabe?

(Sebenza na muntu aliyense wamene bana uza umozindiumozi)

10. Muganiza kuti azimai baja bali napakati bamene bapezeka HIV-positive bangafune tandizo ya PMTC?

Funsisisa

- Matandizo ya bwanji?
- Chifukwa
- Chifukwa chachani?

11. Kodi azimai bamene batengako tandizo ya PMTCT bamauzako nkalidwe yao ya HIV kuli asumbali bao? Ndi ba banja?

Funsisisa

- Chifukwa.
- Chifukwa chachani?

12. Kodi kuzionelamo chingankale nichintu chamene chimalengesa kusa tenga matandizo yogwilizana na PMTCT?

Funsisisa

- Munjila Bwanji?
- Nanga bazimai benengu bamachita bwanji kugonjesa ichi?

13. Muganiza kuti bamuna babantu ndi ba banja bamatandizila kuli bazimai balindipakati bamene batenga matandizo ya PMTCT ngati bayafuna?

Funsisisa

- Chifukwa? Chifukwa chani?
- Bamapasa kutandizila kwabwanji?
- Nimunjila bwanji zamene sibamatandizila?
- Nanga muma dela yao?

14. Nivintu bwanji vamene vina kutandizani kugonjesa njila zina zamene zivaliza zamene takambapo ndipo zina kutandizani kubwela kutenga ma tandizo ya PMTCT pa dela ili?

15. Nivichani vamene muonamonga vingachitiwe kuti vi pepukiseko njila ya azimai bali ndipakati kuti bazitengako matandizo ya PMTCT?

Maliza (mamineti 5):

Zikomo kwambili. Tapitamo mumafunso yatu yonse mukukambisana kwagulu ili ndipo tasala chabe ndi maminati yang'ono. kuliko china chamene mufuna kuikilapo kapena kufunsa?

Interviewer Notes

- Comments about respondents
- Comments on specific questions
- Any other comments

13.8 Tonga Focus Group Discussions Interview Guide

- Ibuzuba bwakubuzya:
- Izina lya muntu ugwasilizya:
- Izina lyabusena/chizyibilo:
- Nkobujanika:

Nchetuyanda:

- Kobambila izichito ziindeneneindene (izibi azibotu) zijatikizya eyi SmartCare kulu gwasho lwa PMTCT.
- Yandaula twaambo tupati itukasya bamakaintu ikutola lubazu mu magwasho a PMTCT.

Izibeleho:

Ipepa lyakusandula ama bopeni

Ima bopeni ngabasikutola lubazu kutegwa babelashe kulembela imapepa akuzumina a mbobapona.

Kobala alimwi bonakuti basikutola lubazu ba saina izipepa zyakuzumina. (5 minutes)

- Bona ikuti basikutola lubazu bamanizya kulemba ipepa lya nkani. (5 minutes)
- Pandulula nzila ya mubandi oyu (5 minutes)

Mbuli pepa lyaku zumina mboli pandulula,zyonse zetutambaule ano zilaba zyama seseke.Zyonse zyumutaambe mumubandi oyu ziyo bambwa kumbali.Echi chilelede kulindiswe loko kulindiswe ikutegwa mwatupa imiyeyo yanu yanchobeni.Tunikubweza majwi anu mumubandi.I tepu liyobambwa muma seseke alimwi imazina anu tawobeleshegwi kulikonse na kwabelesha muma report ngetutikalembe.

Imubandi yesu ulatola ima hola atandila kusika kuli obilo.kuti tumazye zyonse akumanizya muchiindi.inga muziindi ndini kubweza mubandi oyu, pesi nonse mulapegwa ibusena bwakwambaula.Ndalomba kamwambaula kwakuvwika,muntu omwe achiindi chipedwe akwamba mizeyo yanu.Kwina bwinguzi buluzi abitaluzi.swebo tuyanda biyo imiyeyo yanu alimwi tamwelede ikuzumizyana tuyanda ikunvwa imizeyo indeneindene

KUTANGUNA :Bona ikuti basikutola lubazu balimukwambauzyana alimwi libambile ikuti bali pandulule azyobayeyela.Kutanguna:buzya basikutola lubazu ikutu balange muntu ngobatobelana awalo alimwi balibuzye azyintu zishonto alimbabo kutegwa bobilobobilo balipandulule kukabungwe konse.Ko ambila muntu amuntu apandulule mwenhinyina azintu zyo bilo alimbabo.kobapanduluda ikuti na bantu tabayandi kubeesha mazina anchobene inga babelsha bazina akulipangila.Mbuli kulipandulula uku,lipandulule asikukulembela (aliwi kufumbwa muntu ngomulamwi mukubuzya oku uli abusena obu)

NCHETUYANDAULA: pandulula nchetuyandaula mukwi ishana oku mbuli kwindila mukwambauzyana oku,nchetuyandaula nkuzibilao zinji ali SmartCare amagwasho a PMTCT.Tuyaku swilila akwiya kuzwakulindinywe kutegwa kunvwisisya kabotu amagwasho azyomuyeya mbutunga twasumpula agwasho aya.

Imilao yesu: kwaamba ‘tuyanda kunvwa muntu onse zyayeya kutegwa tube amubandi mubotu.Tulabeleka imilao yabuti antomwe sunu?’’Kupa chitondezyo cha mulao omwe (Mbuli kuswilila akupa bulemu muntu zyayeya) alimwi buzya imilao imbi akulemba zebatambe.

Ikuti tibamba MASESEKE,kuibika amundandanda akupandulula.Inga mwayanda kutwambila nkani igamide biyo ndinywe mumubandi oyu,pesi nkani yanu tayeledede kupegwa kumuntu uli onse twamanizya kwambaula oku.

Zitondezyo zyamilao yamubandi oyu:

- Kugwasyana tonse ikutolalubazu kutegwa twalinvwa kwanguluka.
- Kuswililana akupa bulemu muzezo wa umbi.
- Kwina kujata muntu amulomo anikwambaula.
- Tubambe zintu mumaseseke
- Kumuzina mawaile

Bamanizya kwambaula zyonse,amba ‘eyi njitibe milao yesu mumubandi wesu kutegwa tonse twanguluke

1. Kumundipandulwida nzila kuzwa nimwatanguna kwambaula ababelesi bazya buummi ali PMTCT

Kobuzisisya

- Ino mubelesi wazya bumi wakamwambila buti?
- Mwakambaula nzi?
- Mpona ninzi chakachitika?

2. Ninzi nchomuyeya amubelesi wazyabumi?

Kobuzisisya

- Inga mwayeya izintu zibotu akwambauzyana awalo?
- Ino zintu zibi? Tamwelede kwaamba mazina ababelesi.

3. Mwalilembya lili ku SmartCare?

Kobuzisisya:

- Okuli/busena buli?
- Nguni ngumwakambaula awalo?
- Sena mula chitupa cha SmartCare?

4. Sena mubelesi wazyabumi wakamutola kuchibela cha SmartCare?

Kobuzisisya:

- Kamundambila mbumwakalinvwa buya buzuba nimwakali ku chibela cha SmartCare?
- Ninzi chakachitika chakutanguna nimwakasika? Alimwi chakatobela?
- Magwasho abuti ngimwakapegwa?

5. Bakamwambila nzi amagwasho a SmartCare?

Kobuzisisya:

- Wakamwambila nzi alichechi?

6. Mwakambilako muntu uli onse kuti mwakalilembya aba SmartCare?

Kobuzisisya:

- Mwakambila bani?
- Echi chakachitika lili?
- Ino bachita nzi nimwakabambila?

Beleka amuntu omwe omwe utambigwe

- Bakachinvwa echi?
- Sena chachincha echi nikwaba kaindi?

7. Kamupandulula ibantu mbobalailanga eyi SmartCare?

Kobuzisisya

- Balikutondezya izitupa zya SmartCare kumuntu ulionse?

8. Inga mubola zindi zyangaye kubusena obu?

Kobuzisisya

- Nkaambo?

9. Mpafwafwi buti abusena ubo?

Kobuzisisya

- Mweenda buti?
- Palamfu buti?

(Beleka amuntu omwe omwe utambigwe)

10. Inga mubweza chiindi chilamfu buti abusena?

Kobuzisisya

- Chiindi chakulindila?
- Busena bwakulindilila?
- Bulili siside?
- Ino chitola chiindi chilamfu a SmartCare mwezyanya aba lwazi bambi mubunji?

(Beleka amuntu omwe omwe utambigwe)

11. Sena muyeya ikuti bamakaintu bamitide banga bajanwa atuuka twa HIV inga balayanda kubweza magwasho a PMTCT?

kobuzisisya:

- Mishobo ya magwasho?
- Ino?
- Ino Kayi?

(Magwasho ali antomwe a PMCT)

12. Sena bama kaintu ibabweza magwasho a PMTCT inga balamba kubamalumi babo mbobabede akauka ka HIV? A bamukwashi?

Kobuzisisya:

- Ino?

- Ino Kayi?
13. Sena kusalululana kulagwashilizya kupa kutayanda kubweza magwasho a PMTCT azimbi?
Kobuzisisya:
- Munzila nzi?
 - Ino bamwi bama kaintu inga bachiinda buti echi?
14. Sena kuyekuti bamalumi abamukwashi inga balagwashilizya ma makaintu bamitide kubweza magwasho a PMTCT na ayandika?
Kobuzisisya:
- Ino? Ino Kayi?
 - Ndugwasho nzii inga ndobapa?
 - Inga munzila nzi inga mobatagwashi?
 - Ino mumasena mobazwa?
15. Zintu nzi zyakamugwasha kwiinda zintu zikasha ezi zitwambaula awa alimwi zyakamugwasha kujana magwasho a PMTCT abusena bunu?
16. Ninzi chomuyeyela ikuti inga chabambwa ikutegwa chibe chuba kubamakaintu bamitide kuti bajane lugwasho lwa PMTCT.

WRAP-UP (5 mins):

Kuma maninizyo

Twalumba maningi.twainda mumibuzyo yonse yakwa mabuzyana kwesu.Twasyala biyo akaindi kashonto.Kuli chimbi nchemuyanda kuyungihila na kubuzya?

Twalumba loko mukutola lubazu,Kuli dilinki a kakulya kamuntu onse uli wano.

Interviewer Notes

- Comments about respondents
- Comments on specific questions
- Any other comments

Appendix 14: Published Papers

Appendix 14.1: Chapter 4

Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa

A systematic literature review

Sehlukekile Gumede-Moyo, MPH, MBA, Bsc^{a,b,*}, Suzanne Filteau, PhD, Msc, Bsc^a, Tendai Munthali, Msc, BA^{b,c}, Jim Todd, MA, Msc^a, Patrick Musonda, PhD, Msc^b

Abstract

Background: To synthesize and evaluate the impact of implementing post-2010 World Health Organization (WHO) prevention of mother-to-child transmission (PMTCT) guidelines on attainment of PMTCT targets.

Methods: Retrospective and prospective cohort study designs that utilized routinely collected data with a focus on provision and utilization of the cascade of PMTCT services were included. The outcomes included the proportion of pregnant women who were tested during their antenatal clinic (ANC) visits; mother-to-child transmission (MTCT) rate; adherence; retention rate; and loss to follow-up (LTFU).

Results: Of the 1210 references screened, 45 met the inclusion criteria. The studies originated from 14 countries in sub-Saharan Africa. The highest number of studies originated from Malawi (10) followed by Nigeria and South Africa with 7 studies each. More than half of the studies were on option A while the majority of option B+ studies were conducted in Malawi. These studies indicated a high uptake of human immunodeficiency virus (HIV) testing ranging from 75% in Nigeria to over 96% in Zimbabwe and South Africa. High proportions of CD4 count testing were reported in studies only from South Africa despite that in most of the countries CD4 testing was a prerequisite to access treatment. MTCT rate ranged from 1.1% to 15.1% and it was higher in studies where data were collected in the early days of the WHO 2010 PMTCT guidelines. During the postpartum period, adherence and retention rate decreased, and LTFU increased for both HIV-positive mothers and exposed infants.

Conclusion: Irrespective of which option was followed, uptake of antenatal HIV testing was high but there was a large drop off along later points in the PMTCT cascade. More research is needed on how to improve later components of the PMTCT cascade, especially of option B+ which is now the norm throughout sub-Saharan Africa.

Abbreviations: AIDS = acquired immunodeficiency syndrome, ANC = antenatal clinic, ART = antiretroviral therapy, DRC = Democratic Republic of Congo, EID = early infant diagnosis, HIV = human immunodeficiency virus, LTFU = lost to follow-up, MTCT = mother-to-child transmission, NVP = nevirapine, PMTCT = prevention of mother-to-child transmission, WHO = World Health Organization.

Keywords: adherence, loss to follow-up, PMTCT cascade, PMTCT options, retention rate, sub-Saharan Africa

Editor: Leonard Sowah.

Authorship: SGM conceived the idea, carried out the review, and wrote the manuscript. TM and PM appraised the quality of a portion of the included studies for quality control. SF and JT critically reviewed drafts and approved the final manuscript.

Funding/support: The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472.

The authors have no conflicts of interest to disclose.

^aDepartment of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK, ^bSchool of Public Health, University of Zambia, ^cMinistry of Health, Lusaka, Zambia.

* Correspondence: Sehlukekile Gumede-Moyo, Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (e-mail: sehlukekile.gumede@lshtm.ac.uk).

Copyright © 2017 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and build upon the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2017) 96:40[e8055]

Received: 27 December 2016 / Received in final form: 26 July 2017 / Accepted: 30 July 2017

<http://dx.doi.org/10.1097/MD.00000000000008055>

1. Introduction

The Joint United Nations Program on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) over the past 2 decades has documented the heavy burden and impact of HIV on mothers and infants living in resource-limited settings. Among the 260,000 new pediatric infections of HIV worldwide in 2012, 90% of new cases occurred in sub-Saharan Africa.^[1] The use of antiretroviral therapy (ART) by HIV-positive mothers is the cornerstone of strategies to prevention of mother-to-child transmission (PMTCT) during the ante-partum and peri-partum periods and for the duration of breastfeeding.^[2]

The World Health Organization (WHO) in 2010 revised guidelines and offered 2 options: option A and option B. Under option A, pregnant women with a $CD4 \geq 350$ cells/ μ L receive ART prophylaxis from 14 weeks gestation through 1 week postpartum, single-dose nevirapine (NVP) at delivery, and daily lamivudine from delivery through 1 week postpartum. Their infants receive daily NVP from birth through 1 week after the cessation of breastfeeding. Women with $CD4 \leq 350$ cells/ μ L or WHO clinical stage 3 or 4 disease are put permanently on triple-drug ART. Under option B, all women receive triple-drug ART from 14 weeks gestation through the cessation of breastfeeding, and infants receive a daily NVP or zidovudine dose from birth to 4 to 6 weeks.^[2] In 2013, WHO revised its guidelines for the treatment and prevention of HIV and recommended that all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should continue ART for life known as “option B+” while their infants receive daily NVP or zidovudine from birth to 4 to 6 weeks.^[3] Option B+ is now a norm in sub-Saharan Africa, with all the 21 global plan countries implementing it except for Nigeria as of October 2015.^[4]

Effective PMTCT programmes require women and their infants to receive a cascade of interventions including uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, safe child birth practices and appropriate infant feeding uptake, with infant prophylaxis, HIV testing, and other postnatal health care services following delivery.^[5] The global community committed to accelerate progress for PMTCT through an initiative whose goals were to eliminate new pediatric HIV infection by 2015 and improve maternal, newborn and child health, and survival in the context of HIV.^[6] Elimination of new pediatric infections has not been met, so there is a need to investigate why some programs are not effective. This systematic review of the literature was performed to evaluate the impact of implementing the WHO post-2010 PMTCT guidelines in order to inform practices which could help reach PMTCT targets.

2. Methods

2.1. Data sources

The following databases were searched for articles published from January 2010 to October 2016: Africa Wide Information, Medline, Embase, and reference lists from publications provided additional articles. The search was limited to English language journals for studies in sub-Saharan Africa. The following search terms and their variations were combined: prevention of mother to child transmission of HIV; PMTCT cascade; PMTCT options; effectiveness of PMTCT; PMTCT option A; PMTCT option B; PMTCT option B+; antiretroviral treatment; ART; antenatal

care; HIV; HIV-exposed infants' health outcomes; infant feeding; early infant diagnosis (EID), adherence; retention in care; and loss to follow-up (LTFU).

2.2. Study selection

The searched results were exported using reference management software Endnote 7.3 and duplicates were removed. The titles, abstracts, and full texts of potentially relevant studies were reviewed for eligibility. An adapted Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) flow chart was drawn (flow diagram). The selected studies had to include data collected post the WHO 2010 PMTCT guidelines. The inclusion criteria were: retrospective and prospective cohort study designs that utilized routinely collected data with a focus on provision and utilization of the cascade of PMTCT services; studies with particular interest in WHO option A, B, or B+ implementation; and studies from countries which had adopted WHO post-2010 PMTCT guidelines during the data collection period, and studies which evaluated implementation of post 2010 PMTCT guidelines. Qualitative studies, randomized controlled trials, reviews, commentaries, editorials, and modeling studies were excluded. Two independent reviewers (SGM and TM) reviewed the full text articles for inclusion, exclusion and extracted data on outlined outcomes. Ethical approval was granted from London School of Tropical Medicine and Hygiene Research Ethics Committee (Ref: 12086).

2.3. Data extraction

Data were extracted using a standardized data extraction form which summarized key information from relevant studies. The following information was extracted: proportion of pregnant women who were tested during their antenatal clinic (ANC) visits; proportion of women who tested HIV-positive; proportion of women who were already on ART before pregnancy; proportion of women who received their HIV test results; proportion of women tested for CD4 cell count; type of PMTCT option for mothers and their infants; adherence of women to ART; infant feeding methods; infant age when polymerase chain reaction (PCR) was done; mother-to-child transmission (MTCT) rate; proportion of infants reported to die or be LTFU as missing 3 consecutive clinic visits; and retention rate which is the continuous engagement from diagnosis in a package of prevention, treatment, support, and care services. In case of studies where data collection began before 2010 only post-2010 data were extracted.

3. Summary of results

3.1. Study characteristics

A total of 944 potentially eligible full text articles out of 2913 studies based on titles and abstracts were identified. Forty-five met the inclusion criteria (flow diagram) and they originated from 14 countries in sub-Saharan Africa (Table 1). The highest number of studies originated from Malawi (10) followed by Nigeria and South Africa with 7 studies each. The period of data collection was from 2010 to April 2015. The sample sizes for the selected studies ranged from 113 to 2,215,090 participants; the largest sample sizes were from the studies that utilized national data from South Africa and Ghana.

Table 1
Uptake of PMTCT services and infant outcomes.

Author	Data collection period	Country	Tested for HIV during ANC visit	Infant feeding methods	EID	Infant outcomes
Opton A. studies Tengoua et al. ^[47]	2010–2011	Cameroon	23%	31.9% were exclusively breastfed, 35.9% were formula fed 14.4% were mixed fed	12.6% at ≤6wk, 61.1% at >6wk–6mo 26.3% at >6mo	Overall MTCT rate was 11.5%. MTCT rate was 3.7% for infant mother pairs who received prophylaxis; 16.2% for mothers who received prophylaxis and baby without ART; 12% for mother without prophylaxis and infant with Nevirapine and 31.3% for mother baby pair without prophylaxis and Nevirapine
Noubiap et al. ^[42]	2010	Cameroon		44.6% were exclusively breastfed, 33% were formula fed, 22.4% were mixed fed	71.4% at ≤6mo 28.8% at >6mo	Overall MTCT rate 11.6%. MTCT increased with mixed feeding (aOR: 6.7, 95% CI 1.6–28.3; P=.009 MTCT increased if EID at >6mo compared with <=6mo (aOR: 6.5, 95% CI 1.4–29.3; P=.014).
Fenstein et al. ^[40]	2007–2012	DRC		94.4% were exclusively breastfed in 2011–2012	63% by 2 mo in 2011–2012	MTCT rate 11%. 3% dead by 18mo. Among HIV-infected infants, 97% were initiated on ART
Deko-Gyeke et al. ^[14]	2011–2013	Ghana	2011 – 83% 2012 – 76% 2013 – 75%			
Banwat, et al. ^[48]	2009–2010	Nigeria	97.3%	80.3% were exclusively breastfed		MTCT rate 9.6%
Okusanya et al. ^[10]	2010–2011	Nigeria		24.5% were exclusively breastfed, 67.9% were formula fed, 7.6% were mixed fed		MTCT rate 6.3%
Angilele et al. ^[49]	2008–2011	Nigeria				MTCT rates at 18mo were 3.73% for exclusively breastfed infants, 2.43% for exclusively formula fed infants and 14.2% for mixed fed and MF, respectively
Moodley et al. ^[22]	2004–2012	South Africa			97.4% at 4–8wk	MTCT rate was 2.9% by 2012
Bhardwaj et al. ^[18]	2010–2012	South Africa			87% in 2010, 93% in 2011, 100% in 2012	
Hussain et al. ^[14]	2010	South Africa	99.2%		58.9% at birth	
Schnippel et al. ^[17]	2012–2013	South Africa		51% were exclusively breastfed 13% were formula fed 36% were mixed fed		MTCT rate 2.4% in-utero transmission rate was highest among women who required ART but did not initiate treatment (8.5%) compared to 2.7% and 0.4% among women who received ART and women who were not eligible for ART and received PMTCT
Technau et al. ^[19]	2011	South Africa	92%			
Sherman et al. ^[23]	2003–2012	South Africa			73% at 6wk	MTCT rate was 2.4%
Ibeto et al. ^[24]	2012–2013	South Africa			80% at 6wk	MTCT rate was 1.6%
Chidulo et al. ^[38]	2009–2011	Tanzania			91.5% in 2010, 97.8% in 2011	MTCT rate of 9.21% in 2010 and 10.1% in 2011
Mwendo et al. ^[39]	2009–2012	Tanzania		88.6% were exclusively breastfed 7.1% were formula fed 3.9% were mixed fed	77.7% at 1–2mo 16.8% at 3–6mo 5% at 7–12mo	Overall MTCT rate 9.6% The proportion of HIV-infected infants was higher among infants who appeared later for HIV testing (18% at 3–6mo)

(continued)

Table 1
(continued).

Author	Data collection period	Country	Tested for HIV during ANC visit	Infant feeding methods	EID	Infant outcomes
Bennik-Muazzi et al ⁽⁶⁴⁾	2002–2011	Uganda	2010 – 95.5% 2011 – 96%			than among those who presented earlier (6.4% at 1–2 mo) MTCT rate of 5.7% in 2010, and 6.1% 2011
Scott et al ⁽⁶⁵⁾	2011	Zambia		86.4% were ever breastfed 56.8% were exclusively breastfed 22% were mixed fed	22.4% between 0 and 6 wk 59.1% between 6 wk and 6 mo 59.1% between 6 and 12 mo	MTCT rate was 3% MTCT rate was 11% in 2010. Lower rates of positive PCR results were associated with 1) both mother and infant receiving prophylaxis, 2) children never breastfed and 3) mother being 30 years old or greater
Torpey et al ⁽⁶⁷⁾	2007–2010	Zambia				
Gomesa et al ⁽⁶¹⁾	2012	Zimbabwe	96%			
Option A and B Studies						
Koys and Zeeke ⁽⁶⁵⁾	2012	Ethiopia		78.8% were exclusively breastfed 13.3% were formula fed 7.9% were mixed fed		MTCT rate was 10%. Late enrollment to the exposed infant follow-up clinic (aOR = 2.89), rural residence (aOR = 5.05), home delivery (aOR = 2.82), absence of maternal ART (aOR = 5.02) and mixed infant feeding practices (aOR = 4.18, 95) were significantly and independently associated with maternal to child transmission of HIV
Mhuiri et al ⁽¹⁵⁾	2006–2012	Kenya				MTCT rate was 8.9% in 2012. Age at enrollment, nutritional status, residential distance from the hospital, and mothers' HAART status at the time of delivery were independently associated with MTCT of HIV infection MTCT rate 12% MTCT rate of 3.4%
Sutcliffe et al ⁽⁴¹⁾	2010–2012	Zambia			98% of the infants 80.4% of infants	
Okawa et al ⁽⁶⁸⁾	2011–2014	Zambia				
Option A, B and B+ Studies						
Rawizza et al ⁽²⁹⁾	2004–2014	Nigeria			Median age – 1.6 mo; was available for 53% of their infants	MTCT for infants whose mothers received any antenatal and/or delivery care was 2.8% versus 20.0% if their mother received none
Option A and B+ Studies						
Olena et al ⁽⁸⁰⁾	2006–2014	Ethiopia		79% were exclusively breastfed 14.6% exclusive replacement 4.7% were mixed fed	Done for 66.7%	Overall MTCT rate of 4.3%. MTCT rate for infants who received option B+ – 0%. MTCT rate for mother and infant receiving prophylaxis was 3.9% MTCT rate was 4.6% under option A, and 2.6% under option B+
Kamuyango et al ⁽⁸¹⁾	2009–2013	Malawi	94%		82% at 7.6 wk under option A Under option B+, 86.5% at 6.9 wk	
Kim et al ⁽⁸⁾	2010–2013	Malawi				MTCT rate under option A – 2.9, 1.9% in infants born to mothers who received option B+ and 1.1% (continued)

Table 1
(continued).

Author	Data collection period	Country	Tested for HIV during ANC visit	Infant feeding methods	EID	Infant outcomes
Option B Studies Mugierwa et al. ^[65]	2010–2014	Uganda		73.4% exclusively breastfed 26.6% exclusive replacement		for infants with mothers received ART for their own health MTCT rate of 2.6% MTCT was lower among women on ART before pregnancy compared to women who started ART during pregnancy or delivery
Option B+ Studies Price et al. ^[7]	2011–2013	Malawi	90%	98.8% were breastfed	6.4% at 6–9wk 9.5% of at 9wk Not done for 73% of the infants and unknown for 11.1%	
Chen et al. ^[6]	2011–2012	Malawi	81%		80.3% underwent 52.0% at 6–12wk, 28.1% at 12mo	MTCT rate was 4.1% and all had been started on ART by the age of 12mo
Martinez Pérez et al. ^[31]	2011–2012	Malawi			89% at 6wk, and 96% at 24mo	MTCT rate was 5% for tested at 6wk and 8% for those tested at 24mo
Njambi et al. ^[63]	2012–2014	Malawi		43% were exclusively breastfed 50% were mixed fed 4% stopped breastfeeding before registration		
Okafor et al. ^[24]	2009–2011	Nigeria		91.8% were exclusively breastfed 5.5% were mixed fed 2.7% formula fed		MTCT rate of 1.1% at 18 mo
Pfarr et al. ^[11]	2013	Nigeria	75%			
Dzangare et al. ^[64]	2014	Zimbabwe	95%		Done for 71% of infants	

Option A – pregnant women with a CD4 > 350 cells/μL receive ART prophylaxis including daily zidovudine from 14 wk gestation through 1 wk postpartum, single-dose nevirapine at delivery, and daily lamivudine from delivery through 1 wk postpartum. Their infants receive daily nevirapine from birth through 1 wk after the cessation of breastfeeding. Women with women with CD4 < 350 cells/μL or WHO clinical stage 3 or 4 disease are put permanently on triple-drug ART regardless of symptoms. Option B – all women receive triple-drug ART from 14 wk gestation through the cessation of breastfeeding, and infants receive a daily nevirapine or Zidovudine dose from birth to 4–6wk.
Option B+ – all pregnant and breastfeeding HIV-infected women, regardless of CD4 cell count, should continue ART for life.
ANC = antenatal clinic, ART = antiretroviral therapy, DRC = Democratic Republic of Congo, EID = early infant diagnosis, MTCT = mother-to-child transmission, HAART = highly active antiretroviral therapy, LTFU = lost to follow-up, PCR = polymerase chain reaction, PMTCT = prevention of mother-to-child transmission, WHO = World Health Organization.

3.2. Uptake of ANC services

The data on HIV testing during ANC visits were extracted from 8 studies (Table 1) conducted in Malawi,^[7-9] Nigeria,^[10,11] Ghana,^[12] Zimbabwe,^[13] and South Africa.^[14] These studies indicated a high uptake of HIV testing ranging from 75% in Nigeria to over 96% in Zimbabwe and South Africa. The high uptake of HIV testing could have been an attributable to policy changes in integrating HIV testing in ANC and shifting from opt-in to opt-out testing.

The proportion of women who were already on ART prior to ANC visits was reported in 6 studies, from Malawi,^[7-9] Zimbabwe,^[13] Kenya,^[15] and Zambia.^[16] In Zimbabwe only 7% of the women were already on ART during their ANC visits while in Malawi, implementation of option B+, resulted in an increase of women who were already on ART before pregnancy,^[7-9] from 30% before option B+ to 48% after option B+ adaptation. In a matched cohort study of option A and B, in 4 sites receiving external technical support for the provision of PMTCT-related care in Zambia, 48% of women were already on ART prior to their first ANC visit.^[16] Findings are not representative of PMTCT service delivery in Zambia as a whole, since the sites receive technical support for the provision of PMTCT-related care from the Boston University PMTCT Integration Project through the President's Emergency Plan for AIDS Relief (PEPFAR). External support can also influence health facility characteristics and operational aspects of a facility such as capacity, location, staffing, and services provided.

Four out of the 7 studies that had information on CD4 count testing were from South Africa^[17-20] and the rest from Kenya,^[15] Zambia,^[16] and Mozambique.^[21] The proportion of women who had CD4 testing during ANC visits from Kenya, Zambia, and Mozambique was below 60% despite the fact that over the data collection period of these studies, CD4 testing was supposed to be a prerequisite to access care. In South Africa the proportion of women tested for CD4 count increased from 66% in 2010 to 76% in 2012 according to a study that utilized national data.^[19]

3.3. Exposure to PMTCT options

Thirty-five (78%) studies reported on option A (Tables 1 and 2) and they were from the 14 representative countries with South Africa contributing 7 studies.^[14,17-19,22-24] Implementation of option B+ was investigated in Nigeria,^[25,26] Malawi,^[7-9,27-32] Mozambique,^[33] Zimbabwe,^[34] and Ethiopia^[35,36] in 16 studies which were synthesized. The 2 studies which reported in all 3 options (A, B, and B+) were conducted in Malawi^[29] and Nigeria^[25] where the data collection covered a longer period.

3.4. Infant outcomes

The MTCT rate was reported in 29 studies (Table 1) and ranged from 1.1% to 15.1%. MTCT rate was high (above 10%) mainly in studies where data were collected in the early days^[37-42] of the WHO 2010 PMTCT guidelines although South Africa reported a low MTCT rate of 2% during the same period.^[20] In Zambia, there was a reduction in MTCT rate from 12% in 2010^[37] to 3% in a retrospective study conducted from 2011 to 2014.^[43] The lowest MTCT rate of 1.1% was reported from Nigeria^[26]; however, the author indicated that the study involved HIV-positive women who booked for antenatal care in a tertiary institution and were likely to be wealthier and more educated than the general population and perhaps more likely to adhere to ART and other PMTCT interventions

3.5. Exposure to PMTCT options and MTCT rate

In a study from Cameroon, under option A, the MTCT rate was 3.7% for infant mother pairs who both received prophylaxis; 16.2% when only the mothers received prophylaxis; 12% for mothers without prophylaxis whose infants received NVP; and 31.3% when neither mother or infant received prophylaxis.^[44] In Zambia, lower rates of MTCT were associated with both mother and infant receiving prophylaxis: 4.2% compared to 20.1% in a no intervention group at 0 to 6 weeks.^[37] In South Africa, in-utero transmission rate was highest among women who required ART but did not initiate treatment (8.5%) compared to 2.7% and 0.4% among women who received ART and women who were not eligible for ART and received prophylaxis under option A.^[14]

In Ethiopia, absence of maternal ART was significantly and independently associated with maternal to child transmission of HIV (adjusted odds ratio [aOR]=5.02, 95% CI: 2.43, 10.4).^[45]

Results from 2 studies that compared option A and B+ from Ethiopia^[36] and Malawi,^[8] both confirmed supremacy of option B+ over A in terms of MTCT rate. In Ethiopia, none of the infants whose mothers received option B+ had a positive PCR result while the MTCT rate for those under option A was 3.9%.^[36] In Malawi, the MTCT rate was 2.9% under Option A, 1.9% under option B+, and 1.1% for infants whose mothers received ART for their own health.^[8]

Figure 1 shows MTCT rates at the end of data collection year and according to which option was used; only studies showing overall MTCT rates, not rates at younger ages when HIV transmission may have been ongoing in a breastfeeding population, are shown. Option A had higher MTCT rates in most of the studies under review; however, most option A studies preceded the option B+ studies. The general functions of the PMTCT programs have been improving over time with studies carried out after 2013 showing lower MTCT rates even under option A.

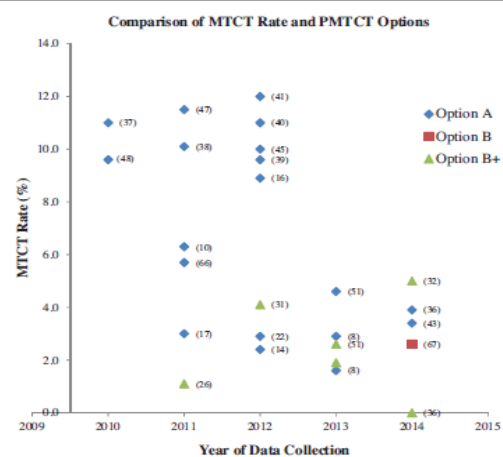


Figure 1. Key – The numbers in brackets are study references and the points are the MTCT rate. MTCT = mother-to-child transmission.

3.6. Timing of ART initiation and MTCT

In Kenya where an MTCT rate of 8.9% was reported, lack of maternal use of ART at the time of delivery was associated with increased risk of MTCT for infants of women who were on option A and B.^[15] In Nigeria, MTCT (0.4%) was lower among women on ART before pregnancy compared to women who started ART during pregnancy or delivery which was at 2%.^[46]

3.7. Impact of infant feeding on MTCT

The impact of infant feeding mode was not explored in most in the analysis of most studies under this review with only 13 studies providing results (Table 2). Exclusive breastfeeding is commonly measured through household surveys by asking mothers/caregivers of sample infants less than 6 months of age regarding intake in the previous day and night. However, there is a lack of uniformity of methods used for collecting exclusive breastfeeding data in the countries under review. Infant feeding methods were reported in studies from Zambia,^[37] Malawi,^[7] Democratic Republic of Congo (DRC),^[40] Ethiopia,^[36,45] Cameroon,^[42,47] Nigeria,^[26,46,48,49] South Africa,^[18] and Tanzania.^[39] High levels of exclusive breastfeeding were reported, with Malawi reporting that 99% of HIV-exposed infants being exclusively breastfed in the first 6 months.

MTCT of HIV was significantly higher with mixed feeding (aOR: 6.7, 95% CI 1.6–28.3; $P=.009$) in Cameroon under option A exposure.^[42] Similarly in Nigeria, MTCT was higher for mixed fed infants at 14.2% compared to 3.73% for exclusively breastfed infant and 2.43% for exclusively formula-fed infants at 18 months.^[49] This was consistent with a study in Ethiopia where mixed infant feeding practices were significantly and independently associated with MTCT of HIV (aOR=4.18, 95% CI: 1.59, 10.99).^[45]

Lower rates of MTCT were found in children who never breastfed in Zambia at 2.5% at 0 to 6 weeks compared to 6.5% those who had been breastfed under option A exposure.^[37]

3.8. Early Infant diagnosis

EID of HIV by PCR was reported in 20 studies from 8 countries (Table 1). The uptake of EID ranged from less than 60% in Nigeria^[25] and Zambia^[37] to 100% in 2012 according to South African national data where it increased from 87% in 2010.^[19] The age at which PCR was done ranged from 4 weeks to 18 months. In South Africa, 80% of exposed infants had PCR results at 6 weeks,^[24] whereas in Malawi 52% underwent testing at 6 to 12 weeks and 28% tested at 12 months.^[31]

3.9. Impact of age at first PCR on MTCT

Age at first PCR had an impact on the MTCT of HIV-exposed infants. In Tanzania, the proportion of HIV-infected infants was higher among infants who appeared later for HIV testing (18% at 3–6 months) than among those who presented earlier (6.4% at 1–2 months) under option A implementation.^[39] The Tanzanian observations were in agreement with the Ethiopian study which reported that late enrolment to the exposed infant follow-up clinic was significantly and independently associated with MTCT of HIV (aOR=2.89, 95% CI: 1.35, 6.21).^[45]

3.10. ART initiation of HIV-positive infants

ART initiation of HIV-positive infants is a key stage of the PMTCT cascade. In this review, it was reported in 3 studies from

DRC,^[40] Zambia,^[41] and Nigeria.^[11] Among HIV-infected infants in DRC, 97% enrolled in 2011 to 2012 were initiated on ART; this was an increase from 61% for infants enrolled in 2007 to 2008.^[40] Lower rates were reported in Zambia where 67% of infants who tested positive started ART by the end of the study^[41] and Nigeria where 75% of HIV-positive infants were initiated on ART.^[11]

3.11. Retention in care

Retention in routine maternal-infant HIV care of HIV exposed infants was explored 3 studies from Zambia, Malawi, and Rwanda. In Zambia, the retention rate of HIV-exposed infants under option A, at 6 months after delivery was 62% compared to 30% of HIV-unexposed infants under the same ongoing routine care conditions.^[16] In Malawi, 72% of HIV-exposed infants remained in care after 12 months under option B+,^[31] whereas in Rwanda under option B, infants' 12-month retention was 81% (95% CI: 76%, 86%).^[53]

In Malawi, the retention in HIV care of women initiated on option B+ was 85%, compared to 93% after 2 years among those initiated on ART because of clinical or CD4 cell count criteria.^[29] These results were consistent with the findings from Rwanda where mothers eligible for ART for their own health were better retained across all the time periods, 66% (CI: 59%, 73%), compared with those not eligible and receiving ART solely for PMTCT, 47% (CI: 37%, 57%), at 12 months, $P<.001$.^[53] Another Malawian study highlighted that initiation of ART on the same day as HIV diagnosis was independently associated with reduced retention in the first 6 months (aOR 2.27; 95% CI: 1.34–3.85; $P=.002$) in under option B+.^[9]

In a retrospective record review of women presenting to antenatal care or maternal and child health services at 34 health facilities in rural Zimbabwe, retention in ART care after 6 months of option B+ initiation was 83%.^[34] In contrast, retention for Rwandan mothers exposed to option B was 68% at 6 weeks postdelivery, decreasing to 58% by 12 months.^[53]

3.12. Lost to follow-up (LTFU)

Data on the magnitude of LTFU (missing 3 consecutive clinic visits) along the PMTCT cascade were reported in 9 studies (Table 2) from Malawi,^[27,28,51] Tanzania,^[38] Kenya,^[15] Nigeria,^[10,25] and Ethiopia.^[35,36] In the studies from Malawi and Ethiopia, this was explored in the context of option B+ while in the other countries it was explored under option A.

In Tanzania,^[38] 61% of infants receiving treatment were LTFU at the time of review, despite the high proportion of guardians and parents who returned for PCR results (92% in 2010 and 98% in 2011). The results were consistent with a study from Malawi where 48% of the HIV-exposed infants were declared LTFU in the database although 96% of them in the cohort had their PCR test done at 24 months.^[54] However, Nigeria reported low rates of LTFU for HIV-infected infants of less than 15%^[11,46] despite that the studies evaluated different PMTCT options. In Kenya, LTFU increased with the age of infants with 9.6% of enrolled infants not returning for any follow-up care, 26.4% dropping out by 9 months and 39% by 18 months of age.^[15]

In Ethiopia under option B+ implementation, the cumulative proportions of women LTFU at 6, 12, and 24 months were 12%, 15%, and 23%, respectively.^[35] Similar results were reported in Malawi where cumulative incidence of LTFU by year 2 was

Table 2
Retention rate, adherence, and magnitude of LTFU*

Author	Data collection period	Country	Retention Rate	LTFU	Adherence to ART
Option A Studies Okusanya et al. ^[10] Chiduo et al. ^[50] Scott et al. ^[19]	2010–2011 2009–2011 2011	Nigeria Tanzania Zambia	62% of HIV exposed were retained in care compared to 30% of comparison unexposed	30% of HIV infected mothers and 25% of exposed infants LTFU 61% of infants LTFU	
Option A and B Studies Nduati et al. ^[15] Sutcliffe et al. ^[41] Okawa et al. ^[43]	2006–2012 2010–2012 2011–2014	Kenya Zambia Zambia	86% of caregivers returned for results and 67% of infants who tested positive started ART by the end of the study	9.6% of enrolled infants did not return for any follow-up care, 39.0% were LTFU before 18 mo of age; 26.4% LTFU at 9 mo, 39% at 18 mo	ART adherence 82.5% during pregnancy, 84.2% at 1 wk postpartum, 81.5% at 6 wk, and 70.5% at 24 wk
Option A, B and B + Studies Kooze et al. ^[29]	2005–2012	Malawi	Women who started ART because of option B+ had retention rate of 85% compared to 93% among women of child bearing age initiated on ART because of clinical or CD4 cell count criteria		
Rawizza et al. ^[23]	2004–2014	Nigeria	66% of the women completed the entire cascade of services including antenatal, delivery and at least 1 infant follow-up visit	21% prior to delivery care with a further 16% lost prior to first infant visit	
Option A and B+ Studies Kamuyango et al. ^[31]	2009–2013	Malawi		Pregnant women were likely to be LTFU compared to nonpregnant women initiating therapy for disease stage or CD4 count	Default and incomplete adherence were more common in the option B+ cohort than under option A
Kim et al. ^[8] Option B Studies Sagay et al. ^[44] Wook et al. ^[53]	2010–2013 2009–2011 2010–2012	Malawi Nigeria Rwanda	Women 58% (95% CI: 52%, 64%), were retained 12 mo postdelivery, infants' 12-mo retention was 81% (95% CI: 76%, 86%)	High LTFU rate at 6–8 wk; 22% were LTFU care and treatment 14.1% of the HIV exposed infants were LTFU between birth and 18 mo Overall, the majority of loss to retention was observed in the 30 d after antenatal registration	
Option B+ Studies Mitiku et al. ^[33]	2013–2015	Ethiopia		The cumulative proportion of patients LTFU at 6, 12 and 24 mo after ART initiation was 11.9% (95% CI: 8.9, 16.0%), 15.7% (95% CI: 12.0, 20.4%) and 22.5% (95% CI: 17.3, 29.2%), respectively. Overall 16.5% were LTFU 17.1% LTFU, 6 mo after initiation 23.9% in all option B+ patients who started ART while pregnant	
Terethani et al. ^[28]	2011–2012	Malawi	82.2% at 6 mo postnatal		

(continued)

Table 2
(continued).

Author	Data collection period	Country	Retention Rate	LTFU	Adherence to ART
Chan et al ^[8]	2011–2012	Malawi	Initiation of ART on the same day as HIV diagnosis was independently associated with reduced retention in the first 6 mo (aOR 2.27; 95% CI: 1.34–3.85; <i>P</i> = .002).		
Haas et al ^[30]	2011–2013	Malawi		The cumulative incidence of LTF by year 2 was 24.5% (95%CI, 23.2%–25.8%) among women who started ART during pregnancy, 20.2% (95% CI, 18.3%–22.2%) among those who started ART while breastfeeding, and 17.0% (95% CI, 15.2%–18.8%) among those who were neither pregnant nor breastfeeding when they started treatment.	70% of women who started ART during pregnancy and breastfeeding adhered adequately during the first 2 y of ART
Tweje et al ^[27]	2011–2013	Malawi	85% at 3 mo; 82% at 6 mo; 79% at 12 mo	20% of these 47% collected ARVs and did not return; 12% collected at 2 visits; 9% at 3 visits and 32% at 4 or more visits	
Martínez Pérez et al ^[31]	2011–2012	Malawi	71.7% of the exposed infants remained in care at 12 mo		
Ngambi et al ^[32]	2012–2014	Malawi		Overall, 48% of HIV-exposed infants were declared LTFU in the database	
Lienas-García et al ^[33]	2013–2014	Mozambique		48.5% of option B+ women were LTFU. The risk of being LTFU was higher in pregnant (aHR: 2.77; 95% CI: 2.18–3.50; <i>P</i> < .001) and lactating (aHR: 1.94; 95% CI: 1.37–2.74; <i>P</i> < 0.001)	
Pharr et al ^[11]	2013	Nigeria		13% of the enrolled infants were LTFU	
Dzangare et al ^[34]	2014	Zimbabwe	Retention in ART care after 6 mo of option B+ initiation was 82.6%		

ART = antiretroviral therapy; ARV = antiretroviral; aHR = adjusted sub-hazard ratio; CI = confidence interval; LTFU = lost to follow-up.
*Retention rate = the continuous engagement from diagnosis in a package of prevention, treatment, support, and care services; LTFU = missing 3 consecutive clinic visits.

24.5% (95% CI, 23.2%–25.8%) among women who started ART during pregnancy, 20.2% (95% CI, 18.3%–22.2%) among those who started ART while breastfeeding, and 17.0% (95% CI, 15.2%–18.8%) among those who were neither pregnant nor breastfeeding when they started treatment.^[30]

The independent risk factors for LTFU were younger maternal age at ART initiation, missing CD4 cell count at ART initiation, ART initiation on the same day of diagnosis, and starting ART at hospital.^[35] The risk of being LTFU was higher in “B+ pregnant” (adjusted sub-hazard ratio [aHR]: 2.77; 95% CI: 2.18–3.50; $P < .001$) and “B+ lactating” (aHR: 1.94; 95% CI: 1.37–2.74; $P < .001$) compared to women on ART for their own health in Mozambique.^[33]

3.13. Adherence

Adherence to ART drugs for PMTCT by the mothers was reported in 2 studies (Table 2) from Malawi^[51] and Zambia.^[43] Adherence during the postpartum period in Zambia^[43] ranged from 71% to 84% at different times postpartum. The results of the study were consistent with the Malawian study where 70% of women exposed to option B+, who started ART during pregnancy and breastfeeding adhered adequately during the first 2 years of ART.^[30] However, default and incomplete adherence were more common in the option B+ compared to the option A in Malawi,^[51] where 4% of women in the option B+ cohort had less than 95% adherence compared to 2% for the option A cohort.

4. Discussion

The global plan toward the elimination of new HIV infections among children by 2015 and keeping their mothers alive prioritized 21 countries in sub-Saharan Africa. The studies in the review originated from 14 of the priority countries. The studies show a continued decline in the incidence of HIV among children, as indicated by low MTCT rates, but the target of a 90% reduction by 2015 was not met, reduction in incidence being only 76% in the 21 priority countries.^[55] South Africa reported low MTCT rates under option A implementation^[24] even from the results of the facility-based cross-sectional study conducted in 2010.^[56] This could have been as a result of their health system which is better resourced than in most of the countries under review.

Many of the studies on the impact of infant feeding methods and exposure to various ART regimens were conducted before the 2010 WHO PMTCT.^[55,57] Although infant feeding results were available from only a minority of studies in this review, the results of the review are in agreement with the findings which led to the current guidelines. In the countries under review breastfeeding is very common, and breastfed infants have an increased risk of MTCT of HIV.^[58] Mixed feeding is also a common practice in sub-Saharan Africa and is an additional risk for postnatal HIV transmission.^[59] As revealed by the studies from Tanzania^[39] and Ethiopia,^[45] where there was increase in MTCT over time, continued breastfeeding in the face of low adherence to ART treatment, is a risk.

Option B+ which initiates lifelong ART to all pregnant and breastfeeding women is now widespread in sub-Saharan Africa, with all the 22 global plan countries implementing it except for Nigeria. As of October 2015, option B+ was being nationally implemented in 14 (Angola, Burundi, Cameroon, Chad, Ethiopia, Kenya, Lesotho, Malawi, South Africa, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe) out of the 21

countries in sub-Saharan Africa, and scale-up continues in 6 countries (Botswana, Cote d'Ivoire, DR Congo, Ghana, Mozambique, and Namibia).^[4] In this review, implementation of option B+ was investigated in Nigeria,^[25,26] Malawi,^[7–9,27–32] Mozambique,^[33] Zimbabwe,^[34] and Ethiopia.^[35,36] Most studies came from Malawi since they were the pioneers of this option; hence, there is a need to explore the impact of implementing the option B+ guidelines and identifying missed opportunities along the PMTCT cascade in other countries which have adopted it.

The implementation of option B+ in Malawi resulted in a 5-fold increase in the numbers of pregnant women being enrolled on ART. Nonetheless, default and incomplete adherence were more common in option B+ implementation.^[43,51] These results were consistent with a qualitative study conducted in Tanzania among mothers who were put on option B+ during pregnancy who indicated various reasons for poor adherence to ART, which included lack of motivation to continue ART after weaning the child and protecting the child from becoming infected, stigma, and poverty.^[60] There is also a need to adjust operational practices related to quality of counseling as it has been indicated to be a predictor of adherence to treatment.^[61] Moreover, a recent study suggested that retention in all postnatal programs, including those outside the context of HIV, is poor globally, elaborating the need for evidence-based intervention strategies and further research on the drivers of disengagement.^[62]

The retention in care of HIV-infected and lactating mothers under option B+ was poor and driven by early losses.^[9,27–29,34,53] Hence, implementation of option B+ requires that policy makers rethink ways of ensuring optimal adherence to ART for maximal suppression of viral replication and avoidance of drug resistance. One possibility is to explore the use of cell phone SMS which has been found to be useful in Africa for improving the quality of care and follow-up of people with HIV/AIDS.^[63,64]

The consolidated guidelines recommend that HIV-exposed infants be tested for HIV between 6 and 8 weeks, at the end of breastfeeding, and at any point they present with illness.^[3] However, in the studies under review the retention rate tended to decrease during the postpartum period.^[16,27–29,32] This reduction in postpartum retention rate implies that HIV-exposed infants will be detached from the health system, thus missing opportunities for PCR testing. A systematic review of mostly sub-Saharan countries found that about a 3rd of HIV-exposed children in standard PMTCT programs fall out of care in 3 months after delivery and a further 45% stop care after their first HIV test.^[65] Furthermore, low rates of infected infants are initiated on ART despite being PCR-tested,^[32,38] raising concerns on the benefits of EID and the referral to care and treatment of these infected infants. Similar results were reported by Chatterjee et al.^[66] in their descriptive analysis of national EID programs in 4 countries where only 22% to 38% of infected infants were initiated on ART. There is a need for strategic and technical developments for ensuring that drop-out rates along the PMTCT cascade are minimal.

4.1. Limitations of the study

The major limitation of the review is that the results of most of the study findings may not be representative of the general health care systems in the countries reviewed as only 2 studies from Ghana and South Africa used national data for analysis. There are also profound variations in the implementation of PMTCT programs across countries. For instance, in Nigeria MTCT was reported to be 1.1%,^[26] which was largely attributed to the study

population which comprised wealthier and more educated women than the general population. There is a research gap of evaluating PMTCT interventions using large cohorts that can be generalized to the whole population.

The limitations of the data sources of this review are mainly due to the retrospective nature posing problems of incomplete recordings. Moreover, the data used in these studies were originally collected for different purposes from this review and therefore hard to compare data when a lot of time points differ because of different timings of key outcomes. However, the advantage of using routinely collected data is that research will be conducted in a timely and cost-efficient manner as data are already collected and available for analysis.^[6,7]

All the studies reported challenges in the documentation of routine services, linkage of HIV diagnosis to care, and active follow-up of those enrolled in care. The data collection systems often lack immediacy as many are paper-based with records completed at each facility and collated centrally. This is likely to be in challenge in most sub-Saharan countries; and therefore, there is a need to improve management of health information systems through the use of modern technology.

5. Conclusion

Irrespective of which option was followed, uptake of antenatal HIV testing was high but there was a large drop off along later points in the PMTCT cascade. More research is needed on how to improve later components of the PMTCT cascade, especially of option B+ which is now the norm throughout sub-Saharan Africa.

There is research gap for studies that investigated the full cascade of interventions that include uptake of antenatal services and HIV testing during pregnancy, use of ART by pregnant women living with HIV, appropriate infant feeding, uptake of infant HIV testing, and other postnatal health care services in the context of the PMTCT option B+ interventions. In view of the gap there is a need for implementation research evaluating real world effectiveness of the 2010 WHO PMTCT guidelines specifically option B+.

Acknowledgments

The authors thank the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472 for the support.

References

- [1] UNAIDS. Global plan towards the elimination of New HIV infections among children by 2015 and keeping their mothers alive. 2011. http://www.unaids.org/sites/default/files/media_asset/20110609_JC2137_Global-Plan-Elimination-HIV-Children_en_1.pdf. Accessed August 17, 2015.
- [2] UNAIDS. Global HIV/AIDS response epidemic update and health sector progress towards universal access. 2011. http://www.unaids.org/sites/default/files/media_asset/20111130_UA_Report_en_1.pdf. Accessed August 17, 2015.
- [3] UNAIDS. Countdown to Zero: Global Plan Towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011–2015. Geneva: 2011. <file:///C:/Users/lsh1405741/Downloads/elimination-of-new-hiv-among-children-in-africa-by-2015-08112013.pdf>. Accessed August 17, 2015.
- [4] The Interagency Task Team on the Prevention and Treatment of HIV Infection in Pregnant Women MaC. Option B+ countries and PMTCT regimen 2015. Available from: <http://emtct-iatt.org/b-countries-and-pmtct-regimen/>. [Accessed Aug 17, 2016]
- [5] Padian NS, et al. HIV prevention transformed: the new prevention research agenda. *Lancet* 2011;378:269–78.
- [6] UNAIDS, Countdown to Zero: Global Plan Towards the Elimination of new HIV Infections among Children by 2015 and Keeping their Mothers Alive 2011–2015. 2011: Geneva. http://www.unaids.org/sites/default/files/media_asset/20121211_Women_Out_Loud_en_1.pdf. Accessed December 22, 2015.
- [7] Price AJ, et al. Uptake of prevention of mother-to-child-transmission using option B+ in northern rural Malawi: a retrospective cohort study. *Sex Transm Infect* 2014;90:309–14.
- [8] Kim MH, Ahmed S, Hosseinipour MC, et al. The impact of option b+ on the antenatal PMTCT Cascade in Lilongwe, Malawi. *J Acquir Immune Defic Syndr* 2015;68:77.
- [9] Chan AK, et al. Same day HIV diagnosis and antiretroviral therapy initiation affects retention in Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi. *J Int AIDS Soc* 2016;19:20672.
- [10] Okusanya BO, Ashimi AO, Aigere EO, et al. Scaling up prevention of PMTCT of HIV infection to primary health centres in Nigeria: findings from two primary health centres in North West Nigeria. *Afr J Reprod Health* 2013;17:130–7.
- [11] Pharr JR, et al. Linkage to care, early infant diagnosis, and perinatal transmission among infants born to HIV-infected Nigerian mothers: evidence from the healthy beginning initiative. *J Acquir Immune Defic Syndr* 2016;72(Suppl 2):S154–60.
- [12] Dako-Gyeke P, Dormoo B, Ayisi Addo S, et al. Towards elimination of mother-to-child transmission of HIV in Ghana: an analysis of national programme data. *BMC Int J Equity Health* 2016;15:
- [13] Gonese E, et al. Is Zimbabwe ready to transition from anonymous unlinked sero-surveillance to using prevention of mother to child transmission of HIV (PMTCT) program data for HIV surveillance?: results of PMTCT utility study. *BMC Infect Dis* 2016;16:97.
- [14] Hussain A, Moodley D, Naidoo S, et al. Esterhuizen pregnant women's access to PMTCT and ART services in South Africa and implications for universal antiretroviral treatment. *PLoS Med* 2011;6:e27907.
- [15] Nduati EW, et al. Outcomes of prevention of mother to child transmission of the human immunodeficiency virus-1 in rural Kenya-a cohort study. *BMC Public Health* 2015;15:1008.
- [16] Scott CA, et al. Uptake, outcomes, and costs of antenatal, well-baby, and prevention of mother-to-child transmission of HIV services under routine care conditions in Zambia. *PLoS One* 2013;8:e72444.
- [17] Schnippel K, Mongwenyana C, Long LC, et al. Delays, interruptions, and losses from prevention of mother-to child transmission of HIV services during antenatal care in Johannesburg, South Africa: a cohort analysis. *BMC Infect Dis* 2015;6:46.
- [18] Technau KG, et al. Timing of maternal HIV testing and uptake of prevention of mother-to-child transmission interventions among women and their infected infants in Johannesburg, South Africa. *J Acquir Immune Defic Syndr* 2014;65:e170–8.
- [19] Bhardwaj S, Barron P, Pillay Y, et al. Elimination of mother-to-child transmission of HIV in South Africa: rapid scale-up using quality improvement. *S Afr Med J* 2014;104:239–43.
- [20] Hussain A, et al. Pregnant women's access to PMTCT and ART services in South Africa and implications for universal antiretroviral treatment. *PLoS One* 2011;6:e27907.
- [21] Gimbel S, et al. What does high and low have to do with it? Performance classification to identify health system factors associated with effective prevention of mother-to-child transmission of HIV delivery in Mozambique. *J Int AIDS Soc* 2014;17:18828.
- [22] Moodley P, Parboosing R, Moodley D. Reduction in perinatal HIV infections in KwaZulu-Natal, South Africa, in the era of more effective prevention of mother to child transmission interventions (2004–2012). *J Acquir Immune Defic Syndr* 2013;63:410–5.
- [23] Sherman GG, et al. Laboratory information system data demonstrate successful implementation of the prevention of mother-to-child transmission programme in South Africa. *S Afr Med J* 2014;104(3 Suppl 1):235–8.
- [24] Ibetu M, Giddy J, Cox V. Closing the gaps: steps towards elimination of mother-to-child transmission of HIV. *S Afr J HIV Med* 2014;15:107–9.
- [25] Rawizza HE, et al. Loss to follow-up within the prevention of mother-to-child transmission care cascade in a large ART program in Nigeria. *Curr HIV Res* 2015;13:201–9.
- [26] Okafor I, Ekwu U, Obi S, et al. Virtual elimination of mother-to-child transmission of human immunodeficiency virus in mothers on highly active antiretroviral therapy in Enugu, South-Eastern Nigeria. *Ann Med Health Sci Res* 2014;4:615–8.

- [27] Tweya H, et al. Understanding factors, outcomes and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi. *Trop Med Int Health* 2014;19:1360–6.
- [28] Tenthani L, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ('Option B+') in Malawi. *AIDS* 2014;28:589–98.
- [29] Koole O, et al. Improved retention of patients starting antiretroviral treatment in Karonga District, northern Malawi, 2005–2012. *J Acquir Immune Defic Syndr* 2014;67:e27–33.
- [30] Haas AD, Msukwa MT, Egger M, et al. Adherence to antiretroviral therapy during and after pregnancy: cohort study on women receiving care in Malawi's Option B+ Program. *Clin Infect Dis* 2016;63:1227–35.
- [31] Martínez Pérez G, Metcalf C, Garone D, et al. HIV testing and retention in care of infants born to HIV-infected women enrolled in 'Option B+', Thyolo, Malawi. *Public Health Action* 2014;4:102–4.
- [32] Ng'ambi WF, et al. Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012–2014. *Trop Med Int Health* 2016;21:995–1002.
- [33] Llenas-García J, et al. Retention in care of HIV-infected pregnant and lactating women starting ART under Option B+ in rural Mozambique. *Trop Med Int Health* 2016;21:1003–12.
- [34] Dzangare J, et al. HIV testing uptake and retention in care of HIV-infected pregnant and breastfeeding women initiated on 'Option B+' in rural Zimbabwe. *Trop Med Int Health* 2016;21:202–9.
- [35] Mitiku I, et al. Factors associated with loss to follow-up among women in Option B+ PMTCT programme in northeast Ethiopia: a retrospective cohort study. *J Int AIDS Soc* 2016;19:20662.
- [36] Olana T, Bacha T, Worku TW, et al. Early infant diagnosis of HIV infection using DNA-PCR at a referral center: an 8 years retrospective analysis *BMC. AIDS Res Ther* 2016;13:29.
- [37] Torpey K, et al. Analysis of HIV early infant diagnosis data to estimate rates of perinatal HIV transmission in Zambia. *PLoS One* 2012;7:e42859.
- [38] Chiduo MG, Mmbando BP, Theilgaard ZP, et al. Early infant diagnosis of HIV in three regions in Tanzania; successes and challenges. *BMC Public Health* 2013;13:910.
- [39] Mwendu EM, et al. Effectiveness of prevention of mother-to-child HIV transmission programmes in Kilimanjaro region, northern Tanzania. *Trop Med Int Health* 2014;19:267–74.
- [40] Feinstein I, Edmonds A, Chalachala JL, et al. Temporal changes in the outcomes of HIV-exposed infants in Kinshasa, Democratic Republic of Congo during a period of rapidly evolving guidelines for care (2007–2013). *AIDS* 2014;28:301–11.
- [41] Sutcliffe CG, van Dijk JH, Hamangaba F, et al. Turnaround time for early infant HIV diagnosis in rural Zambia: a chart review. *PLoS One* 2014;9:e87028.
- [42] Noubiap JJ, Bongoe A, Demanou SA. Mother-to-child transmission of HIV: findings from an Early Infant Diagnosis program in Bertoua, Eastern Cameroon. *Pan Afr Med J* 2013;15:65.
- [43] Okawa S, Chirwa M, Ishikawa N, et al. Longitudinal adherence to ART drugs for PMTCT of HIV in Zambia. *BMC Pregnancy Childbirth* 2015;15:258.
- [44] Saounde Temgoua EM, et al. HIV-1 early infant diagnosis is an effective indicator of the prevention of mother-to-child transmission program performance: experience from Cameroon. *Curr HIV Res* 2015;13:286–91.
- [45] Koye DN, Zeleke BM. Mother-to-child transmission of HIV and its predictors among HIV-exposed infants at a PMTCT clinic in northwest Ethiopia. *BMC Public Health* 2013;13:398.
- [46] Sagay AS, et al. Mother-to-child transmission outcomes of HIV-exposed infants followed up in Jos North-Central Nigeria. *Curr HIV Res* 2015;13:193–200.
- [47] Saounde TEM, Nkenfou CN, Zoung-Kanyi Bissek AC, et al. HIV-1 early infant diagnosis is an effective indicator of the prevention of mother-to-child transmission program performance: experience from Cameroon. *Curr HIV Res* 2016;13:286–91.
- [48] Banwat SB, Ocheke NA, Auta A, et al. Anti retroviral drug prophylaxis in prevention of mother-to-child transmission of HIV infection in a treatment centre in Jos, Nigeria. *J Pharm Bioresour* 2015;11:93–100.
- [49] Anigilaje EA, et al. HIV-free survival according to the early infant-feeding practices: a retrospective study in an anti-retroviral therapy programme in Makurdi, Nigeria. *BMC Infect Dis* 2015;15:132.
- [50] Bannink-Mbazzi F, Lowicki-Zucca M, Ojom L, et al. High PMTCT program uptake and coverage of mother, their partners, and babies in Northern Uganda: achievements and lessons learnt over 10 years of implementation (2002–2011). *J Acquir Immune Defic Syndr* 2013;62:138–45.
- [51] Kamuyango AA, et al. One-year outcomes of women started on antiretroviral therapy during pregnancy before and after the implementation of Option B+ in Malawi: a retrospective chart review. *World J AIDS* 2014;4:332–7.
- [52] Mugerwa JN, Namukwaya Z, Kekitiinwa A, et al. Early Infection Among Ugandan HIV-Exposed Infants Whose Mothers Received Option B+ vs Option A. In: International Antiviral Society, Boston, Massachusetts, USA, March 3–6, 2014.
- [53] Woelk GB, Ndatimana D, Behan S, et al. Retention of mothers and infants in the prevention of mother-to-child transmission of HIV programme is associated with individual and facility-level factors in Rwanda. *J Int AIDS Soc* 2016;19:20837.
- [54] Ng'ambi WF, Ade S, Harries AD, et al. Follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV centre in Lilongwe, Malawi: 2012–2014. *Trop Med Int Health* 2016;21:995–1002.
- [55] World Health Organization. New data on the prevention of mother-to-child transmission of HIV and their policy implications: conclusions and recommendations. Technical Consultation on behalf of the UNFPA/UNICEF/WHO/UNAIDS Inter-Agency Task Team on Mother-to-Child Transmission of HIV. Geneva: WHO, 2001. http://apps.who.int/iris/bitstream/10665/66851/1/WHO_RHR_01.28.pdf. Accessed September 20, 2015.
- [56] Goga AE, et al. First population-level effectiveness evaluation of a national programme to prevent HIV transmission from mother to child, South Africa. *J Epidemiol Commun Health* 2015;69:240–8.
- [57] Little KM, et al. A review of evidence for transmission of HIV from children to breastfeeding women and implications for prevention. *Pediatr Infect Dis J* 2012;31:938–42.
- [58] Coutsoudis A, et al. Late postnatal transmission of HIV-1 in breast-fed children: an individual patient data meta-analysis. *J Infect Dis* 2004;189:2154–66.
- [59] Iliff PJ, et al. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. *AIDS* 2005;19:699–708.
- [60] Ngarina M, et al. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. *BMC Public Health* 2013;13:450.
- [61] Ebuy H, Henock Y, Mussie A. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray. *Northern Ethiop Int J Infect Dis* 2015;33:123–9.
- [62] Myer L, Phillips TK. Beyond Option B+: understanding antiretroviral therapy (ART) adherence, retention in care and engagement in ART services among pregnant and postpartum women initiating therapy in Sub-Saharan Africa. *J Acquir Immune Defic Syndr* 2017;75(Suppl 2):S115–22.
- [63] Siedner MJ, Santorino D, Lankowski AJ, et al. A combination SMS and transportation reimbursement intervention to improve HIV care following abnormal CD4 test results in rural Uganda: a prospective observational cohort study. *BMC Med Global Health* 2015;13:160DOI 10.1186/s12916-015-0397-1.
- [64] Chang LW, Njie-Carr V, Kalenge S, et al. Perceptions and acceptability of mHealth interventions for improving patient care at a community-based HIV/AIDS clinic in Uganda: a mixed methods study. *AIDS Care* 2014;25:874–80.
- [65] Sibanda EL, et al. The magnitude of loss to follow-up of HIV-exposed infants along the prevention of mother-to-child HIV transmission continuum of care: a systematic review and meta-analysis. *AIDS* 2013;27:2787–97.
- [66] Chatterjee A, et al. Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries. *BMC Public Health* 2011;11:553.
- [67] Grzeskowiak LE, Gilbert AL, Morrison JL. Methodological challenges in using routinely collected health data to investigate long-term effects of medication use during pregnancy. *Ther Adv Drug Saf* 2012;4:27–37.

RESEARCH ARTICLE

Open Access



Progress in the performance of HIV early infant diagnosis services in Zambia using routinely collected data from 2006 to 2016

Jasleen Singh¹, Suzanne Filteau¹, Jim Todd¹ and Sehlulekile Gumedde-Moyo^{1,2*} **Abstract**

Background: Early diagnosis and treatment initiation of HIV-infected infants can greatly reduce the risk of infant mortality. The WHO recommends testing HIV-exposed infants at 6 weeks of age and immediate initiation of antiretroviral therapy if positive. This study aimed to determine the feasibility of using an electronic health records system to evaluate the performance of Zambia's HIV Early Infant Diagnosis services.

Methods: A retrospective analysis of routinely collected data from the Zambian SmartCare database was performed for the period January 2006 to December 2016. The study population includes all HIV-infected infants ($n = 32,593$) registered during this period on treatment for HIV. Univariable logistic regression was conducted to identify factors associated with later infant testing and treatment initiation.

Results: The mean age at infant HIV test decreased from 10.10 months in 2006 to 3.49 months in 2016. Infants born in 2015 were almost 4 times more likely to be tested under 2 months of age compared to infants born in 2006 (OR: 3.72, p -value: < 0.001). The mean time from diagnosis to treatment initiation decreased from 220 days in 2006 to 9 days in 2015. There was substantial regional variability with infants in the provinces of Copperbelt, Luapula and Southern performing best in outcomes and Eastern, Lusaka and Western performing the worst.

Conclusions: HIV-exposed infants born more recently have significantly better outcomes than infants born a decade ago in Zambia, which could be as a result of increased attention and funding for HIV programmes.

Keywords: Early infant diagnosis, HIV, PMTCT

Background

Early diagnosis and treatment initiation of HIV-infected infants with antiretroviral therapy (ART) can reduce the risk of early infant mortality by 76% [1]. However, treatment for HIV-infected children lags considerably behind adult treatment and without treatment approximately 50% of HIV-infected infants die before the age of two [2]. The World Health Organisation (WHO) recommends testing HIV-exposed infants by 6 weeks of age and immediate initiation of ART if positive. Despite these recommendations infants are lost at every step of the early infant diagnosis cascade [3].

Zambia has been using the electronic health records system SmartCare for the routine collection of HIV data since 2004. SmartCare was developed to improve continuity of care and provide timely data on maternal and child health HIV interventions for public health purposes. To date no analysis of the paediatric HIV data has been performed. This study was a retrospective analysis of routinely collected data from the SmartCare database over the period 2006 to 2016, to determine if infants are being tested and initiated on treatment in the correct timeframe. This information can be used to inform decisions on improving the provision of early infant diagnosis services in Zambia.

* Correspondence: sehlulekile.gumedde@shmt.ac.uk

¹Department of Population Health, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

²School of Public Health, University of Zambia, Lusaka, Zambia



© The Author(s). 2018 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Methods

Study design

This retrospective analysis of routinely collected data was conducted as part of the SEARCH (Sustainable Evaluation through the Analysis of Routinely Collected HIV data) project which aims to support the utilisation of routinely collected HIV data. The SEARCH project is collaboration between the London School of Hygiene and Tropical Medicine and the Ministries of Health in Zambia and Tanzania. The data source was SmartCare, one of the largest electronic patient monitoring systems in Africa. Introduced as a pilot project in 2004 by the Zambian Ministry of Health with funding from the US Centers for Disease Control (CDC), it has now been rolled out across all ten provinces of Zambia and is used to monitor and plan improvements in the country's HIV services. All facilities in Zambia wishing to dispense ART are required to use SmartCare. Since 2005 SmartCare has been deployed to over 800 facilities in 94 districts, with an enrolment above 900,000 patients. This represents approximately 40% of all clinics in Zambia; these are the largest and busiest ART clinics and the requirement to join SmartCare if clinics wish to prescribe ART means that most Zambian patients on ART care captured in SmartCare databases [4].

Data was extracted by a SEARCH team member from the Zambian SmartCare database modules, Paediatric ART and Under 5 Registration, between the years 2006 and 2016 using a standardised data extraction form. The study population includes all HIV-infected infants registered during this period on treatment for HIV. Age at infant HIV test was determined by linking the Under 5 Registration module (which has infant date of birth) and Paediatric ART module (which has date of infant HIV test). Infants are registered as independent patients from their mothers and the system does not have a link between the mother and infant pairs; therefore, information could not be collected on the mother's treatment, on the proportion of HIV-exposed infants who tested HIV-negative, or on HIV-exposed infants who missed both testing and provision of ART. For this reason, we are focusing this analysis solely on HIV-infected infants born between January 2006 and December 2016 who have received ART.

Statistical methods

Categorical variables were summarised by frequencies and percentages and continuous variables by histograms. Univariable and multivariable logistic regression were conducted with "age at HIV test" and "time from diagnosis to treatment initiation" as the dependent variables and the following independent variables: infant sex, province, year of birth, and season of birth. Season were defined as early dry (June to August); late dry

(September to November); early rainy (December to February) and late rainy (March to May).

Odds ratios with 95% confidence intervals were calculated to identify risk factors for age at test under 2 months and time from diagnosis to treatment under 2 weeks. For the variable 'province' Lusaka was chosen as the reference group because it is the most populous province, and it contains the capital city where the SmartCare project was first rolled out so has the largest number of registered infants. Although multivariable analysis was also conducted for all variables to display adjusted odds ratios, the results showed little difference and so only the univariable analysis results are included in this paper. All analysis was performed using STATA 14 and graphics were produced using STATA and Microsoft Excel.

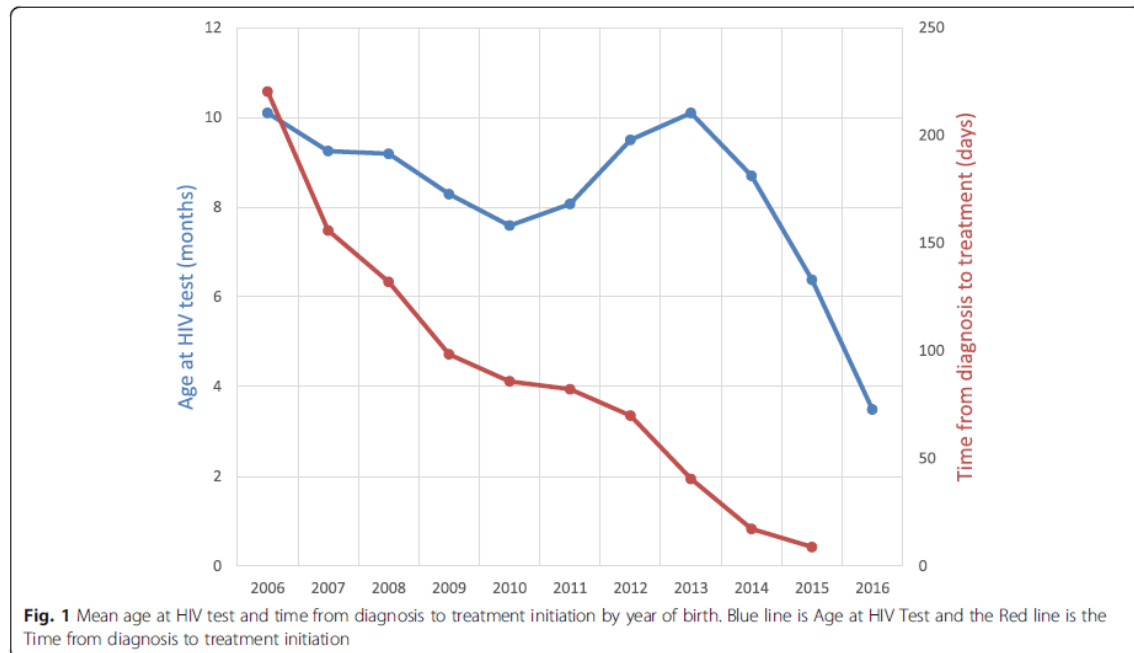
Results

A total of 32,593 HIV-infected infants on ART in Zambia were identified from SmartCare over the period 2006 to 2016. The number of infants in the database on ART increased from 1761 in 2006 to peak at 3720 in 2009 and then steadily decreased to 108 in 2016. Main comparisons over time used 2015 since there were too few infants listed in 2016 for age at testing and none for time to treatment initiation.

Age of diagnosis

For the outcome 'age at infant HIV testing', 20,260 (62.16%) infants had complete data recorded. Looking at the country as a whole, the mean age at HIV testing has steadily decreased from 10.10 months for infants born in 2006 to 3.49 months in 2016 (Fig. 1). Infants born in 2015 were more likely to be tested under 2 months of age compared to infants born in 2006 (OR: 3.72, p -value: < 0.001). For infants born in 2016 an even greater association was found (OR: 5.62, p -value: < 0.001), but this result must be viewed with some caution as there were far fewer infants in the database for the year 2016 ($n = 108$) than 2015 ($n = 386$).

Considering all years together, infants in all provinces, especially Western province (OR: 0.21, p -value: < 0.001) were less likely to be tested under 2 months of age as compared to infants in Lusaka; an exception was Southern province which had an increased odds (OR: 1.83, p -value: 0.001). Figure 2 shows the percentage of HIV tests performed within 2 months of birth in the years 2010 and 2015 by province. All provinces show an overall improvement, particularly Copperbelt, Luapula and Southern. The years 2010 to 2015 were chosen for the comparison to coincide with the changes in prevention of mother-to-child transmission (PMTCT) guidelines in Zambia over this period, as discussed below.



Infants born in the late dry season were more likely to be tested within 2 months than infants born in the early dry season (OR 1.39; *p* value: < 0.001) (Table 1). There was no association found for sex.

Time to ART initiation

For the outcome ‘time from diagnosis to ART initiation’, 10,881 (33.38%) infants had complete data recorded. At the country level the mean time from diagnosis to starting treatment has decreased significantly from 220 days

for infants born in 2006 to 9 days in 2015 (Fig. 1). Infants born in 2015 were more likely to start treatment in under 2 weeks compared to infants born in 2006 (OR 2.29; *p* value: < 0.001).

Infants in all provinces had an increased likelihood of starting treatment within 2 weeks as compared to Lusaka, despite being less likely to be tested under 2 months. Luapula showed the biggest difference (OR: 3.83, *p*-value: < 0.001). The provinces showing the most improvement from 2006 to 2015 were Copperbelt,

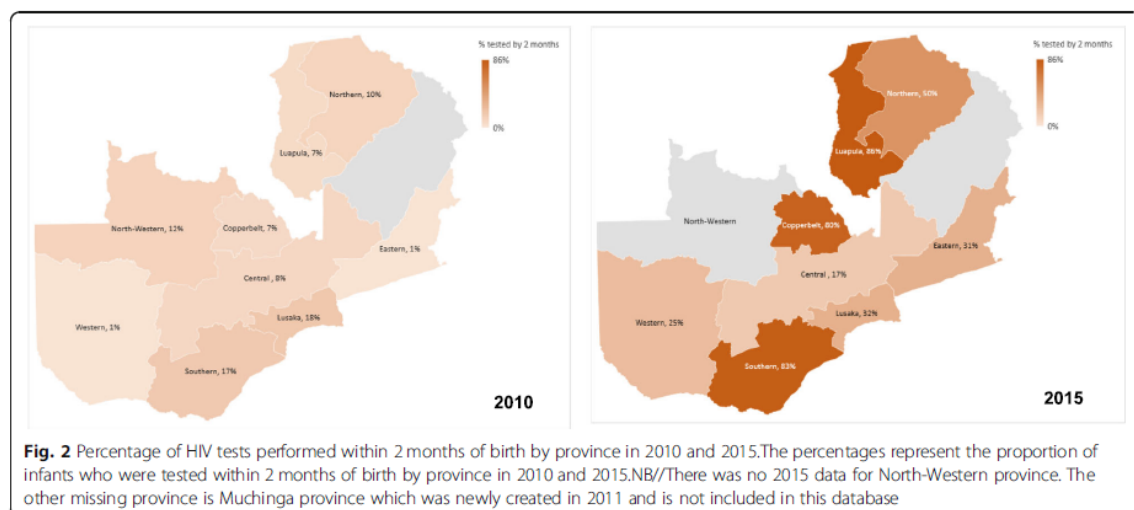


Table 1 Univariable analysis results for sex, season, province and year of birth

Variable	Age at test		Logistic regression for testing at < 2 months			Logistic regression for time from diagnosis to ART < 2 weeks		
	< 2 months n (%)	< 2 weeks n (%)	OR	95% CI	P-value	OR	95% CI	P-value
Sex								
Male	550/10,537 (5.2)	2249/10,537 (21.3)	1.00	–	–	1.00	–	–
Female	603/11,185 (5.4)	2568/11,158 (23.0)	1.03	0.92, 1.17	0.573	1.10	1.03, 1.17	0.004
Season								
Early dry	914/5254 (17.4)	1478/5254 (28.1)	1.00	–	–	1.00	–	–
Late dry	946/4168 (22.7)	1135/4168 (27.2)	1.39	1.26, 1.54	< 0.001	0.96	0.87, 1.05	0.333
Early rainy	926/5364 (17.3)	1509/5364 (28.1)	0.99	0.90, 1.10	0.856	1.00	0.92, 1.09	0.999
Late rainy	912/5474 (16.7)	1611/5474 (29.4)	0.95	0.86, 1.05	0.311	1.07	0.98, 1.16	0.137
Province								
Lusaka	365/5394 (6.8)	822/5394 (15.2)	1.00	–	–	1.00	–	–
Central	94/2288 (4.1)	688/2288 (30.1)	0.59	0.47, 0.74	< 0.001	2.39	2.13, 2.69	< 0.001
Copperbelt	294/4778 (6.2)	1648/4778 (34.5)	0.90	0.77, 1.06	0.210	2.93	2.66, 3.22	< 0.001
Eastern	59/2072 (2.8)	431/2072 (20.8)	0.40	0.31, 0.53	< 0.001	1.46	1.28, 1.66	< 0.001
Luapula	56/1341 (4.2)	547/1341 (40.8)	0.60	0.45, 0.80	0.001	3.83	3.36, 4.37	< 0.001
Northern	57/983 (5.8)	350/983 (35.6)	0.85	0.64, 1.13	0.262	3.08	2.65, 3.57	< 0.001
North-Western	25/883 (2.8)	244/883 (27.6)	0.40	0.27, 0.61	< 0.001	2.12	1.80, 2.50	< 0.001
Southern	394/3366 (11.7)	718/3366 (21.3)	1.83	1.57, 2.12	< 0.001	1.51	1.35, 1.69	< 0.001
Western	24/1577 (1.5)	285/1577 (18.1)	0.21	0.14, 0.32	< 0.001	1.27	1.06, 1.42	0.007
Year of birth								
2006	220/1709 (12.9)	340/1709 (19.9)	1.00	–	–	1.00	–	–
2007	412/2619 (15.7)	547/2619 (20.9)	1.26	1.06, 1.51	0.009	1.06	0.91, 1.24	0.430
2008	528/3475 (15.2)	790/3475 (22.7)	1.21	1.02, 1.44	0.025	1.18	1.03, 1.37	0.020
2009	683/3678 (18.6)	861/3678 (23.4)	1.54	1.31, 1.82	< 0.001	1.23	1.07, 1.42	0.004
2010	675/2718 (24.8)	726/2718 (26.7)	2.24	1.89, 2.65	< 0.001	1.47	1.27, 1.70	< 0.001
2011	446/1812 (24.6)	612/1812 (33.8)	2.21	1.85, 2.64	< 0.001	2.05	1.76, 2.40	< 0.001
2012	191/1384 (13.8)	564/1384 (40.8)	1.08	0.88, 1.33	0.450	2.77	2.35, 3.26	< 0.001
2013	186/1352 (13.8)	605/1352 (44.7)	1.08	0.88, 1.33	0.474	3.26	2.76, 3.85	< 0.001
2014	171/1019 (16.8)	548/1019 (53.8)	1.36	1.10, 1.70	0.005	4.68	3.90, 5.62	< 0.001
2015	137/386 (35.5)	140/386 (36.3)	3.72	2.87, 4.83	< 0.001	2.29	1.80, 2.92	< 0.001
2016	49/108 (45.4)	0/108 (0.0)	5.62	3.71, 8.51	< 0.001	–	–	–

Central and Northern. Female infants were slightly more likely to start treatment in under 2 weeks compared to males (OR: 1.10; *p* value: 0.004). Season showed no significant association.

Discussion

In Zambia the age at infant HIV test has shown a steady decline, with the exception of the period 2010 to 2013 which showed a slight increase. This period coincides with the implementation of new WHO treatment guidelines for PMTCT. Changes in WHO recommendations over the past decade on when to initiate ART in pregnant women have had major implications for the delivery of HIV services, and help explain the trends in

service delivery. From 2010 Zambia adopted Option A, a complex guideline consisting of different maternal treatment regimens during pregnancy, labour and postpartum as well as infant prophylaxis [5]. This complexity of regimen changes, combined with the need for regular clinic visits in early infancy, led to high attrition rates and infants receiving improper doses of daily Nevirapine [6]. Option B+ which was adopted in 2013 [7] removed this barrier by recommending treating all pregnant women with lifelong ART regardless of CD4 count. By simplifying the process considerably, in Malawi (where it was first trialled), switching to Option B+ led to a five-fold increase in the number of pregnant women enrolled on ART in the first quarter of implementation [8].

When Zambia announced its policy for universal ART in 2015, there was an increase in the volume of patients initiating on ART [9]. Zambia has made progress towards elimination of HIV mother-to-child transmission with a reduction in new HIV infections among children from 10,000 in 2010 to 8900 in 2016. This could be as result of improved coverage of pregnant women living with HIV accessing antiretroviral medicines to 86% [10]. In our study we were not able to calculate the MTCT rate because the SmartCare database does not have information on the HIV exposed infants who are not on ART.

All provinces showed a subsequent reduction in age at test between 2013 and 2015 with the implementation of Option B+, in which all pregnant women with HIV are offered lifelong ART regardless of CD4 count [11]. The progress could also be attributed to Option B+ as previous studies have concluded that children born to women who received ART are less likely to be lost to follow-up and more likely to be tested for HIV [12–14]. This suggests that under Option B+ mothers and their infants are more likely to be attached to the health care system. Therefore efforts have to be made to ensure that the infants who are tested and initiated are retained in care. In Tanzania, 61% of infants receiving treatment were lost to follow up at the time of review, despite the high proportion of guardians and parents who returned for PCR results (92% in 2010 and 98% in 2011) [15]. The results were consistent with a study from Malawi where 48% of the HIV-exposed infants were declared lost to follow up (LTFU) in the database although 96% of the them in the cohort had their PCR test done at 24 months [16]. Hence despite the reduction in the age of testing the progress of EID must be enhanced by ensuring continuity in care. In Zambia the estimated percentage of children (aged 0–14 years) living with HIV receiving ART, in 2015 was 61% [17], 3% lower than the adult coverage.

An effective EID service should achieve the following: identify all HIV-exposed infants, provide HIV testing and ensure return of results in a timely manner; retain HIV-exposed infants and their mothers in care; and identify all HIV-infected infants and link them to treatment services to ensure timely initiation of ART [18]. Our data set could not allow us to effectively analyse all these steps hence our conclusion of the progress of EID could have been overestimated as only 33.38% infants had complete data recorded. The poor data quality might have an effect on the external validity of the study. Hence the reasons for poor data quality have been qualitatively explored (*Gumede-Moyo* et al. submitted). It is also likely that poor data entry over these years has impacted the results; SmartCare has evolved from a system solely used to track patients into an extensive database of all patients receiving ART in the country.

This has resulted in a large amount of data being collected for each patient which is very time consuming for the clinician, who often omits collecting data for certain fields they deem irrelevant to their patient's care. In addition, power outages in remote areas of Zambia are a major problem and can occur for prolonged periods of time during the day, limiting the time that data can be entered into the system. This means that data collection is often not up to date and this could contribute to the apparently poor performance of Western province.

Our study is the first to attempt to analyse the progress of EID using the SmartCare database as a source for exposed infants on ART dataset. A more comprehensive dataset of the HIV status of all exposed infants could have been obtained from the ANC and Under 5 paper registers. However, the majority of studies using paper based routine data have also acknowledged the common problem of missing data [19]. This could be assumed to be one of the causes of under-utilisation of routinely collected data which was observed by Munthali et al. [20].

The best performing provinces in 2015 (Fig. 2) for 'percentage of tests performed within 2 months of birth' were Luapula, Southern and Copperbelt; surprisingly Lusaka was the second worst performing province after Western. Of the nine provinces of Zambia (excluding Muchinga province which was created in 2011 and not included in this database), Lusaka and Copperbelt are predominantly urban whereas the remaining are predominantly rural [21]. Previous studies have shown that the burden of HIV is highest in Zambia's 'urban poor' [22, 23], and indeed data from the latest Zambian 2013–14 DHS showed that Lusaka and Copperbelt have the highest adult HIV prevalence, at 16.3 and 18.2% respectively [24]. Despite the similar HIV prevalence and population sizes, Copperbelt saw a more dramatic improvement in age at infant testing between 2013 and 2015 than Lusaka. The stark difference between the performance of Copperbelt and Lusaka is also seen in the percentage of infants tested under 2 months of age, which was amongst the highest in Copperbelt in 2015 compared to 2010, but rose much less in Lusaka during the same period. This regional variability seen could be attributed to the concentration of donor funded programmes in the various provinces. Despite Zambia's classification as a lower-middle income country, it remains heavily dependent on external donors to finance its national HIV response. PEPFAR and the Global Fund account for 95% of donor funding for HIV care [25]. Given external aid makes up the bulk of HIV funding in Zambia, it is possible that decisions on which areas of the country to target may influence the trends in HIV outcomes we have seen at a provincial level.

Infants born in the early dry season tended to be tested earlier compared to infants born in the late dry season, although there was no association found between dry and rainy seasons. Season was chosen as a variable of interest because previous studies in Sub-Saharan Africa have shown an association between being born in the rainy season and poorer outcomes for HIV-exposed infants [26, 27]. Reasons suggested for the higher mortality experienced by infants born in the rainy season include a more contaminated water supply from the rains and food scarcity in the period preceding the harvest [28, 29].

Study limitations

This research has shown that routinely collected data offers a valuable opportunity for the near real-time surveillance of large quantities of data. The SmartCare database of registered infants receiving ART represents a robust sample of the population under study over the stated time period, although we recognise there was a steady decrease in the numbers of infants registered onto SmartCare from 2009 onwards. The large amounts of missing data did not only introduce bias but also compromised the statistical power of a study. Other limitations with using this database are that the database was designed for practical use by healthcare workers and not research so the variables collected are limited to those deemed most useful for the clinical care of patients. In addition, mother-infant pairs are not linked within SmartCare, and so the analysis was restricted to HIV-infected infants on ART and we were not able to analyse outcomes for HIV-exposed uninfected infants. This would be valuable information for any future assessment of mother-to-child HIV transmission prevention and control programs in Zambia.

Conclusions

Early infant diagnosis of HIV is essential to achieve prompt treatment initiation and reduce infant mortality. Infants born more recently have better clinical HIV care than infants born a decade ago in Zambia, which could be as a result of more inclusive treatment eligibility guidelines. Provincial variability in the performance of early infant diagnosis services is substantial. Further research is needed on the reasons for such stark regional disparities in HIV service provision in Zambia, and on addressing missed opportunities for infant testing.

Abbreviations

AIDS: Acquired immune deficiency syndrome; ART: Antiretroviral therapy; CD4: T-lymphocyte cell bearing CD4 receptor; CDC: Centres for disease control and prevention; DHS: Demographic and Health Survey; EID: Early infant diagnosis; HIV: Human immunodeficiency virus; LSHTM: London School of Hygiene and Tropical Medicine; LTFU: Lost to follow up; MTCT: Mother-to-child transmission; PEPFAR: President's emergency plan for

AIDS relief; PMTCT: Prevention of mother-to-child transmission of HIV; SEARCH: Sustainable Evaluation through the Analysis of Routinely Collected HIV data; UNAIDS: Joint United Nations Program on AIDS; WHO: World Health Organisation

Acknowledgements

We would like to acknowledge the support of the SEARCH team and the Ministry of Health in Zambia.

Funding

The study was supported by the SEARCH (Sustainable Evaluation through Analysis of Routinely Collected HIV data) Project funded by the Bill & Melinda Gates Foundation grant number OPP1084472.

Availability of data and materials

The data collected through the SmartCare database belongs to the Zambian Ministry of Health; however any further information pertaining to the database can be addressed by corresponding author sehlulekile.gumedede@lshtm.ac.uk

Authors' contributions

JS conducted the statistical analysis and drafted the manuscript. SGM conducted the data extraction and cleaning from the SmartCare database. SF and SGM supervised the study and JT, as SEARCH project principal investigator, obtained ethical and regulatory approvals and advised on data analysis. All authors have read, commented on and approved the final manuscript.

Ethics approval and consent to participate

The study used secondary data, and hence there was no direct contact with the patients whose individual data was stripped of unique identifiers. Permission to use the data was obtained from the Zambia Ministry of Health and ethical clearance was obtained from the London School of Hygiene and Tropical Medicine (Ref 8410-01) and the University of Zambia Biomedical Research Ethics Committee (Ref 101-04-16).

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 14 June 2018 Accepted: 14 November 2018

Published online: 26 November 2018

References

1. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med*. 2008;359(21):2233–44. <https://doi.org/10.1056/NEJMoa0800971>.
2. Newell L, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*. 2004;364(9441):1236–43. [https://doi.org/10.1016/S0140-6736\(04\)17140-7](https://doi.org/10.1016/S0140-6736(04)17140-7).
3. UNAIDS. 'On the Fast-track to an AIDS-Free Generation'. 2016. [Cited 2017 July 13]. Available from: http://www.unaids.org/sites/default/files/media_asset/GlobalPlan2016_en.pdf
4. Muyunda G. 'Zambia leads the way in SmartCare electronic health records system, a benefit to both providers and patients 2011'. [Cited 2018 September 11]. Available from: <https://www.jhpiego.org/success-story/zambia-leads-the-way-in-smartcare-electronic-health-records-system-a-benefit-to-both-providers-and-patients/>.
5. Ishikawa N, Shimbo T, Miyano S, Sikazwe I, Mwangi A, Ghidini N, Syakantu G. Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia. *PLoS One*. 2014;9(3). <https://doi.org/10.1371/journal.pone.0090991>.
6. Chi H, Stringer A, Moodley D. Antiretroviral drug regimens to prevent mother-to-child transmission of HIV: a review of scientific, program, and policy advances for sub-Saharan Africa. *Curr HIV/AIDS Rep*. 2013;10(2):124–33.

7. Government of the Republic of Zambia Ministry of Health. 'Lifelong antiretroviral drugs (ARVs) for all HIV positive pregnant women in Zambia: Policy guidelines for health facilities in Zambia'. 2013. [Cited 2018 September 11]. Available from: <http://catalogue.safids.net/sites/default/files/publications/Policy-guidelines-for-eMTCT-Option-B+-Zambia-2013.pdf>
8. Kieffer MP, Mattingly M, Giphart A, van de Ven R, Chouraya C, Walakira M, Simonds RJ. Lessons learned from early implementation of option B+. *JAIDS J Acquir Immune Defic Syndr*. 2014;67:5188–94. <https://doi.org/10.1097/QAI.0000000000000372>.
9. Chung N.C, B-MC, Chilengi R, Kasaro M. P., Stringer J. S. A and Benjamin H. Chi B. H. Patient engagement in HIV care and treatment in Zambia, 2004–2014. *Tropical Medicine and International Health*. 2017;22(3):332–9.
10. UNAIDS. UNAIDS Global AIDS Update Data Book. Geneva; 2017. [Cited 2018 September 11]. Available from: http://www.aidsdatahub.org/sites/default/files/publication/UNAIDS_Global_AIDS_Update_2017_Data_book_2017_en.pdf
11. UNICEF. 'Options B and B+: Key considerations for countries to implement an equity-focused approach'. 2012 [Cited 2017 July 7]. Available from: https://www.unicef.org/aids/files/hiv_Key_considerations_options_B.pdf
12. Haas A, van Oosterhout J, Tenthani L, Jahn A, Zwahlen M, Msukwa MT, et al. HIV transmission and retention in care among HIV-exposed children enrolled in Malawi's prevention of mother-to-child transmission programme. *J Int AIDS Soc*. 2017;20(1):21947.
13. Cromwell A, Dow A, Low D, Chirambo C, Heyderman R, Dube Q, et al. (2015) barriers to successful early infant diagnosis of HIV infection at primary care level in Malawi. *Pediatr Infect Dis J*. 2015;34(3):273–5.
14. Feinstein L, Chalachala J, Okitolonda V, Lusiana J, Van Rie A, Chi B, Cole S, Behets F. Temporal changes in the outcomes of HIV-exposed infants in Kinshasa, Democratic Republic of Congo during a period of rapidly evolving guidelines for care (2007–2013). *AIDS (London, England)*. 2014;28(3):301–11.
15. Mercy G, Chiduo B, Zahra P, Bygbjerg C, Jan G, Martha L, Terese K. (2013) Early infant diagnosis of HIV in three regions in Tanzania; successes and challenges. *BMC Public Health* 2013;13(910).
16. Wingston F, Ng'ambi S, Anthony H, Dalitso M, Philip O, Kudakwashe T, Salem G, Sam P. (2016) follow-up and programmatic outcomes of HIV-exposed infants registered in a large HIV Centre in Lilongwe, Malawi: 2012–2014. *Trop Med Int Health*. 2016;21(8):995–1002.
17. UNAIDS. 'Prevention Gap Report'. 2016. [Cited 2018 September 11]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf
18. Sugandhi N, Rodrigues J, Kim M, Ahmed S, Amzel A, Tolle M, et al. HIV-exposed infants: rethinking care for a lifelong condition. *AIDS (London, England)*. 2013;27(Suppl 2):S187–95.
19. Gumede-Moyo S, Filteau S, Munthali T, Todd J, Musonda P. Implementation effectiveness of revised (post-2010) World Health Organization guidelines on prevention of mother-to-child transmission of HIV using routinely collected data in sub-Saharan Africa: a systematic literature review. *Medicine (Baltimore)*. 2017;96(40):e8055.
20. Munthali TMP, Mee P, Gumede S, Schaap A, Mwinga A, Phiri C, Kapata N, Michelo C, Todd J. Underutilisation of routinely collected data in the HIV programme in Zambia: a review of quantitatively analysed peer-reviewed articles. *BMC Res Policy Syst*. 2017;2017:15(51).
21. UNAIDS. 'GARPR Zambia country report'. 2015. [Cited 2017 August 8]. Available from: http://www.unaids.org/sites/default/files/country/documents/ZMB_narrative_report_2015.pdf
22. Chanda-Kapata P, Kapata N, Klinkenberg E, William N, Mazyanga L, Musukwa K, Mwaba P. The adult prevalence of HIV in Zambia: results from a population based mobile testing survey conducted in 2013–2014. *AIDS Res Ther*. 2016;13(1):4. <https://doi.org/10.1186/s12981-015-0088-1>.
23. Kandala NB, Ji C, Cappuccio PF, Stones RW. The epidemiology of HIV infection in Zambia. *AIDS Care*. 2008;20(7):812–9. <https://doi.org/10.1080/09540120701742292>.
24. Central Statistical Office, Zambia; Ministry of Health, Zambia; ICF International. 'Zambia Demographic and Health Survey 2013–14'. 2014. [Cited 2017 August 9]. Available from: <https://www.dhsprogram.com/pubs/pdf/FR304/FR304.pdf>
25. Health Policy Project. 'Sustainable HIV Financing in Zambia: Baseline analysis and prospects for new domestic resource mobilization'. 2015. [Cited 2017 August 20]. Available from: https://www.healthpolicyproject.com/pubs/2876_ZambiaHIVFinancingFeb.pdf
26. Kourtis A. P, Wiener J, Kayira D, Chasela C, Ellington S. R, Hyde L, Jamieson D.J. (2013) Health outcomes of HIV-exposed uninfected African infants. *AIDS*. 27(5), 749–759. <https://doi.org/10.1097/QAD.0b013e32835ca29f>.
27. Zash R, Souda S, Leidner J, Ribaud H, Binda K, Moyo S, Shapiro R. HIV-exposed children account for more than half of 24-month mortality in Botswana. *BMC Pediatr*. 2016;16(1):103. <https://doi.org/10.1186/s12887-016-0635-5>.
28. Lilian RR, Kalk E, Bhowan K, Berrie L, Carmona S, Technau K, Sherman GG. Early diagnosis of in utero and intrapartum HIV infection in infants prior to 6 weeks of age. *J Clin Microbiol*. 2012;50(7):2373–7. <https://doi.org/10.1128/JCM.00431-12>.
29. Francke JA, Penazzato M, Hou T, Abrams EJ, Maclean RL, Myer L, Ciaranello A. Clinical impact and cost-effectiveness of diagnosing HIV infection during early infancy in South Africa: test timing and frequency. *J Infect Dis*. 2016; 214(9):1319–28 <https://doi.org/10.1093/infdis/jiw379>.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

