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Development, Implementation and Utilisation of a Mobile Technology Enhanced, Electronic Medical Record/Clinical Decision Support System for the Co-management of HIV and Pregnancy

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Author's Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) –u updated March 2014. The proposed research study received human research ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number # HR 211/2013

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Abstract

Perinatal antiretroviral therapy can virtually eliminate perinatal transmission of HIV. Extending appropriate application of ART and management of co-morbidities during pregnancy to women living with HIV in underserved settings remains a challenge. Mobile health (mhealth) technologies have been shown to improve ART therapy initiation and adherence, and improve pregnancy outcomes by extending the healthcare workforce via task-shifting and facilitating decentralisation of care, improving data and information access, patient-provider communication, consultation and referral capabilities and data mining and analysis. A mobile technology enhanced, cloud-based, combined electronic medical record (EMR) and passive/active clinical decision support system (CDSS) focused on the antepartum co-management of HIV and pregnancy with birth, breastfeeding, post partum and newborn care planning for point of care use by the clinician was developed and piloted at Kakamega County General Hospital's antenatal care clinic in Kenya. The record has graphic patient education materials and allows for extensive data mining via an application program interface (API).

The EMR/CDSS was developed using the open source, OpenMRS software and the CIEL/MVP concept dictionary. The EMR/CDSS guides the clinician through all aspects of antenatal and HIV care and provides information tabs which reveal diagnostic and treatment information for HIV, opportunistic infections, laboratory analysis, and birth, post partum and newborn management derived from WHO, Kenyan NASCOP, NICE, CDC, Australian and NIH guidelines. Alerts to missing appointments and clinical information and abnormal values provide the active CDSS elements. The system was used on Chromebooks at the point of care in the Maternal Child Health clinic with pregnant women living with HIV. The Chromebooks connected to the server located in Kakamega Town through a virtual private network (VPN) using 3G wireless broadband technology.

Funding challenges delayed the start of the project and led to organisational challenges as the umbrella organisation for the study disbanded. Weather related and Internet service provider related technical challenges delayed the pilot, caused communications failures and undermined record utilisation and supervision during the pilot. The lag between training and implementation, unfamiliarity with laptops, sub-par oversight of clinical staff and project management staff and time constraints undermined proper record utilisation. When utilised, clinical staff reported improvement in data completeness and decision-making secondary to the CDSS elements.

Recommendations for future implementations include using the digital design principals, keeping the knowledge base up to date in a routine fashion, ensuring consistency in programming, operating within an established framework for project management and funds distribution or ensuring that the project has the required funding and time needed to confront and contend with technical and project management challenges, ensuring adequate project management and record utilisation oversight and taking a long term view of the project output.

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My deepest gratitude to the people living with HIV throughout the world, upon whose lives rested and rest the progress that has been made and is still to be made in the face of this epidemic.

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Dedication

This PhD thesis is dedicated to people living with and who have lived with HIV and to the tireless and passionate activists, researchers, practitioners and politicians whose vision has lead to the progress that we see today.

Finally, this thesis is dedicated to my son Julian.

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List of Abbreviations

AIDS- acquired immunodeficiency syndrome

AMPATH – academic model providing access to healthcare

API- application program interface

ART- antiretroviral therapy is the use of a combination of several drugs to limit the rate at which HIV replicates

ARV- antiretroviral drug

CD4- T-lymphocyte cell bearing CD4 receptor

CD8- T-lymphocyte cell bearing CD8 receptor

CDC- United States Centers for Disease Control and Prevention

CDSS- computerised clinical decision support system

CIS- clinical information systems

CMV- cytomegalovirus

CNS- central nervous system

CPOE- computerised provider order entry

CTX- cotrimoxazole

DNA- deoxyribonucleic acid

ELISA- enzyme- linked immunosorbent assay

EHR- electronic health records

EMR- electronic medical records

ETACS – total access communications system, a largely obsolete form of mobile phone system

GALT- Gut associated lymphoid tissue

GFATM- Global Fund to Fight AIDS Tuberculosis and Malaria

GMS – global system for mobile communication

HBsAg- hepatitis B surface antigen

HBV- hepatitis B virus

HCV- hepatitis C virus

HIS- health information systems

HIV- human immunodeficiency virus

ICT- Information communication technology

IPSec- Internet protocol security

IT- Information technology

KS- Kaposi's sarcoma

LAN- Local area network

MVP-CIEL – Millennium Villages Project- Columbia International e-Health Laboratory

PEPFAR- President's Emergency Plan for AIDS Relief

PLHIV- People living with HIV

RNA- ribonucleic acid

SMS- short message service

SSH- Secure socket shell

TB- tuberculosis

UNAIDS- United Nations

UNICEF- United Nations Childrens' Fund

UNPF- United Nations Population Fund

UPIN- unique patient identification number

VCT- voluntary counselling and testing

VPN- virtual private network

VSAT- very small aperature terminal

WHO- World Health Organization

WIMAX- worldwide interoperability for microwave access

Chapter 1 Overview of the thesis

In a reaffirmation of the Millennium Development Goals and continued commitment to the Sustainable Development Goals, on June 7th, 2016 the United Nations General Assembly issued the draft resolution, "Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030" (UN General Assembly, 2016). This document both recognises the achievements that have been made to date in fighting the epidemic, and notes that much work is left to be done. The UNAIDS Fast-track approach envisions 90% of people living with HIV knowing their status, with 90% of those on ART and with 90% of those achieving viral suppression leading to a reduction to 500,000 new infections among adults by 2020. It further envisions that by 2030, 95% of people living with HIV know their status, 95% of those are on ART and 95% of those arebvirally supressed, reducing to 200,000 the number of new infections among adults and also achieving zero discrimination by 2030 (UNAIDS, 2014b). It is in the spirit of these ambitious targets and declarations, and built upon the dedication, suffering and toil of those involved in this fight that this work was embarked upon and has been completed.

1.1 Introduction to the chapter

This chapter provides an introduction to the thesis, the background of the study, justification for the study and the study hypothesis. Chapter summaries follow.

1.2 Background to the study

Nearly 37 million people are currently living with HIV in the world. Seventy-six million people have been diagnosed with HIV since the beginning of the epidemic and 34 million have died. AIDS is currently the leading cause of death for women and adolescent girls of reproductive age worldwide, 14 million children have been orphaned because of AIDS and daily, there are 6000 new infections (UN General Assembly, 2016). Perinatal transmission of HIV is an important avenue of transmission in the AIDS epidemic. Without intervention, mother to child transmission rates of HIV are between 15-45% but can be reduced to below 5% with effective intervention and management (World Health Organization, 2010c). Antiretroviral therapy (ART) during pregnancy reduces mother to child transmission of HIV both by reducing maternal HIV viral load and providing infant pre- and post-exposure prophylaxis (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2013). Recently, mother to child transmission of HIV has accounted for 90% of the infections of HIV in children in low and middle income countries (Scanlon & Vreeman, 2013). Scale up in antiretroviral therapy provision to women during pregnancy has

lead to dramatic decreases in the rates of perinatal transmission of HIV. Sixty-two precent of eligible pregnant women received antiretroviral therapy (ART) during pregnancy in 2012 and 35% fewer cases of perinatal transmission of HIV occurred in 2012 than in 2010. Thirteen percent more pregnant women were receiving ART in the first half of 2014 than the first half of 2013 (UNAIDS, 2014b). The virtual elimination of perinatal transmission of HIV has been cited as an achievable goal for the future (UNAIDS, 2013).

The prevention of perinatal HIV transmission requires a multifaceted approach. Access and adherence to antiretroviral medications, a skilled and knowledgeable caregiving workforce, retention in treatment programs and efficient education, tracking and monitoring of pregnant women with HIV are essential. However, many areas of the world are subject to severe health care staff shortages as well as information deficits; one billion people live in medically underserved areas and one third of countries lack sufficient skilled caregivers (Linder, 2012). These factors contribute to higher than ideal perinatal transmission rates of HIV. E-and mhealth technologies provide an opportunity to compensate for many of these deficits.

The International Telecommunications Union estimated that there would be 6.9 billion cellular service subscriptions by the end of 2014; 2.3 billion of those incorporating mobile broadband services and that number expected to grow to 9.2 billion by 2019 (The Broadband Commission, 2014). This technology is already revolutionising health information delivery in high resource settings and the potential for this technology to revolutionize delivery of health information and health care services is in lower resource settings is enormous as well. As technology and infrastructure continue to develop and wireless coverage continues to grow, the World Health Organization (WHO) has called for the further development and evaluation of electronic health technologies (e-health) and mobile health technologies (mhealth) (World Health Organization, 2011). E-health is described as the transfer of health resources and healthcare by electronic means (World Health Organization, 2013c). Mhealth, a subset of e-health, refers to the application of wireless technology including mobile telecommunication and multimedia technologies to enable healthcare delivery via mobile devices such as smartphones, mobile phones, PDAs, tablet and laptop PCs (Bakshi et al., 2011).

Currently, e-and mhealth systems are extending the geographic access of providers, facilitating patient communication, improving access to patient information, improving diagnosis and treatment and improving data management. (T. Lewis, Synowiec, Lagomarsino, & Schweitzer, 2012a). These systems provide an excellent opportunity

facilitate various aspects of HIV and maternal child health management and care, particularly in resource-constrained settings.

1.3 Aim and objectives

It is underpinned by this background and with the urgent need to effectively support pregnant women with HIV that a mobile technology enhanced, combined electronic medical record and knowledge based, passive-active clinical decision support system (EMR/CDSS) focused on the co-management of HIV and pregnancy has been designed to be used by the clinician at the point of care. This system is Internet based and run on Chromebooks (low cost laptop computers with Internet access) that access wireless broadband services (Google, 2013). The software can also be run on desktop computers and accessed through local area networks (LAN) or on the computer's hard drive.

The system seeks to maximize the utility of healthcare providers and health care facilities, extend the geographic access and patient volume capacities of providers, improve diagnosis and treatment by providing management guidelines for the many facets of HIV and pregnancy co-management, including adherence to ART regimens and retention in programs, engage and educate patients while reminding them of upcoming appointments and improve data management and analysis. It also seeks to improve referral and consultation mechanisms, compensate for health worker shortages and lead to the professional development of healthcare providers. Because of the technology's mobile nature and use of open source software, the system should be appropriate for a high tech, centralized environment as well as a low technology setting lacking a grounded Internet connection and even electricity.

The objectives of the study were:

1. To describe e-health, mhealth, electronic medical records and clinical decision support systems in depth with particular focus on the functionality of e-health and mhealth systems within the realms of pregnancy and HIV care and those that utilise wireless broadband communications and to review and critique the Kenyan National e-Health Strategy 2011-2017.

2. To develop a mobile technology enhanced, combined electronic medical record and clinical decision support system aimed at the co-management of HIV and pregnancy with utility in both centralized and decentralized care environments.

3. To pilot the mobile technology enhanced EMR/CDSS with a small cohort of clinicians in western Kenya

4. To describe the challenges in mhelath deployment within the pilot and in other settings.

5. To provide recommendations for future use of similar mhealth systems in resource limited settings

1.4 Justification

This project seeks to maximize the utility of healthcare providers and health care facilities, extend the geographic access and patient volume capacities of providers, improve diagnosis and treatment, including adherence to ART regimens and retention in programs, and improve data management specifically within the realm of perinatal HIV. It also seeks to improve referral and consultation mechanisms, compensate for health worker shortages and lead to the professional development of healthcare providers for the co-management of pregnancy and HIV. The mhealth technology that this project created includes remote access to a cloud-based, centralised electronic medical record, access to a computerised decision support system and enhancement of referral and consultation capabilities for the management of perinatal HIV. Researching the use of the system developed as a part of this project adds to the evidence base for mhealth and e-health systems in general and specifically for perinatal HIV management. This evidence base will guide governments and funding organisations to most appropriately allocate precious healthcare resources.

Though the current literature does not describe a technology that incorporates all of these aspects, the evidence that versions of each aspect individually has improved patient outcomes, streamlined workflow, improved communication, increased both routine and emergency referrals and removed geographic barriers to treatment is ample, particularly in the areas of maternal child health, HIV/AIDS care and emergency medicine (Bakshi et al., 2011; Chang et al., 2011; Drescher et al., 2011; Espinoza et al., 2011; Garcia, Vargas, Caballero, Calle, & Bayer, 2009; John Haskew et al., 2015; J. Haskew et al., 2015; Karanja et al., 2011; Kubben et al., 2011; Lemay, Sullivan, Jumbe, & Perry, 2012; T. Lewis et al., 2012a; Musoke, 2012; Myers et al., 2012; Olouch, Katana, et al., 2014; Olouch, Kwaro, et al., 2014; Olouch et al., 2012; Shirabad, Wilk, Michalowski, & Farion, 2012; Tamrat & Kachnowski, 2012)

1.5 Significance

Firstly it aimed to improve the quality of care in the co-management of HIV and pregnancy in centralized and decentralized care environment and improve patient health, reduce rates of mother to child transmission of HIV and decrease the burden of neonatal HIV infection. It endeavoured to do this by providing evidence based treatment guidelines and access to participants' medical records and laboratory results and improving consultation and referral capabilities of providers in the decentralized care environment.

Secondly, the project aimed to address physician shortages in low resource environments via the enhancement of the care environment. By removing barriers to clinical and patient information and enhancing referral and consultative capabilities the ability of the workforce to manage HIV in pregnancy would be fostered and improved. In doing so, local capacity is developed, the local knowledge base is widened, professional development occurs, workflow processes could be streamlined and development fostered at the local level. All of these enhancements aim to promote development and equity in a sustainable manner.

Thirdly, the project aimed to add a tool to the open source medical information technology sphere that can be utilized in other care environments. As the EMR/CDSS will be made free and publicly available it has the capacity to be adopted and adapted to many different environments and enhance clinical care broadly using a primary, as opposed to vertical, public health approach. Stakeholders and beneficiaries are one and the same.

Finally, it will contribute to the published evidence base for mhealth's role in modern healthcare delivery. Robust, evidence based support for e-health and mhealth systems must be present in order for low and middle resource nations to justify application of funding to these projects. The WHO has called for the need to develop this evidence base (VanHeerden, Tomlinson, & Swartz, 2012).. As the evidence base for positive user experiences and facilitation of care grows, evidence regarding the affect of these programs on behaviours likely to facilitate virologic suppression remains scant. This study hopes to add to this literature and evidence base.

1.6 Overview of the study location

The pilot of the technology developed for this thesis occurred at Kakamega County General Hospital in Kakamega Town, Kakamega County in the former Western Province of Kenya. Kenya is a country of approximately 38.6 million people. It is located in eastern Africa and bordered by Ethiopia to the north, Somalia to the northeast, Tanzania to the south, Uganda to the west and South Sudan to the northwest. The coastline is along the Indian Ocean to the east. Kenya is bisected by the equator (Republic of Kenya, 2015). Kenya was a British Colony until the Mau Mau rebellion of the 1950s opened the doors to independence in 1963. The economy of Kenya is primarily agricultural and industrial (Republic of Kenya, 2015). Specifics of recent governmental reforms, the health care system, the epidemiology of the HIV epidemic and Kakamega County particulars will be presented in Chapters 2, 3, 4 and 5.

1.7 Overview of the thesis

Chapter One has provided a background to and rationale for the system development, system utilisation and the associated research.

Chapter Two commences with a discussion of the early history of the HIV epidemic. A discussion of the immunology of HIV, the HIV life cycle and how various classes of antiretroviral drugs hinder viral replication follows. The clinical course of untreated HIV infections is presented and this is followed by a description of how HIV infection is diagnosed and how response to antiretroviral therapy is monitored clinically, immunologically and virologically. The history of the HIV pandemic in the early era of antiretroviral therapy is followed by a discussion of how the course of the epidemic differed in low resource settings during this era. A discussion of the 2013 harmonisation of the WHO guidelines across the continuum of care, ART for all, special considerations for pregnancy and a discussion of service integration, decentralisation of care and task shifting follow.

Chapter Three discusses the HIV epidemic in Kenya from epidemiological, political and policy standpoints, including the effects of political devolution on HIV policy implementation. The 2014 and 2016 Kenyan National AIDS & STI Control Programme guidelines for perinatal HIV management are presented.

Chapter Four discusses e-health, mhealth, electronic medical records and clinical decision support systems. It will commence with an overview of the various types of systems in use currently. A literature review of the functionality of e- and mhealth systems, specifically within the realms of pregnancy and HIV care is presented. The Kenyan National e-Health Strategy 2011-2017 is reviewed and critiqued.

Chapter Five discusses the research design and methods used. The rationale and motivation for the study is discussed in detail. The framework will be reviewed and the reader referred to the relevant chapters. A discussion of the literature review and system design periods follow. The study setting, initial visit and training, the launch, continuation and cessation of the study and the return data collecting trip to Kakamega follows. A brief overview of the analysis stage will conclude the chapter.

Chapter Six begins with a brief presentation of the EMR/CDSS and then presents the design principles that underlay the system design and that should be adhered to when designing for the digital sphere in resource- constrained settings. An in depth system description follows. Additional ideal system elements that were not possible due to scope, technical and site restrictions are presented. A summary of the chapter follows.

Chapter Seven presents the challenges faced by this project in a chronologic, systematic and categorical fashion. It begins with a discussion of the financing problems encountered by Uamuzi Bora that necessitated their need to suspend their EMR/CDSS project that the system evaluated in this thesis was to run in conjunction with.

Chapter Eight presents responses to the research objections and questions. Following this is a review of the study output, namely the creation of a mobile technology enhanced, combined electronic medical record and clinical decision support system for the co-management of HIV and pregnancy. Recommendations from the study for community organisations, clinicians, policy and practice and recommendations for future research are reviewed. The significance of the study is reviewed and followed by a discussion of study limitation. A conclusion follows.

Chapter 2 The HIV/AIDS Pandemic

2.1 Introduction to the chapter

This chapter commences with a discussion of the early history of the HIV epidemic. A discussion of the immunology of HIV, the HIV life cycle and how various classes of antiretroviral drugs hinder viral replication follows. The clinical course of untreated HIV infection is presented and this is followed by a description of how HIV infection is diagnosed and how response to antiretroviral therapy is monitored clinically, immunologically and virologically.

The next section presents a history of the HIV pandemic in the early era of antiretroviral therapy and a discussion of how the course of the epidemic differed in low resource setting during this era. A discussion of the evolution of the guidelines for antiretroviral therapy and prophylaxis for pregnant women follows, and details differences between high resource and low resource settings and discusses why the regimens recommended for pregnant women have changed significantly over the past 30 years. The 2013 harmonisation of the WHO guidelines across the continuum of care, ART for all, special considerations for pregnancy and a discussion of service integration, decentralisation of care and task shifting summarise the chapter.

2.2 The early history of the HIV epidemic

In the June 5th 1981 issue of Morbidity and Mortality Weekly Report, 5 case studies of previously healthy homosexual men with *pneumocystic* carinii pneumonia (PCP) and concurrent or previous cytomegalovirus (CMV) infection and mucosal candida infection were reported. By the the time of the report's publication, two of these men had already died. All would be dead shortly after. The editorial note suggested "the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections such as pneumocystosis and candidiasis" (CDC, 1981). This represented the first report of what is now known as Acquired Immunodeficiency Syndrome or AIDS. Further reports noted more clusters of PCP and Kaposi's sarcoma (KS) in New York and California. By the end of 1981, there were a total of 270 case reports and 120 deaths (AIDS.gov, n.d.).

The Centers for Disease Control and Prevention (CDC) first used the term AIDS in 1982. By

the end of that year, the syndrome was reported in an infant that had received a blood transfusion and by early 1983 female sexual partners of men with AIDS were displaying symptoms of the syndrome (AIDS.gov, n.d.). The World Health Organization (WHO) held its first meeting in October of 1983 to establish a system of surveillance and assess the global situation with respect to the virus (AIDS.gov, n.d.). Also in 1983, Dr Robert Gallo of the US National Institutes of Health postulated that a retrovirus was responsible for the syndrome and by the end of that year both Dr Gallo and Dr Luc Montagnier of the Pasteur Institute in France had grown isolates of what would later be known as the Human Immunodeficiency Virus (HIV). By the end of 1984, Drs Gallo and Montagnier jointly announced that the viruses that they had grown were the same and indeed caused AIDS (AIDS.gov, n.d.).

The identification of the virus lead to the development of a screening tool in 1985 which not only allowed the virus to be detected in individuals but also lead to screening of the US blood supply (AIDS.gov, n.d.). By the end of 1985 the virus was given the official name Human Immunodeficiency Virus by the International Committee on the Taxonomy of Viruses and all regions of the world now reported cases of HIV infection and AIDS (AIDS.gov, n.d.).

In February of 1987, the World Health Organization launched the Global program on AIDS and in October, the UN General Assembly designated the WHO to lead the effort against HIV. That same year the WHO announced women with HIV outnumbered men in sub-Saharan Africa (Mann & Kay, 1991).

After elucidation of the virus responsible for AIDS in 1984, efforts towards the development of drugs to combat the virus began. The first antiretroviral drug, AZT, later named Zidovudine (ZDV), was proven to be effective against a murine form of leukaemia and later was shown to hinder the replication of HIV *in vitro* (Vella, Schwartländer, Sow, Eholie, & Murphy, 2012). Secondary to the efforts of activists, healthcare providers, scientists and political pressure, the US Food and Drug Administration rapidly approved AZT for use in 1987 after a short period of clinical trails (AIDS.gov, n.d.). The development of this and other antiretroviral agents ushered in a change in the course of lives of people living with HIV and led to a growing disparity in care and growth of the pandemic between resource rich and resource poor settings (Vella et al., 2012).

2.3 Immunology of HIV infection and principals of antiretroviral therapy

Understanding how the virus infects its host, is transmitted and the mechanisms of action of pharmaceutical agents is key to appreciating the successes and challenges to its control both on an individual level and within the public and global health spheres.

2.3.1 Transmission

The Human Immunodeficiency Virus is transmitted by the blood and body fluids of an infected individual. Semen, cervical secretions, lymphocytes, plasma, cerebrospinal fluid, tears, saliva, urine, breast milk and blood contain the virus, though urine, tears and saliva have not been shown to transmit virus. The recognized routes of infection are sexual (oral, anal and vaginal), via contaminated needles (injection drug use and needle stick injuries), perinatal transmission (from mother to child during pregnancy, birth and breastfeeding) and via organ, tissue and blood donation. There are two distinct types of HIV, HIV-1 and HIV-2. Both viruses cause an indistinguishable clinical syndrome though HIV-2 is less transmissible than HIV-1 and the epidemic is concentrated in West Africa. Generally, and for the purposes of this thesis, "HIV" will refer to HIV-1 unless otherwise specified (Adler, Edwards, Miller, Sethi, & Williams, 2012).

There are numerous risk factors for the transmission of HIV, behavioural, immunologic and virologic. A high viral load increases risk for transmission, especially when the person living with HIV is in the acute stage of infection. Receptive anal intercourse, sex without a condom and sex under the influence of recreation drugs increase likelihood of transmission of HIV, as does the presence of other sexually transmitted infections, particularly those manifesting with genital ulceration. Similarities between the HLA-class-I alleles in serodiscordant couples increases the likelihood of transmission. Male circumcision has been shown to reduce transmission of HIV (Bartlett, 2016).

Perinatal transmission of HIV, the transmission of HIV from infected mother to the foetus or infant could likely occur through a number of different mechanisms. It is thought that one third of infections occur during labour and birth via foetal exposure to HIV from blood and cervical secretions (Kourtis & Bulterys, 2010). Another potential mode of transmission occurs in the days before birth as the placenta begins to separate from the uterine wall or

through other antenatal events that cause maternal and foetal blood to mix such as trauma. HIV has also been isolated from amniotic fluid. Isolation of numerous strains of HIV in the newborn provides evidence that there exists the possibility of multiple transmission events in the peripartum period. Factors influencing perinatal transmission of HIV include a low CD4 count, high viral load at delivery, long periods of membrane rupture, maternal infection, prematurity, vitamin A deficiency, and illicit drug use (Kourtis & Bulterys, 2010; Levy, 2007). Female infants are at twice the risk level for infection compared to male infants (Kourtis & Bulterys, 2010).

It is estimated that 16% of all perinatal HIV transmission occurs through breastfeeding. Colostrum has been shown to be high in both free virus as well as virally infected cells and infection risk is highest in the first three months after birth and when the mother has been newly infected with HIV. The risk of transmission is the highest when the maternal CD4 count is low, the viral load is high and in conjunction with vitamin A deficiency, clinical mastitis, gastric maturity and various immune and genetic factors (Kourtis & Bulterys, 2010; Levy, 2007).

2.3.2 Infection and viral replication

Once HIV has entered the host, the virus is taken up at mucosal surfaces by dendritic cells, macrophages and CD4+ T cells. Binding of the viral envelope protein GP-120 to the CD4 receptor on the dendritic cells found in anogenital mucosa, cervicovaginal epithelium, tonsillar and adenoidal tissue mediates entry. The HIV virus enters the macrophages by endocytosis via the binding of GP-120 with receptors CCR5 and CD4. Binding of GP-120 with CXCR4 causes direct infection of CD4+ T cells (Moir, Chun, & Fauci, 2011; Sax, 2016).

After attachment of the viral envelope to the host cell receptor, the structure of the CD4 protein is altered to enhance entry. The viral envelope and the cell membrane fuse. The ARV class of drugs knows as fusion inhibitors act upon this stage to prevent fusion of the viral envelope with the cell membrane. After fusion, viral core associated RNA will enter the cytoplasm and create reverse transcriptase complexes. Reverse transcriptases synthesise viral RNA into DNA. Another class of ARVs act here to prevent this from happening. This class of drugs is called the reverse transcriptase inhibitors and are either classed as nucleoside or non-nucleoside reverse transcriptase inhibitors depending on their exact mechanism of action. The first antiretroviral drug developed, AZT, is a nucleoside reverse transcriptase

inhibitor (Adler et al., 2012).

Once the copy DNA is produced it then migrates into the cell nucleus where it will be integrated into the host cell's genome. The ARV integrase inhibitors inhibit the action of integration. The host cell will then create viral RNA from this incorporated DNA. Once created, the RNA will return to the cell cytoplasm where the RNA will be translated into viral protein. This viral protein is cleaved by protease and then reconstructed into new virus. The protease inhibitor class of ARVs works by preventing this cleavage. Once reconstructed the new virus leaves the cell by a process called budding (Adler et al., 2012).

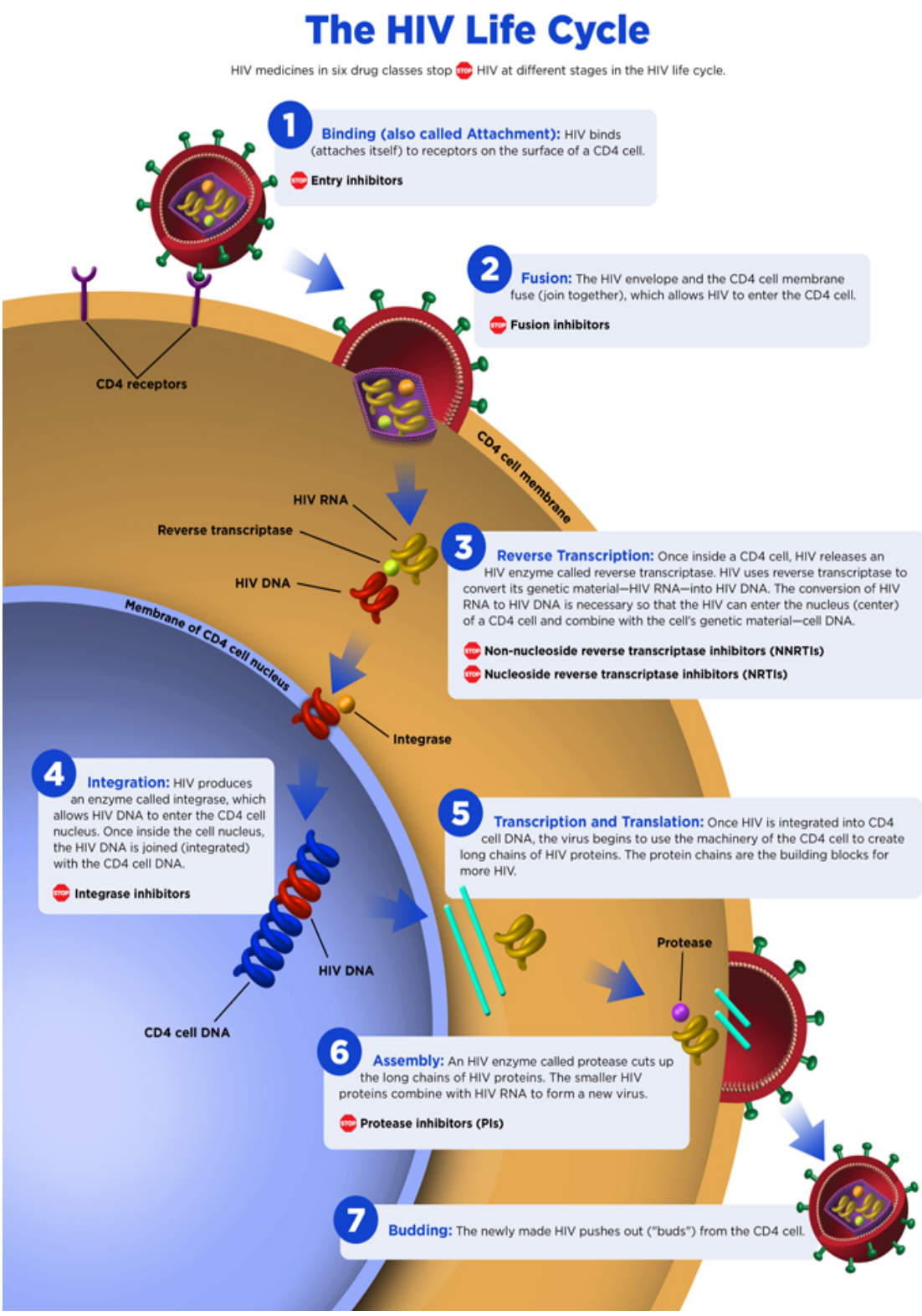
The following table presents the class, mechanisms of action, names and abbreviations of antiretroviral drugs. Currently, antiretroviral drugs are given in combination. This is referred to as highly active antiretroviral therapy (HAART) or combination ART (cART). This type of therapy achieves viral suppression via numerous mechanisms. The evolution of the guidelines in antiretroviral therapy will be discussed further in 2.6 The HIV pandemic in the era of antiretroviral therapy. First line treatment consists of two nucleoside or nucleotide reverse transcriptase inhibitors, referred to as the NRTI backbone, coupled with a non nucleoside reverse transcriptase inhibitor, a protease inhibitor or an integrase inhibitor (Bartlett & Sax, 2016b). Resistant viral strains may require second and third line therapies which may add additional drugs or substitute for drugs to which the virus is no longer susceptible (Adler et al., 2012). A table of approved antiretroviral drugs is presented below.

Table 2-1: Class, mechanisms of action, names and abbreviations of antiretroviral drugs (Medscape, 2014)

Class	Mechanism of action	Name and abbreviation
NRTI- nucleoside/nucleotide reverse transcriptase inhibitor	Competitive inhibition of HIV reverse transcriptase-reverse transcriptase allows HIV RNA to be transcribed into DNA Active against HIV-1, HIV-2	Abacavir (ABC) Didanosine (ddI) Emtricitabine (FTC) Lamivudine (3TC) Stavudine (d4T) Tenofovir (TDF) Zalcitabine (ddC) Zidovudine (ZDV, AZT)
NNRTI- nonnucleoside reverse transcriptase inhibitors	Non-competitive binding to reverse transcriptase-reverse transcriptase allows HIV RNA to be transcribed into DNA Activity against HIV-1	Delaviridine (DLV) Efavirenz (EFV) Nevirapine (NVP) Etavirine (ETR) Rilpivirine (RPV

Class	Mechanism of action	Name and abbreviation
PI-protease inhibitors	Competitively bind to HIV protease- protease cleaves proteins for the creation of viral capsids Activity against HIV-1, HIV-2 Ritonavir is often used to boost activity of other PIs by depleting metabolic enzymes	Atazanavir (ATV) Darunavir (DRV) Fosamprenavir (FPV) Indinavir (IDV) Lopinavir (LPV) Lopinavir/Ritonavir (LPV/r) Ritonavir (RTV) Nelfinavir (NFV) Saquinavir (SQV) Tipranavir (TPV)
INSTI- Integrase strand transfer inhibitors	Selective integrase inhibitors- integrase transports and attaches proviral DNA to host cell DNA Activity against HIV-1	Raltegravir (RAL) Elvitegravir (EVG) Dolutegravir (DTG)
Fusion inhibitors	Inhibit fusion of the HIV virus to CD4 receptor	Enfuvirtide (T-20)
Chemokine receptor antagonists	Selectively binds to the CCR5 coreceptor inhibiting fusion of the HIV virus	Maraviroc (MVC)

Figure 2-1: The HIV lifecycle (AIDSinfo, 2014)



2.3.3 Immune response to HIV infection

After entry of the virus into the host and host's cells, the virally infected cells migrate to regional lymph nodes causing further infection of CD4+ T cells. At this stage, there is an ample supply of susceptible CD4+ T cells and the host immune system is naïve to HIV, leading to a massive initial burst in viral replication. A partially, but not completely effective virus-specific CD8+ T cell response will eventually be elicited leading to the reduction in viral load and the establishment of a set point HIV viral load (Moir et al., 2011; Sax, 2016).
The virus is particularly adept at evading the host immune system through a number of different mechanisms (Adler et al., 2012):

- The portion of the virus that antibodies created by the immune system recognizes is buried deep within the core of the virus and surrounded by glycoprotein spikes, preventing binding of antibodies to this region
- The host's normal interferon-based immune responses are inhibited by the HIV-1 virus
- The reverse transcriptase of the virus is very error prone, which leads to a high rate of mutation of the virus, a mutation rate of about 1/3, this has two effects:
    - To create a new strain that may not be recognized by the immune system
    - These new mutations result in strains of virus that further inhibit the immune system's signalling pathways for immune response activation.
- As detailed above, the viral DNA integrates itself into the host cell's genome. The replication of the virus may not be activated for many years, leading to a persistent reservoir of HIV infection, potentially in the gut associated lymphoid tissue (GALT) and out of reach of the host's immune defence system (Adler et al., 2012; Moir et al., 2011; Sax, 2016).

What causes reactivation of the latent reservoirs is poorly understood (Adler et al., 2012).

2.3.4 The homeostatic period

During the periods of relative homeostasis between the initial acute infection and the severe immune dysfunction that causes AIDS, low levels of viral replication continue along with depletion of the host's immune system. Of particular significance is the depletion of CD4 lymphocytes though multiple avenues of immune dysregulation that are caused by the virus (Adler et al., 2012). Drainage from the lymph nodes to the GALT during the acute phase of

infection leads not only to the massive initial drop in CD4 +T cells, but also may represent the site of chronic low level viral replication as well as the chronic immune activation associated with HIV infection (Sax, 2016). Indeed lymphoid tissue in general is the site of chronic HIV infection. HIV replication continues here along with CD4+ T cell death. During the chronic phase, however, the incomplete immune defence against HIV coupled with the rate of creation of new CD4+T cells is enough to allow both of these factors to remain in relative balance (Bartlett, 2016).

Eventually, the constant immune depletion coupled with the reactivation of high levels of viral replication cause a severely immunocompromised state. It is during this stage that opportunistic infections, infections that would be controlled by a normal immune system, occur and the host, without effective antiretroviral therapy, will eventually succumb (Adler et al., 2012; Moir et al., 2011).

2.4 The clinical course of natural HIV infection

2.4.1 Initial infection

Untreated, the clinical course of HIV infection follows a relatively predictable route. Primary HIV infection, the stage of infection that corresponds with the initial spike in viral replication and immune depletion described above, manifests with symptoms ranging from a mild febrile illness, often accompanied by a rash and lymphadenopathy, to encephalopathy. As these symptoms could easily be attributed to any number of other processes, the diagnosis of acute HIV infection is often missed. Until recently, effective mechanisms for identifying infection in the acute stage have been unavailable, further complicating diagnosis. Individuals with acute HIV infection are highly infectious due to the spike in viral load (Sax, 2016). As most people at this stage are unaware that they are infected with HIV, this is a critical time in HIV transmission (Adler et al., 2012).

2.4.2 Homeostasis

As described above, a period of homeostasis follows the acute stage of infection. During this stage, individuals are generally asymptomatic. This period generally lasts between 5 and 10 years though there are some people who progress from acute infection to AIDS in less than a year and some who have been infected with HIV for much longer than 10 years who have not progressed to AIDS (Adler et al., 2012). These individuals are referred to as elite

controllers and are relatively rare (Sax, 2016).

2.4.3 Reactivation

Eventually, unknown mechanisms cause reactivation of latent reservoirs of HIV, likely in the gut and lymphoid tissue (Moir et al., 2011; Sax, 2016). As gradual immune depletion has been occurring during the period of asymptomatic infection, the immune system is poorly equipped to contend with this increase in replication and the resultant immunosuppression eventually leads to susceptibility to the multitude of infectious processes characteristic of AIDS. In the pre- ART era, management of AIDS focused on pharmacologic therapy as prophylaxis against and to treat these opportunistic infections rather than controlling viral replication. Prior to the discovery and use of antiretroviral therapies, AIDS eventually resulted in death (Adler et al., 2012).

2.5 Diagnostic tools, WHO clinical staging, immunologic and virologic evaluation of HIV disease progression

2.5.1 Diagnostic tools

Early forms of testing for the HIV virus emerged in the mid 1980s. Screening tests evaluated the presence of HIV antibodies in the serum of an infected person and did not differentiate between HIV-1 and HIV-2. These tests required confirmatory testing with a Western Blot assay to confirm the presence of HIV and to differentiate between HIV-1 and HIV-2. These assays had a 'window period' between infection and the ability of HIV to be diagnosed of around 3 months. The newer fourth generation tests have a much higher sensitivity and a much shorter window period as they test for both antibodies to HIV-1 and HIV-2 and the p24 HIV antigen (Bartlett & Sax, 2016a). HIV testing can either be performed in a laboratory or at the point of care. Point of care testing provides a screen for HIV antibodies and returns results in about 30 minutes. This must be confirmed by laboratory analysis. These types of test have high utility when a screening result is essential for management decision making such as when a pregnant woman presents for care in labour who does not know her HIV status. The table below presents the different types of tests used in the diagnosis of HIV, the time to a positive test from infection, and comments about their use (Adler et al., 2012).

Table 2-2 HIV tests (Adler et al., 2012)

Test	Use	Comments
HIV antibody tests	Screening and diagnosis	Positive results returned 21-28 days after infection.
P24 antigen test	Diagnosis	Detect HIV-1 and HIV-2 9-11 days after infection Combined HIV antibody and p24 antigen testing is the current diagnostic standard
Plasma HIV-1 RNA load	Diagnosis and monitoring	Steady state observed 6 months after diagnosis Gold standard for monitoring response to HIV antiretroviral therapy.
Proviral DNA testing	Diagnosis	Diagnosis of babies born to HIV + mothers Used in cases of indeterminate antibody based tests.
Drug resistance monitoring	Monitoring	Monitors resistance to antiretroviral drugs, useful before initiating therapy and in cases of sub-optimal therapeutic response to antiretroviral therapy.
HIV-1 tropism	Monitoring	Detects whether a strain of HIV will positively respond to CCR5 antagonist treatment options

2.5.2 WHO clinical staging

The WHO released clinical guidelines for determining the stage of HIV infection in 1990 for use in low resource settings. This was critical to surveillance and monitoring in regions without access to laboratory analysis. The staging guidelines were subject to a number of revisions, namely to account for the effects of ART on the course of HIV infection. The staging describes the multitude of adverse effects and opportunistic infections that accompany infection with HIV. Though currently not the preferred metric for evaluation of HIV disease progression, the WHO clinical stages will be referred to throughout the following sections and what follows is the 2007 version of the clinical stages for adults and

adolescents.

Clinical stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy (PGL)

Clinical stage 2

- Moderate unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (RTIs, sinusitis, bronchitis, otitis media, pharyngitis)
- Herpes Zoster
- Angular chelitis
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections of fingers

Clinical stage 3

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month
- Unexplained persistent fever above 37.6 degrees (intermittent or constant for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (TB), current
- Severe presumed bacterial infections (e.g. pneumonia, emphyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8g/dl) and/or neutropenia (<500/ml) and/or chronic thrombocytopenia (<50000/ml)

Clinical stage 4

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one

month's duration or visceral at any site)

- Oesophageal candidiasis (or of trachea, bronchi or lungs)
- Extrapulmonary TB
- Kaposi's sarcoma
- Cytomegalovirus (CMV) infection (retinitis or other organ)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculosis mycobacteria infection
- Progressive multifocal leukoencephalopathy (PML)
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated mycosis (histoplasmosis or coccidiomycosis)
- Recurrent non-typhoidal Salmonella bacteraemia
- Lymphoma (cerebral or B cell non-Hodgkin) or other solid HIV-associated tumours
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy (World Health Organization, 2007)

2.5.3 Immunologic staging

Immunologic staging of HIV infection correlates CD4 cell count levels with severity of disease by relating CD4 count to levels of immunosuppression. A normal absolute CD4 count in adults and adolescents is between 500-1500 cells /ml of blood. This type of staging of HIV infection remained a critical element to determining when a person should start antiretroviral therapy for HIV infection and whether a person requires prophylaxis for opportunistic infections until the 2015 guideline revisions for ART initiation (World Health Organization, 2015a). CD4 counts generally rise in response to effective ART and though CD4 counting is not currently used to monitor response to ART, it has been in the past and was at the time that the EMR/CDSS was created. Recurrent CD4 measurements are necessary, however, to determine immunologic response to therapy as well discontinuing or continuing prophylaxis for opportunistic infections in certain settings (World Health Organization, 2007). The following immunologic classifications of HIV associated immunodeficiency are relevant for ages above 5 years:

Table 2-3 Immunologic staging (World Health Organization, 2007)

HIV-associated immunodeficiency	Absolute CD4 value per ml of blood
None or not significant	≥ 500
Mild	350-499
Advanced	200-349
Severe	<200

2.5.4 Viral load monitoring

Viral load measurements are currently considered the most important measurement to monitor response to ART. Viral load measurements should occur before the initiation of therapy and at intervals thereafter. The optimal viral load level would be below detectible limits (generally < 20- 40 copies/ml for the newest tests, the real-time reverse transcriptase polymerase chain reaction (RT-PCR) tests (Caliendo, 2015). The CDC currently considers viral loads above 200 copies/ml to indicate virologic failure- failure of the virus to adequately respond to ART (AIDSinfo, 2013a).

Virologic failure can be caused by numerous factors including poor tolerability of drugs, missed doses and drug resistance. Drug resistance testing is recommended with persistent low level viremea though may be more difficult at levels below 500 copies/ml. Treatment failure is defined as viral load persistently above 1000 copies/ml over a 6 month period and requires regimen change and resistance testing in clinical situations that can support it (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2013a). The highest rates of perinatal transmission of HIV are seen at viral load levels above 1000 copies/ml though perinatal transmission has been noted at undetectable viral load levels as well (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)

2.6 The HIV pandemic in the era of antiretroviral therapy

2.6.1 AZT

The nucleoside reverse transcriptase inhibitor (NRTI) AZT was approved by the US Food and Drug Administration in 1987 as the first antiretroviral agent to control HIV. This drug is also called Zidovudine and carries the abbreviation ZDV. As the WHO guidelines have

consistently referred to the drug as AZT, this thesis will use the same abbreviation. Clinical trials prior to AZT's approval demonstrated better survival rates at 24 weeks of therapy though these effects disappeared by 48 weeks. The drug received US FDA approval for advanced stage AIDS in 1987 despite the modest efficacy and major side effects associated with it (Vella et al., 2012).

AZT monotherapy was the standard of care where it could be afforded through the late 1980s and into the early 1990s. This therapy had modest short-term benefit but did not demonstrate overall increase in life expectancy for those with AIDS, was associated with major and debilitating side effects and the quality of life for those with AIDS remained low and death imminent. By 1989, evidence was emerging of viral resistance to AZT. By 1993 results supporting the lack of effect of AZT on long term survival were presented at the Berlin AIDS conference (Vella et al., 2012).

The Pediatric AIDS Clinical Trail Group 076 results published in 1994, however, did demonstrate that AZT monotherapy was effective in reducing perinatal transmission of HIV by 70% when initiated at 14 weeks of gestation. These results led to further studies evaluating shorter courses of AZT administration to prevent perinatal transmission and AZT monotherapy did become the standard of care for the prevention of perinatal transmission of HIV for many years (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

2.6.2 Early trials of combination therapy

Development of the other early NRTIs zalcitabine (ddC), stavudine (d4T) and didanosine (ddI) in the early 1990s lead to the first combination therapy approaches. These approaches involved using two or three NRTIs together. Clinical trials showed an increase in CD4 count and evidence of better survival rates with combination therapy but this approach retained the problems of high levels of toxicity and major side effects. By 1995 the importance of quantification of circulating viral load levels and the correlations of viral load levels to clinical course became better described as did the mechanisms of drug resistance (Vella et al., 2012). Two new classes of antiretroviral drugs, the non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) were developed during the mid 1990s. Resistance to the first NNRTI, nevirapine developed quickly when used as monotherapy, but when used in combination with 2 other NRTIs, the effects were far superior to other monotherapies or combination therapies (Vella et al., 2012).

Combination therapy approaches were maximised with a double NRTI backbone with the addition of either a PI or a NNRTI. The superior effects of what came to be known as highly active combination antiretroviral therapy or HAART were presented at the Vancouver 11th International AIDS conference in 1996 and the era of HAART was ushered in. The early years of HAART brought many people diagnosed with AIDS back from the brink of death. The debilitating side effect profiles and high pill burdens associated with the drugs kept quality of life poor for many people on ART during the early years of HAART and the cost of this therapy approached $20,000 USD per year. Many high resource governments like Australia (Bowtell, 2005) and the United States (Health Resources and Services Administration, n.d.) were able to subsidise these costs but HAART remained out of reach for most of those in middle and low-income nations (Vella et al., 2012).

2.7 ART in low resource settings

While death rates from AIDS were declining in high-resource areas, antiretroviral therapy availability remained scant to non-existent in low resource settings. Recognising the inability of low- resource nations to be able to afford the high cost of HAART, Peter Piot, director of UNAIDS, launched the Drug Access Initiative in 1997. The first introduction of antiretroviral therapy into sub-Saharan Africa came in December of that year and the international community mobilised to rectify these and other disparities in ART and HIV services access (Vella et al., 2012). The International AIDS Conference in Geneva in 1998 addressed inequities between rich and poor countries, power and autonomy disparities between men and women and the differences in the abilities of governments and civil society to combat the pandemic (Vella et al., 2012). By 1999 AIDS became the number one killer in Africa; a generation was lost to AIDS and millions of orphans and vulnerable children were left in AIDS's wake (AIDS.gov, n.d.).

2.7.1 Focusing on treatment

The Durban International AIDS Conference in 2000 reiterated the need to focus on treatment, prevention and care in the low-resource world and in sub-Saharan Africa in particular (Vella et al., 2012). One hundred and ninety seven nations signed onto the UN Declaration on Millennium Development Goals which included to 'combat HIV/AIDS, malaria and other diseases; halt by 2015, and begin to reverse the spread of HIV/AIDS; achieve by 2010, universal access to treatment for HIV/AIDS for all those who need it; halt by 2015, and begin to reverse, the incidence of malaria and other major diseases'. The

'Accelerating Access Initiative' was created by UNAIDS, WHO, UNICEF, UNPF, the World Bank and the Pharmaceutical Industry to encourage a decrease in antiretroviral drug prices leading the way to a tiered pricing system agreed upon by the European Union, UNAIDS and WHO, among others (Vella et al., 2012).

2.7.2 The TRIPS agreement

While treatment costs for first line therapies continued to drop in high- income nations, the pricing remained prohibitively expensive for low-income countries. Laboratories in Brazil, India and Spain began to produce generic versions of the antiretrovirals and their proof of efficacy was soon established (Vella et al., 2012). In 2000 UNAIDS and WHO created a joint initiative to reduce the costs of drugs in resource limited settings (AIDS.gov, n.d.). The World Trade Organization in November of 2001 adopted the Declaration on the TRIPS (Trade Related Aspects of Intellectual Property Rights) Agreement and Public Health as part of the Doha Declaration. The TRIPS agreement established basic levels of intellectual property protections that must be afforded by WTO partners to each other, but allowed that, while intellectual property protection remained important to development of novel technologies and pharmaceuticals, that in times of national emergency- including public health emergencies, low resource nations could issue licenses to manufacture drugs necessary to combat disease- namely HIV/AIDS, tuberculosis and malaria (Moberg, 2014; World Trade Organization, 2001).

Since the invocation of the TRIPS agreement, however, there has been a steady undermining of its core principles and what exists now is referred to often as TRIPS-plus. TRIPS-plus has arisen mainly as a result of bilateral and multilateral agreements between developed countries and between developed and developing countries, the effect of which has been to increase intellectual property protections for developed countries and erode the flexibility around these protections meant to foster and protect the public health and environmental and social welfare of developing countries as envisioned in the original TRIPS agreement (Moberg, 2014).

2.7.3 The global health agenda in the new millennium

In July of 2002 UNAIDS estimated that the life expectancy in sub-Saharan Africa had

decreased from 62 to 47 years of age because of AIDS and that it was, by far, the number one cause of death. UNAIDS estimated that 10 million young people were affected, 3 million children under fifteen had AIDS, there would be 3.5 million new infections in that year and that 2.4 million deaths could be expected (AIDS.gov, n.d.). The first UN treatment guidelines were issued in 2002 and focused on scaling up antiretroviral therapy using a public health approach and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) was established that same year (The Global Fund, 2014).

The mid 2000's global health HIV agenda focused on increasing access to antiretroviral therapy in low resource settings and developing policies to address these issues. The 2003 creation of PEPFAR, the US President's Emergency Plan For AIDS Relief committed $15 billion US dollars over 5 years to combatting the epidemic. A strong component of this plan focused on treatment. In the same year the United Nations' '3 x 5' plan was launched, aiming to initiate 3 million people on combination ART by 2005. This goal was eventually reached in 2010. The Gleneagles G8 summit of 2005 committed to near universal access to ART in the developing world. During this period, new classes of drugs such as the fusion and entry inhibitors and fixed dose tablets of combination therapies were approved with increased tolerability and simplified dosing schedules (Vella et al., 2012).

2.7.4 Realising gains and Fast-track 2030

Indeed great gains have been made during this millennium. By 2013, new infections were estimated at 2.1 million, a decrease of 38% from 2001, the number of AIDS related deaths had decreased 35% from the peak death rate in 2005 and 13.6 million people were receiving ART by June 2014, an estimated 38% of adults and 24% of children eligibleby guidelines of the time. More young people are aware of HIV prevention behaviours and fewer are initiating sex and reporting multiple partners and more people report using condoms during the 2007-2013 period compared with the 2001-2005 period (UNAIDS, 2014b). There continue to be gaps however among key populations and particularly, sex workers, men who have sex with men and people who inject drugs (UNAIDS, 2014b).

Funding continues to increase across the board but has shifted from deriving from international donations to the most affected countries contributing much funding for their own programs, US$19.1 billion in 2013 by low and middle income countries. The Fast-track approach to ending the AIDS epidemic by 2030 cites the need for US $22-24 billion by 2015 (UNAIDS, 2014b).

The UNAIDS Fast-track approach envisions 90% of people living with HIV knowing their status, 90% of those on ART and 90% of those achieving viral suppression, and a reduction to 500,000 new infections among adults by 2020. It further envisions 95% of people living with HIV knowing their status, 95% of those on ART and 95% of those virally supressed, reducing to 200,000 the number of new infections among adults and zero discrimination by 2030 (UNAIDS, 2014b). This approach requires that goals be achieved through a holistic view and on a sustainable basis. Goals such as: improvement in access to testing and treatment services, confronting deterrents to access to services and the fostering of education, social protection, health and gender equality. Notable to this approach is the understanding that discrimination drives many barriers to effective engagement with services and requires that discrimination be fought alongside HIV (UNAIDS, 2014b).

Fast-track 2030 envisions the avoidance of 21 million AIDS related deaths, 28 million new HIV infections, 5.9 million infections among children and a return of 15- fold on HIV investments between 2015 and 2030 (UNAIDS, 2014b). One must keep in mind, however, that the goal of increasing antiretroviral therapy access, especially for 2nd and 3rd line ARVs will require that generic therapies be available, and this is potentially threatened by the multitude of work-arounds associated with TRIPS-plus (Poku, 2016).

2.8 The evolution of the prevention of perinatal transmission of HIV

2.8.1 The four- pronged approach

There are many facets to the prevention of perinatal transmission of HIV and programmatic approaches have taken into consideration the socioeconomic and biologic factors that lead to the increasingly heavy burden of HIV among women. The World Health Organization has advocated a four-pronged approach to preventing and addressing the perinatal transmission of HIV by:

- The primary prevention of HIV infection among women and their partners
- The prevention of unintended pregnancy through family planning programs
- The prevention of mother-to-child transmission of HIV through the provision of antiretroviral therapy and safe birth practices and infant feeding practices
- The long term care and support of people living with HIV (World Health Organization, 2004)

This section will focus on the third of the four prongs, the prevention of perinatal transmission.

2.8.2 Antenatal and intrapartum care

Antenatal care services provide an opportunity to identify certain pregnancy related high-risk conditions, malnutrition and many other chronic and acute medical conditions that may affect a pregnant women and her foetus as well as promote skilled birthing services. It provides an ideal opportunity diagnose HIV infection and to initiate ART services and provide prophylaxis for and management of opportunistic infections in the peripartum period.

Practices during labour and birth influence the perinatal transmission of HIV to the infant and ART must be used in combination with prudent obstetric practices to minimize transmission. While elective caesarean section prior to delivery in cases of viral load levels above 1000 copies per ml has proven to drastically reduce perinatal transmission rates, elective caesarean delivery is not a safe or feasible option in many parts of the resource constrained world. Optimal intrapartum care for HIV positive women will also include:

- Skilled, facility based labour and birth care
- Minimisation of vaginal examinations
- Use of aseptic techniques when conducting deliveries
- Avoidance of artificial rupture of membranes
- Avoidance of prolonged labour and rupture of membranes
- Avoidance of unnecessary trauma and invasive monitoring techniques
- Minimisation of the risk of post partum haemorrhage
- The use of safe blood transfusion practices (Cunningham et al., 2001; Republic of Kenya Ministry of Health, 2012a).

2.8.3 Antiretroviral drugs during the peripartum period

With respect to the use of antiretroviral therapy during pregnancy, the guidelines have significantly evolved throughout the last two decades as large studies in high, middle and low resource settings have elucidated both efficacy and safety of antiretroviral drugs in pregnancy and the breastfeeding period for the woman, her developing foetus and her infant.

Recommendations generated for resource limited settings have had to additionally take into account cost, availability, programmatic concerns and issues such as the safety of replacement feeding for infants in addition to safety and efficacy profiles of antiretroviral therapy, all utilising the public health approach, and as such, recommendations for resource rich and resource limited settings remain different to this day (World Health Organization, 2006).

2.8.4 Prophylaxis versus treatment

Prior to 2015, guidelines for initiation of ARV for pregnant women made a distinction between treatment for the woman's health and treatment purely for the prevention of perinatal transmission of HIV, as, until 2010, WHO treatment guidelines did not advocate HAART regimens below specific clinical stages and above specific CD4 counts and advocated instead for partially suppressive AZT containing regimens as outlined below for the prevention of perinatal HIV transmission when ART was not needed for the woman's health (World Health Organization, 2010c, 2013a, 2015a).

2.8.5 The evolution of ART regimens for the prevention of perinatal transmission of HIV

The Pediatric AIDS Clinical Trials Group 076 finding of 1994 demonstrated a 68% reduction to 8.3% in the incidence of perinatal transmission of HIV as measured at 18 months of age with AZT monotherapy initiated at 14 weeks of gestation and with 6 weeks of infant AZT prophylaxis in non-breastfeeding populations in the United States and France. Following the early results of this trial, AZT monotherapy became the standard of care for the prevention of mother-to-child transmission of HIV where available (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014). Subsequent to this study, shorter courses of AZT monotherapy regimens were trailed for both mother and infant with an aim to create simplified regimens for resource-constrained environments. Decreases in transmission rates over placebo were seen with these regimens though the regimens with longer antepartum prophylaxis duration were proven to be more efficacious (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

NVP alone and in combination with AZT was trialled after its advent in 1996 and regimens

containing 3TC were added when it became available in 1997, all showing significantly decreased rates of transmission over placebo (World Health Organization, 2001). As with the non-pregnant population, the benefits of triple therapy were evident in pregnant women being treated for their own health by 1998. HAART, along with elective caesarean section before labour for women with viral load levels above 1000 copies/ml and exclusive infant formula feeding, had decreased the rates of perinatal transmission to below 2% in many locations advocating this approach (World Health Organization, 2001).

By 2002, CDC guidelines recommended that all pregnant women living with HIV be placed on AZT irrespective of viral load, CD4 count and clinical staging for the prevention of perinatal transmission of HIV and that all women should also be offered combination antiretroviral therapy, ideally with a regimen containing AZT. At this stage, though some adverse effects of antiretroviral therapies on the developing foetus were understood, including the risk of neural tube defects with first trimester administration of EFV, and haematological disturbances in people taking AZT, the teratogenicity (birth defect) profiles and antepartum effects of many newer ARVs were still unknown. As such, recommendations regarding HAART versus AZT alone or in combination with NVP purely for the prevention of perinatal transmission of HIV in the antepartum period were not firm. Women initiating ARV purely for the prevention of perinatal transmission were encouraged to start after the first trimester. Women already on therapy were given the option of discontinuing if pregnancy was discovered in the first trimester, acknowledging that this would likely cause rebound increases in viral load and decreases in CD4 counts. Though the clear benefits to maternal health with triple therapy were well understood, women needing this therapy were counselled about the option to decline it secondary to poorly understood teratogenicity and foetal adverse effect profiles. The complete avoidance of breastfeeding in high resource nations with safe infant feeding alternatives is advocated to eliminate the potential of HIV transmission through breastfeeding (Mofenson, 2002).

The WHO guidelines for the prevention of mother-to-child transmission has followed a similar course with respect to differentiating between ART for maternal benefit and ARV for the prevention of perinatal transmission as well as discontinuing any ARVs that were started prior to pregnancy until 10 weeks or switching to a non- EFV containing regimen during the first trimester (World Health Organization, 2002). The 2002 WHO guidelines recommended initiating triple therapy for women diagnosed with HIV during pregnancy either at WHO Clinical Stage IV regardless of CD4 count, or if CD4 count was unavailable, or if CD4 count was less than 200 cells per ml and the woman was at WHO Clinical Stage I, II or III. ART was to be initiated after the first trimester, though weighing the risks of maternal health

versus potential foetal benefit of delay. A dual NRTI backbone, generally AZT + 3TC plus a NNRTI, generally ABC secondary to cost and availability, was the recommended regimen for pregnant women in need of treatment for their own health at this time (World Health Organization, 2002).

The World Health Organization advocated for short course, partially suppressive antiretroviral therapy regimes purely for prevention of perinatal transmission until 2010. Though evidence had emerged by the issuance of the WHO 2004 guidelines to the decreased rates of transmission associated with HAART during pregnancy, due to potential difficulties of establishing and maintaining HAART programs in low resource settings, the still poorly understood potential adverse effects of antiretroviral drugs on the foetus and infant and the high cost of HAART regimens, the WHO continued to advocate short course, only partially suppressive regimens for the prevention of perinatal transmission. The 2004 WHO guidelines included the following regimens:

- AZT daily from the third trimester of pregnancy alone with a one-week infant AZT course with or without single dose NVP during labour and for the infant soon after birth.
- AZT plus 3TC daily from the third trimester of pregnancy with a one week infant AZT course with or without single dose NVP during labour and for the infant soon after birth
- Single dose NVP in labour and a single dose of NVP for the baby soon after birth (World Health Organization, 2004)

The WHO acknowledged during this period that breastfeeding still remained an important route of perinatal transmission. The ARVs used during pregnancy and labour did persist in the maternal circulation for some time after birth, which would have some protective effect on transmission while breastfeeding, as did the infant prophylaxis. Evidence was insufficient at this period to recommend continuing antiretroviral therapy purely for the prevention of perinatal transmission during the breast feeding period at this time however (World Health Organization, 2004).

As evidence continued to emerge about both the safety of ART during pregnancy and optimal times to initiate ART in both pregnant and non- pregnant populations, 2006 WHO guidelines revised the CD4 count threshold at which to initiate treatment for the woman's health. The 2006 WHO recommendations advised to treat for maternal health at clinical stages I and II if CD4 count was less than 200 cells/ml. To treat at stage III if CD4 counting capabilities were not available, or if CD4 count was less than or equal to 350 cells/ml. The

WHO recommended treatment for maternal health at clinical stage IV regardless of CD4 count. By this stage, issues of resistance were better understood and guidelines stipulated that a 7 day AZT/3TC tail would be needed to prevent resistance to NVP when single dose NVP had been given during labour (World Health Organization, 2006).

The WHO released new guidelines in 2010 in response to new evidence emerging in support of earlier initiation of ART in pregnant women for the prevention of perinatal transmission and extending this ART through the breastfeeding period. Rates of perinatal transmission in non-breastfeeding populations could be reduced to below 2% and below 5% in breastfeeding populations with the proper application of the new regimen (World Health Organization, 2010a). Key to this recommendation is the understanding that accessibility to replacement feeding is not always affordable, feasible, acceptable, sustainable and safe (World Health Organization, 2010b). Hence, the WHO supported nations to develop individual policy with respect to the promotion of replacement or breastfeeding among HIV positive women and made the following recommendations in settings where national or sub-national authorities are in support of breastfeeding *and* ARV interventions for HIV positive women:

Recommendation 1

Mothers known to be HIV-infected should be provided with lifelong ART or ARV prophylaxis interventions to reduce HIV transmission through breastfeeding according to WHO recommendations.

Recommendation 2

Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

Recommendation 3

Mothers known to be HIV-infected that decide to stop breastfeeding at any time should stop gradually within one month. Mothers or infants who have been receiving ARV prophylaxis should continue prophylaxis for one week after breastfeeding is fully stopped. Stopping breastfeeding abruptly is not advisable.

Recommendation 4

When mothers known to be HIV-infected decide to stop breastfeeding at any time, infants

should be provided with safe and adequate replacement feeds to enable normal growth and development.

Alternatives to breastfeeding include, for infants less than six months of age:

- Commercial infant formula milk as long as home conditions outlined in recommendation #5 are fulfilled;
- Expressed, heat-treated breast milk (see Recommendation #6).
- Home-modified animal milk is not recommended as a replacement food in the first six months of life.

For children over six months of age:

- Commercial infant formula milk as long as home conditions outlined in Recommendation #5 are fulfilled;
- Animal milk (boiled for infants under 12 months), as part of a diet providing adequate micronutrient intake;
- Meals, including milk-only feeds, other foods and a combination of milk feeds and other foods, should be provided four or five times per day. All children need complementary foods from six months of age.

Recommendation 5

Mothers known to be HIV-infected should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status, when specific conditions are met:

- Safe water and sanitation are assured at the household level and in the community; and
- The mother, or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant; and
- The mother or other caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and
- The mother or caregiver can, in the first six months, exclusively give infant formula milk; and
- The family is supportive of this practice; and
- The mother or caregiver can access health care that offers comprehensive child health services.

Recommendation 6

Mothers known to be HIV-infected may consider expressing and heat-treating breast milk as *an interim feeding strategy:*

- In special circumstances such as when the infant is born with a low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; or
- When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis; or
- If antiretroviral drugs are temporarily not available

Recommendation 7

If infants and young children are known to be HIV-infected, mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding as per the recommendations for the general population, that is, up to two years or beyond (World Health Organization, 2010b).

2.8.6 Towards elimination of perinatal transmission of HIV

The WHO now envisioned the elimination of paediatric HIV infection through perinatal transmission (World Health Organization, 2010c). The WHO revised upwards the CD4 count eligibility for ART for maternal health to equal to or below 350 cells/ml and advised that women in need of ART for their own health be initiated on therapy for life. Options for prevention of perinatal transmission were now termed "Option A" which was a partially suppressive regimen and based upon earlier PMTCT regimens or "Option B" which was a fully suppressive triple drug regimen. Both were extended into the breastfeeding period. The correlation between CD4 counts above 250 cells/ml in pregnant women taking NVP and the risk of hepatic abnormalities were acknowledged in these guidelines, though NVP remained a recommended ARV for pregnant women (World Health Organization, 2010a).

By 2012, a WHO technical update streamlined the 2010 guidelines by no longer recommending Option A and adding an option B+, the initiation of antiretroviral therapy in all pregnant women for life. This was in response both to continued emerging evidence about the benefits of early initiation of ART and the importance of ART in prevention of sexual transmission of HIV. Though the ARV components of Options B and B+ at the time of the publication of the programmatic update were of higher cost than continuing with Option A, overall savings were anticipated to make up for the cost increase (World Health Organization, 2012b). The WHO argued that this new fully suppressive regimen

recommendation provides a number of benefits, namely:

Programmatic simplification of adopting a single recommended regimen that does not require CD4 counting for initiation

- Likely overall benefit to women's health
- Likelihood that women will need ART for their own health within 2 years of diagnosis
- Coherence with other ART programs
- Prevention of sexual transmission, especially within serodiscordant couples
- Prevention of perinatal transmission in future pregnancies by pre-conception prophylaxis
- Avoidance of the stopping and starting of drugs and increases in drug resistant strains of HIV (World Health Organization, 2012b)

Table 2-4 2010, 2012 and 2013 WHO recommendations for perinatal ARVs (World Health Organization, 2012b)

	Woman receives treatment if CD4 ≤350 cells/ml Revised to ≤ 500 cells/ml in 2013	Woman receives prophylaxis if CD4 > 350 cells/ml Revised to ≤ 500 cells/ml in 2013	Infant receives:
Option A *Not recommended after 2012*	Triple ARVs starting as soon as diagnosed, continued for life	*Antepartum:* AZT starting as early as 14 weeks gestation *Intrapartum:* at onset of labour, single dose NVP and first dose of AZT/3TC *Postpartum:* daily AZT/3TC through 7 days postpartum	Daily NVP from birth until 1 week after cessation of all breastfeeding; or, if mother is on treatment, through age 4-6 weeks
Option B Option ii	Triple ARVs starting as soon as diagnosed, continued for life	Triple ARVs starting as early as 14 weeks and continued intrapartum and through childbirth if not breastfeeding or until 1 week after cessation of all breastfeeding	Daily NVP or AZT from birth through age 4-6 weeks regardless of infant feeding method
Option B+ Option i	Triple ARVs starting as soon as diagnosed, for life	Triple ARVs starting as soon as diagnosed, for life	Daily NVP or AZT from birth through age 4-6 weeks regardless of feeding method

2.9 2013: The harmonisation of WHO guidelines across the continuum of care

The WHO released The Consolidated Guidelines for HIV Management Across the Continuum of Care in 2013 in response to continued emerging evidence about the importance of earlier initiation of ART, the benefits of ART in the prevention of sexual and occupational transmission of HIV, the importance of ARV prophylaxis in the prevention of perinatal transmission and as pre and post- exposure prophylaxis (World Health Organization, 2013a). The guidelines present a public health approach to management and envision "universal access" to HIV medications- meaning greater than 80% of the eligible population receiving ART services. The public health approach envisions that ART services be equitable, accessible, affordable, comprehensive and sustainable and that the first line regimen be the same for adults, adolescents, older children and pregnant women in order to reduce programmatic complexity (World Health Organization, 2013a).

The guidelines recommend ART for all people living with HIV who are under the age of 5, pregnant or breastfeeding and co-infected with TB or HBV. The guidelines increase the CD4 count threshold at which PLHIV become eligible for ART for their own health to at or below 500 cells/ml (World Health Organization, 2013a). For these populations, a fixed dose, once daily TDF + 3TC (or FTC) + EFV regimen is recommended. Second line regimens consist of a 2 NRTI back bone with a boosted PI component: ZDV + 3TC + ATV/r or LPV/r; or TDF + 3TC + ATV/r or LPV/r (World Health Organization, 2013a). While CD4 counts and clinical staging remain important for individual health evaluation, viral load testing provides the most accurate measure for monitoring response to ART, with the definition of ART failure being a viral load level above 1000 copies/ml (World Health Organization, 2013a).

Options B and Options B+ for the prevention of perinatal transmission received a name change in the 2013 guidelines and reflected the regimens recommended in the 2012 programmatic update and as above:

- **Option i** refers to the initiation of ART for life in pregnant and breastfeeding women
- **Option ii** refers to initiation of ARV for the prevention of perinatal transmission and continuing on only for those who require ART for their own health (World Health Organization, 2013a)

2.9.1 ART for all

In September of 2015 the WHO revised guidelines advocating for initiation of antiretroviral therapy for all, regardless of clinical staging of disease or of CD4 count. This recommendation was based on the results of three major studies revealing the effectiveness of ART in both the reduction of transmission and the decrease of serious HIV and non-HIV related morbidities with early initiation of ART (World Health Organization, 2015a).

The New England Journal of Medicine published the results of the HPTN 052 study in 2011. The HPTN 052 was a RCT that followed 1763 couples serodiscordant for HIV-1 in 13 sites in 9 countries. The partner with HIV was randomised to either treatment according to WHO guidelines, which at the study start was 250 cells/ml. The study found a relative risk decrease in HIV transmission of 96% in the early treatment group. Further, a relative risk decrease of 41% in HIV related adverse events was realised (Cohen et al., 2011).

The improvements in clinical course observed in HPTN 052 with early initiation of ART were confirmed by two further studies, INSIGHT START and TEMPRANO (Cohen et al., 2011; The INSIGHT START Study Group, 2015; The TEMPRANO ANRS 12136 Study Group, 2015). The START study evaluated immediate initiation of ART or initiation deferred to a CD4 count of 350 cells/ml or fewer. A relative risk reduction of 72% was observed in serious AIDS related events and a 39% relative risk reduction in serious non-AIDS clinical events, mainly cancer, were observed (The INSIGHT START Study Group, 2015). The TEMPRANO study conducted in the Ivory Coast recorded relative reductions in severe HIV related illness of 44% and relative reductions from death from any cause of 35%. These results were elicited when ART was combined with IPT for tuberculosis (The TEMPRANO ANRS 12136 Study Group, 2015).

History will tell how these revised guidelines impact upon the epidemic. Certainly universal access to ART services, including prevention of perinatal transmission programs and treatment as prevention will support the goals of reversing the rate of new infections, improving quality of life for people living with HIV and the elimination of perinatal transmission of HIV.

2.9.2 Management of co-infections in the pregnant population

The management of opportunistic infections in the pregnant population can present challenges, as many drugs are not recommended during pregnancy. Additional challenges arise when drug interactions between ARV and therapeutics for OIs exist. The development of multi-drug resistant forms of TB and the high rates of TB infection in the HIV positive population, and particularly among the pregnant population provides an excellent example of a highly complicated management situation. Generally, guidelines for resource limited setting, like those for Kenya, recommend starting all people living with HIV, including pregnant women on prophylaxis for OIs, malaria and in some circumstances, TB (Republic of Kenya Ministry of Health, 2012a). The US National Institutes of Health produces guidelines that delve further into the complexity of prophylaxis and management of OIs specifically during pregnancy and these guidelines have been included in the EMR/CDSS that this thesis is based upon (Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013). The specifics of the recommendations are beyond the scope of this chapter but they may be found in the appendix.

2.9.3 Service integration, decentralisation of care and task shifting

Programmatically, the WHO argues for service integration, decentralisation of care and task shifting to facilitate the rapid increase in ART service delivery that would be needed to achieve coverage as envisioned above and to harmonise and enhance ART service provision (World Health Organization, 2013a).

Service integration requires that ART initiation and maintenance programs be incorporated into:

- Primary care services
- MCH services with good linkage and referral to ongoing care in settings with generalised epidemics
- TB services where high rates of HIV and TB co-infection occur
- In areas of high TB and HIV co-infection, TB management should be incorporated into ART services
- Opioid substitution services (World Health Organization, 2013a)

Decentralisation of care describes ART service provision at most levels of the health care system including:

- Initiation of ART services at hospitals and maintaining ART services in peripheral facilities
- Initiation and maintenance of ART services at peripheral health facilities
- Initiation of ART services at peripheral facilities and maintenance of ART at the community level- in outreach sites, health posts, community based sites and through home visits (World Health Organization, 2013a)

Task shifting extends the ART service delivery of the caregiving workforce beyond the physician to include:

- The initiation and maintenance of ART services by trained, non-physician clinicians, nurses and midwives
- The dispensation of ART drugs by trained and supervised community level health workers (World Health Organization, 2013a)

2.9.4 Chapter Summary

This chapter has summarised the history of the HIV pandemic with emphasis on the evolution of antiretroviral therapy recommendation both for the general population and for the prevention of perinatal transmission. This history has been informed by an immunologic, virologic and pharmacologic explanation of viral transmission, infection, replication and the principals of antiretroviral therapy. Public health policy and implementation has been discussed for low resource environments as advocated by the WHO. This will provide a background for understanding the development of the EMR/CDSS and how EMRs and CDSSs may be helpful in the dissemination and sharing of information in the highly dynamic sphere of HIV medicine.

Chapter 3 History and epidemiology of HIV in Kenya and the national response to the epidemic

3.1 Introduction to the chapter

This chapter discusses the history and epidemiology of HIV in Kenya and the national response to the epidemic from political, programmatic and public health perspectives. Health system responsibilities are reviewed and the Kenya AIDS strategic framework is presented. Obstetric practices in Kenya are reviewed and the NASCOP 2014 recommendations for the management of perinatal HIV infection are presented.

3.2 HIV policy and service management in the context of a devolved Kenya

The HIV epidemic has placed a tremendous strain on the government of Kenya. Management has evolved from a health sector led response to a multi-sectoral response governed by a national authority, a strategic framework and a single monitoring and evaluation system. A discussion of recent political changes in Kenya will lead to a better understanding of policy development and implementation. Kenya underwent a major and highly ambitious process of devolution as stipulated by constitutional ratification in 2010, which has broadly affected the health system and the delivery of HIV related services. The official launch of devolution coincided with the elections held in March of 2013 and created an entirely new level of government at the county level. Forty-seven newly created county governments replaced the previous 8 provinces and 28 districts creating new political and administrative units at one time (World Bank, 2012). The study that this thesis is based on took place in Kakamega County General Hospital, in Kakamega Town, Kakamega County. Kakamega Town was formerly a part of Western Province, which, after March of 2013, ceased to exist in an administrative or political capacity (World Bank, 2012).

Devolution arose out of a long history of post- independence centralization of power, and what many felt was its abuse by the governing elite. Devolution was intended to satisfy a number of goals including the decentralization of power, increase in accountability and transparency, minimizing spatial inequities and improving the delivery of social services by

allowing regional geographic and demographic diversity to inform policy. Devolution in the health sector allows for program management at the county level with most health sector functions allocated to the county governments (World Bank, 2012).

3.2.1 Health service responsibilities in the devolved system

The county government remains responsible for primary care services at the dispensary, health centre, maternity home, public and private hospital and county referral hospital levels as well as professional staff and technical services. The national Ministry of Health resulted from a merger between the former Ministry of Medical Services and the Ministry of Public Health and Sanitation. The Ministry of Health in the devolved government is responsible for:

- National policy development
- Technical support
- Health information systems and communication systems
- Monitoring of quality
- Planning and budgeting
- Major disease control
- Health at the ports, borders and transnational boundary areas
- Standards
- Studies required for administrative and management purposes
- The National Hospital Insurance Fund
- The Kenyan Medical Training College
- The Kenyan Medical Research Institute
- The Kenyan Medical Supplies Authority (KPMG, 2013).

3.2.2 The Kenya AIDS Strategic Framework, 2014/2015-2018/2019, NACC and NASCOP

Within the devolved system, HIV and AIDS policy and services fall under the auspices of both county and national governments and are directed by a number of different strategic plans under the wider Ministry of Health umbrella. The current policy developed specifically to meet the needs of a devolved political environment is the Kenya AIDS Strategic Framework, 2014/2015-2018/2019 (KASF) (Kenyan Ministry of Health, 2014). This

strategic framework aims to provide guidance to counties in regards to coordination and implementation, resource mobilization and allocation, and accountability. Counties can then use the guidelines to develop locally relevant policies. The vision of the plan is for a localized mobilization of a multisectoral response to the HIV epidemic that includes the public sector, private sector, NGOs, FBOs, CBOs and development partners. The KASF is aligned with the goals of Vision 2030 which places health as a key factor in lifting Kenya into middle income nation status by 2030; the Health Sector Strategic Plan; United Nations goals of universal access to care, prevention and treatment, the reduction of new infections, a decrease in stigma and discrimination, and an elevation in reporting standards; as well as regional commitments to IGAE, the East African Community and the African Union Global Commitment to HIV, Tuberculosis and Malaria. The strategic framework is further committed to providing evidence based, high impact and scalable interventions along with sustainable domestic funding sources and solutions (Kenyan Ministry of Health, 2014).

The broad vision of the KASF is to create a Kenya free from HIV infections and AIDS related deaths and also free from the stigma of HIV infection. The stated goal is to contribute to Vision 2030 by providing universal access to comprehensive HIV treatment and care. The specific objectives of the framework are to reduce new HIV infections by 75%, reduce AIDS related mortality by 25%, reduce HIV related stigma and discrimination by 50% and increase domestic financing of the HIV response to 50% during the framework's timeframe (Kenyan Ministry of Health, 2014).

The National AIDS Control Council (NACC), which is under the Ministry of Health umbrella, works with government sectors and county governments with resource distribution and the building of multisecotral plans. It is responsible for resource mobilisation and coordination of all sectors, private, public and donor and aims to ensure efficiency within these sectors (Kenyan Ministry of Health, 2014). The National AIDS and STI Control Programme (NASCOP) was initiated in 1987 to provide guidance on the biomedical interventions to control HIV and other STIs. NASCOP produces guidelines for many aspects of HIV management including prevention of perinatal transmission. The PMTCT guidelines will be presented later in this chapter (Republic of Kenya Ministry of Health, 2012b).

3.3 Epidemiology of HIV in Kenya

3.3.1 Epidemiology

The first case of HIV in Kenya was identified in 1984 and between 1985 and 1995 HIV

prevalence in the population peaked at 10.5%. Largely due to high mortality rates during the 1990s, the rate of infection fell to 6.2% in 2003 and since then has remained relatively stable secondary to the scale up of ART and a decrease in new infections. As in many parts of the world, the greatest burden of HIV infection in Kenya is among women. Data from 2012 estimates the HIV prevalence to be 5.6% in the general population; prevalence among women was 6.9% and among men was 4.2%. Fifty seven per cent of all HIV infections are in women (National AIDS Control Council of Kenya, 2014).

In general, people residing in urban areas have a higher prevalence of HIV than do those from rural areas. Eighty per cent of both HIV infections and deaths related to HIV are among adults over 15 years of age while 20% are in children. The prevalence of HIV among the youth, described as people between the ages of 15 and 24, has fallen from a prevalence of 5.9% in women in 2003 to 3.0% in 2012 and remained at a relatively stable rate for men between 1.1% and 1.5% during that time period. The rate of new infections has declined by about 15% over the past five years, though prevalence rates remain stable because of extended life span with ART (National AIDS Control Council of Kenya, 2014).

Kenya has both a generalized epidemic and concentrated epidemics. People who inject drugs and men who have sex with men have HIV prevalence rates around 18% and sex workers have rates around 29.3%. Geographic granulation of infection prevalence exists as well. The highest rates of infection are seen in Honma Bay County at 27.1% and the lowest at 0.2% in Wajir County. Kakamega County, where the study of the EMR/CDSS took place, has a prevalence rate 5.6% and in line with the national prevalence rate (National AIDS Control Council of Kenya, 2014).

The UNAIDS Gap Report of 2014 has noted many improvements in HIV related statistics in Kenya between 2005 and 2013. AIDS related deaths declined 60% in Kenya during this period, mainly due to increased coverage of ARV. Kenya has also affected a 41% reduction in maternal mortality secondary to AIDS during this same period (UNAIDS, 2014a). Continued increases in access to and availability of ARVs should further propel these decreases in morbidity and mortality. Increases in the availability of condoms, prevention of HIV among children, particularly during the breastfeeding period, and improvement in meeting sexual and reproductive health needs of both men and women by sexual debut have been highlighted by the gap report as areas needing improvement (UNAIDS, 2014a).

3.3.2 Expenditure

Total HIV related expenditure in 2013 was around 72 billion Kenyan Shillings per year; 70% coming from external sources, 17% domestic and 13% coming from households and private sources. Kenya is currently focused on finding sustainable sources of funding, as, with such a large portion of funding coming from external sources, the system is susceptible to fluctuations in global financial markets and economic depressions. Currently, 52% of financing is dedicated to care and treatment while 21% goes towards HIV prevention programs. Eleven per cent of the funding contributes to systems strengthening and collaboration and 8% to the care of and programs for orphans and vulnerable children (National AIDS Control Council of Kenya, 2014).

3.3.3 Challenges and commitments

Kenya committed to achieving Millennium Development Goal 6 and the UNAIDS Strategy- *Getting to Zero 2011-2015*, while remaining keenly aware of the difficulties low and middle income nations would have in achieving these goals. As outlined in the Kenya AIDS Progress Report, 2014 (National AIDS Control Council of Kenya, 2014), Kenya has made significant headway in achieving many of the targets set by these bodies. Prevention strategies have figured largely into this plan. A major focus has been to increase the uptake of HIV testing and there was an increase in the percentages of women and men who have been tested for HIV in the previous 12 months and know their results between 2008/9 and 2012. Integration of testing into antenatal care, STI screening and treatment and sexual and reproductive health services along with home based testing, testing outreach programs and provider initiated testing led to this rise. According to this same report, gaps in prevention programs include low levels of HIV knowledge among young people, continued high rates of early sexual debut, recent increases in those with multiple sexual partners and decreases in condom use among men who have sex with men (National AIDS Control Council of Kenya, 2014).

Achieving universal access to ART is an ongoing goal and through increases of funding allocation, health system expansion, increased training and deployment of health care workers, the reduction of stigma, increasing testing and counselling and increasing HIV awareness, 78.5% of eligible adults are now receiving ART. The target was to reach 1 million people with ART services by 2013 (National AIDS Control Council of Kenya, 2014).

A challenge that Kenya faces in meeting these goals is the shortage of healthcare providers. Kenya averages around 13 doctors, nurses and midwives per 10,000 people, a ratio that the WHO describes as a critical shortage. The rural areas experience staffing shortages of 50-80% (KPMG, 2013). Indeed, it is a stated goal of the devolved government to rectify both staffing shortages and the inequitable allocation of staff between rural and urban areas. Proposed mechanisms include increasing pay and promotional incentives to draw skilled staff to underserved areas (World Bank, 2012).

UNAIDS target #3 is to eliminate new HIV infections among children by 2015 and substantially reduce AIDS related maternal deaths (UNAIDS, 2015) by prevention of HIV, prevention of unintended pregnancy, prevention of HIV transmission to the infant and by increasing care and treatment of women and children with HIV (National AIDS Control Council of Kenya, 2014). NASCOP's treatment guidelines for pregnant and breastfeeding women incorporated the World Health Organization's recommendation of Option B+, initiation of ART by all pregnant women for life, in 2012 (Republic of Kenya Ministry of Health, 2012a). The rate of HIV testing among pregnant women has risen from 68.3% in 2009 to 92.2% in 2012. Currently around 80,000 women are receiving ART during pregnancy and in 2012 70.6% of pregnant and breastfeeding women were receiving ART. More infants exposed to HIV are receiving early HIV prophylaxis and HIV diagnosis though there is certainly room for continued improvement. Transmission rates of HIV from the mother to the baby remained stable during this period of around 14% (National AIDS Control Council of Kenya, 2014)

3.4 Obstetric practices in Western Kenya

Provision of antiretroviral therapy during pregnancy must be coupled with appropriate maternal health, antenatal, birth and postpartum care in order to affect virtual elimination of perinatal transmission of HIV. An analysis of care practices in western Kenya highlight why transmission rates may still remain relatively high despite dramatic increases in the numbers of pregnant women living with HIV having access to ART services during pregnancy.

The Kenyan Service Provision Assessment Survey of 2010 noted HIV prevalence among women in Western Province, which encompassed Kakamega Town in the pre-devolution period, to be 9.2% (Measure DHS, 2010). A comparison of the 2010 and 2014 Kenyan Demographic and Health Surveys reveal significant improvements in measures of maternal health and delivery of care in the Western region of Kenya (Republic of Kenya, 2015). Though 97.2% of pregnant women received antenatal care from a skilled provider in the

Western Region, 47.8% of women's births were attended by a skilled provider in the 2014 survey versus 26% in the 2010 survey and 47% birthed in a health facility, an improvement over the percentage in the 2010, DHS of 27% (Measure DHS, 2010; Republic of Kenya, 2015). In nearby Nyanza province, 34% of pregnancy related deaths were due to the direct obstetric causes of post partum haemorrhage, sepsis and abortion complications. Two thirds of deaths were due to indirect causes, three quarters of these being related to HIV, tuberculosis, malaria and other infectious disease complications (Desai et al., 2013). Increased levels of skilled birth attendance and improved management of infectious disease complications would reduce maternal mortality rates. In Kenya overall, the Kenyan Service Provision Assessment Survey found that only 31% of regular antenatal care providers had been trained in the prevention of perinatal transmission of HIV in the last year. Only 28% of birth care providers were educated in prevention of perinatal transmission and only 24% had been trained in obstetric practices specific to HIV positive women in labour. Most facilities lacked any guidelines related to family planning, opportunistic infection management and antiretroviral therapy management (Measure DHS, 2010).

The same survey indicated that most initial antenatal care visits do not include a medical, surgical, pregnancy and medication history. Further, patient education in relation to common danger signs during pregnancy in the majority of visits was not provided. Lower than ideal rates for education about and provision of intermittent preventative treatment for malaria, administration of tetanus toxoid and counselling about the importance of sleeping under insecticide treated bed nets were observed. Women revealed long wait times as a major problem with antenatal care services (Measure DHS, 2010). Though not statistically significant the overall maternal mortality ratio declined from 520 at the 2008-2009 DHS survey to the 2014 DHS survey (Republic of Kenya, 2015).

DuPlessis, *et al.* (2012) revealed gaps in the provision of HIV services within the essential package of perinatal services that is to include four or greater antenatal visits, counselling, medical history and exam, nutritional assessment, testing for OIs including TB, Prevention with Positives services and the identification of a contraceptive plan. Chart review from a large clinic in Nairobi revealed that only 31% were counselled about contraception and only 10% of patients were screened for TB (Du Plessis et al., 2014). An analysis of recent integration of HIV services into antenatal care found improved patient retention with improved uptake of HIV testing, improved rates of counselling, decreased time to initiation of ART/V, an increase in care quality and a decrease in stigma. The downsides to integration were increases in workloads, training needs, necessary space and organisational conflict (Turan et al., 2012). Though there certainly remains room for improvement in the delivery of

integrated services, the rapid scale of ARV/T for the prevention of perinatal transmission has been challenging and the improvements in service delivery are reassuring.

3.5 NASCOP guidelines for prevention of perinatal transmission

Since the programming of the EMR/CDSS, there has been a revision of the perinatal PMTCT management guidelines with the publication of the Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infections in Kenya, 2016 Edition (Ministry of Health, 2016). As the EMR/CDSS was created and piloted using the most current guidelines of the time, the 2012 guidelines, they will be presented initially.

NASCOP revised its PMTCT guidelines to incorporate the recommendations for initiating Options B and B+ by the WHO in 2012. These guidelines were current during the creation of the knowledge base of the EMR/CDSS and also during the pilot period (Republic of Kenya Ministry of Health, 2012a). The guidelines stress the need for a minimum of 4 antenatal visits and facility based delivery for all women, stressing those women who are living with HIV. Though the WHO Comprehensive guidelines of 2013 ceased to recommend Option A, the NASCOP guidelines continued to (Republic of Kenya Ministry of Health, 2012a; World Health Organization, 2013a), presumably as they were written before the withdrawal of Option A by the WHO and as, programmatically, this may have remained the more feasible option at certain sites.

For treatment for the woman's own health, NASCOP recommended initiating ART at or below CD4 counts of 350/ml at clinical stages 1 and 2 and at clinical stages 3 and 4 regardless of CD4 count. The recommended first line therapy for NVP naïve women or women with a history of NVP exposure > 12 months ago was:

- AZT + 3TC + NVP or EFV
- Or
- TDF + 3TC + NVP or EFV

The guidelines recommend for those with NVP exposure in the past 12 months:

- AZT + 3TC = LPV/r (Republic of Kenya Ministry of Health, 2012a)

For the prevention of perinatal transmission when a woman does not need ART for her own health, Options A, B and B+ are recommended with the following formulations from 14

weeks gestation:

Option A:

- AZT twice daily with the addition of single dose NVP and 3TC in labour with the continuation of AZT and 3TC for 7 days post partum.

Options B and B+

- TDF + 3TC + EFV (the WHO 2013 Consolidated Guidelines recommendation (Republic of Kenya Ministry of Health, 2012a; World Health Organization, 2013a))
- AZT + 3TC + EFV
- AZT + 3TC + LPV/r
- AZT + 3TC + ABC
- Option B should be continued until the period of perinatal transmission has ended if the woman remains at a stage where she does not need treatment for her own health
- Option B+ is continued for life

For all cases these guidelines stipulate that:

- All people living with HIV take cotrimoxazole (CTX) for the prophylaxis of OIs
- EFV be supplanted with NVP in the first trimester
- The use of a PI based regimen in women with a CD4 count above 250 secondary to the increased risk of hepatic toxicity in women taking NVP with high CD4 counts
- Substitution of AZT in women with haemoglobin levels less than 8mg/dl (Republic of Kenya Ministry of Health, 2012a)

The NASCOP guidelines support exclusive breastfeeding for infants of mothers living with HIV unless replacement feeding is affordable, feasible, acceptable, sustainable and safe. NASCOP makes the following infant HIV prophylaxis regimens.

For infants of mothers on HAART (options B and B+):

- Daily NVP x 6 weeks
- For breastfeeding infants of mothers not on HAART:
- Daily NVP until one week after the cessation of breastfeeding

For non-breastfeeding infants: Daily NVP x 6 weeks

All HIV exposed infants require CTX prophylaxis for OIs started at 6 weeks of age and which may be stopped in HIV negative children 2 months after breastfeeding has ended

(Republic of Kenya Ministry of Health, 2012a)

NASCOP stipulates good linkages to care and HIV services for both mothers and infants which includes family planning services for HIV positive women and immunization and growth monitoring services for children (Republic of Kenya Ministry of Health, 2012a).

The 2016 guidelines, in accordance with those issued by the WHO, greatly simplify ART management for all people living with HIV, including pregnant women (Ministry of Health, 2016; World Health Organization, 2015a). The 2016 NASCOP guidelines stipulate that pregnant women be initiated on ART the day of diagnosis, irrespective of CD4 count, clinical staging, viral load and previous NVP exposure, with the preferred regimen being TDF/3TC/EFV (300/300/600mg) as FDC one tablet once daily (Ministry of Health, 2016).

Women already on ART should continue on the current regimen unless part of the regimen is contraindicated in pregnancy. Viral load monitoring is recommended at six months after initiation of treatment and every 6 months thereafter as long as the viral load remains < 1000 copies/ml until the end of breastfeeding then to follow up based on the guidelines for the general population. If the viral load is ≥ 1000 copies/ml it is to be repeated in one month. If it is still ≥ 1000 copies/ml, the recommendation is to change the regimen and repeat in six months following the same algorithm. Women known to be living with HIV and not on ART presenting either in labour or postpartum and breastfeeding are advised to begin ART immediately with once daily FDC (Ministry of Health, 2016).

The current infant prophylaxis regimen recommends weight based dosing of 12 weeks of AZT + NVP followed by NVP for 6 weeks. Infant screening for HIV RNA is recommended at first contact by PCR. The guidelines for labour management and breastfeeding are the same and mirror those of the WHO (Ministry of Health, 2016; World Health Organization, 2015a). It is important to note that the EMR/CDSS designed for this project utilised the 2012 NASCOP guidelines, which were current at the time of design and deployment.

3.5.1 Chapter summary

This chapter has summarised the epidemiology of HIV in Kenya and has presented Kenyan policy with respect to management of HIV in general and HIV during pregnancy. Public and programmatic considerations within the devolved government have been reviewed.

Chapter 4 e-health, mhealth, Electronic Medical Records, Clinical Decision Support Systems, the Current Kenyan e-Health Strategy and Data Mining

4.1 Introduction

This chapter will discuss e-health, mhealth, electronic medical records and clinical decision support systems. It will commence with a discussion of the various types of systems in use currently. A literature review of the functionality of e- and mhealth systems, specifically within the realms of maternal child health and HIV care, resource constrained settings and cloud-based systems will be presented. The Kenyan National e-Health Strategy 2011-2017 will be reviewed and critiqued. Principals of data mining and analysis will be discussed, highlighting the HIV reporting goals laid out by UNAIDS with a specific focus on producing granular data. The chapter will conclude with a summary of the topics discussed.

4.1.1 Ehealth, mhealth and the roles of information technology in healthcare

E-health may be broadly described as the use of information technology and computer systems to facilitate and improve the delivery of health care. Examples of e-health systems include, electronic medical records (EMRs), electronic health records (EHRs), clinical information systems (CIS) and Health Information Systems (HIS). These systems digitise many individual and system based components of paper-based systems. The benefits of digitised formats include the ability to rapidly access individual patient information and also to derive system- wide information. Storage requirements for digitised systems are drastically reduced and labour requirements for filing and retrieving records are minimised (T. Lewis et al., 2012a; World Health Organization, 2013c).

The scope of mhealth technologies has evolved and expanded greatly during the course of the work on this thesis. mhealth was originally considered a subset of e-health with a narrowed definition to include only systems available on devices that do not require fixed telecommunications systems to connect to the Internet and can further be mobilised when

internal batteries are charged. Technologies such as mobile phones, tablets, laptop computers and PDAs are able to connect to wireless broadband systems and have mobile sources of power (World Health Organization, 2011). This definition persists and the scope of the technology has evolved rapidly since 2011 to incorporate many devices that track health metrics and provide point of care patient monitoring and diagnostics. mhealth is a big recipient of venture capital funding and the market for mhealth investment is predicted to grow 55%, from $2.4- $21.5 billion US between 2013-2018 (BCC Research, 2014).

A systematic review noted three main eras of mhealth development and noted three distinct time periods in the development of mhealth projects as the technology for the systems evolved. Prior to 2007, personal digital assistants (PDAs) represented the technology most utilised in mhealth projects, as many young health care workers were starting to adopt these technologies and utilise them to the benefit of their clinical practices. Between 2007 and 2012, basic and feature telephones were the main mode of delivery as these technologies began to become widely adopted by the general public. After 2012 smart devices such as smartphones, tablets and iPods provided the majority of mhealth intervention technology. Despite the lack of research regarding their usage, pagers have remained a constantly utilised mhealth technology throughout these periods, likely due to their reliability (Ali, Chew, & Yap, 2016). The current scope of mhealth technologies incorporates the newer technologies of wearable sensors, portable laboratories, imaging technologies and patient health tracking technologies (Steinhubl, Muse, & Topol, 2015).

The management of chronic disease has been the focus of most mhealth research to date. This is likely due to the prevalence of these conditions in high- income settings, such as Europe and North America where the majority of the research reviewed in this systematic review was derived (Ali et al., 2016). As mobile phone penetration and reliability in low- and middle- resource nations expanded and improved, technologies aimed at infectious diseases and maternal child health have become increasingly created and researched. This was nudged along by donor funding towards the Millennium Development Goals (Ali et al., 2016).

While the original design of the technology for this project and thesis fit into the category of mhealth at the project's inception, it can also be considered a mobile technology enhanced e-health technology. Regardless, an evaluation of mhealth technologies and mobile enhancement to e-health technologies remains extremely relevant as the mobile aspects of the technology designed for this thesis greatly affected utilisation and study outcome.

As noted in Chapter 1, the International Telecommunications Union estimated that there would be 6.9 billion cellular service subscriptions by the end of 2014; 2.3 billion of these would incorporate mobile broadband services with this number expected to grow to 9.2 billion by 2019 (The Broadband Commission, 2014). ITU facts and figures of 2016 put the population covered by mobile cellular networks at 7 billion, or 95% of the world's population (International Telecommunications Union, 2016). As wireless coverage continued to increase and the cost of hardware to decrease, the importance of e- and mhealth strategies for implementation of core development indicators, including the MDGs, was identified. Multiple players have been involved in the mhealth movement: technology companies, telecommunications companies, medical centres, IT start-ups, governments and multilateral agencies are currently collaborating to conceptualise, pilot and bring to scale mhealth projects (mHealth Alliance, 2013). Early mhealth projects in low and middle-resource settings ranged from using mobile phones to convey health information to clients, send appointment reminders to clients, facilitate and coordinate emergency services and provide clinical decision support tools and access to medical records for health workers (World Health Organization, 2011).

The World Health Organization has organised mhealth into different functional categories as described below with examples.

Communication between individuals and health services

- Health call centres
- Health care helplines
- Toll free emergency telephone services

Communications between health services and individuals

- Treatment compliance- reminders to take medications for HIV, TB, contraception, etc. communicated most commonly by SMS
- Appointment reminders- most commonly by SMS, voice message or email
- Community mobilization- rouse support for and participation in public health campaigns such as immunization and VCT for HIV

Consultation between healthcare professionals

- Mobile telemedicine- voice, SMS, email, sharing of images

Intersectoral communication in emergencies

- Intersectoral disaster management- for communication, alerts, emergency

management, reporting and transportation dispatch; voice, SMS, two way radio technology

Health monitoring and surveillance

- Mobile surveys regarding health data such as smoking rates, alcohol use, antenatal care attendance
- Surveillance- reporting of disease outbreaks such as acute watery diarrhoea
- Patient monitoring using diagnostic sensor technology for blood glucose levels, blood pressure, EKG

Point of care access to information

- Information and CDSS- access to relevant literature, education, medication interaction checking and tools to aid in diagnosis and management of health issues
- Patient records- assess to patient electronic medical records (World Health Organization, 2011)

The system that was developed for study will be described in-depth in Chapter 6 Mobile technology enhanced EMR/CDSS for the co-management of HIV and pregnancy design. It will help to keep in mind that it is, briefly, a mobile technology enhanced, cloud-based system that runs on a laptop computer with long battery life and accesses patient records with embedded clinical decision support elements through wireless broadband telecommunications systems. The specific elements of the above system description that it incorporates are: appointment reminders, patient education, consultation between healthcare professionals, surveillance, information, passive and active computerised clinical decision support and access to patient records. The fields of e-health and mhealth have enjoyed rapid expansion and scale up due not only to the increases in knowledge about the benefits and technology sharing but also the rapid penetration of mobile devices, rapid increases in capital investment and funding and user uptake (BCC Research, 2014; Fraser & Blaya, 2010; Steinhubl et al., 2015). Despite this, the evidence base for mhealth technologies remains scant (Steinhubl et al., 2015).

4.1.2 History of electronic medical records and clinical decision support systems

While mhealth technologies have enjoyed rapid scale up since the beginning of the current millennium, the history of electronic medical records and clinical decision support systems

has its genesis in the age of computer development and industry adoption (Atherton, 2011). Health worker and health facility shortages require that all aspects of clinical care be streamlined and that clinicians and administrative staff be utilized to the fullest extent of their training. The e-health and mhealth fields are uniquely positioned to facilitate both of these requirements. Remote and rapid access to patient information through electronic medical records, particularly when coupled with clinical decision support has the potential to support the clinician working in both centralized and decentralized environments (Lemay et al., 2012; Vatsalan et al., 2010). Remotely and electronically available records increase the time available for patient care (Myers et al., 2012).

4.1.2.1 A brief history of electronic medical records

Electronic medical records aim to collect longitudinal patient demographic, clinical, laboratory and often billing information in a coalesced, legible and easily accessible fashion. EHR and EMR genesis lies in the 1960s and 1970s when medical centres began to develop proprietary systems. Notable among these were those produced in the United States by the University of Utah, in collaboration with 3M in the early 1960s. Massachusetts General Hospital and Harvard University developed another system in the late 1960s. The United States Veterans Administration hospital system developed and implemented the VistA system in the 1970s. Industry began to develop these systems in the 1960s as well. Lockheed, TDS Health care and Eclipsys were a few of the early players in the EHR/EMR market (Atherton, 2011).

The United States Institute of Medicine (IOM) understood the need to improve the standard paper record and began to research the utility of EHR/EMR systems in the 1980s. Reports were issued in 1991 and 1997 recommending the use of electronic records to improve patient records overall. By 2000 the IOM argued that electronic record systems were key to overcoming the problem of medical errors, and argued for computerised physician order entry systems in particular, which allow for the order of pharmaceutical agents in a computerised fashion (Atherton, 2011).

Numerous standardised nomenclature systems have been developed to accurately harness patient, laboratory, diagnostic and pharmaceutical metrics (Atherton, 2011). Many of these standardised systems are utilised in electronic medical records both to ensure nomenclature coherence but also as a means of coding metrics to more easily derive system wide data. Numerous standardised nomenclature systems exist for various parameters (Gunter & Terry, 2005). The IOM argued for the creation of a standards organisation aimed at providing a

framework for the standards for integration exchange and retrieval of electronic health information and the Health Level Seven organisation was created with this aim in 1987 (Health Level Seven International, nd).

4.1.2.2 Computerised clinical decision support systems

Computerised clinical decision support systems have roots in the artificial intelligence movements of the 1940s and 1950s. CDSS provide clinical information to practitioners in the care environment and represent an e-health intervention. The type of support provided varies by system. Systems may be described as knowledge based or non-knowledge based (Berner, 2007). Non- knowledge based systems use artificial intelligence and machine learning to create decision algorithms from large amounts of clinical data through pattern recognition. For example, a non-knowledge based system designed to predict cardiac diagnoses from symptoms would be fed large amounts of clinical data of cases with known outcomes to compute likely associations between symptoms, analysis results and diagnoses. The relations between symptoms and outcomes could be rated by likelihood by a variety of different mechanisms to arrive at a list of differential diagnoses (Berner & LaLande, 2007).

One such mechanism of creating these likelihoods would be through use of artificial neural networks. Artificial neural networks create weights of likelihood between the connection between input and output nodes based on large amounts of historical clinical information. These weighted connections are then used to predict outcomes from novel input (Berner & LaLande, 2007).

Genetic algorithm systems are based upon the principals of Mendelian genetics. Fitness between input and output is generated through historical cases as above. Then, random pairings are made between new input and possible outputs that are tested for fitness. The best-fit pairs are retained, hybridized and then retested for fitness. This random pairing continues until the best fit outcome is generated (Berner & LaLande, 2007; Milovic & Milovic, 2012). These non- knowledge types of clinical decision support systems have been shown to improve patient outcomes, minimise errors and reduce the severity of complications (Berner & LaLande, 2007). They are hindered by the sheer amounts data required to program them and the enormous processing power required to run them (Milovic & Milovic, 2012).

Knowledge based systems utilize a set of guidelines from which to supply elements of decision support. The clinical decision support system designed for this project is an

active/passive knowledge-based system. The knowledge base comprises the backbone of the knowledge-based system and is derived from sources chosen by the designer of the knowledge base called the knowledge engineer. This knowledge base may be accessed in a number of different ways. The person utilising the decision support function could access the knowledge base as a reference. There may also be a reasoning and/or inference engine that combines rules from the knowledge base with patient information to derive recommendations and/or alerts in an if-then format. These CDSS elements may be considered "active" in that they actively alert a clinician to a clinical issue of importance or "passive" in that they act as a reference to support clinical decision making (Berner, 2007).

CDSS have the ability to improve quality of care, disease prevention, disease management and drug dosing, management of chronic illness, guideline compliance and decrease variation between practices and practitioners (Shibl, Lawley, & Debuse, 2013). Junglas, Abraham and Ives (2009) investigated the factors affecting mobile charting and CDSS uptake by registered nurses in the United States. Beneficial aspects of mobile technology in the facilitation of patient care included having up to date patient and treatment information at the point of care, the technology was easily transported between locations and workflow processes were streamlined (Junglas, Abraham, & Ives, 2009). General practitioners in Australia were likely to adopt computerized decision support systems when they facilitated consultation and professional development, improved workflow, were easily integrated into the existing practice, were easy to use and when they had trust in the knowledge base of the CDSS (Shibl et al., 2013).

4.1.3 E- and mhealth systems in low- and middle-resources settings

As noted earlier, the development of EMR, CDSS and mhealth systems in low and middle-resource contexts has not been as linear and well financed as those of high resource environments. As provider to patient ratios are low and health care resources scant in much of the low resource world, the potential of EMRs to open up numerous bottlenecks in the care cascade were realized during the scale up of e-health interventions in the high resource world. The Health Metrics Network which was created in 2005, served to advise low-resource nations, those of the African continent in particular, on the adoption and implementation of electronic health information systems (Braa et al., 2010). Recommendations for policy, development and deployment were developed. The first, published in 2005, argued that countries should endeavour to implement a national

framework to guide interoperable sub-systems with the aim of producing aggregated data available in a national repository and the second advised nations on how to do this specifically (Braa et al., 2010).

The challenges to and realities of creating and deploying health information technologies in low resource settings are myriad. Braa, et al. (2010) argue that systems developed for low resource settings must be both scalable and comprehensive. Technical infrastructure and the trained IT workforce may be quite varied from region to region within a continent and within a country. Scalable technologies are those that may be implemented in a paced manner. Comprehensive refers to the technologies' ability to meet most of the needs at all levels and locations of implementation (Braa et al., 2010).

4.1.3.1 Free/Libre Open Source Software in Healthcare (FLOSS-HC)

While proprietary HIS and EMR systems dominate the market in high resource settings, Free/Libre Open Source Software Systems in healthcare (FLOSS-HC) have risen to dominance in the low-resource world. Over the past three decades, numerous HIS technologies have been developed in the low-resource world, often to meet local need, through the open source model (Karopka, Schmuhl, & Demski, 2014).

The idea of open source software was born with the advent of computers. These ideas were put into practice in the mid-1980s and the premise is that the underlying source code is freely available to users to share, study, and modify. FLOSS is generally available by download from the Internet and do not require the payment of without licensing fees. Examples of popular open source platforms include Linux, Android, MySQL and Apache Web Server. The release from licensing fees does not preclude the costs associated with running the software, programming the software or generating income from the development of programs borne out of the software however (Karopka et al., 2014).

There have been numerous FLOSS- HC systems used in the low- resource world, with numerous benefits beyond the absence of licensing fees. Systems are supported by communities of developers and implementers, and sharing of information adds benefit across systems and settings. Many of the FLOSS- HC systems utilised in the low- resource world employ modular architecture, allowing different elements to be chosen from repositories and adapted to local need. GNU Health, District Health Information System, OpenClinic GA,

OpenHIE and OpenMRS are some of the most highly utilised systems in low-resource settings.

OpenMRS is the FLOSS- HC chosen for this project. OpenMRS was born out of a partnership between Moi University in Eldoret, Kenya and The Regenstrief Institute of Medical Informatics at the University of Indiana in the United States. The University of Indiana School of Medicine and Moi University School of Medicine have enjoyed a partnership since the 1990s. During the HIV/AIDS epidemic, the partnership created the Academic Model for Prevention and Treatment of HIV/AIDS (AMPATH). By the mid 2000's the existing IT infrastructure at Moi University became overwhelmed by the data from AMPATH and Paul Biondich and Burke Mamlin, two Informatics experts from the Regenstreif Institute were called in to assess needs. They started work on an HIS for AMPATH (OpenMRS, nd).

Concurrently, Hamish Fraser of Partners in Health, a not-for-profit located in Boston, was working on an HIS project to combat TB and HIV. The PIH and AMPATH founders met at the MedInfo world congress in 2004 and joined forces to start work together. An open source model was chosen and with the addition of developers Ben Wolfe and Darius Jazayeri, OpenMRS was born. The scope of OpenMRS was expanded by the addition of Chris Seebregts of the South African Medical Research Council, who had already been adapting OpenMRS for use in the region (OpenMRS, nd). OpenMRS soon gathered the attention of international partners, helping it to further grow in terms of utilisation and in support of local mentorship of medical informaticians, programmers and developers in the locations where it is implemented. Today OpenMRS is the most highly utilised FLOSS- HC in operation. It allows for and fosters the adoption and adaptation of forms and modules and is supported by a vast network on implementers, developers, programmers and volunteers (OpenMRS, nd). The system developed for this thesis is available for adoption and customisation at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy.

4.1.3.2 Mhealth, care environments and provider extension

As there has not been a technology reviewed to date that focuses on all of the elements contained in the system designed for this project, the literature for elements that reflect those of this system will be reviewed beginning with the ability of mhealth systems to expand care environments in resource and provider limited settings. We will begin with an examination

of the experiences of the use of mhealth systems aimed at provider extension and the decentralisation of care.

Health worker and health facility shortages require that providers be utilized to the fullest extent of their training and that facilities be equipped to respond to population needs. The e- and mhealth fields are uniquely positioned to facilitate both of these requirements. Remote access to patient information, particularly when coupled with clinical decision support has the potential to support the clinician working in both centralized and decentralized environments. Non-physician and non-specialist healthcare workers that possess the general medical knowledge required to implement evidence-based guidelines allow clinicians to maximise their utility. Indeed, randomised controlled trials support home and clinic-based care provided by non-physician healthcare providers for HIV/AIDS management, particularly for improving access to care and adherence to antiretroviral therapy in low, middle and high resource settings (Scanlon & Vreeman, 2013).

Médecins Sans Frontièrs has implemented the decentralized, primary health care focused model of care in numerous locations in southern Africa with comparable or better indicators of virologic suppression, faster enrolment, improved proximity of care and improved acceptance of services (Bedelu, Ford, Hilderbrand, & Reuter, 2007; Elema et al., 2009). Much of the care once provided by physicians has been taken over by non-physician cadres of the workforce with excellent outcomes. Indeed, community-led and primary health care interventions in HIV/AIDS treatment and ART delivery are supported by the WHO (Bedelu et al., 2007). EMRs with CDSS elements assist in providing feedback to practitioners regarding guideline adherence and can aid in the continuing education of healthcare providers (Z. Lewis et al., 2011), a critical imperative as guidelines in HIV and pregnancy care are routinely updated (Shibl et al., 2013). A study of information use by female health workers in rural Uganda found that when information was gained, it was shared amongst the health workers and with the community and led to behavioural changes in both groups. The health of the community was positively impacted through this dissemination of information (Musoke, 2012).

4.1.3.3 Referral and consultation systems

Mobile technologies have been shown to be beneficial to community level healthcare providers from a logistical standpoint as well as a clinical care standpoint. Mobile technologies that incorporate clinical guidelines and consultation and referral mechanisms have shown significant reductions in travel distances and costs incurred by community

health workers and decentralized care programs (Lemay et al., 2012; Vatsalan et al., 2010). Remote, easy access to patient information is beneficial from a case management perspective. It also frees up time for direct patient care (Myers et al., 2012).

4.1.3.4 Access to centralized medical record and laboratory record systems

It is essential that patient and laboratory information be available at the point of care. This information can be made available through e- and mhealth. A study of an e-health driven laboratory system in Peru led to improved system outcomes for HIV treatment. The number of HIV positive people with recorded CD4 counts increased 1.5 fold and the publishing time of these results decreased from 60 days to one day. The processes were found to be streamlined at all levels (Garcia et al., 2009).

4.1.3.5 Mhealth technologies in Maternal and Child Health

A 2016 systematic review and meta-analysis of mhealth technologies focused on maternal and child health in middle- and low- income settings reveals the ongoing need for robust evaluation of these projects. Overall, the authors state that out of 8593 unique references evaluated, only 15 met inclusion criteria and only 2 of these studies were deemed of low bias risk (Lee et al., 2016). These programs tend to be donor funded and small scale. Lee, et al., (2016) find that the research methodology surrounding these projects is of poor quality and there is little evidence to patient outcomes. The focus on rigorous methodology supports the development of the mTERG reporting tool (Agarwal et al., 2016). Despite these overall findings, Lee et al report that there is modest evidence that SMS delivered interventions can improve infant feeding practices and maternal morbidity and mortality were improved in one study evaluating SMS messages sent to pregnant women (Lee et al., 2016).

4.1.3.6 Combined EMR/CDSS in antenatal and HIV clinical care settings

While strictly mhealth solutions focused upon MCH have had mixed results, CDSS coupled with EMRs have shown improvement in many areas of clinical care and in HIV and antenatal care specifically. A 2012 systematic review of the effects of EMR based clinical decision support systems on HIV care in resource constrained settings noted decreases in

missed appointments, missing CD4 counts and a decrease in patient waiting time (Olouch et al., 2012). A randomized controlled trial in Boston found an improvement in ordering rates of CD4 counts, a decrease in the rate of 6 month suboptimal follow up and a decrease in the time to the next scheduled appointment when utilizing a CDSS in HIV care. Further, 90% of clinicians in this study supported the practice (Robbins et al., 2012). A systematic review of the literature in respect to the usage of decision support and clinical information systems in HIV care across a variety of settings found that decision support and clinical information systems together improved guideline implementation in HIV care (Pasricha et al., 2013). Computer generated reminders have been shown to improve CD4 count ordering by clinicians and improve adherence to clinical guidelines (Were et al., 2011). Improvements in adherence to pre-ART guidelines including rates of ordering baseline CD4 counts and a reduction in the time from enrolment to ordering of the baseline CD4 count and increases in the proportion of eligible patients initiating ART was demonstrated in rural Kenyan clinics implementing EMRs (Olouch, Katana, et al., 2014; Olouch, Kwaro, et al., 2014). Implementation of a combined EMR/CDSS in Ghana and Tanzania was not found to increase time spent on ANC visits and positively impacted patient history taking in Ghana (Mensah et al., 2015). Olouch, et al., (2012) point out that, though improvements in certain aspects of care have been seen with these types of systems, more rigorous studies of these systems need to be conducted to conclusively endorse expenditure of precious resources in this sector.

Indeed, evidence continues to emerge in support of EMR usage within the realm of HIV care in resource-constrained settings. The implementation of EMRs with the ability to rapidly identify missed appointments led to improved clinical efficiency, dramatically decreased waiting times to see clinicians, improvement in appointment adherence, a decrease in loss to follow up and improved medication adherence in an HIV clinic in Uganda (Alamo et al., 2012). A large-scale EMR implementation in Nigeria reported improvements in working time and space for data entry staff, improvements in patient care, more efficient government reporting and an improved ability to conduct quality control audits. Furthermore, patients responded favourably to seeing graphic representations of their medical information on the system (Chaplin et al., 2014). EMR systems utilized by clinicians at the point of care have shown reductions in reporting errors. Clinicians also supported the EMR implementation. Most clinicians reported improved clinical care delivery and access to records and also appreciated the automation of tasks (Castlenuovo et al., 2012).

As was discussed in Chapter 2 the complexities of HIV management require that up to date guidelines and patient information be available to clinicians and EMR/CDSS provide both.

Optimal antiretroviral therapy requires monitoring of CD4 counts, viral load and often requires ART resistance testing. Infection with the HIV virus carries with it the risk of opportunistic infection (OI) contraction for which prophylaxis and management is complex. Pregnancy adds an additional layer of complexity to the management of HIV. Thus, it is imperative that clinicians have ready access to current, evidence based and pregnancy specific HIV management information. Many pharmaceutical therapeutics for the management of HIV and co-morbidities are either not suitable in pregnancy, or at certain stages in pregnancy or require unique laboratory monitoring (Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013). As the management of HIV, and the management of HIV during pregnancy, is the subject of much study, guidelines are constantly being updated as new information emerges and in order for clinicians to provide optimal care, this information must be readily available. A combined EMR/CDSS will support the clinical management of an HIV positive pregnant woman, allow the clinician to rapidly consult guidelines in the course of a patient visit, provide educational information to the patient, schedule the next appointment and provide a reminder service and have the ability to recall the patient if needed. Currently, an EMR/CDSS focused on the co-management of HIV and pregnancy is not described in the literature.

4.1.3.7 Cloud-based EMR/CDSS

Within the last 5 years there has been increased interest in locating health IT solutions in the cloud. The cloud broadly refers to the Internet and cloud-based solutions generally rely on the Internet to facilitate the usage of software and systems at a site remote from the device on which it is being utilised. Numerous benefits to cloud-based HIT solutions such as EMR/CDSS have been proposed. Cost and savings should be realised as organisations can rely on one central server from which to operate many systems. This will reduce both the costs of installing and maintaining hardware but also employment costs of an IT professional at multiple locations. Further, decreases in energy costs from running and cooling numerous servers will result from having a centralised server that all units access (Sultan, 2014). Cloud based EMR/CDSS systems can allow for synchronous collaboration between providers at different locations, as both are able to tap into the same record from multiple sites, further improving clinical management and patient outcomes (Wang & Alexander, 2013).

A novel cloud-based system was designed for use in western Kenya and was the progenitor to the system designed for this study by Uamuzi Bora, an NGO dedicated to improving care to people living with HIV by harnessing the power of the Internet and EMRs (Uamuzi Bora, 2013). Indeed, the EMR/CDSS designed for this project combined elements of the EMRs for

HIV and for MCH by Uamuzi Bora and adopted the cloud-based, wireless broadband accessibility technical architecture developed for the Uamuzi Bora project. Their novel system was based in OpenMRS software using Ubuntu Linux. The record was housed on a server located off site from the hospitals and clinics where it was used. At the clinics and in the hospital, the record was run on Chromebooks that connected to the server through a VPN facilitated by WIMAX (worldwide interoperability for microwave access). All connection attempts were logged and audited to ensure security. All identifiable patient information was saved in an encrypted file system and a decryption key stored on removable media in a different secure location. Encrypted identifiable data was held for 6 months then deleted. Anonymised data was compiled daily and accessible via API. The clinical decision support elements of the Uamuzi Bora system were comprised of flags generated in SQL for numerous parameters including out of bounds laboratory values and missing appointments and demographic information (Haskew et al., 2015b).

There are two main differences between the Uamuzi Bora system and the system designed for this project. The first difference is that the EMR/CDSS designed for this project had additional passive clinical decision support elements in the form of clinical guidelines built into the record. The second difference was that the Uamuzi Bora system required retrospective data entry. Clinicians saw patients using the paper forms and then data entry clerks entered the data into the computerised system. The system designed for this project is intended to be used by the clinician at the point of care. A comparison of the results of these systems will be reviewed in Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance.

Haskew, et. al. report improvements in data completeness with both systems. The EMR for antenatal care, when compared with paper records, was shown to improve data completeness at multiple sites in western Kenya and improved rates of screening for tuberculosis, malaria, hypertension, HIV and ART status (Haskew et. al 2015a).

The analysis of the system for HIV care provision found a significant improvement of the number of eligible patients who were started on ART. Pre-implementation, 30% of patients who were eligible for ART had not yet been started on it, post implementation, this dropped to 6%. Significant improvements in data completeness were observed in the recording of clinical information including patient source of testing, the first CD4 count, and the first WHO stage (Haskew, et al., 2015b).

Haskew, et al (2015) note that cloud-based EMR systems have numerous potential benefits,

benefits that informed the creation of this project, as well. They state that access to aggregated anonymised data can inform public health decision making based on current epidemiologic information. Further, the cloud-based model is potentially more cost-effective than clinic based systems as it can be used over a wide geographic range and only incur the costs of maintaining one server as opposed to a server in each location, as is necessary for local systems (Haskew et al., 2015b).

The authors note that potential challenges to cloud-based systems exist. The local mobile data network must be understood as not all environments are able to provide consistent and reliable mobile infrastructure. Further, local and national guidelines for network security must be well understood (Haskew et al., 2015b). These challenges are also cited by Sultan (2014), who adds that cloud-based networks can experience failures of connectivity, which can be detrimental to operations utilising them. Further, they are more susceptible to hacking and data breaches so security of patient information on these systems needs to be maintained and alert to all potential security threats (Uamuzi Bora, 2013). iSanté, an EMR designed for HIV care in Haiti initially utilised an early version of cloud based computing whereby a server located in Washington state, USA was accessed by VSAT satellite communications. Connectivity was so unreliable that this form of communication was abandoned for local servers early on in the implementation period (Lober, Wagner, & Quiles, 2010).

4.1.3.8 The current state of mhealth projects in the African setting

A synopsis of the project for this thesis was included in the African Strategies for Health mHealth Compendium, Volume 5, a compendium of select mhealth projects operating in the African sphere (African Strategies for Health, 2015b). Subsequent to the publication, a survey was conducted with both organisers of projects included in the compendium and other project organisers derived from the African Strategies for Health digital and mobile health listserv. I was surveyed for this study. The results were published in September of 2016 (African Strategies for Health, 2016).

Of the 22 respondents, 13 were working with NGOs or another implementing partner, 4 with a research organisation or university, 2 for the private sector and 1 with a donor organisation. Asked to describe the trends in mobile and digital health over the past 5 years, respondents reported:

- Increased recognition of the importance of digital technology and government

leadership

- Reduced barriers to entry and implementation, particularly increased mobile penetration and improvement in network connectivity as well as the growth of local innovation hubs
- Focus on interoperability, from government, donor and implementing organisations (African Strategies for Health, 2015b).

These trends very much mirror the tenets of the Principles for Digital Development, (digitalprinciples.org, nd), the motivating design paradigm for this project's development, which will be discussed at length in 6.3 Design principles.

Numerous barriers to the scale up were also identified by the respondents, namely:

- Technical infrastructure and device access, including electricity, network connectivity and broadband connectivity
- Funding
- Human resource capacity for digital health systems, particularly at the end user level
- Clear national strategy, standards and leadership (African Strategies for Health, 2016)

Numerous needs for the digital health sphere in Africa were identified:

- The need for establishment of policy and guidelines for digital health at national and organisational levels, especially those that encourage collaboration
- The need for more research to inform policy
- Human capacity building to maintain digital health systems (African Strategies for Health, 2016).

These findings mirror many of the experiences with the system designed for this thesis, which will be explored further in Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance.

4.1.4 EMR/CDSS implementation challenges

Some common challenges to mhealth system implementation in the African setting were reviewed above. Challenges to EMR implementation extend beyond those created by cloud-based systems. Though currently, EMR systems are becoming routine in many high resource settings settings a review of barriers to adoption during the early phases of EMR

implementation may be helpful to foresee challenges that may arise in resource constrained settings. These challenges will be presented briefly here. A systematic review of barriers to the acceptance of medical records from 1998-2009 conducted by Boonstra and Broekhuis (2010) revealed 8 categories of barriers summarised in the figure below.

Figure 4-1 Barriers to EMR implementation (Boonstra & Broekhuis, 2010)

Category	Barrier
Financial	High start up costs
	High ongoing costs
	Uncertainty about return on investment
	Lack of financial resources
Technical	Lack of computer skills of staff
	Lack of technical training and support
	Complexity of the system
	Limitation of the system
	Lack of customizability
	Lack of reliability
	Interconnectivity/Standardization
	Lack of computers/hardward
Time	Time to select, purchase and implement the system
	Time to learn the system
	Time to enter data
	More time per patient
	Time to convert records
Psychological	Lack of belief in EMRs
	Need for control
Social	Uncertainty about the vendor
	Lack of support from external parties
	Interference with doctor-patient relationship
	Lack of support from other colleagues
	Lack of support from the management level
Legal	Privacy and security concerns
Organisational	Organisational size
	Organisational type
Change process	Lack of support from organisational culture
	Lack of incentives
	Lack of participation
	Lack of leadership

Introduction of novel technologies into routine clinical practice will always come with challenges. During the design of this project, mitigation of the challenges reviewed above was hoped to be accomplished to some degree by the adoption of the Principles for Digital Design (digitalprinciples.org, nd) in the design and implementation of the project which is

discussed at length in 6.3 Design principles.

4.1.5 mTERG: mhealth research and reporting guidelines

As mhealth projects reside at the intersection of health and technology, a dire need exists to standardise reporting to establish an evidence base for mhealth interventions. In order to improve and standardise reporting metrics for mhealth projects, the WHO created the mhealth Technical Evidence Review Group, mTERG. The group was composed of experts in mhealth design and implementation. They developed an mhealth evidence reporting and assessment checklist to better report evidence from the myriad mhealth projects deployed worldwide (Agarwal et al., 2016). An mhealth evidence reporting and assessment (mERA) was developed. The checklist features 16 items:

- **Item 1- Infrastructure:** describe, in detail, the necessary infrastructure which was required to enable the operation of the mhealth programme
- **Item 2- Technology platform:** describe, in sufficient detail to allow replication of the work, the software and hardware combinations used in the programme implementation
- **Item 3- Interoperability:** describe how, if at all, the mhealth strategy connects to and interacts with national or regional Health Information Systems (HIS)/ programme context
- **Item 4- Intervention delivery:** elaborate the mode, frequency, and intensity of the mhealth intervention
- **Item 5- Intervention content:** describe how the content was developed/identified and customised
- **Item 6- Usability testing:** describe how the end-users of the system engaged in the development of the intervention
- **Item 7- User feedback**: describe user feedback about the intervention or user satisfaction with the intervention
- **Item 8- Access of individual participants**: mention barriers of facilitators to the adoption of the intervention among study participants
- **Item 9- Cost assessment**: present basic costs of the mhealth intervention
- **Item 10-Adoption inputs/programme entry**: describe how people are informed about the programme or steps taken to support adoption
- **Item 11- Limitations for delivery at scale**: present expected challenges for scaling

up the mhealth intervention

- **Item 12- Contextual adaptability**: describe appropriateness of the intervention to the context, and any possible adaptations
- **Item 13- Replicability**: present adequate technical and content detail to support replicability
- **Item 14- Data security:** describe security and confidentiality protocols
- **Item 15- Compliance with national guidelines or regulatory statutes:** describe how the intervention adheres to practice guidelines established by regulatory bodies
- **Item 16- Fidelity of the intervention**: describe how well the intervention utilised in practice reflects the usage intended by the designers (Agarwal et al., 2016)

Each checklist item has been addressed throughout this thesis.

4.2 Kenya National e-Health Strategy 2011-2017

The "African Regional Meeting on Digital Health for Overcoming Barriers to Ending Preventable Child and Maternal Deaths and Achieving Universal Health Coverage" held in May of 2015 and supported by USAID and the UN Foundation brought together project implementers and stakeholders from the African region to review programs currently in operation, solicit advice from field experts and allow countries to report on digital health programs and progress (African Strategies for Health, 2015a).

Overall, the region has experienced rapid growth in financing for digital technologies. The need for systems interoperability to best enable large scale data management and analysis and the scale up of public-private partnerships was encouraged. Ishrat Husein, the health systems director for USAID's Africa Bureau encouraged digital systems development with the four "C's": "country commitment, conditions conducive for private sector engagement, community focus, and cost effective interventions" (African Strategies for Health, 2015a). Kenya identified the successful implementation of the National e-Health Strategy of 2011-2017 and mhealth taskforce and the promotion of public private partnerships, increasing bandwidth, improving local ICT capacity strengthening and ownership- particularly through institutions of higher education and the establishment of innovation centres as evidence of progress since the last meeting in 2013 (African Strategies for Health, 2015a).

Indeed, the government of Kenya has identified the necessity of electronic information

management systems within the healthcare sector and has placed a focus on their development as a further step towards Vision 2030 in the devolved government. Despite the challenges that come with low to middle income nation status, there are a number of factors beyond sheer political will that place Kenya in a unique position to achieve the goals set out by their e-health strategy.

Kenya's National e-Health Strategy 2011-2017 was developed with devolution in mind and created with the broad mission of harnessing ICT to support improved quality, safety and efficacy within the health system and to use ICT to address skills shortages while moving towards grand scale ups in access and quality objectives as envisioned by the new constitution (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011). Further, the strategy states that ICT should be used to support informed policy, research and investment decisions through data mining of the health system and reporting. Information technology should also be linked with health research to expand the knowledge base of clinicians and to deliver evidence based, high standard care through access to patient health and clinical information, professional development and increased access to clinical decision support. The System should streamline and improve the operation of the national health system and lead to a decrease and in duplication and overcome system fragmentation through improvements in information and data management (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011).

The vision of the strategy and larger ICT system encompasses:

- Telemedicine
- Health information systems
- Information for citizens
- mhealth
- e-learning (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011)

The health information system (HIS) pillar, should provide:

- Patient centric information
- Pharmacy and medical supply chain information management
- Financial information- both insurance and payment
- Health workforce management and training
- Regulation (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011)

Numerous strengths and opportunities for a successful system have been articulated in the strategy, first and foremost being political will. Further to political will, Kenya has a well-developed mobile telecommunications infrastructure, high mobile phone penetration and good fibre optic infrastructure. From a professional perspective, Kenya possesses tertiary training facilities with excellent IT programs. The will and relatively high level of e-literacy among healthcare practitioners coupled with the ability of tertiary medical training institutions to incorporate e-health teaching into curricula will perpetuate and improve these e-literacy levels. Further, many tertiary medical facilities have the infrastructure to support an ICT enabled environment and develop locally relevant e-health solutions (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011).

A WHO 2013 survey of the Kenyan e-health strategy specifically with respect to women's and children's health and implementation reflects these strengths and opportunities in practice (World Health Organization, 2013d). Electronic information systems for births, death and death cause data was implemented in 2012 nationally and at the district level. Resource tracking systems have been successfully implemented and report total health expenditure per capita at the national, district and regional levels. Resource tracking for maternal and child health specifically is available at the national level. Numerous MCH indicators such as MMR immunization rates, under 5 mortality, met need for contraception, skilled birth attendance and pneumonia treatments are electronically monitored and the results available at 5 yearly intervals. ANC coverage, skilled birth attendance, postnatal care, dTAP immunization and breastfeeding statistics are also measured electronically and reported on yearly (World Health Organization, 2013d).

The e-health strategy has clearly been implemented and implemented with many successes. The challenges and obstacles to implementation of the Strategy include the brain- drain and professional skill shortages and emerging public health threats that plague this region of the world. Electricity remains unreliable in many parts of the country and equipment and infrastructure disparities between urban and rural centres hinder the feasibility of rolling out technical aspects of projects in an equitable fashion. The lack of firm data protections policies, bureaucratic inefficiency, underfunding, the risk of cyber security threats and e-health project management inexperience may impede the process oriented aspects of project implementation (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011). These same barriers to implementation were identified by the WHO survey. The need for specific legal frameworks for privacy with respect to health related data, particularly for EMR systems, was highlighted by the WHO. The lack of continuing education in ICT for health professionals already in practice remains a challenge to successful rollout of a

comprehensive and functional e-health system (World Health Organization, 2013d).

4.3 Data mining and granular reporting

Kenya's objectives both with the National e-health policy and the improvements in health service delivery through devolution reflect the goals of granular data reporting and subsequent improvements in subnational allocation of resources laid out by the United Nations (Kenyan Ministry of Health, 2014; Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011; National AIDS Control Council of Kenya, 2014; Republic of Kenya Ministry of Health, 2012b; UNAIDS, 2015). Bi annual reporting of HIV related statistics was requested of UN member states from the period of 2004 -2012 and increased to annually in 2013. This period saw an increase in data being received from 53% of states to 93% of states during the same time period (UNAIDS, 2015).

The UNAIDS Global AIDS Response Reporting Guidelines (2015) specifically highlights the need for disaggregated data (by sex and age) and for subnational data both from geographic locations and key populations. The guidelines note the importance of disaggregated and subnational data for both improvement of resource management and also detection of underlying trends and epidemiologic insights that may not be obvious without analysis of data in this way. Indeed, the improvements and areas for needed improvement identified in the Gap Report discussed in Chapter 2 are the products of disaggregated and sub national data reporting (UNAIDS, 2014a).

EMR/EHR systems have high levels of utility for these purposes as they encompass vast amounts of health related data that can be analysed rapidly for research, epidemiologic, reporting and monitoring and evaluation purposes, yielding improvements in patient and population health, cost savings and improved management and allocation of precious resources (Institute for Health Technology Transformation, 2013; Lesley & Shmerling, 2015; Milovic & Milovic, 2012). An analysis of the potential for big data management in health care underlines the need to improve both the veracity of the data and the granularity of the data if the promises of improvements in outcomes and care delivery are to be recognised (Raghupathi & Raghupathi, 2014). The use of structured data, meaning that it is easy to derive from larger records, such as the coded data used by this system, is key to realising these improvements on a large scale. Interoperability and definition cohesion with other systems in use in the region are key to interpreting and analysing data on a large scale (Institute for Health Technology Transformation, 2013). The elements that this system has incorporated to address these challenges will be discussed in the following chapter.

4.4 Chapter summary

This chapter has discussed the history and various types of e-and mhealth interventions, electronic medical records and clinical decision support systems and provided a literature review of systems that are relevant within the scope of this project. This was followed by a brief discussion of challenges to the implementation and adoption of e-health technologies. A review of the Kenyan National e-health strategy followed. The principals of data mining for reporting and quality assurance were discussed. This chapter should provide a background of evidence for the elements of the specific system designed for the research associated with this thesis to be discussed in Chapter 6 Mobile technology enhanced EMR/CDSS for the co-management of HIV and pregnancy design.

Chapter 5 Research Design and Methods

5.1 Introduction

This chapter will discuss the research design and methods used. It will begin with an overview of the hypothesis, objectives, study design, study sites, sample size and data analysis methods. The rationale and motivation for the study will be discussed in detail. The framework will be reviewed and the reader referred to the relevant chapter. A discussion of the literature review and system design periods will follow. The study setting will be reviewed in terms of demographics, administration, industry, infrastructure and the hospital where the study was conducted. Then, a brief overview of the initial visit and training, the launch, continuation and cessation of the study and the return data-collecting trip to Kakamega will follow. A brief overview of the analysis stage will conclude the chapter.

5.1.1 Aim

To explore whether utilization of a mobile clinical decision support system with access to a centralized electronic medical record and referral and consultation capabilities improves the management of HIV in pregnant women.

5.1.2 Objectives

1. To describe e-health, mhealth, electronic medical records and clinical decision support systems in depth with particular focus on the functionality of e-health and mhealth systems within the realms of pregnancy and HIV care and those that utilise wireless broadband communitcations and to review and critique the Kenyan National e-Health Strategy 2011-2017.

2. To develop a mobile technology enhanced, combined electronic medical record and clinical decision support system aimed at the co-management of HIV and pregnancy with utility in both centralized and decentralized care environments.

3. To pilot the mobile technology enhanced EMR/CDSS for the co-management of pregnancy and HIV with a small cohort of clinicians in western Kenya

4. To describe the challenges in mhelath deployment within the pilot and in other

settings.

5. To provide recommendations for future use of similar mhealth systems in resource limited settings

Pilot site:
The EMR/CDSS was piloted at Kakamega County General Hospital in western Kenya. Details of the study site are reviewed in 3.4 Obstetric practices in Western Kenya, and 5.6 Stage III- Study setting.

Trial design and Study population:
The study focused on pregnant women living with HIV over the age of 18. The study utilised interviews of clinicians who have used the EMR/CDSS. Therefore, eligible participants were:

- Pregnant women over the age of 18 who are have already been identified as being HIV positive or are diagnosed with HIV when they come to the centre.
- Clinicians who have used the tool for patient care

Data collection & Sample Size:
Data collection was to continue until 100 women had been enrolled.

Qualitative analysis: Questionnaires were distributed to the clinicians covers issues such as ease of use of the EMR/CDSS, whether consultation and referral capabilities were improved and whether the provider found that workflow was streamlined (or not).

Reflection of field and contextual challenges: Detailed logs were kept of record development and pilot implementation and challenges and solutions detailed.

5.2 Rationale and motivation for the study

The genesis of the original idea for this project was a result of studying the public health response to HIV in Mumbai, India in 1997 and working clinically as a Certified Nurse-Midwife in New York City, USA. It was the cumulative experiences of caring for women with HIV, working in an environment where pregnant women presented with infectious diseases acquired internationally and being part of a large electronic medical record rollout that lead me to envision the system that I designed for this study. I will explain each aspect individually as they occurred during my career and provide a rationale for the system that I

designed and the rationale behind the study design.

5.2.1 Caring for women living with HIV

I was born in the mid-nineteen seventies in the San Francisco Bay Area, grew up in the eighties and nineties, and moved to New York City in the late- nineties. The HIV/AIDS epidemic was woven into my consciousness from its early days. I recall the ignorance, mythology, fear and stigmatization of the virus, and the people living with it, during my childhood and teen years. I remember watching passionate, angry, intelligent, and vigilant people demand action, fight ignorance and move a nation to act up and act out and demand that response to this true public health threat not be overshadowed and undermined by fear and ignorance and I watched them succeed.

It was at Oberlin College in Ohio, USA in the mid- nineties that my interest HIV and AIDS continued and my consideration of a career in midwifery was born.I realized that the advanced practice nursing profession embodied the perfect blend of medicine, social service, advocacy and activism that I desired. This was confirmed during an internship at Brigham and Women's Hospital in Boston. The midwife I shadowed took care of the woman in the context of her family and her culture, staunchly advocated for her and respectfully put her in informed control of her own care. This was exactly what I wanted to do.

My interest in HIV and AIDS remained piqued during college and I worked in both the Sexual Information Center counselling students about sexual health, and spent a semester in India in the fall of 1997 with the School for International Training. My independent research project that semester focused on HIV and AIDS intervention programs in Mumbai. It was there that the intersection of human rights, HIV/AIDS and women's healthcare and women's rights became truly apparent to me.

After working for a few years in a biomedical research laboratory, I commenced graduate school and completed the Nurse-Midwifery BSN/MS program at Columbia University in 2002. Certified Nurse-Midwives (CNMs) in the United States are independent healthcare providers with prescriptive authority requiring a Master's degree and board certification for entry to practice. The scope of midwifery practice includes women from adolescence through end of life and encompasses primary care, gynaecology, family planning, pre-conceptional, obstetric, post partum and newborn care for the first 28 days of life. Male partners of female clients may be treated for sexually transmitted infections by CNMs.

CNMs “conduct physical examinations; prescribe medications including controlled substances and contraceptive methods; admit, manage and discharge patients; order and interpret laboratory and diagnostic tests and order the use of medical devices. Midwifery care also includes health promotion, disease prevention, and individualized wellness education and counselling. These services are provided in partnership with women and families in diverse settings such as ambulatory care clinics, private offices, community and public health systems, homes, hospitals and birth centers (American College of Nurse-Midwives, 2011).”

Care of women living with HIV was a part of routine midwifery care in New York City when I entered practice in 2003. At Brooklyn Hospital, I joined the PATH (Program for AIDS Treatment and Health) Center, a family practice model HIV care centre. I was one of two midwives who provided prenatal, family planning and gynaecological care to women presenting for HIV care. I met many inspiring women, at all stages of life, from 20 year olds who had been born with HIV to women in their eighties who learned of their HIV positive status when their husbands died of AIDS. Our midwifery clinic was not busy in the early days of the centre and I had time to sit and talk with these women. I learned about what it was like to face not only HIV, but to face the myriad challenges that come with poverty, marginalization and institutionalized racism. I felt honoured to provide them care. I endeavoured to give them the truly respectful, woman centred care that midwifery promises. This desire has informed my professional midwifery career regardless of location as I went on to work at Bellevue Hospital, Brookdale University Medical Centre and in Western Australia. These centres reinforced the importance of interprofessionally respectful, truly interdisciplinary care teams in delivering quality, evidence based, health care.

The science of HIV care from the time I began clinical practice to the present has developed rapidly and it is amazing to me that within the next few years, with increasing access to antiretroviral medications that the elimination of perinatal transmission of HIV worldwide may become a reality. It is essential that clinicians in all areas be aware of the updates to practice that occur so frequently in the HIV arena. Furthermore, they must have access to evidence based guidelines for management of the myriad co-morbidities that come with HIV, and these management guidelines must account for pregnancy as well.

5.2.2 Electronic medical records and clinical decision support systems

My career as a Certified Nurse-Midwife began in 2003. The early stage of my career marked the beginning of the transition from largely paper-based systems for recording clinical notes and receiving paper based reporting of laboratory and radiologic analyses to the beginning of digital reporting and recording of notes and results. My first clinical care appointment was in a small community health centre on the upper west side of Manhattan. This clinic employed a paper based system for the recording of clinical encounters and the reporting of diagnostic and radiologic information. The amount of time wasted by staff waiting for records to be retrieved, or on hold with a laboratory requesting results and then waiting for the results to be faxed was staggering. Prescriptions were written on paper and the possibilities for and realities of fraud were high. We were often forced to care for a patient with drastically limited amounts of clinical information because records were never located. This resulted in sub-optimal care provision, lengthy wait times for patients, and unnecessary staffing expenditures for the clinic as most clinicians worked long overtime hours to compensate for the time wasted waiting for records to be delivered. My next appointment was in a larger hospital that reported inpatient laboratory results in a digital fashion and this was certainly an improvement.

I moved to Bellevue and Gouverneur Hosptials in 2005. Both are a part of the NYC Health and Hospitals System (HHC), the largest municipal hospital system in the United States. HHC was an early adopter of electronic medical record technology with its legacy system beginning in the 1980s (NYC Health and Hospitals Corporation, 2013). Additions and improvements were constantly being made and my tenure saw the application of the EMR to the obstetric and gynaecologic clinics and onto the labour floor. The system was designed to be used across the HHC system that includes 11 acute care facilities and numerous outpatient and long term care facilities. We began transitioning from our paper notes system first by recording both in the paper record and into the EMR. Eventually we were recording only into the electronic record. Laboratory reporting and CPOE systems were eventually added. Boons were increased access to patient information, especially on the labour and delivery floor and elimination of time spent waiting for paper records though at that stage, most historical information prior to the rollout was still only recorded on the paper chart. While only paper records were in use, we would have to request charts to be ferried or faxed from the antenatal clinic or from Gouveneur Hospital, at a different location in the city, which only provided outpatient obstetric services. The EMR employed limited elements of clinical decision support in the form of alerts to drug allergies.

As a clinician, the rollout and extensive tweaking of the system was an interesting and occasionally infuriating process. The EMR was not specifically geared towards obstetric care

and in the early phases did not have the capacity to record antenatal information so that critical information from the previous visits could be viewed without migrating between numerous windows and archived visit information. The American Congress of Obstetricians and Gynecologists' issued antenatal record forms, which were the standard paper records used in antenatal care at the time, provide flow charts that allows clinicians to rapidly compare critical pregnancy data such as history, physical, laboratory data, weight, blood pressure, foetal position, foetal heart rate and urine findings rapidly as seen below in Figure 5-1 ACOG antenatal record. This style of information access was critically missing from the EMR and it had the effect of wasting clinician time and limiting the clinician's ability to analyse trends in the most critical parameters of obstetric care.

Figure 5-1 ACOG antenatal record (ACOG, n.d.)

DATE _____

NAME _____
LAST FIRST MIDDLE

ID# _____ HOSPITAL OF DELIVERY _____

NEWBORN'S PHYSICIAN _____ REFERRED BY _____

FINAL EDD _____ PRIMARY PROVIDER/GROUP _____

BIRTHDATE	AGE	RACE	MARITALSTATUS S M W D SEP	ADDRESS
OCCUPATION ☐ HOMEMAKER ☐ OUTSIDE WORK ☐ STUDENT Type of Work			EDUCATION (LAST GRADE COMPLETED)	ZIP PHONE (H) (O) INSURANCE CARRIER/MEDICAID#
HUSBAND/FATHER OF BABY			PHONE	EMERGENCY CONTACT PHONE

TOTAL PREG	FULLTERM	PREMATURE	AB.INDUCED	AB.SPONTANEOUS	MULTIPLE BIRTHS	ECTOPICS	LIVING

MENSTRUAL HISTORY

LM ☐ DEFINITE ☐ APPROXIMATE (MONTH KNOWN) MENES MONTHLY ☐ YES ☐ NO FREQUENCY:Q_____ DAYS MENARCH _____(AGE ONSET)
☐ UNKNOWN ☐ NORMAL AMOUNT / DURATION PRIOR MENES_____ DATE ONBCPATCONCEPT. ☐ YES ☐ NO hCG+ _____ /_____ /_____
☐ FINAL _____

PAST PREGNANCIES (LAST SIX)

DATE MONTH/ YEAR	GA WEEKS	LENTGH OF LABOR	BIRTH WEIGHT	SEX M/F	TYPE DELIVERY	ANES	PLACEOF DELIVERY	PRETERM LABOR YES/NO	COMMENTS/COMPLICATIONS

PAST MEDICAL HISTORY

	ONeg +Pos	DETAIL POSITIVE REMARKS INCLUDE DATE & TREATMENT				ONeg +Pos	DETAIL, POSITIVE REMARKS INCLUDE DATE & TREATMENT
1.DIABETES					16.D(Rh) SENSITIZED		
2.HYPERTENSION					17.PULMONARY (TB,ASTHMA)		
3.HEART DISEASE					18.ALLERGIES (DRUGS)		
4.AUTO IMMUNE DISORDER					19.BREAST		
5.KIDNEY DISEASE/UTI					20.GYN SURGERY		
6.NEUROLOGIC/EPILEPSY							
7.PSYCHIATRIC							
8.HEPATITIS/LIVER DISEASE					21.OPERATION/HOSPITALIZATIONS (YEAR & REASON)		
9.VARICOSITIES/PHLEBITIS							
10.THYROID DYSFUNCTION							
11.TRAUMA/DOMESTIC VIOLENCE					22.ANESTHETIC COMPLICATIONS		
12.HISTORY OF BLOOD TRANSFS					23.HISTORY OF ABNORMAL PAP		
	AMT/DAY PRE-PREG	AMT/DAY PRE-PREG	#YEARS USE		24.UTERINE ANOMALY / DES		
13.TOBACCO					25.INFERTILITY		
14.ALCOHOL					26.RELEVANT FAMILY HISTORY		
15.STREET DRUGS					27.OTHER		

COMMENTS: _____

SYMPTOMS SINCE LMP

	YES	NO		YES	NO
1.PATIENT'S AGE(35 OR OLDER)			12.MENTAL RETARDATION / AUTISM		
2.THALASSEMIA (ITALIAN, GREEK, MEDITERRANEAN,OR ASIAN BACKGROUND) MCV<80			IF YES,WAS PERSON TREATED FOR FRAGILEX?		
3.NEURAL TUBE DEFECT (MENINGOMYELOCELE,SPINABIFIDA,ORANENCEPHALY)			13.OTHER INHERITED GENETIC OR CHROMOSOMAL DISORDER		
4.CONGENITAL HEART DEFECT			14.MATERNAL METABOLIC DISORDER (EG.INSULINDEPENDENT DIABETES,PKU)		
5.DOWN SYNDROME			15.PATIENT OR BABY'S FATHER HAD A CHILD WITH BIRTH DEFECTS NOT LISTED ABOVE		
6.TAY-SACHS(EG.JEWISH,CAJUN,FRENCH-CANADIAN			16.RECURRENT PREGNANCY LOSS,OR A STILL BIRTH		
7.SICKLE CELL DISEASE OR TRAIT(AFRICAN)			17.MEDICATIONS/STREET DRUGS/ALCOHOL SINCE LAST MENSTRUAL PERIOD		
8.HEMOPHILIA			IFYES,AGENT(S)		
9.MUSCULAR DYSTROPHY			18.ANY OTHER		
10.CYSTIC FIBROSIS					
11.HUNTINGTON CHOREA					

COMMENTS/COUNSELING _____

INFECTION HISTORY	YES	NO		YES	NO
1.HIGH RISK HEPATITIS B / IMMUNIZED?			4.RASH OR VIRAL ILLNESS SINCE LAST MENSTRUAL PERIOD		
2.LIVE WITH SOMEONE WITH TB OR EXPOSED TO TB			5.HISTORY OF STD.GC.CHLAMYDIA.HPV.SYPHILIS		
3.PATIENT OR PARTNER HAS HISTORY OFGENITAL HERPES			6.OTHER(SEE COMMENTS)		

COMMENTS _____

INTERVIEWER'S SIGNATURE _____

INITIAL PHYSICAL EXAMINATION

DATE ____ / ____ / ____ PRE-PREGNANCY WEIGHT _____ HEIGH _____ BP _____

1.HEENT	☐ NORMAL	☐ ABNORMAL	12.VULVA	☐ NORMAL	☐ ABNORMAL
2.FUNDI	☐ NORMAL	☐ ABNORMAL	13.VAGINA	☐ NORMAL	☐ ABNORMAL
3.TEETH	☐ NORMAL	☐ ABNORMAL	14.CERVIX	☐ NORMAL	☐ ABNORMAL
4.THYROID	☐ NORMAL	☐ ABNORMAL	15.UTERUS SIZE	☐ NORMAL	☐ ABNORMAL
5.BREASTS	☐ NORMAL	☐ ABNORMAL	16.ADNEXA	☐ NORMAL	☐ ABNORMAL
6.LUNGS	☐ NORMAL	☐ ABNORMAL	17.RECTUM	☐ NORMAL	☐ ABNORMAL
7.HEART	☐ NORMAL	☐ ABNORMAL	18.DIAGONAL CONJUGATE	☐ NORMAL	☐ ABNORMAL
8.ABDOMEN	☐ NORMAL	☐ ABNORMAL	19.SPINES	☐ NORMAL	☐ ABNORMAL
9.EXTREMITIES	☐ NORMAL	☐ ABNORMAL	20.SACRUM	☐ NORMAL	☐ ABNORMAL
10.SKIN	☐ NORMAL	☐ ABNORMAL	21.SUBPUBICARCH	☐ NORMAL	☐ ABNORMAL
11.LYMPHNODE	☐ NORMAL	☐ ABNORMAL	22.GYNECOD PELVIC TYPE	☐ NORMAL	☐ ABNORMAL

COMMENTS (Number and explain abnormals) _____

EXAMED BY _____

NAME _____

LAST FIRST MIDDLE

DRUG ALLERGY

RELIGIOUS / CULTURAL CONSIDERATIONS _____ ANESTHESIA CONSULT PLANNED ☐ YES ☐ NO

PROBLEMS/PLANS	MEDICATION LIST:	Start Date	Stop Date
1.	1.		
2.	2.		
3.	3.		
4.	4.		
5.	5.		
6.	6.		

EDD CONFIRMATION

INITIAL EDD:

LMP ____ / ____ / ____ = EDD ____ / ____ / ____

INITIAL EXAM ____ / ____ / ____ = ____ WKS = EDD ____ / ____ / ____

ULTRASOUND ____ / ____ / ____ = ____ WKS = EDD ____ / ____ / ____

INITIAL EDD ____ / ____ / ____ INITIAL ED BY _____

18-20-WEEK EDD UPDATE:

QUICKENING ____ / ____ / ____ +22WKS = ____ / ____ / ____

FUNDALHT.ATUMBIL ____ / ____ / ____ +20WKS = ____ / ____ / ____

FHTW/FETO SCOPE ____ / ____ / ____ +20WKS = ____ / ____ / ____

ULTRASOUND ____ / ____ / ____ = ____ WKS = ____ / ____ / ____

FINAL EDD ____ / ____ / ____ INITIAL ED BY _____

VISIT DATE

_____
(YEAR)

COMMENTS:

PROBLEMS: _____

COMMENTS: _____

LABORATORY AND EDUCATION

INITIAL LABS	DATE	RESULT	REVIEWED
BLOOD TYPE	_____ / _____ / _____	A B AB O	
D(Rh) TYPE	_____ / _____ / _____		
ANTIBODY SCREEN	_____ / _____ / _____		
HCT/HGB	_____ / _____ / _____	_____% _____g/dl	
PAP TEST	_____ / _____ / _____	NORMAL/ABNORMAL/ _____	
RUBELLA	_____ / _____ / _____		
VDRL	_____ / _____ / _____		
URINE CULTURE / SCREEN	_____ / _____ / _____		
HBsAg	_____ / _____ / _____		
HIV COUNSELING / TESTING	_____ / _____ / _____	☐ POS ☐ NEG ☐ DECLINED	
OPTIONAL LABS	**DATE**	**RESULT**	**REVIEWED**
HGB ELECTROPHORESIS	_____ / _____ / _____	AA AS SS AC SC AF Ta2	
PPD	_____ / _____ / _____		
CHLAMYDIA	_____ / _____ / _____		
GC	_____ / _____ / _____		
TAY-SACHS	_____ / _____ / _____		
OTHER	_____ / _____ / _____		
8-18-WEEK LABS (WHEN INDICATED)	**DATE**	**RESULT**	**REVIEWED**
ULTRASOUND	_____ / _____ / _____		
MSAFP/MULTIPLE MARKERS	_____ / _____ / _____		
AMNIO/CVS	_____ / _____ / _____		
KARYOTYPE	_____ / _____ / _____	46.XX OR 46.XY / OTHER	
AMINOTIC FLUID(AFP)	_____ / _____ / _____	NORMAL _____ ABNORMAL _____	
24-28-WEEK LABS (WHEN INDICATED)	**DATE**	**RESULT**	**REVIEWED**
HCT/HGB	_____ / _____ / _____	_____% _____g/dl	
DIABETES SCREEN	_____ / _____ / _____	_____ 1HOUR	
GTT (IF SCREEN ABNORMAL)	_____ / _____ / _____	_____ FBS _____ 1HOUR _____ 2HOUR _____ 3HOUR	
D(Rh) ANTIBODY SCREEN	_____ / _____ / _____		
D IMMUNE GLOBULIN(RhIG)GIVEN(28WKS)	_____ / _____ / _____	SIGNATURE _____	
32-36-WEEK LABS (WHEN INDICATED)	**DATE**	**RESULT**	**REVIEWED**
HCT/HGB(RECOMMENDED)	_____ / _____ / _____	_____% _____g/dl	
ULTRASOUND	_____ / _____ / _____		
VDRL	_____ / _____ / _____		
GC	_____ / _____ / _____		
CHLAMYDIA	_____ / _____ / _____		
GROUP B STREP(35-37WKS)	_____ / _____ / _____		

COMMENTS/ADDITIONAL LABS

PLANS/EDUCATION (COUNSELED ☐)

☐ ANESTHESIA PLANS _____
☐ TOXOPLASMOSIS PRECAUTIONS (CATS/RAWMEAT) _____
☐ CHILD BIRTH CLASSESS _____
☐ PHYSICAL/SEXUAL ACTIVITY _____
☐ LABOR SIGNS _____
☐ NUTRITION COUNSELING _____
☐ BREAST OR BOTTLE FEEDING _____
☐ NEWBORN CARSEAT _____
☐ POSTPARTUM BIRTHCONTROL _____
☐ ENVIRONMENTAL/WORKHAZARDS _____

☐ TUBAL STERILIZATION _____
☐ VSAC COUNSELING _____
☐ CIRCUMCISION _____
☐ TRAVEL _____
☐ LIFESTYLE,TOBACCO,ALCOHOL _____

REQUESTS _____

TUBAL STERILIZATION DATE INITIALS

CONSENT SIGNED _____ / _____ / _____ _____

PROVIDER SIGNATURE(REQUIRED) _____

It was thus my objective to include the elements lacking from the HHS record of the time, into the record that I designed for this project, specifically sections that were conducive to the antenatal care environment. The specific elements of The electronic medical record and workflow are discussed in detail in section 6.6.1

It was during this period of rapid deployment and uptake of EMRs in the clinical setting that practice guidelines and practice manuals were being digitised. In the early stages of my

career and as a student, each midwife was required to keep a small pocket sized binder in which he or she had compiled handwritten practice guidelines. I did not find this a useful practice as one was able to actually purchase a small pocket guide to practice in the early days, or to consult a computer based clinical decision support system such as UpToDate (UpToDate, 2016). Eventually, smartphone based clinical decision support practice apps were developed so that the clinician was able to easily access this information during patient care. I began to think at this time about the possibilities of portable CDSS and how they may improve obstetric care specifically.

I moved to Brookdale University Medical Center in 2008. The practice location was a very busy labour floor in a hospital that served an incredibly socio-economically depressed population. Our rates of HIV infection were high and pregnancies were regularly complicated by co-morbidities- infectious, non-communicable chronic, psychosocial, injury and violence related, obstetric and the myriad complications that arise from deprivation and stress such as malnutrition and preterm labour and birth. Most pregnancies would not have been "normal" and the obstetric team was highly experienced in managing the complications that commonly affected our clientele.

The hospital was in close proximity to New York's John F Kennedy Airport, a major international airport serving the New York metropolitan region and pregnant women from other parts of the world were frequently transferred to the hospital with fulminating infectious processes that were not endemic to the New York region and that we had little to no experience with. The proper identification of the pathogenic processes often required an infectious disease consult, which, if in the middle of the night or during a busy work day could take time. Further, the clinical course of infectious disease processes are often altered by pregnancy. Many organisms can also have effects on the foetus and newborn. We were often faced with the conundrum of treating the woman with broad spectrum anti-infective agents immediately which could impair proper identification of the offending organism. I imagined the possibilities of a CDSS that focused specifically on the diagnosis and management of infectious diseases during pregnancy.

I relocated to Western Australia in 2010 and practiced as a Registered Midwife at King Edward Memorial Hospital, the state's only high dependency obstetric unit. King Edward had computer based clinical practice guidelines in each labour room that streamlined and regulated obstetric and midwifery management of the complex cases so often present. These computer-based clinical care and practice guidelines served to regulate care provision across the hospital system, improving care continuity and inter- professional communication. EMR

functionality was introduced slowly during my tenure there with the challenges and successes so common in other settings. Clinical care is often interrupted or slowed down during the training phase and staff disillusionment tended to be high. As I had noted in my previous practices however, once systems are running effectively and the staff has competently incorporated the technology into clinical practice, practice is enhanced overall.

5.2.3 Development of the PhD project

After relocating to Western Australia in 2010 and noting many similar challenges to those discussed previously with respect to management of medically complex cases during pregnancy, I decided to pursue a PhD in International Health at Curtin University. My initial discussion with Professor Jaya Dantas focussed on the design of a mobile CDSS that could aid in the identification and management of the breadth of infectious diseases that may complicate pregnancy. I then narrowed the focus down to the management of HIV during pregnancy and was accepted into the PhD program in February of 2012 with a proposal that reflected the same. The first year was devoted to developing my candidacy proposal and completing coursework, which helped me to incorporate policy and epidemiological concerns into my study and system design in addition to thinking clinically.

After achieving candidacy, I set to work on finding a study location. I was fortunate to be connected with a Kenyan GP and informatics specialist through a friend and midwifery colleague. Through these contacts I was connected with the NGO Uamuzi Bora and Dr John Haskew. Dr. Haskew is an infectious disease physician from the UK who had been working with a global health company called Vestergaard Frandsen. Vestergaard Frandsen started in textiles and uniforms in the 1950s, which moved into vector control and water filtration textiles in addition to other global health projects. They implement thousands of projects around the world including in western Kenya (Vestergaard Frandsen, 2014). Dr. Haskew was a member of the Vestergaard Frandsen team conducting a VCT campaign in conjunction with the Kenyan Ministry of Health in western Kenya. Dr. Haskew realised that tracking and ushering into care individuals identified as living with HIV during this campaign would be a challenge and started the NGO Uamuzi Bora to aid this task (Uamuzi Bora, 2013).

Dr Haskew, Dr Gunnar Rø, and a team designed two EMR/CDSS, one for maternal and child health and the other for HIV management for Uamuzi Bora (Uamuzi Bora, 2013). These records were in use in numerous clinics in western Kenya, including Kakamega County General Hospital, (where the pilot and study for this PhD project took place) from

2009- November 2013 (Uamuzi Bora, 2013). Dr Haskew agreed to host my PhD project in October of 2013, to liaise with study sites and to offer technical assistance with the design of my EMR/CDSS along with Dr Rø utilising the funding sources already in place and in use for Uamuzi Bora. In November of 2013 promised funding was suspended due to budgetary difficulties (Haksew, 2013). Though the funding was reinstated early in 2014, the work of Uamuzi Bora was unfortunately suspended.

At this time I was successful recipient of the Australian Postgraduate Award scholarship, and a Curtin University Postgraduate Students Association grant, which allowed me to self-fund the project with technical support and extensive advice from Drs Haskew and Rø. I was later a recipient of a research scholarship from the Curtin University School of Nursing, Midwifery and Paramedicine which contributed to the study continuation.

The design of the system commenced in early 2014 and is described in detail in Chapter 6 Mobile technology enhanced EMR/CDSS for the co-management of HIV and pregnancy design. In May of 2014, I hired a project coordinator to oversee operations in country. The project coordinator worked with Uamuzi Bora and Vestergaard Frandsen with numerous public health and EMR/CDSS projects in and around Kakamega, Kenya. Vestergaard Frandsen generously donated space in their office in Kakamega for the project. In addition to the office space, Vestergaard Frandsen agreed to manage all distribution of salary to Collins Otwane and to host and manage our numerous accounts with Safaricom, the Internet service provider providing wireless broadband services for the project.

5.3 Framework

The framework utilised for the design and implementation of the EMR/CDSS is the “Digital Design Principles” which is described in 6.3 Design principles (digitalprinciples.org, nd).

5.4 Stage I- Literature review

Because the evidence base for ehealth and mhealth systems is expanding rapidly and the guidelines for and evidence for HIV management is evolving, literature review was conducted and the literature review section of this thesis expanded up until the time of thesis submission. The process began in 2011 when I made the decision to apply to Curtin University’s PhD program. Literature review is to be found in Chapter 2 The HIV/AIDS Pandemic, Chapter 4 e-health, mhealth, Electronic Medical Records, Clinical Decision Support Systems, the Current Kenyan e-Health Strategy and Data Mining, and 6.3 Design

principles.

5.5 Stage II- System design

The system design started in 2014 after the agreement with Uamuzi Bora had been reached. Initially, the EMR was designed in a Microsoft Word format and the backbone textual and computational elements of record were programmed in JavaScript and HTML and utilised many elements of the EMR/CDSS for MCH and HIV that were used by Uamuzi Bora. An outside programmer and recent graduate of the University of Nairobi's Computer Science department was hired to help with the programming of the clinical decision support information tabs which are discussed in 6.6 System architecture and elements.

Once the record was essentially completed it was decided to migrate from the local Uamuzi Bora concept dictionary to the Columbia Earth Institute Laboratory/Millenium Villages Project (CEIL/MVP) dictionary so that data could be aggregated with larger data sets. The benefits and specifics of this decision and this system are discussed in 6.6 System architecture and elements. This process was a combined effort between Dr Rø and myself. Dr Rø was responsible for the technical aspects of the migration. I was responsible for coordinating concepts with codes and for adding additional concepts to the local dictionary.

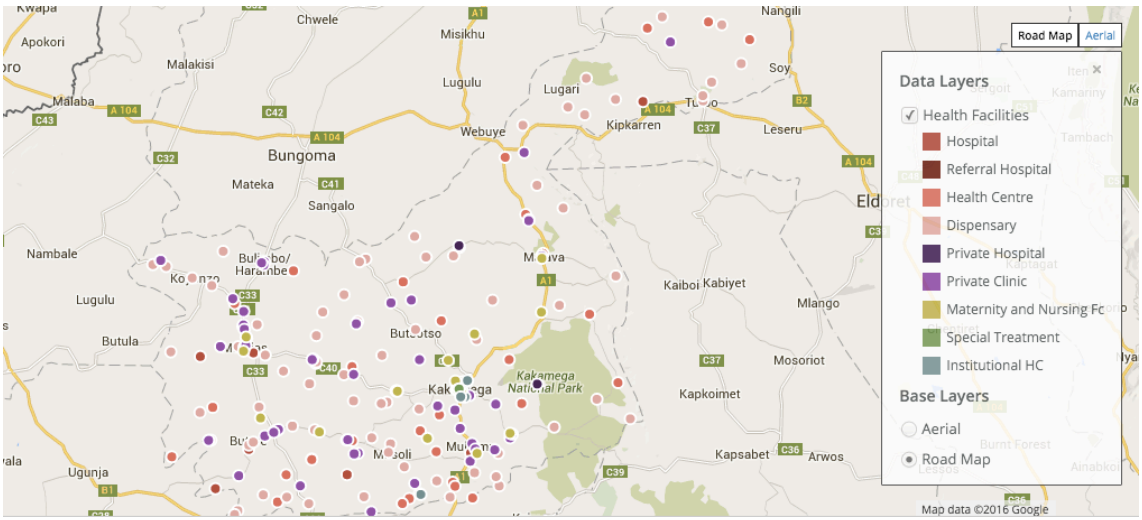
During the design stage, both the project coordinator and I were taking HTML and JavaScript courses online and learning to program the HTML elements of the record ourselves. Dr Rø, the original Uamuzi Bora programmer remained available for the more difficult JavaScript programming. The programming of the EMR/CDSS was essentially complete by November of 2014 when the training and implementation phase began. Mr Otwane and I modified certain elements of the record to reflect requests made by the trainees who would be using it in clinical practice.

5.6 Stage III- Study setting

This section will provide an overview of Kakamega County, Kakamega Town and a brief description of Kakamega County General Hospital. An epidemiologic review of health, HIV and obstetric factors in the area was covered in Chapter 3 History and epidemiology of HIV in Kenya and the national response to the epidemic, 3.3 Epidemiology of HIV in Kenya, and 3.4 Obstetric practices in Western Kenya. Specifics regarding the Kenyan e-health strategy were covered in 4.2 Kenya National e-Health Strategy 2011-2017.

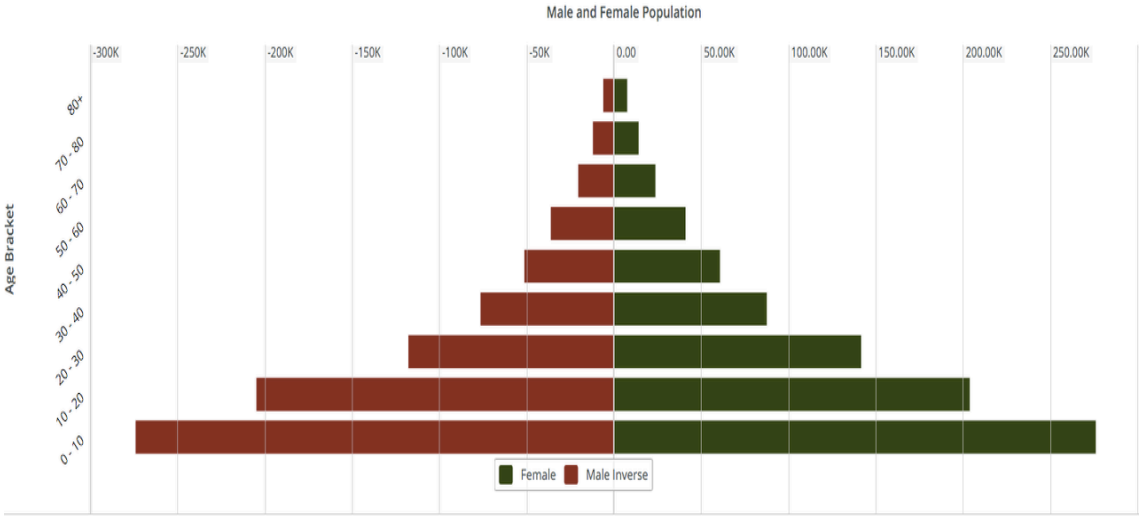
5.6.1 Kakamega demographics

Figure 5-2 Kakamega County map with health facility distribution (Kenya Open Data, 2016a)



Kakamega County is in the former Western Province of Kenya. Its largest town, Kakamega Town, lies 30km north of the equator and has an elevation of 1535m. Kakamega County is the second most populous county in Kenya after Nairobi and according to the 2009 census, Kakmega County had a population of 1,660,651 people (County Government of Kakamega, 2016a). This was projected to rise to 1,929,401 by 2015 (Republic of Kenya Agricultural Sector Development Support Programme, 2016). Kakamega County has a population density of 544 persons per square km on a landmass of 3051.2 sqm. Kakamega comes from the word for “pinch” in the local dialect, which described the way that colonialists ate the staple food, obusuma. Kakamega County has a majority ethnic Luhya population, which is the second largest ethnic tribe in Kenya and represents 14% of the Kenyan population (County Government of Kakamega, 2016a).

Figure 5-3 Kakamega County age pyramid (Kenya Open Data, 2016b)



5.6.2 Kakamega County administration, industry and infrastructure

Kakamega County encompasses 9 constituencies Butere, Mumias, Matungu, Khwisero, Shinyalu, Lurambi, Ikolomani, Lugari and Malava (County Government of Kakamega, 2016a). 49.7% of the country's labour force hails from Kakamega County and agriculture is the main employment activity. Mining, forestry, brick making, construction, service and wage labour are other key industries of employment (Republic of Kenya Agricultural Sector Development Support Programme, 2016). Sugar cane, maize and tea are the main cash crops and beans, cassava, finger millet and sorghum is grown in smaller quantities. Kakamega boasts a large protected old growth rainforest and forest tourism is a fruitful economic activity (Republic of Kenya Agricultural Sector Development Support Programme, 2016).

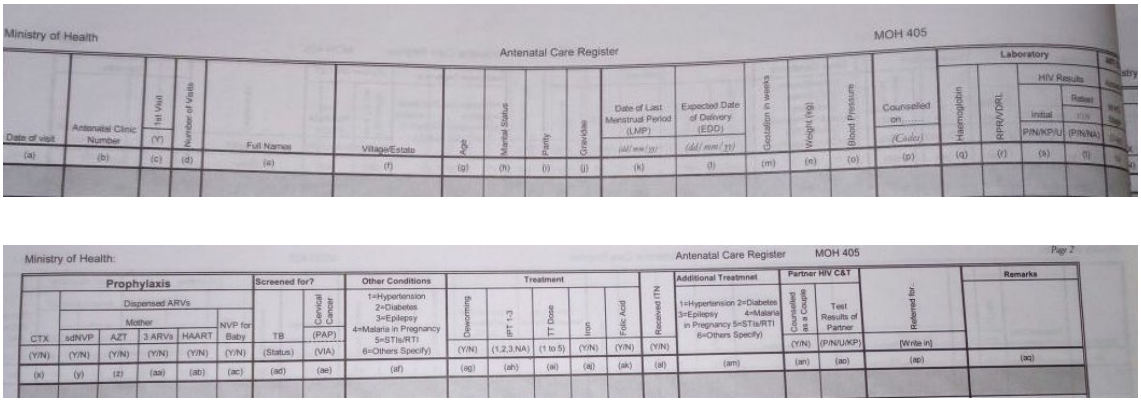
Kakamega County has 3500 km of roads, 260 km of which are paved with bitumen though most roads are described as not routinely passable by the County Government of Kakamega. Currently numerous road improvement projects are underway with sugar companies and the government both contributing funds to the projects (County Government of Kakamega, 2016b). There is 80% coverage from mobile telephones. Along the major roads, fibre optic cable has been laid for telecommunications and Internet services (County Government of Kakamega, 2016b).

5.6.3 Kakamega County General Hospital

Kakamega County General Hospital is the main teaching and referral hospital for Kakamega County and receives referrals from other counties as well. It is a 440 bed, 80 cot facility 2km from the town centre. Kakamega County General Hospital has 2 surgical theatres, 1 maternity theatre and has an emergency department and a radiology department with x-ray and ultrasound services. Currently, the hospital is undergoing major upgrades worth KSH 200 million (www.mygov.go.ke, 2015).

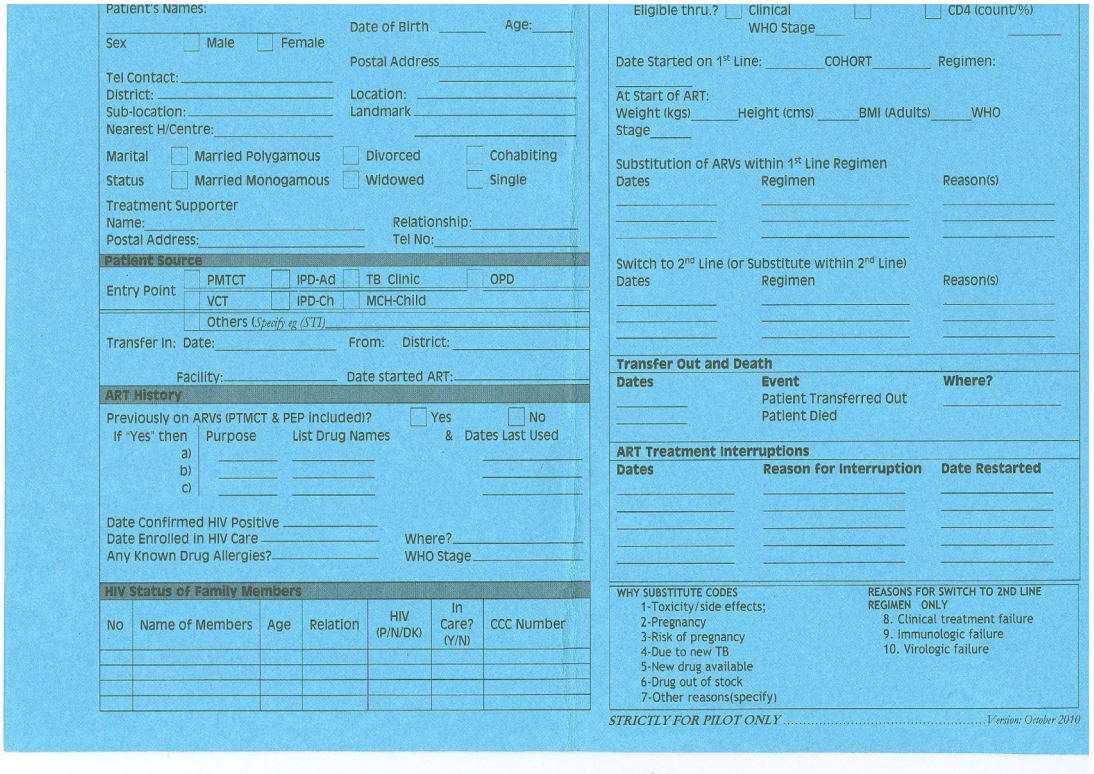
The pilot and launch for this project took place in the outpatient maternal child health unit. There, antenatal and postnatal patients are seen by clinical officers, students, nurses and midwives, with the bulk of the care being provided by nurses and midwives. Antenatal care data is recorded in two fashions. The first is in the MCH care ledger. Each patient seen has her data recorded in a common register according to the order in which she is seen see Figure 5-4 Antenatal care ledger pages 1 & 2.

Figure 5-4 Antenatal care ledger pages 1 & 2



The second method of data recording is in the mother child booklet. This is a booklet that the woman carries on her person. The maternal child health booklet may be accessed here: https://www.k4health.org/sites/default/files/Mother%20and%20Baby%20Booklet%20Sept%202010.pdf

Figure 5-5 Clinical Care Card



While all women living with HIV will be known to the Comprehensive Clinical Care Centre (CCC) for specialty HIV management, routine distribution of ART services during pregnancy are under the purview of the managing clinician in the MCH, whether this be a clinical officer, doctor, midwife or nurse. Mentor mothers represent another link in the care of women living with HIV specifically. Mentor mothers are mothers living with HIV who provide counselling, tracking, emotional and treatment support services (mothers2mothers, nd).

In a typical month, at the Kakamega County General Hospital MCH clinic, around 200- 250 antenatal care patients are seen, of which around 10-15 will be women living with HIV. These numbers are congruent both with Kakamega County and Kenyan national rates of HIV positivity (National AIDS Control Council of Kenya, 2014).

5.7 Stage V- In country visits, training, launch, data collection and conclusion of the pilot

Two trips were made to Kakamega, Kenya. The first was to finalise approval and conduct training for the project and the second was to collect data from the pilot.

5.7.1.1 The initial visit, December 2014

The first visit to Kakamega was in December of 2014. The purpose of this visit was fourfold. The first mission was to meet with the Ministry of Health Officials to secure final approval for the project and the study. The study proposal used to gain in country ethics approval through Moi University Teaching and Referral Hospital's Institutional Research Ethics Committee (IREC) was circulated to all relevant Ministry of Health and Hospital Officials. All had expressed support for the project prior to my visit and required an in person meeting to secure official approval.

The first few days were dedicated to introductions and meeting with the various County Ministry of Health and KCGH officials involved in approval of the project. .

The second objective was to secure final IREC approval from the Moi University Teaching and Referral Hospital in Eldoret. Theoretical approval was received in June, 2013 by IREC but the funds were not able to be transferred electronically as the bank used by IREC only accepted Kenyan Shillings and Westpac Bank in Australia, where the funds were coming

from, was not able to distribute Kenyan Shillings. Final approval was received when IREC received the cash payment.

Once Ministry of Health and Hospital support and final ethical and hospital approvals were received, the details of the training were finalised with Sister Joy, the director of the MCH clinic. It was decided that two sessions would take place. Each session conducted trained the clinicians in all aspects of the study design, the consent process and usage of the EMR/CDSS. Refreshments were provided and vouchers were supplied for lunch.

Eight Chromebooks were available for the training and the training was conducted by tapping in to the EMR/CDSS demo site so that patients created for the purposes of the training were not later erroneously included in the prospective data. Two to three trainees shared a computer and practiced each element of record creation and usage while the same material was being projected from my computer onto a large screen. I was able to visit individually with each team of trainees to help elucidate aspects of the record that were not intuitive.

Figure 5-6 EMR/CDSS training at KCGH

The majority of the trainees expressed satisfaction with the system. The main suggestion was to amend the style of parity recording. It is common to record obstetric parity at KCGH in a n+/-n format such that the first n represents the number of live births. The second n

represents the subtraction of a pregnancy through spontaneous or therapeutic abortion preceeded by the – sign or an additional child, such as a twin or triplet birth, delineated by the + sign. As the system functionality did not accommodate this, it was decided that the parity would be described in as an integer representing live births. Any discrepancy between gravity and parity would be elucidated in the problem list and the pregnancy history section of the record that allowed for more accurate recording of pregnancy outcome.

We also decided as a group to allow the selection of "normal" and "none" as answers to the history and physical sections. Previously, a blank entry would have been considered to be "normal" or "none" by default, in an effort to save time.

The main challenges identified during the training phase were unfamiliarity with the track pad and difficulty typing, though most of the record utilises drop down menus, so this was not expected to cause egregious hinderance. The clinicians expressed worry about the time needed to fill out the initial visit, but agreed that the follow up visits would be easier to enter. All agreed upon changes to the system were made before I departed from Kakamega.

5.7.1.2 The launch

The in-depth, critical details of the challenges encountered in the period leading up to the launch of the system and during the study period will be reviewed and analysed in Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance. A brief overview of the timeline and challenges will be introduced below for the purposes of summary.

After the training, it was decided to delay the launch of the project until January of 2015. This was decided for two reasons. The first was that most of the clinical staff of the MCH was being sent into the field during the remainder of December for a public health campaign. The clinic would be operating with a very limited number of nurses and midwives supplemented by clinical officer, nursing and midwifery students. This is a common occurrence. The MCH in- charges, Mr. Otwane and I felt that it would be sub-optimal to begin the launch when the staff was already operating at minimal staffing levels and also outside the bounds of fairness to the already burdened clinicians.

By the end of January of 2015, the proposed system launch was stymied by numerous environmental, technical and operational challenges. January and February brought heavy storms to the area causing repeated, widespread power outages. One of these storms knocked

down the tower that housed the radio essential to the communications for our project. This was eventually repaired but required that a technical team be sent out to rebuild the tower and install a new radio as ours was damaged.

As was reviewed in Chapter 3, the challenges of reorienting the healthcare system under the new devolved government resulted in high levels of staff dissatisfaction. This period saw the institution of a "go slow" that severely affected clinical operations in the county. The "go-slow" entailed the provision of essential services, as opposed to a strike, but made the launch of the project an impossibility. The technical, operational and environmental challenges resolved to a point that we were able to launch officially on the 6th of March, 2015. In anticipation of the official launch, Mr. Otwane retrained the staff to the use of the system in the first week of March.

A critical element of the EMR/CDSS design was to allow remote access to the system via a VPN. Dr Rø and I were supposed to have access via a password securitised VPN so that we could monitor the system in real time. This VPN was initiated and paid for when the system was set up with Safaircom. The initial security settings of the VPN were not stringent enough to satisfy Dr Rø. Dr Rø required higher levels of security as patient information could be accessed through the VPN. This led Dr Rø to reconfigure the settings remotely. When the reconfiguration was carried out, Safaricom disabled system access via the VPN. In order to reinstate access a Safaricom technician would have to visit the Uamuzi Bora offices and reconfigure the router in person. This took a very long time to occur. When the settings were finally reset to again allow access, they were again not secure enough to comply with standards for electronic patient information securitisation and confidentiality.

As the VPN could be hacked and patient information accessed, the configuration was again modified to increase security to a level acceptable for compliance with standards. This caused VPN access to again be denied and Safaricom was again called out to reconfigure the router settings to allow VPN access. By the time of my second visit to Kakamega VPN access was never achieved in a secure enough fashion to allow it to be operational. The result of this access denial was that neither Dr Rø nor I had the ability to monitor the record.

5.7.1.3 The second visit to Kakamega and prospective

data collection

In mid- October, the failure of a bill to be paid to Safaricom caused the lines used for the project to be suspended and functionality of the system to be obliterated. As 133 patients had now been consented and entered into the system according to reports from the in-charges and Mr Otwane, this would mark the termination of the pilot phase.

My second visit to Kakamega commenced on the 26th of October, 2015. The questionnaires were collected during this visit. Mr. Otwane and I visited the MCH to thank the nurses and midwives, mentor mothers and patients for their help and support.

As reviewed earlier, study data was inaccessible at this time because the VPN was not operational. Over the course of the five days of my stay, Safaricom was communicated with numerous times per day but a technician was never available in the area to come to the office to reconfigure the VPN.

Eventually a Skype call with Dr Rø allowed Mr. Otwane and I, to directly download the data from the server in LINUX using instructions from Dr Rø. The data was emailed to Dr Rø so that he could extract the parameters that I required and return them to me in CSV format. I left Kakamega on the 30th of October. Dr Rø finished the data extraction in mid-December, 2015. Upon inspection, it was immediately apparent that there were numerous incongruities between the data and the pilot design. The most important of which were:

- There were only 67 records entered into the system
- The majority of these records were unpopulated, so did not contain data regarding the parameters requested by me nor required by the system
- The first record entered was on the 26th of September, at the end of the pilot period

It became apparent that the numbers enrolled into the study and the patterns and quality of EMR/CDSS usage were incongruent with the answers on the questionnaires. To confirm this, Dr Rø analysed the number of times the Chromebooks communicated with the server. Aside from the trainings in January, not a single episode of communication was recorded until the end of September, 2015 despite all reports to the contrary.

The decision was made to relaunch the system with improved supervision and oversight. The relaunch of the project was plagued by similar technical, infrastructural and weather related challenges as the first. After 5 ½ months of attempting to restore reliable Chromebook connectivity to the server, the effort was abandoned. An in-depth timeline and discussion of

the myriad factors that led to these outcomes, the implications, analysis and recommendations are discussed in Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance.

5.7.2 Stage VI- Analysis

Qualitative analysis was not possible as the clinicians filled out the questionnaires as if they had indeed been using the system at the point of care, which was not the case, rendering this data void. After the failure of the second round of the study to launch, it was decided that the data analysis would take a "challenges and lessons learned" approach. The decision was made to focus on a reflection of the infrastructural, technical and project management challenges faced during the pilot. The documentation of the technical, infrastructural and weather related challenges was robust and revealing. This allowed timelines of events and delays to be recorded and analysed providing a realistic scenario of the challenges and limitations of a cloud based EMR/CDSS of this scale, run by a small organisation, in this setting. Please see Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance for these discussions.

5.8 Stage VII- Quality and rigor

Numerous safeguards were intrinsic to the design of both the study and the system design. The theoretical underpinnings of the study were tacitly approved when the researcher achieved candidacy in March, 2013. This was followed by ethical approval by the Curtin University Human Research Ethics Committee, which was secured in December of 2013. The delay between candidacy approval and Curtin University Human Research Ethics Committee approvals was due to my maternity leave from April-December 2013.

Ethical approval with Moi University was finalised in December of 2014. The initial application was made in early 2014. IREC required that the supervisory team include someone with in-country experience specifically in the field of health information systems. Dr Haskew was approached and agreed to act as the in county supervisor and added to the supervisory team through Curtin University. The proposal was resubmitted and IREC determined that the supervisor should be a Kenyan national. An extensive online search was initiated through numerous channels including personal contacts and in an online forum for Health IT professionals. Dual recommendations of Professor Peter Waiganjo Wagacha came through both an online forum and also from Dr Judy Wawira Gichoya.

With the addition of Professor Waiganjo Wagacha, a senior lecturer in the Computer Science and Informatics Department at the University of Nairobi and the final payment of the IREC fees, ethical approval was completed in December 2014. Both HREC and IREC ethical approvals were maintained during the implementation and data collection phases of the study. As is evidenced from the discussion of the launch above, numerous factors affected the rigor and the quality of the study itself. These will be analysed and discussed in depth in Chapter 7 Challenges to Successful Implementation and Chapter 8 Discussion, recommendations and significance.

5.9 Chapter summary

This chapter commenced with a discussion of the research design and methods, including the hypothesis and objectives of the project and associated thesis. The rationale and motivation for the design of the EMR/CDSS was elucidated and the development of the PhD project was described in its various stages: identification of the philosophical framework, the literature review, and system design. The demographic details, administration, industry, infrastructure and hospital setting in Kakamega County were described. A discussion of the timeline of in country visits for training and data collection were described as well as an overview of the pilot launch and study period. The analysis stage was briefly covered with a review of quality and rigor of the study.

Chapter 6 Mobile technology enhanced EMR/CDSS for the co-management of HIV and pregnancy design

6.1 Introduction to the chapter

Chapter 5 begins with a brief presentation of the EMR/CDSS and then presents the design principles that underlay the system design and that should be adhered to when designing for the digital sphere in resource- constrained settings. An in depth system description follows. Additional ideal system elements that were not possible due to scope, technical and site restrictions are presented. A summary of the chapter follows.

6.2 Understanding the need

Underpinned by the background and literature review of HIV and the value of EMR/CDSS presented thus far and the urgent need to effectively support pregnant women with HIV, a combined mobile technology enhanced electronic medical record and knowledge based, passive-active clinical decision support system (EMR/CDSS) focused on the co-management of HIV and pregnancy was designed by this writer to be used by the clinician at the point of care. This system is Internet based and run on Chrome Books (low cost laptop computers with Internet access) that access wireless broadband services, but could also be run on a desktop computer and accessed through a fixed broadband connection as well (Google, 2013).

The system seeks to maximize the utility of healthcare providers and health care facilities, extend the geographic access and patient volume capacities of providers, improve diagnosis and treatment by providing management guidelines for the many facets of HIV and pregnancy co-management, including adherence to ART regimens and retention in programs, engage and educate patients while reminding them of upcoming appointments and improve data management and analysis. It also aimed to improve referral and consultation mechanisms, compensate for health worker shortages and lead to the professional development of healthcare providers. Because of the technology's mobile nature and use of open source software, the system is appropriate for a high tech, centralized environment as well as a low technology setting lacking a grounded Internet connection and even electricity.

6.3 Design principles

The Principles for Digital Development, an organisation dedicated to the design and implementation of digital solutions in resource limited settings, and having the support of many multinational organisations such as the United Nations, World Health Organization, UNICEF, the Bill and Melinda Gates Foundation, among many others, has developed a set of principles to guide the design and implementation of digital solutions. This guide will inform the backbone of the discussion of the principles that went into the design of this system (digitalprinciples.org, nd).

6.3.1 Principle 1: Design with the user

Stakeholder and provider input and acceptance is key to successful digital program implementation. End users must have proper training, technical support, and an understanding of how both the knowledge base is derived and also how the system will ultimately aim to improve both clinic performance and workflow (Carter, 2007). Thus, it is imperative that systems be designed with the end users' stipulations and needs (digitalprinciples.org, nd).

The design of this system built on multiple elements of end user needs and input. The EMR/CDSS for the co-management of HIV incorporated two EMR/CDSS previously used at the study site, one for HIV care and the other for antenatal care. Both of these systems incorporated clinical decision support elements as patient flags, though did not include the information tabs that will be described below. These records were developed by the partner NGO to this project, Uamuzi Bora and mirrored in most aspects the Kenyan Ministry of Health paper forms that were already in use. This previous system was shown to improve record completeness in the antenatal care setting by 42.9% (Haskew et al., 2015a). Secondly, the clinical decision support elements of this record drew the knowledge base from multiple sources, with the Kenyan Ministry of Health management guidelines at all points included. Thirdly, during the provider training session, the nurses, midwives, HIV specialist physician, electronic medical records officer and all officers within the county Ministry of Health were given the proposal, access to the record and the opportunity to amend the record to best fit their envisioned user experience with the record being edited in real time.

6.3.2 Principle 2: Understand the existing ecosystem

Principle 2 stipulates that the local ecosystem, practitioners and regulatory framework be well understood (digitalprinciples.org, nd). This project was fortunate that Uamuzi Bora had already been working in the area for some time and many lessons could be learned from their experiences. Relationships with the hospital and county Ministry of Health were established and provided an excellent entrée for this project's introduction and acceptance. This principle was further enhanced as the open source software system utilised by the project was developed in Kenya specifically for the management of HIV and had many stakeholders already aware of the system and local ownership established. Cooperation with all national and county policies was assured and the study received the approval of the Institutional Research and Ethics Committee of Moi University. The project was aligned with both the vision of the local players and also the Kenyan legal framework and policies surrounding clinical care and health information systems (digitalprinciples.org, nd).

6.3.3 Principle 3: Design for scale

Numerous considerations go into designing for scale and these considerations are particularly pertinent to the HIT community. While the project targets a specific subset of diagnoses, namely the peripartum period, HIV and associated co-morbidities, many elements of the record are indeed scalable, customizable and able to be integrated into larger systems. Two aspects in particular make this project align to this principle- namely the use of the open source software system, OpenMRS and the use of the Columbia Earth Institute/Millennium Villages Project concept dictionary, both of which will be described in depth in section 6.6. At the end of the study, the forms used for this record will be published on a Github site so that they may be used in other settings as well as altered to fit the local environment. This principle also suggests that impact be demonstrated before scaling a solution (digitalprinciples.org, nd). The system enjoyed a pilot period, where numerous systems related factors were learned and rectified with the aim of making a small-scale deployment more effective. Studies of the small-scale deployment will inform upward scalability.

6.3.4 Principle 4: Build for sustainability

This principle incorporates three major themes: to plan for sustainability from the project's inception and to ensure long-term financial health, to engage and invest in local developers and communities and to ensure alignment with national strategies (digitalprinciples.org, nd). OpenMRS, the software system used for the design of the EMR/CDSS was developed locally, and a local programmer was used, in conjunction with the designer and the original programmer based in the UK. A local project manager was employed by the project to oversee daily operations, and he had a long and fruitful relationship with the hospital and Ministry of Health through his work with Uamuzi Bora.

This project began on a donor driven model. Indeed, unanticipated shortfalls in funding necessitated a shift in the project scale and goals to accommodate this shortfall. The funding model remains donor driven though, in alignment with the national e-health strategy and active plans for Internet functionality at the study site, a large portion of the costs should be absorbed by the health system without going beyond what was already planned for. As the system utilises the same open source software system likely to be utilised by many Kenyan National EMR systems, elements of this record may be merged with a larger system if deemed appropriate and data can be integrated into larger data sets.

6.3.5 Principle 5: Be data driven

Principle 5 encourages real –time data derivation and analysis throughout the life of the project; using project derived data to inform project decisions and to innovate solutions where gaps exist (digitalprinciples.org, nd). The aim of the project from its inception was to harness the power of data to inform real time decision making both on pilot and study levels but also to supply the relevant authorities within the clinic, hospital and Ministry of Health with data of their choosing to assist in quality assurance, reporting and monitoring and evaluation. During the pilot phase of this study, security elements of the VPN did not allow the programmer and study designer access to the data in a secure enough manner for real-time monitoring via VPN. Encrypted data dumps were available from the hard drive, however, and this was used to gather information about the pilot phase.

6.3.6 Principle 6: Use open standards, open data, open source and open innovation

The usage of open standards, open data, open source and open innovation are key to scalability, particularly in resource- constrained settings. Segregated proprietary systems which hinder interoperability by design are not appropriate to either scale or open standards, nor do they align with the tenets of the primary health care model as espoused by the Alma Ata Declaration (digitalprinciples.org, nd; International Conference on Primary Health Care, 1978). Furthermore as Van Heerden, Tomlinson and Swartz (2012) emphasize, mhealth systems need to be interoperable with e-health systems currently in use. Disparate, proprietary and tailor made systems perpetuate many of the problems already witnessed in vertical public health interventions. Individual systems that do not cohere with systems used regionally and internationally may be useful during the pilot stage but will face challenges in being brought up to scale. Furthermore, they are not sustainable. Using a platform already in existence and used widely in the region will allow a new aspect of the system to be brought to scale rapidly, will adhere to the standards for privacy, security and confidentiality already utilized by those systems and will require minimal training of staff to implement.

Open source software presents a remedy to the problems encountered both in the implementation of proprietary software and with tailor made systems. Open source software authorizes users to copy, modify and adopt the software provided. In turn, the adapted software must be made available to the open source community (Loiterman, 2010). The utilization of open source software also contributes to in-country capacity and economic development as fees are generally given to local developers and implementers rather than an out of country developer (Seegbregts et al., 2009). As such, development is fostered overall, adding to the comprehensive nature of the public health intervention. Central to the design of this system, the software itself is the open source system, OpenMRS. The system is available for demo at www.arantphd.org and download via Github at at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy

6.3.7 Principle 7: Reuse and improve

Principle 7 builds upon principal 6 as it recognises the importance of improving technologies that are already present in the digital sphere (digitalprinciples.org, nd).This principle builds upon the work described above. The system designed for this study integrated two EMR systems that were already in use, based in open source software and piloted at the study site.

The addition of passive and active elements of clinical decision support may be viewed as an improvement.

6.3.8 Principle 8: Address privacy and security

Personally identifiable information, particularly sensitive health information, must be protected and it is incumbent upon the designers of digital solutions to assess and mitigate threats to privacy and security from leakage of information- accidental and intentional, whether digitally derived or as a result of theft of hardware or paper records (digitalprinciples.org, nd). This project has planned for the security of both paper and digital information. The plans have received approval from the Curtin University Human Research Ethics Committee and the Moi University Teaching and Referral Hospital Institutional Research and Ethics Committee.

The OpenMRS EMR system itself requires password access and role privilege-based access. Authorised users must log in and each authorised user is only able to access information as delineated by the system administrator (OpenMRS, 2013). Nurses and midwives involved in direct patient care at the antenatal clinic for women living with HIV have access to patient information, as do the consulting nurses, midwives, clinical officers and physicians in the Comprehensive Clinical Care Unit for HIV care and the labour and birth suite.

The EMR is hosted on a server located in Kakamega, Kenya. It was designed to be accessible securely and remotely via a Virtual Private Network (VPN) and designed to be accessible remotely by password protected IPs, which allow the server to be administered remotely and the data to be backed-up, encrypted and stored daily. The data is also backed-up in an anonymised fashion without identifiable data to allow for operations research. This information was to be accessible to researchers via a REST API remotely and securely. Individual patient medical records are also securitized in a manner that corresponds to strict international standards. Additional communications related security is discussed in section 6.5 The server itself is stored in an alarmed and locked office on the third floor of a shopping centre in Kakamega town. The shopping centre is under armed surveillance 24 hours per day. The server may be erased remotely in the rare event of theft.

6.3.9 Principle 9: Be collaborative

The ninth design principle urges developers to work across sector silos, engage diverse

players to build holistic responses and share processes, information and results under a creative commons license (digitalprinciples.org, nd). This project has engaged players from diverse backgrounds. The system designer and this author has a clinical background as a Nurse-Midwife Practitioner with over 10 years of clinical experience in caring for women living with HIV in addition to experience with EMR/CDSS from a clinical care perspective. The Uamuzi Bora team involved with the project implementation includes an infectious disease doctor with programming capabilities and a computer programmer. The project manager is from the region of the study and has a medical IT project management background as well as programming skills. A local computer scientist helped to program the record as well. All members of the team look forward to sharing results of the pilot with the broader community and endeavour to do so under the creative commons license. As stated previously, the EMR/CDSS code is accessible at at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy. The record may be demo'd at www.arantphd.org.

6.4 The setting

The system was piloted at Kakamega County General Hospital in Kakamega County in western Kenya. The study has received ethical approval from Moi University in Kenya and Curtin University in Australia. The system runs on Chromebooks, communicates with the server directly via SIM air grab of the VPN and was designed to be used at the point of care by the nurses and midwives providing care at the antenatal clinic for HIV+ women in the Kakamega County General Hospital Department of Maternal and Child Health. Four Chrome Books were located at the MCH for routine care. An additional Chromebook resided in the labour and birth suite so that information could be accessed there when women arrived in labour or for triage. The medical and nursing staff at the CCC had a Chromebook to evaluate patient records for the purposes of consultation. The pilot phase of the study did not employ data entry clerks, as this would limit effectiveness of the real time clinical decision support elements of the system.

6.5 Communications

Safaricom, a Kenyan telecommunications company supplies the bandwidth, VPNs and WIMAX for the project. Each Chrome Book is loaded with a SIM card that accesses a VPN via the Safaricom 3G mobile network. The server housing the EMR/CDSS accesses the VPNs via a WIMAX (worldwide interoperability for microwave access) radio transmitter. The server and Cisco router are located in a locked and alarmed office which is under armed security 24 hours per day and has generator back up to ensure continuous operation even in

the event of the frequent power outages that affect this region. The router is connected to a WIMAX radio transmitter on the roof of the building. The router is also connected to the server. The radio transmitter on the roof communicates with a base station that is located about a half a kilometre away. The Chromebooks registered to the project access a VPN via air grab from the Internet. Only registered computers can access the VPN. This cloud-based model of EMR deployment alleviates the need for hospital based Internet infrastructure. Only a single server is maintained centrally. Secure, password securitised IPs allow the designer and the programmer to access the server remotely. Though not the intended usage in this context, the system may be accessed by grounded Internet or used locally downloaded to the computer's hard drive and data stored there.

6.6 System architecture and elements

The EMR is based in the OpenMRS medical record system. OpenMRS is a "highly configurable, scalable and extensible open source EMR application" (Seegbregts et al., 2009). It is an open source software that utilizes the java and JavaScript technical architecture. The software is designed to be implemented by non-programmers and is supported by an open source community of volunteers. The software was originally designed for the AMPATH clinic in Kenya and further developed by Partners in Health and the Regenstrief Institute of Indiana University (Seegbregts et al., 2009). The code base is maintained by an open source development community and has been implemented in hundreds of locations. The software was originally developed with a focus on the management of HIV, AIDS and tuberculosis but has been implemented more extensively in subsequent years (Seegbregts et al., 2009). The customised OpenMRS EMR/CDSS for this project operates on Ubuntu Linux.

The EMR/CDSS utilizes the MVP-CIEL concept dictionary. This dictionary was developed by the Millennium Villages Project and the Columbia International e-health Laboratory and seeks to create a standardized dictionary for medical, laboratory and pharmaceutical concepts that relate to several internationally recognized standards for biomedical terminology including:

- ICD-10- the World Health Organization's medical classification list in its 10th revision.
- SNOMED CT- Systematized Nomenclature of Medicine- Clinical Terms, a comprehensive, multilingual and computer tractable and systematically organized repository of clinical healthcare terminology
- LOINC- Logical Observation Identifiers Names and Codes, a universally

standardized database of laboratory observations

- RxNORM- a repository of pharmaceutical vocabulary (OpenMRS, 2014)

This dictionary was chosen with the objective of utilizing internationally recognized and standardized terminology. It was also chosen so that this particular EMR could be incorporated into larger EMR systems utilizing the same concept dictionary. It further allows for aggregation and analysis of data within and in conjunction with larger systems. Each concept is coded with an identification number and includes a definition, synonyms, search terms, data type (coded, Boolean, text, numeric, etc.) and is mapped to its corresponding standard or standards. The MVP-CIEL may be customized at the local level- meaning that each EMR may have unique terms and definitions that are not part of the larger MVP-CIEL dictionary (OpenMRS, 2014). This particular EMR does have unique local terms.

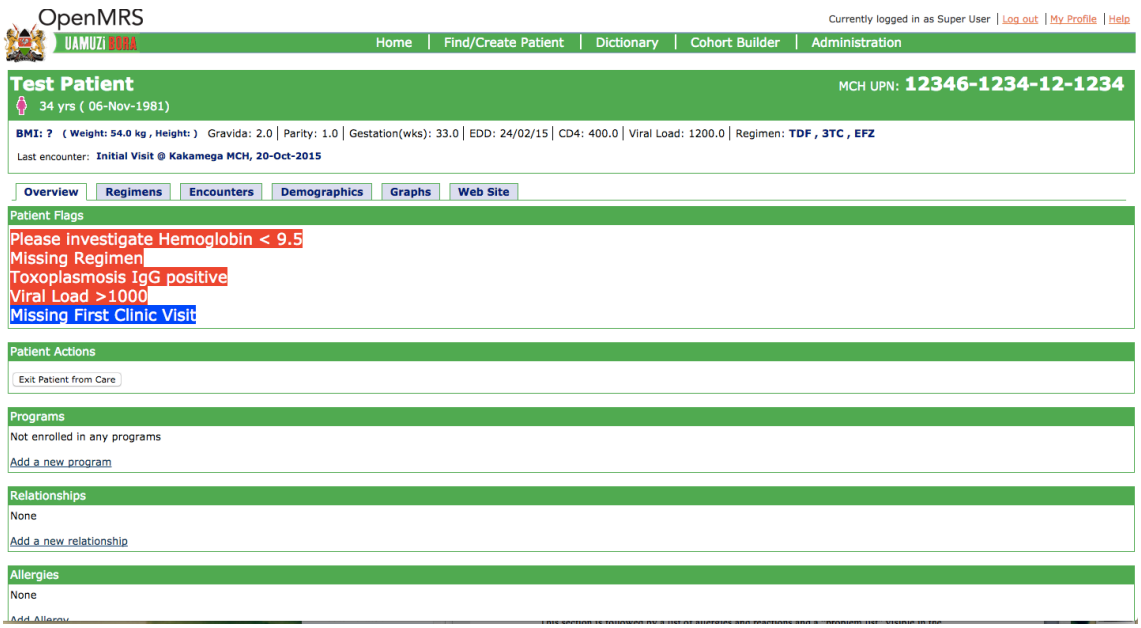
6.6.1 The electronic medical record and workflow

Individual patient records are created utilizing demographic information that will correspond to a generated unique patient identification number. Upon entering an individual patient record the user may access one of four sections.

Overview- this section incorporates:

- **Patient flags**- administrative and clinical values that are either missing or out of bounds.
- **Patient actions**- administrative actions such as exiting a patient from care
- **Program enrolment**- for example enrolment in an HIV in pregnancy program
- **Relationships**- to clinicians, care givers and family members and support persons
- **Regimens**- this section lists all completed, current and future treatment regimens.
- **Encounters**- this section is the clinical care record and it includes the initial visit and the revisit electronic forms
- **Demographics**- this section contains demographic administrative data including contact information and the patient's nearest health centre
- **Graphs**- two graphs chart CD4 count and haemoglobin level over time

Figure 6-1 Patient overview with flags



The EMR's clinical care forms incorporate aspects of both HIV and antenatal care and are organized into two electronic forms: the initial visit and the revisit. The record combines elements of two EMRs designed by a partner NGO in Kenya and utilized up until November of 2013 at five sites in the former Western Province. The HIV and Maternal Child Health EMRs were based off of Kenyan Ministry of Health data paper-based forms and allowed for either point of care or retrospective data entry. The new record does not correspond to any specific Kenyan Ministry of Health paper form but includes all elements from both the HIV and Maternal Child Health paper forms and designed to be used by the treating clinician at the point of care.

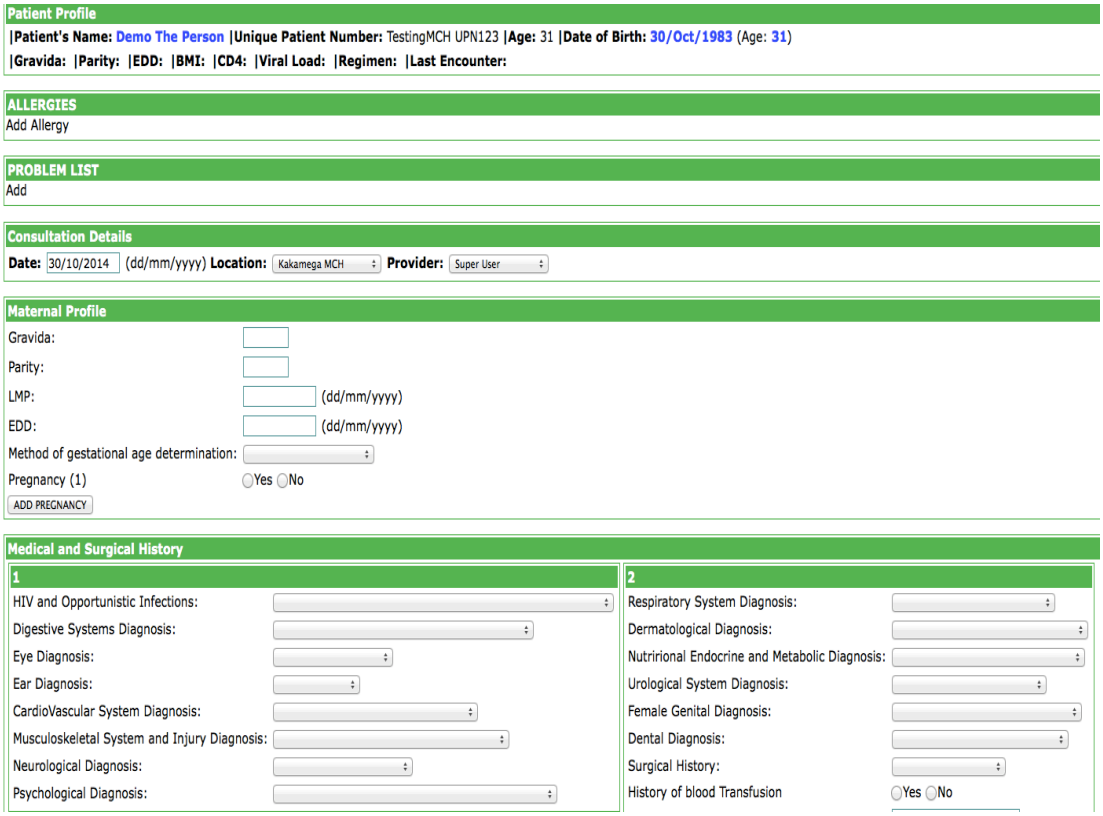
At the head of each electronic encounter form and each section is what is termed the "patient dashboard." This dashboard includes relevant demographic and medical information that the clinician can easily consult without migrating between forms. The information in this section is populated from the EMR. Gravidity and parity are grabbed from the maternal profile and EDD and weeks gestation are automatically calculated from the LMP and/or EDD entry.

This section is followed by a list of allergies and reactions and a "problem list" visible in the clinical care initial visit and revisit forms. This problem list includes relevant history and current concerns (differentiated by either "history of" or "rule out") and medications. Both the patient dashboard and the problem list are at the top of all forms so that the clinician is aware of all relevant treatment issues without having to conduct an extensive record review and migrate between forms. The Allergies and Problem lists carry through to the revisit form

from what has been entered at the initial visit to eliminate double data entry. These lists can be edited. Following the problem list in the initial visit form are the consultation details that specify when and at what facility the encounter took place. A maternal profile and medical and surgical history sections follow.

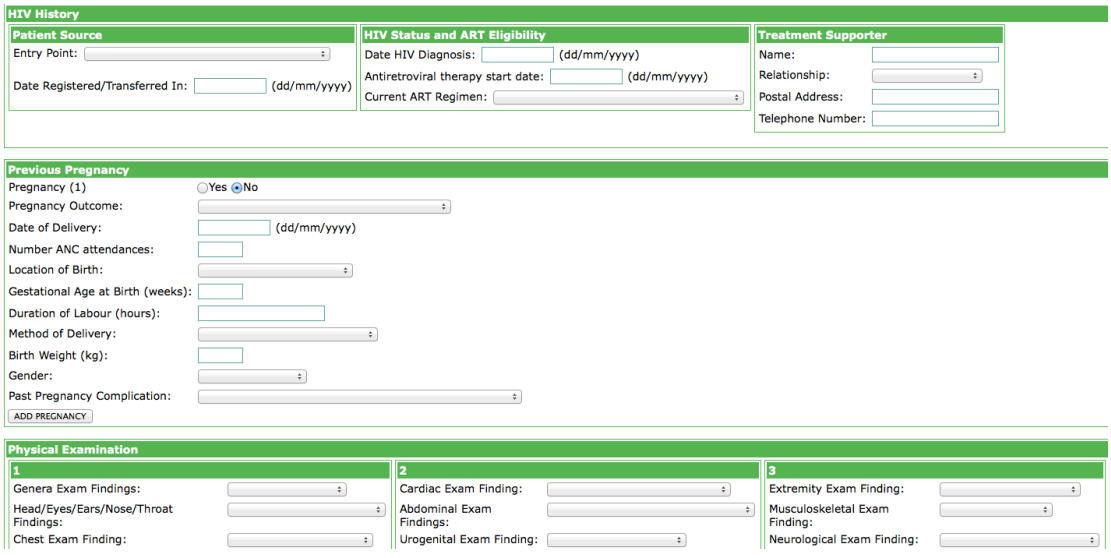
Figure 6-1 Patient profile and history

Pregnancy history and a physical examination section follow an HIV history section. Each



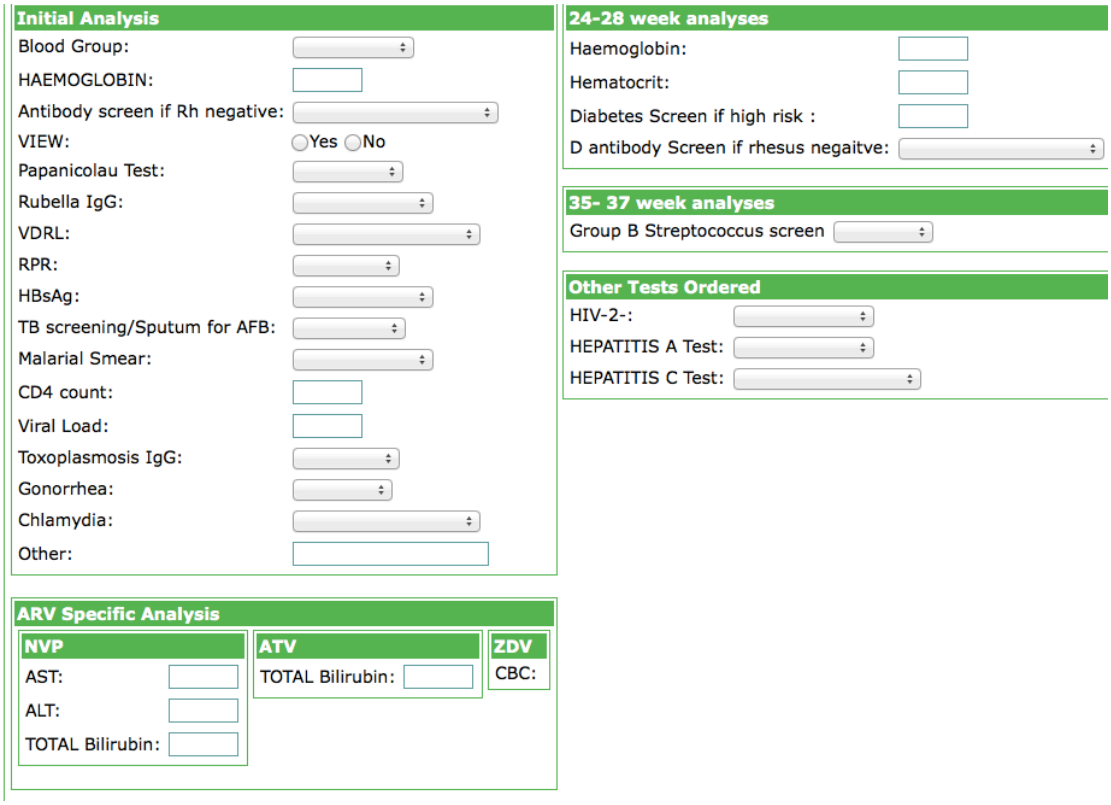
organ system category corresponds to a drop down menu with associated normal and abnormal findings from which the clinician may choose.

Figure 6-2 HIV history, pregnancy history and physical exam



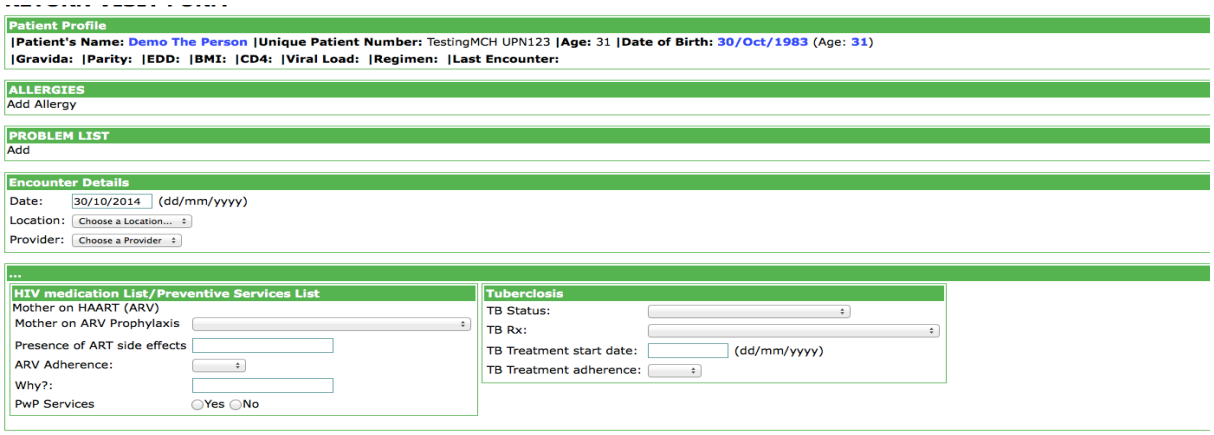
The antenatal laboratory analysis section guides the clinician as to the appropriate analyses to order at specific gestational age ranges and for patients on specific antiretroviral medications. Again, each analysis is associated either with a drop down menu with the coded data set, Boolean, numeric or free text entry sections. The antenatal analysis section will be part of both the initial visit and the revisit forms and the populated sections are visible on both screens.

Figure 6-3 Laboratory analyses



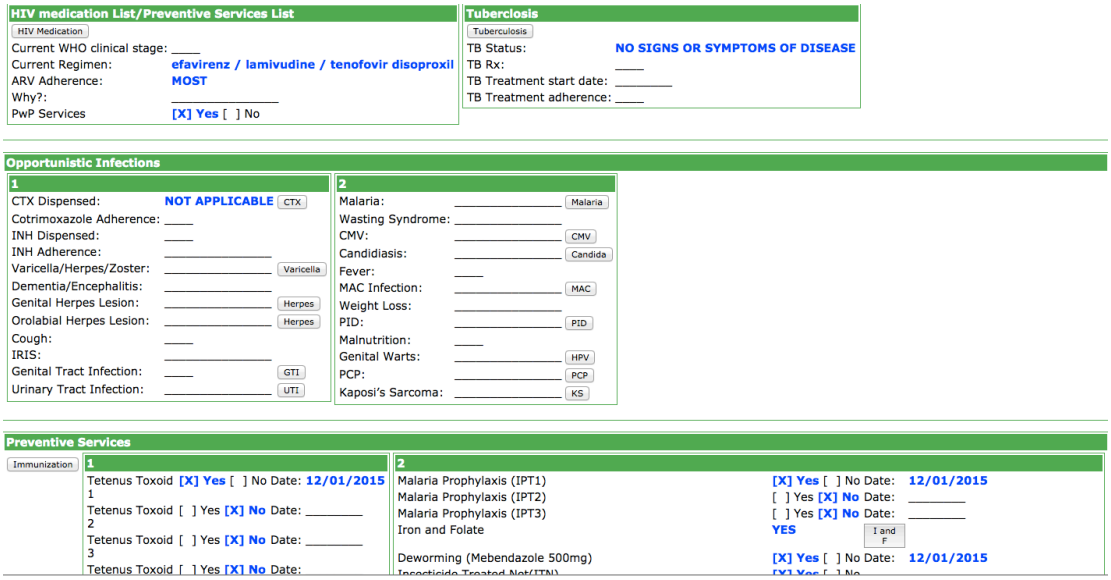
Clinically relevant information from the initial visit form should be added to the problem list by the clinician so that it is immediately visible at subsequent visits without having to do a chart review of the initial visit. If further information is required at revisits, this information is archived under “initial visit” in the “encounters” section of the EMR. The revisit form begins with the patient dashboard, allergies and problem list. Relevant information regarding HIV medications, tuberculosis and preventative services follow

Figure 6-5 Revisit form with HIV medications, tuberculosis and preventative services



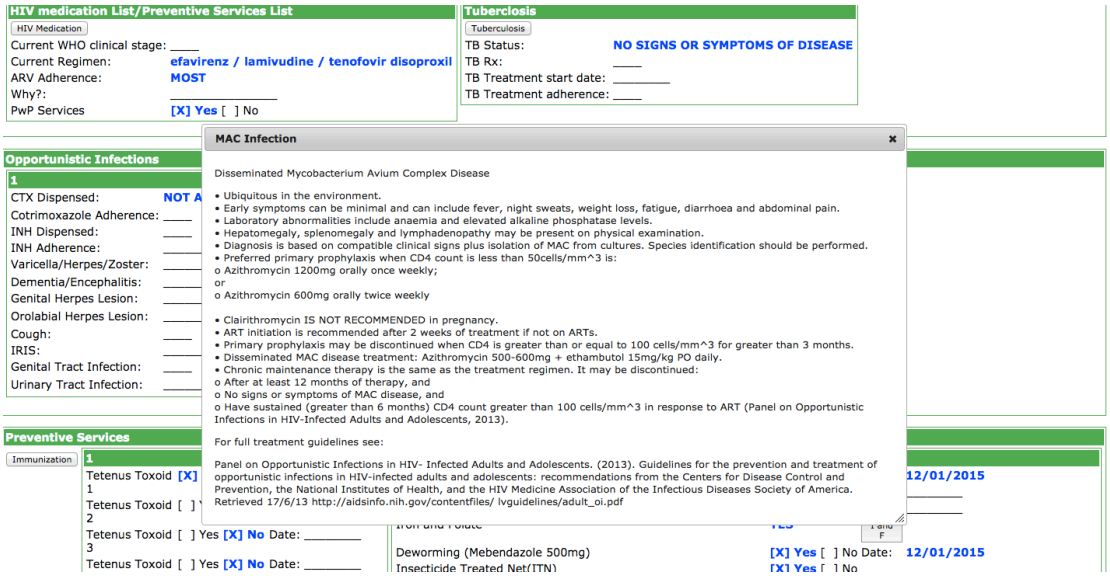
Opportunistic infection (OI) and preventative services information follows.

Figure 6-4 Opportunistic infections and preventative services



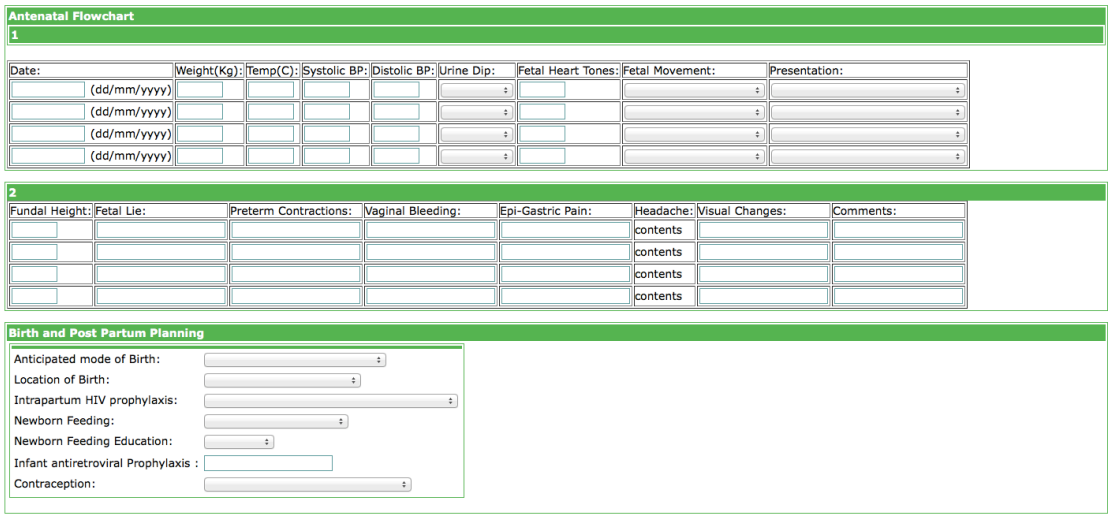
Clinical information tabs are buttons next to varous diagnoses, drugs and laboratory analyses. These information tabs may be clicked upon, opening up a widow with specific information regarding clinical significance and/or epidemiology, diagnosis and management. These tabs will be elaborated upon in section 6.6.3 Clinical decision support. Figure 6-7 shows the same screen with the open information tab for "MAC Infection.

Figure 6-5 Open information tab for MAC infection



The antenatal flow chart follows. This section is designed so that the clinician is easily able to see information from the previous visit and identify trends, for example, a gradual rise in diastolic blood pressure. Birth, intrapartum prophylaxis, newborn feeding and prophylaxis planning and planning for contraception information is presented next

Figure 6-6 Antenatal flowchart and birth and post partum planning

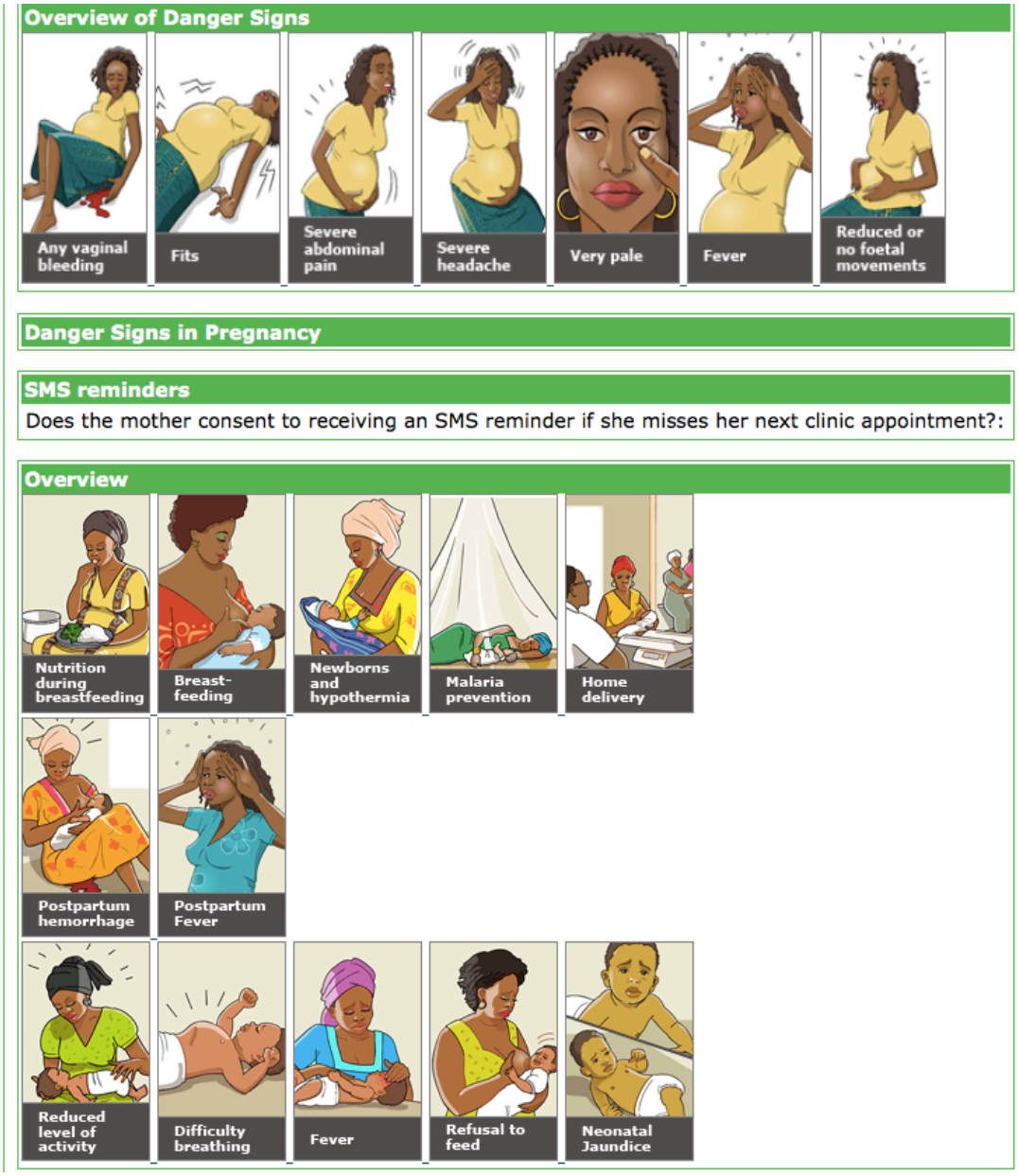


6.6.2 Patient education and communication elements

Graphic representations of educational materials and common danger signs appear in the revisit section as pop out windows with relevant symptom information for patients and

instructions for what to do in case a danger sign is present. These sections are illustrated and will provide patient education that the clinician and the patient can view together. When clicked on, the graphics present a script that the clinician can either read to the patient or that the two can read together, discussing the item of interest (figure 7). Graphs of CD4 count and haemoglobin level over time allow both the clinician and the patient to view trends and can alert to the necessity of intervention or provide positive reinforcement for self-care and intervention practices.

Figure 6-7 Patient Education Graphics



6.6.3 Clinical decision support

Passive and active clinical decision support elements exist throughout the record. The passive elements of the system include both the record itself and the clinical information tabs. As the clinician goes through the record with the patient, he or she is prompted to ask specific questions, conduct specific physical exams, order specific analyses and order certain medications and preventative services. Justifications for each of these elements come from numerous sources. The backbone is the HIV and maternal and child health forms supplied by the Kenyan Ministry of Health combined with standardized practice procedures as delineated by the Kenyan Ministry of Health, American Congress of Obstetricians and Gynecologists and the World Health Organization.

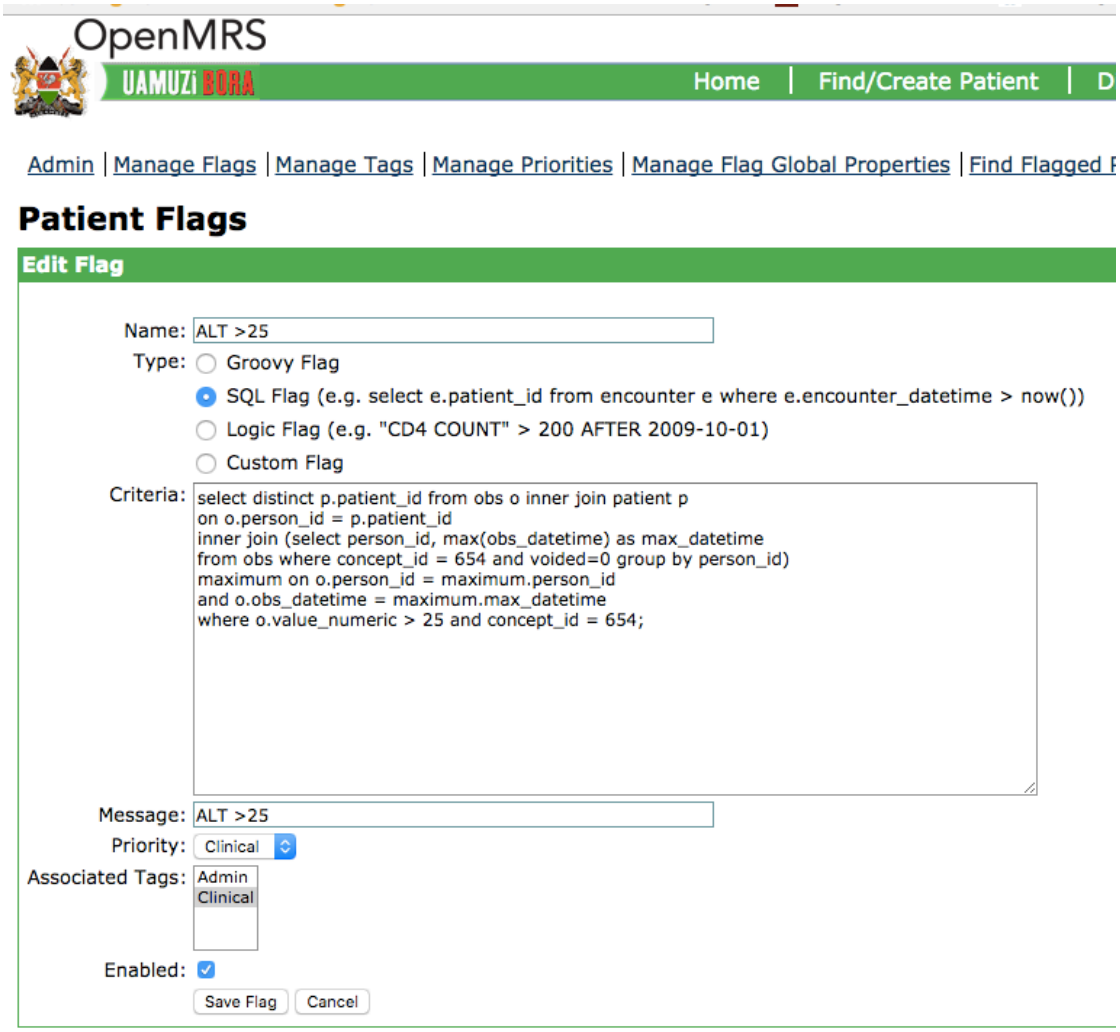
Clinical information tabs are located at relevant points throughout the record and are identified by a symbol. If the symbol is clicked on, a pop out window appears with diagnostic, prophylactic and treatment recommendations for the specific issue. This design was chosen to minimize clutter in the EMR without requiring that a clinician migrate to a different page to review guidelines. The clinician is not required to view the information, but is alerted to the availability of the information if it is needed. Topics relevant to OI management and prophylaxis, laboratory analysis ordering and result management, ART prophylaxis and therapy and preventative services are covered. These guidelines are drawn from WHO, NASCOP, NICE, NIH, CDC, American Society of Colposcopy and Cervical Cytology and South Australian Department of Health Guidelines. All guidelines were current to the time period of the pilot. The content of the information tabs can be seen in Appendix I. They have not yet been updated to reflect the most recent guidelines but will be after the thesis examination period has ended.

The guidelines are intended to act as a reference for the clinician and are not intended to supersede clinical expertise. A disclaimer stating the same is part of the record and should be acknowledged by the clinician at the opening of each patient medical record.

The active CDSS elements consist of clinical and administrative flags. Administrative flags include items such as “missing first clinic visit” while clinical flags denote either missing critical clinical information and/or critical or concerning laboratory values specific to pregnancy. Concerning laboratory values will vary by institution and this section may be edited to reflect local laboratory specifications. The default values used for this record were drawn from Cunningham’s “Protocols for High-Risk Pregnancies: An Evidence Based

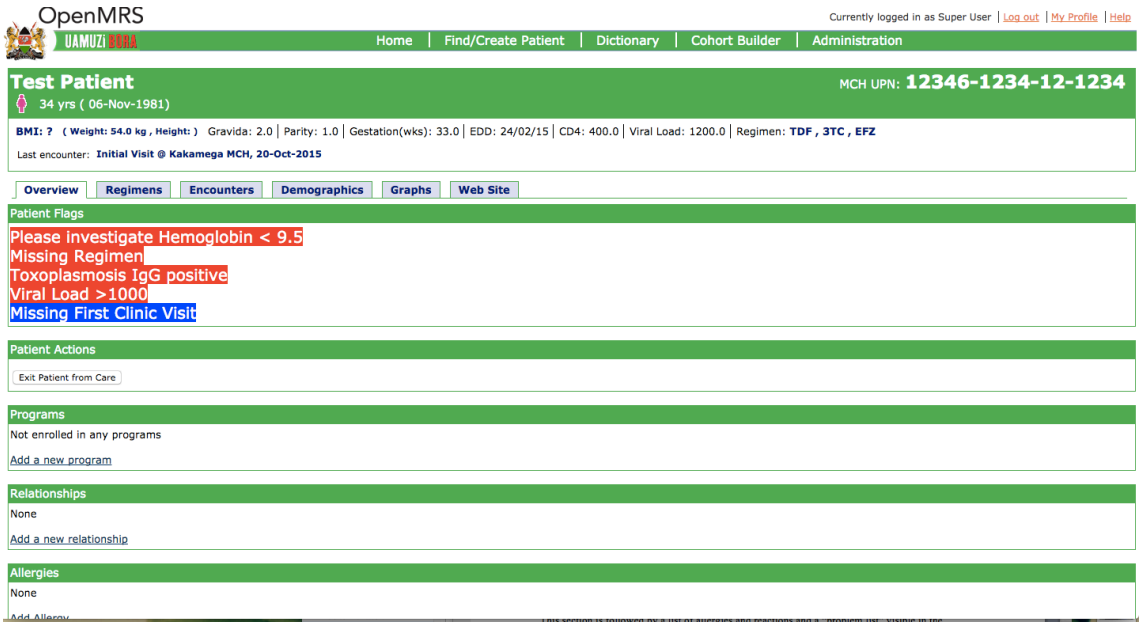
Approach, Fifth Edition" (Cunningham, 2010). Flags were programmed in SQL to meet conjoined specifications for activation. The code for "ALT > 25" can be seen below.

Figure 6-8 SQL code for "ALT > 25" flag



Flags are visible when opening a specific patient record under the "overview" tab. Flags are removed when the relevant information has been entered into the system or the laboratory values have normalized. Red flags alert to clinical information and blue flags to administrative information. All flags for all patients may be generated in a clinic specific summary when required. Ideally, a summary will be generated daily and passed to nurses, midwives, clinicians or administrative staff for review.

Figure 6-9 Patient flag alert



Please see 0 Appendix H Code for the initial visit and revisit forms. Please find the link to the Github page housing the record at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy.

6.6.4 Information sharing

Each clinician treating patients at the clinic was given a Chromebook to use for point of care information entry and clinical guideline consultation. At all times a Chromebook was located on the labour and delivery floor so that clinicians there had access to patient information when they presented in labour or for triage. This is important as decisions regarding obstetric management in the context of HIV require that information about HIV course, viral load, medications taken during pregnancy and the plans for intrapartum prophylaxis, newborn feeding and newborn prophylaxis be available in a timely fashion. By the time a patient paper record can be located, a woman may have already progressed to birth of the baby and the opportunity for the most critical steps in the prevention of perinatal transmission may have been missed.

Another Chromebook was supplied to the CCC physician so that cases that required consultation or referral could be discussed in real time while both clinicians are able to view critical patient information. This clinician was also able to review patient records as soon as the information is entered. This is beneficial from clinician training and clinician oversight perspectives.

A third chrome book was supplied to the medical records officer for the hospital so that critical management functions could be overseen. As described earlier, VPNs and a REST API should have allowed the server to be maintained and backed up and information to be gathered and analysed in an anonymised fashion for both academic and operations research, but this element was never functional.

6.6.5 Ideal additional system functions

The initial design of the system envisioned an SMS recall function that would remind patients of upcoming appointments and send messages with recalls to the clinic. This function was not operating effectively during the pilot and it was abandoned as the technical requirements to make it work were beyond what the available hardware could handle.

Ideally, a computerized pharmaceutical and laboratory order entry system would be included in the above system. Pharmaceutical order entry systems have been shown to reduce medication dosage errors and provide alerts to critical and important drug- drug interactions (Berner, 2007). Analyses of prescribing patterns can aid pharmacies in stock management. Direct laboratory value reporting reduces input error and reduces the likelihood that resulted laboratory values are not entered into the system at all. These elements were not available at the piloting site.

Modern electronic health systems offer services beyond EMR and CDSS to include scheduling, billing, supply chain management and patient interactive tools. Obviously such systems have the potential to impact revenue streams, further impact patient education and appointment adherence and managing pharmaceutical and operational supplies, mitigating the risks of stock-outs (T. Lewis, Synowiec, Lagomarsino, & Schweitzer, 2012b). Resource constrained settings could benefit immensely from these functions.

6.7 Accessing and using the code and record

The code for the project may be accessed for use and adaptation from a Github created for this purpose. It is accessible at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy.

The demonstration site URL is www.arantphd.org. A test patient may be created by creating a UPIN with the format xxxxx-xxxx-xx-xxxx. Alternatively, a pre-created record may be explored by searching for “test patient”.

6.8 Chapter summary

This chapter has described the rationale for developing the EMR/CDSS and highlighted the framework used in the system design and study through the Digital Design Principles. A brief description of the hospital setting follows as well as a description of the telecommunications system utilised. A detailed description of the system architecture and elements is provided along with ideal system functions that were not available for a project of this scale and in this setting. Links to access the code and demo site are given.

Chapter 7 Challenges to Successful Implementation

7.1 Introduction to the chapter

This chapter will endeavour to confront challenges faced by this project in a chronologic, systematic and categorical fashion. It will begin with a discussion of the financing problems encountered by Uamuzi Bora that necessitated their need to suspend their EMR/CDSS project that the system evaluated in this thesis was to run in conjunction with. A discussion of the numerous Internet service provider related challenges will follow. Correlations with similar challenges faced by other cloud-based and wireless systems will be drawn from the literature, though the literature on the subject is currently scant. There is ample literature describing the barriers to implementation of EMRs and CDSSs in general but it is the opinion of this researcher that the impediments presented by the technical infrastructure, organisational and funding paradigm infrastructure, political period of rollout and project management were such that a true evaluation of the pure EMR/CDSS related elements of this project would be corrupt and of lesser value. A discussion and recommendations for future system design and research into cloud-based EMR/CDSSs will be peppered throughout this chapter and expanded upon in Chapter 8 Discussion, recommendations and significance.

7.2 Challenges encountered

7.2.1 Suspension of PEPFAR funding

From the beginning of the site-specific application of this project, financial, infrastructural, political and human resource related challenges stymied implementation. Shortly after the offer was made by Uamuzi Bora to host the EMR/CDSS and run the implementation and study in tandem with their system, Uamuzi Bora had a critical delay in the receipt of funding that necessitated the suspension of their EMR/CDSS system which was fully functional at multiple sites in western Kenya and hosting of this project was delayed.

7.2.2 Receipt of Australian Postgraduate Award

Shortly after funding suspension, Ms Arant Bandy received notification of the receipt of the Australian Postgraduate Award Scholarship. Ms Arant Bandy decided to utilise some of the funds to cover some technical elements of the project and the salary of a project manager, Collins Otwane. Unfortunately, the Safaricom accounts and systems that had been in place for the previous study had already been suspended.

7.2.3 Safaricom account initiation and the period of EMR/CDSS development

Re-initiation and smooth operation of the Safaricom mediated elements of this project proved to be the most detrimental factor affecting this project's success. Safaricom is East and Central Africa's largest communications service provider with over 150 billion KSH in annual revenue. It currently has 25.1 million subscribers in the region. Safaricom was incorporated in 1997 and became a publicly listed company in 2002. Safaricom operates in the voice, data, financial services and business IT spaces. In 2007, Safaricom launched M-PESA, a mobile money transfer service that is widely used by Kenyans (Safaricom, n.d.). Early technical infrastructure was based on an analogue ETACS network and upgraded to GMS in 1997. Safaricom supplies 78% of Kenyans with 3G coverage and 93% with 2G wireless broadband coverage and has invested 32.13 billion KSH in infrastructure in 2016 (Safaricom, n.d.).

7.2.3.1 Delay to Safaricom technical architecture re-initiation and functional operation

After initial costs were agreed upon, Safaricom agreed to re-initiate the 15 SIM lines, 3 VPNs and 3 WIMAX connections from the previous study in an account to now be named and billed to Neel Arant Bandy. A deposit was made by Ms Arant Bandy to Safaricom to reinitiate all elements of the Uamuzi Bora system on the 22nd of January 2014. As this system had been functional and essentially operating smoothly from the period of October 2012- November of 2013, it was not anticipated that re-initiation of the exact same wireless technical infrastructure would present so many challenges. Drs Haskew and Rø reported in conversation that the initial set up of the technical infrastructure required excessive monitoring of Safaricom operations but that once the system was functional, that little over routine management of the Safaricom related elements of the project was required. Neither

publication from the previous Uamuzi Bora system described any Safaricom related challenge as a limitation of either EMR/CDSS system or the associated studies (Haskew et al., 2015a; Haskew et al., 2015b).

Safaricom was to reinitiate all system elements on the 1st of February 2014. The re-initiation did not commence on this day though Safaricom guaranteed that it would be reinitiated as soon as possible. By the 20th of February, the account manager at Safaricom deemed 15 SIM lines too many to be given to an individual and that the account should be run through a registered business instead.

The accounts were set up through Vestergaard Africa, Ltd. as Vestergaard was in charge of funds distribution during the period of the Uamuzi Bora implementation and had experience and a framework for doing this. Ms Arant Bandy would make 6 monthly transfers to Vestergaard Africa, Ltd. to cover the costs of both the Safaricom bills and the salary and taxes for Collins Otwane, the project manager. A contract was negotiated between Vestergaard Africa, Ltd. and Ms Arant Bandy, signed by both parties, and a first instalment was made. This contract was later taken over by Curtin University.

Negotiations ensued between the project manager, Collins Otwane, the accounts team and manager at Safaricom and the finance department at Vestergaard to the details of the new account set up and by the 3rd of March the accounts were approved and re-initiation was to commence. On the 7th of March 2014, Vestergaard was informed by Safaricom that the re-initiation was being suspended because of outstanding bills from the previous Vestergaard accounts with Safaricom, a claim that Vestergaard denied. By the 10th of March, Vestergaard was proven correct in their assertion that all previous accounts had been settled and the re-initiation was scheduled for the following day.

Re-initiation did not proceed the next day as scheduled as Safaricom was required that an entire new set of account applications be submitted. Vestergaard complied and submitted a new set of forms. By the 16th of March, the SIM lines and VPNs were still non functional. In late March, a technical team was dispatched to Kakamega to contend with the WIMAX radio and the Cisco router and SIM line activation and communication with the server was achieved on the 6th of April though the VPNs and IPSecs for remote access by the programmer and researcher were still not functional or accessible.

It took over two and a half months to set up the accounts for the re-initiation of the technical architecture that had been running through Safaricom from 2012-2013. A detailed review of

all communications between Safaricom, Collins Otwane, Neel Arant Bandy and Carrol Ngutu and Nancy Ondieki of Vestergaard would suggest that the disorganisation of the accounts department at Safaricom impeded the early functionality of the system.

Billing challenges persisted through July of 2014, though none were severe enough to completely overturn re-initiation. Safaricom was still billing for closed accounts from the Uamuzi Bora legacy system and threatened to shut down the re-initiation because of non-payment of non-existent accounts- a situation rectified with much effort on the parts of Collins Otwane and the accounts department at Vestergaard. Then it was noted that the bills for the WIMAX were being sent to Dr Haskew and not to Vestergaard, an error on the part of Safaricom as new applications for all elements of the wireless infrastructure had been completed by Vestergaard, another situation that threatened continued operation of the SIM lines. The VPN IPsecs were still not functional at this stage. On the 11th of June 2014, nearly 6 months after the initial payment for re-initiation and through almost six months of payment in full for a non-functional system, all of the SIM lines, VPNs and SSH IPsecVPNs became functional.

In July, the accounts department again threatened to disconnect the lines claiming that the account initiation funds paid in January were never received. Receipts were produced by Ms Arant Bandy. Eventually Safaricom found the receipt for the funds generated on their end.

7.2.3.2 Project management challenges

The job description of Mr Otwane was to liaise with Safaricom and manage the business elements of the project, liaise with the Ministry of Health and Hospital Administration, maintain the IT infrastructure in the Uamuzi Bora office and maintain the Chromebooks and oversee the study at the hospital. At this juncture, a full week's worth of time was dedicated to managing the technical challenges and demands of reinitiating the technical infrastructure.

At this stage, had the continuing challenges in this arena been foreseen, it would have been prudent to employ another person to assist Mr Otwane in his duties. The Uamuzi Bora project employed four people for the job tasked to Mr Otwane. During Uamuzi Bora's EMR/CDSS implementation, Mr Otwane was responsible for technical implementation of the EMR including maintenance of server, Chromebooks and the network, a job description similar to that of the current project. Another project coordinator was responsible for implementation and liaising with the Ministry of Health at an outlying site. There were two

research coordinators responsible for implementation, one in the peripheral clinics and one dedicated to Kakamega CGH. In addition to these project and research coordinators, Dr Haskew was on site in Kenya. Three developers were responsible for the programming elements. They shuttled between Europe and Kenya (Uamuzi Bora, 2013).

Dr Haskew and Ms Arant Bandy did not foresee needing as many project management staff at the inception of the project as the number of patients enrolled in the study was going to be much lower than during the Uamuzi Bora phase and also because, at that stage, the study was limited to 2 sites as opposed to the 5 sites in the Uamuzi Bora study. By the time of the training, this was reduced to one site.

There may also have been a failure to recognise that the technical infrastructure required by this project may have been outside of the scope of familiarity of Safaricom. The cloud-based and wireless broadband connectivity designed by the Uamuzi Bora team was novel. By the time of the launch of this much smaller project, staff migration and turnover at Safaricom meant that many of those familiar with the previous system may have moved to other departments or left the organisation. Though there should have been a template for account management in place, the re-initiation of the accounts may have meant that new personnel were wading their way through the process. Although the technical infrastructure had been functional during the Uamuzi Bora phase of the project, it could have been foreseen that challenges would arise as, overall; there was much unfamiliarity with utilising wireless broadband technology in this fashion. The learning curve could not only be applied to the technical aspects of the system but may justify some of the recurrent problems present in the billing and account management realms.

Another challenge borne out of the difficulties with account management was that it put a significant strain on the finance team at Vestergaard. The Vestergaard finance team agreed to host this project out of goodwill and assumed the responsibility as an addition to its own duties and without compensation. Their finance team was tasked with organisation and payment of the bills, which were erratic, often being sent to the incorrect person, being sent for closed accounts, not being generated for new accounts and often closed without due warning by Safaricom. Furthermore, much of the forensic accounting necessary to reject the numerous incorrect claims levied by Safaricom fell onto the shoulders of the Vestergaard finance team.

Though the VPN IPSec quickly reverted to non-functionality shortly after they started working for the first time in June of 2014, the Safaricom related challenges abated otherwise

from the period of July 2014 until November of 2014 during which time energy was spent finishing the programming and debugging of the record.

7.2.3.3 Challenges encountered during record development

During the period of the establishment of the accounts for the technical architecture, the Uamuzi Bora system was being modified by Gunnar Rø and Neel Arant Bandy. As described in Chapter 6 Mobile technology enhanced EMR/CDSS for the co-management of HIV and pregnancy design, the EMR/CDSS merged elements of the HIV and MCH systems designed by Uamuzi Bora. It then added many elements of antenatal care, modified active CDSS elements and added many passive CDSS elements. Ms Arant Bandy was responsible for the design and content and Dr Rø for the programming of the record. This aspect of the project proceeded relatively smoothly from a development perspective early on.

I-TECH (International Training and Education Center for Health), came to Kakamega CGH in June of 2014 with the aim of implementing the OpenMRS based KenyaEMR. I-TECH was borne out of the University of Washington's Global Health Department and endeavours to strengthen health systems with the end goal being sustainability and local ownership. I-TECH has been working closely with the Kenyan Ministry of Health since 2005 and been promoting and integrating KenyaEMR. Major objectives of the I-TECH program in Kenya are to standardise HIS systems and increase system interoperability (I-TECH, n.d). Uamuzi Bora provided data from their system to I-TECH for integration.

Kenya EMR utilises the CIEL/MVP concept dictionary, while the Uamuzi Bora system concept dictionary was completely custom (see 6.6 System architecture and elements). The data migration from the Uamuzi Bora system into KenyaEMR was going to involve mapping the concepts from the Uamuzi Bora Custom dictionary to the KenyaEMR system. This process entails mapping and linking each concept utilised from the custom dictionary to a corresponding concept in the CIEL/MVP library via code and would be tedious (OpenMRS, n.d.).

As it was now anticipated that this project's EMR/CDSS and KenyaEMR were going to be running simultaneously at Kakamega CGH and because greater concept definition coherence was always an objective of Ms Arant Bandy in designing the system, the decision was made to replace the Uamuzi Bora legacy customised concept dictionary with the CIEL/MVP

dictionary for the EMR/CDSS for HIV and pregnancy co-management.

Dr Rø replaced the dictionary and Ms Arant Bandy investigated the new concept IDs that Dr Rø incorporated into the system. This was an intensely important though very time-consuming exercise for both parties. It extended the time to launch of the record and also put significant time strain on Dr Rø. Uamuzi Bora did provide the data to I-TECH and KenyaEMR, but the implementation, in the end, did not go forward as Kakamega CGH divulged plans to implement their own, local EMR at some stage in the future.

Though the actual concept dictionary migration occurred after a new programmer was hired, during the programming period, the challenges of utilising a programmer that had a legacy based interest and true dedication to the system, but no longer had a direct stake in the project became apparent. Dr Rø was completing a PhD in Theoretical Physics at Durham University in the UK during the phase of record development and the burden of responsibility for all of the programming, especially considering the detail of the passive clinical decision support elements of the record began to negatively influence his primary obligations as a PhD student.

Dr Rø decided that his role as the main programmer of the record was untenable by late August of 2014 and Mr Otwane and Ms Arant Bandy decided to source an outside programmer with experience in OpenMRS. Mr Otwane identified John K'ateino, a recent graduate of the Computer Science program at Masinde Muliro University of Science and Technology. Mr K'atieno had designed a chronic care oriented, OpenMRS based EMR during university and had also applied for an internship with Uamuzi Bora, which did not proceed likely secondary to the suspension of Uamuzi Bora's operation. Mr K'atieno was hired to program the remainder of the record. While the HTML elements of the record, comprising the text and drop box features of the system, were relatively straightforward, many other features were customised by Dr Rø and rather complex JavaScript mediated operations.

Further, Ms Arant Bandy requested that additional elements of the patient information bar visible on all screens automatically calculate EDD and weeks gestation in addition to calculating other pregnancy related information such as gravity and parity and drawing record derived data such as viral load, CD4 count and treatment regimen to populate this field, all of which were all based in JavaScript. The legacy active CDSS elements that needed modification were in an Automated Structured Query Language (SQL) that had also been customised. These elements strayed somewhat from traditional SQL. While Mr

K'atieno was quite adept at the HTML elements of the record, it became clear that the JavaScript and SQL elements would have to be programmed by Dr Rø; a task that he reabsorbed with grace and dedication.

The upside of the programming challenges was that Mr Otwane and Ms Arant Bandy were inspired to learn to program HTML and SQL through online courses and became quite adept at both within a few months. Both also attempted to learn JavaScript online but were unable to master it enough to be functional programmers. The researcher was able to appreciate the time, skills and patience required to program a record and the complexities and time involved in debugging it also. Mr Otwane and Ms Arant Bandy were also able to make small changes as guideline modification as user request required going forward.

7.2.3.4 Challenges encountered during training

The EMR/CDSS content had all been programmed by late November 2014 and Ms Arant Bandy travelled to Kakemega to meet with Ministry of Health Staff, Hospital Administration, Clinical Staff, pay research and ethics fees and to conduct the training on the system (see 5.7.1.1 The initial visit, December 2014). This trip went very smoothly thanks to the hard work of Mr Otwane and the trainings were conducted and the nurses, midwives, doctors and hospital administrative staff were very welcoming of the study and the EMR/CDSS.

The challenges identified during the training of the nurses and midwives mainly had to do with their unfamiliarity with using laptop computers, difficulty typing rapidly and difficulty using the track pads to move the arrow around. Most midwives and nurses were quite adept at using mobile phone technology and were able to type quickly on a smartphone screen, but few had encountered computers or laptops during their professional lives and were not accustomed to using them. Aside from the problem list field, the comments section in the antenatal flowchart and a few demographic elements, the majority of the record utilised drop down menus, but control of the arrow via the track pad remained a rate-limiting factor to the speed of record completion.

This was anticipated to be a challenge during the initial phase of the launch. As patients were only being enrolled into the study at their first visit, and only the women living with HIV were to be enrolled, based on historical clinic data, we did not anticipate that more than 2-3 patients would be entered into the system each day during the early phase of the launch. This was discussed during the training and it was agreed with the clinical staff that this extra work

would be difficult at first but would become easier with time. When the number of enrolees increased to include revisits, the majority of patient data would have already been in the system, available for review. The only additional fields to be entered would be the antenatal flowchart and any additional clinical, medication or laboratory information that had arisen between visits.

Uamuzi Bora's EMR/CDSS utilised data entry clerks to assist with information entry, often retrospectively (Haskew, 2015a). This was acceptable during the utilisation of their record as the clinical decision support elements were mainly flags that could be followed up on between patient visits, or addressed at the next visit. The EMR/CDSS for HIV and pregnancy co-management was designed in such a way that the clinical decision support elements were to be accessed at the point of care, in real time. If the clinician had a question about management s/he could access the guideline in the system while with the patient.

Data entry by a data entry clerk would have negated the most critical design element of the system though it would have streamlined the data entry process and decreased the amount of time to utilise the system. Data entry clerks would have also potentially compromised patient confidentiality, or patient privacy as another, non- clinical person would have been in the room with the patient during the discussion of sensitive medical history. This was discussed during the training and it was thought that the medical students and clinical officer students that were almost always present in the clinic could be harnessed to assist with data entry and their presence in the room, as clinical personnel, would not have caused the patient to feel reluctant to share information. As these students had already received the relevant training and clearance for patient interaction, this did not represent a threat to patient confidentiality either. In hindsight, a dedicated, trained and paid data entry clerk would have been very useful for entering the cumbersome demographic data and even assisting the clinician to enter the historical and review of systems aspects of the initial visit that did not provide this style of clinical decision support.

There were many last minute debugging issues with the record and it was not until the 4th of December 2014 that the SSH IPSec VPNs were finally functional and accessible by Dr Rø. The training was done on the 8th and 9th of December, 2014 and minor adjustments requested by the midwives were programmed into the system. The decision was made by Ms Arant Bandy and Mr Otwane to delay the official launch of the system and in the hospital until after the late December holidays and to launch the system early in the New Year. Please see 0 Appendix L Timeline of progress and impediments to progress in system design, connectivity, implementation and launch from inception to study launch.

7.2.4 Challenges encountered during the launch

Numerous challenges stymied the actual launch of the system. The active clinical decision support elements, the flags, were triggering incorrectly. The flags would show up for missing or out of bounds information even when the information was entered correctly and not out of bounds. Dr Rø and Ms Arant Bandy fixed the flags, which delayed the launch until the second week of February 2015. The SMS reminder function was still dysfunctional and it was later anticipated that this would be impossible to fix, as it had been running on a different server during the Uamuzi Bora EMR period that was no longer available so the decision was made to abandon this function. A flag was operational that flagged for patients who had missed appointments by over one week so that the staff would be able to follow up when weekly reports for missing flags were generated and the decision was made to rely on this instead.

Shortly after the flags were fixed, Kakamega experienced severe storms and flooding. The towers housing the radios for WIMAX mediated VPN connectivity were knocked down and destroyed. Moreover, the entire region of western Kenya was without electricity and power. Broadband communications were not restored to the region until the end of February.
When broadband connectivity was re-established the SSH IPSec VPN connections were tested for functionality and were again non-functional. The router had defaulted to factory settings and erased the reconfigurations that Dr Rø had programmed to ensure the security of patient data transfer for the off-site data back-ups. The decision was made to go ahead with the launch as so much time had elapsed since the trainings without remote access to the server. It was hoped that remote access via SSH IPSec VPN connection would be functional again soon.

7.2.4.1 Effects of the delay to launch

The main effect of the delay to launch was that the midwives had become accustomed to practicing in their usual way, using patient registers and maternal child health cards to record patient information. The second and likely equal effect was that the training on the system was now three months in the past, ample time to forget the intricacies of the system. Furthermore, the week of the launch coincided with trainings of the MCH staff, which took

them offsite, and most initial system usage was done by the medical interns. Despite this the launch went ahead on the 6th of March 2015 and the initial reports were very positive. Please see 0 Appendix M Timeline of period from training to launch.

7.2.5 Challenges encountered during the study period

In keeping with the trajectory of the project thus far, infrastructural, technical, workforce and project management challenges continued during the study period that undermined usage of the system.

7.2.5.1 Infrastructural and technical challenges during the study period

The study period continued to be plagued by infrastructural and technical challenges. Heavy rains at the end of March again compromised the base stations. As noted previously, paper copies of the records were provided and to be filled in when power outages or connectivity failures rendered the Chromebook system non-functional. This was the study "back up" for these technical failures. Sporadic power outages and connectivity issues continued through the duration of the study. Further, it was found that some of the Chromebooks' SIM cards could not access sufficient bandwidth to connect to the VPNs from certain rooms within the clinic. Rooms with better access were reserved for EMR/CDSS usage when needed.

Connectivity issues related to Safaricom billing practices continued during the study period also. By May, most of the lines had been cut again. Safaricom related this cut off to late payment tariffs that had been imposed and not paid. The lines were cut again for billing reasons in July after Safaricom had changed their practice of billing. Per Mr. Otwane, previously, unused data rolled over to the next month and bills were issued when data was low so that accounts could be filled again. The new system eliminated the roll over data and cut the lines off at the end of the billing period if the bills were not paid. Vestergaard and Safaricom were tracing the bills to rectify the situation but the study was again compromised. Though not all of the SIM lines were cut, as each Chromebook had its own SIM account, finding the Chromebooks that still had operational SIM connections would have been cumbersome. In retrospect, if a Chromebook was going to be used and determined non-functional, utilisation of the record for that patient was likely abandoned.

Further forensic accounting revealed that Vestergaard had only been receiving bills for 9 of the 15 SIM lines. At this stage, it was decided to only proceed with those 9 lines in order to cut costs and eliminate the saga of missing bills. During this period of interrupted connectivity because of storms, power outages and billing issues, the SSH IPSec VPN access continued to be non-functional. This was a constant point of contention and discussion between Mr Otwane and Safaricom, as Ms Arant Bandy and Dr Rø were unable to modify the system or confirm usage of the system remotely without the SSH IPSec VPN access being operational. By July, Safaricom agreed to reinstate the SSH IPSec VPN once the billing issues had been rectified. The SSH IPSec VPN access was restored in August but all of the settings had been lost again and security standards were not acceptable for the transfer of patient information.

A meeting between Dr Rø and the technical team at Safaricom was scheduled to rectify this situation. During this time, however, Safaricom was upgrading to 4G in the area, which rendered 3G mediated communications sporadic. Connectivity continued to be a problem through late August. The SSH IPSec VPN access was never restored.

Billing issues emerged again in September, which again negatively affected connectivity. Heavy storm activity ensued around the same time, along with power pole replacement in Kakamega that again lead to sporadic system connectivity and caused major and prolonged power outages to the entire region.

The initial Uamuzi Bora system and this system were novel in their use of wireless broadband to connect to the cloud based record and server via VPN air grab and, as novel technologies, were subject to numerous technological challenges. In 2005, I-TECH, in conjunction with CDC and Haitian Ministère de la Santé Publique et de la Population created a digital patient data reporting system for HIV care for Haiti called iSanté. The iSanté project envisioned a system that could overcome similar challenges to those that this project sought to overcome, namely electricity outages and lack of grounded Internet.

In Haiti at the project's inception, electricity was unreliable and there weren't grounded Internet connections. To overcome these challenges, initially, iSanté systems connected from the facility in Haiti to the server in Washington State, USA by a VSAT (Very Small Aperture Terminal) via Internet communications. Though the iSanté system did not experience challenges due to the service provider, as did this project, it did experience similar challenges in the realm of variable connectivity. The quality of wireless communication became so poor that continuous VSAT mediated data transfer was

abandoned. Eventually the system became local, relying on clinic based servers and Local Access Networks, only using the VSAT technology for bursts of data transfer (Lober et al., 2010). The iSanté system eventually became a point of care EMR system, as was envisioned for this project.

7.2.5.2 Workforce and project management challenges

During the study period, numerous workforce and project management challenges occurred that were not anticipated by the researcher. During devolution (see 3.2 HIV policy and service management in the context of a devolved Kenya and 3.2.1 Health service responsibilities in the devolved system) the health system went from a province based system to a county-based system. This change meant that there was much to be ironed out in terms of financing and management in the following years. Kakamega suffered two nursing strikes during the first 8 months of 2015, one of which shut Kakamega CGH entirely as nurses had not been paid for the months of June and July (The Nation Team, 2015). During the months of June and July, the nurses and midwives of the MCH were on a "go-slow" where only essential functions were being carried out in protest of non- payment.

As the SSH IPSec VPN access was never restored in any functional capacity during the entirety of the study, Ms Arant Bandy and Dr Rø were unable to monitor system usage. Ms Arant Bandy relied on reports given by Mr Otwane on the numbers of patients enrolled into the system, which were reported to him by the MCH in-charge. By the end of June, Mr Otwane received a report from the MCH in-charge that 89 women had been enrolled into the study. The inability of Ms Arant Bandy to remotely review and verify reports of system usage via SSH IPSec VPN assess, seriously undermined the day-to-day operation and validity of the study.

By mid September, with only reports of system functionality and study enrolment, Ms Arant Bandy made plans to travel back to Kakamega to evaluate the study function and consider ending it. Mr Otwane reported at this time that 133 patients had been entered into the system. Power outages and problems with system connectivity continued through September and October. Ms Arant Bandy Arrived in Kakamega on the 26th of October 2015. Please see 0: Appendix N A timeline of relevant events during the study period and actions taken. When Ms Arant Bandy arrived in Kakamega, the system was no longer functioning and the decision was made to end the study.

The purpose of the visit would be to collect the qualitative information, completed

questionnaires, from the clinical staff and to thank them for their help with the project. The second objective was to collect and analyse data from the records themselves.

The questionnaires were collected from the nurses and midwives at Kakamega CGH, in person (see Appendix 0

Appendix J Filled provider questionnaires). The questionnaires, overall, reported satisfaction with the system, though did note that entering information did take extra time. The clinicians noted that they appreciated being able to access treatment information in real time, and that the record was a helpful data-collating tool for each patient. They reported, both in the questionnaires and in person during causal discussions, that they felt that the EMR records were much more complete and accurate than paper records are. The clinicians were thanked and two laptop computers loaded with all of the treatment guidelines from the project were donated to the MCH. The clinicians and Mr Otwane noted at this time that the Mentor Mothers should be thanked as well, as they were instrumental in helping to collect "missing information" through telephone calls to the patients.

Mentor Mothers are HIV positive mothers who act as treatment support and follow up mentors to pregnant women living with HIV at the MCH. The Mentor Mothers follow up missing appointments and make appointment reminders to expectant women living with HIV and provide guidance around subjects such as exclusive breastfeeding and the importance of adherence to antiretroviral drugs (UNICEF Eastern and Southern Africa, 2014). Though appreciative that the Mentor Mothers had helped during the project, Ms Arant Bandy reminded Mr Otwane that missing information should not have been sought, as the record was being used at the point of care, and reiterated that any retrospective data entry would corrupt the study and be a deviation of protocol.

Retrieving data from the server proved challenging as the SSH IPSec VPN access was not functional. Efforts to restore functionality continued from the 26th through the 28th of October but a technician was never able to visit the office. Thus, by the 28th of October with Ms Arant Bandy's departure eminent, the decision was made to download the data directly from the server in an encrypted format and send it by email to Dr Rø.

Dr Rø returned the de-identified data in early December and Ms Arant Bandy viewed it a few days later. A few issues were immediately glaring. First, nowhere near the 133 reported consented and enrolled patients had been entered into the system, only 67 patients were

created- 8 of which had been created during the training, which left 59 patients created during the study period. Second, the majority of the information was missing. Third, all records not created during the training were created between the 26th of September and the 26th of October. Fourth, all of the patients were missing a recorded last menstrual period and many had EDDs that were *before* the date of record creation- leading one to conclude that these records were created retrospectively. Please see Appendix M Appendix O CSV file data from system.

To confirm this, Dr Rø analysed attempts at communication with the server from outside sources, namely, the Chromebooks. His analysis revealed that there were some attempts at communication in early March, but aside from that, there was nothing until the end of September, which was consistent with the data received in CSV format from the server. Please see 0 Webserver requests during the study.

7.2.6 A brief cost analysis

As has been noted previously, the initial challenge to the implementation of this EMR/CDSS was financial. An early loss of funding and the folding of the hosting organisation meant that the technical infrastructure needed to be revived, leading to a recurrence of the start-up costs. These start-up costs were absorbed during the first phase of implementation, mainly because the implementers could not actually predict what, in the end, the cost of start up was actually going to be. During the second phase, the implementers eventually abandoned the project re-launch due to an unacceptable cost /benefit ratio.

Haskew et al. (2015), utilising the same technical infrastructure, were able serve over 4000 clients, making the ongoing costs of running their system acceptable. Uamuzi Bora spent $6000 USD to buy the central server and to establish the online framework and connection. They describe the maintenance costs as $200 per month. Their initial cost for each site was around $500 USD which included the Chromebooks, clinic set-up and training costs and continued maintenance was round $50 USD per month. The Uamuzi Bora system employed an EMR supervisor and the IT systems administrator, which each cost around $500 USD per month. Once the pilot had started, the ongoing expenses were maintenance of the SIM lines, the project manager's salary and extraneous project management costs.

7.2.7 Analysis of the challenges

It was clear by this stage that true data analysis of both the qualitative and quantitative data would be impossible. The system had not been used at the point of care, as it had been designed to be used, as the clinicians were trained to use it, as established by the protocols for usage and as required by study design. As such, there would be no way to measure whether the EMR/CDSS influenced adherence to guidelines. Furthermore, the clinicians had answered the questionnaires *as if* they had been using the system at the point of care, which, clearly they had not been. This rendered the quantitative data useless as the questionnaires had been falsified.

As has been discussed thus far, many challenges confronted this project from its inception. Early on, the loss of critical funding and the suspension of Uamuzi Bora's activities broke down all of the organisational structures in place to support a project of this magnitude. Initially, the Uamuzi Bora designed HIV and MCH records were going to continue running, and the EMR/CDSS designed for this project would be woven into Uamuzi Bora's functional operations and be specifically for pregnant women living with HIV. When Uamuzi Bora as it had been was dismantled, not only was the technical infrastructure that Uamuzi Bora had set up and had maintained for their project lost, all of their project management functions disappeared as well. Aside from Mr Otwane, the project and technical managers associated with the Uamuzi Bora project left for new employment. Dr Haskew also left the project for the WHO, heading up their efforts to fight Polio in the midst of the Syrian refugee crisis. Dr Rø was finishing his PhD in theoretical physics.

Operations now fell to Ms Arant Bandy and to Mr Otwane. Neither were able to anticipate the amount of time, energy and ultimately money, it would take to get a project of this magnitude started and operating functionally from a technical perspective. Had the technical infrastructure been maintained it is possible that this project would have been able to launch and run without the vast Safaricom related challenges that were experienced. Needing to start afresh, with new accounts, new SIM lines, new VPNs, new SSH IPSec VPN access, and a disjointed financing structure proved to be a massive hurdle confronting this project as has been presented throughout this chapter.

The technical aspects of the system, aside from a few days at a time here and there, were never fully functional from the initiation of the accounts on the 22nd of January 2014 through the end of the study when the data from the project was finally retrieved, October 28th 2015- a period of nearly two years where services were being paid for but not fully rendered. As discussed previously, the decision was made to launch the project with only SIM to VPN to server connectivity, while still awaiting oversight through the SSH IPSec VPN, which never

became fully active in any functional way. While patterns of dysfunctional service provision, billing errors, technical errors, system related errors emerged essentially from the first days of setting up the new system, it was difficult to predict when issues would be rectified, when new problems would arise and what they would be as either the Business Accounts, Business Service or the Technical Department at Safaricom was always purporting to be working on the problem and imminent solutions always promised.

Perhaps our organisation did not represent a business customer of sufficient size to warrant the level of attention from Safaricom that this project necessitated. Perhaps our staff of two was not able to put enough pressure on Safaricom to ensure that these detrimental errors in billing and connectivity ceased. The nature of our billing structure going through a third party was a good solution as it allowed the project to continue, but also left much room for error. Mr Otwane and Ms Arant Bandy did not have control over the receipt and payment of bills and, in retrospect, did not have an acceptable method of ensuring that proper bills were being created and that these bills were being paid. As was discussed in 7.2.3 Safaricom account initiation and the period of EMR/CDSS development, an organisation with no real stake in the project aside from a history with Uamuzi Bora and good will and generosity was excessively burdened by the challenges that dealing with Safaricom presented.

Continuing technical challenges encountered after the launch had two major effects, undermining early system functionality and undermining project oversight. Though the launch report from Mr Otwane was positive, connectivity was functioning and patient data was being entered, the server contact logs do not reflect this. No patient data was entered and saved during the early period of the launch whatsoever. Mr Otwane reports helping the midwives from his personal computer, not from a Chromebook. He would have been accessing the demo site server this way and not actually accessing the server in Kakamega that the EMR/CDSS was running from. Upon questioning after the data revealed that no patients were actually entered into the system, Mr Otwane said that he didn't actually help the midwives enter the data himself, as he wasn't in the room with them. It has been difficult to get an accurate account from Mr Otwane as to what he was doing precisely while in the hospital. It is possible that he thought that the training had been sufficient to allow the clinicians to operate the system.

Though Mr Otwane's responsibilities covered both the technical aspects of the project and the running and monitoring of the study at the hospital, the legacy of technical challenges and the continuing technical challenges required that most of his time be spent at the Kakamega office and not on site in the MCH. Without this oversight the actual running of

the project was able to flounder and go largely unsupervised. Unfortunately, in retrospect, this was not effectively communicated to Ms Arant Bandy. Reports were received that did show early enrolment problems related to staffing, power and technical issues, but by two months into the project, the reports from Mr Otwane and the MCH in-charge that enrolment was on track and the system was being used.

Perhaps there was pollution from the previous project that allowed the clinicians to believe that they could actually enter the data in retrospect. Mr Otwane spoke with some of the nurses and midwives involved in the project as to the reasons behind entering the data retrospectively and the lack of usage during the majority of the study period. Sister Zaitun, responsible for the majority of the data entry, stated that she believed retrospective data entry to be acceptable. Another nurse, Alice, stated that she tried to use the system early on in the study but experienced connectivity issues so she abandoned her efforts.

Although SSH IPSec VPN accessibility was continuously promised, it was never active and there should have been a better way to monitor what was actually happening with the system. If we had instituted a data dump earlier, as we had in the end, or had been able to monitor server requests, then the realities of non- usage would have emerged earlier, the situation rectified and we may have been able to evaluate the usage of the system as it was intended to be used.

Again, the iSanté experience is helpful in understanding many of the setbacks and challenges experienced by this project. Although initially envisioned, constructed and used as a data-reporting tool in its early days, it became a point of care EMR for the management of HIV (Matheson et al., 2012). An excellent analysis by Matheson et al., (2012) reveals similar challenges to those experienced by this project namely in terms of real usage and the effects of disasters on the system- both positive and negative.

The iSanté system was piloted at many sites. Though by the time of the analysis, the system was intended to be used at the point of care, four main patterns of actual usage were discovered:

1. Sites were implementing the EMR incompletely
2. Paper was still the main source of patient information and the EMR system was not being used.
3. The primary source of patient information remained paper with some transfer of information to the EMR system
4. There was point of care system usage with paper back up (Matheson et al., 2012).

> Further, it was noted by Matheson et al. (2012) that fluctuations in usage followed disasters and surges of violence or political instability. The researchers noted downturns in usage following outbreaks of violence in 2005, Hurricane Ernesto in 2006, numerous hurricanes in 2008, the earthquake of 2009 and the cholera and election instability that followed.

Certainly natural disasters, though of a much smaller scale than those experienced in Haiti between 2005-2011, negatively impacted the functionality and uptake of the EMR/CDSS designed for this study. From a pattern of usage perspective, the pattern observed in this study likely is better analysed from a provider-to-provider basis as it was only piloted in one clinic. One midwife, Sister Zaitun, was responsible for the majority of the data entry, and she likely represents the pattern of usage depicted in the iSanté system through scenario 3; the primary source of patient information remaining on paper with some transfer of information to the EMR system. Sister Zaitun did report in casual conversation finding that she was made aware of much more missing patient information because of the system's flags. The other clinicians at the site fell into category 1- not completely implementing the EMR system. It is likely that with a longer study, across multiple sites, patterns of usage could be derived and analysed to give as robust an analysis as the review of the iSanté system was able to provide.

Matheson, et al., (2012) recommend evaluation of why the system is not being used routinely if it is not. From their experience, low computer skills and literacy levels, resistance to EMRs in general, inadequate benefits being seen and irregular electricity and internet connectivity emerged as the most common reasons for low implementation (Matheson et al., 2012). Certainly all of these factors played a role in the minimal uptake of the EMR/CDSS system designed for this project. From the electricity, internet and connectivity perspective, the connectivity needed to make this EMR/CDSS system properly operate was never going to function correctly at this location. Perhaps, as with the initial design of iSante project using VSAT connectivity initially and requiring that it be abandoned for a more practical form of data storage and transfer (Lober et al., 2010), the realities of access to the cloud-based EMR/CDSS through wireless broadband with this system was never going to function properly and thus was not practical. For a timeline of data collection and analysis, please see 0: Timeline of challenges encountered during the second site visit and in data collection and analysis.

7.2.8 The decision to re-launch the study

Numerous options for moving forward were discussed between Dr Rø, Dr Haskew, Ms Arant Bandy and Prof Jaya Dantas. The first option was to end the study and move forward with the thesis with the data being "challenges and lessons learned". The second option was to restart the study with stricter protocols for both clinical and project management staff and attempt to collect 6 months worth of data to analyse in the fashion initially envisioned. Ms Arant Bandy, optimistically hoping for a smooth relaunch chose the second option.

7.2.9 The second launch attempt, familiar challenges

Negotiations began with Safaricom in December to relaunch the system with a similar set up used in the initial study. Again, as the components had been in place, it was envisioned that this process would proceed relatively smoothly and we had the assurances from Business Support and Accounts at Safaricom that this would indeed be the case.

As the SSH IPSec functionality had never occurred in any appreciable manner, Mr Otwane received a credit for these service charges to be applied to the relaunch of the project. The decision was made not to rely on the SSH IPSec for system oversight this time around and to instead retrieve information by weekly encrypted data dumps as we had done to retrieve the data set from the pilot. This way, evaluation would not be stymied by a system that proved difficult to initiate and maintain with the level of data security required for patient information protection. As the six-month cost estimate equalled the money remaining with Vestergaard from the last payment by Ms Arant Bandy, it was decided that the costs of moving forward would be justified by the gathering of data according to study design.

Ms Arant Bandy wrote strict study protocols for the clinicians at the MCH as well as a much stricter delineation of duties and responsibilities for Mr Otwane with heightened reporting requirements. These were complete and distributed on the 14th of December 2015. Please see 0 Appendix R Development, utilisation and evaluation of an mhealth tool to aid in the co-management of HIV and pregnancy relaunch protocol.

Though the responsibilities on Mr Otwane were greatly increased, all members of the group, including Mr Otwane believed that as poor oversight and reporting had so detrimentally affected the pilot, they were necessary and acceptable.

Unfortunately, the new protocol was never tested. The restart of the Safaricom accounts was

again mired in vetting, initiation and billing problems after the official restart of the initiation process on the 6th of January 2016. Once these were rectified, after a period of over six weeks, Safaricom initiated upgrades to WIMAX in the Western and Rift Valley regions, followed by power pole replacement in Kakamega delayed the restart by another month. Once the power pole replacements and upgrades were complete, billing issues again arose which cut off service (though the system was still not functional). When the billing issues were rectified, technical and infrastructural challenges arose again.

The SIM cards were active and paid for, filled with data bundles, mapped to the VPN and ready to go but were not connecting to the VPN. They were able to connect to the Safaricom network, indicating that they were functional and within connection range but could not access the VPN in order to connect to the server. Investigation revealed that the VPN was only authorised to accept IPs from the previous pilot system and thus were not establishing connectivity, a Safaricom error. Numerous attempts were made to provide a back end portal for connectivity of the SIM cards to the VPN without success. By mid May, Safaricom decided to reset all of the components in hopes of regaining connectivity. Now over five months out from the decision to relaunch, connectivity of the Chromebooks to the VPN was still non-existent. Ms Arant Bandy decided to suspend the relaunch and close down the EMR/CDSS project. Please see 0 Appendix S Timeline of the attempted relaunch.

7.2.10 The failed re-launch, what went wrong

The reasons for the failure of the second relaunch mirrored the technical and infrastructural challenges that plagued the original system set up and usage pilot. The benefit of having experienced the technical and infrastructural challenges from the first rounds allowed the project team to abandon the relaunch when the time/cost/benefit scenario became unacceptable.

7.3 Chapter Summary

This chapter began with an introduction and was followed by a detailed accounting of the challenges that the system encountered. The challenges have been analysed and compared to two other similar systems, the original Uamuzi Bora system and the i-Santé EMR system for HIV management from Haiti.

Chapter 8 Discussion, recommendations and significance

8.1 Introduction

This chapter begins with a brief review of the research design. Responses to the research objections and questions are provided. Following this is a review of the study output, namely the creation of a mobile technology enhanced, combined electronic medical record and clinical decision support system for the co-management of HIV and pregnancy, the pilot thereof and exploration and reflection of the challenges encountered. Following is a review of recommendations from the study in terms of recommendations for community organisations, clinicians, policy and practice and recommendations for future research. The significance of the study will then be reviewed and followed by a discussion of study limitations. A conclusion will follow.

8.2 A brief overview of the research design

Upon inception, the aim of this endeavour was to create a system that could maximize the utility of healthcare providers and health care facilities, extend the geographic access and patient volume capacities of providers, improve diagnosis and treatment by providing management guidelines for the many facets of HIV and pregnancy co-management, including adherence to ART regimens, engage and educate patients and improve data management and analysis. It also hoped to improve referral and consultation mechanisms, compensate for health worker shortages and lead to the professional development of healthcare providers. It was to be appropriate for a high tech, centralized environment as well as a low technology setting lacking a grounded Internet connection and even electricity. Further, the aim was to provide a literature review of current and past technology within this and similar spheres and to specifically examine the Kenyan National e-Health Strategy within which this system would operate. The pilot of the technology was to reveal operational challenges that would inform recommendations for future implementation projects.

8.3 Discussion

8.3.1 Response to the research objectives

The first objective, to describe e-health, mhealth, electronic medical records and clinical decision support systems in depth with particular focus on the functionality of e-health and mhealth systems in resource- constrained settings and within the realms of pregnancy and HIV care and those that utilise wireless broadband communitcations and to review and critique the Kenyan National e-Health Strategy 2011-2017, was met in Chapter 4 through an in-depth literature review.

The second objective, to develop a mobile technology enhanced, combined electronic medical record and clinical decision support system aimed at the co-management of HIV and pregnancy with utility in both centralized and decentralized care environments, in resource- met and resource- constrained settings, was met and is described in detail in Chapter 5.

The third objective, to pilot the mobile technology enhanced EMR/CDSS with a small cohort of clinicians in Western Kenya, was met, though with limited success from a operational and implementation perspective. Arguably, however, this lead to an enhanced rendering of the fourth objective, which was to describe the challenges in mhealth deployment within this, and other settings and the challenges have been described in chapter 7.

The remainder of this chapter will satisfy the fifth objective, which is to provide recommendations for future use of similar mhealth systems in resource, limited settings.

8.3.2 Outputs from the study

This study rendered two major outputs. The first was the creation of the EMR/CDSS for the co-management of HIV during pregnancy, using open source software, with extensive clinical decision support and data collecting and reporting capabilities, for use in centralised and decentralised environments. This EMR/CDSS is now available for download via GitHub at https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy. Organisations choosing to use the EMR/CDSS will be able to tailor the code to both suit their local environment and amend

and update the knowledge base as required to reflect local and international guidelines. Most critical EMR/CDSS based elements originally envisioned by the designer were achieved and the record itself works quite well. It may be demo'd at www.arantphd.org using the UPIN format xxxxx-xxxx-xx-xxxx or by searching for "test patient"

The mobile technology elements of this system were not able to be fully functional and realised in this setting due to the numerous challenges in wireless broadband connectivity explored previously. Though the qualitative and quantitative data that the researcher originally hoped for was not gathered because of serious and ongoing technological, infrastructural and project management challenges, the data gathered about these challenges, the analysis thereof and the recommendations derived from these challenges represent the second output and a valuable contribution to the literature, particularly with respect to implementing systems that utilise wireless broadband communication technologies. Hopefully this second output will prove useful to other organisations going forward.

8.3.3 Recommendations from the study for designers, implementers and organisations involved in EMR/CDSS implementation

8.3.3.1 Follow the digital design principles and anticipate challenges to implementation

The digital design principles, discussed in 6.3 Design principles, provide an excellent template, reflected by the literature, for the design of health technologies. While many of the principles' spirit was followed including designing for scale, sustainability, using open standards, data and innovation, address privacy and security and reuse and improve were followed with satisfaction, a few elements were not able to be adhered to fully. Though it was not feasible for the scope of this project to design the EMR/CDSS in concert with the MCH clinicians, upon reflection, this would have been ideal. Designing in collaboration with the end user not only allows for an EMR/CDSS that will ultimately satisfy their needs, while also retaining the vision of the designer, it will greatly improve local ownership of the product. This local ownership should enhance uptake and create impetus for successful implementation. Lack of full local understanding of and dedication to the product seriously undermined its usage.

Understanding the existing ecosystem is imperative. This understanding begins with region and its health system and extends to understanding the infrastructural challenges that the region faces. Failure to understand the extent to which infrastructural and technical challenges were going to affect both the utility of the EMR/CDSS on a grand scale but also a local scale, within the clinic itself, again undermined implementation.

Understanding the existing ecosystem applies to understanding the routine functioning of the Internet service provider as well. If there is a choice of provider, all potential providers should be thoroughly vetted to understand their capacity to adequately supply the services needed. Once this has happened and a provider is chosen, a business plan must be drawn up with anticipated costs, timelines and measures for holding the company accountable for unreasonable deviations from this timeline before implementation of the project.

8.3.3.2 Ensure that the knowledge base is up to date

The knowledge engineer must devise a system to ensure that the knowledge base reflects both international and local guidelines. The knowledge engineer for this project subscribed to HIV update alerts from the WHO, NIH and CDC and checked these daily. If there was a change in international guidelines, which happened numerous times during the design and implementation phases of the project, she was able to update clinical decision support elements of the EMR/CDSS to reflect them. The knowledge engineer was then able to investigate what was being done on a local level, if anything, to reflect guideline change and update the knowledge base as necessary. The project manager was able to download the updated clinical decision support elements to the server, print out paper copies and hand-deliver them and the news of the CDSS update to the clinicians in Kakamega. A systematic method for completion of this element must be devised and adhered to.

8.3.3.3 Ensure expertise of system designer and programmer

Ideally, the system designer would also be able to program all or most elements of the record. If the designer and knowledge engineer can program the EMR/CDSS, there will be no discrepancy between vision and output as far as skill in programming allows. Vision may be directly translated and debugging possible as the record is being coded, eliminating barriers in communication and understanding between the system designer/ knowledge engineer and the record programmer.

If this is not possible a programmer must be chosen that has the capability to design all required elements of the system and can demonstrate this before being hired. Modes of communication must be established between the designer/ knowledge engineer and the programmer that allow for ready editing of system functionality in a timely fashion.

Timelines and accountability must also be established before the programming process begins to avoid development delays. Ideally, both the system designer/knowledge engineer and the programmer are able to meet benchmarks together and have in place a prescribed mechanism for resolution when there is discrepancy between what the designer envisions and the programmer is able to create.

8.3.3.4 Alliances and effective structures of organisations

Had this project not faced the massive challenge of the demise of the sponsoring organisation, rollout and implementation should have been much smoother, quicker and the project may have been successful. A project of this size lacked the funding and person power to contend with the myriad challenges discussed in Chapter 7. The recommendation from this research is, if the project addresses a boutique aspect of a larger system, that the project aligns itself with an organisation already functioning in the realm so that all of the technical and infrastructural elements can be utilised or expanded upon. Starting anew with the technological infrastructure doomed this project.

If possible, responsibility for financing the costs of the project should go through the project itself instead of a third party. Recall that the billing for the technical aspects of this project was required to go through a 3rd party- namely a business or NGO registered in Kenya. This lead to myriad problems arising from bills being directed to and paid by a third party and diminished the oversight of the principal investigator and project manager. Billing errors were often not noted until services had been cut. A disseminated structure for account management and receipt and payment of bills provides excessive potential for error. For a project of this size and this cost, as above, alignment with a larger organisation is optimal, unless the project has the financing structure to allow for hiring of a dedicated team. If an alliance is not possible, and the principal investigators are able to provide the time, structure and finances necessary, incorporation as an NGO or CBO may allow the project to handle multiple accounts, as was required in this project, in many jurisdictions.

8.3.3.5 Project management

Ideally, the principal investigator/s should be on site to provide oversight of the project management staff and technical and clinical operations. As the project vision begins with the principal investigator, that person is best equipped to ensure that the objectives of the pilot are met. Further, principal investigator presence and direct involvement may help to make the clinicians and project management staff more committed to the pilot.

In hindsight, one project manager was not sufficient to manage the project. For future projects in this area, one technical manager with IT experience should be at the site of the server and router daily and be responsible for ensuring that the technical architecture is functional there. This technical manager can be responsible for liaising with the Internet service provider, following up billing and service issues and be on site to greet technicians from the field whose arrival is often unpredictable. The technical manager can also oversee financial aspects of the project. The technical manager should keep detailed daily logs reflecting all technical aspects of the project including service issues and interruption, and the follow up of these issues and interruptions. These logs should be uploaded to a shared folder daily so that the principal investigator may be kept abreast of progress.

A second manager, the study manager, should be responsible for all field aspects of the project and be familiar with the objectives, protocols, timeline and technical aspects of the project as they relate to on-site implementation. This study manager should be available to liaise with the government and hospital staff while the project is in the pre-implementation phase. The study manager will be responsible for ensuring that all proposals and protocols have been distributed and that hospital and ethics approvals and fees be maintained and current. When the study begins, this manager will be on site, every day, to help the clinicians with implementation challenges as they arise. Unattended to flags will be generated and the appropriate clinicians alerted to missing information. This manager or a dedicated data entry clerk should assist the staff with data entry aspects of the study that do not require clinical expertise such as demographic data entry.

Ensuring that the clinical site is online, the Chromebooks are powered and have connectivity with the server and ensuring that patients enrolled in the study will be seen with the EMR/CDSS would be the responsibility of this person as well. At the end of each study day,

this manager will ensure congruence between patients enrolled in the study, patients seen on that day and patients having a valid EMR/CDSS record history. Missing appointment lists derived from flags will be generated so that they may be followed up in the morning. The proper shut down, charging and storage of the Chromebooks will be this manager's responsibility. The manager should keep detailed logs of patients seen daily along with any challenges that have arisen. One study manager should be assigned to each study site. These technical and study managers should meet at least weekly to discuss project progress and share challenges and propose solutions whether virtually or in person. The minutes of these meeting should be detailed and shared with the principle investigators. The daily logs should also be shared with the principle investigator, whether in person or online so that daily study activities can be viewed and verified.

8.3.3.6 Oversight and a long term view

Ideally, principal investigators should be on site frequently and able to maintain relationships with all members of the study team. This will increase accountability and improve oversight. As with this project, however, this is often not the case and the principal investigator must devise other methods of ensuring proper system and study oversight.

It is imperative that the principal investigator be able to verify reports from the field, particularly if the investigator is off-site. Ideally, a functional SSH IPSec VPN would be available for a project of this nature so that the server can be accessed daily and enrolment and usage correlated with reports. As discussed above, daily logs from both the IT and study managers should be uploaded to a shared folder so that verification is available and discrepancies and challenges be addressed before they become detrimental to the study's success. If there is not remote access to the server, another mechanism must be in place to ensure that reports from the field and the logs from project management reflect what is on the server. Weekly data dumps from the server reflecting total patients in the system with pertinent information to the study should be accessed and reviewed by the principal investigator so that correlations may be made and inconsistencies responded to promptly.

As Matheson, et al. (2012) point out, organisations should take a long-term view of HIT projects, particularly in low- resource settings. Unfortunately the donor driven and small-scale nature of most of these projects means that few make it out of the pilot phase, certainly a limitation with this project. Perhaps had this project been implemented according to design and without the long period between inception and the beginning of the pilot, the financing structure would have allowed the project to continue for longer, rendering more robust output. Unfortunately this was not the case.

8.3.4 Recommendations for policy makers

As has been noted throughout this thesis as well as through emerging evidence from systematic reviews and surveys of programs and implementers, the small, donor-driven model whereby projects rarely make it past the pilot phase and derive little usable quality evidence for e- and mhealth systems, such as this project, is not a functional one. Successful systems must be sustainable and scalable and these may rely on the collaboration between national stakeholders and private, or non-governmental entities such as the collaboration between I-TECH and the Kenyan Ministry of Health, which provides a good example of a functional system from which to model policy.

Currently, as reviewed in 4.2 Kenya National e-Health Strategy 2011-2017, Kenya is operating under a well defined e-Health strategy that has been implemented with many successes and, currently, Kenya is involved in the rollout of KenyaEMR in consultation with I-TECH. KenyaEMR is an OpenMRS facilitated platform and has been deployed to over 300 sites (I-TECH, n.d). The system designed for this project was created in such a way that it could become either interoperable with KenyaEMR as it used OpenMRS and the CIEL/MVP concept dictionary and at minimum have the ability to share data easily. I-TECH was going to roll out KenyaEMR concurrently with this project, and had completed the Wi-Fi mapping of Kakamega CGH when the project was suspended secondary to Kakamega CGH envisioning the roll out of a local system instead.

This collaboration has fostered numerous components of the successful underpinnings for a national EMR system and allowed I-TECH and the Ministry of Health to begin to achieve numerous HIS tenets that align both with the Kenya National e-Health Strategy 2011-2017 and with the recommendations from the National e-Health Strategy Toolkit as recommended by the WHO and ITU (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011; World Health Organization & International Telecommunications Union, 2012).

Specifically, I-TECH and the Kenyan MOH have worked together to achieve many foundational elements necessary for a successful rollout of a national system and ensure that local facilities are able to effectively handle transitions to electronic HIS. At the national

level, the collaboration has standardised the HIS to ensure that systems are both interoperable and that data collection is accurate and complete. The collaboration is also working to improve standards for data quality and also conducting data analyses on key indicators and working to address quality of care through this EMR gathered data. This data will be available to guide future research (I-TECH, n.d).

I-TECH and the Kenyan Ministry of Health are also ensuring smooth and well supported HIS rollout at the local level through a number of different mechanisms. As identified by the Ministry of Medical Services & Ministry of Public Health & Sanitation in the Kenyan National e-Health Strategy 2011-2017, electricity remains unreliable in many parts of the country and equipment and infrastructure disparities between urban and rural centres can hinder the feasibility of rolling out technical aspects of projects in an equitable fashion (Ministry of Medical Services & Ministry of Public Health & Sanitation, 2011). Pre-planning site assessments ensure that barriers and challenges to successful rollout from both technical and organisational perspectives are identified prior to the HIS implementation and allow the rollout to be tailored to the unique challenges of each site (I-TECH, n.d).

Further, standardised curricula have been developed to train health care administrators and system users to ensure consistency of usage across sites and improve the accuracy of data. At the local clinic level, the preparation of health managers and administrators will enable the on-site training of facility staff and ensure that administrators and users are well prepared in advance of the rollout to meet the demands of implementation. This is facilitated by e-learning technologies (I-TECH, n.d). This will also ensure that, once the rollout is complete and the EMR operational in the local setting, that there is sufficient local ownership to transition to facility based management. Further to this, the collaboration trains and supports local developers and implementers in line with the principles of FLOSS-HC, Alma Ata and OpenMRS (I-TECH, n.d; International Conference on Primary Health Care, 1978; Karopka et al., 2014). Towards the vision of a more comprehensive HIS, the collaboration is creating a National Unique Patient Identifier, a Gender Based Violence database and open-source laboratory information systems (I-TECH, n.d).

8.4 Limitations of the study

The primary limitation of this study was the failure of the pilot to gather qualitative and quantitative data hoped for, for future robust analysis of the likely effects of a mobile technology enhanced, combined electronic medical record and clinical decision support systems on the transmission of HIV in the peripartum period. As has been reviewed

throughout the thesis, the unrelenting technical, infrastructural, budgetary, clinical and project management challenges encountered limited the mobile technology elements of the the system and stymied implementation of the system and lead to the abandonment of the pilot.

8.5 Significance of the study

The primary significance is the development of a unique, freely available, open source EMR/CDSS for the co-management of pregnancy and HIV. The record is unique in the amount of clinical information contained within it, and especially designed for the co-management of pregnancy, HIV and the multitude of co-morbidities associated with HIV and may serve the clinician and the patient at the point of care. This resource may be downloaded freely and adapted to a variety of situations.

8.5.1 Significance for pregnant women living with HIV and the clinicians who care for them

A system has been created that coalesces patient specific clinical information and active and passive clinical decision support elements specific to the co-management of HIV in the Kenyan setting. The system provides the opportunity to enhance the patient care experience by providing clinicians with a cloud based, wirelessly accessible repository of patient specific information, which under ideal technical infrastructural situations provides detailed patient information to the clinician at the point of care. This information is available without grounded Internet and electricity.

Further, the patient's specific clinical situation may be interpreted through the active clinical decision support elements of the system. Clinical care is enhanced as current guidelines (as of the pilot) are embedded in the record as passive clinical decision support elements for an extensive array of aspects of pregnancy care, HIV care and the specific care of the pregnant woman living with HIV. This has been accomplished through study and understanding of the scientific, clinical, public health, financial and historical underpinnings of the HIV epidemic with specific detail to pregnancy and the Kenyan context.

8.5.2 Significance for system designers and researchers in the e-Health field

An important manner in which this study is of significance is that it has described the creation process of an OpenMRS based, combined passive/active EMR/CDSS with mobile technology enhancements for use in a resource constrained environments. The literature review has provided a background for understanding the different types of EMR/CDSS and E- and mhealth systems. It has highlighted the successes and challenges of similar systems to the time of the pilot of the system created for this study with particular attention to cloud based systems and those in the maternal child health and HIV spheres.

The research study associated with the project outlined and examined the myriad barriers to successful implementation of a mobile technology enhanced, cloud- based EMR/CDSS in this particular resource constrained environment. While the majority of the originally intended study objectives with respect to robust quantitative data collection and analysis were not realised, the qualitative data may serve to act as a guideline to anticipate challenges when designing and implementing a study of this size, budget and nature from infrastructural and technological standpoints. It has further notified those intending to pilot similar projects in the region of potential pitfalls related to the Internet Service Provider, the weather and the condition of the wireless broadband communications in the area.

Additionally, the study has elucidated potential project management challenges and offered advice as to how to structure project management and project oversight going forward both from IT and clinical site management perspectives. Further, it has elucidated how budgetary difficulties and complex financing structures may impede program implementation and study output and made recommendations for organisational collaboration if possible.

Finally, a critique of the technology with respect to the digital design principles has been undertaken, rendering suggestions for improvement of system design both from technical and collaborative perspectives.

8.6 Conclusion

This study endeavoured to undertake the design of a novel, mobile technology enhanced, combined electronic medical record and active/passive clinical decision support system aimed at the co-management of pregnancy and HIV. Though the mobile technology elements were stymied in their full implementation in this setting, the record designed has been made available for demonstration, adoption and adaptation through a demonstration site and a Github armed with the code for the record. The system could be fully functional in a setting that had consistent access to 3G/4G wireless broadband or grounded internet or when used as

a local record housed on a hospital based server.

A discussion of the pathophysiology and clinical components of HIV and HIV care have been presented and a timeline of the public health and pharmacological interventions to date have been presented to enhance understanding of this project's context and to provide a rationale for why current guidelines are required for the ever evolving clinical care environment. The history and epidemiology of HIV in Kenya has been described to provide rationale for specific system elements from technical and public health infrastructural perspectives and clinical care perspectives so that this particular system my be viewed in context.

The background and literature review details the history, challenges and successes of electronic medical record and clinical decision support systems and provides rationale for the continued development of these systems and evidence of their utility, particularly in resource constrained settings. The system design and implementation has been described in granular fashion and the successes and challenges detailed with suggestions for designers, implementers and organisations implementing similar types of systems.

Finally this study has provided a tool to the m and ehealth, maternal child health and HIV communities to further enhance care of HIV positive women in resource-constrained settings. It is hoped that this study provides a backbone for future projects, implementation and research.

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Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged."

Appendix A Curtin Ethics Approval

Curtin University

Memorandum

To	Associate Professor Jaya Earnest, Nursing and Midwifery
From	Professor Peter O'Leary, A/Chair, Human Research Ethics Committee
Subject	Protocol Approval **HR 211/2013**
Date	19 December 2013
Copy	Jennifer Neel Arant Nursing and Midwifery

Office of Research and Development
Human Research Ethics Committee

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for providing the additional information for the project titled "*Development, Utilisation and Evaluation of a Mobile Health Application to Aid in the Management of HIV in Pregnancy*". The information you have provided has satisfactorily addressed the queries raised by the Committee. Your application is now **approved**.

- You have ethics clearance to undertake the research as stated in your proposal.
- The approval number for your project is **HR 211/2013.** *Please quote this number in any future correspondence*.
- Approval of this project is for a period of four years **19-12-2013** to **19-12-2017**.
- Your approval has the following conditions:
  i) Annual progress reports on the project must be submitted to the Ethics Office.
- **It is your responsibility, as the researcher, to meet the conditions outlined above and to retain the necessary records demonstrating that these have been completed.**

Applicants should note the following:

It is the policy of the HREC to conduct random audits on a percentage of approved projects. These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on follow-up of participants.

The attached **Progress Report** should be completed and returned to the Secretary, HREC, C/- Office of Research & Development annually.

Our website https://research.curtin.edu.au/guides/ethics/non_low_risk_hrec_forms.cfm contains all other relevant forms including:

- Completion Report (to be completed when a project has ceased)
- Amendment Request (to be completed at any time changes/amendments occur)
- Adverse Event Notification Form (If a serious or unexpected adverse event occurs)

Yours sincerely

Professor Peter O'Leary
A/Chair Human Research Ethics Committee

Appendix B Moi University Teaching and Referral Hospital Institutional Research and Ethics Committee Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2014/32
Approval Number: 0001191

6th June, 2014

Ms Neel Arant Bandy
Centre of International Health
School of Nursing and Midwifery
Curtin University

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
06 JUN 2014
RECEIVED
P.O. Box 4606-30100 ELDORET

Dear Ms Neel,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Development, Utilization and Evaluation of a Mobile Health Application to Aid in the Management of HIV in Pregnancy".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1191*** on 5th June, 2014. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 29th May, 2015. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc Director - MTRH Dean - SOP
Principal - CHS Dean - SON
Dean - SOM Dean - SOD

Appendix C English and Swahili patient information and consent forms

Centre for International Health
School of Nursing and Midwifery
Faculty of Health Sciences

Participant Information Sheet

A mhealth tool to aid in the co-management of HIV and pregnancy

My name is Neel Arant Bandy and I am a midwife and a doctoral candidate and student in the Centre for International Health at Curtin University of Technology in Western Australia. I am conducting a research study that aims to understand how delivery of care during pregnancy for HIV positive women is affected by the utilisation of a mobile clinical decision support system and electronic medical record by the healthcare provider.

The main aim of the research is to identify how treatment and management is changed by the introduction of a decision support system and electronic medical record specific to HIV in pregnancy. This system provides your healthcare practitioner with access to the most up to date guidelines for the co-management of HIV and pregnancy as well as access to your medical record ensuring that he or she has the most current information to treat your HIV and manage your pregnancy. The tool also allows your practitioner to discuss your case with other healthcare providers and refer you to another centre for care if needed.

I hope to understand how this system affects the treatment that you receive. The care recommended for you will be based on the most up to date information available and in accordance with the World Health Organization and the Kenyan Ministry of Health guidelines. Any discussion about your care will be with a health care practitioner associated with your clinic and will not be discussed with anyone outside of your routine care environment such as partners, children, friends or family members. No information will be linked to your name or your likeness in any writing or publication. All of your medical information will be stored as it would during your routine care at your clinic.

I would be most grateful if you would assist me with this project. The project hopes to improve the care given to HIV positive pregnant women and their babies and your assistance could be beneficial to you, your community and women living with HIV worldwide. There are no identifiable risks to you or your baby as a result of participating in the study. The results of the project will be made available for your perusal at your clinic after the project has been completed.

Your participation in this project is voluntary and will not affect your ability to receive care at the clinic. You are free to ask questions about the project at any time. If at any point you would no longer like to participate in the project you are free to end your participation without any penalty and your care will revert to routine care without the use of the clinical decision support system.

This study has been approved by the Moi University Institutional Research and

Ethics Committee, approval number FAN:IREC 1191 and the Curtin University Human Research Ethics Committee, approval number HR 211/2013. The Curtin University Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

THANK YOU VERY MUCH FOR TAKING THE TIME TO TALK TO ME

Please contact the following with queries, complaints or for communication in regards to the research:

Neel Arant Bandy
PhD Candidate
Centre for International Health
School of Nursing and Midwifery
Curtin University of Technology
Perth, Western Australia
jennifer.arant@postgrad.curtin.edu.au

Dr. Jaya Earnest
Associate Professor
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Collins Epereje Otwane
Project Coordinator
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Centre for International Health
School of Nursing and Midwifery
Faculty of Health Sciences

Appendix D Participant Consent Form

A mhealth tool to aid in the co-management of HIV and pregnancy

Consent Form for Participants

Date……..

Neel Arant Bandy, a doctoral student at the Centre for International Health in the School of Nursing and Midwifery at Curtin University of Technology, is the investigator for this project.

- I have read the information sheet for this project and have agreed to participate in the study on the use of a mhealth tool to aid in the co-management of HIV and pregnancy.
- I have been informed of and understand the purposes of the study.
- I am participating voluntarily and understand that I can withdraw from the study at any time.
- I understand that information regarding the treatment I receive may be used in reports and publications and that this information will not be linked to my name.
- I am able to ask questions of the project at any time.

I would like to participate in this study YES NO

Signed……..

Print Name……..

Date……

Centre for International Health
School of Nursing and Midwifery
Faculty of Health Sciences

Kifaa cha mhealth kinachotumika kwa kushughulikia maswala ya HIV na uja uzito.
Ujumbe Wa Mgonjwa

Jina langu ni Neel Arant Bandy.Mimi ni mkunga, msomi na mtahiniwa wa kimatibabu katika chuo kikuu cha kiafya cha Curtin huko Magharibi mwa Australia. Ninafanya utafiti unaolenga kubainisha jinsi matumizi yamtambo wa rununu kufanya maamuzi ya kiafya, na kuweka rekodi za matibabu kielektroniki kumeshawishi shughuli ya kujifungua kwa wamama wanaoishi na virusi vya HIV, baada ya kliniki dhidi ya virusi hivyo wakati wa uja uzito.

Lengo kuu hasa la utafiti huu ni kujua jinsi kujumuishwa kwa mpango huu wa kielektroniki ulivyobadilisha shughuli za kimatibabu na namna ya kuzimudu shughuli hizo, hasa wakati wa uja uzito.

Mtambo huu humpa mhudumu wako wa afya fursa ya kupata maelekezo yaliyokamilika kuhusu mbinu za kuthibiti virusi vya HIV na uja uzito pamoja na kuona rekodi zako za kiafya ili kuhakikisha kuwa anao ujuzi wa kisasa wa kupambana na kushughulikia hali yako ya HIV na uja uzito mtawalia.

Mtambo huu pia humwezesha kujadili hali yako na wahudumu wengine wa afya na kukupa huduma za uhamisho wa kimatibabu hadi kwenye zahanati nyingine panapo haja.

Nataraji kuelewa jinsi mbinu hii imeathiri au kuboresha matibabu unayopokea.
Huduma unaokulenga wewe utazingatia kikamilifu maelezo kutoka kwa SHIRIKA LA AFYA DUNIANI (WHO) pamoja na WIZARA YA AFYA HUMU NCHINI.

Uamuzi wowote kukuhusu na huduma za kiafya unazopewa utabaki tu na mhudumu wa afya; na hautajadiliwa na mtu yeyote wa kando kama vile; mwenzio wa kazi/biashara,watoto, jamaa au marafiki.

Huduma na maelezo unayoyapata yanaweza kuwekwa wazi kwa uma, japo kuhusishwa na jina lako,au chochote kinachoweza kukutambulisha.

Nitashukuru sana iwapo utanisaidia kwa ajili ya mradi huu, kwa sababu mradi huu unatrajia kuboresha huduma wanaopewa wamama wajawazito wanaoishi na virusi vya HIV pamoja na watoto woo. Hivyo Masada wako quenda ukawa wa mhimu sana kwako, kwa jumuiya yako na kwa wamama na watoto wa namna hii ulimwenguni mwote.

Naomba nikujulishe kuwa hakuna athari zozote zitakazoletwa kwako wala kwa mototo wako kwa ajili ya kushiriki kwenye utafiti huu. Matokeo ya mradi huu yatapatikana kwenye kituo chako cha afya kwa kudurusu pale utafiti huu utakapokamilika.

Kumbuka kuwa, kushiriki kwako kwenye utafiti huu ni kwa hiari/kujitolea na hautaathiri uwezo au haki zako za kupokea huduma za kliniki. Vilevile uko huru kuuliza maswali unapotaka. Iwapo utahisi kutoshiriki kabisa kwenye utafiti huu, uko huru kutamatisha shughuli hiyo pasipo na adhabu yoyote dhidi yako na huduma yako ya kliniki zitaendelea tu kama kawaida, japo nje ya mradi huu bali kwa namna ya awali.

This study has been approved by the Moi University Institutional Research and Ethics Committee, approval number FAN:IREC 1191 and the Curtin University Human Research Ethics Committee, approval number HR 211/2013. The Curtin University Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

ASANTE SAN KWA KUCHUKUA MUDA WAKO KUONGEA NAMI

Kwa maoni,maswali,malalamishi au mawasiliano kuhusu mradi na utafiti, wasiliana n

Neel Arant Bandy
PhD Candidate
Centre for International Health
School of Nursing and Midwifery
Curtin University of Technology
Perth, Western Australia jennifer.arant@postgrad.curtin.edu.au

Dr. Jaya Earnest
Associate Professor
Centre for International Health
School of Nursing and Midwifery
Faculty of Health Sciences
Curtin University of Technology
Perth, Western Australia
j.earnest@curtin.edu.au

Dr. Roseline Atieno
The Medical Superintendent
Kakamega County General Hospital
Kakamega County
P.O Box 15, Kakamega
0722331585
roselineatieno@yahoo.com

Collins Epereje Otwane
Project Coordinator
Uamuzi Bora
Tuskys Mall
Kakamega, Western Province, Kenya.
0710383086
collins.otwane@uamuzibora.org

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School of Nursing and Midwifery
Faculty of Health Sciences

Kifaa cha mhealth kinachotumika kwa kushughulikia maswala ya HIV na uja uzito.
Fomu ya kukubali kushiriki

Tarehe…….
Neel Arant Bandy, msomi na mtahiniwa wa chuo cha afya cha Curtin ndiye mtafiti wa mradi huu.

- Nimesoma habari kwenye ukurasa huu na nimekubali kushiriki kwenye utafiti wa matumizi ya mtambo wa 'Mhealth' ili kuimarisha shughuli za kumudu virusi vya HIV wakati wa uja uzito.
- Nimeshaelezwa na kuelewa madhumuni ya utafiti huu.
- Nimeelewa kuwa ninashiriki kwa hiari na ninaweza kujiondoa wakati wowote.
- Naelewa kwamba matibabu ninayoyapokea yanaweza kutumika kwa ripoti na kuwekwa wazi kwa uma pasipo kuhusisha jina langu wala chochote cha kunitambulisha.
- Niko huru kuuliza maswali kuhusu mradi na utafiti huu wakati wowote.

Ningependa kushiriki kwenye utafiti huu NDIYO LA

Sahihi……

Jina……

Tarehe ……..

Appendix E Provider information and consent forms

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School of Nursing and Midwifery
Faculty of Health Sciences

Provider Information Sheet

A mhealth tool to aid in the co-management of HIV and pregnancy

My name is Neel Arant Bandy and I am a midwife and a doctoral candidate in the Centre for International Health at Curtin University of Technology in Western Australia. I am conducting a research project that aims to understand how delivery of care during pregnancy for HIV positive women is affected by the utilisation of a mobile health application by the healthcare provider.

The aim of the project is to identify how treatment and management of HIV in pregnancy is changed by the introduction of a combined clinical decision support system and electronic medical record specific to HIV in pregnancy utilised by the healthcare provider at the point of care. It also aims to evaluate whether provider workflow is streamlined and whether consultation and referral capabilities are enhanced.

This tool will provide a computerised decision support system that reflects best evidence based practice guidelines for the co-management of HIV and pregnancy, access to each patient's electronic medical record at the point of care and the ability to consult with a practitioner at a different facility and refer a patient to another facility if needed.

The project will compare treatment modalities in the pre- intervention and post-intervention groups. Information regarding the perceived usefulness of the tool by the healthcare provider will be collected by questionnaire.

I would be most grateful if you would assist me with this project. As a healthcare provider you would be asked to utilise the mhealth tool for medical record review and completion,

management decision-making and consultation and referral when necessary. You will be asked to respond to a questionnaire at the end of the project.

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Faculty of Health Sciences

The questionnaire will query you regarding experience of use, management decision-making and experience with consultation and referral. This information will be written. Information regarding treatment given to patients and your answers to the questionnaire will be collected and may be used in reports and publications associated with the project. None of the information will be linked to your name.

Your participation in this project is voluntary. You are free to ask questions about the project at any time. If at any point you would no longer like to participate in the project you are free to end your participation without penalty.

THANK YOU VERY MUCH FOR TAKING THE TIME TO TALK TO ME

Neel Arant Bandy, CNM, RM, RN
PhD Candidate
Centre for International Health
Faculty of Health Sciences
School of Nursing and Midwifery
Curtin University of Technology
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jennifer.arant@postgrad.curtin.edu.au

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Collins Epereje Otwane
Project Coordinator
Uamuzi Bora

Tuskys Mall
Kakamega, Western Province
Kenya
Collins.otwane@uamuzibora.org

This study has been approved by the Moi University Institutional Research Committee (Approval Number FAN:IREC 1191) and the Curtin University Human Research Ethics Committee (Approval Number HR211/2013). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth 6845 or by telephoning 9266 9223 or by emailing hrec@curtin.edu.au.

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School of Nursing and
Midwifery
Faculty of Health Sciences

A mhealth tool to aid in the co-management of HIV and pregnancy

Consent for Healthcare Providers

Date……..

Neel Arant Bandy of the Centre for International Health in the School of Nursing and Midwifery at Curtin University of Technology is the investigator for this project

- I have read the information sheet for this project and have agreed to participate in the study on the use of a mhealth tool to aid in the co-management of HIV and pregnancy.
- I have been informed of and understand the purposes of the study.
- I am participating voluntarily and understand that I can withdraw from the study at any time.
- I agree to utilise the mhealth tool for the management, review, charting, consultation and referral of participants enrolled in the project.
- I am sharing information on my experience with the mhealth tool and understand that my name will not be associated with my answers.
- I consent to having my answers to the questionnaire audio recorded.
- I am able to ask questions of the project at any time.

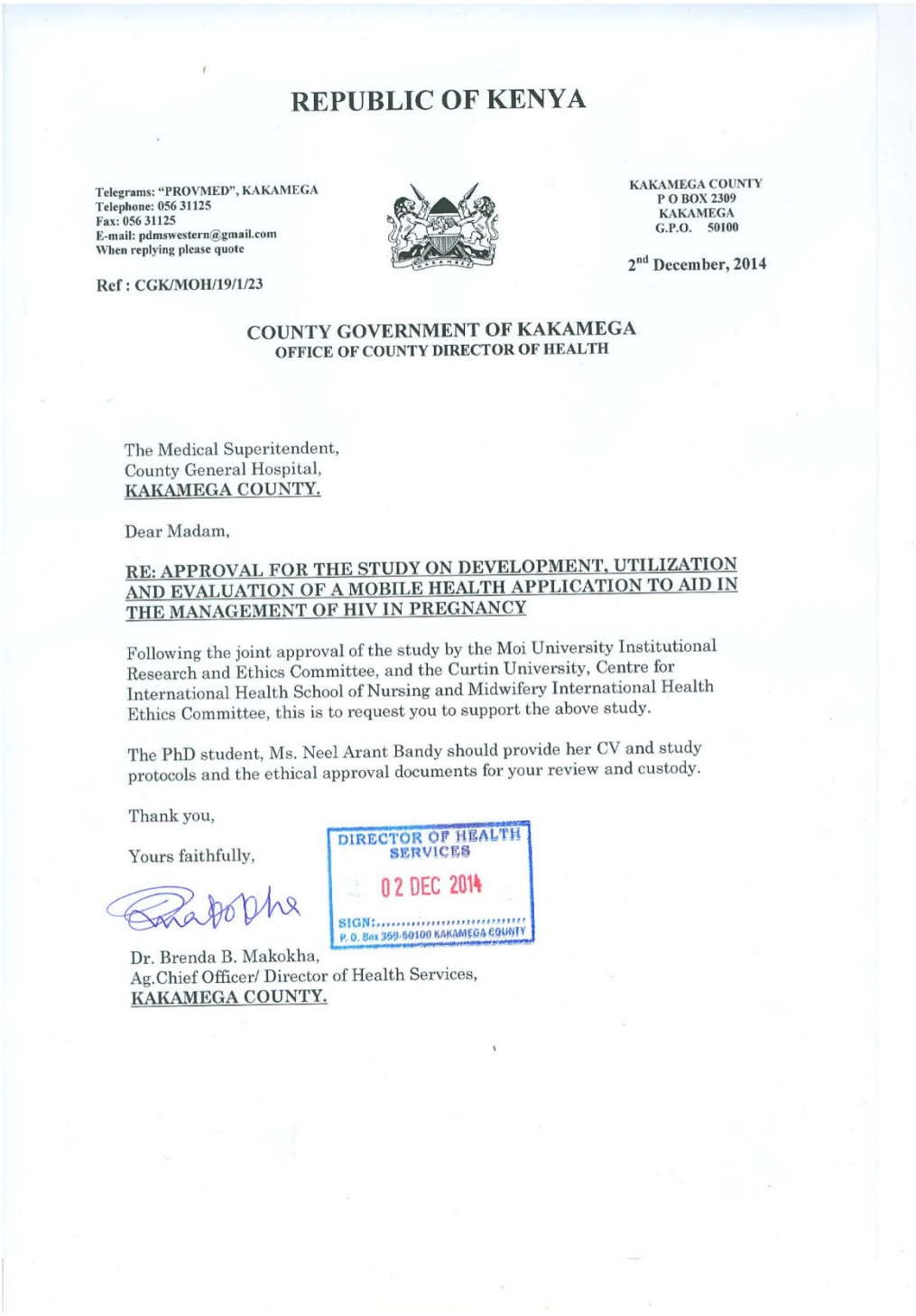
I agree to participate in this project YES NO

Signed……..

Print Name……..

Date…….

Appendix F County Ministry of Health and Kakamega County General Hospital Approvals



REPUBLIC OF KENYA

Telegrams: "PROVMED", KAKAMEGA
Telephone: 056 31125
Fax: 056 31125
E-mail: pdmswestern@gmail.com
When replying please quote

KAKAMEGA COUNTY
P O BOX 2309
KAKAMEGA
G.P.O. 50100

Ref : CGK/MOH/19/1/23

2nd December, 2014

COUNTY GOVERNMENT OF KAKAMEGA
OFFICE OF COUNTY DIRECTOR OF HEALTH

The Medical Superitendent,
County General Hospital,
KAKAMEGA COUNTY.

Dear Madam,

RE: APPROVAL FOR THE STUDY ON DEVELOPMENT, UTILIZATION AND EVALUATION OF A MOBILE HEALTH APPLICATION TO AID IN THE MANAGEMENT OF HIV IN PREGNANCY

Following the joint approval of the study by the Moi University Institutional Research and Ethics Committee, and the Curtin University, Centre for International Health School of Nursing and Midwifery International Health Ethics Committee, this is to request you to support the above study.

The PhD student, Ms. Neel Arant Bandy should provide her CV and study protocols and the ethical approval documents for your review and custody.

Thank you,

Yours faithfully,

DIRECTOR OF HEALTH SERVICES
02 DEC 2014
SIGN:.....
P. O. Box 369-50100 KAKAMEGA COUNTY

Dr. Brenda B. Makokha,
Ag.Chief Officer/ Director of Health Services,
KAKAMEGA COUNTY.

REPUBLIC OF KENYA

Telegrams: "PROVMED", KAKAMEGA
Telephone: 056 31125
Fax: 056 31125
E-mail: pdmswestern@gmail.com
When replying please quote

KAKAMEGA COUNTY
P O BOX 2309
KAKAMEGA
G.P.O. 50100

Ref : CGK/MOH/19/1/23

2nd December, 2014

COUNTY GOVERNMENT OF KAKAMEGA
OFFICE OF COUNTY DIRECTOR OF HEALTH

Cash Point
Please accept 5000/= from the bearer for research
3/12/14

The Medical Superitendent,
County General Hospital,
KAKAMEGA COUNTY.

Dear Madam,

RE: APPROVAL FOR THE STUDY ON DEVELOPMENT, UTILIZATION AND EVALUATION OF A MOBILE HEALTH APPLICATION TO AID IN THE MANAGEMENT OF HIV IN PREGNANCY

Following the joint approval of the study by the Moi University Institutional Research and Ethics Committee, and the Curtin University, Centre for International Health School of Nursing and Midwifery International Health Ethics Committee, this is to request you to support the above study.

The PhD student, Ms. Neel Arant Bandy should provide her CV and study protocols and the ethical approval documents for your review and custody.

Thank you,

Yours faithfully,

DIRECTOR OF HEALTH SERVICES
02 DEC 2014
SIGN:.....
P. O. Box 369-50100 KAKAMEGA COUNTY

MEDICAL SUPERINTENDEN
KAKAMEGA COUNTY GENERAL HOSPITAL
03 DEC 2014
P. O. Box 1...
Sign:.....

Dr. Brenda B. Makokha,
Ag.Chief Officer/ Director of Health Services,
KAKAMEGA COUNTY.

Appendix G Itinerary for 12/2014 Kakamega in country visit

Date	Activities
Monday 1/12/14	Arrived Kisumu International Airport at 7:50 am, drove to Kakemega and checked into Golf Hotel. Met with Mr. Otwane to review intinerary and gain familiarity with hospital and Ministry of Health Officials.
Tuesday 2/12/14	Meeting with the County Health Management Team, Kakamega CGH Medical Superintendent and the MCH In-charge in Kakamega. The Director, Dr. Baraza gave us the final approvals for the proposal and a letter of authority to conduct training at the Hospital. We were assured maximum support from both of the County Health Management team members Mr. Omusotsi and Mrs. Brenda.
Wednesday 2/12/14	Visit to the research site for acquaintance and invitation to training. Paid a visit to the Medical Superintendent office, Dr. Rose and she received the project proposal, encouraged more research to be done in collaboration with the hospital and stamped all the necessary documents and approvals for the project after which we headed to the Hospital's Administrator's office who gave us an entry letter and handed us over to The Hospital's Records Department who took us to the MCH again for a re-introduction. We had a meeting with the nurse in charge of MCH, Mrs Joy, together with her deputy Mrs Dorothy Brown, and planned for the 2-day training. The nurses and midwives were organised into 2 groups that would work in shifts over the 2 days of training. Later we paid the hospital's research fees and headed back to the office.
Thursday 3/12/14	Fine-tuned the system in preparation for the launch. Extracted retrospective data from Uamuzi Bora system.
Friday 4/12/14	Visited the Moi University School of Medicine Teaching and Referral Hospital Institutional Research Ethics Committee and made the research payment in Kenyan shillings as electronic bank transfer in US Dollars not accepted by IREC bank.

Date	Activities
Monday 8/12/14	Part 1 Training conducted and feedback and recommendations from clinicians recorded.
Tuesday 9/12/14	Part 2 training conducted and feedback and recommendations from clinicians recorded. Visit to the Medical Director's office to thank her for the opportunity to conduct research at KCGH.
Wednesday 10/12/14	Review of the system and made changes in accordance with clinician recommendations.
Thursday 11/12/14	Departure/Kisumu International Airport. (7.10 p.m.)

Appendix H Code for the initial visit and revisit forms

Initial Visit Form Code

```
<htmlform>
<!-- new code -->

<script src="../../scripts/colorbox/jquery.colorbox-min.js" type="text/javascript"></script>

<link href="../../scripts/colorbox/css/colorbox.css" media="all" rel="stylesheet"
type="text/css" />

<script src="https://code.jquery.com/jquery-1.10.2.js"></script>
<script src="https://code.jquery.com/ui/1.10.4/jquery-ui.js"></script>
<link rel="stylesheet" href="https://code.jquery.com/ui/1.10.4/themes/smoothness/jquery-
ui.css"/>

                        <script type="text/javascript">
                                var $j = jQuery.noConflict();

                        /* variable used in js to know the context path */
                        var openmrsContextPath = '/demo/mch';
                        var dwrLoadingMessage = 'Loading...';
                        var jsDateFormat = 'dd/mm/yyyy';
                        var jsTimeFormat = 'hh:mm';

                        /* prevents users getting false dwr errors msgs when leaving pages
*/
                        var pageIsExiting = false;
                        if (typeof(jQuery) != "undefined")
                           jQuery(window).bind('beforeunload', function () { pageIsExiting
= true; } );

                        var handler = function(msg, ex) {
                                if (!pageIsExiting) {
                                        var div =
document.getElementById("openmrs_dwr_error");
                                        div.style.display = ""; // show the error div
                                        var msgDiv =
document.getElementById("openmrs_dwr_error_msg");
                                        msgDiv.innerHTML = 'A javascript error has
occurred:' + " <b>" + msg + "</b>";
                                }

                        };
                        dwr.engine.setErrorHandler(handler);
                        dwr.engine.setWarningHandler(handler);
                </script>
```

```
<!-- end of new code -->

<script type="text/javascript">
if(jQuery){
//To calculate the EDD from LMP by adding 280 days
$j(document).ready(function(){

  $j("#w16-display").change(function(){
   lmp=$j("#w16-display").val();
   year=parseInt(lmp.substr(6,4));
   day=parseInt(lmp.substr(0,2));
   month=parseInt(lmp.substr(3,2)-1);
   date=new Date(year,month,day)
   new_date=new Date(date.getTime()+280*24*3600*1000)

   date=new_date.getDate()
  if( date &lt; 10 ){
      date ="0"+ String(date)
    } else {
      date=String(date)
    }
   month=new_date.getMonth()+1
   if ( month &lt; 10){
      month= "0"+String(month)
   } else {
      month = String(month)
     }

   string=date+"/"+month+"/"+String(new_date.getFullYear());
   string2=String(new_date.getFullYear())+"-"+month+"-"+date
  lmp=$j("#w18-display").val(string);
  $j("#w18").val(string2);

  });
  $j(".trigger").each(function(i,obj){

   if($j(this).find(':radio').attr("id")==undefined){
   var disableField = "#enable_disable"+$j(this).attr('enable_disable');
   if($j(this).find('.value').html().toString()[9] =="Y"){
   $j(disableField+"_yes").show();
   }
  }
  });

   $j(".trigger").find(":radio").change(function(){
     var disableField = "#enable_disable"+$j(this).parent().attr('enable_disable')+"_yes";
     var enableField = "#enable_disable"+$j(this).parent().attr('enable_disable')+"_no";

     var value=$j(this).val();
     if (value=="true"){
         $j(disableField).show();
         $j(enableField).hide();
     }else{
          $j(disableField).hide();
          $j(enableField).show();
```

```
    }
});

 <!-- new code -->
 $j("a.dangerous-signs").each(function() {
  $j(this).colorbox({
    width:"300",
    height:"580",
    title: $j(this).attr('data-desc'),
    onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
  });
 });
 <!-- end of new code -->
<!-- new code -->
 $j("a.colorbox").each(function() {
  $j(this).colorbox({
    width:"300",
    height:"580",
    title: $j(this).attr('data-desc'),
    onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
  });
 });
 $j("a.colorbox-wide").each(function() {
  $j(this).colorbox({
    width:"500",
    height:"520",
    title: $j(this).attr('data-desc'),
    onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
  });
 });
 <!-- end of new code -->
});
 }

beforeSubmit.push(function() {
   var ret=true;
   $j(".trigger").each(function(i,obj){
    if( $j(this).find('input[type=radio]:checked').val()!==undefined){
   $j(this).find('.error').html('').hide()
   }else{
   ret=false;
   $j(this).find('.error').html("Required field").show()
   }
   });

   return ret;
});

</script>

        <macros>
                paperFormId = MoH 216
                headerColor = #00B551
                fontOnHeaderColor = white
        </macros>
```

```
<style>
	.section {
		border: 1px solid $headerColor;
		padding: 2px;
		text-align: left;
		margin-bottom: 1em;
	}
	.sectionHeader {
		background-color: $headerColor;
		color: $fontOnHeaderColor;
		display: block;
		padding: 2px;
		font-weight: bold;
	}
	table.baseline-aligned td {
		vertical-align: baseline;
	}
	/*new code*/
	.overview-dangerous-signs{
	}
	.overview-dangerous-signs img{
	  width: 90px;
	  height: 180px;
	}
	/*end of new code*/
</style>

<span style="float:right">Paper Form ID: $paperFormId</span>
<h2>Initial Visit Form</h2>

<section headerLabel="Patient Profile">
  <table class="baseline-aligned">

	<tr>
<td><strong>|Patient's Name:</strong></td>
		<td><lookup class="value" expression="patient.personName"/></td>

<td><strong>|Unique Patient Number:</strong></td>
		<td><lookup expression="patient.getPatientIdentifier(5)"/></td>
<td><strong>|Age:</strong></td>
		<td><lookup expression="patient.age" /></td>

<td><strong>|Date of Birth:</strong></td>
		<td><lookup class="value" complexExpression="#if(
\$patient.birthdateEstimated ) ~#end"/> <lookup class="value"
expression="patient.birthdate"/>
		 (Age: <lookup class="value" expression="patient.age"/>)</td>
	</tr>

  </table>

</section>

<section headerLabel="Consultation Details">
	<table class="baseline-aligned">
```

```
                        <tr>
                                <td><strong>Date:</strong> <encounterDate
default="today"/></td>
                                <td><strong>Location:</strong> <encounterLocation
default="1"/></td>
                        <td><strong>Provider:</strong> <encounterProvider
default="currentuser"/></td>

                        </tr>

                </table>
        </section>

<section headerLabel="Problems and Allergies">
Problem List:<br />
<obs conceptId="162667" style="textarea" rows="10" cols="80"/>
<br />
<br />
Allergies:<br />
 <obs conceptId="162668" style="textarea" rows="10" cols="80" />

</section>
<section headerLabel="Maternal Profile">
                <table class="baseline-aligned">
                        <tr>
                                <td>Gravida:</td><td><obs conceptId="5624" /></td>
                        </tr>
                        <tr>
                                <td>Parity:</td><td><obs conceptId="1053" /></td>
                        </tr>
                        <tr>
                                <td>LMP:</td><td><obs conceptId="1427" /></td>
                        </tr>
                        <tr>
                                <td>EDD:</td><td><obs conceptId="5596"
allowFutureDates="true" /></td>
                        </tr>
<tr>
                                <td>Method of gestational age
determination:</td><td><obs conceptId="160697" /></td>


                        </tr>
        <tr><button class="showFormEntryDialog" style="margin-left: 2em; margin-
bottom: 0.5em">Enter Form</button>

                        <script type="text/javascript">
                                var r = confirm("Welcome to the Initial Visit Form. The
treatment guidelines presented in this record are intended as a guide and should not
supersede clinical judgement");
if (r == true) {
   x = "You pressed OK!";
} else {
   x = "You pressed Cancel!";
}
```

```
</script>
</tr>
                    </table>
            </section>
        <section headerLabel="Medical and Surgical History">
                    <table class="baseline-aligned">
<tr><td>
<section headerLabel="1">
                    <table class="baseline-aligned">
                                        <tr>
                                        <td>HIV and Opportunistic Infections:</td><td><obs
conceptId="160170" /></td>
</tr>
<tr>
                        <td>Digestive Systems Diagnosis:</td><td><obs conceptId="160171"
/></td>
                                </tr>
                                <tr>
                                        <td>Eye Diagnosis:</td><td><obs conceptId="160172"
/></td>
</tr>
 <tr>
                        <td>Ear Diagnosis:</td><td><obs conceptId="160173" /></td>
                                </tr>

<tr>
                                        <td>Cardiovascular System Diagnosis:</td><td><obs
conceptId="160174" /></td>
</tr>
<tr>
                        <td>Musculoskeletal System and Injury Diagnosis:</td><td><obs
conceptId="160175" /></td>
                                </tr>
<tr>
                                        <td>Neurological Diagnosis:</td><td><obs
conceptId="160176" /></td>
</tr>
<tr>
                         <td>Psychological Diagnosis:</td><td><obs conceptId="160177"
/></td>
                                </tr>

                                <tr>
                                        <td>Respiratory System Diagnosis:</td><td><obs
conceptId="160178" /></td>
                                </tr>

<tr>
                        <td>Dermatological Diagnosis:</td><td><obs conceptId="160179"
/></td>
                                </tr>
                    </table>
            </section>
</td>
<td>
```

```
<section headerLabel="2">
                    <table class="baseline-aligned">

                                <tr>
                                            <td>Nutrirional Endocrine and Metabolic
Diagnosis:</td><td><obs conceptId="160180" /></td>
                                </tr>
<tr>
                          <td>Urological System Diagnosis:</td><td><obs conceptId="160181"
/></td>
                                </tr>

                                <tr>
                                            <td>Female Genital Diagnosis:</td><td><obs
conceptId="160213" /></td>
                                </tr>
                                <tr>
                                            <td>Dental Diagnosis:</td><td><obs conceptId="160182"
/></td>
                                </tr>
<tr>
                          <td>Surgical History:</td><td><obs conceptId="162605" /></td>
                                </tr>
<tr>                      <td> History of intimate partner violence:</td><td><obs
conceptId="160658"/></td>
                    </tr>

<tr>
                                  <td>History of blood Transfusion</td><td> <obs
conceptId="1871" style="yes_no"/></td>
                                </tr>
<tr>
                     <td> Family History:</td><td><obs conceptId="161011"/></td>
                    </tr>

<tr>
                          <td>Other:</td><td><obs conceptId="161011" /></td>
                                </tr>
                     </table>
          </section>
</td>
</tr>
                     </table>
</section>

 <section headerLabel="HIV History">
                    <table class="baseline-aligned">
<tr><td>
<section headerLabel="Patient Source">
                    <table class="baseline-aligned">
                                <tr>
                                            <td><obs conceptId="160540" labelText="Entry Point:"
id="entryPoint"/></td>
                                </tr>
                                <tr>
```

```
                                    <td><obs conceptId="162597" labelText="Date
Registered/Transferred In::" id="entryDate"/></td>
                                </tr>
                        </table>
                </section>
</td>
<td>
<section headerLabel="HIV Status and ART Eligibility">
                        <table class="baseline-aligned">

                        <tr>
                                    <td><obs conceptId="160554" labelText="Date HIV
Diagnosis:" id="positiveDate"/></td>
                                </tr>
                        <tr>
                            <td><obs conceptId="160553" labelText="Initial WHO clinical
Stage:"/></td>
                        </tr>
                                <tr>
                                    <td><obs conceptId="159599" labelText="Antiretroviral
therapy start date:"/></td>
                                </tr>
<tr>
                                    <td><obs conceptId="1088" labelText="Current ART
Regimen:"/></td>
                                </tr>
                        </table>
                </section>
</td>
<td>
<section headerLabel="Treatment Supporter">
                        <table class="baseline-aligned">
                                <tr>
                                    <td>Name:</td>
                                    <td><obs conceptId="162606"/></td>
                                </tr>
                                <tr>
                                    <td>Relationship:</td>
                                    <td><obs conceptId="160640"/></td>
                                </tr>
                                <tr>
                                    <td>Postal Address:</td>
                                    <td><obs conceptId="160641"/></td>
                                </tr>
                                <tr>
                                    <td>Telephone Number:</td>
                                    <td><obs conceptId="160642"/></td>
                                </tr>
                        </table>
                </section>
</td>
</tr>
```

*To access the full Initial Visit form code as it appeared for the 2014 launch of the pilot, please visit https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy *

Revisit Form Code

```
<htmlform>
<!-- new code -->

<script src="../../scripts/colorbox/jquery.colorbox-min.js" type="text/javascript"></script>

<link href="../../scripts/colorbox/css/colorbox.css" media="all" rel="stylesheet"
type="text/css" />
<script>
$j(document).ready(function(){

for(var i=1;i&lt;32;i++){
$j( "#hello"+i).dialog({ autoOpen: false,width:900 });
$j( "#say_it"+i).click(function() {
$j("#hello"+$j(this).attr("id").substr(6)).dialog( "open");
});
}
});
</script>
                    <script type="text/javascript">

                                        var $j = jQuery.noConflict();

                                /* variable used in js to know the context path */
                                var openmrsContextPath = '/demo/mch';
                                var dwrLoadingMessage = 'Loading...';
                                var jsDateFormat = 'dd/mm/yyyy';
                                var jsTimeFormat = 'hh:mm';

                                /* prevents users getting false dwr errors msgs when leaving pages
*/
                                var pageIsExiting = false;
                                if (typeof(jQuery) != "undefined")
                                   jQuery(window).bind('beforeunload', function () { pageIsExiting
= true; } );

                                var handler = function(msg, ex) {
                                        if (!pageIsExiting) {
                                                var div =
document.getElementById("openmrs_dwr_error");
                                                div.style.display = ""; // show the error div
                                                var msgDiv =
document.getElementById("openmrs_dwr_error_msg");
                                                msgDiv.innerHTML = 'A javascript error has
occurred:' + " <b>" + msg + "</b>";}

                                };
                                dwr.engine.setErrorHandler(handler);
                                dwr.engine.setWarningHandler(handler);
                    </script>
<!-- end of new code -->

<script type="text/javascript">
```

```
if(jQuery){

$j(document).ready(function(){
    lmp=$j("#lmp").html();
    today=new Date()
    weeks=Math.floor((today.getTime()-Date.parse(lmp))/(1000*3600*24*7))
     $j("#weeks").html(String(weeks))

  for(var i=0;i&lt;10;i++){
  ht=$j("#o_row"+i).html()
  $j("#row"+i).html(ht)
 $j("#o_row"+i).html(" ")

   }

  if($j("#npl").find("span.value").html()==""){
    $j("#npl").find("span.value").html($j.trim($j("#pl").html()))
  }
 if($j("#na").find("span.value").html()==""){
    $j("#na").find("span.value").html($j.trim($j("#a").html()))
  }
  if($j("#npl").find("span.value").html()==null){
  if(getValue("npl.value")==""){
   setValue("npl.value",$j.trim($j("#pl").html()))
   } if(getValue("na.value")==""){
   setValue("na.value",$j.trim($j("#a").html()))
   }}
   $j(".trigger").each(function(i,obj){

    if($j(this).find(':radio').attr("id")==undefined){
    var disableField = "#enable_disable"+$j(this).attr('enable_disable');

    if($j(this).find('.value').html().toString()[9] =="Y"){
    $j(disableField).show();
    }
   }
   });

    $j(".trigger").find(":radio").change(function(){
      var disableField = "#enable_disable"+$j(this).parent().attr('enable_disable')+"_yes";
      var enableField = "#enable_disable"+$j(this).parent().attr('enable_disable')+"_no";

      var value=$j(this).val();
      if (value=="true"){
          $j(disableField).show();
          $j(enableField).hide();
      }else{
           $j(disableField).hide();
           $j(enableField).show();
      }
    });

  <!-- new code -->
  $j("a.dangerous-signs").each(function() {
    $j(this).colorbox({
```

```
      width:"300",
      height:"580",
      title: $j(this).attr('data-desc'),
      onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
    });
  });
  <!-- end of new code -->
 <!-- new code -->
  $j("a.colorbox").each(function() {
    $j(this).colorbox({
      width:"300",
      height:"580",
      title: $j(this).attr('data-desc'),
      onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
    });
  });
  $j("a.colorbox-wide").each(function() {
    $j(this).colorbox({
      width:"500",
      height:"520",
      title: $j(this).attr('data-desc'),
      onComplete: function(){ $j('.cboxPhoto').css('margin-top','0px')}
    });
  });
  <!-- end of new code -->
});
 }

/*
beforeSubmit.push(function() {
    var ret=true;
    $j(".trigger").each(function(i,obj){
     if( $j(this).find(':radio:checked').attr('checked') == true){
    $j(this).find('.error').html('').hide()
    }else{
    ret=false;
    $j(this).find('.error').html("Required field").show()
    }
    });

    return ret;
});
*/
</script>

        <macros>
                paperFormId = MoH 216
                headerColor = #00B551
                fontOnHeaderColor = white
        </macros>

        <style>
                .section {
                        border: 1px solid $headerColor;
                        padding: 2px;
```

```
                        text-align: left;
                        margin-bottom: 1em;
                }
                .sectionHeader {
                        background-color: $headerColor;
                        color: $fontOnHeaderColor;
                        display: block;
                        padding: 2px;
                        font-weight: bold;
                }
              .contrast{
    background-color: #B2E9CB;
visibility: hidden;
    }
                table.baseline-aligned td {
                        vertical-align: baseline;
                }
                /*new code*/
                .overview-dangerous-signs{
                }
                .overview-dangerous-signs img{
                  width: 90px;
                  height: 180px;
                }
                /*end of new code*/
        </style>

        <span style="float:right">Paper Form ID: $paperFormId</span>
        <h2>Return Visit Form</h2>

      <section headerLabel="Patient Profile">
          <table class="baseline-aligned">

                <tr>
<td><strong>|Patient's Name:</strong></td>
                        <td><lookup class="value" expression="patient.personName"/></td>

<td><strong>|Unique Patient Number:</strong></td>
                        <td><lookup expression="patient.getPatientIdentifier(5)"/></td>
<td><strong>|Age:</strong></td>
                        <td><lookup expression="patient.age" /></td>

<td><strong>|Date of Birth:</strong></td>
                        <td><lookup class="value" complexExpression="#if(
\$patient.birthdateEstimated ) ~#end"/> <lookup class="value"
expression="patient.birthdate"/>
                                (Age: <lookup class="value" expression="patient.age"/>)</td>
                </tr>
          </table>
<table class="baseline-aligned">
<tr>

                                        <td>Gravida:</td><td><lookup
expression="fn.latestObs('5624').valueNumeric"/></td>
                                        <td>Parity:</td><td><lookup
```

```
expression="fn.latestObs('1053').valueNumeric"/></td>

                                        <td>LMP:</td><td id="lmp"><lookup
expression="fn.latestObs('1427').valueDatetime" /></td>

                        <td>Regimen:</td><td><lookup
expression="fn.latestObs('1088').valueCoded.name"/></td>

                                        <td>BMI:</td><td><obs conceptId="1342" /></td>

</tr>
<tr>
<td>CD4:</td><td><lookup expression="fn.latestObs('5497').valueNumeric"/></td>

                        <td>Weeks gestation</td><td id="weeks"></td>

                                        <td>Viral Load:</td><td><lookup
expression="fn.latestObs('856').valueNumeric"/></td>

                                        <td>EDD:</td><td><lookup
expression="fn.latestObs('5596').valueDatetime"/></td>
                                                </tr>

</table>
      </section>

<section headerLabel="Problems and Allergies">
Problem List:<br />
<div style="display:None" id="pl"><lookup
expression="fn.latestObs('162667').valueText"/></div>
<obs conceptId="162667" style="textarea" rows="10" cols="80" id="npl"/>
<br />
<br />
Allergies:<br />
<div style="display:None" id="a"><lookup
expression="fn.latestObs('162668').valueText"/></div>
 <obs conceptId="162668" style="textarea" rows="10" cols="80" id="na" />

</section>

      <section headerLabel=" Encounter Details">
            <table class="baseline-aligned">
                  <tr>
                        <td>Date:</td>
                        <td><encounterDate default="today"/></td>

                        <td>Location:</td>
                        <td><encounterLocation default="1"/></td>

                        <td>Provider:</td>
                        <td><encounterProvider default="currentuser"/></td>
                  </tr>
<tr><button class="showFormEntryDialog" style="margin-left: 2em; margin-bottom:
0.5em">Enter Form</button>
```

<script type="text/javascript">
var r = confirm("Welcome to the Return Visit Form. The treatment guidelines presented in this record are intended as a guide and should not supersede clinical judgement.");
if (r == true) {
x = "You pressed OK!";
} else {
x = "You pressed Cancel!";
}
</script>
</tr>
</table>
</section>

<section headerLabel="...">
<table class="baseline-aligned">
<td>
<section headerLabel="HIV medication List/Preventive Services List">
<table class="baseline-aligned">
<td>
<button id="say_it1" type="button">HIV Medication</button>
<font face="Georgia" size="2">

NASCOP recommendations ART in pregnant and lactating women (2014)

Criteria for Treatment:
</br>
•All HIV-infected pregnant women irrespective of CD4 count, WHO stage or gestation age*

•All HIV-infected breastfeeding women irrespective of CD4 count, WHO stage*

*Note for pregnant and breastfeeding women
</br>
The use of ART in pregnant and breastfeeding women markedly reduces the transmission of HIV infection from mother to child.

The women should also be screened and treated for opportunistic infections including TB

</br>
All HIV-infected pregnant women should have baseline laboratory and other necessary diagnostic evaluations including Hb, rhesus blood group and ABO typing, VDRL, urine analysis and STI screening
</br>
ALT and creatinine levels for women eligible for HAART
</br>
OI prophylaxis and micronutrient supplementation: multivitamins and co-trimoxazole (CTX)- one double strength or two single strength tablets once daily for all PLHIV (sulphur-based intermittent presumptive malaria treatment should not be given to women who are on CTX prophylaxis)
First Line:
</br>
Regimen Options:
First line ART regimen to start in all women with previous exposure to NVP through PMTCT -

Less than 24 months since previous NVP Exposure:

Preferred:
TDF* + 3TC + ATV/r***

*** Hyperacidity and hence use of over the counter antacids are common occurrence in pregnancy. Caution should be exercised in pregnant women initiating ART regimens containing ART/r who concomitantly use antacids. LPV/r remains an alternative in such cases. Service providers should actively ask about OTC medications.

First Line:
Alternatives:
TDF + 3TC + LPV/r or

AZT + 3TC + ATV/r or

AZT + 3TC + LPV/r*

First Line:
</br>
More than 24 months since previous NVP exposure:

Preferred:
</br>
TDF* + 3TC + EFV

First Line:
</br>
Alternatives:
</br>
TDF+3TC+NVP or

AZT + 3TC + EFV or

AZT + 3TC + NVP

Second Line:
</br>
Not specified

Third Line:
</br>
ARVs for constituting a third line ART regimens are not readily available, however if an ART client is in need of third line, clinical summary form should be sent to the National Therapeutics TWG through 3rdline@nascop.or.ke (link sends e-mail) for guidance on further management. The patient should continue with current 2nd line ART with intensified adherence efforts including adherence counseling, Direct Observed Treatment Supervision(DOTS) and home visits.

WHO recommendations for initiation of ART in pregnancy

Option B+

Recommended by the WHO for generalized epidemics, where CD4 count testing and partner testing is limited and where breastfeeding duration is long and fertility is high.

TDF + 3TC (or FTC) + EFV for life

The updated NIH guidelines of 2014 recommend EFV only after 8 weeks of pregnancy secondary to teratogenicity concerns, unless a woman presents for care already on EFV and the regimen is effective and well tolerated(Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

Women who receive an NNRTI based ART regimen that is discontinued after delivery should receive a dual-NRTI regimen alone or with a PI for 7-30 days in order to reduce the likelihood of development of a NNRTI resistance (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

Option A
No longer recommended by the WHO due to complexity of management and equivalent efficacy of Option B (World Health Organization, 2013)

Panel on HIV infected pregnant women and prevention of perinatal transmission recommendations for ARV initiation in ARV-naïve pregnant women

*To access the full revisit form code as it appeared for the 2014 launch of the pilot, please visit https://github.com/neelarant/EMR_CDSS-for-HIV-Pregnancy *

Appendix I Passive Clinical Decision Support guidelines from the information tabs

NASCOP recommendations ART in pregnant and lactating women (2014)

Criteria for Treatment:
•All HIV-infected pregnant women irrespective of CD4 count, WHO stage or gestation age*
•All HIV-infected breastfeeding women irrespective of CD4 count, WHO stage*
*Note for pregnant and breastfeeding women

The use of ART in pregnant and breastfeeding women markedly reduces the transmission of HIV infection from mother to child. The women should also be screened and treated for opportunistic infections including TB

All HIV-infected pregnant women should have baseline laboratory and other necessary diagnostic evaluations including Hb, rhesus blood group and ABO typing, VDRL, urine analysis and STI screening

ALT and creatinine levels for women eligible for HAART

OI prophylaxis and micronutrient supplementation: multivitamins and co-trimoxazole (CTX)- one double strength or two single strength tablets once daily for all PLHIV (sulphur-based intermittent presumptive malaria treatment should not be given to women who are on CTX prophylaxis)

First Line:
Regimen Options:

First line ART regimen to start in all women with previous exposure to NVP through PMTCT -

Less than 24 months since previous NVP Exposure:
Preferred: TDF* + 3TC + ATV/r***

*** Hyperacidity and hence use of over the counter antacids are common occurrence in pregnancy. Caution should be exercised in pregnant women initiating ART regimens containing ART/r who concomitantly use antacids. LPV/r remains an alternative in such cases. Service providers should actively ask about OTC medications.

First Line:
Alternatives:
TDF + 3TC + LPV/r or
AZT + 3TC + ATV/r or
AZT + 3TC + LPV/r*

First Line:
More than 24 months since previous NVP exposure:
Preferred:

TDF* + 3TC + EFV

First Line:
Alternatives:
TDF+3TC+NVP or
AZT + 3TC + EFV or
AZT + 3TC + NVP

Second Line:
Not specified

Third Line:
ARVs for constituting a third line ART regimens are not readily available, however if an ART client is in need of third line, clinical summary form should be sent to the National Therapeutics TWG through 3rdline@nascop.or.ke (link sends e-mail) for guidance on further management. The patient should continue with current 2nd line ART with intensified adherence efforts including adherence counseling, Direct Observed Treatment Supervision(DOTS) and home visits.

WHO recommendations for initiation of ART in pregnancy
Option B+
Recommended by the WHO for generalized epidemics, where CD4 count testing and partner testing is limited and where breastfeeding duration is long and fertility is high.
TDF + 3TC (or FTC) + EFV for life

The updated NIH guidelines of 2014 recommend EFV only after 8 weeks of pregnancy secondary to teratogenicity concerns, unless a woman presents for care already on EFV and the regimen is effective and well tolerated (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

Women who receive an NNRTI based ART regimen that is discontinued after delivery should receive a dual-NRTI regimen alone or with a PI for 7-30 days in order to reduce the likelihood of development of a NNRTI resistance (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

Option A: No longer recommended by the WHO due to complexity of management and equivalent efficacy of Option B (World Health Organization, 2013). Panel on HIV infected pregnant women and prevention of perinatal transmission recommendations for ARV initiation in ARV-naïve pregnant women

Preferred Regimen	Comments
Preferred Two-NRTI Backbone	
ABC/3TC	ABC to be avoided in patients +for HLA-B*5701
TDF/FTC or 3TC	TDF has potential renal toxicity
ZDV/3TC	Potential for haematologic toxicity
PI Regimens	
ATV/r+ a Preferred Two-NRTI Backbone	
LPV/r + a Preferred Two-NRTI B	Once daily LPV/r is not recommended for pregnant women, twice daily dosing preferred
NNRTI Regimen	
EFV+ a Preferred Two-NRTI Backbone	Secondary to teratogenicity concerns, use only after 8 weeks of pregnancy
Alternative Regimens	
PI Regimens	
DRV/r + a Preferred Two-NRTI Backbone	Less experience in pregnancy than ATV/r and LPV/r
SQV/r + a Preferred Two-NRTI Backbone	Baseline ECG advised due to potential PR and QT elongation. Contraindicated with cardiac disease
NNRTI Regimen	
NVP + a Preferred Two-NRTI Backbone	Caution with administration in women with CD4 counts > 250 cells/mm^3. Caution with ABC co-administration.
Integrase Inhibitor Regimen	
RAL + a Preferred Two-NRTI Backbone	Limited use in pregnancy. Consider when PI administration a concern.
Insufficient Data to Recommend	
DTG; EVG/COBI/TDF/FTC fixed drug combination; FPV/r; MVC; RPV	
Not Recommended	
ABC/3TC/ZDV; d4T;ddI;IDV/r;NFV;RTV;ETR;T20;TPV	

(Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)

Pregnant women who are currently receiving ARV
• If the regimen is well tolerated and effective it should be continued.
• EFV should be continued in pregnant women presenting in the first trimester if the current regimen has achieved virologic control.
• Drug resistance testing should be carried out on those with detectable viremia on cART (>500-1000copies/ml).
Pregnant women who are not currently on ARV but have been in the past
• A detailed history of all previous ARV usage should be taken including efficacy, tolerance, adherence issues and results of prior resistance testing.
• Drug resistance testing should be done for all eligible (viral load > 500-1000 copies/ml). If the woman presents for care late in pregnancy, ART should be initiated prior to the receipt of results.

• If the woman previously received ARV for her own health or is not achieving virologic suppression on the current regimen, HIV specialist consultation is recommended.

Acute HIV infection in pregnancy

• If acute HIV infection is suspected during pregnancy, an HIV antibody test should be performed in conjunction with a plasma HIV RNA test.
• All women with acute or recent HIV infection should start an ARV regimen as soon as possible. Because of the high viral load in acute HIV infection, rates of perinatal transmission and transmission from breastfeeding are high.
• Genotypic resistance testing should be conducted in conjunction with initiation of ARV drugs. Regimens may be modified but treatment initiation should not be delayed.
• A ritonavir-boosted PI- based regimen is the preferred ARV therapy (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

For a comprehensive HIV drug interaction tool see:
http://www.hiv-druginteractions.org
For full treatment guidelines including dosage recommendations see:

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014
http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf
Ministry Of Health Kenya - Guidelines On Use Of Antiretroviral Drugs For Treating And Preventing HIV Infection Rapid Advice (2014) taken from
https://aidsfree.usaid.gov/resources/guidance-data/treatment/kenya#n5171
Republic of Kenya Ministry of Health. (2012). Guidelines for Prevention of Mother to Child Transmission (PMTCT) of HIV/AIDS in Kenya (Fourth Edition ed.). Nairobi: National AIDS and STI Control Programme.
World Health Organization. (2013). Clinical guidelines across the continuum of care: HIV diagnosis and ARV drugs for HIV preventionConsolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, recommendations for a public health approach. Retrieved from
http://www.who.int/hiv/pub/guidelines/arv2013/download/en/.

Anti-D prophylaxis recommendations

Women should be screened for presence or absence of the Rh (D) antigen with their first antenatal screening bloods. Confirmatory screenings (for D antigen and anti-D antibodies) should be conducted prior to the administration of blood products. A minimum of 2 screens is required prior to administration of blood products.

Potentially sensitising events for women who are Rh (D) negative:

- Birth
- Amniocentesis
- Cordocentesis
- Other in-utero surgery
- Antepartum haemorrhage
- Chorionic villus sampling
- Ectopic pregnancy
- External cephalic version
- Abdominal trauma/ fall
- Intrauterine death
- Termination of pregnancy

At all points anti- D immune globulin should be administered as soon as possible and within 72 hours of the potentially sensitising event.

Prior to 12 weeks of gestation (confirmed by ultrasound):
In uncomplicated spontaneous abortion anti-D administration is not necessary
In cases of therapeutic abortion 250 i.u of anti-D immunoglobulin should be administered intramuscularly to known D negative women who are not sensitised to D.
Recurrent bleeding that stops prior to confirmed 12 weeks of gestation does not require anti-D immunoglobulin

Between 12-20 weeks gestation:
250 i.u. intramuscularly should be administered to known D negative women who are not already sensitised to D. If these women experience recurrent bleeds they should receive 250 i.u. anti-D at a minimum of 6 weekly intervals.

After 20 weeks gestation:
The volume of foetal-maternal haemorrhage (FMH) must be determined by acid elution

(kleihaur). If the volume is > 4ml, this must be confirmed by flow cytometry. At least 500 i.u of anti-D should be administered intramuscularly and more should be given if the FMH is known to be >4ml to D negative and non-sensitised women.

If these women experience recurrent bleeds anti-D 500 i.u should be given at a minimum of 6 weekly intervals. FMH should be estimated every 2 weeks. If the 2 weekly FMH is positive, a minimum of 500 i.u should be given (more if FMH > 4 ml) regardless of the

Following birth:

Cord blood, or a neonatal heel stick sample should be analysed for ABO and D type of the neonate. Maternal samples for confirmatory ABO and D type and FMH should be collected after 30-45 minutes of the FMH to allow the foetal blood to disperse adequately in the maternal circulation. At least 500 i.u should be administered to the unsensitised D- negative mother of the D positive neonate known to have a maternal-foetal haemorrhage of <4ml. Additional 125 i.u. of anti-D immune globulin should be administered for each additional ml of FMH. In cases of FMH > 80 ml, intravenous anti-D administration should be considered.

Routine anti-D immunoglobulin administration of 500 i.u. intramuscularly should be administered at 28 and 34 weeks of pregnancy to D-negative and non- sensitised women. Alternatively 1500 i.u of anti-D may be given as a single dose at 28 weeks. Previous administration of anti-D should not affect routine antepartum or post partum prophylaxis (British Committee for Standards in Haematology, 2008).

Contraceptive considerations for women living with HIV

Method	Comments	Use in HIV+ people
Condoms	Male & female condoms available. Provide protection against STIs/HIV and pregnancy. Requires correct use each time and partner cooperation.	Can and should be used at all stages of HIV infection Can and should be used by patients on ART Correct and consistent use is recommended regardless of the use of other methods of contraception (dual contraception).
Hormonal methods- progesterone only and low dose combined pills, depot medroxyprogesterone acetate (DMPA) injections, etonorgestrel and levonorgestrel implants	Very effective and easy to use long and short term. Reversible. Serious complications rare. Use with caution or avoid with known CV disease, hepatic conditions, high blood pressure, smoking and thromboembolic disorders. Combined hormonal contraceptive methods should be avoided in the first 21 days for women without other VTE risk factors and for 42 days post partum for those with VTE risk factors secondary to unacceptably elevated VTE risk(Centers for Disease Control and Prevention, 2011).	Not on ART- use without restriction. On ART- when used as emergency contraception use without restriction DMPA can be used while on ART. Concurrent use of condoms encouraged. The following drugs interact with hormonal contraceptives. Alternative contraception should be considered: All RTV boosted PIs. FPV, NFV. NNRTIs NVP, EVF. Anti-TB drugs- Rifampicin and Rifabutin Others- Griseofulvin, Phenobarbitone, Carbemazepine, Phenytoin
Copper intrauterine contraceptive device	Highly effective (close to 100%), long-term, reversible. Can be used for 12 years. Screen and treat for bacterial STI prior to insertion. Not recommended with high risk sexual lifestyles.	Very reliable. Can be used in HIV+ women without stage 4 disease/AIDS defining illness. When on ART and WHO stage 4 symptoms controlled may be used. Concurrent condom use encouraged.
Sterilisation	Very effective for couples and individuals who do not want more children. Considered permanent. Safe, simple surgical procedure	No reason to deny unless acute HIV related infection or stage 4 disease. When resolved and after immune reconstitution may proceed.

		Concurrent condoms use encouraged.

(Centers for Disease Control and Prevention, 2011; Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014; Republic of Kenya Ministry of Health, 2012a)

Centers for Disease Control and Prevention. (2011). Update to CDC's U.S. medical eligibility criteria for contraceptive use, 2010: revised recommendations for the use of contraceptive methods during the postpartum period. *Morbidity and Mortality Weekly Report, 60*(26), 878-883.

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014 http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

Republic of Kenya Ministry of Health. (2012). Guidelines for Prevention of Mother to Child Transmission (PMTCT) of HIV/AIDS in Kenya (Fourth Edition ed.). Nairobi: National AIDS & STI Control Programme.

Cotrimoxazole use in the first trimester

Trimethoprim antagonises folate in bacteria but does not have the same level of effect in the human. Per Schaefer, Peters and Miller (2007) folate depletion in the normal woman from trimethoprim at therapeutic doses is unlikely. If needed in the first trimester, normal folate supplementation levels (0.5mg) may be considered for theoretical reasons (Schaefer, Peters, & Miller, 2007).

The U.S. National Institutes of Health (2013) cite elevated risk of neural tube, cardiovascular, urinary tract malformations and multiple anomalies after first trimester trimethoprim exposure. Various studies cited a decrease in risk with folic acid supplementation but also an increased likelihood of treatment failure. The NIH (2013) recommends that if folate supplementation be given with trimethoprim that it be confined to the teratogenic window and that foetal anatomical evaluation be done at 18-20 weeks (Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013).

In all cases, the likelihood of serious morbidity or mortality from opportunistic infection should be weighed against the first trimester risks of trimethoprim exposure.

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Schaefer, C., Peters, P., & Miller, R. K. (2007). *Drugs During Pregnancy and Lactation treatment options and risk assessment* (Second ed.). London: Academic Press.

Disseminated Mycobacterium Avium Complex Disease management in pregnant women

- Ubiquitous in the environment.
- Early symptoms can be minimal and can include fever, night sweats, weight loss, fatigue, diarrhoea and abdominal pain.
- Laboratory abnormalities include anaemia and elevated alkaline phosphatase levels.
- Hepatomegaly, splenomegaly and lymphadenopathy may be present on physical examination.
- Diagnosis is based on compatible clinical signs plus isolation of MAC from cultures. Species identification should be performed.
- Preferred primary prophylaxis when CD4 count is less than 50cells/mm^3 is:
  - Azithromycin 1200mg orally once weekly; or
  - Azithromycin 600mg orally twice weekly
    - Clairithromycin IS NOT RECOMMENDED in pregnancy.
    - ART initiation is recommended after 2 weeks of treatment if not on ARTs.
    - Primary prophylaxis may be discontinued when CD4 is greater than or equal to 100 cells/mm^3 for greater than 3 months.
    - Disseminated MAC disease treatment: Azithromycin 500-600mg + ethambutol 15mg/kg PO daily.
    - Chronic maintenance therapy is the same as the treatment regimen. It may be discontinued:
      - After at least 12 months of therapy, and
      - No signs or symptoms of MAC disease, and
      - Have sustained (> 6 months) CD4 count > 100 cells/mm^3 in response to ART (Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013).

For full treatment guidelines see:

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Urinary Tract Infections during pregnancy

The following are adapted from the South Australian Perinatal Practice Guidelines for urinary tract infections in pregnancy.

Midstream sterile urine culture is the gold standard for diagnosis

E. *coli* is the pathogen in >80% of cases.

Staphlococcus saprophyticus, group B streptococci and gram negative strains such as klebsiella, proteus and enterococcus are other likely strains.

Asymptomatic bacteriuria

ASB is bacteriuria >100,000cfu/ml without symptoms.

ASB has been associated with low birth weight and preterm birth.

30% will go on to develop acute cystitis and 50% to develop pyelonephritis if left untreated.

Bacteriuria >100,000/ml with 2 or more organisms likely represents contamination.

Treatment:

Start antibiotics based on sensitivity testing.

Trimethoprim can potentiate folate deficiency. Avoid in the first trimester if possible.

Nitrofurantoin should be avoided near term (>36 weeks) because of the possibility of newborn haemolytic anaemia due to glutathione instability.

E. *Coli*

Cephalexin- 500mg orally twice daily for 5 days

Or

Nitrofurantoin 100mg orally twice daily for 5 days

Or

Trimethoprim 300mg orally for 5 days

Gram negative bacteria

Norfloxacin 400mg orally twice daily for 5 days

Repeat MSSU 48 hours after treatment completed

Group B streptococcus

Penicillin V 500mg orally twice daily for 5 days
GBS bacteriuria requires GBS prophylaxis in labour (see below for protocol).

Acute Cystitis
+ MSSU with associated symptoms such as dysuria, suprapubic pressure, abdominal tenderness, pyuria and urinary frequency without fever

Treatment:
Cephalexin 500mg orally twice daily for 5-7 days
Or
Nitrufurantoin 50mg orally every 6 hours for 5-7 days
Or
Amoxycillin+clavulanate 500 + 125 mg oral, twice daily for 5-7days (only if < 20 weeks of gestation and no alternatives available)

Pyelonephritis
MSSU + clinical diagnosis of pyrexia, chills, rigor, flank pain; potentially nausea and vomiting and dysuria
Monitor foetal wellbeing and for signs and symptoms of preterm labour
Blood cultures, high and low vaginal swabs, full blood picture with renal function tests and urine test for protein
Admit for antimicrobial treatment
Manage pyrexia
Anticipate dehydration, monitor urine output and correct with IV fluids

Gentamicin 5 mg / kg (*maximum initial dose 480 mg) intravenously as a single daily dose for 3 days, or until sensitivities are available. Serum levels should be taken if ongoing gentamicin treatment is required
* The actual weight of the woman may be used to calculate gentamicin dosing, except in the obese woman weighing 100 kg or over. In this case, calculate dose according to a maximum weight of 100 kg
And
Ampicillin [or amoxycillin] 2 g intravenous initial dose then 1g intravenous every 4 hours for 3 days
Or
Cefazolin 1-2 g intravenously every 6 to 8 hours over 3 days
Or

Ceftriaxone 1 g intravenously once a day over 3 days OR

Cefotaxime 1 g intravenously every 8 hours over 3 days

After 3 days:

Cephalexin 500 mg oral 6 hourly for 10 days

Or

Trimethoprim 300 mg oral daily for 10 days (avoid in first trimester and in pregnant women with established folate deficiency, low dietary folate intake, or for women taking other folate antagonists)

Or

Amoxycillin+clavulanate 500 + 125 mg oral twice daily for 10 days (if < 20 weeks of gestation and no other treatment available)

Recurrent infections

Treat based on MSSU

Consider prophylaxis after two or more cases of cystitis or pyelonephritis

Prophylaxis:

Nitrofurantoin 50mg orally every night (caution near term secondary to risks of newborn haemolytic anaemia)

Or

Cephalexin 250mg orally at night

Or

Trimethoprim 150mg orally at night (avoid if possible in first trimester) (Department of Health Government of South Australia, 2013)

For full treatment guidelines please see:

Department of Health Government of South Australia. (2013). Urinary tract infections in pregnancy. *South Australian Perinatal Practice Guidelines* Retrieved 06/03/2014, 2014, from http://www.sahealth.sa.gov.au/wps/wcm/connect/4bf52c004eee77c8bfa3bf6a7ac0d6e4/2013_04_29_urinary+tract+infections+in+pregnancy.pdf?MOD=AJPERES&CACHEID=4bf52c004eee77c8bfa3bf6a7ac0d6e4

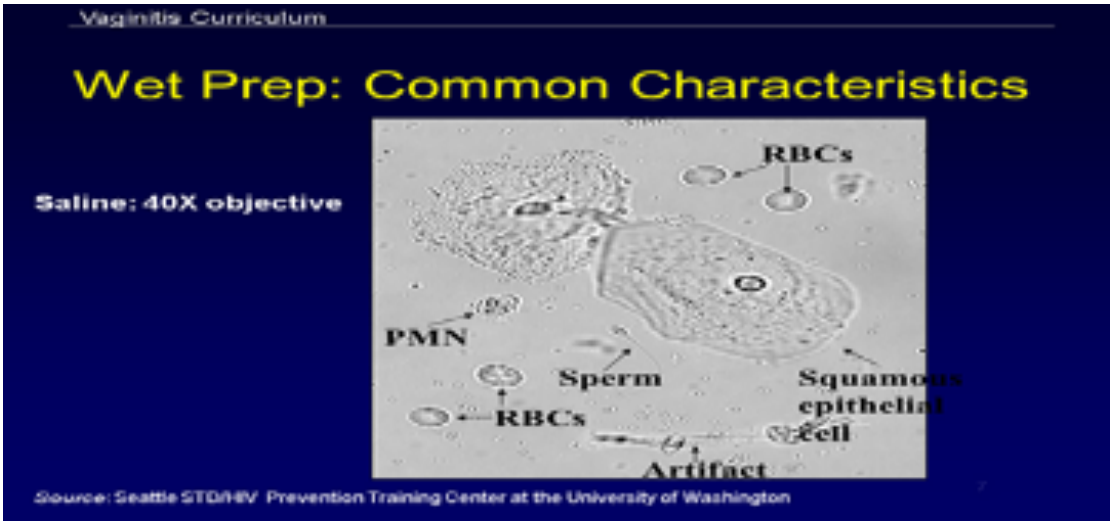
Management of diseases of the genital tract in HIV affected pregnancy

Please see Kenyan NASCOP "Algorithms for managing common STI syndromes" at the link below:

http://nascop.or.ke/library/STI/Revised%20ST1Chart%20.pdf

The following are adapted from US Centers for Disease Control and Prevention 2010 STD treatment guidelines

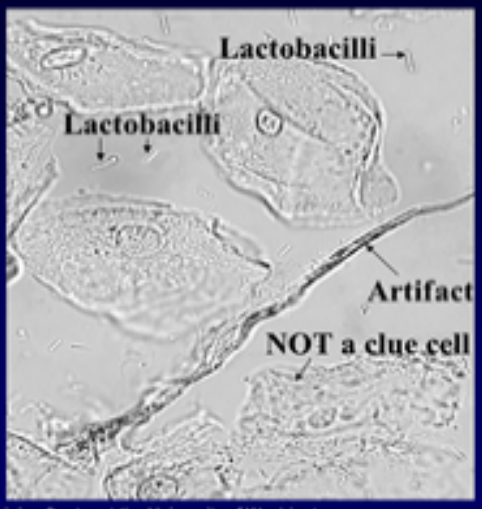
Discharge may be collected from the lateral vaginal wall and a wet mount made with a drop of 0.9% saline. The slide should be overlaid with a cover slip and examined under both 10x and 40x power. Adding a drop of 10% KOH will allow for the visualisation of yeast and pseudohyphae in candida infections and a positive amine/fishy odor in bacterial vaginosis.



Vaginitis Curriculum

Wet Prep: Lactobacilli and Epithelial Cells

Saline: 40X objective



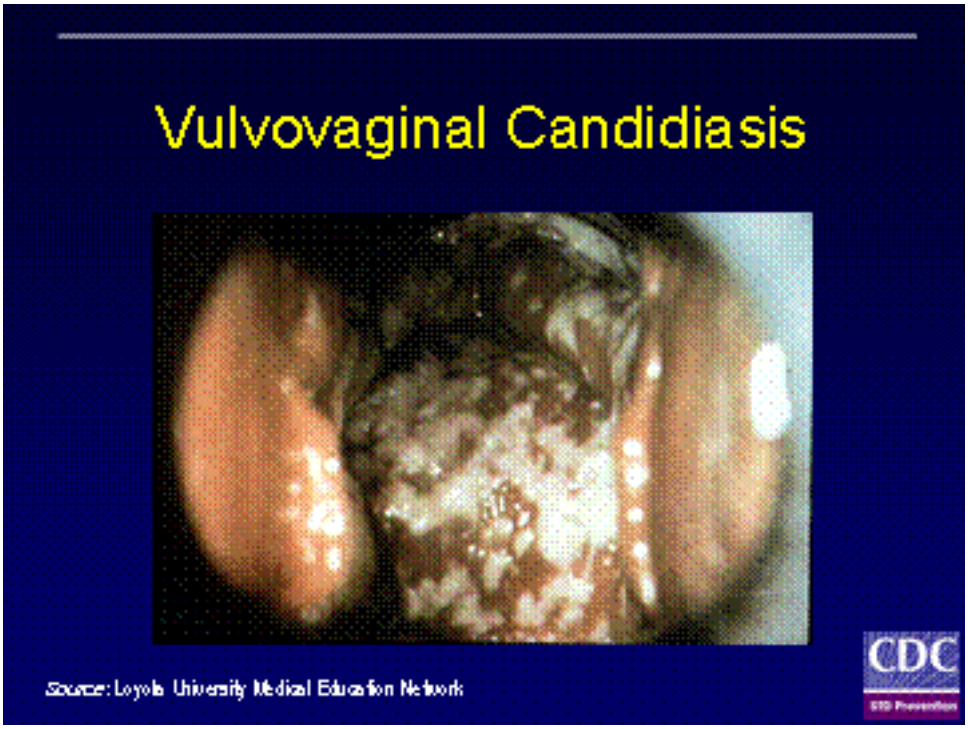
Source: Seattle STD/HIV Prevention Training Center at the University of Washington

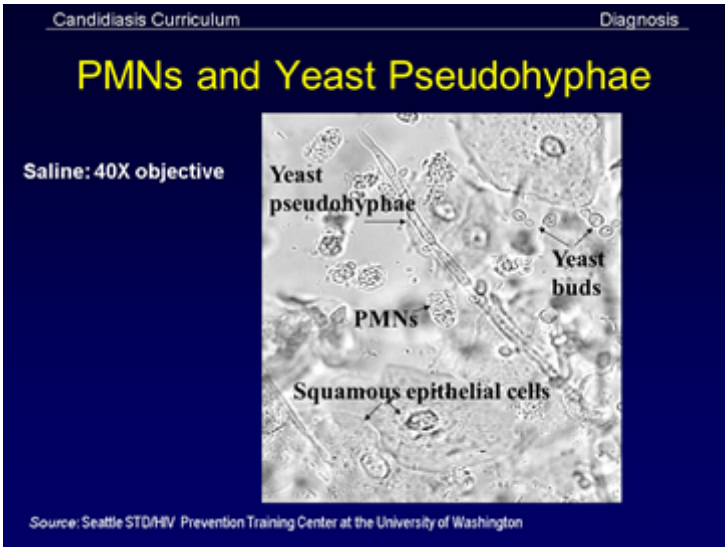
Vaginitis Curriculum

Vaginitis Differentiation

	Normal	Bacterial Vaginosis	Candidiasis	Trichomoniasis
Symptom presentation		Odor, discharge, itch	Itch, discomfort, dysuria, thick discharge	Itch, discharge, ~70% asymptomatic
Vaginal discharge	Clear to white	Homogenous, adherent, thin, milky white; malodorous "foul fishy"	Thick, clumpy, white "cottage cheese"	Frothy, gray or yellow-green; malodorous
Clinical findings			Inflammation and erythema	Cervical petechiae "strawberry cervix"
Vaginal pH	3.8 - 4.2	> 4.5	Usually ≤ 4.5	> 4.5
KOH "whiff" test	Negative	Positive	Negative	Often positive
NaCl wet mount	Lacto-bacilli	Clue cells (≥ 20%), no/few WBCs	Few to many WBCs	Motile flagellated protozoa, many WBCs
KOH wet mount			Pseudohyphae or spores if non-*albicans* species	

Candidiasis





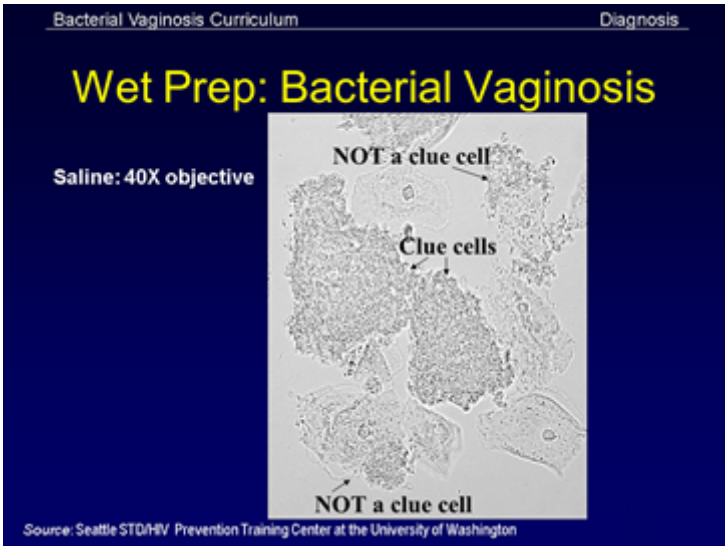
Vulvovaginal candidiasis is a common infection in pregnancy. Rates of candidiasis are also elevated in HIV+ women.

Diagnosis: Wet mount, clinical features, culture, DNA probe

Treatment:

Topical azole treatment for 7 days is the only acceptable treatment for vulvovaginal candidiasis in pregnancy. See the section on treatment of oropharyngeal and vulvovaginal candidiasis as an OI for more information.

Bacterial Vaginosis



Treatment of Bacterial Vaginosis is recommended for all symptomatic pregnant women. Although BV has been associated with premature rupture of membranes, preterm labour and birth, intra-amniotic infection and post partum endometritis the only documented benefit of therapy is a reduction in symptoms and signs of vaginal infection.

Diagnosis: Clinical features, wet mount, KOH prep, DNA probe

Treatment:

Metronidazole 500mg orally twice per day x 7 days

Or

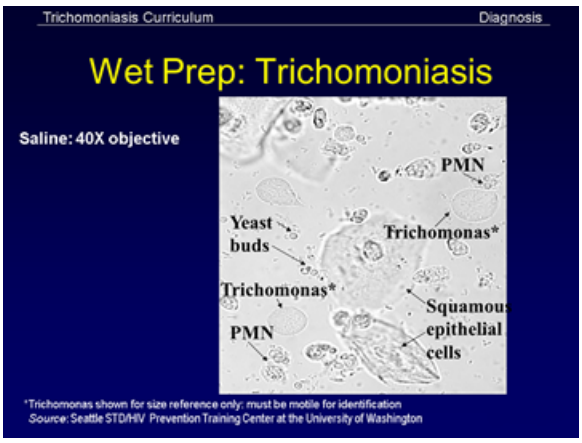
Metronidazole 250mg orally three times per day x 7 days

Or

Clindamycin 300mg orally twice per day x 7 days

HIV + women are more likely to experience a recurrence of BV symptom

Trichomoniasis



Trichomoniasis has been associated with premature rupture of membranes, preterm birth and low birthweight. Treatment of trichomoniasis with Metronidazole has not been associated with a reduction of these adverse events. Trichomoniasis in the HIV+ woman has been associated with increased vaginal viral shedding of HIV. For this reason treatment is recommended for HIV + women.

Diagnosis: Clinical features, wet mount DNA probe, cultures and nucleic acid amplification tests.
The regimen recommended for treatment in HIV + women is:
Metronidazole 2g orally in a single dose.
This regimen is acceptable in pregnancy.

Gonorrhea
All pregnant women should be screened for Gonorrhea when presenting for care. Women at high risk (new or more than one sex partner) should be rescreened in the third trimester. Presumptive treatment for Chlamydia is recommended in the United States when treating Gonorrhea

Diagnosis:
Urine/vaginal/endocervical specimens can be subjected to nucleic acid amplification, culture and nucleic acid hybridization tests.

Treatment:
250mg Ceftriaxone intramuscularly x 1
plus (for presumptive treatment of Chlamydia)
Azithromycin 1g orally x 1
Alternative:
Azithromycin 2g orally x 1
Treatment failure is unlikely though reinfection is common. Patients should be encouraged to be retested after 3 months. Partners should be referred for evaluation and treatment

Chlamydia
All pregnant women should be screened for Chlamydia when presenting for care. Women at high risk (new or more than one sex partner) should be rescreened in the third trimester.

Diagnosis:
Urine/vaginal/endocervical specimens can be subjected to nucleic acid amplification, culture,

direct immunofluorescente, EIA, and nucleic acid hybridization.

Treatment:

Azithromycin 1g orally x 1

Test of cure should be performed 3 weeks after completion of treatment. All pregnant women treated for chlamydia should be rescreened in 3 months. Sex partners should be referred for treatment (Centers for Disease Control and Prevention, 2010b)

For full guidelines and further information see:

Centers for Disease Control and Prevention. (2010). Prevention of sexually transmitted diseases treatment guidelines 2010. Retrieved 20/02/2014, from http://www.cdc.gov/std/treatment/2010

Group B Beta Haemolytic Strep (GBS)

Adapted from the Centers for Disease Control and Prevention 2010 Guidelines for the Prevention of Perinatal Group B Streptococcal Disease

Group B streptococcus is a leading cause of infectious early neonatal morbidity and mortality. Identification of GBS colonised women and the use of antibiotics as prophylaxis during labour has reduced the incidence of neonatal group B streptococcus disease. GBS screening by lower vaginal and rectal swabs is recommended from 5 weeks before delivery- negative predictive value decreases with cultures > 5 weeks before delivery

Women who are penicillin allergic with a history of anaphylaxis, angioedema, respiratory distress and/or urticaria after receiving penicillin or a cephalosporin should have antibiotic susceptibility testing performed on GBS isolates.

GBS prophylaxis is recommended if:
GBS screening is positive late in pregnancy
GBS bacteriuria is present at any time during pregnancy
Previous infant with invasive GBS disease
Unknown GBS status at onset of labour and, delivery at less than 37 weeks gestation, rupture of membranes 18 hours or greater, temperature at or above 38 degrees Celcius.
Prophylaxis:
Preferred therapy: Penicillin G, 5 million units IV initial dose, then 2.5-3.0 million units every 4 hours until delivery
Or
Ampicillin, 2g IV initial dose, then 1g IV every 8 hours until delivery
If the woman is penicillin allergic ***without*** a history of the following after receiving penicillin or a cephalosporin- anaphylaxis, angioedema, respiratory distress and/or urticaria then she may have:

Cefazolin 2g IV initial dose, then 1gIV every 8 hours until delivery
If the woman is penicillin allergic ***with*** history of anaphylaxis, angioedema, respiratory distress and/or urticaria if the isolate is susceptible to clindamycin and erythromycin she may be prophylaxed with:

Clindamycin, 900mg IV every 8 hours until delivery
If the isolate is not susceptible to clindamycin and erythromycin she may be prophylaxed

with:

Vancomycin, 1g IV every 12 hours until delivery (Centers for Disease Control and Prevention, 2010a)

For full guidelines and further information see:

Centers for Disease Control and Prevention. (2010a). Prevention of perinatal group B streptococcal disease, revision of CDC guidelins 2010. *Mortality and Morbidity Weekly Report, 59*(RR10), 1-32.

Centers for Disease Control and Prevention. (2010b). Prevention of sexually transmitted diseases treatment guidelines 2010 Retrieved 20/02/2014, from http://www.cdc.gov/std/treatment/2010

Gestational diabetes screening recommendations

Risk factors for gestational diabetes include

- Family history of type II diabetes
- History of macrosomia
- Obesity
- Maternal age >25 years

WHO guidelines, 2013

Hyperglycaemia first detected at any time during pregnancy should be classified as either:
Diabetes mellitus in pregnancy
Diagnosed at any time during pregnancy by one of the following criteria

- fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl)
- 2- hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) following a 75 g oral glucose load
- random plasma glucose ≥ 11.1 mmol/l (200mg/dl) in the presence of diabetes symptoms

Or
Gestational diabetes mellitus
Diagnosed at any time during pregnancy by one or more of the following criteria

- fasting plasma glucose 5.1-6.9 mmol/l (92-125 mg/dl)
- 1- hour plasma glucose ≥ 10.0 mmol/l (180 mg/dl) following a 75g oral glucose load
- 2- hour plasma glucose 8.5-11.0 mmol/l (153-199 mg/dl) following a 75 g oral glucose load (World Health Organization, 2013b)

World Health Organization. (2013). Diagnostic criteria and classification of Hyperglycaemia first detected in pregnancy. Retrieved 22/04/2014, from World Health Organization

Hepatitis B and Hepatitis C in HIV affected pregnancy

Hepatitis B

- Screen for HBsAg, anti-HBc and anti-HBs in pregnancy if unknown
- Vaccinate susceptible women.
- HBsAg can be detected ~ 4 weeks after exposure in acute infection.
- Chronic HBV infection- persistent HbsAg detected on two occasions, 6 months apart. These patients should be tested for HBeAg, anti-HBe and HBV DNA. The

presence of serum HBV DNA and persistent or fluctuating ALT elevation signifies active disease.

- Past infection that has resolved is identified by positive anti-HBc and anti-HBs but negative HBsAg.
- High HBV DNA levels are associated with perinatal transmission and passive-active immunoprophylaxis failure though perinatal transmission has been documented at undetectable HBV DNA levels as well (AIDSinfo, 2013a).
- Women with HBV infection should be screened for hepatitis A virus as they are at increased risk from complications from hepatitis co-infection. Non-immune women should be vaccinated (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).
- Asymptomatic-acute infection in pregnancy should receive supportive therapy (AIDSinfo, 2013a).
- Pregnant women with HIV/Hepatitis B co-infection should be given ART with anti Hepatitis B activity.
- Tenofivir with lamivudine or emitricitabine is the preferred dual NRTI backbone (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).
- Interferon alpha is an abortafacient and SHOULD NOT be given in pregnancy (AIDSinfo, 2013a).
- Newborns should receive Hepatitis B immune globulin and Hepatitis B vaccination with in 12 hours of birth with second and third Hepatitis B vaccine doses at 1 month and 6 months of age. Post vaccination testing for immunity should be done after completion of the vaccine series and between 9-18 months.
- Decisions regarding mode of delivery should be made based on obstetric indications and HIV status (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)

Hepatitis C

- Individuals seropositive for anti-HCV should have confirmatory HCV DNA testing.
- Hepatitis C treatments, Interferon and Ribavarin are CONTRAINDICATED in pregnancy (AIDSinfo, 2013a).
- ARV considerations for HCV infected women are the same as for pregnant HIV infected women without HCV co-infection (AIDSinfo, 2013a)
- HIV/HCV co-infection risks liver toxicity in women on ARVs. Monitoring should be performed 1 month after initiation of ARVs and every 3 months thereafter.

- HCV/HIV co-infection should be managed by a specialist.
- Hepatitis C infection should be evaluated at 3 months post partum to allow pregnancy related changes to resolve.
- Caesarean delivery DOES NOT reduce rates of perinatal transmission of Hepatitis C (AIDSinfo, 2013a).
- Infants born to women with HCV should be evaluated with anti- HCV antibody testing after 18months of age with confirmatory viral load testing. If testing is required prior to 18 months then two negative tests are required after two months with one being at or after 12 months as viremia is intermittent (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)

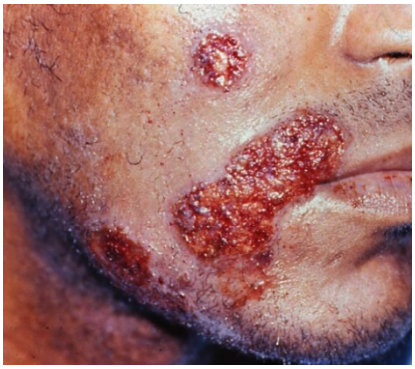
(Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)

For further information see:

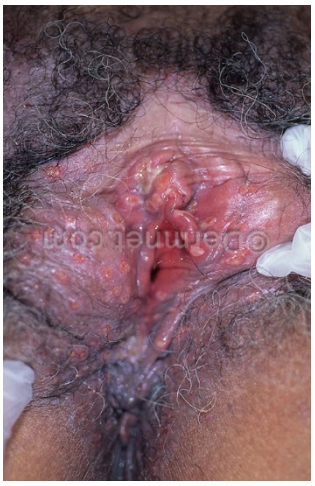
Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013) Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014 http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

Herpes simplex virus in HIV affected pregnancies



(Herpes simplex images, 2012)



(Herpes simplex image genital, 2014)

- Herpes simplex infections can be diagnosed clinically or with viral cultural, HSV DNA PCR and HSV antigen detection.
- The clinical course consists of a sensory prodrome followed by lesional evolution from papule to vesivle, ulcer and crust stages in orolabial herpes. Mucocutaneous manifestations are only visible as ulcers.
- Pregnant women are at increased risk of visceral HSV disease which can be fatal.
- Pregnant women may be offered episodic treatment with Acyclovir 400mg 3 times per day, or, Valacyclovir 1g PO 2 times per day. Treatment duration is 5-10 days for orolabial lesions and 5-14 days for genital lesions.
- HSV-2 transmission risk to the infant is low in recurrent infection. The highest risk of transmission exists in primary infections near delivery.
- Pregnant women with recurrent genital HSV lesions may be offered prophylaxis with Acyclovir 400mg PO 2 times per day, or, Valacyclovir 500mg PO 2 times per day from 36 weeks gestation until delivery.
- Caesarean section is indicated if genital HSV lesions or prodromal symptoms are present at the onset of labour (Panel on Opportunistic Infections in HIV-Infected

Adults and Adolescents, 2013)

For full treatment recommendations see:
Herpes simplex image genital. (2014).
Herpes simplex images. (2012). from
http://depts.washington.edu/hivaids/derm/case1/discussion.html

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13
http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

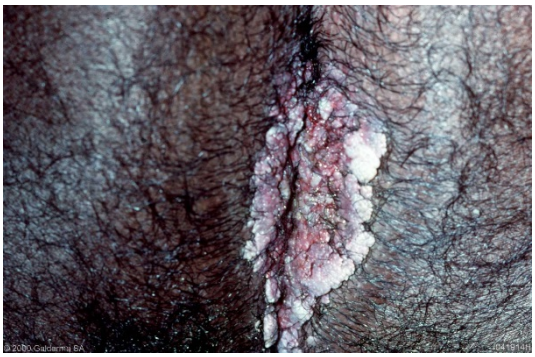
HIV-2 Infection during pregnancy

- Consider in women from countries or women whose partners are from countries where HIV-2 is endemic and who are ELISA HIV antibody positive but have consistently indeterminate western blot testing and HIV-1 viral loads at or below detectable limits.
- HIV-2 is endemic in many West African countries including Ivory Coast, Ghana, Cape Verde, Gambia, Mali, Senegal, Liberia, Guinea, Burkina Faso, Nigeria, Mauritania, Sierra Leone, Guinea Bissau, Niger, Sao Tome, and Togo; Angola; Mozambique; parts of India and France and Portugal.
- HIV -2 has a 5- fold lower rate of sexual transmission and a 20-30 fold lower rate of perinatal transmission. Without intervention perinatal transmission rates are between 0-4%.
- Two NRTIs and a boosted PI is recommended for pregnant women who require treatment for their own health with the preferred treatment being Lopinavir/ritonavir plus zidovudine/lamivudine or abacavir/lamivudine or tenofovir/emtricitabine.
- Optimal regimens have not been determined for pregnant women who do not require treatment for their own health though the following approached have been recommended: a boosted PI- based regimen (dual NRTI plus ritonavir boosted lopinavir) with the drugs stopped post partum or zidovudine prophylaxis alone during pregnancy and birth.
- NNRTIs and enfuvirtide have no activity against HIV-2 and should not be used for either treatment or prophylaxis.

- In cases of HIV-1 and HIV-2 co-infection a regimen should be chosen according to HIV-1 monoinfection guidelines but ensuring that the regimen also has activity against HIV-2.
- Infants born to HIV-2 + mothers should receive the 6 week zidovudine prophylactic regimen (see intrapartum management guidelines) (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

For full treatment guidelines see:
Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014
http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

HPV disease management in pregnancy affected by HIV



(Genital Wart Image, 2014)

- HIV + women require cervical cytology screening yearly at minimum
- Perform cervical cytology screening at first the first antenatal visit if there is no normal screen recorded within the previous 12 months
- If all previous cervical cytology screens are normal may repeat yearly, if not every 6 months
- Pregnant, HIV + women are at increased risk for genital warts which may be managed with bichloroacetic acid., trichloroacetic acid, cryotherapy, excision and laser therapy.
- Podophyllin and podofilox are contraindicated in pregnancy.
- Evidence is insufficient to recommend Imiquimod

- Genital warts have been associated with early-onset recurrent laryngeal papillomatosis; this risk is not reduced with caesarean section
- Cesarean section in cases of genital warts is recommended only when the risk of obstruction and excessive bleeding exists
- ASC-US should be managed in the same manner as non-pregnant women
- Can defer colposcopy for ASC-US until 6 weeks post partum
- CIN without invasive disease should be managed 6 weeks post partum
- Abnormal cytology and lesions suspicious for high grade or cancer should be evaluated colposcopically and biopsied.
- Endocervical curettage may not be performed in pregnancy
- Vaginal delivery is not recommended in cases of cervical cancer
- HPV vaccination is not recommended in pregnancy at this time(AIDSinfo, 2013a)

Provider applied therapy for genital warts:
Cryotherapy: apply until lesion is frozen and repeat every 1-2 weeks for 4 weeks until lesions are no longer visible.

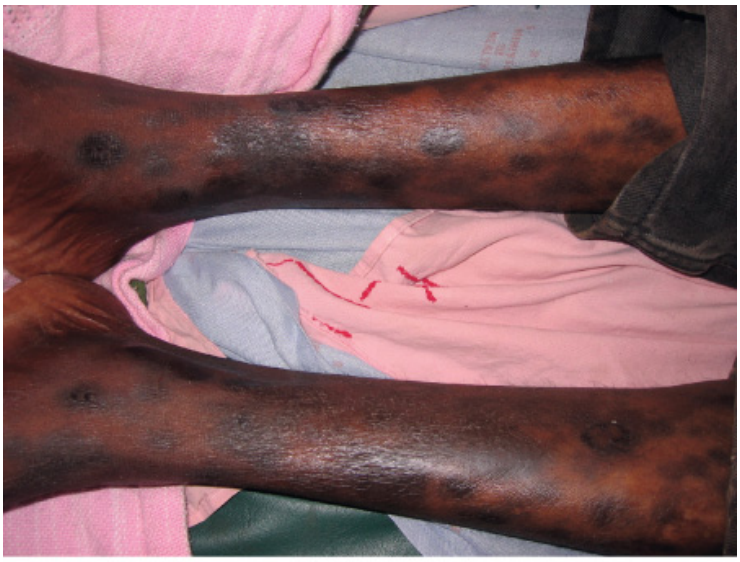
TCA or BCA cauterization: 80-90% aqueous solution. Apply to wart and allow to air dry until the development of a white frost. Repeat weekly for up to six weeks or until lesions are no longer visible.

For abnormal cervical cytology management algorithms see:
http://www.iedea-ea.org/joomla/index.php?option=com_attachments&task=download&id=262

http://www.asccp.org/Portals/9/docs/Algorithms%207.30.13.pdf
For full treatment guidelines see:

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Human herpesvirus-8 disease/Kaposi's sarcoma



Source: Knoop KJ, Stack LB, Storrow AB, Thurman RJ: *The Atlas of Emergency Medicine, 3rd Edition:* http://www.accessmedicine.com

(Kaposi's Sarcoma image)

- Clinical manifestations of KS are varied but generally consist of nontender, purplish, indurated skin lesions.
- HHV-8 seropositivity does not appear to affect pregnancy outcome.
- Initiation and optimization of ART is recommended for HHV-8 and KS management during pregnancy (AIDSinfo, 2013a).
- Antiviral therapy specifically for HHV-8 IS NOT RECOMMENDED.
- Vertical transmission and neonatal KS occurs infrequently.

AIDSinfo. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Kaposi's Sarcoma image. Retrieved 20/05/14, 2014, from http://accessmedicine.mhmedical.com/searchResults.aspx?q=kaposi+sarcoma&f_SemanticFilterTopics=kaposi+sarcoma&fl_SiteID=53&fl_TopLevelContentDisplayName=Images&adv=True

Immunization recommendations for HIV infected pregnant women

- In general, immunogenicity is improved in immunocompetent individuals with CD4 > 200cells/mm^3.
- If the vaccine is given at a CD4 count <200 cells/mm^3 consideration should be given to repeating the vaccination when the CD4 count has risen above 200 cells/mm^3.
- Live, attenuated viral and live bacterial vaccines should be avoided in the immunocompromised patient and are contraindicated in the pregnant patient.
- No evidence of risk exists to the pregnant woman or foetus with inactivated virus or inactivated bacterial vaccines or toxoids.
- In all cases likely benefit must outweigh risk.

Vaccine	Pregnancy recommendations	HIV recommendations
Hepatitis A	Acceptable if indicated and non-immune	Consider for all non-immune Check serologic response one month after completed series
Hepatitis B	Acceptable if indicated and non-immune	Check serologic response one month after completed series
HPV	Contraindicated	Not contraindicated though limited evidence in HIV+ population
Influenza (Inactivated)	Recommended during flu season	Recommended yearly
Influenza LAIV	Contraindicated	Contraindicated Contraindicated in close contacts
MMR	Contraindicated Vaccinate non immune women post partum as for HIV+	Contraindicated in persons with CD4<200cells/mm^3 Recommended in non-immune persons with CD4>200cells/mm^3
Meningococcal MCV4	Acceptable if indicated	Recommended if risk factor is present
Pneumococcal PCV 13	Insufficient evidence to recommend	Recommended for all
Pneumococcal PPSV22	Safety during the first trimester has not been established	Recommended for all
Tdap	Recommended	Recommended
Varicella/Zoster	Contraindicated	Contraindicated in individuals with CD4<200 cells/mm^3 Consider in VZV seronegative individuals with CD4count>200 cells/mm^3

(Centers for Disease Control and Prevention, 2013; U.S. Department of Health and Human

Services, 2011)

For full guidelines please see:

Centers for Disease Control and Prevention. (2013). Guidelines for vaccinating pregnant women Retrieved 17/03, 2014, from http://www.cdc.gov/vaccines/pubs/preg-guide.htm

U.S. Department of Health and Human Services. (2011). Guide for HIV/AIDS Clinical Care. Retrieved 17/03/2014, from U.S Health Resources and Services Administration, HIV/AIDS Bureau http://aidsetc.org/sites/default/files/resources_files/CM_Jan2011 %281%29.pdf

Intrapartum management algorithms for HIV+ pregnant women and recommendations for infant ARVs

Management as adapted from the Kenyan NASCOP PMTCT guidelines

Optimal Intrapartum Care

The following guidelines should be followed for all women admitted to labour and delivery units

- Minimise vaginal examinations.
- Use aseptic techniques in conducting delivery.
- Avoid routine artificial rupture of membranes (ARM).
- Avoid prolonged labour by use of a partograph.
- Avoid unnecessary trauma during delivery.
- Minimise the risk of postpartum haemorrhage.
- Use safe blood transfusion practices.
- Provide emotional support during labour.
- Induction of labour is associated with increased perinatal transmission of HIV.
- Implement the Community Health Strategy, to achieve maximal skilled birth attendance/hospital delivery.

No ARVs taken in pregnancy

Mother in early labour (up to 1 hour before delivery)

Mother:

Intrapartum period; Give mother SdNVP 200mg at onset of labour+ AZT 600mg OR AZT 300mg BD + 3TC 150mg BD in labour and delivery

Postpartum: Give mother AZT 300mg and 3TC 150mg BD for 7days. Assess for ART eligibility and initiate HAART as indicated

Infant:

Breastfeeding infant

Daily NVP from birth until one week after all exposure to breast milk has ended

Non-breastfeeding infant

NVP for 6 weeks

Mother received AZT 300mg BD in pregnancy

Intrapartum and post-partum period regimen are the same as above

Mother received HAART in Pregnancy

Regardless of the duration of HAART received, continue the regimen through labour and delivery and the postpartum period

Infant NVP recommendations are the same as above (Republic of Kenya Ministry of Health, 2012a)

Intrapartum management algorithms for HIV+ pregnant women- adapted from the US National Institutes of Health guidelines and the Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission

No ARVs taken in pregnancy

Give Zidovudine as continuous infusion during labour

2mg/kg zidovudine IV loading dose over 1 hour, followed by continuous infusion of 1mg/kg/hour until delivery

The benefits of caesarean delivery for the prevention of perinatal transmission after rupture of membranes and in labour are unclear. Management of these patients should be individualised.

Infant of HIV+ ARV naïve pregnant women

- Prophylaxis with a combination ARV drug regimen started as close as possible to time of birth.
- Zidovudine given for 6 weeks with three doses of NVP- at birth, 48 hours later and 96 hours after the second dose.
- Artificial infant feeding is recommended if affordable, feasible, acceptable, sustainable and safe.

Women on ARVs with viral load >1000copies/ml identified prior to labour and rupture of membranes

- If virologic response is appropriate, continue ARV regimen and recommend scheduled caesarean delivery at 38 weeks by best obstetrical dating to reduce likelihood of HIV transmission

- If caesarean delivery is elected follow routine caesarean delivery management (including prophylactic antibiotics), counsel risks related to surgery, anaesthesia and post partum infection.
- Continue ARV medications on schedule as much as possible
- Administer a 1 hour loading dose of zidovudine and continuous IV zidovudine for 2 hours prior to caesarean delivery (3 hours total)

Women on ARVs with viral load >1000copies/ml presenting in labour or after rupture of membranes

- Begin IV zidovudine administration as above immediately while continuing ARV regimen. If oral zidovudine is part of the ARV regimen, it may be held while IV zidovudine is being administered.
- Individualise management (vaginal vs. caesarean delivery) based on clinical factors.
- If caesarean delivery is chosen administration of the IV loading dose of zidovudine should be completed before surgery.
- Women should be informed of the risks associated with caesarean delivery and if indicated for prevention of perinatal transmission of HIV should be weighed against likely benefit to the infant.

Women on ARVs with sustained viral load ≤ 1000 copies/ml

- Continue ARVs as scheduled.
- IV zidovudine administration is at the discretion of the treating clinician but appears not to confer additional benefit.
- Caesarean delivery is not recommended for prevention of perinatal transmission in women on cART with viral load levels consistently ≤ 1000 copies/ml.

Women on ARVs with undetectable viral load

- Counsel that perinatal transmission rates are less than 1% with undetectable viral load.
- Continue ARV administration as scheduled.
- IV zidovudine administration is at the discretion of the treating clinician but appears not to confer additional benefit.
- There is no evidence of benefit of caesarean delivery in women receiving cART with an undetectable viral load, and the risks of caesarean delivery likely outweigh the benefits in this population.

In women who receive a CYP 3A4 enzyme inhibitor such as a PI, methergine should be avoided for the treatment of post partum haemorrhage unless no alternative treatments are available and usage outweighs risk. If used, the lowest effective dose for the shortest possible duration should be administered. The combination of these drugs may result in exaggerated vasoconstriction.

Women receiving a CYP 3A4 enzyme inducer such as nevaripine, efavirenz or etravirine, methergine activity will be reduced and alternative uterotonics/ higher doses of methergine may be required.

Infants of women on ARVs

- Start zidovudine as soon as possible after birth and continue for 6 weeks.
- A 4 week zidovudine regimen may be considered when the infant was ≥ 35 weeks of gestation at birth and the mother has received cART during pregnancy with consistent viral suppression and no concerns related to maternal adherence.
- Artificial infant feeding is recommended if affordable, feasible, acceptable, sustainable and safe.

Infant Zidovudine dosage recommendations

≥35 weeks' gestation at birth: 4 mg/kg/dose PO twice daily, started as soon after birth as possible and preferably within 6–12 hours of delivery (or, if unable to tolerate oral agents, 3 mg/kg/dose IV, beginning within 6–12 hours of delivery, then every 12 hours). Duration of therapy is from birth to 4-6 weeks.

≥30 to <35 weeks' gestation at birth: 2 mg/kg/dose PO (or 1.5 mg/kg/dose IV), started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours at age 15 days. Duration of therapy is from birth to 6 weeks

<30 weeks' gestation at birth: 2 mg/kg body weight/dose PO (or 1.5 mg/kg/dose IV) started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours after age 4 weeks. Duration of therapy is from birth to 6 weeks.

Nevaripine dosage recommendations for infant if mother received no ARVs in pregnancy

Weight Band Dosing

Birth weight 1.5-2 kg: 8 mg TOTAL for each dose orally

Birth weight >2 kg: 12 mg TOTAL for each dose orally

3 doses in the first week of life

• 1st dose within 48 hours of birth (birth–48 hours)

• 2nd dose 48 hours after 1st

• 3rd dose 96 hours after 2nd

Infants should be tested for HIV infection by HIV NAT at baseline, 4-6 weeks, 3 months and 6 months of age to determine HIV status.

If the infant is found to be HIV positive while receiving prophylaxis, the prophylaxis should be discontinued and cART should be initiated. Resistance testing should be performed and the cART regimen should be modified accordingly.

HIV antibody assays may be used in infants greater than 18 months of age.

(Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2012, 2014)

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission.. (2012). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Retrieved 21/1, 2013, from http://aidsinfo.nih.gov/contentfiles/lvguidelines/peri_recommendations.pdf

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014 http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

Republic of Kenya Ministry of Health. (2012). Guidelines for Prevention of Mother to Child Transmission (PMTCT) of HIV/AIDS in Kenya (Fourth Edition ed.). Nairobi: National AIDS & STI Control Programme.

Iron and folate supplementation recommendations

The WHO (2012) recommends daily folate (0.4mg) and iron (30-60mg elemental iron) supplementation for all pregnant women throughout pregnancy.
If anaemia is diagnosed in pregnancy supplementation with 120mg elemental iron with 0.4mg folate is recommended until the haemoglobin concentration normalises at which point the normal dosage is reverted to (World Health Organization, 2012a).
Folate dosage of 4mg/day is recommended for women with a history of neural tube defects through 10-12 weeks gestation (U.S. Preventitive Services Task Force, 2009).

NASCOP (2012) recommendations:
Haemoglobin 8-10: Look for treatable causes and manage. Give haematinics irrespective of gestation.
Haemoglobin 6-8: AZT contraindicated. Initiate ART irrespective of CD4 with TDF in place of AZT. Transfuse if >36 weeks gestation and if < 36 weeks gestation give haematinics.
Haemoglobin less than 6: AZT contraindicated. Initiate ART irrespective of CD4 with TDF in place of AZT. Transfuse irrespective of gestation.
(Republic of Kenya Ministry of Health, 2012a)

Republic of Kenya Ministry of Health. (2012). Guidelines for Prevention of Mother to Child Transmission (PMTCT) of HIV/AIDS in Kenya (Fourth Edition ed.). Nairobi: National AIDS & STI Control Programme.

U.S. Preventitive Services Task Force. (2009). Folic acid for the prevention of neural tube defects, 2014, from http://www.uspreventiveservicestaskforce.org/uspstf09/folicacid/folicacidrs.htm
World Health Organization. (2012). Guideline: Daily iron and folic acid supplementation in pregnant women. Retrieved 18/03/2014, from World Health Organization http://apps.who.int/iris/bitstream/10665/77770/1/9789241501996_eng.pdf?ua=1

Malaria prophylaxis and treatment in HIV affected pregnancy

•ITNs should be given to all pregnant women as early as possible and women should be counselled to sleep under them.

• In Malaria endemic areas in Africa, starting as early as possible in the second trimester, IPTp-SP is recommended for all pregnant women at each scheduled ANC visit until the time of delivery, provided that the doses are given at least one month apart and ensuring that at least three doses are given.

•SP should not be given during the first trimester of pregnancy; however, the last dose of IPTp-SP can be administered up to the time of delivery without safety concerns.

•IPTp-SP should be administered as DOT of three tablets sulfadoxine/pyrimethamine (each tablet containing 500mg/25mg SP) giving the total required dosage of 1500mg/70mg SP

•SP can be given with food or on an empty stomach

•SP should NOT be administered to women receiving co-trimoxazole prophylaxis due to a higher risk of adverse events

•WHO recommends the administration of folic acid at a dose of 0.4 mg daily; this dose may be safely used in conjunction with SP. Folic acid at a daily dose equal or above 5mg should not be given together with SP as this counteracts its efficacy.

• Malaria should be confirmed by peripheral blood smear or rapid diagnostic testing.

• Malaria affects both mother and foetus.

• P. falciparum infection is associated with an increased risk of anaemia, severe disease, preterm birth and low
birth weight.

• If the blood stage is unknown treat as uncomplicated P. falciparum infection.

• Treat pregnant women in the first trimester and with uncomplicated P. falciparum infection with 7 days of quinine and clindamycin.

•Treat pregnant HIV+ women with uncomplicated P. falciparum infection after the first trimester with artemether and lumefantrine or artesunate and mefloquine or dihydroartemisinin and piperaquine.

• Artisunate and SP combination treatment is acceptable in pregnancy after the first trimester but contraindicated in patients on CTX.

•Artisunate and amodiquine combination treatment is acceptable in pregnancy after the first trimester but contraindicated in persons taking EFV or ZDV(AZT) for HIV.

• Treatment for 7 days with quinine is recommended for chloroquine
resistant P. vivax infection in the first trimester and ACT or choloroquine thereafter. Blood

glucose should be monitored in pregnant women taking quinine as it may cause hypoglycaemia.

• Treat severe cases of malaria with intravenous or intramuscular artesunate at all trimesters for at least 24 hours and until able to tolerate oral medication. After 24 hours of parenteral therapy, complete treatment with 3 days of ACT if able to tolerate oral medication.

• If the above therapy is not available and awaiting transfer to higher level facility where it is, give a single intramuscular dose of artesunate and refer. If artesunate is unavailable, use intramuscular quinine.

• Atovaquone-proguanil, tetracyclines and primaquine are not recommended during pregnancy (Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013; World Health Organization, 2015b).

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

World Health Organization. (2015). *Guidelines for the treatment of malaria- 3rd edition* Retrieved from http://apps.who.int/iris/bitstream/10665/162441/1/9789241549127_eng.pdf?ua=1&ua=1

Monitoring response to ART and drug resistance testing

- Viral load monitoring is the preferred approach to diagnose treatment success or failure.
- Viral load should be tested early after ART initiation (within 6 months) and repeated every 12 months in the non-pregnant adult population (World Health Organization, 2013a).
- Viral load reduction is generally seen 12-24 weeks after ART initiation in pregnant women (AIDSinfo, 2013b).
- Treatment failure is defined as viral load persistently above 1000 copies/ml over a 6 month period (two consecutive measurements three months apart).
- If viral load monitoring is unavailable, CD4 count and clinical monitoring may be used to detect treatment failure with targeted viral load monitoring if available (World Health Organization, 2013a).
- Adequate response to therapy is an increase in CD4 count 50-150 cells/mm^3 per year with an accelerated response in the first three months (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2013a).
- Drug resistance testing is recommended for all HIV infected individuals at entry into care, including for pregnant women.
- Genotypic testing is preferred in ART- naïve patients.
- Drug resistance testing should be used to guide in the selection of drugs in cases of virologic failure and with suboptimal virologic response. With HIV RNA levels between 500-1000 copies/ml, resistance testing may be unsuccessful but should still be considered.
- Phenotypic testing should be done in conjunction with genotypic testing with known or complex resistance profiles, particularly to PIs.
- In addition to drug resistance testing at entry to care, pregnant women with detectible HIV RNA on ART should have drug resistance testing performed(Panel on Antiretroviral Guidelines for Adults and Adolescents, 2013b).
- Perinatal transmission of resistant strains of virus is unusual, though has been reported (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014)
- Women experiencing failure of virologic suppression during pregnancy (persistent viral load > 20-75 copies/ml) need to be evaluated for adherence, tolerability issues, dosage correctness and absorption issues (such as nausea and vomiting or lack of

food). They should be evaluated for resistant virus and managed in consultation with an HIV specialist. ARV regimen change should be considered (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

- An automated HIV-2 resistance analysis tool is available freely online at http://www.hiv-grade.de (Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission, 2014).

Panel on Antiretroviral Guidelines for Adults and Adolescents. (2013a). Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents, laboratory testing, plasma HIV RNA testing Retrieved 3/3, 2013, from http://aidsinfo.nih.gov/Guidelines/HTML/1/adult-and-adolescent-treatment-guidelines/5/

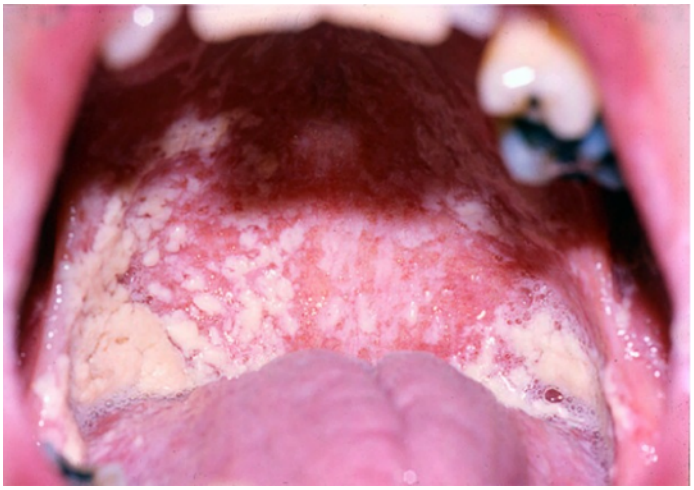
Panel on Antiretroviral Guidelines for Adults and Adolescents. (2013b). Guidelines for the Use of antiretroviral agents in HIV-1-infected adults and adolescents. Laboratory Testing. Drug-resistance testing. Retrieved 08/04/2013 http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/6/drug-resistance-testing

Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2013c). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States Retrieved 2/10, 2013, from http://aidsinfo.nih.gov/contentfiles/lvguidelines/peri_recommendations.pdf

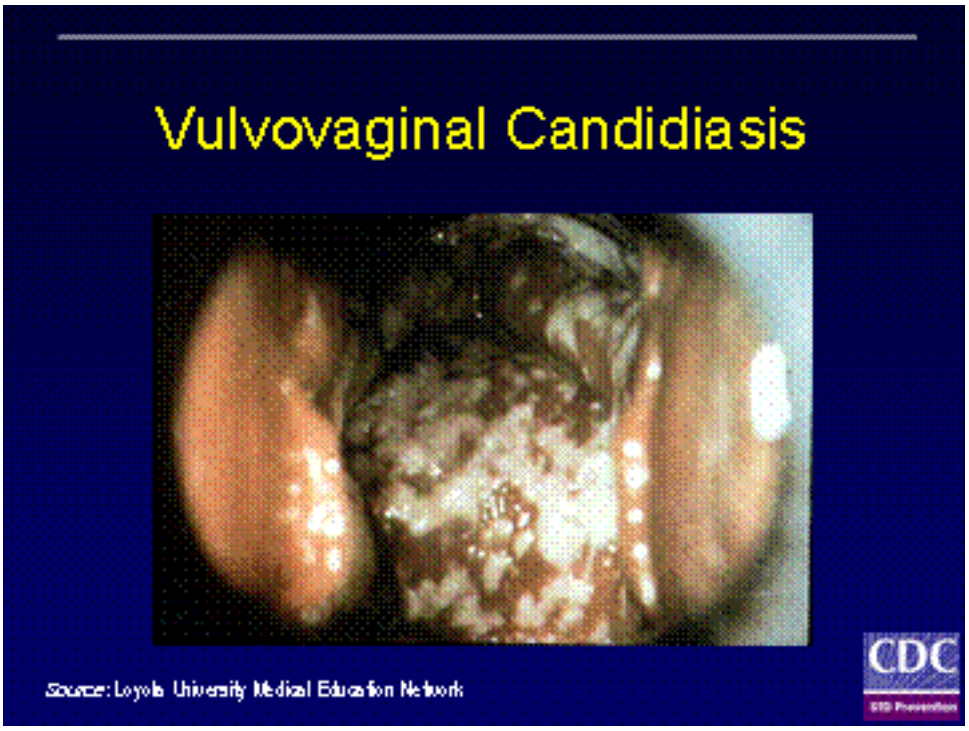
Panel on Treatment of HIV Infected Pregnant Women and Prevention of Perinatal Transmission. (2014). Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to preduce perinatal HIV transmission in the United States. Retrieved 08/04/2014 http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf

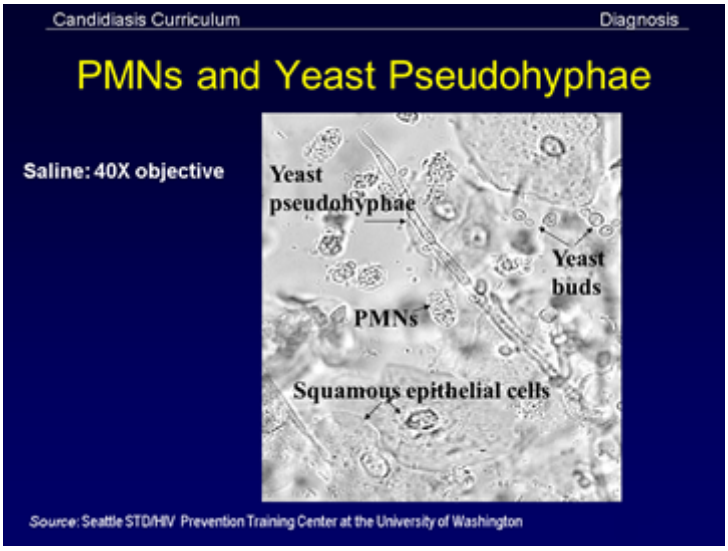
World Health Organization. (2013). Clinical guidelines across the continuum of care: HIV diagnosis and ARV drugs for HIV preventionConsolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, recommendations for a public health approach. Retrieved from http://www.who.int/hiv/pub/guidelines/arv2013/download/en/.

Mucocutaneous candidiasis in HIV affected pregnancy



("Oropharyngeal Candidiasis Image,")





Diagnosis: Wet mount, clinical features, culture, DNA probe

- Pregnant women are at increased risk of vaginal candidiasis.
- Topical therapy is the treatment of choice in oral and vaginal candidiasis in pregnancy.
- Topical azole therapy for 3-7 days is the treatment of choice in pregnancy for vaginal candidiasis..
- Single dose episodic therapy with fluconazole has not been associated with birth defects but chronic treatment with high dose fluconazole has been associated with fluconazole embryopathy.
- Systemically absorbed azoles SHOULD NOT be used during pregnancy.
- Though chronic suppressive therapy is generally not recommended unless patients experience severe or frequent recurrences, pregnant women on suppressive therapy for chronic candidiasis should be switched to Amphotericin B in the first trimester.
- Neonates born to women on amphotericin B therapy near delivery should be evaluated for renal dysfunction and hypokalemia.

Oropharyngeal candidiasis

Preferred topical therapy:

Clotrimazole troches 10mg orally 5 times per day; or

Miconazole mucoadhesive buccal tablet 50mg applied to mucosal surface over canine fossa once daily (do not swallow, chew or crush tablet)

Vulvovaginal candidiasis

Topical azole therapy (clotrimazole, butoconazole, miconazole, tioconazole or terconazole) for 3-7 days as vaginal suppository, ovule or cream.

(Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013)

For full treatment information see:

Oropharyngeal Candidiasis Image. Retrieved 22/05/14, from http://depts.washington.edu/hivaids/oral/case1/discussion.html

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Pelvic Inflammatory Disease in pregnant women

- Clinical diagnosis of PID is imprecise.
- Empiric treatment should be considered when sexually active women at risk for STIs experience pelvic pain and no other cause can be found *plus* clinical findings of cervical motion tenderness, uterine tenderness or adnexal tenderness.
- The presence of the following additional factors increase specificity of the diagnosis: oral temperature > 38.3, abnormal cervical or vaginal mucoprurulent discharge, abundant WBCs on saline microscopy of vaginal fluid, elevated ESR, elevated C-reactive protein and documentation of Gonorrhea and/or Chlamydia.
- Hospitalization and parenteral treatment is recommended for pregnant women suspicious for pelvic inflammatory disease
- No specific additional recommendations for HIV+ women
- Parenteral therapeutic regimen as recommended by the Centers for Disease Control and Prevention

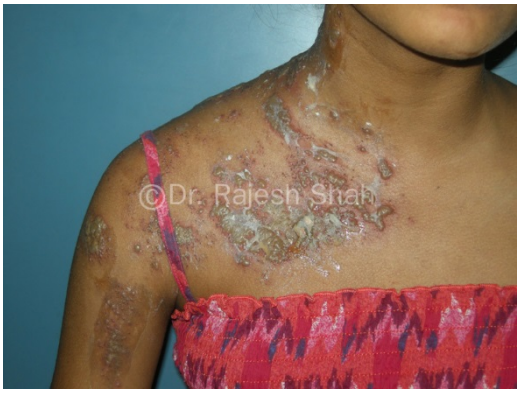
Recommended Parenteral Regimen B

Clindamycin 900 mg IV every 8 hours PLUS **Gentamicin** loading dose IV or IM (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3–5 mg/kg) can be substituted.

Although use of a single daily dose of gentamicin has not been evaluated for the treatment of PID, it is efficacious in analogous situations. Parenteral therapy can be discontinued 24 hours after clinical improvement; ongoing oral therapy should consist of clindamycin 450 mg orally four times a day to complete a total of 14 days of therapy. (Centers for Disease Control and Prevention, 2010b)

Varicella Virus Disease in HIV positive pregnant women

("Varicella Zoster, primary infection, image,")



("Herpes Zoster Image,")

- Primary varicella infection is characterised by a rash with a central distribution that starts on the head, then trunk, then the extremities. The lesions evolve from macule to papule to vesicle to pustule to crust. It is accompanied by pruritus, fever, headache, malaise and anorexia. Visceral involvement in HIV+ people is common.
- Herpes zoster is the result of latent varicella reactivation and involves a painful cutaneous eruption with a dermatomal distribution- most commonly the thoracic dermatomes followed by cranial, cervical, lumbar and sacral dermatomes. An erythematous maculopapular rash is followed by clear vesicles and pain then by pustulation and scabbing. The lesions typically persist for 2-3 weeks.
- Pregnant women should not receive the varicella vaccine or the herpes zoster vaccine.
- Congenital varicella risk in neonates of HIV- seronegative pregnant women is 0.4% during the first trimester, 2.2% from 12-20 weeks and negligible thereafter.
- If a close contact is diagnosed or suspected to have varicella or herpes zoster,

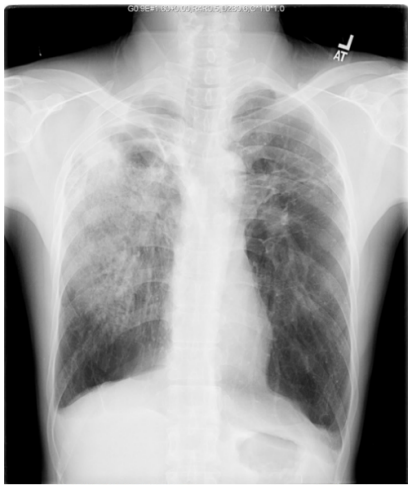
administration of Varicella Ig is recommended within 10 days for maternal benefit. It is unknown if there is foetal benefit. Vaccination should be deferred for 5 months after receiving varicella Ig.

- Infants born to women with varicella infection diagnosed 5 days prior to 2 days after birth should receive varicella Ig prophylaxis to reduce neonatal varicella morbidity risk.
- Post exposure prophylaxis VariZIG 125 IU/10kg- max 625IU as soon as possible and within 10 days of exposure.
- Alternative post exposure prophylaxis- Acyclovir 800mg PO 5 times per day x 5-7 days, or, Valacyclovir 1g PO 3 times per day x 5-7 days begun 7-10 days after exposure.
- Treatment of primary uncomplicated Varicella infection – Valacyclovir 1g PO 3 times per day x 5-7 days, or, Acyclovir 800mg 5 times per day x 5-7 day.s
- Treatment of severe or complicated primary varicella infection- Acyclovir 10 mg/kg q 8hours for 7-10 days. May switch to oral agent after defervescence if no visceral involvement is suspected
- Treatment of Herpes Zoster/Shingles- Valacyclovir 1g PO 3 times per day x 7-10 days or Acyclovir 800mg PO 5 times per day x 7-10 days(AIDSinfo, 2013a)

For full treatment guidelines see:

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Tuberculosis management in HIV + Pregnant Women



("Chest X-Ray, Tuberculosis, Image,")

Characteristic infiltrates with cavitation seen in the right upper lobe

- All pregnant women should be screened for TB if no negative screen is documented.
- Diagnosis of LTBI involves a positive IGRA or TST for persons with no clinical or radiographic evidence of disease. In advanced HIV, individuals should be retested after CD4 counts are ≥ 200 cells/mm^3 as false negative screenings are possible at lower CD4 counts. Individuals should be rescreened yearly.
- Diagnosis of active disease should be targeted to the involved organ system but should always involve chest radiograph (with abdominal shielding to minimise risk to the foetus). Sputum smear and culture should be performed in individuals suspicious for TB even in the absence of positive finding on chest radiograph. It is possible to have falsely negative sputum smears in individuals with advanced disease and non-cavitary involvement. Nucleic- acid amplification testing can be useful in this situation.
- Drug susceptibility testing should be conducted on all positive cultures.
- Obstetrical complications of TB include preterm birth, low birth weight and intrauterine growth restriction.
- The risk of maternal and neonatal mortality in HIV and TB co-infected pregnant women is high.
- Congenital TB, though uncommon, has been reported.
- Preventative treatment of latent tuberculosis during pregnancy should be considered and should include ART, isoniazid and pyridoxine.
- ART should be initiated in all HIV and TB co-infected persons as well as in all

pregnant women.

- ART should be initiated within 2 weeks of TB treatment for those with CD4 count< 50 cells/mm^3 and within 8-12 weeks for all others.
- Many significant interactions between ARVs and drugs used in the treatment of tuberculosis exist.

Treating Latent Tuberculosis Infection:

Indications: positive screening test, no evidence of active TB and no history of prior treatment for active or latent disease. Close contact with an infectious person regardless of screening test result.

Preferred therapy:

INH 300mg daily + pyridoxine 25mg orally daily

OR

INH 900mg orally twice weekly (by directly observed therapy) + pyridoxine 25 mg orally daily.

Alternative therapy:

Rifampin 600mg PO daily x 4 months

Treating Active TB Disease

Empiric therapy should be started in HIV + persons with radiographic and clinical signs of TB. Drug sensitivity testing should be performed.

DOT is recommended for all HIV related TB

- Isoniazid is non-teratogenic but associated hepatotoxicity may be greater during pregnancy and the post partum period- monthly monitoring of liver transaminases is recommended
- Rifampin is non-teratogenic in humans
- Pyrazinamide has limited use history in pregnancy but is non-teratogenic in animals. The WHO and International Union Against Tuberculosis and Lung Diseases recommend its use during pregnancy. If NOT used the treatment duration should be at least 9 months
- Ethambutol does not have evidence of teratogenicity in humans but does in rabbits and rodents at high doses. Ocular toxicity has been reported in adults but not in foetuses exposed in utero.

Recommended therapy for drug-sensitive TB:

Intensive phase (2 months)

Daily DOT (5-7 days per week)

INH + RIF + PZA + EMB (if TB is susceptible to INH and RIF then EMB may be discontinued).

Continuation Phase

INH+ RIF daily (5-7 days per week) or three times per week.

Duration of Therapy (based on number of doses received, not calendar time):

Pulmonary, drug susceptible TB- 6 months

Pulmonary TB and positive culture after 2 months of treatment- 9 months

Extrapulmonary TB with CNS involvement 9-12 months

Extrapulmonary TB with bone or joint involvement 6-9 months

Extrapulmonary TB in other sites- 6 months

Dosages and interactions:

Drug	Daily dosing	Three times per week dosing
Isoniazid	5 mg/kg; usual dose 300mg	15 mg/kg; usual dose 900mg
Rifampin (not recommended in conjunction with the PIs- ETR, RPV or EVG/COBI/TDF/FTC	10mg/kg; usual dose 600mg	10 mg/kg; usual dose 600mg
Pyrazinamide (weight based dosing) 40-55 kg 56-75 kg 76-90 kg >90 kg	 1000mg 18.2-25.0 mg/kg 1500mg 20.0 -26.8 mg/kg 2000mg 22.2 – 26.3 mg/kg 2000mg consider therapeutic monitoring	 1500mg 27.3- 37.5 mg/kg 2500mg 33.3- 44.6 mg/kg 3000mg 33.3- 39.5 mg/kg 3000mg consider therapeutic monitoring
Ethambutol (weight based dosing) 40-55 kg 56-75 kg 76-90 kg >90 kg	 800 mg 14.5-20.0 mg/kg 1200mg 16.0- 21.4 mg/kg 1600mg 17.8- 21.1 mg/kg 1600mg consider therapeutic monitoring	 1200 mg 21.8- 30.0 mg/kg 2000 mg 26.7- 35.7 mg/kg 2400 mg 26.7- 31.6 mg/kg 2400 mg consider therapeutic monitoring

Experience with second-line drugs in pregnancy is limited. Therapy for MDR-TB should not be withheld, and should be managed by a specialist. The following should be taken into consideration:

- Streptomycin use is associated with a 10% rate of eighth nerve toxicity in

infants with *in utero* exposure.

- 2% of children exposed to long term *in utero* exposure to kanamycin therapy like streptomycin have documented hearing loss.
- Theoretical risk for ototoxicity with *in utero* exposure to amikacin and capreomycin exist but has not been documented, therefore these may be useful alternatives when an aminoglycoside is needed.
- Quinolones have caused arthropathy in animal studies but studies of use in pregnant humans have failed to show increased rates of arthropathy or birth defects. Fluroquinolones may be used for MDR-TB if use is required based on susceptibility testing.
- Para-aminosalicyic acid is not teratogenic in rabbits or rats. One study indicates a possible increase in limb and ear abnormalities with first trimester exposure, other studies fail to associate risk of defects. Use with caution.
- Ethionamide use during pregnancy is limited. Studies in mice rats and rabbits have associated high dose exposure with anomalies, but not doses equivalent to those used in humans- avoid unless necessary.
- Cycloserine lacks data from animal studies and there are no reports of human use.
- Rifabutin is not recommended during pregnancy (Schaefer et al., 2007).

(Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2013)

For full treatment guidelines see:

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. (2013). Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Retrieved 17/6/13 http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Appendix J Filled provider questionnaires

Curtin University

Centre for International Health
School of Nursing and Midwifery
Faculty of Health Sciences

A mhealth tool to aid in the co-management of HIV and pregnancy

Healthcare Provider Questionnaire

1. Did you find that utilisation of the mhealth system enabled you to access up to date information regarding clinical management of HIV in pregnancy?

Yes, From the additional information in the system

2. Did you find that treatment and management was modified from your routine practice because of the system? If so, how?

Yes, I read additional treatment information on the system.

3. Did you find that your ability access to patient information, such as demographic, co-morbidity, laboratory result information was changed from the norm in your routine practice? If so, how and what influence did this have on your management decisions?

No

Did you have the opportunity to utilise the consultation or referral capacity of the mhealth system? How do you feel this compared to your routine channels for consultation and referral?

NO, I could not consult via the system since most nurses are busy on other clients far from the laptops

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School of Nursing and Midwifery
Faculty of Health Sciences

4. How did system utilisation impact upon your workflow?

Slowed the workflow to the system hanging due to a Safaricom network problem or power blackout problems.

5. Please comment on the ease of use of the mhealth system.

A bit challenging as it needs previous knowledge in computer

6. In what ways did the use of the mhealth system impact upon your interaction with the patient?

- It made me identify missing information that about the patient and hence I could ask the patient about the missing information.

7. Would you adopt this system and incorporate it into your practice going forward? Why?

Yes, it helps in making follow ups on defaulters by bringing up their names
- It also helps in identifying missing patients data and hence get quality data once they are rectified.

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School of Nursing and Midwifery
Faculty of Health Sciences

A mhealth tool to aid in the co-management of HIV and pregnancy

Healthcare Provider Questionnaire

1. Did you find that utilisation of the mhealth system enabled you to access up to date information regarding clinical management of HIV in pregnancy?

Yes, by reading the extra treatment information on the m-health system.

2. Did you find that treatment and management was modified from your routine practice because of the system? If so, how?

Yes, because of flags | warnings that alerted me for any missing information.

3. Did you find that your ability access to patient information, such as demographic, co-morbidity, laboratory result information was changed from the norm in your routine practice? If so, how and what influence did this have on your management decisions?

Yes, I could see warnings for missing data or tests then rectify that

Did you have the opportunity to utilise the consultation or referral capacity of the mhealth system? How do you feel this compared to your routine channels for consultation and referral?

NO, because of more clients to see and time constrains.

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Faculty of Health Sciences

4. How did system utilisation impact upon your workflow?

Due to double entry in the booklet and system it slowed down the work flow.

5. Please comment on the ease of use of the mhealth system.

Hard, in the begining but with time it gets easier.

6. In what ways did the use of the mhealth system impact upon your interaction with the patient? — the time per. patient was increased (additional like 5-10 minutes)
— I could ask the patient more information due to missing data highlighted.

7. Would you adopt this system and incorporate it into your practice going forward? Why?

Yes,
Because of the educational nature of the additional information it offers and also for having all the patient information in one place when they leave.

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School of Nursing and Midwifery
Faculty of Health Sciences

A mhealth tool to aid in the co-management of HIV and pregnancy

Healthcare Provider Questionnaire

1. Did you find that utilisation of the mhealth system enabled you to access up to date information regarding clinical management of HIV in pregnancy?

Yes, Since I would ~~not~~ get more treatment guidelines and information from the system.

2. Did you find that treatment and management was modified from your routine practice because of the system? If so, how?

Yes, I learnt new treatment guidelines from the additional treatment information that the system has.

3. Did you find that your ability access to patient information, such as demographic, co-morbidity, laboratory result information was changed from the norm in your routine practice? If so, how and what influence did this have on your management decisions?

No, most of the information in the system is already in the clients registers which is ~~easy~~ easily accessable like when the system is experiencing network challenges or Power failures.

Did you have the opportunity to utilise the consultation or referral capacity of the mhealth system? How do you feel this compared to your routine channels for consultation and referral?

NO

Most nurses are always up and down with other duties to enable them consult through the system.

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Faculty of Health Sciences

4. How did system utilisation impact upon your workflow?
- Not that much, rarely used the system, I mostly used the paper records.

5. Please comment on the ease of use of the mhealth system.
- Easy to use if there was a data clerk to enter the data.

6. In what ways did the use of the mhealth system impact upon your interaction with the patient? Not very much, I mostly used the paper records as opposed to the system.

7. Would you adopt this system and incorporate it into your practice going forward? Why?
Yes, For Preservation of Patient data even after they are done with clinic.

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Faculty of Health Sciences

A mhealth tool to aid in the co-management of HIV and pregnancy

Healthcare Provider Questionnaire

1. Did you find that utilisation of the mhealth system enabled you to access up to date information regarding clinical management of HIV in pregnancy?

Yes I accessed more information on treatment from the system

2. Did you find that treatment and management was modified from your routine practice because of the system? If so, how?

Not very much, I had knowledge of most of the information, treatment guidelines in the system.

3. Did you find that your ability access to patient information, such as demographic, co-morbidity, laboratory result information was changed from the norm in your routine practice? If so, how and what influence did this have on your management decisions?

Yes, it was much easier to get all the information in one place and saved alot of time in data retrieval

Did you have the opportunity to utilise the consultation or referral capacity of the mhealth system? How do you feel this compared to your routine channels for consultation and referral?

No, it was not easy to get someone to be on the system Laptop at the same time with you due to your nursing staff.

Curti

Centre for Inte
School of Nursi
Faculty of Heal

4. How did system utilisation impact upon your workflow?

It made the work a little bit slow
I was alone checking the client
entering data on the book and in

5. Please comment on the ease of use of the mhealth system.

Easy but needs alot of practice to
used to.

6. In what ways did the use of the mhealth system impact upon your interact with the patient?

It was challenging to do other
at the same time write in the c
booklet and putting the data in th

7. Would you adopt this system and incorporate it into your practice going forward? Why?

- Yes, it might help in capturing all
data and do follow up on the
- It makes data retrieval easy too
time.

Appendix K Flags

Flags

Name	Tags	Priority	Status		
ALT >25	Clinical;	Clinical	Enabled	Preview	Delete Flag
AST > 23	Clinical;	Clinical	Enabled	Preview	Delete Flag
Diastolic BP > 90	Clinical;	Clinical	Enabled	Preview	Delete Flag
Group B streptococcus screen positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
HIV Status	Clinical;	Clinical	Enabled	Preview	Delete Flag
HbsAg	Clinical;	Clinical	Enabled	Preview	Delete Flag
Hematocrit <28	Clinical;	Clinical	Enabled	Preview	Delete Flag
Hemoglobin < 9.5	Clinical;	Clinical	Enabled	Preview	Delete Flag
Hepatitis A positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Hepatitis C positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Malarial Smear positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing Appointment >1 week	Admin;	Admin	Enabled	Preview	Delete Flag
Missing Blood Group	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing CD4 Count	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing Clinic Visit	Admin;	Admin	Disabled	Preview	Delete Flag
Missing EDD	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing First Clinic Visit (Maternal)	Admin;	Admin	Enabled	Preview	Delete Flag
Missing Method of gestational age Determination	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing Parity	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing Program Enrolment Date	Admin;	Admin	Disabled	Preview	Delete Flag
Missing Program Enrolment Location	Admin;	Admin	Disabled	Preview	Delete Flag
Missing Regimen	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing Viral Load	Admin; Clinical;	Clinical	Enabled	Preview	Delete Flag
Missing gravida	Clinical;	Clinical	Enabled	Preview	Delete Flag
On NVP and CD4 > 250	Clinical;	Clinical	Enabled	Preview	Delete Flag
On ZDV/AZT and Haemoglobin<8	Clinical;	Clinical	Enabled	Preview	Delete Flag
RPR Positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Serum Glucose > 8.5mmol	Clinical;	Clinical	Enabled	Preview	Delete Flag
Systolic BP > 140	Clinical;	Clinical	Enabled	Preview	Delete Flag
TB Screening Positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Toxoplasmosis IgG positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
VDRL Positive	Clinical;	Clinical	Enabled	Preview	Delete Flag
Viral Load >1000	Clinical;	Clinical	Enabled	Preview	Delete Flag

Appendix L Timeline of progress and impediments to progress in system design, connectivity, implementation and launch from inception to study launch

Date	Occurrence and actions
6/12/2013	Notified by John Haskew that expected PEPFAR funding to UB project delayed. Decision made to suspend EMR study and all operations.
8/12/2013	Notification of Australian Postgraduate Award Scholarship and Neel Arant Bandy offered to utilise some funds to continue the project. John Haskew agreed to system continuation and transfer of funding responsibilities to Neel Arant Bandy.
17/1/2014	Discussion of costs with John Haskew, agreed to supply a deposit of KES 49,980 and monthly payments to Safaricom of KES 47,480 to cover Safaricom lines (one line per Chromebook and VPN for remote access). Restart scheduled for 1/2/2014. Agreed to hire Collins Otwane as Project Manager at 45,000 KES per month beginning 1/5/2014.
1/2/2014	Re-initiation of Safaricom SIM lines and VPNs scheduled for today. Not completed by Safaricom.
4/2/2014	Notified by Collins Otwane of a delay by Safaricom in reactivating the lines. Safaricom anticipated reactivation by the end of the following week.
20/2/2014	Safaricom will not reinstate the lines as there are too many to be registered to one person, Neel Arant Bandy. The proposal was made to have the lines billed to Vestergaard Africa, Ltd as was the agreement under Uamuzi Bora and for Neel Arant Bandy to supply funds to Vestergaard Africa, Ltd.
26/2/2014	Agreement reached between Neel Arant Bandy and Carrol Ngutu, Finance and Administrative Manager for Vestergaard Frandsen East Africa.
27/2/2014 -3/3/2014	Discussions between Safaricom and Vestergaard to confirm the reactivation of the 3 WIMAX lines and 15 sim lines for Chromebooks.
7/3/2014	Notified by Safaricom that reactivation suspended due to outstanding bill of 6,000 KES from previous Vestergaard accounts.
10/3/2014	Confirmation by Safaricom that the outstanding bill had actually already been paid and all accounts had been settled when the previous Uamuzi Bora lines were closed.
11/3/2014	The Safaricom lines have not been reactivated, despite being promised reactivation on this day.

Date	Occurrence and actions
13/3/2014	The lines remain inactive. Safaricom's credit department requires that new account application forms for all lines and fixed Internet at the Vestergaard office in Kakamega be generated. New account application forms submitted by Vestergaard.
15/3/2014	Correspondence from Collins Otwane to Gilbert Masero of Safaricom expressing disappointment that lines not yet activated.
16/3/2014	Reply from Gilbert Masero that 3 WIMAX lines have been reconnected. SIM lines pending VPN reactivation. Expect that this will be complete by 17/3/2014.
25/3/2014	Lines have not been reconnected. A new project manager has been assigned to the project by Safaricom.
28/3/2014	Safaricom technical team visited the Kakamega office to set up the router configurations. Due to their late hour of arrival, they were not able to access the Tuskys Megamall roof to align the WIMAX radio to the best available base. The technical team cannot return until the following week.
31/3/2014	Safaricom due to return to the Kakamega office. The meeting was rescheduled for 1/4/2014 due to Vestergaard meeting at the office and request for privacy.
6/4/2014	SIM lines reported as connected, not all are working.
7/4/2014	8 of 15 lines functional. There is no VPN access by either Gunnar Rø in the UK or Neel Arant Bandy in Australia.
16/4/2014	Billing confusion between Vestergaard and Safaricom as bills being generated for old, closed lines despite new applications being made for the new accounts. 3 VPNs are still not functional. Discussions between Collins Otwane and Rachael Achieng in regards to the same. Situation worked out and new bills generated.
22/4/2014	Rachael Achieng of Safaricom notified that the 3 VPNs are still not functional.
24/4/2014	Given network performance monitor username and password by Safaricom.
14/5/2014-8/6/2014	Business support at Safaricom unable to access server and router, requesting reboot to confirm configurations for IPSec. Gunnar Rø unable to access server remotely as the VPN IPsecs remain non-functional. Safaricom also not able to access remotely and report that physical connection on Kakamega end is to blame.
8/6/2014	Uamuzi Bora did not receive funding to reinstate their project. Data gathered is to be migrated to I-TECH and KenyaEMR who will be taking over EMR activities at the former Uamuzi Bora sites. I-TECH is aware of the PhD project for Ms. Arant Bandy and supportive of it.

Date	Occurrence and actions
11/6/2014	All lines and VPNs now functional and accessible. Rachael Achieng notified that 2 of 3 WIMAX bills not being sent to Vestergaard as agreed, but being sent to John Haskew.
3/7/2014- 14/7/2014	Safaricom claims that initial payment for institution of lines never received. Receipt of initial payment made on 22/1/2014 forwarded to Rachael Achieng of Safaricom. Safaricom then requests a trace be made on the transfer as they do not have a record of receipt of payment. The receipt is eventually found and the account remains open.
8/2014	Meetings with County Health Management team regarding the roll out of two EMR systems at the same time, Ms. Arant Bandy's system and the KenyaEMR/I-TECH system. The decision made with the county team to conduct the two rollouts simultaneously after much discussion as Ms. Arant Bandy's rollout focused solely on pregnant women living with HIV.
18/8/2014	I-TECH, citing the desire of Kakamega CGH to institute their own HMIS has declined to implement KenyaEMR at the hospital. Ms. Arant Bandy's project is unaffected and will continue as planned pending technical achitecture completion and EMR/CDSS completion.
2/9/2014	John K'atieno a recent Computer Science graduate of Masinde Muliro University of Science and Technology hired to program remainder of the EMR/CDSS. Neel Arant Bandy and Collins Otwane are both studying HTML in order to assist with this effort.
16/9/2014	The decision made my Ms. Arant Bandy to replace the Uamuzi Bora local concept dictionary with the Columbia International eHealth Laboratory/Millenium Villages Project concept dictionary. This dictionary is also utilised by KenyaEMR and will allow for concept coherence and data migration between the two systems. Local terms have been added to the CIEL/MVP Uamuzi Bora dictionary. Gunnar Rø facilitates this repacement and all concept IDs rewritten.
28/11/2014- 3/12/2014	VPN access again impossible. Gunnar Rø, Collins Otwane and Safaricom in constant communication and trying to rectify the issue. The EMR/CDSS is nearing completion with minor bugs being rectified. Ms. Arant Bandy in Kakamega and all meetings with County Ministry of Health and KCGH officials complete and all approvals granted. See 5.7.1.1 The initial visit, December 2014 for details.
4/12/2014	Gunnar Rø is now able to connect to the server through the VPN.
4/12/2014-	EMR/CDSS debugging continues. Gunnar Rø assisting with many elements. Connectivity through VPN continues.
8/12/2014- 9/12/2014	Both rounds of training staff at KCGH complete and the VPN and server are working correctly. Minor changes to be made to EMR/CDSS over the end of December by Gunnar Rø as required by KCGH staff.

Appendix M Timeline of period from training to launch

Date	Occurrence and action
11/1/2015-18/1/15	Flags are triggering incorrectly and future dates not enterable in system. Gunnar Rø has fixed the future date entry error. John K'atieno has been contacted to rectify the issue with the incorrect triggering of flags as he programmed them initially. The official launch has been delayed until the flags are triggering correctly.
18/1/2015-9/2/2015	Flags continue to trigger incorrectly, John K'atieno difficult to reach, he has agreed to fix them but has not. Neel Arant Bandy has completed an SQL course in an attempt to fix them herself but OpenMRS format slightly different. The SMS reminder feature is not functioning correctly.
11/2/2015	Gunnar Rø and Neel Arant Bandy have fixed the majority of the flags and disabled the non-functional flags. The SMS reminder system is not working. The decision is made to proceed to the launch without the reminder system.
16/2/2015	Launch delayed because of heavy downpours, which knocked down the towers housing the transmitters in Kakamega and have wiped out power and Internet connectivity in the Western Region of Kenya. Safaricom technicians are on site and attempting repairs.
18/2/2015	Electrical power has been restored but the broadband communications are still down.
22/2/2015	The broadband has been restored in the Western Region, however the VPN is not functioning because the router configuration has reset to default setting and needs to be reconfigured.
1/3/2015	The flags are working but the SMS reminder system is not. Gunnar Rø feels this will be difficult to restart. The decision was made to go ahead with the launch and remove the SMS reminder function. The in-charge at the MCH anticipates acceptability of the launch for the following week.
4/3/2015	The launch scheduled for this day but delayed as the Medical Superintendent is not on site. The Medical Superintendent and the MCH staff agree that the launch will go ahead 6/3/2015
6/3/2015	The launch has commenced and been reported as welcomed and successful. It has been decided that medical students will be utilised to help enter data into the system, especially retrospective data. Anticipated challenges include the following week being short staffed because of nurses and midwives being in meetings on strengthening MCH practices. The medical students on internship will be seeing patients and utilising the system at the point of care. Collins Otwane will be on site to do all trainings of students and staff as required.

Date	Occurrence and action
8/3/2015	The launch report has been received by Neel Arant Bandy. Collins Otwane has been reminded that, unless there is a power failure or the system is down and paper copies of the record have been filled in, there is to be no retrospective data entry as the system is designed to be used at the point of care and patients enrolled at their first visit.

Appendix N A timeline of relevant events during the study period and actions taken

Date	Occurrence and actions
23/3/2015	Collins reports that 4 new patients were seen the previous week but not entered into the system as there were heavy rains in Kakamega and the base station was compromised. Safaricom is working on the issue and the records have been marked and will be entered retrospectively.
29/3/2015	Safaricom has moved the base station to a new tower to avoid future weather related outages. There were no new clients seen in the clinic since the last report.
7/4/2015	The MCH in-charge has reported to Collins that 2 new patients have been registered into the system.
20/4/2015	Collins Otwane reports being on site at the hospital with the MCH nurses and midwives. He does not report any problems with the system.
27/4/2015	Collins Otwane has reported that he has been printing out weekly summaries of flags of errant values and missing data and giving them to the midwives but there isn't much information as few women have been entered into the system thus far. A plan was made to print reports weekly so that midwives may follow up on them. Another plan was to enrol women at their first and second visits in order to increase enrolment. Neel Arant Bandy is waiting for a new user name and password to access the SSH IPsecVPN to review enrolment. We have reviewed that women enrolled will have a sticker on their paper file and in the MCH register to denote that they are part of the study.
6/5/2015	Collins Otwane reports that the midwives and nurses are slowly getting accustomed to the system and are able to take their time with it as there continue to be very few new women to enrol into the study. There has been an issue with billing between Vestergaard and Safaricom that has lead to the expiration of the certificates of some of the lines. Vestergaard and Safaricom are rectifying the billing issue. Enough Chromebooks remain active to continue EMR/CDSS utilisation.
11/5/2015	The Safaricom billing issues continue as new tariffs have been added for lateness of payment. There have been no new enrolments into the system.
24/5/2016-2/6/2015	Correspondence with Collins Otwane advises a progress report will be submitted on 25/5/2016. There was no correspondence with Collins between 24/5/2015- 2/6/2015. Collins was travelling to his family home because of an urgent family matter. Upon his return 2/6/2015 he reports that all of the lines are again functional.
2/6/2015-15/6/2015	Communication between Neel Arant Bandy and Collins Otwane difficult as emails are being redirected to spam folders on both ends using Gmail. Settings have been reviewed and both are checking spam folders routinely.

Date	Occurrence and actions
16/6/2015-19/6/2015	Collins has reported that there is a "go-slow" in effect in Kakamega County currently as the government has not paid health sector workers for some time. There have been few enrolments. The in-charge at the MCH has yet to report on the number of enrolees and Collins is awaiting her official report. Neel Arant Bandy is not able to access the server via SSH IPsec VPN access.
28/6/15	The SSH IPsec VPN access is not working. Safaricom has committed to rectifying the issue. The MCH in-charge has reported to Collins that 89 women have been enrolled into the study so far. Collins reports that he has been printing reports of patient flags weekly.
8/7/2015	Collins Otwane reports that the "go-slow" has ended and that the MCH clinic has returned to normal operations. The SSH IPsecVPN remote access has yet to be restored. Discussions with Safaricom reveal that they have changed their billing system. Previously, unused data rolled over to the next month and bills were issued when data needed to be purchased again. Under the new system, at the end of 30 days, service is cut off for all of the lines and VPNs are cancelled until the new bill is paid. Collins is in communication with Vestergaard and Safaricom to rectify the situation.
22/7/2015	Collins Otwane has been communicating with Vestergaard about the payment for the Safaricom lines. Bills have gone missing and only 9 of the lines have receipts. Safaricom will reinstate the SSH IPsec VPNs access once the billing and receipts have been rectified. It has been decided that the study will continue with only 9 lines instead of 15 to cut costs and simplify billing. Only 2-3 Chromebooks are needed in the MCH at a time to satisfy the number of patients enrolled or being enrolled. The remaining four are in the CCC, Labour and Birth Suite, with the Medical Superintendent and with the Medical Records Department.
3/8/2015	The tracing of the bills and receipts between Safaricom and Vestergaard continues. The SSH IPsec VPN access has been restored but all configurations have been lost. Gunnar Rø will have a Skype call with the technical team at Safaricom to restore the required configurations. Safaricom is currently testing all of their 4G systems, which has been negatively affecting connectivity of the Chromebooks to the server.
3/8/15-16/8/15	There have been numerous attempts to communicate with Collins Otwane. He reports that he has been ill with acute Malaria.
23/8/2015	Collins Otwane reports that he will be visiting the hospital 24/8/16 and will reply with a report of numbers and system functionality.
1/9/2015	The report was not received. Correspondence from Collins Otwane states that he went to his family home for the weekend and was stranded there for over a week because of extensive flooding and a washed out bridge and power outages. Power has been restored and he will be travelling back to Kakamega soon pending the repair of the bridge.

Date	Occurrence and actions
6/9/2015	Collins Otwane is back in Kakamega. The MCH staff report to him that the system has been non-functional. The SSH IPsec VPN access is still non-functional. Neel Arant Bandy has notified Collins that she is planning a second visit to Kakamega to wrap up the study and collect the qualitative data.
13/9/2015	Collins reports that there were again billing issues between Vestergaard and Safaricom and the lines were all cut. Vestergaard is tracing the bills and will pay them. The MCH in-charge reports that, to date, 133 patients have been enrolled into the system and that a few have come for 2nd and 3rd visits but most have been seen only once. The SSH IPsec VPN is still not functional.
28/9/2015	Collins Otwane reports that there have been extensive power outages to the Kakamega area as power poles are being replaced and this has affected system utilisation and connectivity.
12/10/2015	Collins Otwane reports that the power outages have caused extensive challenges to the system utilisation. He reports that paper forms are filled out sporadically for retrospective entry but that for the most part, these have been neglected.
14/10/2015	Gunnar Rø has noted that though the study data and EMR/CDSS is likely functional on the server, he has not been able to remotely back up the data from the UK. If the VPN remains non-functional the data can be downloaded directly from the server and Gunnar can receive it in an encrypted file over email and extract the needed study data.
26/10/2016	Neel Arant Bandy on site in Kakamega.

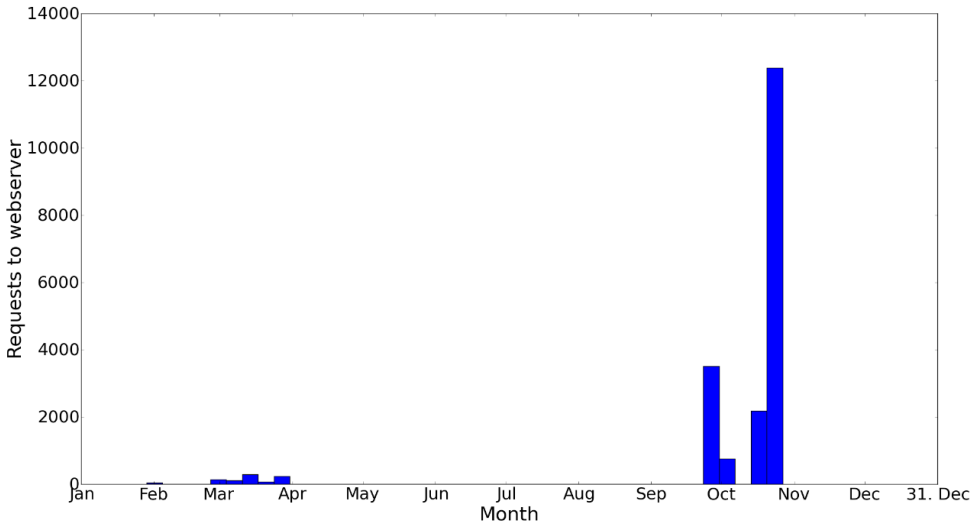
Appendix O CSV file data from system

age	Art regimen	ART Start date	CD4 count	On CTX?	EDD	Entry point	hiv_ date diagnose d	iWHO clinical stage Initially	LMP	ID	Date Record created	Viral load	WHO stage current
0	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	2	12/8/14 17:57	Missing	Missing
31	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	12	12/9/14 7:55	Missing	Missing
38	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	13	12/9/14 8:09	Missing	Missing
44	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	14	12/9/14 8:09	Missing	Missing
17	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	15	12/9/14 8:09	Missing	Missing
17	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	16	12/9/14 8:10	Missing	Missing
38	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	17	12/9/14 8:10	Missing	Missing
38	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	18	12/9/14 8:13	Missing	Missing
31	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	28	9/26/15 13:59	Missing	Missing
26	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	29	9/26/15 15:53	Missing	Missing
33	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	30	9/26/15 16:24	Missing	Missing
33	NEVIRAPI NE	4/16/15 0:00	27	YES	8/18/15 0:00	Adult inpatient service	9/23/14 0:00	WHO STAGE 3 ADULT	Missing	31	9/27/15 12:27	Missing	Missing
33	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	32	9/27/15 12:32	Missing	Missing
31	TDF/3TC/ EFV	3/3/15 0:00	350	YES	9/12/15 0:00	Prevention of maternal to child transmission program	3/2/15 0:00	WHO STAGE 1 ADULT	Missing	33	9/27/15 12:37	Missing	WHO STAGE 1 ADULT
31	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	34	9/27/15 12:43	Missing	Missing
41	NEVIRAPI NE	6/16/15 0:00	413	YES	9/27/15 0:00	Prevention of maternal to child transmission program	5/11/11 0:00	WHO STAGE 3 ADULT	Missing	35	9/27/15 12:48	Missing	WHO STAGE 3 ADULT
29	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	36	9/27/15 12:56	Missing	Missing
44	AZT/3TC/ EFV	4/2/15 0:00	146	YES	9/15/15 0:00	Prevention of maternal to child transmission program	4/2/15 0:00	WHO STAGE 1 ADULT	Missing	37	9/27/15 13:02	Missing	Missing
29	TDF/3TC/ EFV	3/26/15 0:00	400	YES	8/4/15 0:00	Prevention of maternal to child transmission program	3/23/15 0:00	WHO STAGE 1 ADULT	Missing	38	9/27/15 13:06	Missing	WHO STAGE 1 ADULT
31	NEVIRAPI NE	8/4/11 0:00	488	YES	11/15/1 5 0:00	Voluntary counseling and testing program	11/4/08 0:00	WHO STAGE 2 ADULT	Missing	39	9/27/15 13:11	Missing	WHO STAGE 3 ADULT
36	TDF/3TC/ EFV	9/1/12 0:00	Missing	YES	10/2/15 0:00	Voluntary counseling and testing program	8/23/12 0:00	WHO STAGE 3 ADULT	Missing	40	9/27/15 13:15	Missing	WHO STAGE 3 ADULT
24	TDF/3TC/ EFV	4/10/15 0:00	273	YES	9/30/15 0:00	Adult inpatient service	4/10/15 0:00	WHO STAGE 1 ADULT	Missing	41	9/27/15 13:19	Missing	WHO STAGE 1 ADULT
26	TDF/3TC/ EFV	4/14/15 0:00	389	YES	9/8/15 0:00	Prevention of maternal to child transmission program	4/13/15 0:00	WHO STAGE 1 ADULT	Missing	42	9/27/15 13:31	Missing	WHO STAGE 1 ADULT
30	NEVIRAPI NE	8/5/10 0:00	Missing	YES	9/11/15 0:00	Prevention of maternal to child transmission program	8/5/10 0:00	WHO STAGE 1 ADULT	Missing	43	9/27/15 13:34	Missing	WHO STAGE 1 ADULT
29	TDF/3TC/ EFV	6/4/15 0:00	Missing	YES	7/18/15 0:00	Prevention of maternal to child transmission program	3/18/15 0:00	WHO STAGE 1 ADULT	Missing	44	9/27/15 13:38	Missing	WHO STAGE 1 ADULT
36	NEVIRAPI NE	4/26/10 0:00	396	YES	8/5/15 0:00	OTHER NON-CODED	9/28/09 0:00	WHO STAGE 1 ADULT	Missing	45	9/27/15 14:10	Missing	WHO STAGE 2 ADULT
28	TDF/3TC/ EFV	Missing	300	YES	7/9/15 0:00	Pediatric inpatient service	Missing	WHO STAGE 2 ADULT	Missing	46	9/27/15 14:21	Missing	WHO STAGE 2 ADULT

age	Art regimen	ART Start date	CD4 count	On CTX?	EDD	Entry point	hiv_ date diagnosed	iWHO clinical stage Initially	LMP	ID	Date Record created	Viral load	WHO stage current
39	NEVIRAPINE	4/24/08 0:00	695	YES	7/2/15 0:00	Prevention of maternal to child transmission program	6/8/07 0:00	WHO STAGE 2 ADULT	Missing	47	9/27/15 14:28	Missing	WHO STAGE 3 ADULT
33	NEVIRAPINE	5/17/12 0:00	655	YES	0205-07-12 00:00:00	OTHER NON-CODED	12/15/09 0:00	WHO STAGE 2 ADULT	Missing	48	9/27/15 15:05	Missing	WHO STAGE 2 ADULT
28	NEVIRAPINE	6/27/13 0:00	769	YES	6/29/15 0:00	Tuberculosis treatment program	5/2/15 0:00	WHO STAGE 3 ADULT	Missing	49	9/27/15 15:09	Missing	WHO STAGE 3 ADULT
31	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	50	9/27/15 15:33	Missing	Missing
32	LAMIVUDINE / NEVIRAPINE / ZIDOVUDINE	5/22/12 0:00	631	YES	10/31/15 0:00	OPD (outpatient department)	5/21/12 0:00	WHO STAGE 1 ADULT	Missing	51	9/27/15 15:38	Missing	WHO STAGE 1 ADULT
31	TDF/3TC/ EFV	1/31/12 0:00	378	YES	8/22/15 0:00	OPD (outpatient department)	1/31/12 0:00	WHO STAGE 1 ADULT	Missing	52	9/27/15 15:43	Missing	WHO STAGE 1 ADULT
41	NEVIRAPINE	2/11/15 0:00	Missing	YES	7/31/15 0:00	Pediatric inpatient service	2/10/15 0:00	WHO STAGE 1 ADULT	Missing	53	9/27/15 15:51	Missing	WHO STAGE 1 ADULT
27	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	54	10/3/15 13:15	Missing	Missing
0	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	55	10/3/15 13:25	Missing	Missing
27	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	56	10/3/15 13:29	Missing	Missing
36	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	57	10/3/15 13:38	Missing	Missing
0	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	58	10/3/15 13:49	Missing	Missing
23	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	59	10/3/15 13:56	Missing	Missing
25	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	60	10/3/15 14:01	Missing	Missing
23	TDF/3TC/ EFV	1/15/15 0:00	586	YES	6/7/15 0:00	Prevention of maternal to child transmission program	1/15/15 0:00	WHO STAGE 1 ADULT	Missing	61	10/3/15 14:06	Missing	WHO STAGE 1 ADULT
24	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	62	10/3/15 14:15	Missing	Missing
27	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	63	10/4/15 16:11	Missing	Missing
35	NEVIRAPINE	9/19/14 0:00	438	YES	4/3/15 0:00	Prevention of maternal to child transmission program	2/21/07 0:00	Missing	Missing	64	10/20/15 15:47	Missing	UNKNOWN
28	Missing	6/25/13 0:00	Missing	Missing	Missing	Prevention of maternal to child transmission program	12/18/09 0:00	WHO STAGE 1 ADULT	Missing	65	10/20/15 15:55	Missing	Missing
30	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	66	10/20/15 16:17	Missing	Missing
32	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	67	10/20/15 16:25	Missing	Missing
37	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	68	10/20/15 16:28	Missing	Missing
29	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	69	10/20/15 17:00	Missing	Missing
34	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	70	10/20/15 17:05	Missing	Missing
28	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	71	10/20/15 17:09	Missing	Missing
21	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	72	10/20/15 17:11	Missing	Missing
22	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	73	10/20/15 17:15	Missing	Missing
28	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	74	10/20/15 17:18	Missing	Missing
25	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	75	10/20/15 17:23	Missing	Missing
39	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	76	10/20/15 17:30	Missing	Missing
34	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	77	10/20/15 17:36	Missing	Missing
22	NEVIRAPINE	10/9/14 0:00	Missing	YES	1/11/15 0:00	Prevention of maternal to child transmission program	10/9/14 0:00	WHO STAGE 1 ADULT	Missing	78	10/25/15 11:13	Missing	WHO STAGE 1 ADULT

age	Art regimen	ART Start date	CD4 count	On CTX?	EDD	Entry point	hiv_ date diagnose d	iWHO clinical stage Initially	LMP	ID	Date Record created	Viral load	WHO stage current
26	TDF/3TC/ EFV	10/31/12 0:00	400	YES	7/27/15 0:00	Prevention of maternal to child transmission program	6/9/11 0:00	WHO STAGE 1 ADULT	Missing	79	10/25/15 11:33	Missing	WHO STAGE 1 ADULT
27	TDF/3TC/ EFV	Missing	390	YES	3/6/15 0:00	Voluntary counseling and testing program	2/17/09 0:00	WHO STAGE 1 ADULT	Missing	80	10/25/15 12:22	Missing	WHO STAGE 1 ADULT
30	TDF/3TC/ EFV	Missing	934	YES	7/2/15 0:00	Missing	Missing	Missing	Missing	81	10/25/15 12:41	Missing	WHO STAGE 1 ADULT
36	NEVIRAPI NE	12/22/14 0:00	Missing	YES	2/14/15 0:00	Prevention of maternal to child transmission program	12/17/14 0:00	WHO STAGE 2 ADULT	Missing	82	10/26/15 4:09	Missing	WHO STAGE 2 ADULT
37	LAMIVUD INE / NEVIRAPI NE / ZIDOVUDI NE	1/3/11 0:00	Missing	YES	Missing	Voluntary counseling and testing program	12/7/10 0:00	WHO STAGE 3 ADULT	Missing	83	10/26/15 4:20	Missing	WHO STAGE 3 ADULT
28	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	84	10/26/15 4:34	Missing	Missing
23	TDF/3TC/ EFV	1/22/15 0:00	Missing	YES	3/24/15 0:00	OTHER NON-CODED	6/16/15 0:00	WHO STAGE 1 ADULT	Missing	85	10/26/15 4:38	Missing	WHO STAGE 1 ADULT
28	NEVIRAPI NE	4/22/15 0:00	205	YES	9/7/15 0:00	Adult inpatient service	4/21/15 0:00	WHO STAGE 1 ADULT	Missing	86	10/26/15 4:55	Missing	WHO STAGE 1 ADULT

Appendix P Webserver requests during the study



Appendix Q Timeline of challenges encountered during the second site visit and in data collection and analysis

Date	Occurrences and actions
26/10/2016	Ms Arant Bandy is onsite in Kakamega
26/10/2016-29/10/2016	Constant communication with Safaricom in an attempt to restore SSH IPsec VPN access so that Dr Rø can download quantitative data from the server. Waited in the Uamuzi Bora offices for three days for the promised Safaricom technician who failed to make a site visit to restore access.
29/10/2016	Qualitative questionnaires received and reviewed. Please see 5.7.1.3 The second visit to Kakamega and prospective data collection
28/10/2016	Downloaded information directly from the server in LINUX. Dr Rø gave Mr Otwane and Ms Arant Bandy the code to type into the system to release the data over a Skype video call. The data was downloaded successfully and emailed to Dr Rø in encrypted format.
29/10/2016	Ms Arant Bandy requested the following information in de-identified format from the data dump: Age, Patient ID, EDD, LMP, Entry point, HIV diagnosis date, Initial WHO stage, Current WHO stage, ART start date, Current ART regimen, CTX dispensed, CD4 count, Viral Load
31/10/2016	Ms Arant Bandy departed Kakamega
26/11/2015	De-identified information received from Dr Rø in CSV format.
6/12/2015	Ms Arant Bandy evaluated the data in Excel format. Sixty-seven records entered total. Noted that LMP was missing from all entries and much information was missing from other fields as well. Further evaluation in CSV revealed that the first 8 records were entered during the training and of the following 59, all were entered between 26/9/15 and 26/10/15. There were no entries of records between the beginning of the study 6/3/2015 and 27/9/2015.

Date	Occurrences and actions
6-9/12/2015	Dr Rø and Mr Otwane contacted to address discrepancies. Considered th possibility that information had not been saved correctly or that data had been lost. The decision was made to retrieve the data month by month from the server. Dr Rø noted that 23 records were created on 27/9/2015 by one person, Sister Zaitun. Alerted Dr Haskew to the situation.
10/12/2015	Dr Rø has made a log of contact with the server. There have been no attempts at contact with the server from any of the Chromebooks between March and the end of September. It was postulated that Mr Otwane may have been entering information onto the demo server, but there was little activity there that was not accounted for by Ms Arant Bandy's test patients and the update of Malaria guidelines in late March/early April.
10-14/12/2015	Mr Otwane's discussions with nurses and midwives at the MCH reveal that they did attempt to use the system early on but encountered connectivity issues and did not use the system again until they began retrospective data entry in September. Per the nurses and midwives report, the believed that retrospective data entry was acceptable.
14/12/2015	The decision was made by Ms Arant Bandy to restart the study as soon as possible with stricter guidelines, protocols and reporting metrics in place for Mr Otwane.

Appendix R Development, utilisation and evaluation of an mhealth tool to aid in the co-management of HIV and pregnancy relaunch protocol

Enrolment:

- Pregnant women living with HIV, whether diagnosed at this pregnancy or earlier at their first visit will be inducted into the system and followed for all subsequent visits until the end of pregnancy or the end of the study, whichever occurs first.
- We will endeavour to enrol 120 patients before ceasing enrolment in hopes of capturing 100 patients with sufficient data to include in the study.
- The woman will be given the translated information sheet to read, sign and date if she consents to be in the study. If required, the information sheet will be read to her and this will be indicated on the information and consent form.
- A paper file and corresponding electronic file will be created for each patient enrolled and consented with a copy of the consent form to remain with Collins (the other copy is to remain on site if this is required by the hospital). In addition to this, a list of patients will be created that have been enrolled into the study. This list is to be updated as patients are enrolled. A copy of this list will remain with Collins and another copy will remain with the clinic. An updated copy will be sent to Neel each day.
- Collins, will assist the MCH staff with entering the demographic patient information into the EMR so that clinical staff may devote their time to clinical activities and the electronic documentation thereof.
- A notation should be made on the patient MCH card to indicate that she is part of the study so that her electronic medical record may be accessed for revisits when she presents to the clinic and a similar notation will be made in the register. This may be a coloured mark next to the name or UPIN. This will allow clerical and clinical staff to be prepared for the patient visit and not waste time starting up, signing in and connecting the computers when the patient arrives in the room.

Follow up and monitoring:

- Each day, at the end of the day, the hard drive will be monitored to ensure that all patients enrolled in the study do indeed have a corresponding EMR. This will be cross-referenced with the list of patients as well as the consent forms. If a patient's record is

found to be deficient in any above element, it should be rectified as soon as possible. If rectification is not possible then the patient should not be included in the study.

- Each morning, a list of patient flags and defaulters will be generated. This will be given to the clinical staff for follow up. Follow up documentation will be entered into the EMR as a separate visit with actions documented in the comments section of the flow chart, ie: “patient recalled by telephone for haemoglobin of 7, will present to clinic tomorrow”. This information will be entered by the person recalling the patient under their username.
- If a patient EMR will no longer be in use, this will be documented :
- in the EMR under the comments section of the antenatal flow chart ie: “gave birth, date”, “transferred to a new facility, date “deceased, date”, etc.
- on the list of study participants
- in the individual patient file with the consent form
- in the MCH register

Project manager’s daily responsibilities

- Each morning, print out a copy of the defaulters and the flags and bring them to the clinic
- Ensuring that all Chrome Books are charged, running and connected to the server each morning before the clinic starts including the chrome book in the CCC.
- Ensure that the chrome book in the labour and delivery suite is charged and connected each day. Review with staff how to access patient records and determine if a labouring woman is a part of the study.
- Ensuring that all nurses/midwives are prepared to enter information for patients into the EMR each day and assisting them within the bounds of patient confidentiality
- Entering new patient demographic data into the system and keeping track of all new patients enrolled into the study, ensuring that each has:
    - A valid EMR file created and an initial visit and return visit forms created and saved via accessing the patient list from the server and cross checking it
    - A paper file created with the consent form. One copy will remain at the study site and one at the UB offices. These will be scanned and a corresponding electronic file created.
    - Lists of patients enrolled, paper and electronic
    - a marked patient card indicating that she is part of the study.
    - A mark in the MCH register corresponding with the patients name or UPIN that she is a part of the study

- Ensure that all chrome books are charging and locked up at the end of the day.
- Sending an email to Neel each day detailing new patients enrolled with the last four digits of the UPIN and detailing any issues encountered with the system that day. If the patient enrolment can be verified with a screen shot of the hard drive, this would be good- this can also be accomplished with a shared drop box. We need to discuss how this can be accomplished in a de-identified manner so that it can be sent via email.
- Liaising with Safaricom to rectify any connectivity issues and keeping a detailed log of interactions with Safaricom including; the name of the person communicated with, date and time
- Plan for rectification & Follow up if the situation has not been rectified
- Keeping a meticulous daily log detailing problems encountered that affected enrolment and follow up each day, ie: strikes, campaigns, power outages, connectivity issues.
- Filing and keeping track of bills from Safaricom and other project related expenses.
- Downloading to the server changes made to the record by Neel or Gunnar and updating the paper knowledge base at the MCH when required.
- Potential travel and distribution of funds for research fees and ethics approvals.

The reseacher's responsibilities:

- Maintenance of the knowledge base of the system and ensuring that this remains up to date by keeping abreast of guideline changes by monitoring WHO, NIH and NASCOP guidelines consistently.
- Addressing any practice related questions or concerns presented by clinical staff as they relate to the EMR.
- Confirming daily study records with respect to enrolment, etc. and supervising Collins in his duties.
- Maintenance of ethical approvals and research fees.
- Regularly updating Prof Dantas and Dr Haskew as they require.

In case of power or connectivity issues:

- Paper copies of the initial and return visit forms will be created in the rare event of a connectivity issue or if power is down and the chrome books are not charged. The paper version of the knowledge base will be available for clinician consultation. Two copies are currently with the MCH. This will be documented and it will be ensured that data is entered into the system when connectivity has been restored. A note will be made of this both in the daily log and in the patient record under the comments section in the antenatal flow chart ie: "information entered retrospectively from paper form due to

(event), date, entered by."

Appendix S Timeline of the attempted relaunch

Date	Occurrences and actions
6/1/2016	Mr Otwane spoke with Rachael Achieng of Safaricom for a 6-month budget quote.
8/1/2016	The 6-month budget finalised. It is congruent with the money left over with Vestergaard.
12/1/2016	Mr Otwane discussed the application process with Ms Achieng, she has promised to speed up the vetting process.
14-19/1/2016	Calls from Safaricom Customer Service Support to confirm the account details.
20/1/2016	New application forms required for re-request of WIMAX services, Mr Otwane completes this.
25/1/2016	Mr Otwane completes the client data bundle forms for Safaricom.
28-29/1/2016	Refresher training conducted at the MCH with the clinical staff.
5/2/2016	EMR/CDSS is updated to reflect most current guidelines.
5/2/2016	Refresher training conducted in the CCC and on the labour ward.
6/2/2016	Ms Achieng contacted regarding the delay of the application process. She again promises assistance.
9/2/2016	Mr Otwane speaks with Customer Support Services at Safaricom to rectify account details.
10-11/2/2016	Second round of refresher training in the CCC and labour ward.
15/2/2016	Mr Otwane travels to Nairobi to finalise the application process in person.
18/2/2016	The application process has been updated to reflect the vetting of Uamuzi Bora.
19/2/2016	Safaricom technicians visit Kakamega to set up the router in the office for Internet connectivity.
20-24/2/2016	Safaricom begins a WIMAX upgrade for the Western and Rift Valley regions.
26/2/2016	Scheduled update of the router in the Uamuzi Bora office by Safaricom technicians but wasn't completed because they ran out of time.
1/3/2016	Visit to Kakamega office by Safaricom technicians to manually update with new software to pick up the update rolled out the previous week. This was done with all clients in Kakamega as many were reporting fluctuating Internet connectivity.

Date	Occurrences and actions
4-6/3/2016	Mr Otwane has sent the SIM numbers to be activated and mapped to the Uamuzi Bora APN, a new account was created and bills will be sent to Vestergaard. When payment has been completed the SIM cards can be activated and the VPN tested.
7/3/2016	Safaricom has stalled the reactivation of WIMAX in the Western and Rift Valley regions until technicians can confirm upgrades and authorise reactivation.
15/3/2016	Safaricom technicians have finalised the set up in the Uamuzi Bora offices. The Internet was tested and is fine. The SIM numbers to be mapped to the Uamuzi Bora APN were submitted and Vestergaard notified to prepare payments to Safaricom when a new account number has been generated by Safaricom.
18-20/3/2016	Power maintenance and electric power pole replacement in Kakamega District causes a 3-day power blackout.
21/3/2016	Ms Arant Bandy approves payment by Vestergaard to Safaricom. Safaricom is finalising the new Uamuzi Bora account with a request for the SIM cards to be bundled with 1.5GB data per sim card.
23/3/2016	Safaricom has rejected Ms Arant Bandy's request as it did not come on letterhead, but came via email. A letter was generated on Uamuzi Bora letterhead to resubmitted to Safaricom.
25-28/3/2016	Easter holiday
6/4/2016	All of the SIM cards have received their data bundles. The SIM cards were able to connect to the Safaricom network but they could not connect to the VPN and the server. The router from the UB office was connecting to the radio but the network fluctuates.
7/4/2016	The network connection at the hospital was tested and was disconnecting after one minute.
8/4/2016	Testing continues and Safaricom states they are working on the connection.
12-15/4/2016	Mr Otwane hospitalised with chronic Malaria.
16/4/2016	Mr Otwane in communication with Safaricom technical support about the fluctuating connection. Safaricom has discovered that the SIM cards were given a new IP address which was preventing the connection as the VPN was only authorised to allow the old IP address.
19/4/2016	Safaricom technicians install a back route for the new IP address that was issued and the old IP addresses were removed from the router configurations.
1-3/5/2016	Labour Day public holidays

Date	Occurrences and actions
4/5/2016	Given approval by the Deputy Medical superintendent for the study extension.
11/5/2016	Despite the reprogramming of the back route, the connectivity issues persist. Safaricom has given new IP addresses to the SIM cards and the VPN has been refreshed.
16/5/2016	The refresh has not fixed the connectivity issue and Safaricom Business Support has decided to completely reset the router and VPN settings.
18/5/2016	Trainings done for new nurses that have joined the MCH.
23/5/2016	The router was refreshed by Safaricom technicians and the new IP addresses were able to connect via the VPN.
30/5/2016	Ms Arant Bandy makes the decision to end the relaunch.