CLINICAL AUDIT ON MANAGEMENT OF HIV EXPOSED UNINFECTED INFANTS (HEIs) 0-24 MONTHS OLD IN 2016/17 AT THE LEA TOTO PROGRAM, NAIROBI, KENYA.

By

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DECLARATION

This dissertation proposal is my original work and has not been presented for the award of a degree in any other university or academic forum.

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ACRONYMS AND ABBREVIATIONS

ART Antiretroviral therapy

ARV Antiretroviral

AZT Zidovudine

CHW Community health worker

EID Early infant diagnosis

EMR Electronic medical records

EMTCT Elimination of mother to child transmission

HEU HIV exposed uninfected

HIV Human Immunodeficiency Virus

HUU HIV unexposed uninfected infants

IPT Isoniazid preventive therapy

KEPI Kenya expanded program on immunization

KNH Kenyatta National Hospital

MOH Ministry of health

MTCT Mother to child transmission

NACC National Aids Control Council

NVP Nevirapine

PCP Pneumocystis jirovecii pneumonia

PCR Polymerase Chain Reaction

PMTCT Prevention of mother to child transmission

STATA Data Analysis and Statistical Software

UNAIDS Joint United Nations Programme on HIV/AIDS

UoN University of Nairobi

VL Viral load

WHO World Health Organization

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DEFINITION OF TERMS

Breastfeeding: Process of feeding the infant on the mother's milk, either directly from the breast or by giving expressed breast milk. Exclusive breastfeeding is recommended for the first six months of life and continued breastfeeding with complementary feeding until 2 years of life.

For the HIV exposed infant all breastfeeding must be accompanied by Anti-retroviral drug administration – current recommendation is combination therapy for the mother and prophylaxis for the infant 6 weeks of AZT and NVP followed by another 6 weeks of NVP.

Complementary feeding: The child receives both breast-milk and solid (semisolid or soft) foods. Usually recommended after first 6 months of life.

Early infant HIV diagnosis: Testing children for HIV infection at first contact ideally within the first 48 hours after delivery for an HIV exposed child and confirmed with testing at age 4-6 weeks of age, in order to provide lifesaving treatment or prophylaxis for HIV. The term may also apply to testing of exposed infant as soon as mother is diagnosed with HIV in the context of new infected or previously undiagnosed individual.

EMTCT: elimination of mother-to-child transmission of HIV to ensure that MTCT of HIV is controlled and reduced to a very low level that it ceases to be a public health problem. This target <50 new pediatric infections per 100,000 live births and a transmission rate of either <5% in breastfeeding populations or <2% in non-breastfeeding populations. (8)

Exclusive Breastfeeding: the infant receives only breastmilk (including expressed breast milk or from a wet nurse) and nothing else except Oral Rehydration Solution, vitamins, minerals and medicines. This is recommended for the first six months of life.

Growth monitoring: The regular recording of a child's weight, in order to document growth. The child's size measurements must then be plotted on a growth chart coupled with some specified remedial actions if the weight is abnormal in some way.

HIV Virological testing: This maybe detection of viral nucleic acid (DNA and RNA polymerase chain reaction (PCR), antigen testing (P-24 antigen tests) or viral culture. The standard in clinical practice in HIV DNA and RNA PCR. In this study diagnosis of HIV may have been by detection of HIV-DNA or RNA by use of polymerase chain reaction and other

nucleic acid detection techniques. HIV DNA PCR is a qualitative test (i.e. it gives a yes/no diagnosis for HIV infection). HIV RNA detection provides additional quantitative information on virological status, and the same technology/equipment is used for monitoring the response to treatment and possible therapeutic failure.

Isoniazid preventive therapy: Administration of isoniazid to prevent active tuberculosis in children who are HIV infected or exposed. Usually recommended for children who have contact with persons with tuberculosis and without active TB.

PCP prophylaxis: Administration of cotrimoxazole to prevent pneumocystis jirovecii pneumonia in children who are HIV infected or exposed.

PMTCT - prevention of mother-to-child transmission of HIV-includes primary prevention of HIV, prevention of unintended pregnancies, effective access to testing, counselling, antiretroviral therapy (ART), safe delivery practices, and appropriate infant feeding practices (including access to antiretroviral drugs) to prevent HIV transmission to infants

Serological HIV testing: Diagnosis of HIV by detection of antibodies against HIV. It may not distinguish HIV infection or exposure in children aged less than 18 months due to presence of maternal antibodies in this age group.

ABSTRACT

Back ground: The majority of infants born to HIV-infected women, are HIV-exposed uninfected (HEU). Effective clinical management of these children will prevent seroconversion, severe illness and malnutrition. To ensure quality care the Ministry of health has guidelines for standard evidence based care that all providers follow.

Objectives: A clinical audit to determine proportion of HEU children aged less than 24months enrolled in Lea Toto program that accessed and adhered to Kenyan National guidelines in the following components: early infant HIV diagnosis (EID), anti-retroviral prophylaxis, immunization, retention in care, and management of nutrition and infectious co-morbidity.

Methods:

Design, Setting and Participants

This was a clinical audit conducted at Lea Toto program a faith based NGO which has for the past 20 years provided health services to families of children affected by HIV and currently serves up to 3,100 HIV-positive children and up to 15,000 family members annually. The study participants were HEU children 0 to 24 months old on follow up in 2016-2017.

Children were classified as HEU on the basis of their first HIV PCR test being negative. After informed consent a standardized clinical audit tool was used to abstract data from the electronic medical records of the HEU infants. The tool was used to collect information on timing and results of the early infant HIV diagnosis, ART prophylaxis, nutrition status, morbidity, immunization and adherence to follow up.

Results: A total of 322 electronic medical records of HEU infants at Lea Toto program were evaluated. Age on enrolment into the program was from 3 days of age to 20 months of age. The mean age of first HIV PCR test was 2.01 months. A total of 287(89.13 %) of the first HIV PCR were done at Lea Toto. Overall 299 (92.8%) of the 322 participants received ART prophylaxis, 144 (44.7 %) the recommended combined Zidovudine (AZT) + Nevirapine (NVP) prophylaxis, and 155 (48%) only NVP. Only 217 (67.39%) participants started ART prophylaxis on first day of life and up to 219 (68.01%) HEU were on the ART prophylaxis for 3 months, while 25(7.8%) receive a shorter course of prophylaxis because of loss to follow-up or no longer at risk, and 78 (24.2%) received more than 3 months prophylaxis due to heightened risk of infection from

maternal viral non-suppression.. The 23 (7%) who did not received ART prophylaxis were enrolled into the program after they had been weaned off breastfeeding and reports of ART prophylaxis could not be verified. Overall 265 (82.3%) received cotrimoxazole prophylaxis. There were 214 (66.45%) participants who reported exclusive breastfeeding for 6 months, 58 (18%) for 5 months and only 10 (3%) for less than a month. Overall 72 (22.4%) had some malnutrition including 43 (13%) moderate malnutrition, 13 (4%) stunted, 9 (3%) wasted, while 7 (2%) both wasted and stunted. Only 26 (8.1%) of the 322 participants were admitted to hospital during the period of audit. Only 4 (1.2%) children seroconverted. Factors associated with seroconversion were late enrolment, inappropriate ART prophylaxis and incomplete HIV testing.

Conclusion and recommendation:

Children enrolled in the Lea Toto program are accessing the essential HIV care package. Late enrollment into the program was associated with increased likelihood of malnutrition and HIV infection. There is need for continuing medical education (CME) to address the observed low PCR testing rate at 9 months and inappropriate use of CTX before the age of 6 weeks of life.

CHAPTER ONE: INTRODUCTION

Pediatric HIV exposure and infection remains a major cause of childhood morbidity and mortality. In 2014, 150,000 children died from HIV-related causes worldwide (1). In 2015, 1.4 million children aged <15 years were estimated to be living with HIV, with the vast majority living in sub-Saharan Africa (2).

Vertical transmission of HIV from mother to child is the main route by which childhood HIV infection is acquired. About 90% of the infected infants acquired the HIV virus from their HIV-positive mothers during pregnancy, delivery, or through breast-feeding. (3) Without treatment, the likelihood of HIV passing from mother-to-child is 15% to 45%. However, antiretroviral treatment and other effective PMTCT interventions can reduce this risk to below 5 %(4).The most effective way to tackle pediatric HIV globally is to reduce mother-to-child transmission.

Since 2011 to 2015 globally the annual number of HIV-infected children has declined by 50 %(5) .Kenya reduced number of new HIV infections among children by 49% between 2013 and 2015. More than half (24) of the 47 counties significantly reduced their new HIV infections among children (6).

Improving PMTCT means large numbers of (HEU) children are being born. Infants born to HIV infected women are HIV-exposed but the majority remain uninfected. HEU infants suffer greater morbidity and mortality compared to HIV-unexposed uninfected (HUU) peers (7).

Despite progress in PMTCT programs, there were 100,000 new pediatric HIV infections in 2016 in Kenya (8). More than 50% of infant HIV infections occurred in the postpartum period, reflecting the need for greater attention to the HEU children. Early diagnosis and treatment are necessary to prevent morbidity and mortality in HIV-infected children.

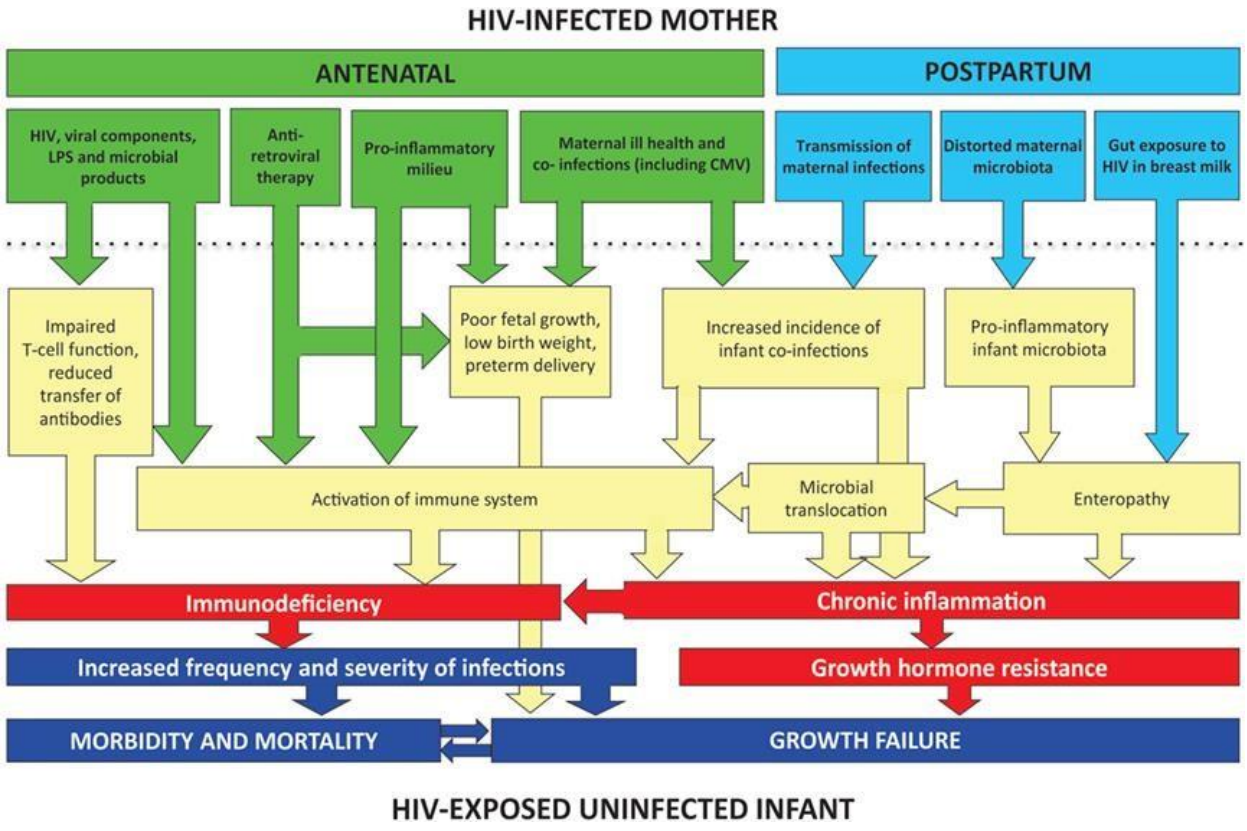
The global community including WHO and member states is moving towards elimination of mother to child transmission of HIV (EMTCT). The goal of EMTCT is to ensure that MTCT of HIV is reduced to a very low level, such that it ceases to be a public health problem. The minimum EMTCT impact targets are to reduce MTCT to < 5% and reduce HIV pediatric infections to less than 50 per 100,000 live births. (8)

CHAPTER TWO: LITERATURE REVIEW

With increasingly effective PMTCT, the population of HEU infants is growing. HEU children are at increased risk of mortality, morbidity and slower early growth than their HIV-unexposed counterparts. This association is hypothesized to be driven by a combination of biologic and socio-economic risk factors. Other factors include advanced maternal HIV disease or death, disruptions in family and socio-economic structures, insufficient infant vaccine and other immunological responses. Altered child health care-seeking behavior, increased pathogen exposure in the home and suboptimal infant feeding practices are other aggravating factors. The flow chart below shows the factors affecting HEU infants. These factors affect the outcomes of HEU infants especially if PMTCT is not adhered to.

Figure 1: Flowchart showing factors affecting HEU infants.

Adapted from ZVITAMBO study group trial (35).



2.1 Trends of PMTCT and pediatric HIV

Since 2011, globally the annual number of HIV-infected children has declined by 50%. There is 66% decline in new HIV infections among children in Sub-Saharan Africa (9).

Kenya reduced number of new HIV infections among children by 49% between 2013 and 2015. More than half (24) of the 47 counties significantly reduced their new HIV infections among children (10).

Seven of the 47 Counties have achieved the target of Less than 5% MTCT rate ahead of the 2019 target. These include Nairobi, Nyeri, Kiambu, Nandi, Nakuru, Elgeyo Marakwet, Bungoma (11).

Approximately 97,400 paediatric HIV infections have been averted due to PMTCT scale up in 2013 through to 2015, free maternity services and introduction of option B+ in Kenya (11). There 22 counties that have achieved a PMTCT coverage of 80% or more, out of these, 13 had more than 90% coverage. (12)

Figure 2: Bar graph showing the PMTCT coverage and new HIV pediatric infections in sub-Saharan global plan countries 2000-2015

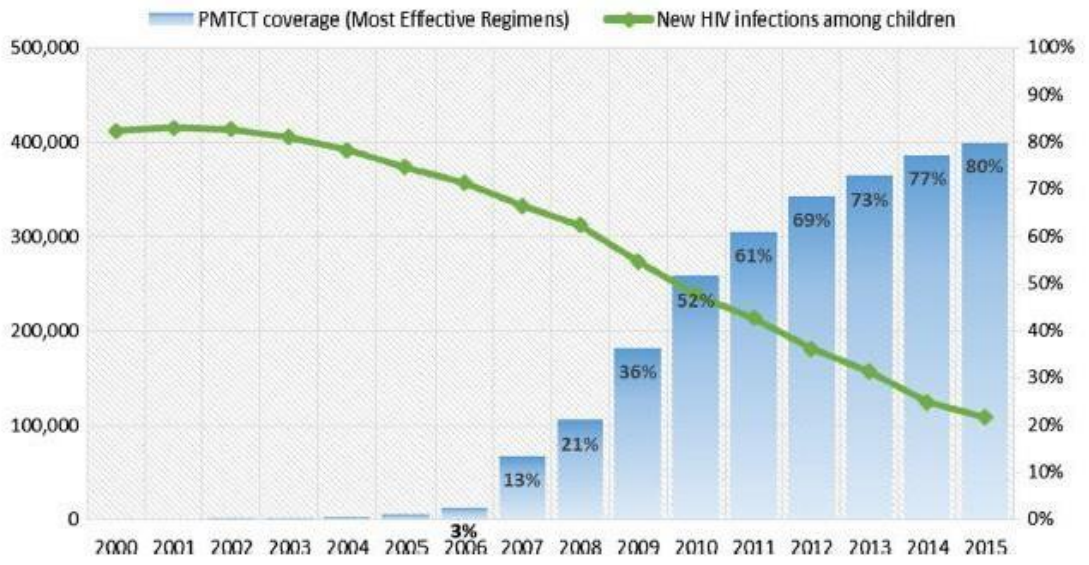


Fig. 4 Trends in percentage of pregnant women living with HIV receiving effective antiretroviral medicines for PMTCT and new HIV infections among children 0–14, 21 sub-Saharan African Global Plan countries, 2000–2015. *Source* UNICEF, PMTCT progress reporting, 2002–2006; WHO/UNICEF Universal Access Progress Reporting, 2007–2010; UNAIDS/UNICEF/WHO Global AIDS Response Progress Reporting databases, 2011–2015; UNAIDS 2016 estimates, July 2016

2.1.1 Evolution of PMTCT guidelines:

The WHO PMTCT Guidelines have been changing over time as shown in appendix 2. The basis for these changes is evidence that new pediatric HIV infections can be reduced through proven PMTCT interventions. These interventions include maternal and infant antiretroviral therapy, early infant diagnosis and appropriate infant nutrition.

The 2006 WHO PMTCT guidelines recommended starting lifelong ART for pregnant women with a CD4 count equal to or below 200 cells/mm3, usually the stage at which the immune system is no longer strong enough to prevent opportunistic diseases. (13)

The 2010 WHO guidelines promoted starting lifelong ART for all pregnant women with severe or advanced clinical disease (stage 3 or 4), or with a CD4 count at or below 350 cells/mm3, regardless of symptoms which is also safe and effective in reducing mother to child transmission of HIV (MTCT). (13)

The 2010 revised PMTCT guidelines refer to the following two key approaches: Pregnant and breastfeeding women who were not eligible for life-long therapy had two options:

(i) Maternal ART prophylactic monotherapy with AZT coupled with daily administration of NVP to the infants from birth (within 6–12 hours), until 1 week after all exposure to breast milk has ended or if breastfeeding stops before the age 6 weeks, for a minimum of 4 to 6 weeks following birth. This approach was also known as option A or

(ii) Option B: Maternal short-term triple ARV prophylaxis during pregnancy, delivery and breastfeeding. All infants regardless of **infant** feeding mode NVP or AZT for 4 to 6 weeks.

The 2015 WHO guidelines recommend Option B+, that is lifelong antiretroviral treatment is provided to all pregnant and breastfeeding women living with HIV regardless of CD4 count or WHO clinical stage. Treatment should be maintained after delivery and completion of breastfeeding for life. (14)

The changes in infant ART prophylaxis are:

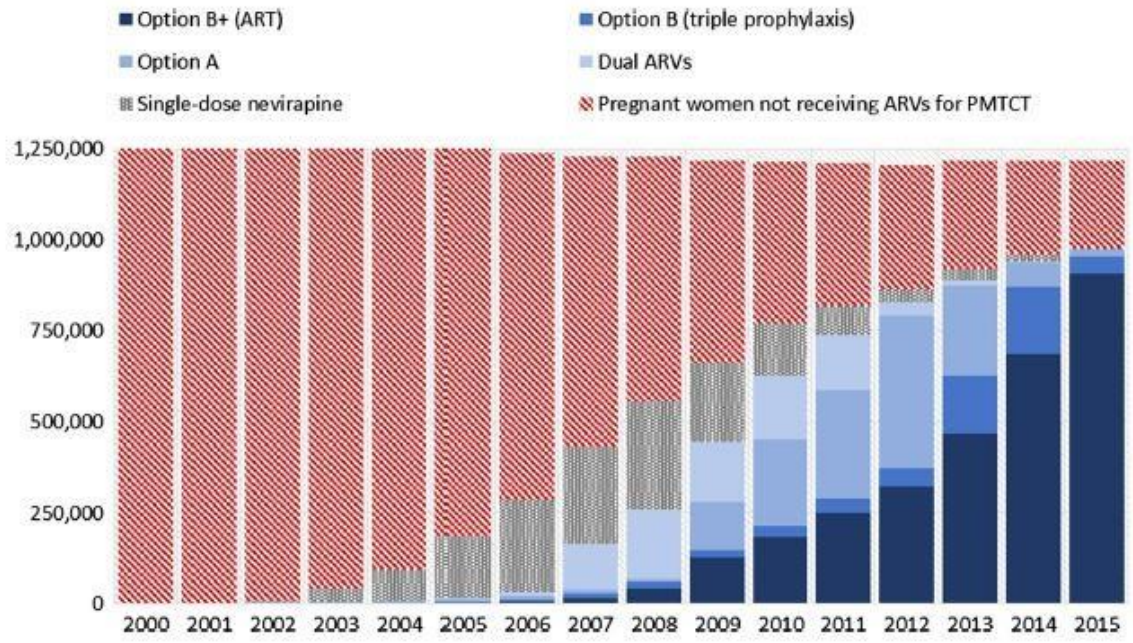
- In 2006 Prophylaxis regimens for exposed infants was nevirapine and zidovudine for 7 days.

- In 2010, there were 2 options for maternal prophylaxis which in turn determine infant prophylaxis. Irrespective of the mode of infant feeding, the maternal triple ARV prophylaxis (option B) should be coupled with daily administration of NVP or twice-daily AZT to the infant. That is from birth (within 6–12 hours) or as soon as feasible thereafter until 4 to 6 weeks of age. (22)

- In 2010, for breastfeeding infants and maternal prophylaxis is option A .i.e. maternal zidovudine only. This should be coupled with daily administration of NVP to the infants from birth (within 6–12 hours), until 1 week after all exposure to breast milk has ended.

- In 2015 according to Kenyan national guidelines, prophylaxis recommended is 12 weeks of infant prophylaxis. That is zidovudine and nevirapine for 6 weeks, followed by nevirapine for 6 weeks. (23).

Figure 3 Graph showing changes in PMTCT by regimen in 21 sub-Saharan African countries since 2000-2015.



Distribution of the number of pregnant women living with HIV receiving antiretroviral medicines for PMTCT by regimen, 21 sub-Saharan African Global Plan countries, 2000–2015. *Source* UNAIDS/UNICEF/WHO Global AIDS Response Progress Reporting database, 2016

2.2 Early Infant HIV Diagnosis

Starting perinatally infected infants on ART therapy by 7 weeks of life is associated with significantly better survival compared to treatment initiation later in infancy. Therefore, early infant diagnosis is critical for reducing HIV-associated mortality in children. It is recommended that all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or at the earliest opportunity thereafter. (15) If breastfeeding, the infant may still be at risk for acquiring HIV infection and will need age-appropriate retesting 6 weeks or more after cessation of breastfeeding. (15)

It is also recommended that well, HIV-exposed infants undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Those who have reactive serological assays at 9 months should have a virological test to identify HIV-infected infants who need ART. (15)

In the non-breastfed or never-breastfed infant, a negative serological test result at or above the age of 9 months can be used to rule out HIV infection. (15)

In children older than 18 months, maternal HIV antibodies are usually no longer detectable. The presence of HIV antibodies in this population is therefore a quick and reliable means of definitively diagnosing HIV infection. (15)

In Kenya, MOH introduced the EID programme in the country in 2006 which intended to test all HIV exposed children. This enables provision of treatment for those who are infected and follow-up preventive support for the uninfected. National EID testing and treatment algorithms have been standardized with the WHO guidelines. All HIV exposed infants should be tested using PCR tests from 6 weeks of age or the first contact. ART should be initiated in all PCR+ infants regardless of their clinical or immunological status. The algorithm further recommends HIV antibody testing among infants whose initial PCR test is negative at 9 and 18months or at 2months after cessation of breastfeeding whichever comes earlier. Since the inception of the EID programme up to date more than 3,000 EID testing sites are active in Kenya. Nairobi County having the largest number of 192 testing centers.

In 2014, in Kenya only 42% of HIV-exposed infants received a timely diagnostic test for HIV and has not improved with repeated targeted efforts. This challenge is not unique to Kenya, only 39% of children in low-income countries were estimated to have access to HIV testing within the recommended 2 months of birth in 2012. (16) There is some evidence that some of the missing infants may have already succumbed to their infection.

There were common reported challenges in access to services for early infant diagnosis. These included weak sample referral networks, long turnaround time, and limitations in supply chain management. Integration of services for EID with other programs, e.g. immunizations, pediatric care, and health outreach in the community, were integral to success of EID . (17)

2.3 Breastfeeding and Complementary Feeding in HIV Exposed Uninfected Infants

Protection and promotion of breastfeeding in resource-limited settings has been emphasized by WHO. This is because of its significant reduction in infant morbidity and mortality (18).
Previously in the 1990s data regarding risk of MTCT through breast milk prompted the complete

avoidance of breastfeeding by HIV-infected mothers. Previously in women who started breastfeeding had to wean rapidly by 4–6 months postpartum (19).

Subsequently, evidence of high mortality of non-breastfed or early weaned infants born to HIV-infected mothers has been published. There is data on the protective effect of antiretroviral use by mothers or infants with respect to the breast-milk transmission of HIV (20). Therefore, it is now recommended that breastfeeding in HIV-infected women be continued throughout infancy while using antiretroviral therapy. (21) After 6 months of age, to meet their evolving nutritional requirements, HEU infants should receive nutritionally adequate and safe complementary foods 9.i6and continue breastfeeding.

2.4 Infant ARV prophylaxis

Infant ARV prophylaxis has undergone changes, even in WHO guidelines as outlined in appendix 2. In 2006 Prophylaxis regimens for exposed infants was nevirapine and zidovudine for 7 days. In 2010, there were 2 options for maternal prophylaxis which in turn determine infant prophylaxis. Irrespective of the mode of infant feeding, the maternal triple ARV prophylaxis (option B) should be coupled with daily administration of NVP or twice-daily AZT to the infant. That is from birth (within 6–12 hours) or as soon as feasible thereafter until 4 to 6 weeks of age. (22)

For breastfeeding infants, maternal prophylaxis there is option A –maternal zidovudine only. Should be coupled with daily administration of NVP to the infants from birth (within 6–12 hours), until 1 week after all exposure to breast milk has ended. If breastfeeding stops before the age 6 weeks, for a minimum of 4 to 6 weeks following birth. (22)

In infants receiving replacement feeding only, maternal ARV prophylaxis (option A) should be coupled with daily administration of infant NVP. Infant may also get NVP plus twice-daily AZT from birth (within 6–12 hours), until 4–6 weeks of age. (22)

In 2015 according to Kenyan national guidelines, prophylaxis recommended is 12 weeks of infant prophylaxis. That is zidovudine and nevirapine for 6 weeks, followed by nevirapine for 6 weeks. (23).

If a breastfeeding mother refuses to start ART but agrees to provide infant ARV prophylaxis, provide 6 weeks of AZT+NVP, followed by daily NVP until 6 weeks after complete cessation of

breastfeeding. If mother has VL ≥ 1,000 continue infant prophylaxis until confirmed viral suppression or 6 weeks after complete cessation of breastfeeding. (23)

2.5 Co-trimoxazole prophylaxis

Co-trimoxazole is a combination of two antibiotics sulfamethoxazole and trimethoprim. Cotrimoxazole, is recommended for HIV-exposed children to prevent the development of serious, often fatal, opportunistic infections, notably PCP.WHO estimate that only 8% of children exposed to HIV were initiated on co-trimoxazole prophylaxis by two months of age.
(41) Ideally, all HEU infants should be started on co-trimoxazole prophylaxis at six weeks of life. A randomized controlled trial among HIV-infected children in Zambia demonstrated that mortality was reduced by half and the number of hospital admissions was significantly reduced among children using co-trimoxazole. (42) Co-trimoxazole prophylaxis also protects against episodes of malaria, estimated 99.5% protection from pooled data (43). Co-trimoxazole prophylaxis is a low-cost intervention, with a unit cost of only about US$ 0.03 per child per day, or about US$ 10/year.

2.6 Immunization

HIV exposure can alter the efficacy and safety of vaccines and affect the susceptibility of the patient to the diseases for which immunization can confer protection. Immune responses to a variety of vaccines are reduced in HEU infants.

Because of their success in achieving high population coverage, routine immunization services have been used as a platform to deliver other health interventions, including vitamin A supplementation, deworming treatments, and insecticide-treated bed nets. Integrating other primary health care services with routine immunization visits is recommended in the World Health Organization and United Nations Children's Fund's Global Immunization Vision and Strategy, 2006–2015.In addition, the World Health Organization PMTCT Strategic Vision, 2010–2015, recommends integration of PMTCT services with maternal, newborn, and child health programs.
All HIV-exposed infants and children should receive all Expanded Programme for Immunization vaccines, including Haemophilus influenzae type B and pneumococcal vaccine, as early in life as possible, according to the recommended national schedules.

2.7 Growth monitoring

Children's growth reflects their health and nutritional status well. Growth failure, however, is common among children who have HIV exposure. HEU infants merit special attention as they have additional needs to ensure growth and development and depend on adults for adequate care. Regular, ongoing follow-up and monitoring of growth, particularly weight gain, height, head circumference and other measures of growth are essential to document the effect of HIV exposure-upper-arm circumference when used in combination with other clinical signs (bilateral pitting edema) has been found to be a useful and highly practical indicator of wasting-associated mortality risk.

2. 8 Morbidity in HIV exposed uninfected (HEU) children

The HEU have higher mortality and morbidity than unexposed infants. This may be due to increased exposure to infectious pathogens or compromised immune development.

A likely major cause of this impaired health is less exposure to breast milk as mothers are either less able to breastfeed. Mothers maybe stop breastfeeding early to protect their infant from HIV infection. Breastmilk is necessary for good nutrition status and adaptive immunity.

Other contributing factors are parental illness or death resulting in reduced care of the children and possibly exposure to antiretroviral drugs. It has been observed that the death of the mother poses an 8-fold risk increase in death of an infant independent of HIV status. (24)

The explanation for worse outcomes in HEU infants could be related to an altered immune system state. HEU infants have altered cell-mediated immunity, including impaired T-cell maturation (25). Pre-vaccination vaccine-specific antibody levels are often lower in HEU than HU. (26). HEU infants are often found to have lower absolute neutrophil counts as compared to HU infants. (27).

Their developing immune system is altered by HIV exposure, predisposing them to increased postnatal infections. HIV exposure was associated with a lower proportion of B cells in general and memory B cells. In particular, largely due to a lower proportion of un-switched memory B cells. (28)

Table 1:Studies on morbidity of HEU infants

Author	Setting	Study design	Results	Conclusion
Gichuhi C, et al, 2009. (31)	KNH-Kenyatta National Hospital, Nairobi,Kenya.	Prospective cohort study	Followed 351 HEU infants from neonatal period up to 1 year of age. 16 infants died (post-neonatal mortality rate of 47/1000 live births), 14 (8.8%) before six months of age.	The commonly identified medical conditions included bronchopneumonia, diarrhea and failure to thrive.
Wamalwa D. et al (32)	Infants born to HIV positive mothers at KNH evaluated for TB using T-Spot	Observational cohort	Early TB infection was 10.9% among 6 month-old HEU infants. Infants with positive T-SPOT.TB were more likely to have prolonged fever and maternal active TB	There was a high prevalence of TB infection in this cohort of HEU infants. This necessitates systematic TB screening and IPT.
Obimbo E. et al (33)	HEU infants followed from birth until last negative HIV test or at 1 year of age at KNH.	Retrospective cohort	Among 388 HEU infants, 113 hospitalizations were reported (35/100 infant-years). 90 % hospitalizations were due to one or more infectious diseases (26/100 infant-years), primarily pneumonia (n=40), gastroenteritis (n=17) and sepsis (n=14).	Breastfeeding was associated with reduced risk of hospitalization

Table 2:Studies comparing morbidity of HEU infants with HUU infants

Author	Setting	Study design	Results	Conclusion
Odundo E. et al (34)	In 2 western Kenya hospitals	Cross sectional study	Cryptosporidium spp. was more commonly identified in the stool of the 60 HEU children <24 months of age who were tested for parasites (12.2%) as compared to the 44 HIV-unexposed children <24 months who were tested for parasites (4.7%)	HIV-infection and HIV-exposure status were both associated with specific enteric pathogens. Cryptosporidium spp. 3 times more common in HEU compared to HIV-unexposed children. These associations were independent of measured potential confounding and mediating factors.
Koyanagi A. et al,2011((35)	Sick child clinic in Zimbabwe	ZVITAMBO trial	Compared with not-exposed infants, sick clinic visits were 1.2 times more common among HEU infants. Morbidity is higher among HEU infants and increases with severity of maternal disease, but is significantly higher for all mothers with CD4 cell count <800 cells/μL.	Increased risk of sick-child visits to clinic throughout the first year for HEU infants, as well as increased risk of hospitalization in the neonatal period.

Table 3: Studies on nutrition of HEU infants

Author	Setting	Study design	Results	Conclusion
Mbatia G. et al (36)	Kesho bora study	Study in 5 African countries.	751 HEU infants between 0 and 2.9 months of age. For the entire 0–6-mo age interval, non-breastfeeding infants tended to have greater morbidity risks than did breastfeeding infants (OR: 1.22; 95% CI: 0.99, 1.50; *P* = 0.058).	Absence of breastfeeding was associated with slightly increased risks of maternal-reported morbidity.
Mwiru R. et al, 2011.(37)	666 HEU infants in outpatient setting in Tanzania.	Randomized control trial.	EBF was associated with a 51 % decreased risk of cough, a 56 % reduced risk of cough and fever.EBF was associated with a 71 % reduced risk of acute diarrhea.	EBF is significantly associated with reduced risk of respiratory, diarrhea and nutritional morbidities during the first 6 months of life among children born to HIV-infected women.
Nduati R.et al (38)	HEU evaluated depending on feeding mode	Prospective cohort	Among infants in the Formula Fed (FF) and Breastfeeding (BF) groups, 56% and 60%, respectively, experienced stunting by 2 y. The slower rate of decline in length growth with FF may reflect benefits of micro nutrients.	Despite being uninfected, HIV-1–exposed infants showed frequent growth faltering, suggesting the need for vigilance in recognizing stunting within PMTCT programs

Table 4: Studies on early infant HIV diagnosis and prophylaxis

Author	Study design	Study setting	Results	Conclusion
Izudi J. et al|(41)	Interventional study	ANC unit of Kaabong Hospital, Uganda.	DNA-PCR testing increased from 20 to 100% between June 2014 and July 2015.	The integration of EID laboratory services, patient health education on importance of EID, regular EID CMEs for health workers, and use of community structures (expert clients and peer mothers) significantly improved EID outcomes and quality.
Girma M. et al.(42)	Prospective observational study	HIV-positive pregnant mothers and their newborns attending PMTCT services at seven health centres in Addis Ababa.	Of 435 infants born alive 98.6% received nevirapine prophylaxis. The mother-to-child HIV transmission rate was 0.7% after a median of 6.7 weeks (IQR 6.4-10.4), but EID results were received for only 46.6% within 3 months of birth.	High retention in PMTCT services, triple maternal ART and high infant nevirapine prophylaxis coverage were associated with low mother-to-child HIV transmission. Declining post-partum ART adherence and challenges of EID linkage require attention
Sutcliffe C. et al(43)	Interventional study	Macha, Zambia from 2013 to 2015 among mothers of HEU infants. Mothers were interviewed about mobile phone use and willingness to be contacted directly or through their rural health center.	6% of mobile phone owners were reached by study staff and 98% of mothers without mobile phones were contacted through their rural health center. With increases in the availability of texted results (38 vs. 91%) and arrival of the texted result prior to the hardcopy report (27 vs. 83%). Texted results arriving at the clinic before the hardcopy were received a median of 19 days earlier.	Mobile phone and text messaging technology has the potential to improve early infant diagnosis
Ashiono E. et al(44)	Retrospective cross-sectional study .	2,642 records of HIV-exposed infants analysed.	(42.4%) infants had DNA PCR within the first 6 weeks of age. 72.1%) infants received prophylactic antiretrovirals	EID, maternal & infant prophylaxis were associated with lower rate of MTCT.

CHAPTER THREE: STUDY JUSTIFICATION

Mother-to-child transmission of HIV has been reduced from 14 %(2013) to 8.3 % (2015) in Kenya. (29) The majority of infants born to HIV-infected women, thus, are HIV-exposed uninfected. With high prevalence of HIV infection, especially women of reproductive age[4], HEU infants can comprise a significant proportion of children.

Similarly, the HEU infants form the majority of children aged under 24 months of age in the Lea Toto program. This group faces challenges of unique morbidities in term of severity and frequency of infections. Other factors such as early infant diagnosis, infant prophylaxis, nutrition status, loss to follow up will feature in this study. This is an audit on clinical management of HEU infants.

The morbidity rates of HEU infants are higher than HIV-unexposed (HU) peers. This relates in part to the elevated risk of HEU infants suffer from infectious disease. Specifically, increased risk for contracting infections, higher risk for severity of infection, greater rates of hospitalization, and mortality have been documented in HEU as compared to HU infants. (30)

There are publications on HIV-exposed uninfected (HEU) children in Kenya mainly in research settings. This study seeks to add to the knowledge on HIV-exposed uninfected (HEU) children especially outside the research setting.

The results of this study will inform the Lea Toto program on the clinical management of HIV-exposed uninfected (HEU) children.

3.1 : Research Question

1. Is the clinical management of HEU infants aged 0-24 months at Lea Toto in accordance with national Kenyan guidelines in regards to;

a. ART prophylaxis

b. Early infant diagnosis

c. Infant feeding (EBF and Complementary feeding)

d. Co-trimoxazole prophylaxis

e. Immunization

f. Growth monitoring

g. Recommended follow-up

2. Determine the risk factors for severe illness, seroconversion, and severe malnutrition among HEU children.

3.2 : Study Hypothesis

The hypothesis stated in null:

1. HEU children enrolled in Lea toto program are not receiving recommended care package.

2. Non-adherence to the recommended care package has insignificant impact on vital status and morbidity of HEU children enrolled at Lea toto program.

CHAPTER FOUR: STUDY OBJECTIVES

4.1 Overall Objectives

To evaluate adherence to Kenyan National guidelines in the clinical management of HIV exposed uninfected (HEU) infants aged 0-24 months at Lea Toto program.

4.2 Specific objectives

To determine proportion of HEU children aged < 24months enrolled in Lea Toto program who accessed and adhered to Kenyan National guidelines in the following components:

a) Recommended ART prophylaxis- 12 weeks of infant prophylaxis.i.e. Zidovudine and nevirapine for 6 weeks, followed by nevirapine for 6 weeks. (23).

b) Early infant HIV diagnosis-at 6 weeks age or first contact (if seen after 6 weeks age)

c) Co-trimoxazole prophylaxis-from 4-6 weeks of age to 6 weeks after exclusive breastfeeding stops.

d) Adherence to infant and young child feeding guidelines i.e. exclusive breastfeeding for 6 months then weaning with appropriate foods.

e) Recommended immunization schedule as per KEPI

CHAPTER FIVE: RESEARCH METHODOLOGY

5.1 Study Design

This was a clinical audit study conducted at the Lea Toto Program Nairobi, Kenya in 2018. The study evaluated the clinical management of HIV exposed uninfected infants. This was measured against the recommended Kenya national guidelines. It was a retrospective review of the PMTCT experience in the first 2 years of HEU infants. Data was extracted from the source documents (program EMR) using a standard tool.

Study period: The data collection was in January to February 2018 upon ERC approval. The data collected was for children on follow up since January 2016 while less than 2 years of age.

5.2 Study Setting

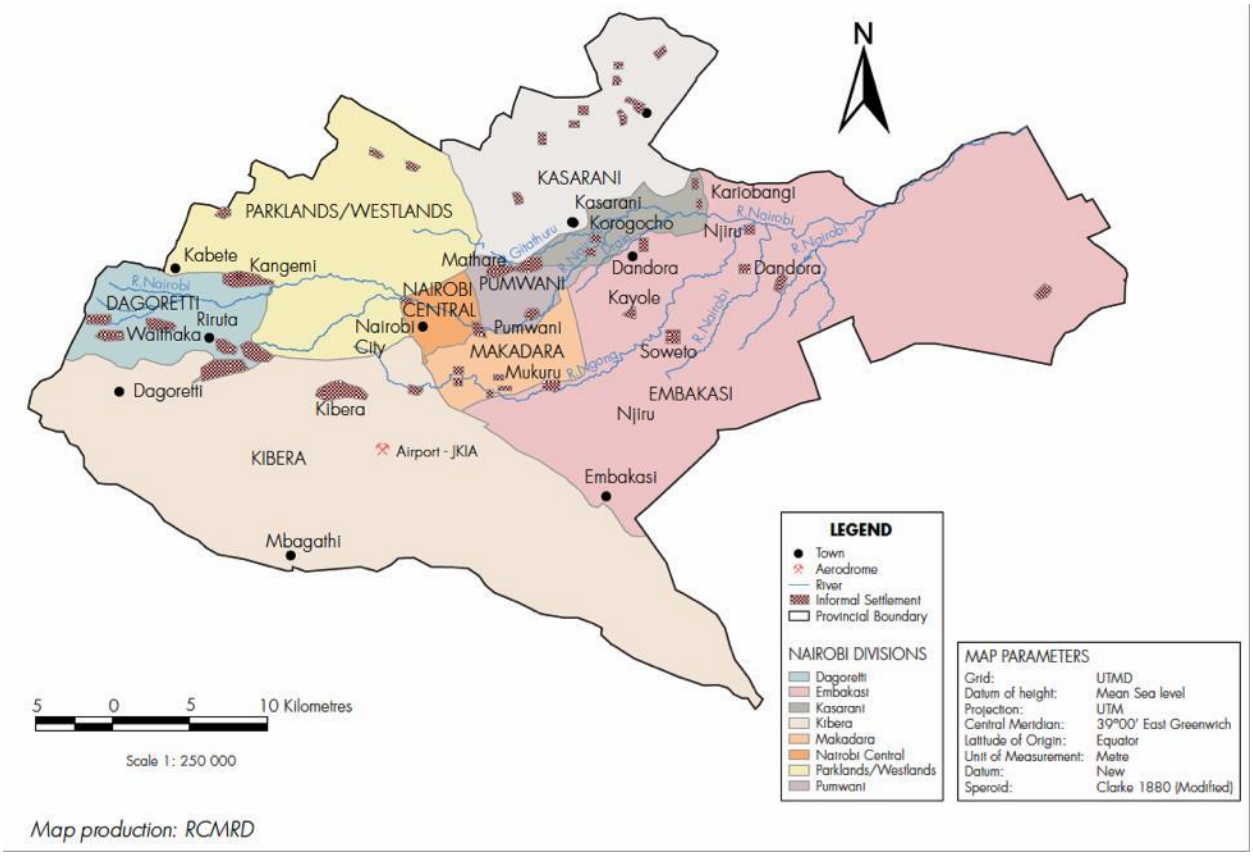
The study was conducted at the Lea Toto program in Nairobi, Kenya. The program manages children who are HIV infected or HIV exposed but uninfected according to the Kenya National guidelines. The children can be as young as 1-day old to 18 years of age. Admission into the program is at any age. The program is community based. It has 8 health facilities.

Each facility has a team including a clinical officer, nurse, nutritionist, counsellor, social worker pharmacy technologist, records officer and community health workers. The children join the program by referral from other health facilities or self-referral by parents or caregivers.

On their first visit the child is registered to the program. They have their vital signs taken by the nurse and nutritional assessment by the nutritionist. The clinical officer takes further history and examines the child and sends them for necessary lab test and gives appropriate prescriptions. The clinician also refers patients who need further management such as inpatient admissions. The lab technologists take patients' blood and other samples for necessary lab tests. The tests are conducted in the facility's lab or main program's lab. The pharmacy issues medicines as per the prescriptions. The pharmacy team monitors for adverse effects of medicines. The counsellor compiles social history of patients and counsels on adherence and other issues eg pretest and posttest counselling. The clinical data is keyed into a computer system which is maintained centrally by monitoring and evaluation team. Patients are on continuous follow-up as scheduled. Patients are not charged fees for services rendered or medicines dispensed.

Lea Toto program also provides livelihood support and as a result attracts children to their facilities away from the County health facilities that also provide the HIV care services without livelihood support.

Figure 4 MAP OF Nairobi informal settlements



The health facilities are located in Kibera, Kangemi, Mukuru, Kariobangi, Dandora, Kawangware, Dagoretti, and Zimmerman. These areas are shown in figure 4. The catchment population in these facilities are of low socio-economic class.Many of them living in informal settlements bearing the same name as the clinics within the city of Nairobi. Most of people living in these informal settlements are unemployed and living on less than $1.00 per day. Persons living in the informal settlements of Nairobi are disproportionately affected by the AIDS epidemic. (40)

The city of Nairobi has an estimated night time population of 3 million people. The city of Nairobi has the highest burden of people living with HIV 177, 155 of the estimated 1.6 million living with HIV in Kenya.

5.3 Study Population

The study population was HEU children who have been followed up in the first 2 years of life in 2016 and 2017 in Lea Toto program. The study included HEU infants who were followed from 0-24 months of age, having been in the program for at least 3 months.

5.4 Case Definition

The study participants were children on follow up while less than 2 years of age in the program.

5.4.1 Inclusion Criteria:

The children recruited met the following criteria to be included into the study:

1. Child's age was 0 to 24 months while on follow up at the Lea Toto program. By end December 2017 the child should be less than 5 years old.

Child had been on follow up for at least 3 months in 2016-2017 while less than 2 years of age.

2. Child was born to HIV infected mother, whether alive or deceased.

3. Child was confirmed HIV negative by PCR at first EID testing. [Subsequent HIV infection maybe as a result of poor adherence to the HIV prophylaxis and other care guideline]

5.4.2 Exclusion Criteria:

Children meeting any of the following exclusion criteria were excluded from the study:

a. Child enrolled after they achieved the age of 21 months.

b. Lack of consent (by parent, guardian or institution) to access medical records, if identifiable information will be used.

c. Child with incomplete medical records.

5.5 Sample Size Determination

The Sample Size was determined using calculation formula in Epi Info, for clinical audit studies.

$$n = \frac{c2Np(1-p)}{(A2N) + (c2p[1-p])}$$

n=is the sample size required=322

N=is the whole target population in question=503

P= is the average proportion of records expected to meet the various criteria (1-p) is the average proportion of records not expected to meet the criteria=50%

A= is the margin of error deemed to be acceptable (calculated as a proportion) e.g. for 5% error either way A = 0.05

C= is a mathematical constant defined by the Confidence Interval chosen i.e. (how sure we need to be of the result) =1.96=95% confidence interval

An expected incidence of 50% i.e. that standards was met 50% of the time. It gave the sample size needed in order to be 95% sure (degree of confidence) that the results obtained from the sample were within 5% (degree of accuracy) of the results you would have obtained for your whole population if you had collected data on all of them.

5.6 Sampling Procedure

Potential study participants were identified by proportionate stratified random sampling in the 8 facilities. The sample size of each facility was proportionate to the population of the facility when viewed against entire population of the program. Hence the facility with more patients had a larger proportion of sample size. Proportionate sampling was applied to ensure all facilities are represented. Every patient within the audit population had an equal chance of selection within their unit.

At each facility all the patients' records (who meet inclusion criteria) were assigned unique study numbers. Study participants were selected by computer randomization that generated true random numbers using atmospheric noise. The records then selected were analyzed for missing

data. Records found to be incomplete were noted and replaced by random selection of another participant.

This resulted in the sample being representative of the characteristics of the whole population, due to random selection reducing the possibility of any systematic bias that would make the selected group different in character from the overall population. To ensure representative results this method was used in conjunction with a calculated sample size.

The records selected were analyzed for necessary information as outlined in data collection tool (appendix 1). Records with missing information were noted. The missing details were noted. The reason for incomplete information was also be noted. This formed part of audit results. It will be used to give feedback on where and why patients' records are incomplete.

5.7: Data Collection, Management and Analysis

5.7.1: Study Procedures:

The data collection was done by the principal investigator. The data was collected in January to February 2018 upon approval by UON-KNH ethics committee**.**

Permission to access medical records was sought from the board of management at the Lea Toto program (attached see consent form-Appendix 3). Once the board granted permission, the principal investigator was assigned a read-only account in programs' electronic medical records. The principal investigator was trained on how to access patients' records by the program's ICT staff. The 8 health facilities were allocated random days for data collection. Permission was sought from the facility in-charge to access patients' records (attached see consent form-Appendix 3). The electronic medical records were accessed only for purpose of extracting data, using a read-only account. The relevant details to this study were as per the data collection tool (appendix 1).

Study participants were identified using serial numbers and no personal identification details recorded. All identifiers such as names, residence,facility name were assigned unique serial numbers .No patient information will be released to an unauthorized third party without prior written approval from the ethics committee. This will ensure protection of health information.

5.7.2 Screening procedures:

Patients' records were screened to ensure study participants met the inclusion criteria. The participants should be younger than 5 years by time of data collection in January 2018.They should be HIV exposed but uninfected on basis of PCR test.They should have been on follow up at the age of 0-24 months. They should have been on follow up for at least 3 months. The participants' records was also be screened to ensure they are complete for all details as per data collection tool.

Data abstraction: A standardized structured questionnaire was used to abstract de-identified data from electronic medical records of the patients. Specifically the tool collected data on the demographic characteristics (age, sex, whether orphaned, maternal education status and use of cART), early infant HIV diagnosis (defined as DNA PCR testing at 6-8 weeks of life), subsequent HIV testing, ART prophylaxis (drugs used and duration), feeding and nutrition status (duration of exclusive breastfeeding, timing of complementary feeds, anthropometric measurements of the child) , morbidity (cause of illness and hospitalization), immunization and adherence to follow up.

5.7.3 Data Collection:

Data was collected by use of a structured clinical audit tool (see appendix 1).

Data was collected in all the 8 facilities. This involved retrieving electronic medical records of the patients. The data will be collected by the principal investigator in January to February 2018.

The data collected included:

Demographic data: gender, current age, age at enrollment in program, caretakers of the child, residence and facility child is attending, vital status of the child (alive or dead) and if still alive, whether they were still on follow up at the age of 24 months.

Details of early HIV infant diagnosis: age at diagnosis and results of first and any repeat testing.

Details of serological HIV testing: age at testing and outcome of tests.

Details of ARV prophylaxis: what ARV was started and at what age, at what age was prophylaxis stopped.

Details of co-trimoxazole prophylaxis: at what age was prophylaxis started and stopped.

Details of primary immunization: is the child appropriately immunized as per KEPI?

Nutrition care of HEU infant: duration of exclusive breastfeeding, whether child continues to breastfeed with complementary feeding,

Growth monitoring and promotion – regularity, and promptness and appropriateness of response for growth faltering [is weight plotted on a growth chart, if not plot and check whether there ever was growth faltering, and how was that responded to]

Regularity of visits – are there clear appointment dates, and does the child attend scheduled visits.

5.7.4 Measurable Outcomes

Primary outcome:

The primary outcome evaluated was whether there is appropriate clinical management of the HEU infants as per current Kenya national guidelines. The following components of clinical care were evaluated.

1. Timeliness of Early infant diagnosis and follow up testing.

- Was the first HIV PCR test done at 6 weeks of age or first contact with the program, if less than 18 months of age?
- Was there HIV PCR testing at 2 weeks after exclusive breastfeeding stopped or after attained 6 months and 9 months of age?
- Was there serology testing at 18 months ± 1 month?
- What was the outcome of the testing?

2. Adequacy of ART prophylaxis

- Has the child ever received ART prophylaxis?

- Is the child on correct ART drugs?
- Is the child on correct duration of ART prophylaxis? 12 weeks nevirapine and 6 weeks zidovudine. Some children enrolled before the new guidelines were implemented could have been on Nevirapine only.
- Adherence to ARV prophylaxis is defined as: Patient has been started on correct antiretroviral, at the right time, on correct dose, for the correct duration and has followed the medical advice.

3. Co-trimoxazole prophylaxis***:***

- Has the child ever received cotrimoxazole prophylaxis?
- Was the child on cotrimoxazole prophylaxis since 4-6 weeks of age?
- Was the child on cotrimoxazole prophylaxis up to at least 6 weeks after exclusive breastfeeding?
- Was the child on correct dose of cotrimoxazole?

4. Primary immunization***:***

- Has the child ever received any immunization?
- Is the child fully immunized?
- What is the timeliness of Immunization:
    - Various antigens within 2 weeks of schedule
    - schedule completed on time – measles, rubella vaccine at 18 months
- What immunization has child missed and why has child missed immunization(s)?

5. Breastfeeding:

- Was the child ever breastfed?

- Was there exclusive breastfeeding up to 6 months? If not what was the duration of exclusive breastfeeding?
- Is the child still breastfeeding?
- If weaned was the child weaned before or after 6 months?

6. Growth monitoring and promotion

- Does the child have anthropometric measures taken on every visit?
- Is there documentation of anthropometric measures?
- I s there timely detection of growth faltering?
- What is the response to abnormal anthropometric measures? Is the response appropriate?

7. Regularity of visits –Are there clear appointment dates? Does the child attend scheduled visits-at least within 1 week? Why does the child miss appointment(s)?

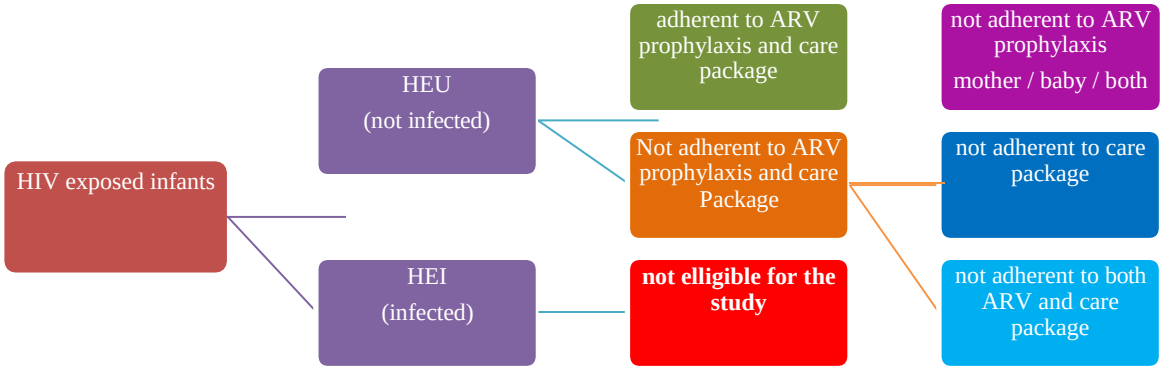
5.8 Data Management

Data was collected and recorded in all the 8 facilities using data collection forms i.e. clinical audit tool (appendix 1).A read only account in the program's EMR system was allocated to the principal investigator. Data was collected by the principal investigator. The investigator got details for study participants on their clinical management since enrollment.

The Data thus obtained was reviewed daily by the primary investigator to identify any errors and omissions before being put into STATA software for analysis. After data entry, hard copies of forms were organized into clearly labeled folders and stored in locked storage units. Access to these files will be limited to authorized persons only. Electronic copies of the data will be kept in the above-mentioned databases, which will only be accessible to relevant staff and will be password protected. Research data will be stored until February 2027. Research project data that is no longer required following the end of the data retention default period (duration of Master of Medicine project, examination, defense and manuscript up to February2027) will be destroyed, subject to the demands of the publication cycle, continuing or follow-on projects. All original hard-copy project data and documentation will be shredded and electronic data will be deleted from computer memory and CD or DVDs destroyed.

5.9 Data Analysis

Figure 5: Categorization of participants



Descriptive statics was used to describe the study population and included age, sex, whether orphaned, age at enrolment into the program, where they live and facility which they were recruited from, whether still in follow-up at age of 2 years and vital status. Further clinical data will be major morbidity (diarrhea and vomiting, pneumonia, malaria, meningitis, or TB (suspected or confirmed) and whether they have been admitted in hospital. Means were used for continuous variables and proportions for categorical ones.

Access to EID-The proportion of children offered EID was total number of children tested as proportion of all HEU children of eligible age group enrolled in the designated time period while timeliness will be testing at point of enrollment.

HIV exposed uninfected (HEU) The total number of children tested/ or identified as HEU based on referral notes on enrolment into the program formed the study population for subsequent analysis. Those enrolled on basis of referral note will require accompanying evidence of a negative PCR test. They should have a repeat PCR in the program which is negative.

Adherence to ARV prophylaxis was analyzed as:

- whether correct drugs were provided,
- whether they were started on time
- Whether they were used for the correct duration of time.
- Ascertain whether the children were given the medicines by parents/guardians. The program has means of knowing if children take their medicine. These include pill counts on clinic appointments, use of patient support groups and psychosocial counseling.
- Review adherence counseling notes

The proportion was estimated by the children who adhered divided by all eligible HEU children.

Adherence to Care package -Each component was analyzed as a binary value (yes/no) [eg. EBF for 6 months yes/no] and then a composite score calculated to determine degree of adherence/access to the care package.

Children who adherent to both the ARV package and other care components were compared to those that are not adherent to determine bivariate and independent predictors of adherence to the comprehensive HEU care package using logistic regression analysis technique. P values derived for chi square tests or Fishers exact tests (for small numbers/ cell count) were used to determine statistical associations. Relative risk and 95% Confidence intervals were computed to determine the significance of these relationships.

All analysis was based on a significance level of 0.05.

5.11 Study Limitations

1. Short period of study as limited to MMed curriculum timelines, this gives no room for re-audit due shortage of time. A re-audit will show if recommendations of the first audit add value.

2. Study design limitations:

Retrospective review of records means there may be missing data. The participants with missing data were replaced. The magnitude and reasons for missing data was captured and discussed in this study.

3. Study setting limitations: Data obtained did not include maternal details of PMTCT. The program manages children only. The study was conducted in the facilities as clinical management of children continued. This means further details during management added after the audit will not be captured in the study.

5.12 Ethical Considerations

Ethical approval was obtained from Kenyatta National Hospital and University of Nairobi (KNH/UON) Ethical Review Committee (ERC) before the study.

Permission was sought from the Lea Toto board of management which is led by the chairperson. The board was requested to allow the investigator to audit electronic records of children aged 0-24 months in 2016-2017 at Lea Toto program. At the facility level, permission was sought from the facility in-charge. These two custodians of the EMR were asked for informed consent. The parents/guardians upon enrolment at the program were informed about possible use of health information for research purposes. Informed written consent was to be sought from the parent if identifiable data was to be obtained. Waiver of consent was applied for access to EMR of participants especially since no identifiable data was be used and no modification of medical management.

All the questionnaires had no identifiers including names of facilities and residence information. There were unique codes for these details to ensure confidentiality. A link log was created in a separate booklet that will link the subjects' numbers on the questionnaires with their names and record codes. The data containing the identity of the subjects will be kept securely under lock while not in use and will not be shared with third parties and all identifiers will be removed during electronic data entry

The study was be carried out based on the ethical standards set out in the ERC guidelines. These standards are as outlined below.

Informed consent:

Informed written consent was obtained from the board of management at Lea Toto program to gain access to EMR. Informed written consent was obtained from facility in-charge at each Lea Toto program to gain access to EMR.

Confidentiality

Strict confidentiality was maintained throughout the entire study period, held in trust by the investigators, research staff and study institutions. Study participants were identified using serial numbers and no personal identification details recorded. No patient information was released to an unauthorized third party without prior written approval from the ethics committee.

The information obtained from the study will then be disseminated through the board of management at Lea Toto. Contacts of the researchers will be given for any further clarifications if need arises.

The results of this study will only be released to the relevant authorities .i.e. the board of management at the program. The results will only be used for academic purposes and quality improvement of healthcare provision.

CHAPTER SIX: RESULTS

A total of 322 electronic medical records of HEU infants at Lea Toto program were evaluated. The study was conducted in January and February 2018.All the eight facilities of Lea Toto participated in the study. At each facility all the patients' records (who meet inclusion criteria) were assigned unique study numbers. Study participants were selected by computer randomization.

Table 5 : Number of children (age 0-24 months) on follow up in clinics and enrolled in study

Clinic	Total HEU followed up N=503	Total infected children N=33	Total No. of children in clinic .N=556	No. of HEU children in study N=322	% of HEU children in study
Dandora	33	4	37	21	6.57
Kariobangi	67	6	73	43	13.32
Dagoretti	38	-	38	24	7.55
Zimmermann	91	2	93	58	18.09
Kawangware	63	3	66	40	12.52
Mukuru	80	6	86	52	15.9
Kibera	71	7	78	45	14.12
Kangemi	60	5	65	39	12

Table 5 shows the proportion of children on follow up in different clinics and the children enrolled in this study. There was proportional random stratified sampling, hence the clinic with more children had a larger proportion of children enrolled in the study.

5.1 Demographic Characteristics of Participants

Current age of participants

The current age of the participants was ranging from 3 to 24 months. The participants were stratified in age groups for the sample size to be representative.

Table 6: current age at time of study

Age group	N=322	%
0-6 months	80	24.8%
7-12 months	80	24.8%
13-18 months	81	25.1%
19-24 months	81	25.1%

Table 7: Age at enrolment into Lea Toto Program

Age at enrolment	N=322	%
0-2 weeks	50	15.53%
3-5 weeks	63	19.57%
6 weeks	86	26.71%
7 weeks -9 weeks	58	18.01%
10 weeks-6 months	37	11.49%
7 -12months	21	6.52%
13-24 months	7	2.17%

The children were enrolled into the program from as early as 3 days of age up to 20 months of age.50 (15%) of the study participants were enrolled before 2 weeks of age into Lea Toto. The majority were enrolled at 6 weeks of age .i.e. 86 participants (26.8%).There were 28(8.6%) children enrolled after 6 months of age. The mean age of enrolment was 2.85±0.5 months with median age of 1.5 months (IQR 3). Most of the children enrolled later, because their mothers knew their HIV status after giving birth.

Gender

Table 8: gender profile of study participants

		n=322	
Gender	Male	160	49.6%
	Female	162	50.3%

There were 162(50.3%) female and 160 (49.6%) male participants.

Referral sources to the Lea Toto program

The study participants were referred to Lea Toto by various means.CHWs referred 125 (38.8%) participants to the program, 87 (27%) by fellow caregivers with children in the program and 58 (18.1 %) were referred from other health facilities. There were 52(16.1 %) participants who were self-referrals by their parents or caregivers.

Table 9: caregivers' characteristics

Caretaker	No.	%
Both Parents	182	56.5
Mother only	114	35.4
Father only	2	0.7
Orphan	24	7.4

Table 10: Caregivers Education background

Education level	primary	Secondary	tertiary	Never attended
Mother	167(56.42%)	94(31.7)%	26(8.78%)	9(3.04%)
Father	82(43.68)%	78(41.57%)	27(13.9%)	3(1.58%)

Table 11: Caregivers' Occupation

Caretakers occupation	Mother	Father
Salaried employment	17(5.74%)	25(13.6%)
Casual labor	79(26.68%)	89(46.84%)
Self employed	49(15.2%)	10(4.8%)
Unemployed	151(51.7%)	66(34.73%)

Table 12: Caretakers' age

Age group	Mothers NO. & %	Father NO.& %
< 18 years	7 (2.36%)	0
18-20	61(20.6%)	6(3.15%)
21-30	169(57.1%)	94(49.4%)
31-40	42(14.2%)	63(33.15%)
41-50	17(5.74%)	24(12.63%)
>51	0	3(1.58%)

Most children were under the care of both parents. There were 7 (2.36%) mothers who were under 18 years of age. These mothers were clients at the Lea Toto program. The mean age of the mothers was 29.1±1.2 years and the median was 30 years.

Most mothers at 151(51.7 %) were unemployed, 47(31.12%) of these mothers were single parents.

Most mothers at 167 (56.42%) had only attained primary level of education. There were 9 (3.04%) mothers who never attended school.

5.2 Early infant diagnosis and subsequent HIV testing

The timing of the first HIV PCR test among study participants was from 3 days to 20 months of age, and 251 (91.5%) had first PCR done at 6 weeks as recommended. The mean age of first HIV PCR test was 2.0±0.5 months and the median was 6 weeks age (IQR 4.5).

Table 13: Age at first HIV PCR testing

Age groups	No. of HEU enrolled N=322	No of HEU who had first PCR N=322	%PCR at first contact
0-2 weeks	50	44	88%
3-8 weeks	189	183	96.8%
9weeks-6months	55	73	132%*
7-24 months	28	16	57.1%

*There were 6 patients enrolled when 3-8 weeks old but had 1st PCR done at 9 weeks-6 months. There were 12 children enrolled when 7-24 months old and had PCR done at 9 weeks – 6months at other facilities before enrolment.

The PCR testing at first contact was from 57-96%, highest among children enrolled at 3-8 weeks. Some children enrolled later had PCR done before enrolment

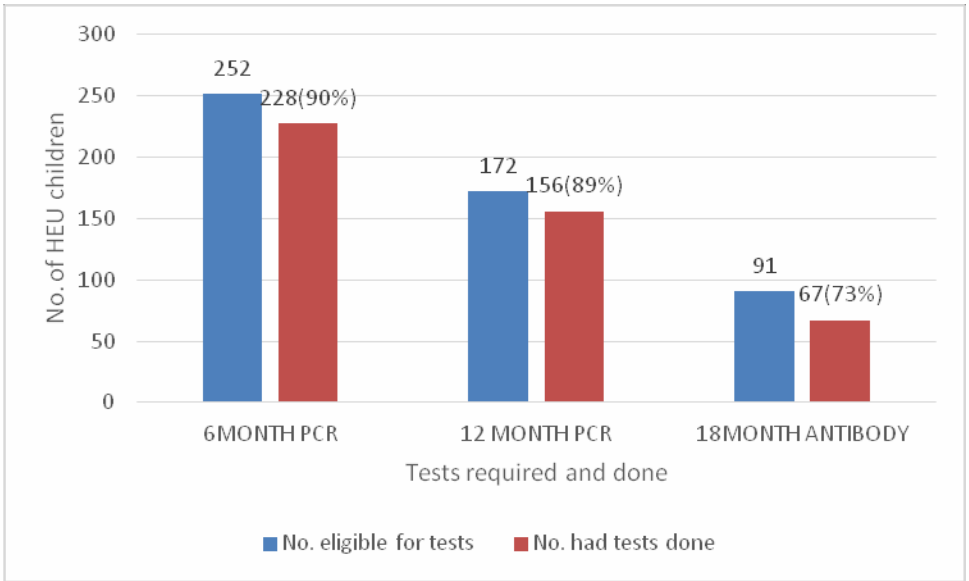
The results of the first HIV PCR for all the participants were negative, as required of the inclusion criteria.

The subsequent HIV testing was as shown in the table below. These results are stratified .e.g. for participants aged 6 months and above, 90.6% had the 6 month HIV PCR test.Testing after cessation of breastfeeding was not regularly practiced in the program.

Table 14: Subsequent HIV testing

Recommended subsequent HIV tests	No of HEU children eligible for HIV tests* N=322	No. of HEU children who had tests done timely**N=322	% uptake of HIV tests
6 months + 1 week	252	228	90.6%
9 months	202	84	41.6%
12 months	172	156	89.7%
18 months	91	67	73.6%
*These were children currently eligible for tests during study period **This indicates children who received the test within the recommended age.			

Figure 6: Subsequent recommended HIV testing



The 6 month PCR had the most uptake with the 18 month antibody test having the least uptake.

5.3 ART and cotrimoxazole prophylaxis

From 2016 according to Kenyan national guidelines, ART prophylaxis recommended is 12 weeks of infant prophylaxis. That is zidovudine and nevirapine for 6 weeks, followed by nevirapine for 6 weeks. (23).

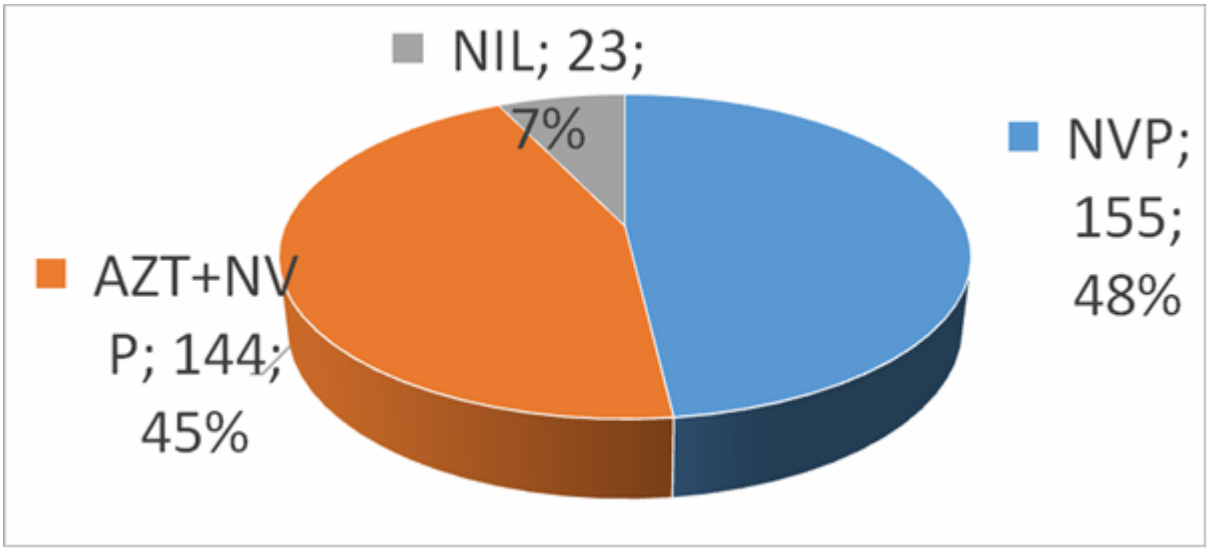
Overall 299 (92.8%) of the 322 participants received ART prophylaxis, 144 (44.7 %) the recommended combined Zidovudine (AZT) + Nevirapine (NVP) prophylaxis, and 155 (48%) only NVP.

There were 89 (27.6%) children enrolled before start of ART prophylaxis, 79(87%) were documented to have started ART prophylaxis upon enrolment.

Only 217 (67.39%) participants started ART prophylaxis on first day of life even before enrolment in the program. There were 25(7.8%) children received a shorter course of prophylaxis because of loss to follow-up, orphaned children whose HIV test was negative and children who were on follow up in other institutions where prophylaxis was done for shorter duration of time. Another 78 (24.2%) children received more than 3 months prophylaxis due to heightened risk of infection because their mothers had not achieved viral suppression, mothers not on HAART or diagnosed in the postnatal period.

There were 23(7.2%) study participants who did not receive any ART prophylaxis in the program. These were children who had either completed ART prophylaxis in other facilities before enrolment at Lea Toto, those enrolled after they had ceased breastfeeding or their mothers were diagnosed with HIV after they had stopped breastfeeding or orphaned children whose EID HIV test was negative.

Figure 7: ART prophylaxis received by HEU infants



Overall 265 (82.3%) participants were on cotrimoxazole prophylaxis. The prophylaxis was started as early as day 1 of life to 9 months of age. The majority of participants 178 (55.28%) were started at 4-6 weeks of age. There were 13 (4.03%) of participants started before 4 weeks of age. Appropriate discontinuation of cotrimoxazole prophylaxis was done for 51 (15.83%) at 18 months.

5.4 Morbidity of HEU infants at Lea Toto program

The common diseases affecting the participants were as shown in Table 13.

Table 15: Morbidity and age at diagnosis

Diagnosis	No. of children affected	%	Median age at diagnosis
Acute respiratory illness	303	94.09	9 months
gastroenteritis	153	47.51	7 months
Eye discharge	67	20.8	2 months
Skin rash	40	12.42	8 months
TB	3	0.93	13 months

Most of these were managed as outpatient. The children received their treatment for free at Lea Toto facilities. The common diseases affecting the participants were as shown in Table 3. Overall 303 participants experienced at least one episode of acute respiratory infection (ARI), 12 (3.7%) severe enough for hospital admission. From the medical records, the severity of ARI was not clarified. Only 3 (0.9%) children were diagnosed with tuberculosis. Other than TB, median age at diagnosis of these conditions was in the first year of life. Most of these conditions were managed as outpatient. The children received free treatment at Lea Toto facilities.

The rate of hospital admissions was 8.07% with 26 of the participants being admitted.

Table 16: Conditions necessitating hospitalization.

Diagnosis	No. of participants	% of participants	Median age at diagnosis(in months)
Gastroenteritis	16	4.9%	8
Acute respiratory illness	12	3.72%	10
Tuberculosis	2	0.62%	13
Neonatal sepsis	3	0.93%	1
Neonatal Jaundice	1	0.31%	1
Prematurity	4	1.24%	1
Anemia	3	0.93%	4
Malaria	5	1.55%	9

5.5 Feeding history and nutrition Status of the participants:

Overall 282 participants reported that they exclusively breastfed their infants among them 214 (66.45%) who reported 6 months of exclusive breastfeeding, 58 (18%) for 5 months and 10 (3%) for less than a month. None of the mothers had chosen replacement feeding. Overall 254 (78.8%) children were breastfed as recommended .i.e. exclusive breastfeeding for 6 months then addition of appropriate complementary feeds while continuing to breastfeed for at least 12 months. The total duration of breastfeeding even after introduction of complementary feeding was not documented.

Overall 72 (22.4%) experienced some malnutrition including 43 (13%) with moderate malnutrition [Weight for age (W/A) range -1 to -2 standard deviation (SD)], 13 (4%) stunted [height for age (H/A) Z score < -3], 9 (3%) wasted [weight for height (W/H/) Z score < -3], while 7 (2%) both wasted and stunted. The median age for diagnosis of wasting was 13 months and the range was 2-24 months. The median age of stunting was 14 months with a range of 10-24 months. Out of 29 participants with severe malnutrition, 26(89.65%) were appropriately diagnosed and managed. The plotting of child's weight and height in recommended growth charts was not regularly done.

Figure 8: Nutrition status of HEU children

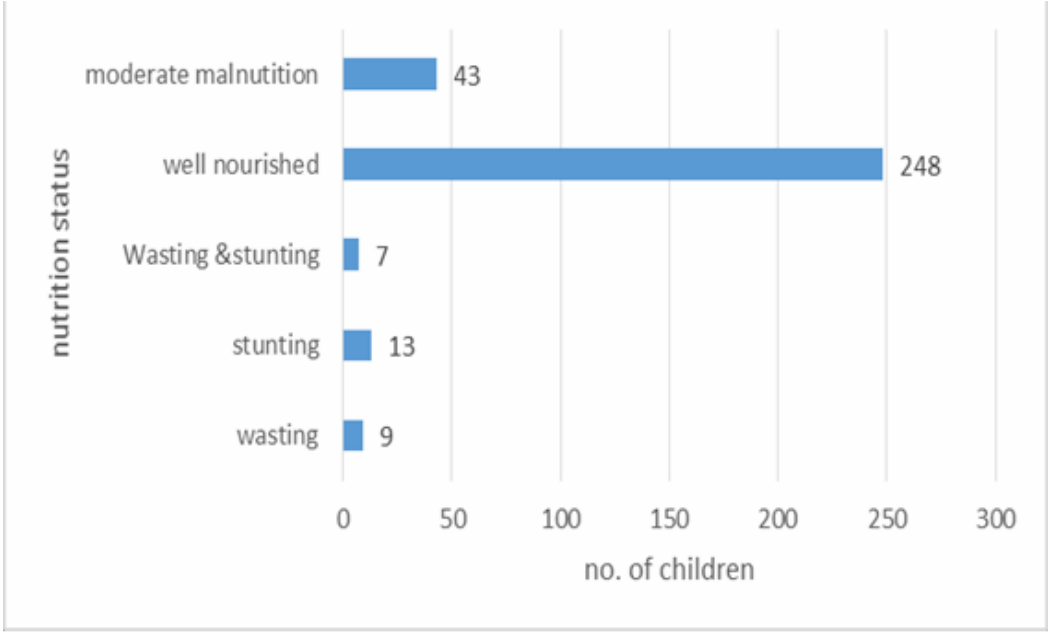


Table 17:Factors associated with nutrition status of HEU infants

Variable	HEIs without severe malnutrition n=291	HEIs with severe malnutrition n=29		O.R (95% C.I)	p value
Wasting WHZ>-3 Stunting Wasting stunting	291 291 291	9(2.79%) 13(4.04%) 7(2.17%)		-	
Age at enrolment 0-6 months 7-18 months	272(93.47%) 22(7.56%)	9(2.79%) 20(6.21%)	**Age at diagnosis** 8(2.48%) 21(6.52%)	1.0 (ref) 27.5 (11.2,65.5)	<o.oo1
Mother's education Primary & Never attended Secondary &Tertiary	158(54.3%) 112(38.49%)	18(5.6%) 8(2.48%)		1.59 (0.67-3.79)	0.02
Mother's occupation Unemployed Working mother	151(51.89%) 143(49.14%)	17(5.28%) 8(2.48%)		2.01(0.84-4.81)	0.01
Exclusive breastfeeding for 6months Yes No	184(63.23%) 107(36.77%)	14(4.34%) 15(4.65%)		1.84(0.85-3.96)	0.01
Nutrition management Appropriate Inappropriate	- -	26(8.07%) 3(0.93%)		-	

The HEU children with severe malnutrition were compared to those that were well nourished. They were comparable in terms of mother's education status as well as employment status. A similar proportion of children(both well nourished and not) were exposed to exclusive breastfeeding for 6 months. The only difference between well nourished and poorly nourished HEU was the age at which they enrolled into the program. Only 20% of the malnourished HEU enrolled into the program by 6 months of age compared to 93.4% of the well nourished HEU. Children enrolled in the program after the age of 6 months had 27 fold increased risk of being malnourished – OR=27.5 [(95% CI 11.2,65.5), $p < 0.001$Fischer's exact test].

5.6 Patient follow up and defaulting rate:

Majority of study participants at 246 (76.3%) were on ongoing follow up without missing clinic appointments. There were 53 (16.4%) participants who were officially discharged after negative antibody test at 18 months.

There were 23 (7.14%) participants who were lost to follow up. Loss to follow up was defined as missing a scheduled clinic appointment for more than 1 week. Out of 23 participants who were lost to follow up, only 11 resumed follow up at the program.

The median age of loss to follow up was 9 months. The reasons for loss to follow up include: lack of transport means/monies, relocation, mother's illness and mothers were busy at work.

5.7 Immunization status of participants according to KEPI

The immunization status was up to date for 301 (93.7%) of participants on their first visit to the program. Out of 301 participants, only 204 (67.77%) had their immunization status updated to the last clinic visit. Lack of proper documentation of immunization status was noted .This may be attributed to children being immunized at other clinics (Lea Toto doesn't offer immunization services) and immunization card/book not presented during consultations at Lea Toto.

The reasons for missed immunization were home delivery, hospital admissions and abandoned, orphaned children.

5.8 Seroconversion:

There were 4 children whose subsequent HIV tests turned positive. Their characteristics are described in the table below.

Table 18:Factors associated with seroconversion in HEIs

Variable	Seroconversion N =4	No seroconversion N =318	O.R	CI 95%	P Value Fischers exact test
Mother's education Primary & Never attended Secondary &Tertiary	2 2	165 92	1.7	0.24 to 1.2	0.05
Mother's occupation Unemployed Working mother	3 1	148 144	2.9	0.3 to 2.8	0.07
Exclusive breastfeeding for 6months Yes No	1 3	213 105	6	0.6 to 5.9	0.1
Current age 0-12 months 13-24 months	1 3	159 159	3.0	0.30-29	0.6
Age at enrolment 0-12 months 13-24 months	1 3	311 7	13.3	12.28-1445	0.001
ART prophylaxis- Appropriate Not appropriate	1 3	318 -	undefined	-	0.02

EID Complete Incomplete	 1 3	 238 80	 8.7	 0.8-84.5	 0.1
Nutrition status Normal malnutrition	 - 4	 241 77	 undefined	 	 0.008
Hospital admission Yes No	 2 2	 19 299	 15.7	 2.1-117.9	 0.04

Three of the four HIV infected children were aged 13-24 months and they had been enrolled when they were aged 13-24months. Again 3 of the 4 infected children did not receive the appropriate ARV prophylactic regimen and they did not access EID. All 4 children who sero-converted were malnourished and 2 of them were admitted into hospital. The 4 children who seroconverted were of similar age to those that did not. However among the infected, 3 (75%) out of 4 children were enrolled in the second year of life compared to 7 (2%) of 318, OR 13.8 [(95% CI 12.3-1445), p=0.001]. All 318 children who did not sero-convert received appropriate ARV prophylaxis compared to the 3 (75%) of the 4 who were infected (p=0.02)

All children who sero-converted were malnourished compared to 77 of the 318 children who were not infected and this difference was significant (p=0.008 Fischer's exact test). The infected children experienced a higher hospital admission rate compared to those who were not infected 2 (50%) compared to 19 (5.9%) OR=15.7 (2.1,117.9).

5.9 Missing details in medical records

Table 19: Missing details in medical records

Details missing	No. of medical records
Demographic characteristics:	
Current age	-
Age at enrolment	-
Gender	-
Referral source	4
Residence	3
Who is the child's caregiver?	
Care giver's age	1
Caregiver's education	2
Caregiver's occupation	1
First HIV PCR results	-
Subsequent HIV results	**4**
ART prophylaxis (specific medicines)	3
Date started ART prophylaxis	7
Date finished ART prophylaxis	8
Morbidity	
Whether the child has been unwell?	-
Whether the child has been admitted?	2
Nutrition status	
Weight	2
Height	3
MUAC	12
Immunization:	
Is child fully immunized?	14
What immunizations has child missed?	26

The immunization status was not regularly updated, since the program doesn't offer KEPI services.

5.10 : Program performance

Table 20_ Program performance

	ART	**CTX**	**EID**	**6 months PCR**	**9 month PCR**	**18 month antibody testing**
Number receving service at enrollment (a)	217	178	298	216	81	81
Number eligible for the service (b)	322	293	322	252	202	91
Number provided the service (c)	295	265	322	239	135	86
Effectiveness of the program c/b	91%	90.4%	100%	94.8%	66.8%	94.5%
Service coverage (a+c)/a+b	95.7%	94.05%	100%	97.2%	76.3%	97.1%

Table 20 shows the performance of the program over the period of observation. There was effective coverage of the essential HIV care package for the children enrolled into the program other than the 9 month HIV test.

CHAPTER SIX: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

6.1 Discussion

The study participants 294(91.3%) were mainly enrolled at 0-6 months of age, especially at 6 weeks of age 86 (26.8%). This corresponds to the timing of first or second HIV PCR test.These children also come for refill of their prophylaxis and adjusting of doses at 6 weeks of age.

Community health workers (CHWs) referred children from the community to the program for nutritional and medical management of various ailments. The children enrolled in later months are on continuing nutrition management and are on follow-up even after negative test at 18 months. It was observed that the program worked closely with CHWs.This is vital in ensuring ongoing follow up at home and community health outreach.

The children's caregivers were mainly both parents 182 (56.5%) but majority were separated. Most parents were unemployed or in casual labor. Most mothers at 151(51.7 %) were unemployed, 47(31.12%) of these mothers were single parents. The socioeconomic status of the families of HEU children is critical for their care. Most children from broken homes, young and unemployed mothers suffered malnutrion.Fortunately with regular growth monitoring and promotion at the program, malnutrition was appropriately diagnosed and managed. The program also offer family food support and other livelihood needs such as rent, beddings and transport monies to needy families.

The program receives children after they have been delivered in other facilities and already on ART prophylaxis. This proved to be challenging. Sometimes one has to rely on mother's history on when prophylaxis was started and if the medicines are adhered to.

Despite the national HIV guidelines amendment to include zidovudine as part of prophylaxis, most children enrolled early 2016 were on nevirapine prophylaxis only. There were only 144(45%) on AZT+NVP. The program staff then have to start the zidovudine later than recommended. This is critical as appropriate ART prophylaxis ensures HEU children don't seroconvert. The program needs to give feedback to referring health facilities if the children are not on appropriate ART.

The duration of ART prophylaxis for some participants were not appropriate. For instance its recommended if a breastfeeding mother refuses to start ART but agrees to provide infant ARV

prophylaxis, provide 6 weeks of AZT+NVP, followed by daily NVP until 6 weeks after complete cessation of breastfeeding. If mother has viral load ≥ 1,000copies/micromoles, continue infant prophylaxis until confirmed viral suppression or 6 weeks after complete cessation of breastfeeding. These special recommendations were not followed in the above mentioned circumstances and these children were put on similar prophylaxis as children whose mothers were on HAART and virally suppressed. This is challenging since the mothers are not managed at the program.

The national guidelines recommends that all HIV exposed infants should receive Co-trimoxazole prophylaxis from 6 weeks of age to 6 weeks after exclusive breastfeeding stops. WHO estimate that only 8% of children exposed to HIV were initiated on co-trimoxazole prophylaxis by two months of age (23). Similarly at the program some children (17%) were not on cotrimoxazole prophylaxis at any point of management.

There were challenges with early infant HIV diagnosis. The tests were conducted when the child was enrolled at first contact, for 287(89.13%) participants especially if not done at referring facility. This may not be the same timings as recommended by national guidelines. For instance a child enrolled at 5 months age will have a PCR test at enrolment. The same child is expected to have HIV PCR at 6 months age. Some children were no longer brought to the clinic once their PCR test turned negative and child was not breastfeeding. This resulted in low turnout for the 18 month antibody tests. However the social worker and CHWs organize for home visits to ensure children resume follow up.

The turnaround time for HIV PCR results was as long as 2 months. For instance there were 3 infants who were initially managed as HEU as results were pending, but their first HIV PCR turned positive. These children had initial high viral loads due to late start of HAART.

The above mentioned challenges hindered full turn out of the recommended HIV tests. In our study there was only 79% uptake of the 6 week PCR test. In a review by Celleti (16) only 39% of children in low-income countries were estimated to have access to HIV testing within the recommended 2 months of birth.

According to a study by Ashiono (44) in a retrospective cross-sectional study that analyzed 2,642 records of HIV-exposed infants in north rift Kenya, (42.4%) infants had DNA PCR within the

first 6 weeks of age. In that study only 72.1% infants received prophylactic antiretroviral, in this study ART prophylaxis was given to 92.8% of participants at Lea Toto program.

According to the ZVITAMBO trial (35), compared with not-exposed infants, sick clinic visits were 1.2 times more common among HEU infants. In a cohort study in Uganda (45), non-breastfeeding HEU, from 6-11 months compared with non-breastfeeding HUU had a higher risk of hospitalizations, severe febrile illness, severe diarrhea and severe malnutrition. In this study at Lea Toto HEU children were seen severally for various diseases, some even before scheduled appointments. There were study participants who ended up being hospitalized due to the severity of their illness. There were others who required further specialized treatment e.g. recurrent eye discharge not responding to treatment.

In a study by Gichuhi (31) that followed 351 HEU infants from neonatal period up to 1 year of age, common medical conditions included bronchopneumonia, diarrhea and failure to thrive. These were similar to the medical conditions leading to hospital admissions in this study.

Malnutrition was observed in majority of study participants. The children who were not exclusively breastfed had higher risk of malnutrition OR=1.84 95%CI 0.85-3.96 and severe illness. More than half (56%) of the participants with wasting were not exclusively breastfed. Among the children who were treated for severe illness requiring admission and specialist follow up, 58.1% (OR: 1.22; 95% CI: 0.99 p) were not exclusively breastfed for 6 months.

The immunization status of the children was mainly recorded in the first visit to the program. The follow up immunizations after first visit was not recorded for most of the children. The immunization of HEU infants is critical in ensuring disease prevention. HEU infants have altered cell-mediated and humoral immunity, this coupled with lack of immunization increases their risk to acquire severe childhood illnesses which are preventable.

The children lost to follow up before official discharge, majority 13 out of 23 did not resume follow up. There was no documentation on home visits or phone call to ascertain child's whereabouts.

The seroconversion rate in this study was 1.24 %(95% C I: 0.34, 3.15). Factors associated were late enrolment to program, incomplete EID and inappropriate ART prophylaxis. A meta-analysis including 9 studies, 3688 mother-baby pairs in Ethiopia (46), the pooled prevalence of MTCT of HIV was 9.93%. Associated factors with MTCT of HIV include: mixed feeding, absence of infant ARV prophylaxis, home delivery, and absence of maternal PMTCT intervention.

The program is different from research based programs. The program's facilities are located in the community, increasing accessibility. Furthermore the program works with CHW to ensure community involvement. It is also run by local (Kenyan) technical staff, with guidance from national guidelines with minimal supervision. This makes the model more sustainable. Most research based programs are run by specialists and researchers, sometimes from international organizations who have oversight by international organizations. Most research based programs run for a limited period of time.

6.1.1 Limitations:

Although the study had limitations, every attempt was made to minimize their effects on the study outcome.

The study results were based on documentation of patients' details in the program's EMR.The validity of this information could only be ascertained by trusting that the program's healthcare professionals were accurate in their documentation.

The management of HEU children has been changing based on changes made in national HIV management guidelines. This means all children could not be subjected to a single, standard criteria.

Lack of PMTCT maternal details in child's medical records.This mainly because the program caters to children only

There were missing details in some of the patients' records. These records were excluded from the study. Ideally all records were to be audited for proper evaluation to be done.

6.2 Conclusion:

Overall 299 (92.8%) of the 322 participants received ART prophylaxis. The PCR testing at first contact was from 57-96%, highest among children enrolled at 3-8 weeks. The 6 month PCR had the most uptake (90%) with the 18 month antibody test having the least uptake (73%).

There were 9(2.79%) participants with weight for height Z score > -3SD. Stunting was observed in 13(4.03%) study participants. Out of 29 participants with severe malnutrition, 26(89.65%) were appropriately diagnosed and managed. The children who were not exclusively breastfed had higher risk of malnutrition OR=1.84 95%CI 0.85-3.96.Among the children who were treated for severe illness requiring admission and specialist follow up, 58.1% (OR: 1.22; 95% CI: 0.99 p) were not exclusively breastfed for 6 months.

Children enrolled in the Lea Toto program are accessing the essential HIV care package. Late enrollment into the program was associated with increased likelihood of malnutrition and HIV infection.

6.3 Recommendations

- The HEU children require regular HIV testing as recommended in the national guidelines. This will ensure seroconverted infants are detected early.
- ART prophylaxis need to be appropriate i.e correct medicines, correct duration. Children with special circumstances .e.g. Mom is not HAART need appropriate adjustments of ART prophylaxis.
- Immunization status needs to be regularly monitored and documented.
- Cotrimoxazole prophylaxis should be administered to all children, it aids in prevention of illnesses such as gastroenteritis, pneumonia.
- Regular growth monitoring and promotion will ensure timely diagnosis and management of malnutrition.
- There needs to be follow up for children who have defaulted clinic appointments.
- The referral sources can be advised to refer children early to ensure prompt, appropriate management at the program.
- The program's EMR system needs to be adjusted to include maternal details e.g. antenatal details, ARV use, viral suppression, and labor and delivery details.

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STUDY TIMELINE

ACTIVITY	START	END	DURATION
Concept development	Sep 2016	Oct 2017	2 months
Concept presentation to Prime K for funding	Oct 2017		1 month
Concept presentation to faculty	April 2017	May 2017	2 months
Proposal to ERC	June 2017	August 2017	3 months
Data collection	September 2017	October 2017	2 months
Data entry	September 2017	January 2018	2 months
Data analysis	September 2017	Jan 2018	2months
Posters to faculty	May 2018	May 2018	1 month
Handing in books for marking	End of May 2018	June 2018	Month
First internal marking	June 2018		
Student corrections	1st 2 weeks of July 2018		
2nd internal marking	Last 2 weeks of July 2018		
Books sent to external examiner	August 2018		

Clinical audit on HEU infants care at Lea toto program

BUDGET FOR RESEARCH

ITEM	QUANTITY	UNIT PRICE	TOTAL (KSH)
SUPPLIES			
Biro Pens	8	20.00	160.00
Pencils	8	10.00	80.00
Box file	5	150.00	750.00
Spring files	4	100.00	400.00
Pencils sharpener	1	50.00	50.00
White out pen	4	150.00	600.00
Folder	6	50.00	300.00
Staple	1	500.00	500.00
Paper Punch	1	600.00	600.00
Staple Romover	1	250.00	250.00
Dicta phone	1	15,000.00	15,000.00

Note book	8	100.00	800.00
TOTAL SUPPLIES			**19,490.00**
OTHERS			
Printing	15	10.00	150.00
Photocpying	8250	2.00	16,500.00
Final proposal booklet	12	1,500.00	18,000.00
Ethic committee fee	1	2,000.00	2,000.00
A poster	4	3,000.00	12,000.00
TOTAL OTHER			**48,650.00**
Transport	**1**	40,000.00	40,000.00
Communication	**1**	5,000.00	5,000.00
Data Stastitian	**1**	15,000.00	15,000.00

Research Assistant & other related Expenses			
Cost of training for Research Assistants (2 days training)	12	800.00	9,600.00
Payment to research Assistants	8	2000.00	16,000.00
Dissemination cost	8	5,000.00	40,000.00
TOTAL PERSONNEL			**55,600.00**
TOTAL EXPENSES			**164,250.00**

Appendix I: Clinical Audit Tool

Study Tittle: Clinical audit on management of HIV exposed uninfected (HEU) infants aged 0-24 months in 2016/17 at the lea Toto program, Nairobi, Kenya.

Date of data collection…….

Study ID…….

Research Instructions:

- The principal investigator will fill in the necessary details below as recorded in the program's EMR.
- No identifiable data such as patients name,facility name or residence addresses will be indicated in this tool.
- This form needs to be completely filled to be deemed valid.

Demographic data

1. (a) Current age of patient (in months) …….....

……

(b)Age at enrollment in program (in months)

……..……..……

……

2. Gender male ☐ female ☐

3. Who referred the child to the Lea toto program (choose appropriately)

- Self-referral by parent ☐
- Referred from another health facility ☐
- Others (specify)…….

4. Who is the caretaker of the child, (tick as appropriate) .What is their level of education and occupation?

Caretaker	Tick	Education (primary,secondary,tertiary	Occupation of caretaker
Motheronly			
father only			
Both mother and father			
Other relatives or guardians			

5. Which health facility is patient on follow up (tick as appropriate) and where do they reside?

Health facility	Tick	Area of residence (sub county and location
LT1		
LT2		
LT3		
LT4		
LT5		

LT6		
LT7		
LT8		

Early infant HIV diagnosis and follow up tests

6.a) Age at which first DNA PCR was done……..

(b)Where was the first PCR done……..

7. What was the result of first DNA PCR……

8. Did the participant have the following HIV test and what was the result?

Age at time of testing	Test done(PCR/antibody)	Done: yes/no	Result of test
Birth to <6 weeks age	PCR		
6 weeks	PCR		
6 months&1 week	PCR		
9 months	PCR		
18 months	Antibody		

ART, PCP prophylaxis and IPT

9. (a)At what age was IPT, ARV and PCP prophylaxis was started and completed(specify in table below)?……

ART, PCP prophylaxis and IPT	Age started	Age stopped
ART prophylaxis		
PCP prophylaxis		
IPT		

(b) Did the participant take all the medicines as prescribed?What means were used to determine if all medicines were taken as prescribed?.....

(c) Did the participant have adherence issues?(Yes/No)What were the issues?.....

(d) Was adherence counselling done?(Yes/No)How many sessions?.....

(e) What were the reasons for non adherence to medicine?.....

(f)What interventions were done for non –adherence?.....

(g) Did the child later on adhere to medicines and medical advice after interventions?.....

…….

10. (a)What ART prophylaxis was child started on (specify details in table below)……

ART prophylaxis	Age started	Age stopped
NVP		
AZT		
Others(specify and reason why this specific drug was given)		

Morbidity of HIV exposed infant

11. Has the child ever been unwell since birth……..….

12. What was ailing the child and at what age……

……

13. (a)Has the child ever been admitted for any illness (specify illness and duration of admission)

Nutrition

14. What was the mode of feeding for first 6 months of life……

……

15. At what age were other foods other than breast milk introduced……..……..

16. Is the nutritional status of the child appropriate? If not what nutrition management was done?

17. Specify nutritional issues according to WHO Z scores.

Nutritional status	Age at diagnosis	Nutrition management
Wasting > or = -3		
Stunting> or =-3		
Underweight -1 or - 2		
Wasting with edema		
overweight		

18. Until what age was the child on follow up until official discharge from the program, if not at what age was child lost to follow-up……..

19. Are the reasons for loss to follow up known? If yes, what are the reasons…….

……

20. Did the child resume follow up and after how long?……

……

21. Is the child fully immunized for age as per KEPI? Yes/No. If not what immunisations has the child missed and what is the reason?.....

22. What is the vital status of the patient?

Alive ☐ Deceased ☐

Appendix 2: Informed Consent Form (ICF) for parents

2a) Consent (English)

Informed Consent Form (ICF) for parents of children between the ages of 0 and 24 months who are HEU and on follow up at Lea Toto program in 2016/17.

Principal investigator: Dr. Edith Wacera Kagunda

Institutions: University of Nairobi and Lea Toto program

PART I: Information Sheet

I am Dr. Edith Wacera Kagunda a postgraduate student at the University of Nairobi, Department of Pediatrics. I am conducting a study as part of the requirement for the degree of Master of Medicine in Pediatrics. The study aims to evaluate the management of HEU children aged 0-24 months in 2016/17 at the Lea toto program.

HIV exposed but uninfected children form the majority of children born to HIV positive mothers. Their care is critical to ensure they remain HIV negative. They need to be diagnosed early and started on appropriate ART prophylaxis. They also need to be fully immunized according to KEPI. They also require regular growth monitoring and promotion. They also face unique challenges when they are unwell and require appropriate management of illness.

Evaluation of their clinical management is necessary and a quality improvement exercise.

The benefits of your child participating in this study are: to ascertain the child has appropriate clinical management which ensures better outcomes. It will also highlight area of improvement in clinical management. Your child will not have alterations in their management as per national guidelines.

By participating in this research it is possible that your child's health information will be discussed and disseminated for academic and research purposes. No personal particulars such as names, residence will be disclosed to any persons except authorized research personnel.

If you do not wish your child to take part in this research, your child will be provided with the established standard treatment available at the lea Toto program. This treatment is according to Kenya national guidelines.

As I seek your participation, I would like to bring to your attention the following ethical considerations which will guide your participation.

1. Participation in this study is purely voluntary.

2. If you choose not to consent, all the services your child receives in the program will continue as per the standard of care.

3. After you read through the explanations, please feel free to ask any questions that will allow you to understand the nature of the study.

5. Any information collected from this research including details on your demographic characteristics will be treated as strictly confidential. It will not be shared with or given to anyone except the researchers and hospital ethics board.

6. The knowledge obtained from this study will be made available to the general public and the results published for future scientific purposes.

7. The study protocol has been reviewed by the ethics committee. The protocol can be accessible to you should you choose to know the details.

This proposal has been reviewed and approved by the Ethics, Research and Standards Committee of Kenyatta National Hospital and University of Nairobi {KNH/UON-ERC}, whose task it is to make sure that research participants are protected from harm.

Information on researchers: Please feel free to contact the following if you have any questions about the study or would like any further information: Principle investigator: Dr.Edith Wacera. Telephone number: 0722 571424

PART II: Certificate of Consent

I, the undersigned, as the legal guardian do hereby consent for my child to participate in this study whose nature, purpose and objectives have been fully explained to me. I am aware that participation is voluntary and that there are no consequences to withdrawal from the study. I have been informed that all data provided will be used for the purposes of study only.

Name of Participant (Printed)

Name of Parent/Guardian (Printed)

Signature of Parent or Guardian

Date

Statement by the researcher/person obtaining consent

I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands that the following will be done: The program's EMR will be accessed to gather information intended for this study only. There will be no identifiable or personal details disclosed to unauthorized persons. I confirm that the parent was given an opportunity to ask questions about the study, and all the questions asked by the parent have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

(A copy of this ICF has been provided to the participant.)

Name of researcher/person obtaining consent (printed)

Signature of researcher/person obtaining consent

2 b)Fomu ya Ruhusa ya Kibali (ICF) kwa wazazi wa watoto kati ya umri wa miezi 0 na 24 ambao ni HEU na kufuatilia katika mpango wa Lea Toto mwaka 2016/17.
Mtafiti mkuu: Dr Edith Wacera Kagunda
Taasisi: Chuo Kikuu cha Nairobi na programu ya Lea Toto

SEHEMU YA I: Karatasi ya Taarifa
Mimi ni Dk. Edith Wacera Kagunda mwanafunzi wa chuo kikuu cha Chuo Kikuu cha Nairobi, Idara ya Pediatrics. Ninafanya utafiti kama sehemu ya mahitaji ya shahada ya Mwalimu wa Dawa katika Pediatrics. Utafiti huo una lengo la kutathmini usimamizi wa watoto wa HEU wenye umri wa miezi 0-24 mwaka 2016/17 katika mpango wa Lea toto.
VVU hufunuliwa lakini watoto wasioaminika huunda watoto wengi waliozaliwa na mama wenye VVU. Huduma yao ni muhimu ili kuhakikisha kuwa bado hawana VVU. Wanahitaji kupatikana mapema na kuanza kwenye dawa nzuri ya ART. Pia wanahitaji kuwa na chanjo kamili kulingana na KEPI. Pia huhitaji ufuatiliaji wa kawaida na uendelezaji. Pia wanakabiliwa na changamoto za kipekee wakati wao hawana afya na wanahitaji usimamizi sahihi wa ugonjwa.
Tathmini ya usimamizi wao wa kliniki ni muhimu na zoezi la kuboresha ubora.
Faida za mtoto wako kushiriki katika utafiti huu ni: kuhakikisha mtoto ana usimamizi sahihi wa kliniki ambayo inahakikisha matokeo mazuri. Pia itaonyesha eneo la kuboresha katika usimamizi wa kliniki. Mtoto wako hatakuwa na mabadiliko katika usimamizi wao kulingana na miongozo ya kitaifa.
Kwa kushiriki katika utafiti huu inawezekana kwamba maelezo ya afya ya mtoto wako yatashughulikiwa na kusambazwa kwa madhumuni ya kitaaluma na utafiti. Hakuna maelezo binafsi kama majina, makaazi yatafunuliwa kwa watu wowote isipokuwa wafanyakazi wa utafiti wenye mamlaka.
Ikiwa hutaki mtoto wako atashiriki katika utafiti huu, mtoto wako atapewa na tiba ya kawaida iliyopatikana katika programu ya lea Toto. Tiba hii ni kulingana na miongozo ya kitaifa ya Kenya.
Ninapotaka kushiriki kwako, ningependa kukuelezea mambo yafuatayo ya kimaadili ambayo itasaidia ushiriki wako.
1. Kushiriki katika utafiti huu ni kikamilifu kwa hiari.
2. Ikiwa unachagua kutobali, huduma zote mtoto wako anazopata katika programu itaendelea kulingana na kiwango cha huduma.
3. Baada ya kusoma kwa maelezo, tafadhali jisikie kuuliza maswali yoyote ambayo itawawezesha kuelewa asili ya utafiti.

5. Taarifa yoyote iliyokusanywa kutoka kwa utafiti huu ikiwa ni pamoja na maelezo juu ya sifa zako za idadi ya watu itachukuliwa kama siri ya siri. Haitashirikiwa au kupewa mtu yeyote isipokuwa watafiti na bodi ya maadili ya hospitali.
6. Maarifa yaliyotokana na utafiti huu yatapatikana kwa umma na matokeo yaliyochapishwa kwa madhumuni ya kisayansi.
7. Itifaki ya utafiti imechungwa na kamati ya maadili. Itifaki inaweza kupatikana kwako unapaswa kuchagua kuchagua maelezo.

Pendekezo hili limepitiwa na kupitishwa na Kamati ya Maadili, Utafiti na Viwango vya Hospitali ya Taifa ya Kenyatta na Chuo Kikuu cha Nairobi {KNH / UON-ERC}, ambao kazi yake ni kuhakikisha kuwa washiriki wa utafiti wanalindwa dhidi ya madhara.
Taarifa juu ya watafiti: Tafadhali jisikie huru kuwasiliana na yafuatayo ikiwa una maswali kuhusu utafiti au ungependa maelezo zaidi: Mtafiti wa kanuni: DrEdith Wacera. Nambari ya simu: 0722 571424

SEHEMU YA II: Hati ya Ruhusa
Mimi, aliyeandikwa chini, kama mlezi wa kisheria hukubali kwa mtoto wangu kushiriki katika utafiti huu ambao asili yake, madhumuni na malengo yameelezewa kikamilifu kwangu. Ninajua kuwa ushiriki ni wa hiari na kwamba hakuna madhara ya kujiondoa kutoka kwenye utafiti. Nimeambiwa kuwa data zote zinazotolewa zitatumika kwa madhumuni ya kujifunza tu.
Jina la Mshiriki (Kuchapishwa)
Jina la Mzazi / Mlezi (Kuchapishwa)
Saini ya Mzazi au Mlezi
Tarehe

Taarifa ya mtafiti / mtu kupata idhini
Nimesoma kwa usahihi karatasi ya habari kwa mzazi wa mshiriki, na kwa uwezo wangu wote kuhakikisha kuwa mtu anaelewa kuwa yafuatayo yatafanyika: EMR ya programu itafikia kukusanya maelezo yaliyopangwa kwa ajili ya utafiti huu tu . Hakutakuwa na maelezo ya kutosha au ya kibinafsi yanayofunuliwa kwa watu wasioidhinishwa. Ninathibitisha kwamba mzazi alipewa fursa ya kuuliza maswali kuhusu utafiti, na maswali yote aliyouliza na mzazi yamejibu kwa usahihi na kwa uwezo wangu mkubwa. Ninathibitisha kwamba mtu huyo hakujazimishwa kutoa idhini, na ridhaa imetolewa kwa uhuru na kwa hiari.
(Nakala ya ICF hii imetolewa kwa mshiriki.)
Jina la mtafiti / mtu anayepata idhini (iliyochapishwa)
Sahihi ya mtafiti / mtu kupata idhini

Appendix 3: (Consent) Informed Consent Form (ICF) for chairperson of board of management-Lea toto and facility in-charge.

Study Title: Clinical audit on management of HIV exposed uninfected (HEU) infants aged 0-24 months in 2016/17 at the lea Toto program, Nairobi, Kenya.

Principal investigator: Dr. Edith Wacera Kagunda

Institutions: University of Nairobi and Lea Toto program

PART I: Information Sheet

I am Dr. Edith Wacera Kagunda a postgraduate student at the University of Nairobi, Department of Pediatrics. I am conducting a study as part of the requirement for the degree of Master of Medicine in Pediatrics. The study aims to evaluate the clinical management of HEU children aged 0-24 months at the Lea toto program.

HIV exposed but uninfected children form the majority of children born to HIV positive mothers. Their care is critical to ensure they remain HIV negative. They need to be diagnosed early and started on appropriate ART prophylaxis. They also need to be fully immunized according to KEPI. They also require regular growth monitoring and promotion. They also face unique challenges when they are unwell and require appropriate management of illness.

Evaluation of their clinical management is necessary and a quality improvement exercise.

The benefits of this study are: to ascertain appropriate clinical management which ensure better outcomes. It will also highlight areas of improvement in clinical management. There will be no alterations in their management as per national guidelines.

As I seek your participation, I would like to bring to your attention the following ethical considerations which will guide your participation.

1. Participation in this study is purely voluntary.

2. Patients who choose not to consent, all the services received in the program will continue as per the standard of care.

3. After you read through the explanations, please feel free to ask any questions that will allow you to understand the nature of the study.

4. Any information collected from this research including details on your demographic characteristics will be treated as strictly confidential. It will not be shared with or given to anyone except the researchers, Lea toto board of management and UON ethics board.

5. The knowledge obtained from this study will be made available to the general public andthe results published for future scientific purposes.

6. The study protocol has been reviewed by the ethics committee. The protocol can be accessible to you should you choose to know the details.

This proposal has been reviewed and approved by the Ethics, Research and Standards Committee of Kenyatta National Hospital and University of Nairobi {KNH/UON-ERC}, whose task it is to make sure that research participants are protected from harm.

Information on researchers: Please feel free to contact the following if you have any questions about the study or would like any further information: Principal investigator: Dr.Edith Wacera. Telephone number: 0722 571424

PART II: Certificate of Consent

I, the undersigned, as the legal custodian of program's EMR do hereby consent for EMR to participate in this study whose nature, purpose and objectives have been fully explained to me. I am aware that participation is voluntary and that there are no consequences to withdrawal from the study. I have been informed that all data provided will be used for the purposes of study only.

Name of Participant (Printed)

Name of Chairman Board of management/Facility in-charge (Printed)

Signature

Date

Statement by the researcher/person obtaining consent

I have accurately read out the information sheet to the board of management/facility in-charge, and to the best of my ability made sure that the person understands that the following will be done: The program's EMR will be accessed to gather information intended for this study only.No identifiable or personal details will be disclosed to unauthorized persons.I confirm that the parent was given an opportunity to ask questions about the study, and all the questions asked by the parent have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

(A copy of this ICF has been provided to the participant.)

Name of researcher/person obtaining consent (printed)

Signature of researcher/person obtaining consent

Date

Appendix 4: Key revisions in the recommendations from 2006 to 2010

2010 recommendations	2006 recommendations
1. ANTIRETROVIRAL THERAPY FOR HIV-INFECTED PREGNANT WOMEN WHO NEED TREATMENT FOR THEIR OWN HEALTH	
ARV eligibility criteria	
All women with CD4 of ≤350 cells/mm^3, irrespective of clinical staging All women with clinical stage 3 or 4, irrespective of CD4 cell count	Women in clinical stage 1 and 2 with CD4 of <200 cells/mm^3 All women in clinical stage 4, irrespective of CD4 cell count Women in clinical stage 3, with CD4 of <350 cells/mm^3, if available; if the CD4 cell count is not available, all women in stage 3 should be treated
When to start ART in pregnant women	
As soon as feasible	As soon as feasible
Recommended first-line regimens for pregnant women	
AZT + 3TC + NVP or AZT + 3TC + EFV or TDF + 3TC (or FTC) + NVP TDF + 3TC (or FTC) + EFV	AZT + 3TC + NVP
Prophylaxis for infants born to pregnant women on ART	

2010 recommendations	2006 recommendations
All infants regardless of **infant** feeding mode NVP or AZT for 4 to 6 weeks	AZT for 7 days
2. <u>ANTIRETROVIRAL PROPHYLAXIS</u> FOR PREGNANT WOMEN WHO DO NOT NEED TREATMENT FOR THEIR OWN HEALTH	
When to start ARV prophylaxis	
As early as 14 weeks of pregnancy	Starting at 28 weeks of pregnancy
Prophylaxis regimens for the mother	
Option A: AZT during pregnancy plus sd-NVP + AZT + 3TC tail during labour and delivery plus AZT + 3TC for 7 days postpartum (may omit sd-NVP and intrapartum and postpartum AZT + 3TC if >4 weeks AZT; in this case, continue maternal AZT twice daily during labour and stop at delivery) Option B: AZT + 3TC + LPV/r or AZT + 3TC + ABC or AZT + 3TC + EFV or TDF + 3TC (or FTC) + EFV	AZT during pregnancy plus sd-NVP + AZT + 3TC during labour and delivery plus AZT + 3TC for 7 days postpartum
Prophylaxis regimens for exposed infants	

2010 recommendations	2006 recommendations
Option A: Breastfeeding infants NVP from birth until 1 week after all exposure to breastfeeding Non-breastfeeding infants NVP or sd-NVP + AZT for 4 to 6 weeks Option B: All infants regardless of **infant** feeding mode NVP or AZT for 4 to 6 weeks	sd-NVP + AZT for 7 days
Related infant feeding recommendation for known HIV-infected women	
National authorities should decide whether health services will principally counsel mothers to either breastfeed and receive ARV interventions or avoid all breastfeeding, as the strategy that will most likely give infants the greatest chance of **HIV**-free survival Where breastfeeding is judged to be the best option: Exclusively breastfeed for the first 6 months, introduce appropriate complementary food thereafter, and continue breastfeeding for 12 months Wean gradually within 1 month	Exclusive breastfeeding for the first 6 months unless replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS) At 6 months, continue breastfeeding with additional complementary food if AFASS is not met Wean within a period ranging from about 2–3 days to 2–3 weeks

2010 recommendations	2006 recommendations
Adapted from: Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants: Recommendations for a Public Health Approach: 2010 Version. Geneva: World Health Organization; 2010.	