EFFICACY OF PHONE USE ON ADHERENCE TO NEVIRAPINE PROPHYLAXIS AND RETENTION IN CARE AMONG HIV-EXPOSED INFANTS IN PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV: A RANDOMIZED CLINICAL TRIAL.

A RESEARCH PROPOSAL FOR DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE DEGREE OF MASTERS OF MEDICINE (MMED) IN PAEDIATRICS AND CHILD HEALTH, UNIVERSITY OF NAIROBI

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DECLARATION

This dissertation is my original work, and has not been presented for a degree in any university or published anywhere.

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DEDICATION

I dedicate this book to the dearest and most phenomenal woman in my life, my mother, Jane K. Kebaya, and my late father, Charles K. Kebaya, who endeavored to ensure that my siblings and I realized our dreams in life, no matter how unrealistic they were. Their unwavering and unconditional love and support inspired us to reach our fullest potential in life. And to my mother, whose resilience these past two years has only made me appreciate her even more. I am equally grateful for the support accorded to me by siblings.

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LIST OF ABBREVIATIONS

AIDS - Acquired Immune Deficiency Syndrome

ARV-Antiretrovirals

CD4- Cluster of Differentiation 4

HAART – Highly active antiretroviral therapy

HIV-Human Immunodeficiency Virus

NVP-Nevirapine

MCH - Maternal and Child Health

PMTCT- Prevention of Mother-to-Child transmission of HIV

UN - United Nations

WHO - World Health Organization

ABSTRACT

Background

HIV is a major contributor to infant mortality. A significant gap remains between the uptake of infant and maternal ARV regimens and only a minority of HIV-exposed infants receives prophylaxis and safe infant feeding. Losses to follow-up of HIV-exposed infants are associated with shortcomings of facility-based PMTCT models with weak community support of linkages. The rapid expansion of mobile phone coverage in Africa, and in Kenya, presents an opportunity to strengthen linkages between caregivers and health providers. Mobile phone use offers an option to improving care and promoting retention for the mother-baby pairs, which is a major challenge in efforts to achieving an HIV-free generation.

Objectives

To compare self-reported adherence to infant nevirapine (NVP) prophylaxis and retention in care over 10 weeks in HIV exposed infants randomized to 2-weekly mobile phone calls (intervention) versus no phone calls (control).

Design

Open label Randomized controlled trial

Methods

One hundred and fifty HIV infected women drawn from 3 health facilities in Western Kenya and their infants were randomly assigned to receive either phone-based reminders on PMTCT messages or standard health care messages (no calls) within 24 hours of delivery. The group in the intervention arm received phone calls fortnightly. At 6 and 10 weeks following

randomization we collected data on infant adherence to nevirapine, mode of infant feeding, early HIV testing and retention in care in both study arms. All analyses were intention to treat.

Results

Seventy five women were each randomized to the intervention and control arms respectively. At 6 weeks follow-up 68 (90.7%) of participants in the intervention arm reported adherence to infant NVP prophylaxis, compared with 54 (72%) participants in the control group ($p = 0.005$). Participants in the intervention arm were also significantly more likely to be retained in care than those in the control group. At 6 weeks 59 mother-infant pairs (78.7%) attended scheduled visits with the visits coinciding with the appointment date versus 44 (58.7%) in the control arm ($p = 0.009$). At 10 weeks the revisit rates were 69.3% (52) in intervention arm and 37.3% (28) in control arm for the 150 mother-infant pairs evaluated ($p < 0.001$).

Conclusion

These results suggest that phone calls can be an important tool to improve adherence to infant NVP prophylaxis and retention in care for HIV exposed infants.

BACKGROUND AND LITERATURE REVIEW

1. INTRODUCTION

HIV is a major contributor to infant mortality. Prevention of mother-to-child transmission of HIV (PMTCT) provides drugs, counseling and psychological support to help mothers safeguard their infants against the virus[1]. PMTCT strategies reduce the risk of mother-to-child transmission from nearly 40% to less than 5%, as shown in figure 1.Without intervention, every child born of a HIV-positive mother has a 40% risk of contracting HIV.

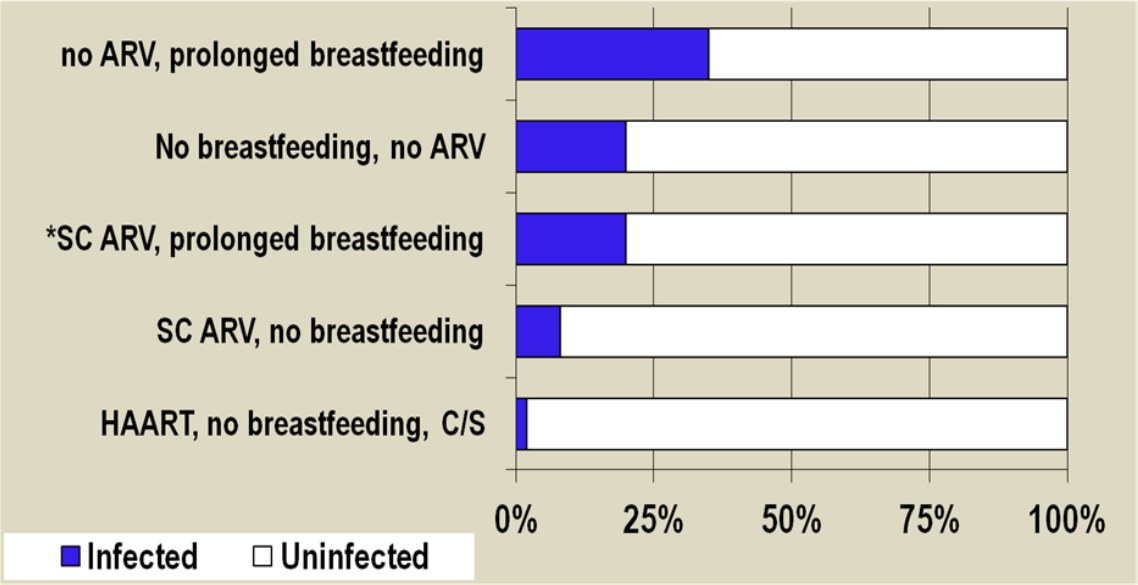

Figure 1: Variable Risk of Mother-to-Child HIV-1 Transmission. ***With or Without Interventions*[1]**.

CS- Caeserian section

Ensuring PMTCT is provided to all women who need it is the most effective way to end mother-to-child HIV transmission by 2015, and reach the United Nation's MDG 6.Hence, ensuring that no child is born with HIV is an essential step towards achieving an AIDS-free generation.

However, despite the gains, far too few pregnant women and their infants have access to this preventive treatment. In 2010, an estimated 350 000 new HIV infections occurred among children under the age of 15, with 90% of these children getting the infection through vertical transmission[2]. Such trends have resulted in nearly three million children living with HIV and almost 250,000 HIV related deaths annually as shown in Figure 2.

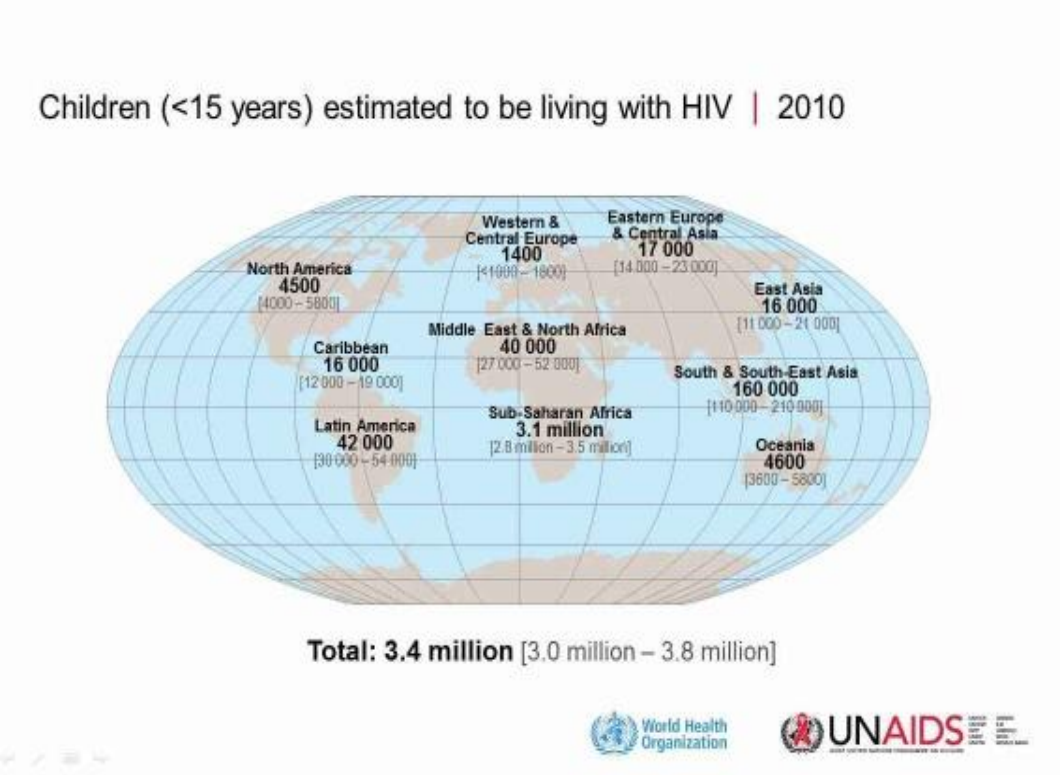

Figure 2: Children (<15 years) estimated to be living with HIV[2].

Kenya is one of the 22 priority countries for eliminating mother to child transmission of HIV (MTCT)[2]. In 2009, the PMTCT program in Kenya embarked on a five-year initiative to eliminate mother to child transmission of HIV[3]. The overall target is reduction of mother to child transmission rate to less than 5% by 2015.Figure 3 demonstrates the four-pronged strategy and Kenya's country targets. Remarkable progress has been made so far in achieving the MDG

4, 5 and 6 (Appendix IX); however, much is still needed in countries affected by high levels of HIV/AIDS.

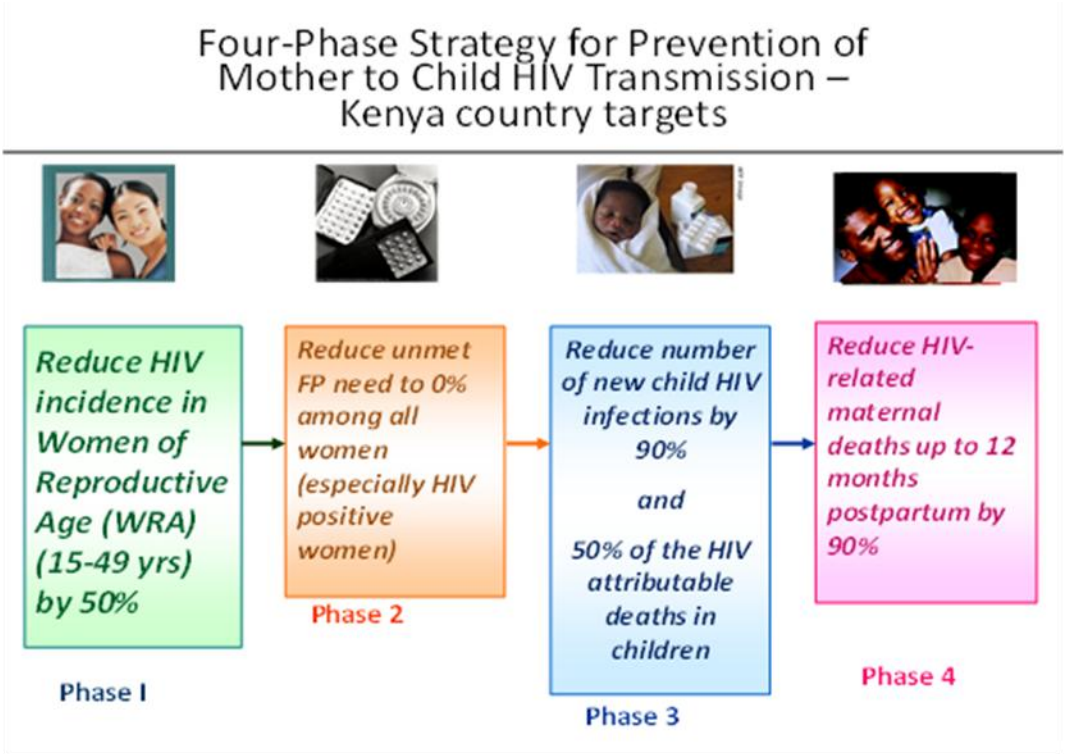

Figure 3: Elimination of Mother to Child Transmission of HIV: Kenya Country Targets[4]

Some of the challenges in provision of quality PMTCT services include low utilization of ANC services with about 52% of pregnant women making at least four antenatal clinic visits; few facility-based deliveries; inefficacious regimes for PMTCT; human resource constraints; lack of integration of early infant diagnosis in Maternal, Newborn and Child Health (MNCH) services, resulting in missed opportunities for pediatric treatment and poor continuum of care for mother-baby pairs, leading to loss to follow up of HIV-exposed infants. Conducted Ministry of Health data audit also revealed critical gaps in quality of data and service delivery at facility level in high prevalence districts[3].

1.1. Literature review

1.1.1. Antiretroviral (ARV) prophylaxis among infants born to mothers living with HIV

With a combination of ARVs for mother and baby, infants of HIV infected mothers may be protected from infection during pregnancy, delivery and the prolonged period of breastfeeding. ARVs are used for both treatment of HIV disease and for PMTCT in HIV positive pregnant women and their infants, as shown in table 1 and appendix X.

Table 1: Antiretroviral prophylaxis for HIV-exposed infants[4]

Scenario	**Infant intervention**
Mother on HAART	NVP for 6 weeks
Mother not on HAART and Baby breastfeeding	NVP till 1 week after cessation of breastfeeding
Baby not breastfeeding	NVP for 6 weeks

The coverage of infant antiretroviral prophylaxis increased in accordance with the increasing uptake of ARVs by pregnant women living with HIV. Globally, in 2010, 42% of an estimated 1.49 million infants born to mothers living with HIV received ARVs for PMTCT versus 20% in 2007[2].Despite overall progress, a significant gap remains between the uptake of infant and maternal ARV regimens. Although the gap between the numbers of mothers and infants reached by antiretroviral prophylaxis partly reflects the inadequacy of monitoring and evaluation systems to capture the data on the services provided, bridging the gap will also require strengthening follow-up mechanisms within and outside health care systems[1].

Epidemiology of Pediatric HIV and PMTCT in Kenya

An estimated 1.4 million adults aged 15-64 years are infected with HIV/AIDS with the HIV prevalence being higher among women[5], [6]. With an estimated population of 38.6 million in the year 2010, the number of HIV-exposed infants was estimated to be 97,272 and at least 38,900 HIV-positive babies were born, assuming a 40% transmission without any interventions (Table 2).

Table 2: Estimated magnitude of MTCT in Kenya[4]

Population (Estimates)	38.6 million
Births per annum	1.5 million
HIV prevalence in mothers	6.2%
Total number of births to HIV-infected mothers exposed to MTCT assuming no multiple pregnancy	97,272
Number of HIV positive infants per annum in Kenya assuming 40% transmission	38,900

The national PMTCT Program started in 2002, and since then over 60% of health facilities countrywide provide PMTCT services. As a result, over 80% of pregnant women are counseled and tested for HIV and 79% of the HIV positive women receive ARVs for prophylaxis[7]. However, 33% still receive single dose nevirapine, a regimen being phased out in response to new WHO guidelines[2].Only 63% of HIV-exposed infants receive ARV prophylaxis (figure 3) and only 35% of the HIV-exposed infants receive a Polymerase Chain Reaction (PCR) HIV test six weeks after birth[7]. Currently, many HIV exposed infants are falling through the cracks and cannot be accounted for by 18 months. By 2009, it was estimated that MTCT rate was 27% at

18 months. Use of more efficacious regimens and provision of extended infant prophylaxis for the duration of breastfeeding is expected to drastically reduce the MTCT rates.

Cascade of PMTCT services in Kenya

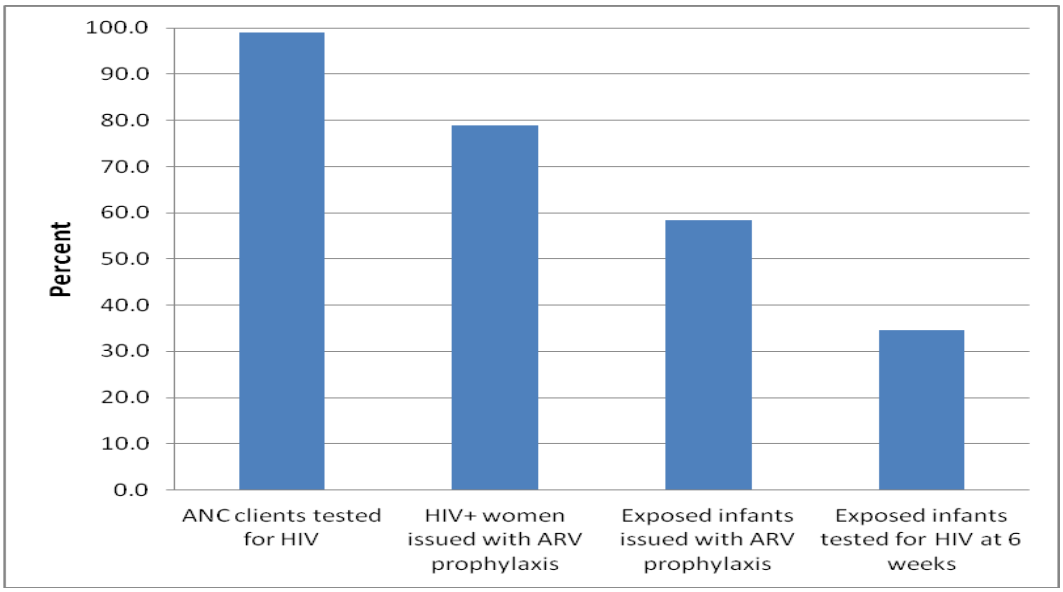

Figure 4: Kenya PMTCT Cascade[7]

1.1.2. Infant feeding within the context of PMTCT

The recommended feeding options for a HIV exposed infant are exclusive breastfeeding with ARVs or exclusive replacement feeding for the first 6 months[4] (see Appendix VIII). Breastfeeding by a mother living with HIV exposes the infant to HIV. And research suggests increased risk of mother to child transmission of HIV with prolonged duration of breastfeeding, mixed feeding and breast disease. However, avoidance of breastfeeding places the infant at increased risk of death due to diarrhea, pneumonia and malnutrition. Mothers living with HIV need to balance these competing risks when deciding how to feed their newborn children[1].

Despite years of experience, services to support mothers living with HIV in making safer infant-feeding decisions remain inadequate in many countries: HIV counseling during antenatal care may be insufficient; health workers may not always provide women with sufficient information on alternative options with regard to their individual circumstances to help them make an informed choice[9] and HIV testing of HIV-exposed infants at six weeks of age (for the purpose of early infant diagnosis) may be mistakenly used as a time to revise feeding practices. In these circumstances, the practices of feeding HIV-exposed infants generally do not optimize their chances of healthy survival free of HIV infection[2].

Research studies have demonstrated that ARV interventions can reduce HIV transmission through breastfeeding. The MmaBana[10], BAN[11] and Kesho Bora[12] randomized controlled trials reported postnatal transmission rates of 1–3% when mothers living with HIV with CD4 count greater than 200 per mm^3 were given 3 ARV drugs during the course of breastfeeding. The BAN[11] and Malawi PEP[13]studies which assessed the impact of giving NVP daily to the breastfeeding infants of mothers living with HIV, reported MTCT rates of 1.8% when infants received NVP daily for up to 6 months of breastfeeding. For infants of mothers who are not eligible to receive HAART, evidence suggests that the use of ARVs by mothers during the period of breastfeeding or giving an ARV prophylaxis to the infant while breastfeeding can reduce transmission, thereby making breastfeeding a safer option for mothers living with HIV. These interventions, combined with knowledge about the benefits of exclusive breastfeeding, offer an important opportunity to accelerate efforts to achieving an HIV-free generation[1].

Taking into consideration the aforementioned concerns faced by HIV-positive mothers with regard to breastfeeding; the phone call intervention will act as a reminder to reinforce safe infant feeding with continued ARV prophylaxis for the infant.

1.1.3. Infant HIV-1 testing and diagnosis

Early infant diagnosis (EID) refers to making of HIV diagnosis in infants and young children before 18 months of age[4]. EID is required to reliably identify HIV infection among infants and children and initiate care and treatment interventions in a timely manner. All HIV-exposed infants should receive early virological testing at or around 4 to 6 weeks of age[1]. Infants with a positive virological test result should be assumed to be HIV-positive and started on antiretroviral therapy immediately, to improve chances of survival; and HIV infection should be confirmed by repeat viral testing as shown in figure 5. Globally, the uptake of HIV testing among children remains low and many children living with HIV still go undiagnosed. In 65 countries, only 28% of children born to mothers living with HIV were tested for HIV within the first two months of life[2]. Efforts to improve early infant diagnosis and postnatal follow-up with integration of HIV services with services for MNCH are needed to provide a continuum of HIV prevention and care for women and children[1].HIV infection follows a more aggressive course among infants and children than among adults. One third of children living with HIV die before the age of one year and almost 50% by the second year. This therefore underscores the need for early HIV diagnosis of HIV-exposed infants. Findings from the "Children with HIV Early Antiretroviral Therapy" study (CHER)[14]demonstrated that giving ART to HIV-infected infants beginning at an average age of seven weeks made them four times less likely to die in the next 48 weeks, compared with postponing ART until signs of illness.

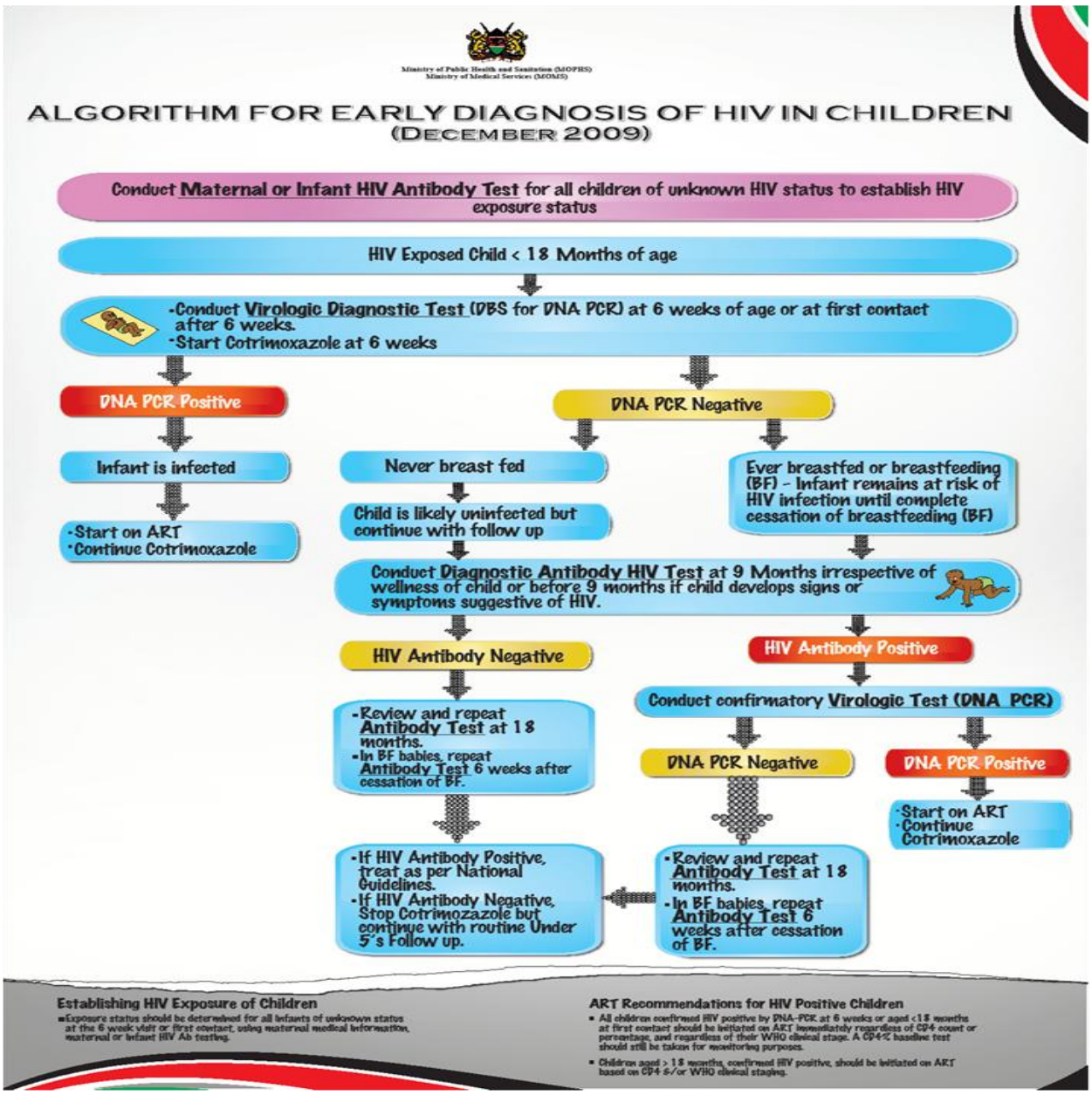

Figure 5: Algorithm for Early Infant Diagnosis of HIV-1 Infection in Children[4]

An important strategy countries such as Swaziland and Zambia use to improve the follow-up of known HIV-exposed infants is including HIV-specific information on child health cards to better enable health care workers to identify infants needing HIV testing, and innovative approaches such as using mobile phones to connect with mothers living with HIV and their infants[2].Closer

home, the Kenyan Mother Baby Booklet has been used to follow up the mother-baby pair in the postnatal period.

1.1.4. Providing a continuum of care for the mother-baby pairs

To be effective, evidence-based preventive, treatment and care interventions for pregnant women living with HIV, mothers and their children must be provided within a continuum of care. However the data suggest that several critical gaps remain along this continuum at the end of 2010[1]. A critical gap lies in providing ARVs to mother-baby pairs. Only 42% of infants born to mothers living with HIV in 2010 received ARVs versus 45% of mothers who received ARVs for PMTCT. Data show a significant gap between the number of children born to mothers living with HIV who received antiretroviral prophylaxis (42%) and those that continued into the critical services for early infant diagnosis (28%) and co-trimoxazole prophylaxis (23%) [2].To maximize the effectiveness of programs for preventing mother-to-child transmission of HIV, integrated packages of services must be systematically targeted at the facility level, and systems should be developed to track and improve performance at every step of the cascade through follow-up mechanisms and links to the essential treatment, care and support services.

1.1.5. Factors affecting uptake of PMTCT services and retention in care of HIV exposed infants

Losses to follow-up and patient retention pose critical challenges to the successful care and treatment of HIV-exposed and infected children. Studies have shown frequent late entry and high drop out among infants enrolling for care and early infant diagnosis in Kenya[16]. Majority of infants enrolled after 2 months of age, with more than 80% being referred for care from acute or

chronic clinical services. This suggests that infants were referred and enrolled when they fell sick, rather than for scheduled follow up of PMTCT (figure 6).

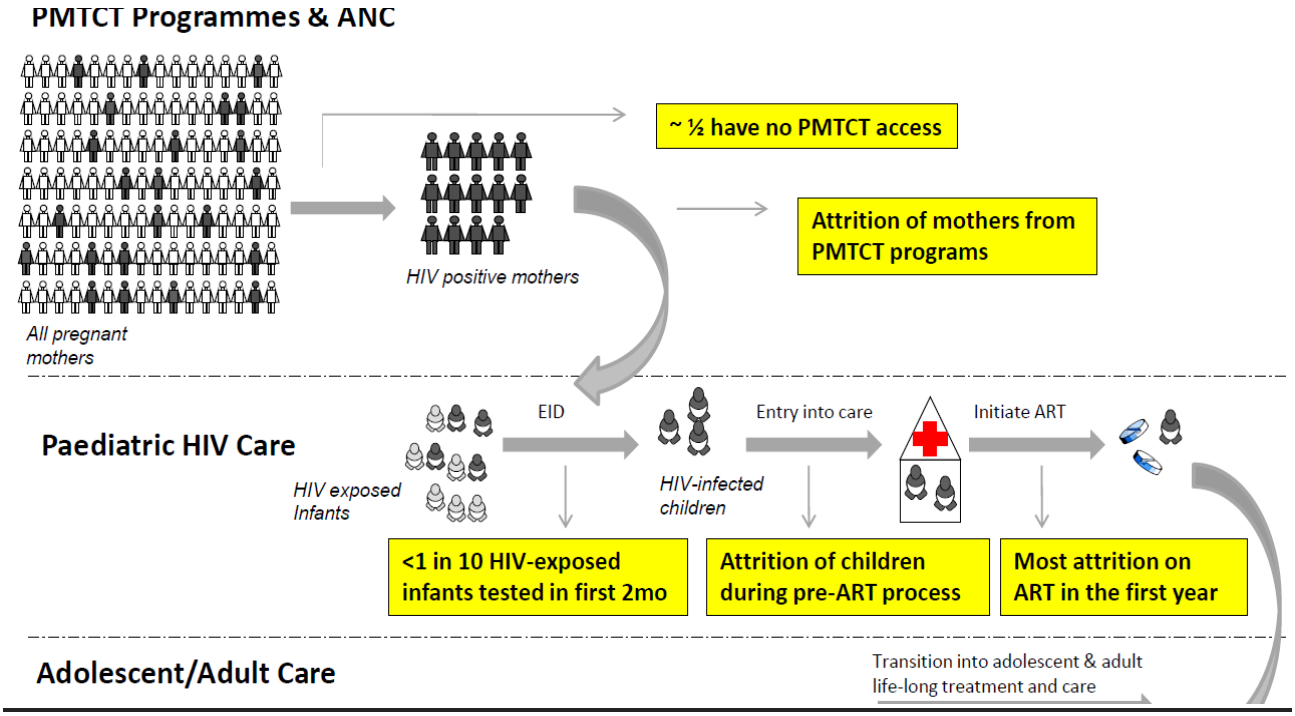

Figure 6: Losing HIV-Exposed infants: The HIV Care Continuum[15]

Two-thirds of the infants who dropped out had mothers who were also 'lost to follow up' for HIV care. In rural Malawi, a study evaluating PMTCT program revealed a progressive loss to follow up of HIV positive mothers of up to 81% postnatally[17]. Household and community factors influenced retention, including stigma and constrained social support networks [16, 18].Given the high level of poverty, and especially in resource-limited countries, travel and other indirect costs associated with repeated visits to the hospital were important. Another barrier to uptake of PMTCT services as seen in rural Africa was that many women opt to deliver at home[16].

Fully integrating EID into PMTCT has the potential to improve uptake and retention by including more specific EID training within the PMTCT syllabus to empower service providers with adequate knowledge and understanding of EID[16].In most settings in Kenya, HIV-exposed infants are enrolled and cared for in exclusive HIV clinics. The PMTCT program is moving towards integrating EID services and postnatal testing within MCH services; offered together with immunizations, growth monitoring and other maternal child health care services. This is a potentially attractive strategy considering high levels of immunization coverage, and the possibility of reducing costs to caregivers by combining visits[16].

1.1.6.Use of mobile phone technology for PMTCT

By the end of 2010, Allied Business Intelligence (ABI) Research forecasted over five billion mobile subscriptions, with an approximate 4.8 billion connections having already been reached by the end of the year's first quarter[19]. Much of this growth was registered in developing markets in Africa and the Asia-Pacific region. Africa remains the fastest growing mobile market with a year over year growth of over 22%. Falling monthly tariffs and ultra-low-cost mobile handsets have democratized the reach and use of the mobile phone, and aggressive roll-outs by mobile operators in these countries will see the current rate of subscriber addition maintained for some time to come. These trends are currently evident in Kenya.

In Kenya, the situation is no different; mobile phones are becoming widespread, with 42 mobile phone subscriptions per 100 people in 2008, compared to an average of 32 per 100 for Sub-Saharan Africa as a whole [20, 21].By October 2012, with a population of around 42million, Communication Commission of Kenya (CCK) had announced that the country's total number of mobile subscribers was an incredible 29.7million. This number firmly makes Kenya as one of the countries in Africa with the highest mobile penetration rates of 75.4 %, signifying a growth of

17.5% from 25.2 million recorded in the 2010/2011 period. The Kenyan market has accepted the mobile phone as a primary form of communication. This access to mobile phones has even surpassed access to banks which were present here long before the mobile phones. Mobile phones are used intensely for both personal and commercial use, as attested to since the invention of m-pesa (mobile money transfer service in Kenya) [22].

Thus, the rapid expansion of mobile phone coverage in Africa presents an opportunity to scale-up the HIV/AIDS response in resource-poor settings. A wide range of medical services could be improved by providing patient-focused support and management through the health-care system[23].If mobile phone use does improve health outcomes in resource-limited settings, this mobile health technology could be included in health-system strategies and help improve health development goals[24].Studies have been conducted in other resource-constrained settings, e.g. India, and have been shown to improve ART adherence among HIV-positive patients and adherence improves health outcomes[25, 26]. Other studies conducted in rural health facilities in Kenya showed that mobile health innovations can improve HIV treatment outcomes. Patients who received the SMS support were more likely to report adherence to ART and were more likely to have their viral load suppressed below detection levels than patients who received the standard care alone[26, 27].Use of phone call reminders, has also been used to assist adolescents adhere with HIV medications. This relatively inexpensive strategy does not require an extensive amount of daily staff time[28].The use of the mobile phone has also been used in other health strategies; for example, improve Malawi's child malnutrition surveillance[29].

JUSTIFICATION

High rates of loss to postnatal follow up in PMTCT have largely been attributed to poor and weak linkages between the clients and health workers. Use of the mobile phone to follow up on these mothers and their infants, is an important strategy to incorporate in order to scale up PMTCT interventions. There are no similar studies done, with special emphasis on PMTCT strategies, and so this study sought to address the significance of using the mobile phone with the aim of improving retention and care in the PMTCT program. Also taking into consideration the aforementioned concerns faced by HIV-positive mothers with regard to breastfeeding, the phone call intervention acted as a reminder to reinforce safe infant feeding with continued ARV prophylaxis for the infant. Information derived from this study will be useful to the PMTCT program in the health facilities hosting the study, and hopefully inform policy at the national level too.

RESEARCH QUESTION

What is the effect of mobile phones on adherence to ART prophylaxis and retention in care among the HIV-exposed infants?

We hypothesized that the phone call intervention would improve adherence and retention in PMTCT compared to patients who only receive the standard of care without the said intervention (control).

Broad objective

- To determine the efficacy of mobile phone use on adherence to ART prophylaxis and retention in care among the HIV-exposed infants in Prevention of Mother to Child Transmission of HIV

Primary Objective

- To compare retention in care(at 6 and 10 weeks) and self-reported adherence to infant ART prophylaxis in HIV exposed infants randomized to 2-weekly mobile phone call verses control (no phone call)

Secondary Objectives

- To determine whether cell phone intervention improves early infant diagnosis and promotes safe infant feeding

METHODS

STUDY DESIGN

The study used a randomized control designin3health facilities randomized to two arms (intervention or control) to determine the effect of mobile phone technology on infant ART prophylaxis adherence, early infant diagnosis, safe infant feeding practices and ultimately, retention in care to 10 weeks postpartum. Within this design, the scope of activities in the 2 arms was as follows:

1) **Intervention**: arm, where PMTCT services were offered (early HIV infant diagnosis, support and enrollment in care and treatment) and MNCH services (support safe infant feeding options, immunization and growth monitoring). In addition to the aforementioned services, HIV-infected mothers were called on phone by a clinician (the researcher), every two weeks, to remind them of/ and reinforce key PMTCT messages (ARV adherence, exclusive breastfeeding, EID, follow-up schedule) and enquire into how they were doing. Study participants also called to ask questions and report concerns.

2) **Comparison**: arm, where PMTCT services were offered (early HIV infant diagnosis, support and enrollment in care and treatment) and MNCH services (support safe infant feeding options, immunization and growth monitoring). Mothers were contacted by the clinician, but had a phone number they could call if they had a problem.

STUDY SITE

The study was conducted at Jaramogi OgingaOdinga Teaching and Referral Hospital (JOOTRH), Kisumu East District Hospital (KEDH)and Lumumba Health Centre. These are government health facilities situated in Kisumu East District County. JOOTRH has a busy maternity ward with approximately 500 deliveries per month, with 35-55 HIV positive pregnant mothers, delivering per month. KEDH has approximately 250 deliveries per month. The estimated HIV prevalence among pregnant women presenting at ANC is 15%. At KEDH, approximately 90% of pregnant women are receiving antenatal HIV counseling and testing, and uptake of more efficacious maternal ARVs during pregnancy was nearly 62% (excluding single dose nevirapine). Approximately 44% of women deliver in a health care facility, the proportion of HIV-exposed children accessing infant ARV prophylaxis was 65.6% and proportion tested for HIV by eight weeks was 59%. As of 2011, the overall MTCT rate was 7.7%.The estimated HIV prevalence among pregnant women presenting at ANC at Lumumba Health Centre was 20%.

STUDY PERIOD

From the time of delivery to 10 weeks postpartum.

STUDY POPULATION.

HIV Positive women who deliver at JOOTRH, KEDH and Lumumba Health Centre.

Inclusion criteria

1. HIV- positive women who delivered within the last 24 hours at the study site
2. Willingness to enroll infant into the study after delivery
3. Willing to stay in the study area for at least 3 months after delivery
4. Own a mobile phone on which they can receive calls

Exclusion criteria

1. Mothers, with no access to a phone
2. Mothers who declined to participate in the study
3. Mothers, whose HIV status was unknown, and who declined test

Note: Patients were not provided with cell phones or network airtime credit

SAMPLING PROCEDURE

The researcher trained the 3 research assistants on how to use the data tools and how to obtain written consent from participants. Women who met the inclusion criteria were approached by a recruiter and the study introduced to them. Information on the study's purpose, procedures, risks and benefits, as well as confidentiality and voluntariness of participation was provided to all potential participants as part of the informed consent process. Women who agreed to participate in the study signed a written consent and were interviewed to collect on demographic, socioeconomic and biomedical data. Enrolled mothers were assigned into either intervention or control groups using computer generated block randomization method.

Follow up procedures in the intervention arm

The researcher called all subjects in the intervention arm every 2 weeks (10 weeks follow-up for each participant), on Monday mornings, to remind them and reinforce key PMTCT messages (nevirapine prophylaxis, exclusive breastfeeding of the HIV-exposed infants, early infant diagnosis, scheduled immunizations) and enquired into how they were doing. Calling was inexpensive (at four Kenya shillings per minute).Study participants were also allowed to call to ask questions and report concerns on infant health. All cell phone communications between the researcher and study participants were recorded in a study log.

Follow up procedures in the Control group

Participants randomized to the control arm received their usual standard of care (SOC) clinic support but were not called by the clinician. They were however free to call the researcher at any time on their own initiative.

SAMPLE SIZE CALCULATION

Sample size with 80% power to detect 20% increase in self-reported adherence to infant ART prophylaxis will be calculated as follows:

$$n = \frac{2\left(Z_{1-\alpha} + Z_{\beta}\right)^2 P_{av}(1 - P_{av})}{(P_1 - P_2)^2}$$

n -The sample size required in each group

$Z_{1-\alpha/2}$ refers to the level of significance (5%)/ 95% confidence interval = 1.96

$Z_{1-\beta}$ refers to the power of obtaining difference between the two groups; set at 80% = 0.84

P_1 - Percent of controls with self-reported adherence to ART = 47%[27]

P_2- Percent of intervention group with self-reported adherence to ART (24% higher than controls) 67%

P_{av} – average outcome in the two groups = (47% + 71%)/2 = 59%[29]

Substituting into the formula:

$$n = \frac{2(1.96 + 0.84)^2 0.59(1 - 0.59)}{(0.47 - 0.71)^2}$$

Sample size (n) required in each group was 75. A total number of participants to be randomized into intervention and control groups were 150.

STUDYPROCEDURES

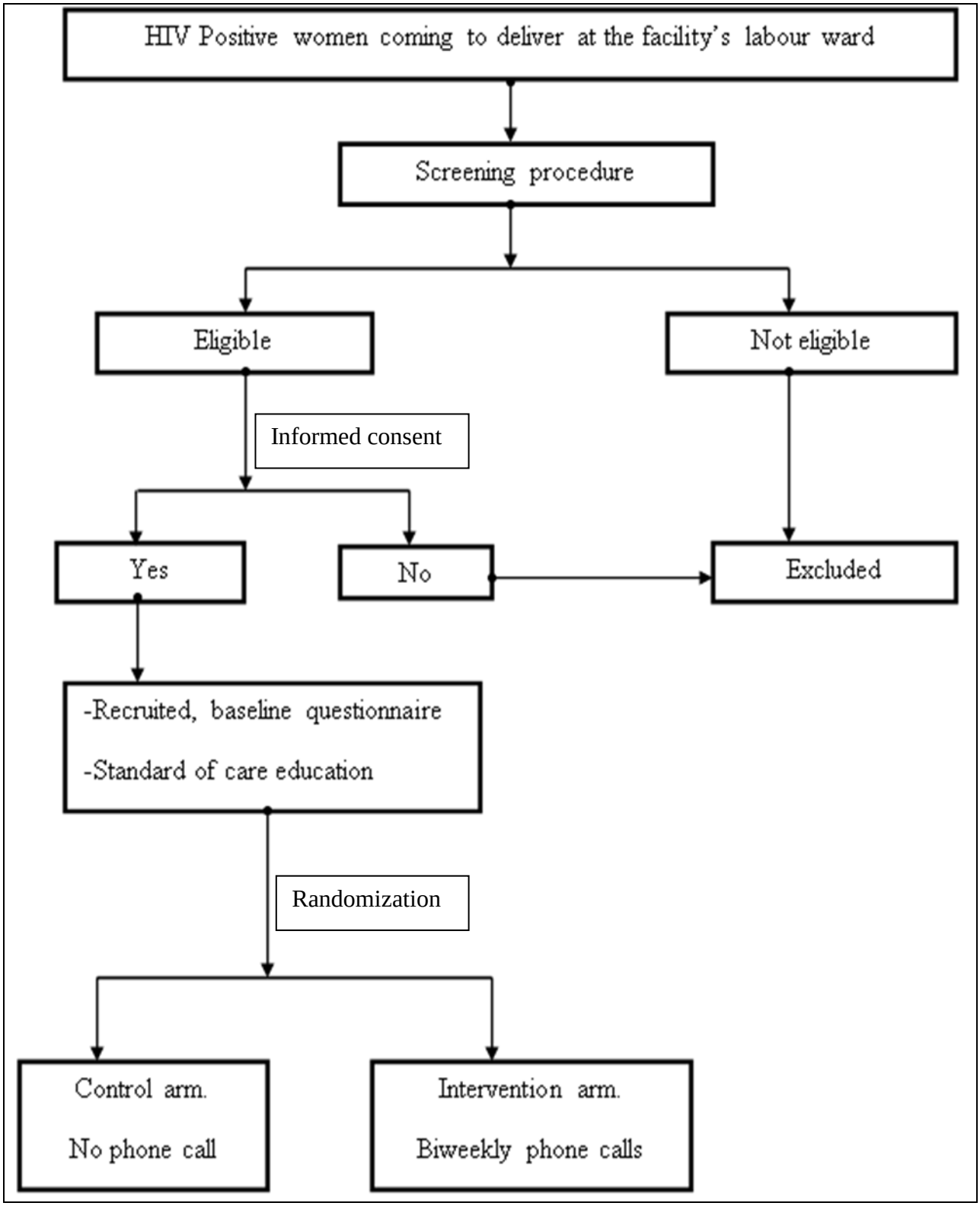

Figure 7: Study procedure

CASE DEFINITIONS AND OUTCOME MEASURES (6 AND 10 WEEKS).

The following were measured at 6 and 10 weeks after delivery:

1. **Adherence to nevirapine** - At discharge, each mother was issued with nevirapine for her infant. Adherence was measured as not having missed more than 3 doses for the first 6 weeks of life.
2. **Retention in care**- At discharge, each mother-infant pair was given a clinic return date at 6 weeks. Retention in care was measured as keeping the scheduled appointment date, hence, any mother who came on a different date was not included.
3. **Safe infant feeding**- safe feeding is defined as exclusive breastfeeding for the first 6 months of life.
4. **Timing of EID** - EIDis a test done, preferably by the 6 weeks' clinic visit, and at subsequent visits for those that missed out.

Follow-up activities in both arms

At 6 and 10 weeks scheduled clinic appointments, data was collected on infant adherence to nevirapine, retention to care, safe infant feeding and early infant diagnosis.

ETHICAL CONSIDERATIONS

1. The study was conducted after getting approval from the University of Nairobi, Kenyatta National Hospital Ethics and Research Committee (Appendix XIII) and Jaramogi Oginga Odinga Teaching and Referral Hospital Ethics and Research Committee.

2. A valid, informed consent was sought from the mothers prior to inclusion in the study. No mother was victimized for declining to participate in the study, as this was a voluntary process.
3. The nature of the study was explained to the personnel at JOOTRH, KDH and Lumumba labour wards and MNCH.

DATA MANAGEMENT AND ANALYSIS

Data from the questionnaires were coded and entered into Microsoft Access 2007 database. Data entry and cleaning were conducted concurrently with data collection. SPSS version 17.0 was used to analyze data. Both intention to treat and per protocol analyses were conducted. Baseline characteristics were analyzed and presented for both intervention and control groups. Similarities between the two groups was shown by comparing the baseline characteristics using Chi square/ Fishers' exact tests and Student's t / Mann Whitney U test for categorical and continuous variables respectively. The effect of the mobile phone intervention was measured by comparing self-reported adherence to ART prophylaxis, EBF, EID and the retention rates in PMTCT follow up at six and ten weeks. Adherence and retention were compared, analyzed and presented as proportions of patients with the characteristic in the group. Both outcomes were compared between the two groups using Chi square test and the impact of the intervention was shown using relative risks with 95% confidence interval. Furthermore, early infant diagnosis and feeding options were compared between the two groups using Chi square test and the likelihood of having the outcome in the intervention group shown using relative risk ratio. All statistical tests were performed at 95% confidence level (5% level of significance).

RESULTS

Between 19th September 2013 and 31st January 2014, a total of 150 HIV positive mothers and their newborn babies were randomly assigned to a mobile phone intervention at 3 health facilities in Kisumu, Kenya. Figure 8 shows the number of participants enrolled in the study and the numbers included in the intention to treat (ITT) and per protocol analyses according to study group and the different follow up times (6 and 10 weeks). 91 mother-infant pairs were ineligible and a majority of these (61) were not from the study area, while 15 of these lacked a mobile phone and another 15 mothers did not give consent. A single mother-infant pair was excluded from 6 week per protocol analysis due to an early neonatal death (after 36 hours). The main reasons for exclusions from analysis at the ten-week time point was loss to follow-up (n = 7 and n = 20 within intervention and control groups, respectively) or being on option A antiretroviral therapy (terminates nevirapine prophylaxis at 6 weeks) thus implying infants on this option were ineligible for evaluation of ARV adherence outcome at 10 weeks. After all exclusions 68 mother-infant pairs in intervention group and 55 pairs in control group were included in the 10-week per protocol analysis.

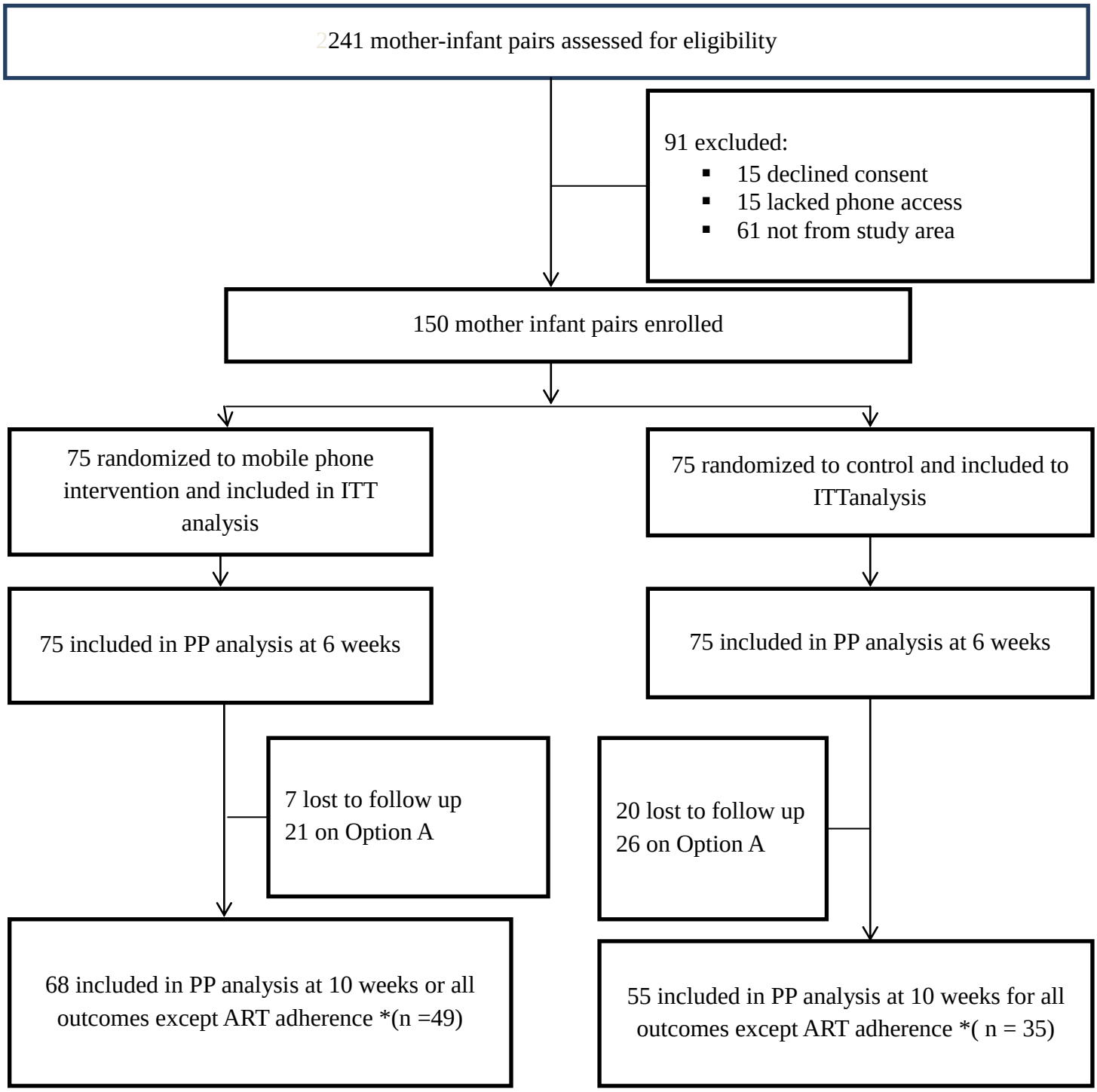

Figure 8: Flow chart of Mother-infant recruitment in study

There were no major differences in baseline characteristics between the 2 treatment groups for all maternal and newborn factors except maternal employment status and tertiary education level (table 3).

Table 3: Maternal and newborn characteristics according to mobile phone intervention allocation

Characteristics	Intervention (n = 75) n (%)	Control (n = 75) n (%)	P value
Maternal characteristics			
Mean age in years (SD)*	25.9 (4.7)	26.9 (5.5)	0.240
Married	66 (88)	65 (86.7)	0.806
Employment status			
Employed	19 (25.3)	32 (42.7)	0.025
ANC attendance	74 (98.7)	75 (100)	0.316
Mother has other living children	55 (73.3)	53 (70.7)	0.716
Education level			
Tertiary	6(8)	15(20)	0.034
Secondary	24(32)	21(28)	0.593
Primary	44(58.7)	39(52)	0.412
None	1(1.3)	0	NA
Socioeconomic factors			
Single roomed housing	35 (46.7)	37 (49.3)	0.744
Electricity within house	43 (57.3)	38 (50.7)	0.413
Cemented floor	21 (28)	21 (28)	1.00
Newborn characteristics			
Male	36 (50)	36 (50)	1.00
Mean birth weight (SD)*	3104.1 (557)	3095.8 (529.8)	0.337
Place of birth			
KDH	50 (66.7)	54 (72.9)	0.479
JOOTRH	15 (20)	15 (20)	1.00
Lumumba	9 (12)	5 (6.8)	0.262
Other	1 (1.3)	-	NA
Mode of delivery			
SVD	63 (84)	62 (82.6)	0.827
CS	12 (16)	12 (16)	1.00

*** Figures represent mean (SD)**

The odds of employment among mothers in the control group were two-fold higher than for mothers in the intervention group (OR = 2.25, 95% CI 1.12 – 4.50, p = 0.025), while the odds of mothers in the control arm receiving tertiary education were two-fold higher than for mothers in the intervention arm (OR = 0.35, 95% CI 0.1-1.02, p = 0.034).

Most mothers in both treatment groups were currently on HAART (68.9% for treatment versus 58.7% in control) as demonstrated in table 4. The proportion of participants receiving Option A did not differ between intervention (28%) and control arms (34.7%). At least 80% of mothers had disclosed HIV status to their partners (84.7% versus 83.3%) and more than half of partners had been tested for HIV (56% versus 58.7%).Among the 47 mother-infant pairs on Option A,

Table 4: Comparison of maternal HIV related information according to treatment group

	Intervention (n = 75)	**Control (n = 75)**	**P value**
Characteristics	n (%)	n (%)	
Currently on HAART	51(68.9)	44(58.7)	0.193
Currently on Option A*	21 (28)	26 (34.7)	0.379
Mean CD4 count (SD)**	406.2 (241.9)	443.1 (242.1)	0.436
HIV status disclosure to partner	61 (84.7)	60 (83.3)	0.82
Partner tested for HIV	42 (56)	44 (58.7)	0.741
Known HIV positive partner	31 (41.3)	31 (41.3)	> 0.99

***Option A (See appendix X)**

**** Figures represent mean (SD)**

the mean CD4 count was 573.3 (SD 266.6) and mean birth weight 3291.5 (SD 576.7). Most infants were delivered through SVD (n = 42, 89.4%), to married women (n = 39, 83%) with

living children (n = 32, 68.1%) and partners whose HIV status was frequently reported either as unknown (n = 22, 47.8%) or positive (n = 17, 37%). 14 (29.8%) infants on option A were being breastfed and all these breastfed infants were on nevirapine prophylaxis. All mothers of infants in this group reported that they practiced exclusive breastfeeding.

Primary outcomes

Adherence to NVP prophylaxis

Self-reported ART adherence rates were significantly different between the 2 groups at 6 weeks: 68 mother-infants reported adherence to NVP prophylaxis in the intervention arm (90.7%) versus 54 mother-infants (72%) in the control arm (OR = 3.8, 95% CI 1.5-9.5, p = 0.005) as shown in figure 9.

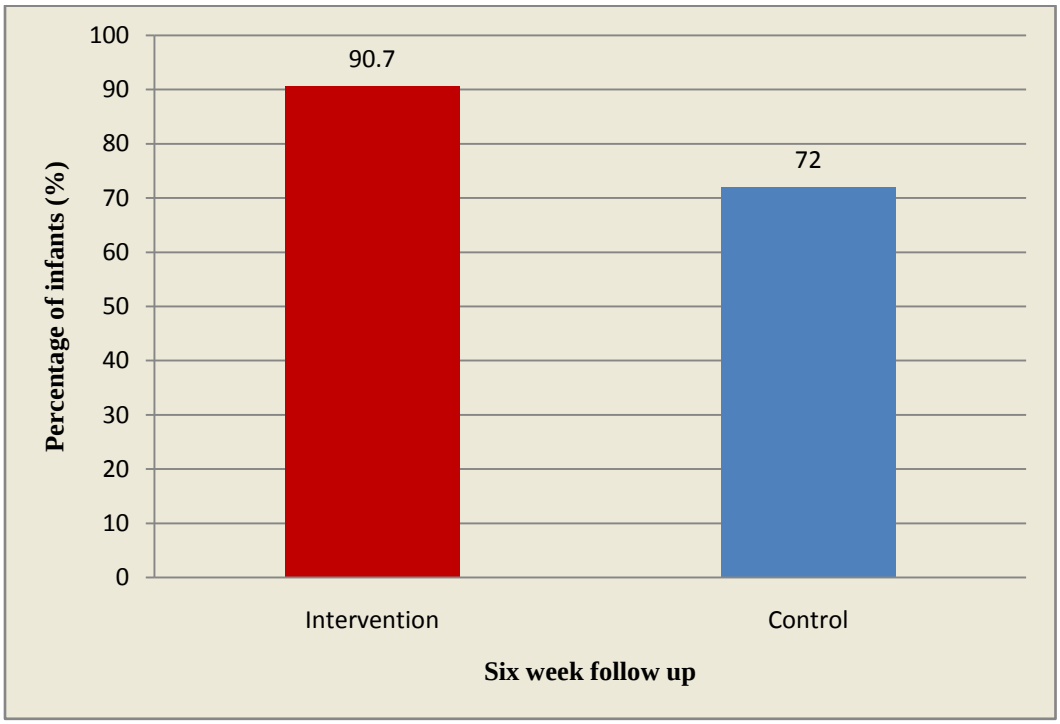

Figure 9: Adherence to infant nevirapine prophylaxis

We did not report the 10 weeks results as only 47 mothers who were on Option A were analyzed. The majority of the mothers were on HAART and their infants stopped taking NVP by 6 weeks.

Retention in care

In the intention to treat analysis, at 6 weeks 59mother-infant pairs (78.7%) attended scheduled visits with the visits coinciding with the appointment date versus 44 (58.7%) in the control arm (OR = 2.6, 95% CI 1.3-5.3, p = 0.009). At 10 weeks the revisit rates were 69.3% (52) in intervention arm and 37.3% (28) in control arm for the 150 mother-infant pairs evaluated (OR = 3.8, 95% CI 1.9-7.5, p < 0.001).

Table 5: ITT and PP analysis of mobile phone intervention effect on retention in care at 6 and 10 weeks

	Intervention N = 75	**Control N = 75**	**OR (95% CI)**	**P value**
Intention to treat analysis				
6 weeks (n =150)	59/ 75 (78.7)	44/ 75 (58.7)	2.6(1.3-5.3)	0.009
10 weeks(n=150)	52/ 75 (69.3)	28/ 75(37.3)	3.8(1.9-7.5)	<0.001
Per protocol analysis				
6 weeks (n =150)	59/75 (78.7)	44/74 (58.7)	2.6 (1.3-5.3)	0.009
10 weeks (n=123)	52/68 (76.5)	27/55 (49.9)	3.8 (1.9-7.5)	0.438

The findings of per protocol analysis were similar to the intention to treat analysis with significant differences reported between the intervention groups for all two primary outcomes: retention in care OR = 2.6, 95% CI 1.3-5.3; ART adherence, OR = 3.6(1.4-9.1); and week 10 retention in care OR= 3.4(1.6-7.3).

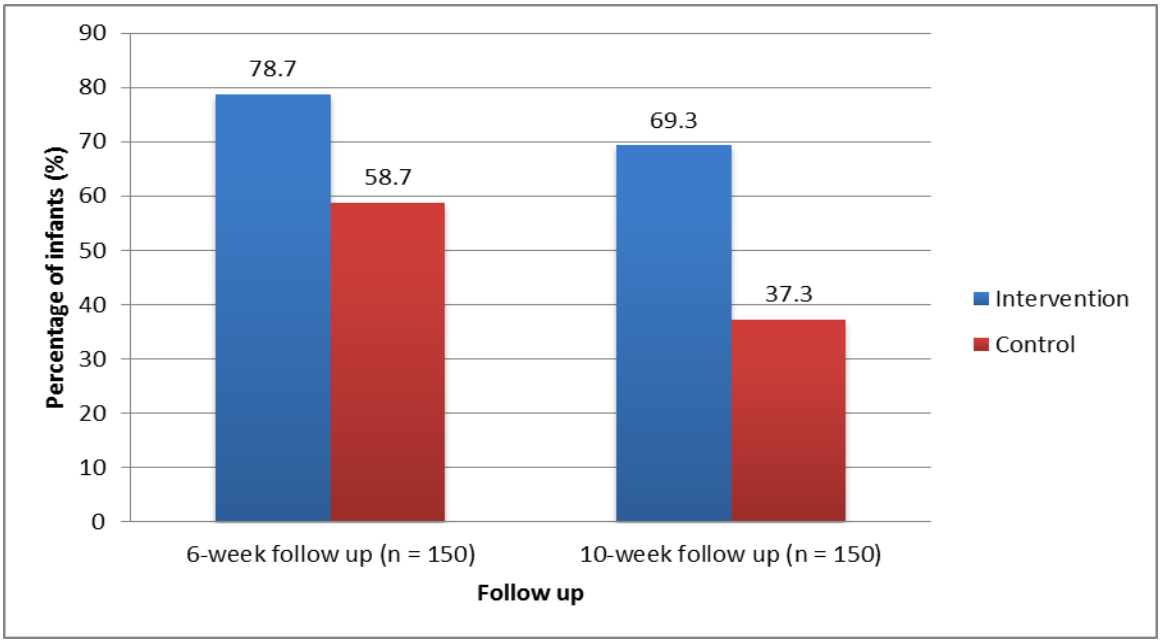

Figure 10: Retention in care

Impact of mobile phone use on EID and adherence to safe infant feeding

At 6 weeks, 53 infants (70.7%) had a PCR taken for EID in the intervention arm versus 44 (58.7%) in the control arm. At the tenth week, we had an additional 1 infant tested (54 in total) in the intervention arm, compared to 2 more (46 in total) in the control arm. Figure 11 shows that the testing rate increased by 1.3% (95% CI -1.3% to 4.0%) in intervention group compared to an increase of 2.7% (95% CI -1.1% to 6.4%) in control group.

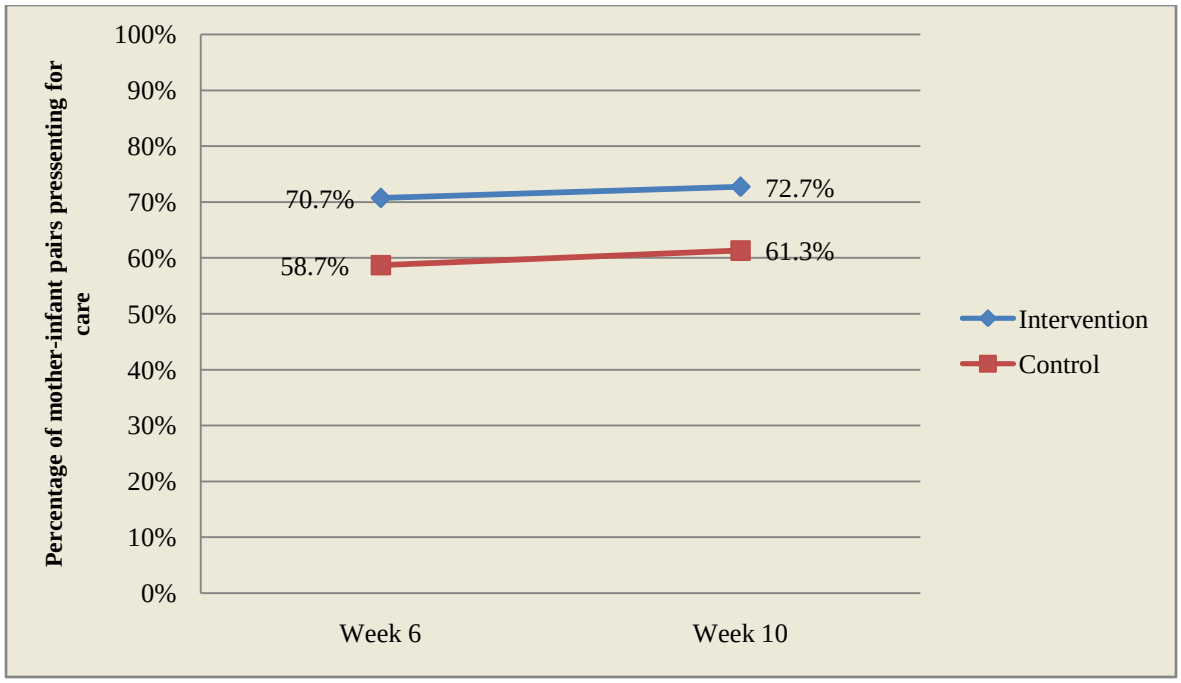

Figure 11: Comparison of EID at 6 and 10 weeks

Table 6 presents the analysis of impact of mobile phone intervention on secondary outcomes. The odds of EID testing at 6 and 10 weeks were not significantly different between the intervention and control groups [week 6: 70.7% versus 58.7%, OR = 1.7 (0.9-3.3) and week 10: 72.7% versus 61.3%, OR = 1.6 (0.8-3.2)]. All mothers reported 100% breastfeeding rates at 6 weeks follow-up visit, and the rate of exclusive feeding at 10 weeks was 88% in the intervention group compared to 64% in the control group, OR = 4.0 (1.6-10.5), which was statistically significant .

Table 6: Secondary outcomes

	Intervention	Control	OR (95% CI)	P value
Early infant diagnosis				
6 weeks (n =150)	53 /75(70.7)	44 /75 (58.7)	1.7 (0.9-3.3)	0.126
10 weeks (n =150)	54/ 75 (72.0)	46/ 75 (61.3)	1.6 (0.8-3.2)	0.167
Safe infant feeding				
6 weeks (n = 150)	All were breastfeeding			
10 weeks (n = 150)	66 / 75(88)	48 / 75 (64)	4.0 (1.6-10.5)	0.001

DISCUSSION

In this randomized control trial, we showed that the mobile phone reminders improved infant ART adherence and retention in care of HIV-exposed infants. Our data indicate that biweekly phone calls improved adherence to infant NVP prophylaxis at 6 weeks to 90.7%, compared with no phone call (72%). In our small sample, the biweekly reminders were also effective at improving retention in care at 6 weeks for the mother-infant pairs (78.7% in the intervention arm compared to 58.7% in the control arm). Our results were much better than national data which demonstrated that only 63% of exposed infants receive ARV prophylaxis at 6 weeks[11].The results of this study have important implications as Kenya strives to meet its stated goals of reducing the MTCT rate to less than 5% by 2015[12] and achieving the MDG 4, 5 and 6.

Overall, there is limited data about use of the mobile phone to promote ART adherence in the HIV-exposed infants; however, there are several studies that have been conducted in the adult HIV population that have demonstrated the efficacy of the same. Our results were comparable with a study done in Kenya to show the effect of short message service (SMS) reminders on adherence to ART among patients attending a rural clinic[13]. In that study the intervention was effective in 53% of participants receiving weekly SMS reminders achieving adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group ($p = 0.03$). It was also noted that participants in the intervention group were also significantly less likely to experience treatment interruptions exceeding 48 hours during the 48-week follow-up period than participants in the control group (81 vs. 90%, $p = 0.03$). Therefore, these results, like our study, suggested that phone reminders can be an important tool to achieve optimal treatment response in resource-limited settings.

In this study, early infant diagnosis and safe infant feeding showed trends in a positive direction but may have not shown statistical significance. Our study lacked power to attain that. However, our study showed EID rates of 70.7% in the intervention arm and 58.7% in the control arm at 6 weeks after birth, which is higher than the national rates of 35%[11]. On safe infant feeding, at 6 weeks visit all mothers in both arms reported exclusively breastfeeding their infants; this, could be attributed to the level of counseling in the PMTCT program. And, although the results for safe infant feeding were not statistically significant at 10 weeks, we showed a difference between the 2 groups (97.3% compared to 89.4%, p-value = 0.09). This was a relatively small study, and with a larger study we might be able to show a difference.

Randomization was successful in both arms, but it is worth pointing out that at baseline, there was a difference in both maternal employment status and tertiary education level [(the odds of employment among mothers in the control group were 2-fold higher than for mothers in the intervention group, while the odds of mothers in the control arm receiving tertiary education were 2-fold higher than for mothers in the intervention arm (p = 0.034)]. This could have attenuated our findings as a mother's education can exert a positive influence on her children's health and survival and a more educated mother is more likely to adhere to instructions that an uneducated one. However, this was not evident in our final analysis as we still saw great differences in the 2 arms.

There were several limitations to our study. First, it was noted that self-report on adherence to infant nevirapine and exclusive breastfeeding can be an inaccurate method of obtaining information. Further research could incorporate facility level data to verify adherence to

nevirapine in infants and exclusive breastfeeding. Additionally, a major drawback was a health care provider industrial action that took place for 3 weeks in December 2013.This not only affected the recruitment process, but also potentially hampered the follow up process in both arms. Another limitation was the customary use of mobile phones by more than one individual in some homes which posed a confidentiality risk. Further research on mobile phone use will need to continue to address issues of confidentiality. Also, our study did not review EID results due to the short period within which this study was carried out, which limited our ability to review results and have a clear picture on transmission rates. Lastly, in the 10 week follow-up of the mother-infant pairs, only 1 death (within 48 hours) was reported within the intervention arm. The mother reports that neonate was in good general health upon discharge and breastfeeding, but died in her sleep on her first night as home. She however declined to consent for postmortem. It is difficult to fully ascertain the number of deaths in both arms due to the losses to follow-up.

CONCLUSION

These results suggest that phone calls can be an important tool to improve adherence to infant nevirapine prophylaxis and retention in care for HIV-exposed infants.

RECOMMENDATIONS

-Larger studies and evaluation of cost effectiveness will be critical for understanding the true benefits and best implementation strategies of mobile phone use for follow-up in PMTCT programs.

-Further research for a longer period of time, preferably 18 months, is recommended. This will also allow for the researcher to receive EID results and look at transmission rates, which we were not able to evaluate with this study.

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APPENDIX I: PARENT INFORMATION SHEET

Mother-Infant Pair No……

Investigator and study title

My name is Dr. Lilian Kebaya from the University of Nairobi, Department of Pediatrics and Child Health. I am conducting a study to evaluate the efficacy of mobile phone use on self-reported adherence to ART and retention in care.

Emergency telephone numbers: Dr. Lilian Kebaya, Department of Paediatrics, University of Nairobi, 0711493717. Supervisors: Prof. R. Nduati-0722235323; Prof.Wamalwa–0721239493Ethical Review Committee Chairperson: Prof. A.N. Guantai-(020) 726300-9

Investigator's statement

We thank you for your willingness to participate in this study. Before you decide whether to take part, we would like to explain the purpose the study. We also want to explain the risks and benefits, and what would be expected of you if you agree to be in the study. It is important that you understand that your participation in this study is voluntary. This form will help you decide if you want to take part in the study. Once you understand the study, you can choose to be a part of the study or not. If you choose to be a part of this study, we will ask you to sign your name or make your mark on this form. We will give you a copy to keep. This process is called informed consent.

It is important that you know the following:

- You do not have to be in this study if you do not want to join.
- You may decide not to take part in the study or to withdraw from the study at any time.

Purpose of the study

Prevention of mother-to-child transmission of HIV (PMTCT) provides drugs, counseling and psychological support to help mothers safeguard their infants against the virus, therefore ensuring that no child is born with it. It is possible to interrupt this preventable burden on our innocent babies. This can be achieved by ensuring that the babies get their daily Nevirapine doses as prescribed by the healthcare provider, is exclusively breastfed or given any other safe infant replacement feeding option for the first 6 months of life and at six-eight weeks of life, the infant should be tested for HIV and the results communicated to the parents. To maximize the effectiveness of these practices, we would like to use the mobile phone to call the mothers and remind them of these practices in the prevention of mother-to-child transmission of HIV.

Study procedures

If you decide to take part in this study, you shall be followed up for three months from today. This will require that we administer to you a questionnaire at the beginning of the study. We shall be calling you fortnightly to remind you of the key PMTCT messages (Infant Nevirapine prophylaxis, safe infant feeding, and early infant diagnosis). You will be asked to bring the child to this clinic for the scheduled immunizations (at six and ten weeks).

At every planned clinic visits:

- We shall administer a questionnaire during the MCH visits (six and ten weeks) on adherence to ART, safe infant feeding and early infant diagnosis.
- We will ask several questions about the child's health and if the child missed any medicines and how / what you have been feeding the child.

At any time in the study

- If your child is sick he/ she will be seen by the medical staff at the clinic and treated.
- If your child is unwell, or if you have any concerns, you are allowed to call us on the number provided.

Risks and/or discomforts

- If you notice that the child is not well, please come to the clinic or to the nearest health facility.
- We shall not take any blood from you or your child for laboratory tests during this study.

Benefits

While taking part in the study, we shall be calling you every two weeks to follow up on your infant's wellbeing and to remind you on what you already know on the importance of PMTCT. You or others may benefit in the future from information learned in this study. You will get counseling on how best to give your child nevirapine and on safe infant feeding practices.

Other issues

Costs to you

There is no cost to you for being in this study. The researcher shall incur all the calling costs.

Confidentiality

Efforts will be made to keep all personal information related to you and your child confidential. Any publication of this study will not use your name or identify you personally.

Problems or questions

If you ever have any questions about the study you should contact Dr Lilian Kebaya. If you have questions about your rights as a research participant, feel free to contact:

Prof. A.N. Guantai (the Chair of the KNH ERC)

Secretary, KNH/UON-ERC,

Kenyatta National Hospital,

Hospital Rd, along Ngong Rd,

P.O.Box 20723, Nairobi

Tel: (020) 726300-9

Fax: 725272

APPENDIX II

INFORMED CONSENT (English version)

Mother-Infant Pair No……

I, Mr./Mrs./Ms ……., the parent of (Child's Name)……., agree to the above and give consent for me and my child to be included in this study.

As explained to me by……..

I understand the purpose of this study and conditions of participation.

Sign…….. Date……..

Witness Sign…….. Date……

IDHINI YA MZAZI WA MTOTO (Kiswahili)

Mother-Infant Pair No……

IDHINI YA MZAZI WA MTOTO (Kiswahili)

Mimi……. nimzaziwa (jina la mtoto)…….
NimekubalikushirikikatikautafitihuukamanivyoelezwanaDaktari……
……

Sahihi……. Tarehe…….

Shahidi…….. Tarehe…….

APPENDIX III: CHECK LIST

1. HIV Status: Positive ☐

Negative ☐

Unknown ☐ ; willing to be tested: Yes ☐ No ☐

2. Are you willing to participate in this study and enroll infant into the study after delivery?

Yes ☐

No ☐

3. Do you have access to a mobile phone on which you can receive calls on a regular basis (own phone)?

Yes ☐

No ☐

4. Are you willing to stay in the study area for at least 3 months after delivery?

Yes ☐

No ☐

APPENDIX IV: BASELINE QUESTIONNAIRE

1. Code number of mother-infant pair:_____ Date: __/__/____

2. i)Age of the mother: _____
   ii) Place of Birth: _____
   iii) Mode of Delivery: SVD_____ CS_____

3. i) Date of birth of the baby:__/__/____
   ii) Gender: _____
   iii) Birth weight: _____

4. Marital status:

   Married ☐
   Single ☐
   Divorced ☐
   Separated ☐
   Widowed ☐

5. Residence ☐

6. How many rooms?
   One ☐
   Two ☐
   Three ☐
   > Three ☐

7. Amount of house rent in Kenya shillings:

< 3 thousand ☐

3-5 thousand ☐

5-10 thousand ☐

10-15 thousand ☐

> 15 thousand ☐

Lives in own house ☐

8. Do you have electricity? Yes ☐ No ☐

9. Flooring Material:

Earthen ☐

Cement ☐

Wood ☐

10. Level of education:

Tertiary ☐

Secondary Complete ☐

Secondary Incomplete ☐

Primary Complete ☐

Primary Incomplete ☐

None ☐

11. Employment Status: Employed ☐ Not Employed ☐

12. If employed:

Professional/technical ☐

Skilled/Manual ☐

Unskilled/Manual ☐

Domestic Services ☐

Agriculture ☐

Small Scale business ☐

13. Did you attend ANC during pregnancy? Yes ☐ No ☐

14. Date HIV test was taken: __/__/____, or gestation (if tested during pregnancy) _____

15.i. Did you disclose your HIV status to your partner? Yes ☐ No ☐

ii. Has your partner been tested for HIV? Yes ☐ No ☐ Unknown ☐

iii. If yes, what is his HIV status? Positive ☐

Negative ☐

Unknown ☐

16. i. Do you have other living children? Yes ☐ No ☐

ii. If yes, have they been tested for HIV? Yes ☐ No ☐

iii. If deceased, age(s) at death _____; Probable cause of death (if known) _____

17. i). What was your last CD4 count? _____; if yes, date/gestation taken _____

ii).What was your last viral load (if taken)? ____; if yes, date taken/gestation_____

18. i) Are you on ARVs? Yes ☐ No; ☐ late/gestation started _____

ii) Current HAART regimen: _____

iii) If not on HAART, were you on AZT (Option A) during pregnancy? Yes ☐ No ☐

iv) If yes, date started __/__/____ or gestation started _____

19. Date Mother-baby pair due for first clinic visit: __/__/__

20. Telephone Number: _____

APPENDIX V: LOG CALLS-INTERVENTION ARM

Serial Number	Mother-Baby Pair Number	Name	Telephone Number	Call 1	Call 2	Call 3	Call 4	Call 5	Call 6	Call 7
1				**Date** __/__/___						
2										
3										
4										
5										
6										
7										
8										
9										
10										

Calls made by mothers (from both arms)

Name	Telephone Number	Date	Concerns raised	Comments and/or recommendations made

APPENDIX VI: FOLLOW-UP QUESTIONNAIRES

FIRST VISIT

1. Age of infant _____

2. Adherence to clinic visits:

   i. Clinicname: ☐

   ii. Date of first visit: __/__/____

3. Adherence to Infant NVP Prophylaxis:

   i. Was Mother given NVP Prophylaxis for baby at ANC or after delivery? (Check ARV dispending tool)

   Yes ☐ No ☐

   ii. Is Mother on HAART?

   Yes ☐ ☐

   If yes, is infant breastfeeding? Is infant on NVP prophylaxis?

   Yes ☐ No ☐ Yes ☐ No ☐

   iii. Was mother on Option A(during pregnancy)?

   Yes ☐ No ☐

   If yes, is infant breastfeeding? Is infant on NVP prophylaxis?

   Yes ☐ No ☐ Yes ☐ No ☐

iv. Has the infant missed any NVP doses? Yes ☐ No ☐

If yes, how many? ☐

4. Safe infant feeding:

i. What have you been feeding your infant on since birth? Breast milk ☐

Formula ☐

Other (Specify)

_____

ii. If breastfeeding, have you given infant anything to eat or drink other than breast milk?

Yes ☐ No ☐

iii. If yes, specify item(s) ☐

5. Timing of EID (Check HEI register): Date __/__/____

6. Date Mother-baby pair due for second clinic visit: __/__/__

SECOND VISIT

1. Age of infant _____

2. Adherence to clinic visits:

   i. Date of second visit: __/__/____

3. Adherence to Infant NVP Prophylaxis:

   i. Was Mother given NVP Prophylaxis for baby at ANC or after delivery? (Check ARV dispending tool)

   Yes ☐ No ☐

   ii. Is Mother on HAART?

   Yes ☐ No ☐

   If yes, is infant breastfeeding? Is infant on NVP prophylaxis?

   Yes ☐ No ☐ Yes ☐ No ☐

   iii. Was Mother on Option A(during pregnancy)?

   Yes ☐ No ☐

   If yes, is infant breastfeeding? Is infant on NVP prophylaxis?

   Yes ☐ No ☐ Yes ☐ No ☐

. iv. Has the infant missed any NVP doses? Yes ☐ No ☐

If yes, how many? ☐

4. Safe infant feeding:

i. What have you been feeding your infant on since birth? Breast milk ☐

Formula ☐

Other (Specify) ☐

ii. If breastfeeding, have you given infant anything to eat or drink other than breast milk?

Yes ☐ No ☐

iii. If yes, specify item(s) ☐

5. Timing of EID (Check HEI register): Date __/__/____

6. Results of EID, if available (Check HEI registers):_____

APPENDIX VII: FEEDING INFANTS AND YOUNG CHILDREN BORN TO HIV-INFECTED MOTHERS[4]

A. Operational Guidelines on Infant feeding (0-6 months)

The following should guide infant feeding for the first six months:

1. All mothers who are HIV negative or are of unknown HIV status should be encouraged and supported to exclusively breastfeed for the first six months and continue breastfeeding with appropriate complementary feeding introduced thereafter.
2. All HIV positive mothers should be given information on available infant feeding options and counselled using recent scientific information on benefits and challenges for each option in order to help them make an informed choice.
3. All HIV positive mothers who choose to breastfeed should be encouraged and supported to exclusively breastfeed for the first six months and continue breastfeeding up to one year with appropriate complementary feeds. Infants of these mothers should be provided with NVP prophylaxis for up to one week after complete cessation of breastfeeding.
4. HIV positive mothers who meet AFASS(Acceptable Feasible Affordable Sustainable and Safe) criteria and chose not to breastfeed should be encouraged and supported to do exclusive replacement feeding for the first six months and appropriate complementary feeding introduced thereafter. Infants of these mothers should be provided with NVP prophylaxis for six weeks.
5. In special circumstances determined by clinicians involving infants who cannot breastfeed e.g. orphans or abandoned babies or where the mother has condition like

mastitis preventing breastfeeding the infant should be provided with exclusive replacement feeding with appropriate complementary feeds introduced thereafter.

B. Operational Guidelines on Feeding Children six months and older

The following should guide feeding for children six months and older:

1. From six months, milk alone is not adequate to meet the baby's nutritional requirements.
2. Complementary foods should be introduced with continued breastfeeding or with replacement feeding until a nutritionally adequate diet can be sustained without milk.
3. Abrupt cessation of breastfeeding should be discouraged to avoid psychological trauma for both the mother and the baby.
4. From 6 months animal milk can be introduced and should continue as an important component of the child's diet.
5. Complementary foods should be prepared from locally available family foods.

APPENDIXVIII: MILLENNIUM DEVELOPMENT GOALS (WHO)

The United Nations Millennium Development Goals are eight goals that all 191 UN (United Nations) member states have agreed to try to achieve by the year 2015. The United Nations Millennium Declaration, signed in September 2000 commits world leaders to combat poverty, hunger, disease, illiteracy, environmental degradation, and discrimination against women. The MDGs are derived from this Declaration, and all have specific targets and indicators.

The Eight Millennium Development Goals are:

1. To eradicate extreme poverty and hunger;
2. To achieve universal primary education;
3. To promote gender equality and empower women;
4. To reduce child mortality;

   Target 5: Reduce by two thirds, between 1990 and 2015, the under-five mortality rate

   - Children 1 year old immunized against measles, percentage
   - Children under five mortality rate per 1,000 live births
   - Infant mortality rate (0-1 year) per 1,000 live births
5. To improve maternal health;

   Target 6: Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio

   - Births attended by skilled health personnel, percentage
   - Maternal mortality ratio per 100,000 live births
6. To combat HIV/AIDS, malaria, and other diseases;

   Target 7: Have halted by 2015 and begun to reverse the spread of HIV/AIDS
7. To ensure environmental sustainability; and

8. To develop a global partnership for development.

The MDGs are inter-dependent; all the MDG influence health, and health influences all the MDGs. For example, better health enables children to learn and adults to earn. Gender equality is essential to the achievement of better health. Reducing poverty, hunger and environmental degradation positively influences, but also depends on, better health.

APPENDIX IX: COVERAGE OF ANTIRETROVIRAL PROPHYLAXIS TO PREVENT THE MOTHER TO CHILD TRANSMISSIONS OF HIV[2]

For pregnant women living with HIV who are not eligible for treatment, WHO recommends two efficacious antiretroviral regimen options for prophylaxis to reduce transmission during the perinatal period and while breastfeeding. For the first time, antiretroviral medicine to either the mother or the infant is recommended throughout the breastfeeding period, in settings where breastfeeding is the safest option for feeding the infant.

For **option A**, the mother takes zidovudine during the antenatal period, starting from as early as 14 weeks of pregnancy. A single dose of nevirapine and lamivudine is added during labour, and zidovudine and lamivudine are continued for seven days after delivery as a "tail" to decrease the risk of nevirapine resistance. If the mother breastfeeds, the baby will receive nevirapine syrup from birth until one week after all exposure to breast-milk has ended. If the mother is giving the baby replacement feeding, he or she will only get either nevirapine or zidovudine from birth until 4–6 weeks of age.

For **option B**, the mother takes a prophylaxis regimen consisting of three antiretroviral medicines during pregnancy, labour and after delivery until one week after all exposure to breast-milk has ended. Infants born to mothers on option B receive either nevirapine or zidovudine from birth until 4–6 weeks of age, regardlessof their feeding method. WHO recommends four possible triple antiretroviral prophylaxis regimens for option B, with the choice of regimen to be made at the country level.

Importantly, a single dose of nevirapine is no longer recommended as a standard practice.

APPENDIX X: TIMELINE / TIME FRAME

Table 7: Timeline

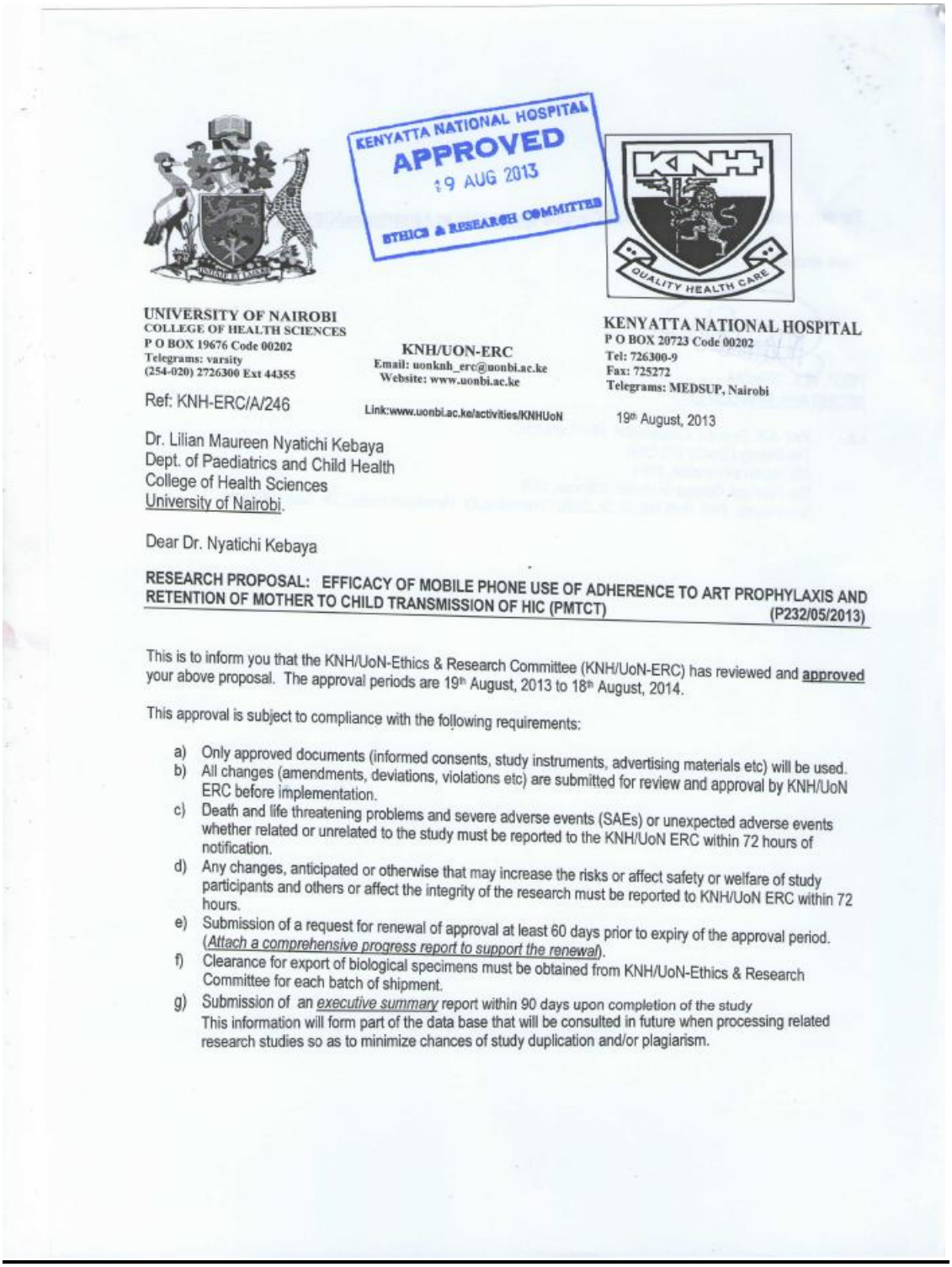
Activity	Dec 12	Jan 13	Feb 13	Mar 13	Apr 13	May 13	Jun 13	Jul 13	Aug 13	Sep 13	Oct 13	Nov 13	Dec 13	Jan 14	Feb 14	Mar 14
Proposal development	■	■														
Proposal defense			■													
Submission to ERC				■	■	■	■	■								
Data collection									■	■	■	■	■			
Data analysis and report writing												■	■	■	■	■
Poster presentation																■

APPENDIX XI: BUDGET

Table 8: Budget

Item	**Number**	**Unit Cost**	**Total**
KNH/UON Ethics committee	1	2000	2000
JOOTRH Ethics Committee	1	6000	6000
Poster print	1	1500	1500
Phone	1	5,000	5,000
Airtime / per call / per min=4 Ksh(Safaricom network) fortnightly	Estimated call time = 4 Ksh (75 participants in the intervention arm, and each call lasts approximately 2-3 minutes)	5000	5,000
Research Assistants	3 Clinical Officers: Recruiting of mothers and follow up of the mother-baby pairs at their respective clinics	15000 each for the Clinical officers, for 5 months	225000
Travel costs/per trip	3 return trips to Kisumu by bus	3,000	9,000
Accommodation (October 2013)	1200 per day	30 days = 36,000	36,000
Stationery	Pens, pencils, envelopes, erasers, files for each mother-infant pair Printing costs	5,500 2,000	5,500 2,000
Data Analysis	1	30,000	30,000
Miscellaneous	XXX	5,000	5,000
Total			**332,000**

APPENDIX XII: ETHICS APPROVAL



KENYATTA NATIONAL HOSPITAL
APPROVED
19 AUG 2013
ETHICS & RESEARCH COMMITTEE

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
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(254-020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
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Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/246

19th August, 2013

Dr. Lilian Maureen Nyatichi Kebaya
Dept. of Paediatrics and Child Health
College of Health Sciences
University of Nairobi.

Dear Dr. Nyatichi Kebaya

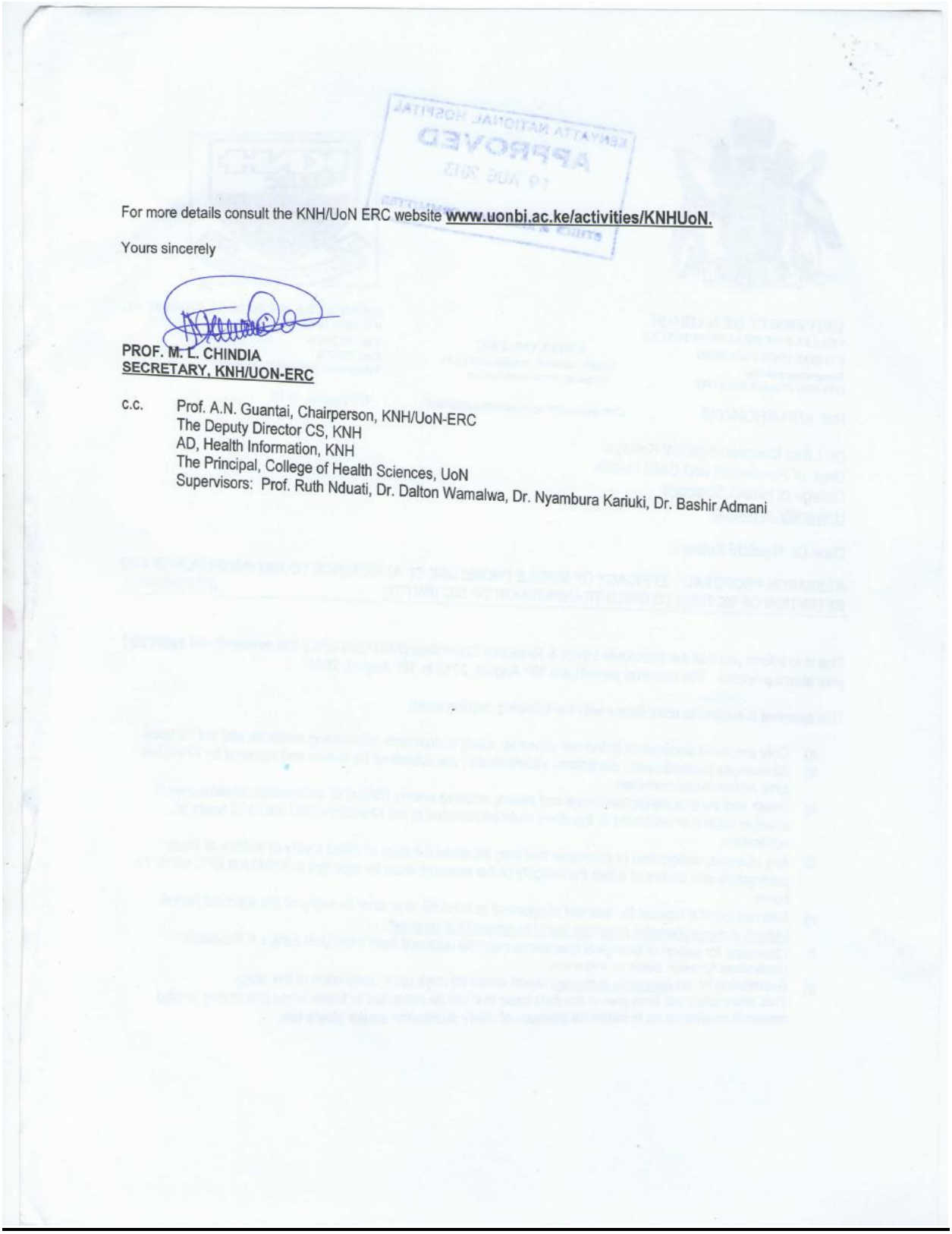
RESEARCH PROPOSAL: EFFICACY OF MOBILE PHONE USE OF ADHERENCE TO ART PROPHYLAXIS AND RETENTION OF MOTHER TO CHILD TRANSMISSION OF HIC (PMTCT) (P232/05/2013)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 19th August, 2013 to 18th August, 2014.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

Figure 12: Ethics approval, part I



For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN.**

Yours sincerely

PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. Prof. A.N. Guantai, Chairperson, KNH/UoN-ERC
The Deputy Director CS, KNH
AD, Health Information, KNH
The Principal, College of Health Sciences, UoN
Supervisors: Prof. Ruth Nduati, Dr. Dalton Wamalwa, Dr. Nyambura Kariuki, Dr. Bashir Admani

Figure 13: Ethics approval, part II