Mobile Phone Communication for Improving Uptake of Antiretroviral Therapy in HIV-infected Pregnant Women: Review

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ABSTRACT

Background: About 1.4 million pregnant women are living with HIV in low and middle-income countries with about 91% of these women residing in sub-Saharan Africa. HIV-infected pregnant women face several challenges that could decrease antiretroviral therapy adherence. Studies reported challenges such as poor mental health, lack of social support, fears of infecting children, medication side effects, cultural factors, economic instability, nausea and vomiting during pregnancy. This review investigated whether mobile phone text messaging could improve antiretroviral therapy in during and after pregnancy. Objectives: To assess the effectiveness mobile phone text messaging for improving adherence to antiretroviral therapy in HIV-infected pregnant women. To investigate whether mobile phone text messaging could improve follow-up in HIV-exposed infants. Search methods: We searched Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, MEDLINE via PubMed, Web of Science, CINAHL (EBSCO). Furthermore, we searched studies through HIV/AIDS conferences websites: International AIDS conferences, The European AIDS Clinical Society (EACS) conferences, International AIDS Society Conference on HIV Pathogenesis and Treatment (IAS). Two authors extracted data in the study eligibility form. Selection criteria: We selected randomized controlled trials (RCTs) assessing mobile phone text messaging as reminders for antiretroviral therapy uptake in HIV-infected pregnant women. Data collection and analysis: Two authors independently identified and assessed all studies that met inclusion criteria. Study design, characteristics of study populations, interventions and controls and study results were extracted by two review authors. Also, the risk of bias of included studies was assessed independently by two reviewers. We reported the results narratively as meta-analysis was not feasible because of differences in the study design. We reported the odds ratio with 95% confidence intervals for the different outcomes. Main results: We identified five eligible studies; three ongoing and two completed studies. Findings from the included studies showed that mobile phone text messaging did not increase antiretroviral therapy initiation (OR 1.79 95%CI 1.09 to 2.94, 307 participants, 1 study). However, there was an increase in maternal clinic attendance and HIV tested infants; (RR 1.66 95%CI 1.02 to 2.70, 381 participants, 1 study) and (OR 2.01 95%CI 1.03 to 3.92, 325 participants, 1 study), respectively. The overall quality of evidence was assessed as moderate. None of the included studies reported on adherence to antiretroviral therapy. Authors’ Conclusions: The review revealed that mobile phone text messaging may improve maternal clinic attendance and number infants tested for HIV compared to the standard care. Mobile phone communication did not improve ART initiation compared to standard care. Further studies are needed to evaluate the value of mobile phone communication in promoting adherence to antiretroviral drugs among pregnant women and reduction of mother-to-child transmission of HIV.

Keywords: HIV-infected, Pregnant, Phone Communication, Uptake.
1. INTRODUCTION

Around 1.4 million pregnant women are living with HIV in low and middle-income countries with about 91% of these women residing in sub-Saharan Africa. HIV-infected pregnant women are facing several challenges that could decrease antiretroviral therapy adherence in antepartum as well as in postpartum. The main goal of this study was emphasized on assessing the effectiveness mobile phone text messaging for improving antiretroviral therapy initiation on antenatal and postpartum care in HIV-positive women. Also, the study was focused on investigating whether mobile phone text messaging could improve follow-up in HIV-exposed infants.

This review included two randomized controlled trials. Both trials were conducted in sub-Saharan Africa (Kenya and Botswana). They compared short weekly text messages against standard care. The findings showed that mobile text messaging did not improve the rate of initiation of antiretroviral drugs among pregnant women. However, there was some improvement in the rate of clinic attendance and number of infants tested for HIV. Further studies are needed to evaluate the value of mobile phone communication in the prevention of mother-to-child transmission of HIV.

Background

Description of the condition

In 2015, about 36 million people were living with the human immunodeficiency virus (HIV) (UNAIDS 2016). In December 2015, 17 million people HIV-infected were accessing antiretroviral therapy (UNAIDS 2016). Among them, 77% of pregnant women HIV-infected had access to antiretroviral medicines to prevent mother-to-child transmission (PMTCT) (UNAIDS 2016). Sub-Saharan Africa is the most affected region, with 25.6 million people living with HIV in 2015(WHO 2016). Among them, 58% were women (UNAIDS 2016) In Sub-Saharan Africa, mother-to-child transmission (MTCT) is the highest in the world. Antiretroviral therapy (ART) use in antepartum and postpartum period is crucial both for preserving maternal health and for PMTCT of HIV (Nachega 2012). In 2015, about 77% of pregnant women living with HIV had access to antiretroviral treatment to prevent MTCT (UNAIDS 2016).Therefore, in Sub-Saharan Africa, gaps in access to treatment persist in some countries.

Pregnant women living with HIV face daily challenges maintaining their health and that of their babies including physical and mental health (Rotheram-Borus 2011). A recent review highlighted that psychiatric symptoms, particularly depression, and mental health vulnerabilities are widespread among HIV-infected women globally and have a potential to affect psychological well-being, quality of live and salient clinical outcomes (Kapetanovic 2014). Then, receiving a positive HIV diagnosis during pregnancy often elicits feelings of anxiety, depression and social isolation (Rochat 2006; Rotheram-Borus 2011). Poor mental health and a lack of social support are, in turn, associated with decreased adherence to ARV medication, and faster disease progression (Starace 2002; Cook 2006; Rotheram-Borus 2011). Also, to decrease social support and mental health, WLH face other challenges such as fears of transmitting the infection to their baby and Impact on ability to raise children (Faithfull 1997). Studies have revealed that poor adherence ARV continues to be one of the most frequent reasons for poor treatment outcomes and/or lack of sustained treatment benefits (Conway 2007; Reynolds 2008).

Despite improved treatment coverage and meaningful reductions in MTCT in sub-Saharan Africa over the past several years, continued improvements in PMTCT programs are required if Millennium Development Goals. Recently, most sub-Saharan Africa Ministry of Health introduced the option B+ which expands lifelong highly active antiretroviral therapy (HAART) to all HIV-infected pregnant women independent of CD4 cell count and clinical staging (Schwartz 2015). In HIV-infected pregnant women, option B+ presents to increase treatment access globally and its potential in improving mothers’ and babies’ health, reduced stigma and opportunities to breastfeed (Matheson 2015). Option B+ has been adopted by several sub-Saharan countries (Schouten 2011; Republic of Zambia Ministry of Health 2013; Herlihy 2015). Then, the adequate measure should be taken in Sub-Sahara particularly, and in developing countries to strengthen option B+. Thus, several interventions should be explored to integrate Option B+ successfully in developing countries. In this review, we explore the effects of mobile phone communication in improving adherence to ARV during pregnancy and improving HIV-related outcomes.
Description of the intervention
Mobile health can be defined as the practice of medical and public health via mobile communication devices (Torgan C 2009; health alliance 2012 Catalani 2013). Most resource-limited settings have well developed cellular telecommunication networks, and mobile phone ownership worldwide has grown dramatically from 1 billion in 2002 to 4.1 billion in 2008 (Pop-Eleches 2011). Actually, there are more than 7 billion mobile phone ownership worldwide (The world in 2015). As wireless telecommunications networks have spread rapidly throughout sub-Saharan Africa, South Asia, and other resource-limited settings with high HIV prevalence, sending text messages on wireless mobile telephones has become an extremely popular means of communication among people in all sectors of society (Horvath 2012; iTWire 2011). Mobile phone text messaging, also called short messaging service (SMS), has been proposed as an approach to improve adherence rate (Horvath 2012; Mbuagbaw 2012). Furthermore, health programs that use mobile communication technologies are emerging with the aim of strengthening health systems (Kaplan 2006; Krishna 2009; Lester 2010; Padma 2010). If mobile phone use does improve health outcomes in limited resource settings, this mobile health technology could thus be included in health-system strategies and help health development goals (Rabkin 2009; Lester 2010). A study conducted in South Africa has revealed that the short message service (SMS) improves HIV health care service delivery by enhancing communication between health workers and patients, and also as an appointment reminder (Mukund 2010).

How the intervention might work
Reviewing the literature on adherence intervention, we find that this field of HIV adherence interventions is quite broad. Major reviews of adherence interventions conducted mainly in developed countries revealed that the most effective are typically patient-based, behavioral interventions designed to build patient knowledge and efficacy through practical medication management skills (Amico 2006; Simoni 2006; Scanlon 2013). Nowadays, biomedical scientists involved in clinical trial research and health care providers charged with treating persons living with HIV are interested in social and behavioral interventions to improve adherence (Chesney 2000). In particular, there is interest in understanding the factors that account for patients’ difficulties in adhering to care (Chesney2000). While some social and behavioral scientists have become very involved in developing measures of adherence, studying explanatory factors and developing programs to improve patient adherence, others (Giami 1996 Abelhauser, 1998; Chesney 2000) have argued, ‘‘l’arbre qui cache la foret’’. (Chesney 2000). That means patient adherence is multidisciplinary and complex.

Given the dearth of research in this area and the potential opportunities that SMS provides healthcare providers and PLWH, Coomes proposed a conceptual model (Figure 1) that integrates the communication functionality of SMS with important psychosocial factors that could mediate the impact of SMS communication on health outcomes (Coomes 2012). This model is based on the limited but growing research that has used SMS across various disease conditions to assist patients in self-management or adherence (Coomes 2012).

In most countries affected by HIV, the use of mobile phones to improve HIV-related health outcomes is emphasized as emerging evidence that stipulates reminder messages can increase adherence to ART and retention in care, decrease then viral load and treatment interruptions, and improve communication with healthcare personnel (Mbuagbaw, 2013).

Why it is important to do this review
Prevention of mother-to-child transmission is a cornerstone strategy in reducing infant mortality due to HIV infection (UNAIDS 2010; Jennings 2013). However, an estimated of 330,000 children acquired HIV worldwide in 2011, over 90% through mother-to-child transmission (Jennings 2013). Current strategies for preventing HIV infections in infants can reduce the risk of transmission from an estimated 30% to less than 2% (Jennings 2013). However, in resource-limited countries, low adherence and retention limit the utility of facility-based PMTCT services to ensure appropriate prophylaxis and treatment from pregnancy to delivery and pursuing in the postnatal period until stop breastfeeding (Jennings 2013). A systematic review has shown that many factors could affect adherence of antiretroviral in pre –and post-natal periods (Nachega 2012). Morning sickness is common in early pregnancy and may contribute to reduced adherence during this period (Nachega 2012). Nausea and vomiting affect 70–85% of pregnant women in early pregnancy and may be exacerbated by other medications e.g. Zidovudine (ZDV), particularly those that may also have common gastrointestinal side-effects. Heartburn also occurs in later pregnancy and may affect medication taking behaviors (Nachega

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Then, HIV Symptom Index Score (symptom burden) (Koole 2016) could be estimated high in HIV-infected pregnant women. Furthermore, physical, economic and emotional stresses, including the stresses and demands of caring for a new baby might interfere with ART uptake, and then make adherence more difficult in the postpartum period (Nachega 2012). Adherence in early pregnancy may also be affected by maternal concerns about the safety of ART drugs for the fetus (Nachega 2012).

A recent study concluded that HIV-infected women on suppressive combination antiretroviral therapy, the risk of viral rebound is increased during postpartum, especially in the first 3 months, which may be related to reducing adherence (Huntington 2015). Also, postpartum viral rebound was linked with fewer prenatal visits and later gestational week of starting prenatal care (Cavallo 2010; Adams 2015). Indicating then the need for effective adherence interventions as well as in prenatal and postpartum period.

A recent systematic review found high-quality evidence of efficacy in intervention using short weekly message (Horvath 2012; Finitsis 2014) and World Health Organization guidelines include a strong recommendation to consider text messaging "for promoting adherence to ART as part of a package of adherence interventions (WHO 2013; Finitsis 2014)". We did not find any review that evaluated the effects of mobile phone communication for improving PMTCT outcomes. Therefore, this systematic review aims to provide some evidence on the use of mobile phone communication for improving adherence to ARVs during pregnancy.

Fig.1 Conceptual model of the communication functionality of short message service (SMS), showing psychosocial factors that could mediate the impact of SMS communication on health care quality and health outcomes (Coomes 2012)

**Objectives**

To assess the effectiveness mobile phone text messaging for improving adherence in antiretroviral therapy in HIV-infected pregnant women.

To investigate whether mobile phone text messaging could improve follow-up in HIV-exposed infants.

2. METHODS

**Criteria for considering studies for this review**

**Types of studies**

We considered randomized controlled trials (RCTs) that evaluated the efficacy of mobile phone communication for improving the therapy in HIV-infected pregnant women.
Types of participants
HIV-positive pregnant women, on HAART or about to start HAART.

Types of interventions
- Experimental: Daily, weekly or monthly SMS reminders or other forms of mobile phone communication aimed at reminding the patient about adherence to ARVs, expected to respond within 48 hours, clinician to response, non-responders called and calls.
- Comparison: Standard care or no mobile phone communication.

Types of outcome measures

Primary outcomes
A. Maternal outcomes
   - Initiation of antiretroviral therapy
   - Maternal clinical attendance (ante and postpartum)
B. Infant outcome
   - Mother to child transmission of HIV

Secondary outcomes
- Number of infants tested for HIV

Search methods for identification of studies

Electronic searches
Until 5 May 2016, we searched the following electronic databases:
- CENTRAL (Cochrane Central Register of Controlled Trials)
- Scopus
- MEDLINE via PubMed
- Web of Science
- CINAHL (EBSCO)

Both text words and Medical subject heading (MeSH) terms, for example pregnant women, adherence, antiretroviral, antiretroviral therapy, HAART, HIV, acquired immunodeficiency syndrome, SMS, texting, text message, short message service, cell phone, phone, telephone, mobile health, mHealth, mobile phone, short message and randomized controlled trial were used in the search strings. Furthermore, we used Boolean search in different combinations with the adaptation of the literature search strategy that will be convenient to each database. We suggested the following search strategy:

(Pregnant women) OR (pregnant) OR (pregnancy) OR (pregnancies) OR (gestation) OR (mother to child transmission) OR (vertical transmission) OR (mtct) OR (pmtct) OR (perinatal transmission)
AND
(Cellular phone) OR (telephone) OR (mobile phone) OR (text message*) OR (testing) OR (short message*) OR (cell phones) OR (SMS) OR (short message service) OR (text) OR (mobile health) OR (telemedicine) OR (health) OR (health communication) OR (health education) OR (behavior) OR (ehealth)
AND
(Antiretroviral therapy) OR (anti-retroviral agents) OR (antiretroviral) OR (ART) OR HAART
AND
(Randomized controlled trial) OR (controlled clinical trial) OR (randomized controlled trials) OR (random allocation) OR (double-blind method) OR (single-blind method) OR (clinical trial) OR (trial) OR (clinical trials) OR (clinical trial) OR (single* OR double*) OR (treble* OR triple*) AND (mask* OR blind*) OR (placebos) OR (placebo*) OR (random*)

Searching other resources
We conducted an electronic search for potentially eligible studies through conferences websites: International AIDS conferences, The European AIDS Clinical Society (EACS) conferences, International AIDS Society Conference on HIV Pathogenesis and Treatment (IAS). We also searched for unpublished and ongoing studies in prospective clinical trial registries such as ClinicalTrials.gov and WHO International Clinical Trials Registry Platform.

3. ANALYSIS

The methodology used for collecting and analyzing data was based on the guidance of the Cochrane Handbook of Systematic Reviews of Interventions (Higgins 2011). Authors (JT and CO), working independently, reviewed the abstracts of all studies identified through database searches or other resources. Where there was any question of eligibility, we obtained the full text of the article for closer examination.

Selection of studies
Two review authors (JT and CO) evaluated the studies obtained from the literature search for eligibility criteria. Titles and abstracts were independently screened to obtain the full text of eligible studies. In the cases of disagreement, the resolution was reached by consensus.
Data extraction and management
We used a data extraction sheet to capture data and entered the data into Review Manager Software RevMan 5. Two authors (JT and CO) extracted data independently for each included study. In the event of disagreements, authors discussed for further clarifications. The data extraction sheet included the following information:

- Trial characteristics: trial design, the risk of bias assessment, the number of participants included and excluded length of follow-up (in weeks) and lost to follow-up (number of patients).
- Participant characteristics: country of origin, sample size, setting, age, date of the study, the range of gestational age, antenatal or postpartum period, education, comparison group.
- Intervention characteristics: duration of intervention (in weeks, intensity per week and total time expressed in hours).
- Type of intervention: e.g. SMS.
- Outcomes: Primary and secondary outcomes relevant to this review.

Assessment of risk of bias in included studies
We assessed independently the risk of bias using the Cochrane risk of bias tool (Higgins 2011). The recommended approach for assessing the trial quality in studies included in Cochrane Reviews is based on six domains (sequence generation, allocation concealment, blinding of participants, personnel and outcomes, incomplete outcome data, selective reporting and other issues). The first step of the tool implied describing what was reported to have happened in the study. The second step of the tool involved assigning a judgment relating to the risk of bias for that entry regarding the high, low or unclear risk of bias. If any disagreement remains unresolved, the third author was consulted in order to make a final decision.

Measures of treatment effect
We used the latest version of the Review Manager 5.3 software provided by the Cochrane Collaboration for preparing the review and for statistical analysis (RevMan 2011). We used odds ratio and risk ratio as the principal categorical outcome measure of effect, with 95% confidence intervals (CI). The results were presented in the forest plots.

Unit of analysis issues
The unit of analysis was individuals.

Dealing with missing data
We did not find any missing data when assessing included studies.

Assessment of heterogeneity
We planned to assess heterogeneity on the interventions, outcomes, and studies through visual inspection of the forest plot and by a chi-squared test to demonstrate whether the observed differences in results are compatible with chance alone. However, we included a very limited number of studies and did not assess for heterogeneity.

Assessment of reporting biases
We did not assess for reporting bias due to a limited number of studies.

Data synthesis
Included studies were very few, and their study designs were different. Then, it was not appropriate to combine the results of the studies statistically. We present narratively an overview of the findings. We used Review Manager 5 (RevMan 2011) provided by the Cochrane Collaboration for preparing the review and for statistical analysis. We presented the results in the forest plots and then interpreted different results.

Subgroup analysis and investigation of heterogeneity
Subgroup analyses was not undertaken to investigate heterogeneity because of a limited number of studies.

Sensitivity analysis
We did not do sensitivity analysis.

4. RESULTS

Results of the search
Figure 2 shows the study selection flow diagram. The literature search yielded 4907 articles. After screening titles and abstracts, 20 articles were selected for critical reading. Five studies met the inclusion criteria, and two were included in the analysis. There were 2 completed trials and 3 ongoing studies. Studies were succinctly described in annex tables: Characteristics of included studies, Characteristics of excluded studies and Characteristics of ongoing studies.

Included studies
Two randomized control trials were identified as meeting the inclusion criteria. One study was a cluster trial while the other was a Parallel-group, unblinded, randomized controlled trial. Details of these trials (Dryden-Peterson 2015; Odeny 2014); are shown in
the “Characteristics of included studies” (Table 1) and bias risk (Table 2). Three other studies were ongoing trials (Davey 2012; Mwapasa 2014; Ong’ech 2014). See Characteristics of ongoing studies (Table 3)

Fig. 2 Selection flow diagram

<table>
<thead>
<tr>
<th>Table (1) Characteristics of included studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dryden-Peterson 2015</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Methods</th>
<th>stepped-wedge cluster randomized trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>366 HIV-infected pregnant women enrolled in PMTCT. 169 in the intervention group and 156 in control group (analyzed for CD4 before 26 weeks gestation). 154 in the intervention group and 153 in control group (analyzed for ART before 30 weeks gestation). A study conducted in the antenatal clinic, Gaberone/Botswana.</td>
</tr>
<tr>
<td>Interventions</td>
<td>The Tokafatso intervention included: An automated sending SMS every 4 weeks from the second week until the twelfth week. A 1-2 hour participatory session for clinic staff. Longitudinal support by study team member to antenatal clinics.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary: Dichotomous measure ART initiation before 30 weeks gestation:</td>
</tr>
</tbody>
</table>
Intervention group: 56/154  
Control group: 37/153  
**Secondary:** Dichotomous measures:  
CD4 before 26 weeks gestation:  
Intervention group: 100/169  
Control group: 79/156  
Impact on Specific Elements of the prevention of MTCT cascade:  
Intervention group: 168/169  
Control group: 155/156  

<table>
<thead>
<tr>
<th>Odeny 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
</tr>
</tbody>
</table>
| **Outcomes** | Maternal clinic attendance (8 weeks post-partum)  
SMS group: 38/194  
Control group: 22/187  
infant HIV DBS testing (8 weeks post-partum)  
SMS group: 172/187  
Control group: 154/181  
Mother to child transmission of HIV  
SMS group: 2/187  
Control group: 3/181 |

Table (2) Bias Risk

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgment</th>
<th>Support for judgment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear Risk</td>
<td>Not enough information to judge 'Yes' or 'No.'</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High Risk</td>
<td>... the envelope was opened revealing the names of the 2 clinics to receive the intervention…</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low Risk</td>
<td>Clinics and the study team were blinded to randomized order.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low Risk</td>
<td>Records were used to assess the outcome…</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High Risk</td>
<td>The reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing</td>
</tr>
</tbody>
</table>
data across interventions intervention groups. The analysis intention to treat was not used. The data has not been able to be re-included.

<table>
<thead>
<tr>
<th>Selective reporting (reporting bias)</th>
<th>Low Risk</th>
<th>The study protocol is available. Also, primary and secondary outcomes of interest have been reported.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other bias</td>
<td>High Risk</td>
<td>The population seems to be different in some baseline characteristics.</td>
</tr>
</tbody>
</table>

**Odeny 2014**

<table>
<thead>
<tr>
<th>Random sequence generation (selection bias)</th>
<th>Low Risk</th>
<th>A block randomization scheme with variable block sizes was used.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low Risk</td>
<td>Opaque sealed envelopes were used.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High Risk</td>
<td>Neither participants nor personnel was not blinded.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low Risk</td>
<td>The outcomes were extracted from clinic records.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low Risk</td>
<td>There was no differential loss to follow-up.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low Risk</td>
<td>The study protocol is not available, but it is clear that the published reports include all expected outcomes.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low Risk</td>
<td>This study appears to be free of other sources of bias.</td>
</tr>
</tbody>
</table>

**Table (3) Characteristics of ongoing studies**

**Davey 2012**

<table>
<thead>
<tr>
<th>Study name</th>
<th>Evaluating SMS reminders in improving ART and PMTCT adherence in Mozambique: challenges in achieving scale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td>Randomized control trial</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>HIV-infected women</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Weekly SMS reminders</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Reducing HIV-related morbidity and mortality. Prevent mother to child transmission.</td>
</tr>
<tr>
<td><strong>Starting date</strong></td>
<td>Not provided</td>
</tr>
<tr>
<td><strong>Contact information</strong></td>
<td>D. Joseph Davey, Susannah Hares, W. Ponce, A. Nguimfack, D. Traca, C. Sousa Absolute Return for Kids (ARK), Mozambique, 251 Ho Chi Minh, Maputo, Mozambique Absolute Return for Kids (ARK), London, UK University of Eduardo Mondlane, Mozambique <a href="mailto:dvora.davey@arkonline.org">dvora.davey@arkonline.org</a></td>
</tr>
</tbody>
</table>

**Mwapasa 2014**

| Study name | Mother–Infant Pair Clinic and SMS Messaging as Innovative Strategies for Improving Access to and Retention in eMTCT Care and Option B+ in Malawi: A Cluster Randomized Control Trial (The PRIME Study) |

**Methods**  | Cluster randomized control trial  
---|---  
**Participants**  | pregnant women HIV-positive  
**Interventions**  | mother–infant pair clinics, which deliver integrated HIV and non-HIV services,  
| mother–infant pair clinics plus electronic text message (SMS) reminders for mother–infant pairs who miss scheduled eMTCT follow-up clinics, and current standard of care.  
**Outcomes**  | Proportion of HIV+ mothers retained in eMTCT care at 12 months post-partum  
| Proportion of HIV-exposed infants retained in eMTCT care at 12 months postpartum  
| Some HIV-infected pregnant women received recommended HIV and non-HIV services during preceding scheduled visits.  
**Starting date**  | August 2015  
**Contact information**  | Victor Mwapasa, George Pro, Jobiba Chinkhumba, Mavuto Mukaka, Emily Kobayashi, Adrian Stuart, Andrews Gunda, Jessica Joseph, Nandita Sugandhi, Frank M. Chimbwandira, and Michael Eliya.  
| Faculty of Public Health and Family Medicine, University of Malawi College of Medicine, Private Bag 360, Chichiri, Blantyre 3, Malawi  
| vmwapasa@medcol.mw  

_Ong’ech 2014_

| Study name | Mobile Phone Technology for Prevention of Mother-to-Child Transmission of HIV: Acceptability, Effectiveness, and Cost  
---|---  
**Methods**  | Cluster randomized control trial  
**Participants**  | 600 HIV-infected pregnant women  
**Interventions**  | HIV-infected pregnant women and male partners within the PMTCT program are engaged in multi-directional mobile communication for PMTCT  
**Outcomes**  | Primary:  
| The proportion of women who completed PMTCT from antenatal to six weeks post-partum.  
| Initiation of infant prophylaxis, facility delivery and receipt of results of weeks early infant diagnosis(DNA PCR)  
| Secondary:  
| Uptake ARV prophylaxis/ART during labor, delivery and postpartum  
| Self-reported maternal adherence to ARV prophylaxis/ART during pregnancy.  
| Time to initiation of ARV prophylaxis.  
**Starting date**  | May 2011  
**Contact information**  | Not provided  

**Excluded studies**  
Fifteen studies were excluded from the review with reason (Brar 2014; Clouse 2015; Dean 2012; Fayorsey 2015; Ishola 2015; Jennings 2013; Lema 2014; Mushamiri 2015; Odeny 2014a; Ross 2013; Rotheram-Borus 2011; Sando 2014; Schwartz 2015 Stinson 2015; van Heerden 2013).

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Table (4) Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brar 2014</td>
<td>Qualitative study design</td>
</tr>
<tr>
<td>Clouse 2015</td>
<td>Qualitative study design</td>
</tr>
<tr>
<td>Dean 2012</td>
<td>Qualitative study design</td>
</tr>
<tr>
<td>Fayorsey 2015</td>
<td>Randomized control trial, using outreach worker/counselor (Mama Mshauri) to visit HIV-infected pregnant women</td>
</tr>
<tr>
<td>Ishola 2015</td>
<td>Randomized control trial assessing other outcomes</td>
</tr>
<tr>
<td>Jennings 2013</td>
<td>Qualitative study design</td>
</tr>
<tr>
<td>Lema 2014</td>
<td>Community health worker interventions other than mobile phone interventions</td>
</tr>
<tr>
<td>Mushamiri 2015</td>
<td>Cluster randomized control trial sending SMS via electronic software (APAS) to community health workers who visited the expected mother in her home for reminding of her upcoming appointment.</td>
</tr>
<tr>
<td>Odeny 2014a</td>
<td>Qualitative study</td>
</tr>
<tr>
<td>Ross 2013</td>
<td>Randomized control trial assessing other outcomes (depressive symptoms)</td>
</tr>
<tr>
<td>Rotheram-Borus 2011</td>
<td>Community-based interventions different than mobile phone interventions</td>
</tr>
<tr>
<td>Sando 2014</td>
<td>Community workers interventions</td>
</tr>
<tr>
<td>Schwartz 2015</td>
<td>Nonrandomized control trial with retrospective control group</td>
</tr>
<tr>
<td>Stinson 2015</td>
<td>The pragmatic cluster randomized controlled trial assessed the effectiveness of Lay Health Worker Support To Strengthen PMTCT.</td>
</tr>
<tr>
<td>van Heerden 2013</td>
<td>Cluster randomized control trial, assessing the acceptability and feasibility of using mobile phones to collect data from pregnant women living with HIV who were enrolled in the PMTCT program.</td>
</tr>
</tbody>
</table>

OUTCOMES:
Primary:
The proportion of women who completed PMTCT from antenatal to six weeks post-partum.
Initiation of infant prophylaxis, facility delivery and receipt of results of weeks early infant diagnosis (DNA PCR)

Secondary:
Uptake ARV prophylaxis/ART during labor, delivery and postpartum
Self-reported maternal adherence to ARV prophylaxis/ART during pregnancy.
Time to initiation of ARV prophylaxis.

Risk of bias in included studies
The risk of bias in included studies was described in Figure 2 and Figure 3.

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Allocation (selection bias)
The two trials reported adequate generation of the random sequence (Dryden-Peterson 2015; Odeny 2014). Only one trial had adequate allocation concealment (Odeny 2014).

Blinding (performance bias and detection bias)
Clinics and the study team were blinded (Dryden-Peterson 2015); either participants or personnel were unblinded (Odeny 2014). Meaning then, Dryden-Peterson 2015 seemed to be low of performance bias.

Incomplete outcome data (attrition bias)
In Dryden-Peterson 2015, loss to follow-up was imbalanced in intervention and control group. Odeny 2014, intention to treat analysis was used, minimizing then attrition bias.

Selective reporting (reporting bias)
We did not find any evidence of publication bias. Publication bias could not be assessed formally because of a limited number of studies.

Other potential sources of bias
No other potential sources of bias were identified in the included studies.

Effects of interventions
Antiretroviral therapy initiation
One study reported on this outcome and found that there was a statistically significant difference between mobile phone text messaging and standard care (OR 1.79 95% CI 1.09 to 2.94, 307 participants, 1 study). The study reported adjusted odds ratio that rates of ART initiation remained low, with 56 (36.4%) women registering under Intervention versus 37 (24.2%) women under Usual Care initiating ART before 30 weeks gestation, aOR 1.06 (95%CI 0.53–2.13, P = 0.87) figure 4.
Maternal clinical attendance (ante and postpartum)

Maternal clinical attendance was 1.66 times higher in mobile phone text group compared to the standard care. The outcome was reported by Mobile phone messaging significantly increased clinic attendance by up to 66% (RR 1.66 95%CI 1.02 to 2.70, 381 participants, 1 study). P-value was 0.04. Figure 5.

Number of infants tested for HIV

The number of HIV tested infants appears to increase in mobile phone text messaging (OR 2.01 95%CI 1.03 to 3.92, 325 participants, 1 studies); meaning that the odds of HIV tested infants is increased by 101% in mobile phone text messaging group compared to the standard care. The 95% CI is as low as 1.03 and as high as 3.92. The p-value was 0.04, showing a statistically significant result. Figure 6.

Mother To Child Transmission of HIV (MTCT)

One study reported on this outcome. The study found no statistically significant difference in the rate of MTCT among the mobile phone communications group and the standard care group (OR 0.64 95%CI 0.11 to 3.88, 368 participants, 1 study, P-value 0.63). Figure 7.
5. DISCUSSION

This systematic review has attempted to find evidence for mobile phone text messaging in improving antiretroviral therapy adherence in HIV-infected pregnant women. Two trials were included. According to different outcomes, the lowest sample size of HIV-infected pregnant women was 307 and the highest 368. The finding indicated that mobile phone text messaging did not increase antiretroviral therapy initiation in the intervention group compared to the control group. Maternal clinic attendance was increased 1.83 times in intervention group compared to the control group. Lastly, HIV tested infant was increased 2.01 times in intervention group compared to the control group. The studies found no difference in the rate of mother to child transmission of HIV.

Overall completeness and applicability of evidence

We conducted a comprehensive search of the literature without any date or language limitation. Major electronic databases were used in our search and wide search terms were used. This review included very few studies. These results should be considered in a context of several limitations in included studies. Both studies were conducted in sub-Saharan Africa, and the findings are likely to be an application in other similar settings.

Quality of the evidence

The quality of evidence was assessed using the GRADE approach. We looked at various factors that could influence our level of confidence in the evidence; including study designs, the risk of bias, inconsistency, indirectness and imprecision and publication bias. We assessed the quality of evidence for each of the outcomes of interest. We assessed the quality of evidence for each outcome using each of these criteria. Our level of confidence in the effect estimates was reduced due to the imprecision of the results across all outcomes. The overall quality of evidence was assessed as moderate.

Potential biases in the review process

The number of trials included in data analysis was very low. Statistical heterogeneity was not applicable. We also reduced potential bias in the conduct of this review by having two of the authors independently scan through the search output, extract data, and assess the methodological quality of each study.

Agreements and disagreements with other studies or reviews

A recently published systematic review, included 9 randomized control trials, evaluating the impact of using of mobile phone text-messaging in improving HIV treatment outcomes, revealed that text messaging interventions to promote ART adherence (Finitsis 2014). Another review published in 2012, including 2 high-quality randomized control trials demonstrated that mobile phone text-messaging at weekly intervals, whether the messages be short or long, is efficacious in enhancing adherence to ART to enhance adherence to ART in patients with HIV infection (Horvath 2012).

6. CONCLUSION

Implications for practice

In summary, the evidence has shown that mobile phone text messaging may improve not rate of initiation of HAART among HIV-infected pregnant women. However, mobile phone communication may improve clinic attendance among HIV-infected pregnant women and also increase the number of infants tested for HIV. However, the review did not find any significant difference in the rates of mother to child transmission of HIV. Also, the included studies did not report on the effect of mobile phone communication on adherence. Nowadays, several technology interventions among which computer-delivered interventions, internet approaches, mobile phone technologies, and electronic dose monitoring
with triggered messaging and data-informed counseling are explored to improve antiretroviral therapy adherence (Amico 2015). The results could be estimated meaningful in general. Hence, in HIV-infected pregnant women, many barriers are interacting as shown in Figure 1. Envisaging a single intervention in HIV-infected women could lack efficacy in improving HIV outcomes. Policy makers should propose the combination of more than two community-based interventions to strengthen the Option B+ in HIV-infected pregnant women. For example, home visits associated with mobile phone intervention could be suggested. Electronic adherence monitoring with text message dosing reminders would be another field of research in increasing antiretroviral adherence in pregnant women. A recent randomized control trial found that electronic monitoring with text reminders for late doses reduced the frequency of treatment interruptions without a difference in neither adherence nor HIV RNA suppression in the context of high levels of adherence support (Orrell 2015).

Implications for research
Further well-designed studies are needed to evaluate the effects of mobile phone communication among pregnant women on other clinically relevant outcomes, including adherence to ARVs and mother to child transmission of HIV.

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