

Effectiveness of conditional cash transfers for uptake and retention in HIV prevention of mother-to-child transmission services in low- and middle-income countries: a systematic review protocol

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ABSTRACT

Objective: This systematic review will identify and synthesize evidence on the effectiveness of conditional cash transfers for the uptake and retention in prevention of mother-to-child transmission services in pregnant and/or breastfeeding women with HIV infection in low- and middle-income countries.

Introduction: Regardless of the effectiveness of prevention of mother-to-child transmission services, uptake and retention in such services remains poor in low- and middle-income countries. This review intends to evaluate the effectiveness of conditional cash transfers in improving uptake and retention in such services for pregnant and/or breastfeeding women with HIV infection.

Inclusion criteria: This review will consider studies that evaluate the impact of conditional cash transfers on uptake and retention in prevention of mother-to-child transmission services in pregnant and/or breastfeeding women with HIV. Studies will compare conditional cash transfers with no intervention or other interventions. Only studies carried out in low- and middle-income countries will be eligible for inclusion.

Methods: Eight databases will be searched. Publication status will not be considered as a criterion for inclusion. Studies published in English since 2000 will be considered, because prevention of mother-to-child transmission services were first introduced in that year. Following the search, two independent reviewers will screen titles and abstracts against the inclusion criteria, critically appraise eligible studies for methodological quality using JBI critical appraisal tools, and extract data from included studies using a standardized data extraction tool. Where possible, quantitative data will be pooled using statistical meta-analysis.

Systematic review registration number: PROSPERO CRD42021236729

Keywords: conditional cash transfer; HIV; PMTCT; pregnant women; vertical transmission

JBI Evid Synth 2022; 20(4):1120–1126.

Introduction

Human immunodeficiency virus (HIV) remains a major public health issue globally. In 2019, 38 million people were living with HIV, of whom 1.8 million were children (0 to 14 years of age). There were 1.7 million new infections in the same year, of which 150,000 were in children.¹ The vast majority of HIV infections in children are acquired in utero, during birth, or while being breastfed.²

One of the key approaches for HIV prevention is the elimination of mother-to-child transmission of HIV, which is also known as vertical transmission.³ Prevention of mother-to-child transmission (PMTCT) programs constitute a range of services to women of reproductive age who are at risk of or living with HIV infection. These services should be offered before conception and during pregnancy, labor, and breastfeeding. The cascade of PMTCT services targets both the mother and the infant. Interventions targeting the mother include preventing HIV infections and unwanted pregnancies among women with HIV and providing them with lifelong antiretroviral therapy (ART). Interventions involving infants consist of

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The authors declare no conflicts of interest.

DOI: 10.11124/JBIES-21-00098

diagnosis at four to six weeks of age and 18 months of age (or when breastfeeding ends), and ART initiation for infants exposed to HIV as soon as possible.⁴ In the absence of treatment, rates of HIV transmission from mothers to children can be between 15% and 45%. However, this risk could be reduced to less than 5% if treatment is provided during pregnancy and breastfeeding.⁴

Regardless of the effectiveness of PMTCT services, uptake and retention in PMTCT services remains poor in low- and middle-income countries.⁵ Retention of such services is lower compared with uptake. This is because PMTCT services risk loss-to-follow-up at every step of service delivery – from the first contact to postnatal follow-up.⁶ As a result, in some countries, more infants are infected during the postnatal period through breastfeeding rather than during pregnancy or labor because more women leave care.³ This underscores the importance of retention in care.

In 2019, only 85% of pregnant women living with HIV were accessing antiretroviral medicines. This fell short of the target for 2018, which was 95%.^{7,8} In 2018, 160,000 children were newly infected with HIV while the target by UNAIDS was fewer than 40,000.⁹

Barriers to the use of and adherence to PMTCT services are numerous. According to a systematic review by Brusamento *et al.*,¹⁰ lack of awareness about HIV, ART, and vertical transmission; lack of full male partner engagement; low level of education; and psychological issues after diagnosis have been identified as key barriers at an individual level. The study further notes that at a community level, stigma and fear of status disclosure to partners, family, and community members were identified as the main barriers. Cultural barriers, such as a preference for traditional healers and traditional birth attendants, and non-facility deliveries were also reported as important barriers.¹⁰ Supply-side barriers include poor handling of clients by health workers, staff shortages, and problems of access to services.¹¹ There are also economic barriers, such as opportunity cost, cost of transport, and distance to health facilities. Among the socio-economic barriers, transport costs and distance were the most commonly cited barriers.^{12,13}

The potential of PMTCT services to be an effective tool to eliminate mother-to-child transmission of HIV will remain untapped unless the various barriers to uptake and retention are addressed.¹⁰

Studies show that addressing the social determinants of health lead to better health. Cash transfers are considered one of the tools that could help address this problem.¹⁴ Cash transfer is defined as a direct transfer of money to an eligible household to increase the household's real income. The recipients of the assistance are generally people who are at risk of sliding into poverty in the absence of cash transfers.¹⁵ Conditional cash transfer (CCT) programs give money to people in need to help fulfill specific behavioral conditions, such as children's school enrollment, timely vaccinations, or regular attendance of pregnant women at health care facilities.¹⁶ The positive impact of CCTs on the uptake of preventive services by children and pregnant women is supported by evidence from several studies.¹⁵

Primary studies on the impact of CCTs on uptake and retention in PMTCT services have shown promising results. A study in Nigeria¹⁷ has demonstrated that pregnant women with HIV who were involved in a CCT program were very likely to give birth in a health facility, and more infants received early infant diagnosis compared with pregnant women with HIV in standard care. A study in the Democratic Republic of Congo has shown that CCT increased uptake and retention in PMTCT services for pregnant women compared with standard care.¹⁸ There is scant evidence to guide decision-makers and implementers in low- and middle-income countries to optimize PMTCT services in general. There is also little evidence on the effectiveness of interventions to enhance uptake and retention in PMTCT care in mothers and their infants.⁵ The proposed review intends to evaluate the effectiveness of CCT in improving uptake and retention in PMTCT services for pregnant and/or breastfeeding women with HIV in low- and middle-income countries. The review will focus on low- and middle-income countries because these countries bear the disproportionate burden of the HIV epidemic.¹⁹ In 2009, approximately 91% of the world's total HIV-1-infected population (around 30 million people) resided in low- to middle-income countries.²⁰

We conducted a preliminary search of *JB* Evidence Synthesis, PROSPERO, and the Cochrane Database of Systematic Reviews, and no protocols or systematic reviews on the topic were identified. The objective of this review will be to identify and synthesize evidence on the effectiveness of CCT for the uptake and retention in PMTCT services for

pregnant and/or breastfeeding women in low- and middle-income countries.

Review question

What is the effectiveness of CCTs for the uptake and retention in PMTCT services for pregnant and/or breastfeeding women with HIV in low- and middle-income countries?

Inclusion criteria

Participants

The review will include studies on pregnant and/or breastfeeding women with HIV and their infants or children. Only studies carried out in low- and middle-income countries will be eligible for inclusion. Low- and middle-income countries will be identified based on the classification by the World Bank.²¹ Studies conducted only in high-income countries will be excluded.

Intervention

This review will consider studies that evaluate the impact of CCT on uptake and retention in PMTCT services in pregnant and/or breastfeeding women with HIV. Conditional cash transfers are defined as programs that give money to people who are at risk of falling into poverty to help fulfill specific behavioral conditions, such as timely vaccinations or regular attendance of pregnant women at health care facilities.¹⁶ Only studies that consist of direct cash (monetary) transfers will be considered. Studies that involve in-kind transfers will not be considered for inclusion. Cash transfers should be conditional on uptake and/or retention in PMTCT services. Studies with unconditional cash transfers will not be included.

Comparator

This review will consider studies that compare the impact of CCT with no intervention or with other interventions, such as food, transport support, provision with cellphone minutes, or male involvement, for pregnant and/or breastfeeding women to improve uptake and retention in PMTCT services.

Outcomes

The primary outcomes of this review will be the percentage of:

- i. pregnant and/or breastfeeding women with HIV enrolled in ART

- ii. women with HIV giving birth in health facilities
- iii. women and their infants/children retained in the PMTCT service up to the last ART regimen, as defined by the PMTCT regimen undertaken, regardless of missing clinic visits.

Secondary outcomes will include the percentage of infants:

- i. completing post-exposure HIV testing at four to six weeks after birth
- ii. exposed to HIV testing positive for HIV
- iii. exposed to HIV with health defects (eg, neural tube defects, heart defects, major limb malformations).

Types of studies

The review will consider all study designs for inclusion: experimental (randomized controlled trials, cluster controlled randomized trials, non-randomized controlled trials, and quasi-experimental studies) and observational studies (prospective and retrospective cohort studies, case-control studies, before and after studies, and analytical cross-sectional studies).

Methods

The systematic review will follow the JBI methodology for systematic reviews of effectiveness.²² The protocol has been registered in PROSPERO (CRD 42021236729).

Search strategy

The search strategy will aim to identify both published and unpublished studies. A preliminary search of MEDLINE and CINAHL will be conducted to identify articles on the topic. Words in titles and abstracts of articles and index terms used to describe the articles found in the preliminary search will be used to create a full search strategy for MEDLINE. The search strategy will be adapted for each included database and/or information source. The reference lists of all included studies will be checked for additional studies.

Only studies published in English will be included as this is the only international language spoken by the study team. Studies published since 2000 will be included as PMTCT was introduced in that year.²³

Databases to be searched include the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (PubMed), Embase (Ovid), and CINAHL (EBSCO). Sources of unpublished studies/gray

literature to be searched include ProQuest Dissertations and Theses, OpenGrey, WHO International Clinical Trials Registry Platform, and ClinicalTrials.gov.

Study selection

After the search, all identified citations will be collated and uploaded to EndNote v.X9 (Clarivate Analytics, PA, USA) and duplicates removed. Following a pilot test, two or more independent reviewers will screen titles and abstracts for assessment against the inclusion criteria for the review. Studies that are potentially relevant will be retrieved in full. Details of selected citations will be imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia).²⁴

Two or more independent reviewers will evaluate the full texts of selected articles in detail against the inclusion criteria. Reasons for exclusion of papers at the full-text level will be recorded and reported in the systematic review. Any disagreements that arise between the reviewers during the selection process will be resolved through discussion or with the involvement of additional reviewer(s).

The study inclusion process and the results of the search will be reported and presented in full in the final systematic review using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.²⁵

Assessment of methodological quality

Two independent reviewers will critically appraise eligible studies for methodological quality using standardized critical appraisal tools from JBI for experimental and quasi-experimental studies.²² Requests for missing or additional data for clarification, where required, will be made by contacting authors of papers. Any disagreements that arise will be resolved through discussion or with a third reviewer. The results of the critical appraisal will be reported both in narrative and table format. All studies will undergo data extraction and synthesis (where possible) regardless of their methodological quality.

Data extraction

Two independent reviewers will extract data from studies included in the review using the standardized data extraction tool from JBI SUMARI.²⁴ The data extracted will consist of details about the populations,

study methods, interventions, and outcomes of significance in line with the review objective. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer. When additional or missing data are required, authors of papers will be contacted.

Data synthesis

Studies will, where possible, be pooled in a statistical meta-analysis using JBI SUMARI.²⁴ Effect sizes will be presented as either odds ratios (for dichotomous data) and weighted (or standardized) final postintervention mean differences (for continuous data). Confidence intervals (95%) will be calculated for analysis. The standard χ^2 and I² tests will be used to assess heterogeneity statistically. Statistical analyses will be conducted using random or fixed effects based on established guidance.²⁶ Subgroup analysis will be conducted to identify the potential sources of heterogeneity across studies. Sensitivity analyses will be conducted to examine the influence of each study on the final results by leaving out one study at a time. Findings will be presented in a narrative format, including tables and figures, when statistical pooling is not possible. A funnel plot will be generated using META-FUNNEL (Stata Corp LLC, Texas, USA) to assess publication bias if there are 10 or more studies included in a meta-analysis. The Egger test²⁷ for funnel plot asymmetry will be performed where appropriate.

Assessing certainty in the findings

The certainty of evidence will be determined using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach,²⁸ and a Summary of Findings (SoF) will be created using GRADEpro GDT 2020 (McMaster University, ON, Canada). The SoF will include estimates of relative risk, absolute risks for the treatment and control, and a ranking of the quality of the evidence. Quality of evidence will be ranked based on the directness, risk of bias, precision, heterogeneity, and risk of publication bias of the review results. The outcomes reported in the SoF will be the percentage of:

- i. pregnant and/or breastfeeding women with HIV enrolled in ART
- ii. women with HIV giving birth in health facilities
- iii. women and their infants/children retained in the PMTCT service up to the last ART regimen as defined by the PMTCT regimen undertaken, regardless of missing clinic visits

- iv. infants completing post-exposure HIV testing at four to six weeks after birth
- v. infants with HIV exposure testing positive for HIV
- vi. infants with HIV exposure with health defects (eg, neural tube defects, heart defects, major limb malformations).

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Appendix I: Search strategy

MEDLINE (PubMed)

Search conducted July 8, 2021.

Query	Search	Records Retrieved
#1	((((((((pregnant woman[Text Word]) OR (pregnant women[Text Word])) OR (expectant woman[Text Word])) OR (expectant women [Text Word])) OR (breastfeeding[Text Word])) OR (newborn[Text Word])) OR (neonate[Text Word])) OR (infant[Text Word])) OR (pregnant woman[MeSH Terms])) OR (infant[MeSH Terms])) OR (neonate[MeSH Terms])	1,482,320
#2	((((((((conditional cash transfer[Text Word]) OR (cash transfer[Text Word])) OR (cash allowance[Text Word])) OR (transfer of money [Text Word])) OR (transfer of cash[Text Word])) OR (financial incentive[Text Word])) OR (money transfer[Text Word])) OR (cash benefit[Text Word])) OR (financial support[Text Word])) OR (cash incentive[Text Word])	10,237
#3	((((((((((((((((vertical transmission[Text Word]) OR (mother-to-child transmission[Text Word])) OR (retention in care[Text Word])) OR (prevention of mother-to-child transmis-sion[Text Word])) OR (PMTCT[Text Word])) OR (HIV-infection[Text Word])) OR (early infant diagnosis[Text Word])) OR (EID[Text Word])) OR (uptake of PMTCT[Text Word])) OR (lost to follow-up[Text Word])) OR (infant ART initiation[Text Word])) OR (pre-exposure prophylax-is[Text Word])) OR (treatment uptake[Text Word])) OR (vertical transmission[MeSH Terms])) OR (HIV-infection[MeSH Terms])) OR (lost to follow-up[MeSH Terms])) OR (pre-exposure prophylaxis[MeSH Terms])) OR (patient compliance[MeSH Terms])) OR (prenatal care[MeSH Terms])) OR (postnatal care[MeSH Terms])) OR (patient compliance[Text Word])) OR (prenatal care[Text Word])) OR (postnatal care[Text Word])	457,975
#4	((((((((((((pregnant woman[Text Word]) OR (pregnant women[Text Word])) OR (expectant woman[Text Word])) OR (expectant women [Text Word])) OR (breastfeeding[Text Word])) OR (newborn[Text Word])) OR (neonate[Text Word])) OR (infant[Text Word])) OR (pregnant woman[MeSH Terms])) OR (infant[MeSH Terms])) OR (neonate[MeSH Terms])) AND (((((((((((conditional cash transfer[Text Word]) OR (cash transfer[Text Word])) OR (cash allowance[Text Word])) OR (transfer of money[Text Word])) OR (transfer of cash[Text Word])) OR (financial incentive[Text Word])) OR (money transfer[Text Word])) OR (cash benefit[Text Word])) OR (financial support [Text Word])) OR (cash incentive[Text Word])))) AND (((((((((((vertical transmission[Text Word]) OR (mother-to-child transmission [Text Word])) OR (retention in care[Text Word])) OR (prevention of mother-to-child transmission[Text Word])) OR (PMTCT[Text Word])) OR (HIV-infection[Text Word])) OR (early infant diagnosis[Text Word])) OR (EID[Text Word])) OR (uptake of PMTCT[Text Word])) OR (lost to follow-up[Text Word])) OR (infant ART initiation[Text Word])) OR (pre-exposure prophylaxis[Text Word])) OR (treatment uptake[Text Word])) OR (vertical transmission[MeSH Terms])) OR (HIV-infection[MeSH Terms])) OR (lost to follow-up[MeSH Terms])) OR (pre-exposure prophylaxis[MeSH Terms])) OR (patient compliance[MeSH Terms])) OR (prenatal care [MeSH Terms])) OR (postnatal care[MeSH Terms])) OR (patient compliance[Text Word])) OR (prenatal care[Text Word])) OR (postnatal care[Text Word]))	122