

# **An evaluation of alternative methods to reducing mother-to-child HIV transmission in sub-Saharan Africa**

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**Abstract.** Despite the availability of antiretroviral therapies (ARTs), mother-to-child transmission of HIV continues to be a major problem in areas where access to such services is limited. In this paper, we examine three different projects aimed at increasing the uptake of ARTs as a method of preventing mother-to-child transmission of HIV (PMTCT). Projects in Kenya and South Africa were evaluated. First, results from clinical trials in Kenya show that triple-antiretroviral use in pregnant mothers can be a safe and more effective method of reducing HIV transmission compared with traditional single-dose prophylaxis. These effects, however, may not hold outside a clinical setting. We then turned our attention to evaluations of strategic interventions to increase PMTCT uptake in target populations. A pilot program in Western Kenya suggests integration of PMTCT services in existing maternal and child health facilities can increase utilization of preventive measures, although these results are limited and site-specific. Similarly, an assessment of Mothers to Mothers (m2m) in South Africa finds that participation in a HIV-mentoring program can increase PMTCT uptake among pregnant HIV-positive women. The extent of program impact, however, may be exaggerated given the context of evaluation, and non-generalizable. Finally, we examine the broader implications of these findings, concluding with recommendations of policies to increase uptake of PMTCT services in resource-limited settings and suggestions for future research.

## Introduction

In their 2010 report, the WHO estimated that 15.7 million women and 2.1 million children<sup>1</sup> worldwide are currently living with HIV. Of these women, 12 million can be found in sub-Saharan Africa, where women account for approximately 60% of all HIV infections. The rate of new HIV infections and the absolute number of individuals living with HIV in this region continues to pose a major global health challenge. Sub-Saharan also has the highest rate of HIV infections among children, with 91% of all new infections among children in 2008<sup>2</sup>. Infections in children are predominantly a result of HIV transmission from mother to child<sup>3</sup>. Given the effectiveness of new antiretroviral therapies (ARTs) in reducing transmission rates, however, there is the potential for significantly reduced. Whether or not we meet this challenge, however, will depend upon the extent to which new policies and programs can facilitate greater access to and utilization of ARTs in high-risk areas.

There are currently a wide variety of programs for preventing mother-to-child transmission (PMTCT), that direct interventions at one or more of the following stages: 1) reducing the rate of HIV infection in women, 2) reducing unintended pregnancies among HIV-positive women, 3) reduction of HIV transmission during pregnancy and infant-feeding, and 4) support for HIV-infected women and/or children after birth. In this review, we focus on interventions in the

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<sup>1</sup> Individuals under the age of 15.

<sup>2</sup> WHO, 2010, p.84.

<sup>3</sup> UNAIDS, 2010.

third, perinatal period, during which time prophylaxis treatments for pregnant mothers can be used to lower the rate of children born with HIV.

We evaluate three studies examining both the efficacy of available ARTs in reducing mother-to-child transmission (MTCT) rates, and the effectiveness of two different strategies at improving ART uptake. We chose three different studies conducted in sub-Saharan Africa, given the prevalence of the problem in this region. Studies were evaluated based on their empirical methodology, and results assessed with the context of this approach. Given the potentially large effects anti-retroviral treatments can have on reducing mother-to-child transmission, it is necessary that we find appropriate strategies to facilitate the uptake and delivery of ARTs, as part of a set of complementary PMTCT services, and reduce the high number of children living with HIV worldwide.

### **Efficacy of ARTs in preventing mother-to-child transmission**

#### **1. Results from a Clinical Trial on Triple-Antiretroviral Prophylaxis**

The Kisumu Breastfeeding Study (KiBS) in Kisumu, Kenya, is a single trial conducted between July 2003 and February 2009 examining the safety and effectiveness of a triple-antiretroviral regimen, administered during the perinatal period, in preventing mother-to-child transmission of HIV. HIV-infected pregnant women took three key drugs: zidovudine, lamivudine, and either nevirapine (NVP) or nelfinavir. The goal was to improve upon the rate or reduction in mother-to-child transmission over traditional single-dose NVP, which is widely used across sub-Saharan Africa as part of anti-retroviral treatment, while increasing the rate of infant survival. The study assesses the effect of the regimen on target outcomes, as

well as the safety, toxicity, and potential issues of a triple-ARV prophylaxis on mothers and infants.

Participants were recruited through existing PMTCT programs in antenatal clinics of two hospitals, both of which serve low-income populations of Kisumu and surrounding areas. Participants were selected based on certain WHO enrolment criteria, and had to be HIV positive with intent to breastfeed<sup>4</sup>. Effects were measured only on women to whom the program was offered, and actually enrolled. Thus, estimates are not representative for the entire sample of the population, but only treatment-on-treated.

Results showed that treatment was successful in reducing infant viral loads to undetectable levels. These reductions were statistically significant at the 1% level, which suggests that the triple-prophylaxis ARVs can be highly effective in diminishing the rate of HIV transmission due to MTCT. The intervention showed a reduction in the rate of HIV-transmission to 4.2% at 6 weeks and 6.7% at 18 months (significant at the 5% level). These rates are less than half of the corresponding rates of 11.8% and 15% observed with single-dose maternal and infant NVP. The intervention showed no improvement, however, on reducing the incidence of infant mortality compared with single-dose NVP.

#### Empirical evaluation

The study takes into account a wide variety of outcomes, including severe adverse events (SAE) for infants exposed to low dose ARVs through maternal breast milk and for mothers exposed to triple doses ARVs. They found that mothers

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<sup>4</sup> Other criteria included a minimum age of 15 years, gestation of 34-36 weeks, and no previous ARV exposure.

showed symptoms of pneumonia, malaria, diarrhea, and anemia with the treatment, though there were no child deaths or SAE attributable to the intervention.

Empirical limitations, however, limit the relevancy of these findings. The authors used results from a study on NPV in Uganda as a comparison group. While this initial study was conducted in an area with similar characteristics to Kisumu, it does not represent a statistically identical counterfactual. The decision not to create a concurrent control group of women taking NVP was made due to cost constraints and anticipated difficulties in enrolling adequate numbers for a trial. The resulting issue is that we cannot attribute differences estimated effect to drug efficacy alone. Given the geographical differences, there is at least one known factor that could be contributing to difference in response to treatment between groups. The study could not account for all observed and unobserved factors that might explain differences in outcomes.

The length of the study, in which participants are tracked over 6 years, may also raise concern. Other health interventions could have been operating simultaneously that had an effect on observed outcomes. Additionally, there is possible bias in data collection on non-objective variables, such as survey of women regarding adherence to ARVs or infant feeding recommendations, which may have resulted from pressure on the part of study staff.

Self-selection bias is another reason results may not be generalizable to larger contexts. Because participants elected to be included in the trial, these may have been individuals who were committed to PMTCT measures and follow-up. Difference in outcomes observed with the comparison group could have been due to

underlying differences in motivation. There was also intense follow-up on the part of KiBS resulting in good adherence to the trial protocol. In other contexts where resources are limited and follow-up is poor, we may not see the estimated effects of the treatment.

### Program Assessment

The intervention method used in this study follows a simple regimen that does not require different drugs at different time points during and following pregnancy, and can be made available to HIV-infected women regardless of CD4 cell count. This is an improvement on treatments that require women receive the results of their CD4 count before beginning anti-retroviral therapy, given high rates of attrition in latter cases. While the study shows positive effects of triple-antiretroviral prophylaxis in increasing PMTCT effectiveness, there are problems of external and internal validity when analyzing conclusions on a larger scale.

### **Strategies to Improve PMTCT Uptake**

#### 2. Effectiveness of Integration of PMTCT services on facilitating uptake

Recently, there has been a greater amount of interest in assessing how integration of PMTCT services into existing maternal and children health structures can improve uptake and delivery. While there have been a number of evaluations in this area relying on observational data, there are few available experimental studies with high internal validity that can offer strong or generalizable evidence on the effectiveness of such interventions.

Nonetheless, we chose to review a pilot project expanding PMTCT services at a large health facility in Western Kenya, as a starting point to examine what kinds of measures might be taken to better integrate PMTCT services into prenatal care. We

look at whether integration into existing health structures do in fact facilitate greater ART coverage and reduce MTCT transmission rates, as well as other possible project impacts that should be evaluated.

### Summary of Results

The 2002 study was conducted at New Nyanza Provincial General Hospital (NNPGH) in Kisumu, Kenya. A before-and-after approach was adopted to analyze the effects on pregnant women who visited the facility, before and after intervention to integrate PMTCT services into existing prenatal care. The intervention included changed testing protocol from an “opt-in” to “opt-out” approach<sup>5</sup>, pre- and post-test counseling, and infant feeding counseling upon dispensing ART (nevirapine) to infected mothers.

Two methods of data collection were used: computer-entered and manually counted data compiled from hospital nurses. The authors found no significant differences between the data collected from these two methods, though only the hand-counted data were used in the analysis. The treatment was carried out at the facility-level, although only one facility (NNPGH) is examined. Data were collected on the number of women who received pre-test counseling on their first ANC visit, the number who were tested and received same-day test results, and the number who receive post-test counseling and ARTs. The authors compared results from the period 4 – 12 months after PMTCT services were more fully integrated (November 2002 – August 2003), with the same period from the previous calendar year (November 2001-August 2002), prior to changes.

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<sup>5</sup> Rather than requiring women to approve of HIV testing (“opt-in”), testing was routinely performed on all pregnant women, who reserved the right to refuse testing (“opt-out”).

The study found significant changes in the measured outcomes after changes in routine care were implemented. The number of women who received pre-test counseling increased by 15 percentage points. Although there was only a 3 percentage point increase in the number of women who then agreed to HIV-testing, there was a total 18 percentage point increase in the overall number of pregnant women who were tested. Similarly, the overall number of women who learned their HIV status after their first visit increased by 13 percentage points. Finally, the number of HIV-infected women who received ART drugs also increased by 13 percentage points. These findings were each significant at the 1% level. There was, however, no significant difference in the number of women receiving post-test counseling before and after the intervention.

#### Empirical Issues

The initial findings suggest that integration of PMTCT services into routine prenatal care can be effective in improving uptake and facilitating access to ARTs. Methodological flaws, however, limit the significance of these results; conclusions are site-specific and non-generalizable to a wider range of settings.

The major critiques of this evaluation would be its lack of a valid counterfactual group and limited sample size, which bring into question both the internal and external validity of the study. Foremost, it is unclear that the observed changes in PMTCT outcomes are due to implementation of the program alone, as the authors are unable to control for other time-varying factors between the two periods. Because the program does not follow a given group of individuals but looks rather at the number of pregnant women treated for prenatal services in each period, it fails to account for a wide variety of external factors that could affect the

total number and composition of women who visit the facility in each period. No information is provided on the age, background, or economic characteristics of the women included in the study. The authors fail to create a valid counterfactual group, and statistical differences between women in each period are not evaluated. Thus, there may be external factors affecting outcomes that are not accounted for, and causality cannot be established.

The study also lacks external validity, because the program only evaluates the effects of the intervention on a small sub-set of the population. This sub-set consists of those individuals who already have access to NNPGH. Because this facility is located in an urban center, the results are not largely applicable across Kisumu District, as women in further rural areas may not be affected at all by implementation of the program. Thus, there is an inherent selection bias, as participants in the study are not representative of the target population. We must conclude that any observable effects are specific to the context of the study, and cannot be widely generalized to other regions in sub-Saharan Africa.

#### Program Assessment

While the study provides some initial insight to the potential impact of greater integration of PMTCT services on improving uptake, there are a number of issues left unresolved. First, the design of the study makes it difficult to disaggregate between the different components and services that were implemented, and their respective impact on observed outcomes. While an “opt-out” approach to testing may have been effective in increasing the number of women who received pre-test counseling, it is not clear then whether pre-test counseling had any further effect on increasing the number of women who were tested, or if this increase carried over

from the new “opt-out” approach alone. Similarly, the authors are unable to evaluate the size of the impact pre-test counseling itself may have had on increasing the number of women who then learned their HIV status. More information about women’s motivations for refusing testing, or decisions to follow-up with post-test counseling, could be useful in formulating appropriate policies to facilitate uptake of these services.

Similarly, there are a number of additional relevant outcomes that are not considered in the scope of this study. The evaluation does not examine post-birth outcomes, or whether infant feeding counseling has any actual impact on mothers’ behavior. There is no information on whether prophylaxis treatments to women are actually used by those women, or whether a significant reduction in MTCT rates was actually observed. This is likely due to a lack of funding to pursue follow-up measurements, yet such information is integral for our analysis of the effectiveness of the program intervention on key targets.

The authors also fail to measure whether integration of PMTCT services could potentially have a negative effect on hospitals’ ability to provide overall care. Here, it would be prudent to examine the effect of the program on changes in total healthcare expenditures or employee hours, as a way to estimate cost-effectiveness of the intervention, and possible impact on the quality of health services. Further evaluations in this respect will help determine whether integration of PMTCT services could overburden resource-limited healthcare facilities. If such is the case, integration may not be an effective solution in the absence of public funding, and more attention should be given back to strengthening stand-alone programs.

Despite its methodological issues, the study provides some evidence that integration of PMTCT services into existing prenatal care can improve uptake. The use of two different data collection methods, and a comparison of the results from each, does strengthen the reliability of the data, and we can acknowledge that general improvements in target outcomes were observed during the evaluation period. There is, however, no indication that such changes at the health-facility level are effective in reaching the target population, or that they improve the quality of care received. Integration of PMTCT services alone, without improving outreach, may be ineffective in increasing access for a large part of the population, particularly those who are currently unable to access prenatal care.

As with other integrated PMTCT programs, as well as stand-alone programs, we continue to see high rates of attrition at each intervention step, although results show that a greater percentage of women do continue to follow-through with each treatment step in the post-intervention period. Regarding low rates of post-test counseling, the authors suggest that social stigma and negative perceptions surrounding HIV could play an important role in explaining why some women continued to refuse HIV testing or follow-up after receiving test results. This highlights a major gap in PMTCT intervention that cannot be addressed through greater integration of services alone, but likely requires a more direct approach in reaching out to women and communities where HIV is prevalent, but may be highly misunderstood. One such program that has received considerable attention is Mothers to Mothers, which has expanded across sub-Saharan Africa and is examined in greater detail in the following section.

### 3. Potential effect of peer-mentoring on improving uptake of PMTCT services

Horizons Systems Health Trust, a health NGO, conducted an impact evaluation on the effectiveness of mothers2mothers (m2m), a peer support program aimed at offering education and psychological support to HIV positive mothers and helping ensure they use local treatment options to prevent mother-to-child transmission of HIV. M2M works by pairing pregnant HIV positive women with HIV positive mothers as mentors, who meet with them and provide information and support. The impact evaluation examined whether m2m is effective in achieving its goals.

The study was conducted in the semi-urban KwaZulu-Natal area of South Africa. This area has HIV rates of 39%, the highest in the nation. A number of other HIV treatment and information programs were also active in the area at the time of the study. Participants were women between ages 18 and 49 who knew their HIV status, and were 6-9 months pregnant or less than 12 weeks postpartum. Baseline survey data from three intervention sites were collected in 2005 prior to the introduction of m2m. Follow-up data was collected in 2006 and was approximately double the size of the baseline (695 vs. 361) to include an equal number of participants and non-participants in the study. Data was collected on PMTCT knowledge, HIV status, use of Nevirapine, infant feeding practices, referral to follow-up care, and psychological well-being. Participants in m2m formed the treatment group, while non-participants acted as a control. There was no randomization of the groups; instead, women self-selected to participate in the mentor program. Women who met with a mentor 2 or more times were evaluated in the treatment group.

### Summary of Results

The study found that participants on average had greater knowledge of HIV-related issues. A greater number of participants were informed that HIV positive mothers can transfer HIV to their children, and that breastfeeding can lead to transmission of HIV. Both findings were significant at the 5% level. These suggest, at least, that m2m helps inform women about MTCT. The program also showed strong effects on willingness to disclose HIV status to others. Postpartum participant mothers were 12% more likely to have disclosed their HIV status. This finding was significant at the 1% level. Pregnant participants were also more likely to disclose their HIV status, but this effect was not significant. Together, this suggests that m2m helps to remove the social stigma surrounding HIV.

In terms of increasing uptake of PMTCT services, postpartum participants were also significantly more likely to receive ARTs during breastfeeding, for themselves and for infants. There was no significant effect on the number of pregnant mothers receiving ARTs. The treated group was also significantly more likely to practice safe breastfeeding, and women who participated in the program were significantly more likely to use contraception and get regular CD4 testing after having given birth.

### Empirical Evaluation

While the impact evaluation estimates a potentially large effect of m2m on target outcomes, the study itself lacks both internal and external validity. Because the study was conducted in an urban area of South Africa, with a relatively large number of both stand-alone PMTCT programs and PMTCT services provided in large health facilities. This location limits the extent to which these results can be

generalized to other regions in sub-Saharan Africa, especially more rural areas. Furthermore, increased activity or number of other HIV programs might have affected the results, although we might assume that both treatment and control groups would be affected in the same way.

A greater concern is the issue of internal validity due to lack of randomization. Because program was not routinely offered to participants in randomly generated treatment and control groups, there is a selection bias. Baseline statistics show that, in fact, pregnant women included in the treatment group were significantly more educated and older than those pregnant who did not enroll in the program, who were then included in the control group. The study compares outcomes on individuals who enrolled versus those who did not participate in the program, despite the fact that there is an inherent difference between these two groups. Because data were not collected blindly, this may have also introduced bias. Additionally, all results were self-reported rather than objectively measured.

#### Program Assessment

Together, the findings suggest that there may be a causal link between improving available information, social climate, and support structures for women living with HIV on increasing uptake of PMTCT services. The psychological survey also shows significantly improved well-being on various metrics for both pregnant and post-partum participants in the treatment. The estimated impact suggests that further attention to how complementary social measures can impact uptake of PMTCT services should be considered.

It may have been preferable, however, to employ falsification tests to see whether outcomes in treatment and comparison groups would be moving in tandem

in the absence of the program. This would require additional rounds of data collection prior to the introduction of m2m, but would give a better estimate of the extent of m2m's impact on facilitating uptake. Currently, the lack of a randomized experiment limits the significance of findings regarding m2m's impact. Further studies comparing outcomes between areas where m2m is active to those where the program is not offered, would give a better idea of the true impact of m2m.

The study gives some indication about the potential impact peer-mentoring may have on improving utilization of PMTCT services, but we cannot draw conclusive statements regarding these effects. Furthermore, because m2m relies on existing PMTCT programs to be effective, it does not provide any new suggestions on how access to such services can be increased in the absence of established programs. Thus, the impact of programs such as m2m are only applicable in settings where existing PMTCT services, whether integrated or stand-alone, are already available.

### **Concluding Recommendations**

Our evaluations of these three methods and their effectiveness at improving PMTCT outcomes suggests that reducing the incidence of mother-to-child transmission of HIV can be accomplished through the use of more effective anti-retroviral therapies, or with greater application of complementary or facilitative services. In resource-limited settings, this does not necessarily require a scaling-up of PMTCT services, but rather an adjustment of the types of services provided, or changing the context in which these services are provided.

A review of triple-antiretroviral prophylaxis treatment suggests that such regimens may be both safe and effective in improving the efficacy of anti-retroviral therapies. There is, however, further research that should be done in this area before such treatments might be reasonably implemented. First, an experimental study to evaluate the effectiveness of triple-antiretroviral treatment against single-dose ARTs should be conducted. It is possible that a methodological comparison of these two treatments will show that the improved efficacy of the extended regimen is not replicable outside of clinical settings, given potentially high rates of attrition in target populations.

Our overview of alternative strategies for improving PMTCT uptake suggest that both greater integration of services with existing prenatal care facilities, and the introduction of socially-oriented programs, such as peer-mentoring, have the potential to facilitate the uptake of these services, given certain conditions. Integration of services into one facility, counseling, and follow-through with one provider can improve the number of women who are tested for HIV and learn their results. Integration into existing maternal health structures, however, is not shown to have an effect on reaching women who may have the least access to PMTCT services. Further research is necessary to evaluate programs that can target underserved populations who have least access to PMTCT services.

Given the findings from the mothers2mothers evaluation, we suggest that complementary programs targeted at increasing awareness and providing information to pregnant mothers on ARTs should be pursued, where existing PMTCT programs are already available. Peer-mentoring can be effective in

improving utilization of these existing resources. Given the high attrition rates of women who receive HIV-testing but do not follow-up, such programs can be important in ensuring that ARTs are correctly administered and appropriate infant feeding recommendations are followed.

Overall, addressing the problem of high rates of HIV infection in children requires coordination between existing maternal and child health structures, and programs targeted at delivery of PMTCT services. Improved information regarding available services can be effective in increasing utilization, but more information is needed to understand how social programs may play a role in improving uptake.

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