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Improving PMTCT Uptake in Rural South Africa

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Abstract

Introduction—Despite the widespread availability of prevention of mother-to-child transmission (PMTCT) programs, many women in sub-Saharan Africa do not participate in PMTCT. This pilot study aimed to utilize partner participation in an intervention to support PMTCT uptake.

Methods—Couples ($n = 239$) were randomized to receive either a comprehensive couples-based PMTCT intervention or the standard of care.

Results—Compared to the standard of care, participants receiving the intervention increased HIV- and PMTCT-related knowledge ($F_{1,474} = 13.94, p = .004$) and uptake of PMTCT, as defined by infant medication dosing (74% vs. 46%, $\chi^2 = 4.69, p = .03$).

Discussion—Results indicate that increasing male attendance at antenatal clinic visits may be “necessary but not sufficient” to increase PMTCT uptake. Increasing HIV knowledge of both partners and encouraging *active male participation* in the PMTCT process through psychoeducational interventions may be a strategy to increase the uptake of PMTCT in South Africa.

Keywords

PMTCT; male involvement; South Africa

Introduction

Prevention of mother-to-child transmission (PMTCT) programs have played a major role in reducing child mortality associated with HIV/AIDS and improving maternal health.^{1,2} Guidelines for the use of antiretroviral (ARV) therapies to reduce transmission have been

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implemented in countries most affected by the HIV pandemic, especially those in sub-Saharan Africa.³ The PMTCT program in South Africa consists of HIV counseling and testing (HCT) and the offer of ARV prophylaxis for seropositive mothers and their newborns as well as referral of HIV-positive mothers and their families for CD4 assessment for antiretroviral therapy (ART).¹ However, despite the widespread availability of PMTCT, less than 70% of the mothers provided with medication take it themselves or provide it to their newborns,⁴⁻⁸ which resulted in high rates of vertical transmission in sentinel surveys conducted in various South African provinces in 2009 and 2010.^{9,10} Recent revisions to the SA PMTCT protocol (eg, lifelong provision of ARV drugs for women with CD4 > 350 and prophylaxis starting in the second trimester for those with higher CD4 counts) have been associated with reductions in maternal transmission, but vertical transmission rates of 12% to >20% continued to be reported in 2010 community health center reports in South Africa's Mpumalanga Province.¹⁰ Such rates may also be attributable in part to limitations in health care systems and failure of health service provision to integrate PMTCT, maternal/child health, and postnatal follow-up.

Prevention of mother-to-child transmission program failure occurs at several stages of the process in South Africa.¹¹ Implementation of PMTCT programs in already overburdened clinical settings presents multiple challenges, including systemic (eg, failure to offer ARV prophylaxis, home delivery), social (eg, stigma, lack of disclosure), individual (eg, maternal failure to ingest medication or provide it to the infant, failure to obtain antenatal testing), and interpersonal (eg, lack of male involvement, intimate partner violence [IPV]) factors.¹² Recent efforts to increase PMTCT include broadening the scope of involvement in care of the mother to include her male partner¹³ throughout the various stages of antenatal and postpartum care.¹⁴⁻¹⁷ However, although increasing male participation generally has been viewed as supportive of PMTCT,^{8,18} involvement, defined as clinic attendance alone, may not be sufficient to significantly impact PMTCT uptake,¹⁶ that is, the *quality* of participation in care and the type of support these men provide for their pregnant partners must also be addressed.¹⁹

The HCT for pregnant women has typically been on an individual and gender-specific basis in PMTCT programs. However, a couple's approach to HCT and antenatal care may facilitate communication about HIV serostatus, thereby reducing one of the major barriers to acceptance of ARV prophylaxis by mothers for themselves and their newborns as well as encouraging adoption of preventive behaviors within couples and reducing HIV transmission during and following pregnancy.^{20,21} Limited knowledge of the PMTCT process may also be a contributing factor to lack of male involvement²² and contribute to the overall perception of the male partner's minimal role in the antenatal care/ PMTCT process. While male involvement has been increasingly encouraged^{8,23-25} and male participation has met with some success,^{16,26} no randomized clinical trials of the influence of male partners as key contributors to PMTCT uptake have been conducted. In addition, while male involvement may be desirable, sustaining male participation has proven difficult.^{1,18,27} Both HCT and prevention strategies for couples could also strengthen HIV prevention efforts in Southern Africa,²⁸ where the majority of HIV infections occur in stable relationships.

As a precursor to a large-scale clinical trial, this pilot study was designed to test whether participation in a combination of 2 evidence-based interventions, a couples risk reduction intervention and a medication adherence intervention, would significantly improve uptake of the PMTCT protocol by women. The study sought to determine whether male participation in the intervention would significantly impact PMTCT uptake compared to male attendance at antenatal visits only, utilizing the existing public health program linking antenatal care, HCT, and PMTCT services as the standard of care.

Method

This study was funded as a supplement to a center grant by a PEPFAR/NIAID collaboration for advancing implementation science in PMTCT, targeting existing PEPFAR sites. University of Miami Miller School of Medicine Institutional Review Board, Human Sciences Research Council Research Ethics Committee, and the Mpumalanga Provincial Department of Health approvals were obtained prior to the onset of the study. All procedures followed were in accordance with the ethical standards of the review committees mentioned previously and with the Helsinki Declaration of 1975, as revised in 2000. This study protocol is registered at clinicaltrials.gov, number NCT01448512. All participants provided informed consent prior to enrollment and the initiation of study-related procedures.

Participants and Setting

Pregnant women who had completed HCT and were 24 to 30 weeks' pregnant and 18 years of age were recruited and if interested, were asked to invite their male partner to enroll as a couple (n = 239 couples). Couples then returned to provide informed consent and baseline assessments. Despite the drive to encourage women to book earlier in care to take advantage of PMTCT care, women were enrolled late in pregnancy as most women in the region did not present for care until late gestational age. Participants were recruited from 12 antenatal clinics (ANCs) in Gert Sibande and Nkangala districts of Mpumalanga Province, South Africa. Antenatal HIV prevalence rates ranged from 15.4% to 38.2%. Couple status was verified by screening to ensure enrollment of genuine primary sexual partners. South African 2009 PMTCT guidelines did not require women to receive their HIV test results and male partners were not required to undergo HCT, though those who are tested are strongly encouraged to receive their results and involve their male partners. Those testing HIV seropositive during antenatal care (n = 82) were referred for CD4 and liver function evaluation; those with CD4 counts \leq 350 were referred for ART, those $>$ 350 were referred for HIV prophylaxis. The confidentiality of the serostatus of all participants was maintained throughout the study. Women who tested HIV negative at antenatal care entry (baseline) were retested at 32 weeks' gestation.

Intervention—The PartnerPlus intervention adapted a couples' behavioral HIV risk reduction intervention²⁹ and a medication adherence intervention³⁰ to create a platform for a comprehensive couples-based PMTCT intervention. The intervention consisted of 4 successive weekly sessions of 90 to 120 minutes each and addressed HIV, safer sex, sexual negotiation, and PMTCT issues. Sessions were closed, structured, of gender-concordant groups limited to 10 participants, led by trained gender-matched facilitators, and conducted

in ANCs. Sessions utilized a cognitive-behavioral skill training approach to improve adherence to treatment during pregnancy, communication related to sexual and interpersonal negotiation, conflict resolution, medication adherence, HIV and PMTCT knowledge, male and female condom use, and disclosure issues. The intervention was designed for seropositive, discordant, and seronegative couples. While the information presented did not apply equally to every participant, facilitators related information in a variety of contexts, for example, adherence, was presented to participants as relating to not only medication but also clinic visits and pregnancy treatment guidelines. The group-based cognitive-behavioral HIV risk reduction intervention was guided by the theories of reasoned action³¹ (ie, attitudes and subjective norms influence intentions that in turn influence beliefs about behavior) and planned behavior³² (ie, perceived behavioral control influences intentions and resulting behavior) to predict sexual barrier use. The adherence component of the intervention utilized the Information Motivation Behavioral Skills Model,³³ in which the components of medication adherence (adherence-related information, motivation, and behavioral skills) function together to promote adherence. Using a manual of the intervention, facilitators applied cognitive-behavioral strategies to the components of the intervention (eg, reframing thoughts, heightening participants' awareness of their reactions to condom use in their sexual relationships, and reframing automatic thoughts that may impede barrier use, HIV status disclosure, and open communication). Sessions also addressed IPV and antecedents to conflict and violence, and each session included relaxation techniques to use during stressful interactions (deep breathing, imagery, or meditation). Group strategies included establishment of a safe environment for sharing personal experiences, role-playing negotiation, problem solving and communication skills, and hands-on experiential training with condoms.

While all sessions were gender separate, participants were given "homework" to work on as a couple at home. Each subsequent week, participants were encouraged to share their experiences and apply cognitive-behavioral skills in problem solving.

Control condition participants received the standard of antenatal care (plus PMTCT, if HIV seropositive) and group time-matched sessions consisting of health-related videos on diabetes, hypertension, alcohol misuse, and exercise. All participants were provided with male and female condoms at each session.

Design

This pilot study was conducted in accordance with randomized controlled trial methodology, using a 2×2 comparison (condition \times time). To avoid contamination between conditions, the 12 ANCs were randomly assigned to a condition in a 1:1 ratio. Six sites provided the PartnerPlus intervention (experimental group) and 6 sites provided time-matched health education sessions (control group).

All women were provided the standard antenatal care visits. The SA PMTCT treatment protocol was offered to all women identified as HIV seropositive prior to delivery.³⁴

Measures

Participants were recruited between January 2010 and July 2011. Participants were administered assessments at study entry and postintervention by trained assessors; at 32 weeks, pregnant HIV status was reassessed; and at postdelivery, dried blood spots (DBS) were collected to determine whether ARV drugs were taken.³⁵

Preintervention assessments were conducted at ~24 weeks' gestation and postintervention assessments occurred 1 month following the intervention, at ~24 to 32 weeks' gestation. Assessments of HIV status occurred at 32 weeks' gestation. At 6 weeks postdelivery, blood tests were assessed by polymerase chain reaction (PCR) to determine infant HIV status. All biological assessments were part of the existing PMTCT protocol. Participants were compensated 100 South African Rand (R100) per assessment and R50 per intervention session for time and transportation. All study materials, for example, consent, assessment, and intervention, were translated into the major local languages (Zulu and Swati). No literacy restrictions were used as assessments were interviewer administered by trained assessors; study assessors were not drawn from clinic staff and did not participate in the provision of the PartnerPlus intervention (Figure 1).

Demographics

Data on age, educational level, employment status, household and personal income, residential status (urban or rural), and HIV status (if known) were collected from the participant. HIV serostatus was confirmed from clinic records.

Knowledge of HIV and PMTCT

HIV knowledge concerning HIV transmission, condom use, PMTCT, and AIDS was assessed using 13 items adapted from an AIDS-related knowledge scale. The scale had been previously adapted for use in South Africa by the study team. HIV knowledge was scored for the number of correct responses (Yes, No), with Don't Know responses scored as incorrect (score = 0), and the possible range of scores 0 to 13 expressed as the percentage correct. The HIV knowledge test demonstrated heterogeneous item content; Cronbach α was .54 for this study sample. A subset of 4 PMTCT-specific questions were scored and analyzed separately to assess PMTCT-specific knowledge, these items included "Do pregnant women who are HIV positive, transmit HIV to their babies?" "Can an HIV-positive mother infect her baby with HIV during pregnancy?" "Can a HIV-positive mother infect her baby with HIV during delivery?" and "Can a HIV-positive mother infect her baby with HIV during breastfeeding?" Because repeated testing of the same variables was performed in the analyses of HIV and PMTCT knowledge, all resulting *P* values were adjusted for false discovery rate according to the methods detailed by Benjamin and Hochberg.³⁶

Medication Uptake

The PMTCT medication uptake was assessed using 7 items addressing medication use by mothers and infants prior to, during, and following birth. Questions were scored using yes,

no responses, and a single scale representing the self-reported percentage of medication provided by mothers to their infants.

HIV Serostatus and ARV Uptake

HIV serostatus for couples and infants was confirmed using clinic record data (baseline and 32-week HCT, 6-week infant PCR). Maternal and infant blood samples were collected post-delivery using DBS at 3 to 7 days postpartum. Samples were analyzed for the presence of nevirapine (NVP), zidovudine (ZDV), efavirenz (EFV), lamivudine (3TC), and stavudine (d4T), the medication regimens for highly active antiretroviral therapy (HAART) and PMTCT in South Africa at the time of this study. Nevirapine was assessed due to its association with breastfeeding infants longer term.

Session and Clinic Attendance

Session and clinic attendance was obtained from study facilitators and clinic records. Female participants self-reported the number of clinic visits attended during pregnancy following enrollment in the study and the number of clinic visits attended by their male partner.

Statistical Analyses

Data analyses with dichotomous variables were conducted using chi-square tests of independence and Fisher exact test. Continuous variables were assessed using repeated measures analysis of variance and *t* tests. Dependent variables included HIV- and PMTCT-related knowledge, attendance, disclosure, and PMTCT uptake. The independent variables for analyses included gender and study condition. All tests were performed with a 2-tailed significance level of .05, using IBM Statistical Package for the Social Sciences (SPSS) version 19.0.

Results

Demographics and HIV Serostatus

Participants ($N = 478$) were an average of 28 ± 7 years of age; the majority were unemployed (58%) and living in rural areas (71%). Half of the sample (49%) reported no income and less than 12 years of education (53%). Experimental condition participants were more likely to live in an urban area than controls ($\chi^2 [n = 478] = 8.3, P = .004$). At baseline, 32% ($n = 76$) of women were seropositive. While the exact gestational age at which women enrolled was not available, all female participants were enrolled between 24 and 30 weeks' pregnant. Demographic information is further detailed in Table 1.

At postintervention, 35% ($n = 82$) of female participants were HIV positive. In all, 87% of males ($n = 208$) were also tested for HIV, and 21% ($n = 43$) were positive. The participant HIV serostatus is shown in Table 2. Among HIV-seropositive men, 12 (28%) accurately disclosed their serostatus to their partners postintervention. Among women, just under 50% had accurately disclosed at baseline, and there was no increase in disclosure among women across the course of the study.

Knowledge of HIV and PMTCT

At baseline, there was no difference in HIV and PMTCT knowledge between conditions ($t_{476} = .94, p = .35$). Postintervention, HIV and PMTCT knowledge increased only in the intervention condition; while the level of participant HIV and PMTCT knowledge did not change in the control condition ($F_{1,474} = 13.94, p = .004$). Knowledge did not change by gender over time or by gender within condition over time. Table 3 details the results of HIV and PMTCT knowledge by gender and condition.

At baseline, there was no difference in the mean PMTCT-specific knowledge scores between conditions ($t_{476} = .53, p = .60$). PMTCT-specific knowledge differed by condition over time ($F_{2,474} = 25.27, p = .004$); scores increased in the intervention condition, while decreasing in the control condition. PMTCT-specific knowledge did not change by gender over time or by gender within condition over time (see Table 2).

Attendance

Attendance at ANC appointments was high in both conditions; female participants attended an average of 5.7 ± 1.5 prenatal clinic visits; their male partners reported attending an average of 2.3 ± 1.8 visits. There was no difference in the number of visits between rural and nonrural participants or between employed and unemployed participants, nor was the number of visits associated with income or education. There was a non-significant trend in the difference between the intervention and control conditions in the number of visits attended by women ($t_{201.5} = 1.76, p = .08$) and no difference in the number of visits attended by men ($t_{223} = -1.3, p = .18$). The number of visits attended within couples was modestly correlated ($r = .17, p = .01$).

Similarly, there was no difference in the overall study session attendance by condition among women ($3.1 \pm .85$, intervention, $3.3 \pm .81$, control; $t_{236} = -1.8, p = .08$). Intervention session attendance by men was higher in the control condition ($3.3 \pm .87$) than in the experimental condition ($3.1 \pm .85$; $t_{236} = -2.5, p = .01$).

PMTCT Medication Uptake and Infant Serostatus Outcomes

Of those women who were HIV seropositive at postintervention ($n = 82$), only 57 disclosed their serostatus to the study assessor postpartum. Of those, 95% ($n = 54$) reported taking all of their medication during the last 4 days of pregnancy and 86% (49) reported taking NVP and/or ZDV (83%, $n = 53$) during delivery. Two-thirds ($n = 38$) reported their infant was administered ZDV and 84% ($n = 48$) reported their child received NVP; however, only 61% ($n = 35$) reported they subsequently gave their infant every dose of medication prescribed. Women in the experimental condition were more likely to report giving their infant every dose of HIV medication (74% versus 46%, $\chi^2 = 4.69, p = .03$).

In the experimental condition, women successfully delivered 30 infants, and 7 were miscarried. In the control condition, women successfully delivered 37 infants, and 6 were miscarried. There was no difference in the percentage of live births by condition ($\chi^2(82 \text{ df}) = .48, P = .49$). Confirmatory data was obtained on a subset of women who agreed to be tested for the presence of ARV drugs on their own and their infant's blood by DBS ($n = 24$

mothers and 25 infants; 12 intervention and 12 control mothers, 13 intervention and 12 control infants). Anti-retroviral medication was detected in 75% of intervention condition mothers ($n = 9$) and 50% of control mothers ($n = 6$; Fisher Exact test, $p = .19$) and 92% of intervention condition ($n = 12$) and 75% of control infants ($n = 9$; Fisher Exact test, $p = .32$). Figure 2 details the results of DBS testing. Of the 6 women who seroconverted during the study, DBS data were available for 1 infant and mother. No ARV drugs were detected in the mother, while medication was detected in the infant sample. All women who completed DBS testing reported never skipping medication in the previous 3 months, that is, perfect adherence. Among the 4 infants testing negative for ARV medication via DBS, all mothers reported giving their infant 100% of prescribed doses, that is, perfect adherence.

All infants were tested for HIV at 6 weeks of age. Four infants were confirmed HIV seropositive; 3 born to mothers in the control condition (total infants = 39, HIV positive = 8%), 1 to a mother in the intervention condition (total infants = 30, HIV positive = 3%). Of the 4 babies, 1 completed DBS testing (intervention condition), and medication was detected in both mother and infant.

Discussion

This pilot study sought to test whether participation in a combined couples risk reduction and medication adherence intervention would improve PMTCT reach and effectiveness and to determine whether male participation would significantly impact the uptake of PMTCT treatment by pregnant women. Male involvement increased in both conditions, while HIV and PMTCT knowledge increased only in the intervention condition. While the sample of infants was very small, and could have been influenced by random variation, the intervention condition was associated with better PMTCT uptake, as defined by medication uptake and infant serostatus outcomes.

Increasing male participation to enhance uptake of and commitment to the PMTCT medical protocol for pregnancy and newborn care has been identified as a potentially critical strategy in sub-Saharan Africa.^{8,26} Prevention programs to increase male involvement in Tanzania, Botswana, Zambia, and Kenya have met with some success.^{15,16,27} Men's attitudes regarding involvement in PMTCT and antenatal care programs have been linked to the perception that male participation is superfluous.²⁸ Problems with attendance have included lack of specific information regarding the importance of PMTCT and conflicts between PMTCT programs and work schedules. This study suggests that men may attain a level of comfort in clinics following exposure, but as noted earlier, the quality of involvement appears to remain a key to increasing PMTCT uptake.¹⁹

Male attendance at ANC visits in both experimental and control conditions dramatically increased in comparison with the number of visits reported in other programs.^{16,37} In fact, female clinic attendance exceeded the World Health Organization (WHO) recommendations (4 antenatal visits).³⁸ Study session attendance was higher in the control arm, but this was likely due to the increased flexibility of scheduling associated with the individual versus group condition. However, in both conditions, clinic visits may have occurred simply as a result of men attending experimental or control sessions held at the clinics. The intervention

group significantly increased both overall HIV knowledge and PMTCT knowledge, however, in comparison with the control condition. It is clear, therefore, that male involvement must be more than just “presence” at the ANC. It must also include active participation in a program that provides them both information and opportunity for exploration of those factors relevant to both maternal and infant well-being.

While some men and women may have tested for HIV or have been aware of their HIV status prior to participation in the study, the study identified an increase in disclosure among men during and following participation. It is interesting to note that while study participation increased the likelihood of HIV status disclosure among men in both conditions, it did not increase disclosure among women. This perhaps is most readily explained by the fact that women may have “more to lose” by disclosure than their male partners, given gender power inequities within couple relationships. Women may also be more likely to disclose to family and friends and less likely to disclose to male partners. This finding notwithstanding the fact that women in the intervention condition had significantly greater adherence to PMTCT medications for both themselves and subsequently their newborns than those in the control condition suggests that male involvement *and* their participation in the intervention amounted to “*active* participation.”

Limitations

This 18-month pilot study established the feasibility of conducting such interventions in rural settings in South Africa and created the foundation for a large-scale clinical trial, demonstrating 100% participant retention through the study as well as increased PMTCT participation by both men and women. The study sample included HIV-positive, -negative, and sero-discordant couples. In addition, some participants did not disclose their HIV serostatus to assessors, resulting in a reduced sample size to assess infant and maternal adherence. As such, the small sample size of HIV seropositive women and infants in the study precluded definitive conclusions. Future studies should include the use of audio computer-assisted self-interview (ACASI) technology to encourage more accurate self-report. In addition, subsequent studies can utilize the current study results to estimate the sample size necessary to answer relevant hypotheses concerning partner influence on PMTCT uptake and outcomes. Such studies should also have sufficient resources to follow all participants through delivery (clinic or home delivery) and follow participants for 1 year to provide complete HIV incidence data on exposed infants. Additionally, men’s reluctance to test for HIV and both men’s and women’s hesitance to disclose their HIV status remains an important impediment to HIV risk reduction.

Conclusions

It is important to recognize the important contribution of male partners to the success of PMTCT programs. However, the old expression “necessary, but not sufficient” is particularly apt in attempting to understand the nuances of partner participation. Male attendance at antenatal visits was high in both experimental and control conditions, but only the experimental group demonstrated significant improvements in PMTCT outcomes,

confirming the need for psychoeducational programs to *actively* engage both HIV-seropositive pregnant women and their male partners in the PMTCT process.

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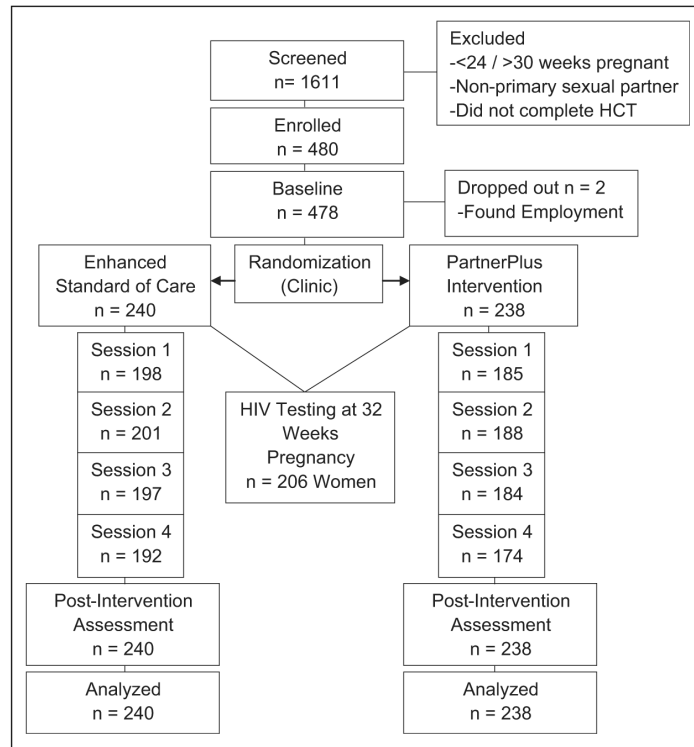


Figure 1.
CONSORT flow diagram.

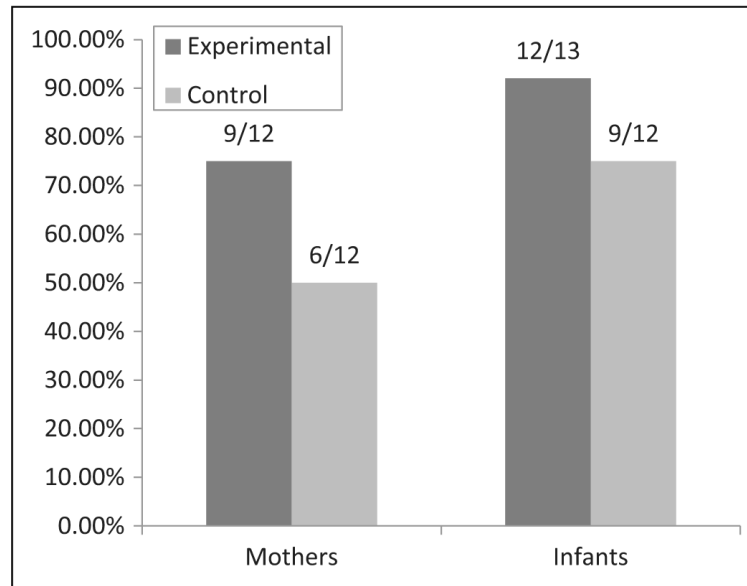


Figure 2. Presence of ARV medication detected (postnatal) via DBS testing. ARV, antiretroviral medication; DBS, dried blood spots.

Table 1

Demographics.

Measure	Total N (%) or Mean (SD)	Intervention n = 238	Control n = 240	<i>t</i> / χ^2	<i>P</i> ^a
Age	28.2 (7.1)	28.3 (6.8)	28.1 (7.4)	.27	.79
Personal income (Rand, per month)	888 (1758)	761.8 (1418.0)	1014.7 (2036.8)	1.6	.12
Employment				.57	.45
Unemployed	344 (72)	175 (74)	169 (70)		
Employed	134 (28)	63 (27)	71 (30)		
Education				2.7	.10
<Grade 12	253 (53)	135 (57)	118 (50)		
Grade 12 or more	225 (47)	103 (43)	122 (51)		
Residence				8.3	.004
Rural	340 (71.1)	155 (65)	185 (77)		
Settlement/urban	138 (28.9)	83 (35)	55 (23)		

^aStatistically significant variables are noted in boldface.

Table 2

HIV Serostatus.

	Men, n = 239	Women, n = 239
HIV serostatus (baseline)		
Positive	38 (16)	76 (32)
Negative	144 (60)	163 (68)
Did not test	57 (24)	0 (0)
HIV serostatus (postintervention)		
Positive	43 (21)	82 (35)
Negative	165 (69)	124 (52)
Did not test/retest	31 (10)	33 (13)

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Table 3

HIV and PMTCT Knowledge Pre- and Postintervention by Condition and Gender.

	Baseline M (SD)	Postintervention M (SD)	<i>F</i> 1,474 <i>df</i>	<i>P</i> ^a
HIV and PMTCT knowledge				
Main effect	10.4 (1.7)	10.6 (1.8)	3.1	.16
Condition × time			13.9	.004
Intervention	10.4 (1.6)	10.9 (1.7)		
Control	10.5 (1.8)	10.4 (1.8)		
Gender × time			.55	.74
Male	10.3 (1.8)	10.5 (1.9)		
Female	10.6 (1.6)	10.7 (1.7)		
Condition × gender × time			.02	.97
PMTCT-specific knowledge				
Main effect	2.8 (1.1)	2.7 (1.2)	4.1	.11
Condition × time			25.2	.004
Intervention	2.8 (1.2)	3.0 (1.1)		
Control	2.9 (1.1)	2.4 (1.2)		
Gender × time			.01	.97
Male	2.8 (1.1)	2.6 (1.2)		
Female	2.9 (1.1)	2.8 (1.1)		
Condition × gender × time			.35	.76

Abbreviations: PMTCT, prevention of mother-to-child transmission; SD, standard deviation.

^a*P* values adjusted for multiple comparisons using false discovery rate, experiment-wide $\alpha = .05$.