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HIV Prevention Counseling Intervention Delivered During Routine Clinical Care Reduces HIV Risk Behavior in HIV-Infected South Africans Receiving Antiretroviral Therapy: The Izindlela Zokuphila/Options for Health Randomized Trial

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All authors declare that they have no conflicts of interest.

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SA Options Team
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Abstract

Context—Sustainable interventions are needed to minimize HIV risk behavior among people living with HIV (PLWH) in South Africa on antiretroviral therapy (ART), a significant proportion of whom do not achieve viral suppression.

Objective—To determine whether a brief lay counselor delivered intervention implemented during routine care can reduce risky sex among PLWH on ART.

Design—Cluster randomized 16 HIV clinical care sites in KwaZulu Natal, South Africa, to intervention or standard-of-care.

Setting—Publicly funded HIV clinical care sites.

Patients—1891 PLWH on ART received the HIV prevention counseling intervention (n = 967) or standard-of-care counseling (n = 924).

Intervention—Lay counselors delivered a brief intervention using motivational interviewing strategies based on the Information—Motivation—Behavioral Skills (IMB) model during routine clinical care.

Main Outcome Measures—Number of sexual events without a condom in the past four weeks with partners of any HIV status, and with partners perceived to be HIV-negative or HIV-status unknown, assessed at baseline, 6, 12, and 18 months.

Results—Intervention participants reported significantly greater reductions in HIV risk behavior on both primary outcomes, compared to standard-of-care participants. Differences in STI incidence between arms were not observed.

Conclusion—Effective behavioral interventions, delivered by lay counselors within the clinical care setting, are consistent with the strategy of linking HIV care and HIV prevention and integrating biomedical and behavioral approaches to stemming the HIV epidemic.

Key words/Phrases

South African HIV Epidemic; Prevention with Positives; HIV Risk Reduction; IMB Model

INTRODUCTION

Since the beginning of the South African epidemic, an estimated 2 million adults have died from HIV/AIDS[1,2], 6.1 million South Africans are currently living with HIV[3], the prevalence in the 15–49 year age range is 17.9%[3], and the incidence is 1.43% per year

among those aged 15–49[4]. Over 370,000 HIV infections and 240,000 AIDS-related deaths occur in South Africa each year[3].

South Africa's HIV Testing and Counselling campaign and rollout of antiretroviral therapy (ART) are well established[5]. More South Africans are learning their HIV status and entering clinical care[6], presenting a unique opportunity to link HIV treatment with HIV prevention behavioral interventions for persons living with HIV (PLWH) on ART. PLWH on ART constitute a large and growing population of great significance for impacting South Africa's epidemic[7]. Specifically, these individuals, like PLWH everywhere, are variably adherent to ART[8] and to safer sex practices[9–11], despite clinic-based standard-of-care ART education and counseling and safer sex promotion. Treatment failure with continuing detectable viremia among South African PLWH on ART is not uncommon[12,13] and ART resistance has occurred in a sizable proportion of individuals who have been treated and have experienced therapeutic failure[14–19]. South African PLWH on ART who have experienced treatment failure may serve as relatively healthy but infectious vectors for transmission of drug susceptible and drug resistant virus and may contribute to the maintenance or exacerbation of South Africa's HIV epidemic. These individuals represent one potential leading edge of the country's generalized HIV epidemic and merit priority for behavioral safer sex interventions to avert forward HIV transmission. PLWH who engage in unprotected sex also place themselves at risk for other sexually transmitted infections (STI), associated morbidity, accelerated progression of HIV disease[20–22], and potential superinfection with drug resistant HIV[23–26].

Despite the need for evidence-based safer sex behavioral interventions for PLWH on ART in South Africa and their potential efficacy and efficiency when delivered in the clinical care setting, too few large- scale South African research studies, conducted as rigorous experimental trials in the clinical care context, have been reported[27–31]. In the United States and other resourced countries, more randomized controlled trials of HIV risk reduction behavioral interventions designed for PLWH and delivered in clinical care settings have been reported[32–42] (See 32 for an overview of twenty studies in this area.) We extensively modified the U.S. Options project—a quasi-experimental intervention resulting in significant decreases in HIV risk behavior among PLWH in an HIV clinical care setting[34] – for the South African cultural context, HIV risk dynamics, and health care setting. We conducted a successful pilot study of this intervention in South Africa[28] and brought it to scale. The current research widely implemented and rigorously evaluated this intervention in the South African HIV clinical care setting to assist PLWH on ART to reduce HIV risk behavior. We hypothesized that over 18-months, PLWH participating in the intervention compared to those receiving standard of care (SOC) would demonstrate significantly greater reductions in HIV sexual risk behavior.

METHODS

Randomization

Sixteen urban, peri-urban, and rural Primary Healthcare Clinics and Community Health Centers in the uMgungundlovu and uMkhanyakude health districts of KwaZulu-Natal, South Africa, paired based on geography and other relevant clinic characteristics (e.g., catchment

area, patient population, clinic resources), were cluster randomized to intervention (8 clinics) or SOC (8 clinics) arms. These health districts report among the highest rates of HIV in South Africa; antenatal clinic attendee prevalence is 39.8% and 41.1%, respectively[4]. See Figure 1 for study design.

Participants

HIV-infected participants on ART (N = 1891) were recruited from clinical care sites from June 2008 - May 2010. Inclusion criteria were documented HIV infection, receiving HIV care at a participating clinic, prescribed ART, and minimum age 18 years. To maximize statistical power (≥80%) to detect changes in HIV risk behavior, enrollment targets specified a minimum of 16 clinics with a minimum of 125 participants per site and used a sampling strategy oversampling those reporting recent HIV risk behavior. Sampling targeted a 60:40 distribution of those reporting risk behavior during the past 4 weeks on a pre-enrollment screener vs. those not reporting risk. Similar numbers of HIV-infected women and men on ART were recruited.

Procedures

Clinic staff referred eligible PLWH to a research assistant who described the study and screened interested patients for risky sex in the past 4 weeks. Patients meeting criteria were invited to take part in the study and provide informed consent. Participation consisted of (1) completing audio computer-assisted self-interview (ACASI) and interviewer-administered questionnaires (in isiZulu or English) at four time points over 18-months (baseline, 6, 12, and 18 months), (2) providing biological samples assessing sexually transmitted infections (STIs) at three time points (baseline, 12, and 18 months), and (3) consenting to medical chart reviews for CD4 count, HIV viral load, STIs, and health status. As part of routine clinical care, participants in the intervention (n = 967) and SOC (n = 924) arms received counseling from lay counselors concerning issues relevant to PLWH on ART (e.g., adherence education and counseling).

Participants at the eight intervention clinics (n = 967) received brief (10–15-minute), theory and evidence-based, tailored, one-on-one counseling sessions with trained lay counselors concerning sexual risk behavior reduction. Intervention sessions were integrated into PLWHs' routine clinical care during the 18-month study period. SOC participants received standard of care safer sex promotion messages from counselors, typically involving standard condom promotion messaging. Assessments were carried out by a different individual in a separate research setting at the four specified time points within the 18 month study.

Intervention and SOC participants were compensated for completing measures (R70 ~US $10 per assessment) but not for participation in one-on-one counseling. The study was conducted according to the principles of the Helsinki Declaration and approved by ethics committees at University of Connecticut (USA), University of KwaZulu-Natal (South Africa), Centre for Addiction and Mental Health (Canada), the Research Committee of the KwaZulu-Natal Department of Health, and relevant District Health Offices.

Outcome Measures

The primary outcome measures for intervention evaluation were ACASI-reported number of sexual events without condoms (penile-vaginal or penile-anal) over the past 4 weeks with all partners, regardless of perceived partner serostatus, and number of sexual events without condoms over the past 4 weeks with partners perceived to be HIV-negative or -status unknown. Additional outcome measures included interviewer assessment of participants' number of unprotected sexual acts during the past 4 weeks, inconsistent condom use over the past 4 weeks and over the past 3 months (1 = "never" to 5 = "always"), and condom nonuse over the past 6 months ("When did you last have sex without a condom?").These partially overlapping interviewer-delivered measures were included to provide multiple, potentially convergent endpoints assessed via alternative methodologies (ACASI and interviewer) over varying time periods. Data were cleaned prior to analyses; values entered on ACASI surveys judged to be due to touch screen over-sensitivity (e.g., the same number in duplicate [i.e., 88] or triplicate [i.e., 888]) were set to missing (affecting <1.7% of the data, unrelated to study arm).

Self-collected biological samples (vaginal tampons for women, urine samples for men) at baseline, 12, and 18 months assessed incident STIs including *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in men and women and *Trichomonas vaginalis* in women. (The 12-month STI testing was abandoned midway through collection due to financial constraints). Specimens were transported to the laboratory within 48 hours[43].

Intervention

The *Izindlela Zokuphila/Options for Health* HIV risk reduction counseling intervention for PLWH on ART was delivered by lay counselors on an ongoing basis integrated within routine HIV clinical care visits and based on the Information-Motivation-Behavioral Skills (IMB) model of health behavior change[44,45]. It consisted of brief, collaborative, patient-centered, face-to-face discussions between a lay counselor and a patient. Motivational Interviewing (MI) techniques[46,47] were used to: (a) assess the patient's sexual risk behavior, (b) identify informational, motivational, and behavioral skills barriers to safer sex, (c) explore strategies the patient could use to address barriers, and (d) negotiate an achievable, individually-tailored behavior change (or maintenance) goal. This intervention demonstrated acceptability, feasibility, and fidelity in South African pilot projects[27,28] and was adapted for the current study. At the end of each intervention session, lay counselors completed an "Options Record Form" (ORF) serving as a guide for continuing counseling at subsequent sessions and as a measure of intervention fidelity. The full study protocol is available at www.chip.uconn.edu/southafricaoptions.

Lay Counselor Training and Support

Lay counselors from intervention sites (N = 48) participated in an intensive 5-day training to criterion.[27,28]. Telephone consultation, direct observation, and booster trainings provided ongoing support to lay counselors, who were already employed as clinic staff at intervention and control sites. One additional study-supported lay counselor was hired at each intervention site to assist with intervention delivery; one was hired at each control site to provide resource parity.

Analytic Approach

Pretest equivalence and attrition analyses were conducted to identify covariates (any baseline variable that was non-equivalent between randomized groups or significantly associated with attrition or missing assessments). Sites were randomized to intervention or SOC control condition, and individuals within sites were assessed on 4 occasions (baseline, 6, 12 and 18 months) on the primary and additional risk-related outcomes. Intention to treat (ITT) outcome analyses used generalized linear mixed effects modeling with non-normal outcome distributions (negative binomial) and AR(1) covariance structure to account for the correlated nature of longitudinal data[48,49], negative binomial distributions of outcome measures[49,50], and clustering of over time assessments within participants within research site. Analyses used 'time' as a continuous variable, with the interaction between time and condition used to determine effect of study condition on changes in risk behavior over time. We repeated analyses using 'time' in the class statement to evaluate effects by assessment interval. We found that negative binomial[51] (versus Poisson) distribution on count-based outcomes and AR(1) as opposed to other structures were preferable. Outcomes were evaluated with SAS version 9.3[52] using PROC GLIMMIX which accounts for repeated observations of the same individual over time, nested within clinical care site, and estimates missing observations via all available pairs. Missing data were infrequent; analyses are expected to be robust and consistent with outcomes that adopt multiple imputation strategies to recover larger gaps in data coverage[53,54]. All main analyses were repeated to determine robustness of effects controlling for identified covariates and participant sex. The potential impact of baseline rates of risky sex was included in the models, as baseline risk set the intercept for each individual's slope for change over time, although we also compared study arms for potential baseline differences. Newly diagnosed STIs at 18 months relative to baseline were evaluated for study arm differences using simple chi-square tests and logistic regression.

RESULTS

Patient Characteristics

1891 HIV+ patients on ART (mean age 37.3 years; range 18–78 years) were enrolled. At baseline, approximately two-thirds had been on ART less than two years, 30% had CD4+ counts < 200 cells/uL, and approximately one in four (26.1% of men, 22.2% of women) with chart-based viral load data (N=961 of 1891 [51%]) at baseline had detectable viral load. Table 1 provides additional patient characteristic data. Intervention and SOC participants had equal clinical care visits ($\bar{x}$ = 11, SD = 4.68, range 1–24) over study participation. About 75% of routine clinical care visits included contact with a lay counselor, and in the intervention arm about 75% of visits with counselor contact included intervention sessions. 903 (93.3%) intervention arm participants were exposed to the intervention, receiving an average of five intervention counseling contacts (range 0 to 15, SD = 2.86, normally distributed).

Baseline Equivalence and Attrition

Baseline levels of primary and additional risk outcomes, CD4, and viral load did not differ by condition. Five demographic variables, identified as potential covariates based on non-

equivalence between arms at baseline, were used as covariates in intervention outcome analyses (see Table 1).

Thirteen percent (246/1891) of participants discontinued participation before the 18-month assessment. This was evenly distributed between intervention (13.0%) and SOC (13.0%) arms and unrelated to covariates identified in pre-test equivalence analyses or to categorical baseline risk variables. Sex was related to attrition; stratified by study arm, men were lost to follow-up more than women in the SOC condition (17% of men, 10% of women, p = 0.001), with a similar trend in the intervention condition (15% of men, 11% of women, p = 0.06), not an uncommon finding in studies involving HIV care in South Africa[55–58]. Men and women did not differ in inclusion in the ITT analysis (93% of men and 95% of women had sufficient data for inclusion), but we nonetheless considered sex in the covariate-controlled intervention effects analyses. Missing any risk variable assessment at any point was experienced by 316 (16.7%) participants but was unrelated to condition ($X^2 = 0.09$, p = 0.78) or sex ($X^2 = 0.20$, p= 0.65), and differential measurement attrition by study arm did not occur. Study withdrawals were not related to study arm; there were no adverse events due to intervention exposure.

Analyses of HIV Risk Behavior Outcomes

ITT analyses indicate that, compared to SOC participants, intervention participants showed significantly greater reductions in HIV risk behavior on the primary outcome variables. Over the past four weeks, intervention participants indicated significantly greater reductions in number of sex events (penile-vaginal or penile-anal) without a condom with any partner regardless of serostatus, and in number of sex events without a condom with partners perceived to be HIV-negative or -status unknown (Table 2; Figures 2 and 3).

Reported number of sex events without a condom with partners regardless of perceived serostatus during the past 4 weeks decreased over time for each group (time effect −0.46, p < .0001 for intervention;- 0.22, p <0.0001 for SOC). However, membership in the intervention condition was associated with greater risk reduction compared to SOC (interaction effect −0.22, p < .002). Study arms significantly differed in favor of the intervention condition at 6, 12 and 18 month assessments for number of events without a condom during the past four weeks with partners regardless of serostatus (see Figure 2). Similar results were found for number of sexual events without a condom during the past four weeks with partners perceived to be HIV-negative or -status unknown. Events without a condom involving these partners decreased over time for intervention and control participants (time effect −0.72, p <0.0001 in the intervention condition; −0.31, p < 0.0001 in the control condition), with the intervention condition associated with greater reduction in sex without a condom (interaction effect −0.41, p < 0.0001). The arms significantly differed in number of sexual events without a condom with HIV-negative and -status unknown partners at 12 and 18-month assessment intervals (see Figure 3).

Repeating analyses controlling for covariates and sex produced similar results. Analysis of the additional outcome data (interviewer administered measures of number of unprotected sexual acts during the past 4 weeks, consistency of condom use during the past 4 weeks and 3 months, and condom nonuse during the past 6 months) produced similar results with

intervention participants reporting significantly greater reductions in all additional measures of risk behavior over various time frames, compared to control participants (data not shown).

STI Findings

STI data were available for 1873 (99%) participants at baseline and 1571 (83%) at 18 months. Missing STI data at 18 months was marginally associated with study arm (15.3% of intervention vs. 18.6% of SOC participants were missing STI data at 18 months; $X^2 = 3.82_{(1,1891)}$, $p = 0.06$). Excluding 221 participants with a confirmed STI at baseline (111 intervention, 110 control), incident STIs were evaluated for those without STI at baseline who had one at month 18. 53 (7.4% of valid cases) intervention and 44 (6.8% of valid cases) control participants had new STIs at month 18 ($X^2_{(N=1366)} = .17$, ns). Additionally, new STIs did not differ by study arm considered within sex or by specific STI. Results were also unchanged when examining percent of participants with any STI at each time point, regardless of baseline STI status.

DISCUSSION

The findings support the efficacy of our intervention for reduction of HIV risk among HIV-infected South Africans on ART. Intervention compared to SOC participants reported consistent, statistically significant, meaningful reductions in each primary and in each additional risk behavior endpoint. Findings indicated greater intervention than SOC reductions in unprotected sex with all partners and with partners perceived to be HIV-negative or -status unknown. Similar reductions in risk were observed on all additional outcome measures including unprotected sex overall and with HIV-negative or status unknown partners, across assessment intervals from four weeks to six months, as assessed by interviewer and ACASI methodologies. These intervention effects were obtained controlling for site-level differences, which, when significant, were generally small, and few in number, and occurred despite matching sites on key variables, and when controlling for covariates and sex of participant. The intervention was delivered during routine clinical care visits, on an ongoing basis, by trained lay counselors, nearly all already employed at clinical care sites. This approach provides effective and continuing intervention exposure linking HIV treatment with HIV prevention while deploying existing resources effectively.

Results demonstrated a substantial decline in HIV risk behavior and persistence of reduced risk behavior supported by the continuing presence of the intervention. With over-sampling of sexually risky individuals, participants reported roughly two unprotected sexual events with any partner, and approximately one with an HIV- or -status unknown partner during the past four weeks, at study baseline. At 18 months, intervention participants engaged in roughly one-quarter as much risky behavior with any partner, and one-seventh as much risky behavior with partners perceived to be HIV- or -status unknown, compared to their baseline risk, and engaged in significantly less risk than SOC participants at almost every post-baseline assessment. While the current intervention was designed to be an ongoing component of routine clinical care and thus a final post-intervention follow-up period was

not part of the study design, results showed sustained reductions in risk behavior in the presence of the intervention, as intended.

Our intervention is highly compatible with an integrated behavioral and biomedical approach to HIV prevention incorporating ART treatment and adherence to reduce viral load[59] and HIV risk reduction to prevent forward transmission from PLWH who are not virally suppressed— 25% of our sample. As such, our intervention represents an important addition to the integrated behavioral and biomedical HIV prevention armamentarium. It has considerable promise for widespread and sustainable dissemination at low cost with existing clinic personnel in low resource settings. The major costs of implementation as a standard approach to integrated behavioral and biomedical HIV risk reduction would involve training lay counselors already on staff in the intervention protocol and training an existing site mentor to provide ongoing intervention fidelity support.

While this research has several strengths, limitations are present. Although the intervention achieved significantly greater risk reduction than the SOC at nearly all assessment points, the SOC also exhibited a significant, although significantly less robust, reduction in risk. Reduction of HIV risk behavior in control conditions of intervention research is commonly observed[60–63] and may be a result of research-related attention and monitoring of sexual behavior. A second, important limitation is that we did not observe significant intervention impact on the STI outcome. This would have been a desirable complement to our self-reported outcomes that focus directly on unprotected sexual events, but which are nonetheless subject to potential reporting bias. Complexities in collection and interpretation of STI data as proxies for sexual risk behavior include the inability to account for individuals who acquired symptomatic STIs and were successfully treated between STI assessments, and individuals assessed with an STI and referred to treatment, who did not successfully complete treatment or clear the infection. Failure to observe intervention impact on STI endpoints is present in a number of published HIV prevention behavioral intervention trials[63,64]. With the current intervention effects replicating on diverse measures of risk behavior (ACASI, interview, asked as count data, as estimates of frequency of condom use, and for varying time intervals), confidence in the integrity and accuracy of the behavioral risk reduction findings may be increased. Finally, although retention was high, among those who left the study early, men were overrepresented across study arms. The percent loss was low in each arm, however, and intervention results were maintained when controlling for sex, suggesting that intervention effects should be generalizable to men and women living with HIV and treated with ART in the South African clinical care setting.

CONCLUSION

Our intervention provides effective, efficient, continuing support for HIV risk reduction among HIV-infected South Africans on ART. It is compatible with an integrated behavioral and biomedical approach to stemming HIV and holds promise for sustainable and widespread dissemination efforts linking treatment and prevention to curtail the South African epidemic. Our intervention, integrated within the clinical care setting and utilizing existing staff, represents an empirically-supported strategy to leverage existing resources

and structures to promote HIV risk reduction among HIV-infected individuals on ART in generalized epidemic, resource-limited, sub-Saharan settings.

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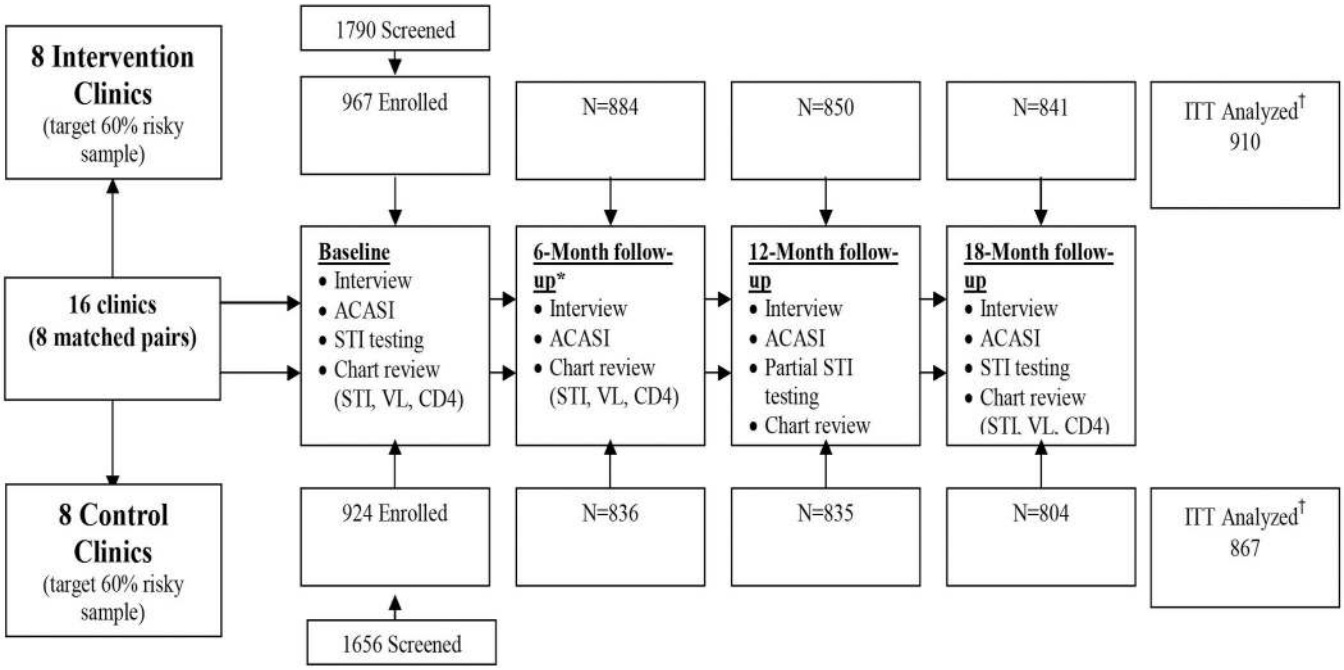

Figure 1. Study design, recruitment and assessment flow Intervention and Standard of Care Arms

†GEE analyses required two of more assessment periods with a valid score on the primary ACASI collected risk behavior variable to be included in the ITT. 94% of randomized participants met this criterion in the intervention arm and in the control arm.

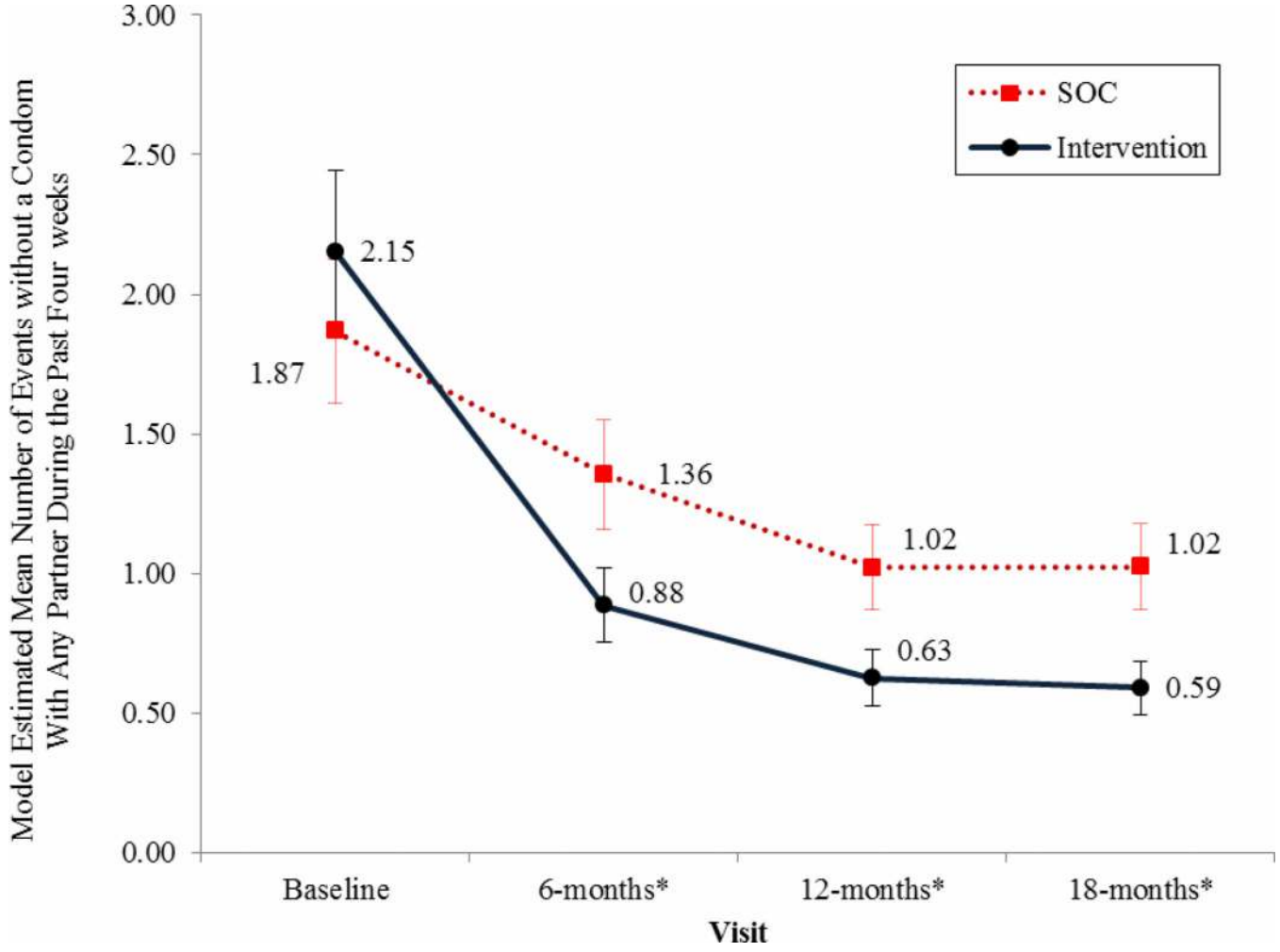

Figure 2. Model Estimated Mean Number of Events without a condom with any Partner During the Past Four weeks

Results indicate a statistically significant decrease favoring the intervention arm at each assessment point with a 72% total reduction in events without a condom from baseline by 18-months in the intervention group versus a 45% reduction in the control arm.

Error bars represent +/− 1 standard error with non-overlap in errors between group estimates reflecting significant group differences, also designated with * $p < 0.05$.

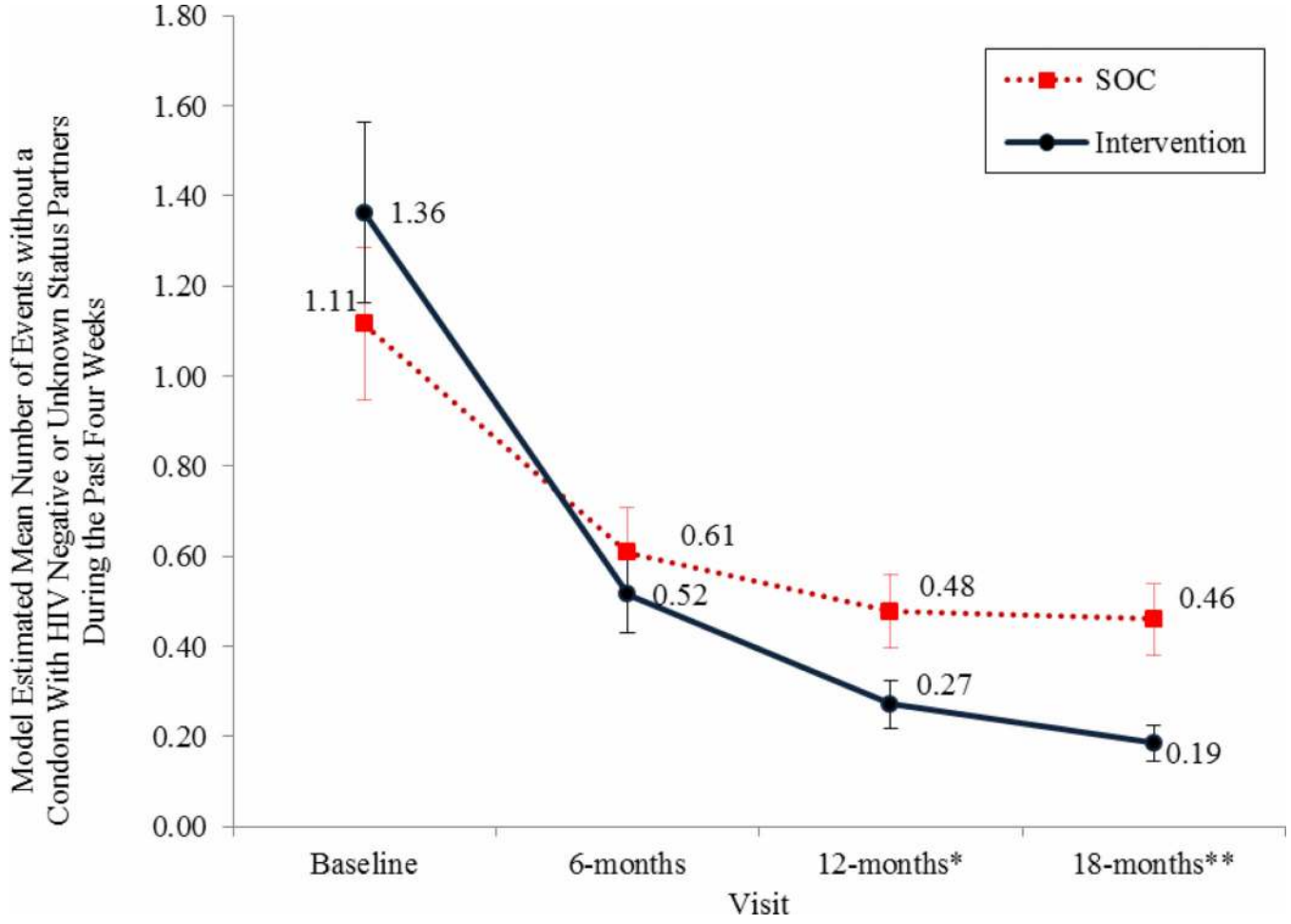

Figure 3. Model Estimated Mean Number of Events without a Condom with Partners Perceived to be HIV-negative or HIV-status unknown During the Past Four weeks

Results indicate a statistically significant decrease favoring the intervention group with an 86% total reduction in events without a condom from baseline by 18-months in the intervention group versus a 59% reduction in the control arm.

Error bars represent +/− 1 standard error with non-overlap in errors between group estimates reflecting significant group differences, also designated with * $p < 0.05$ and ** $p < 0.01$ on over time axis.

Table 1

Characteristics of Study Participants.

Characteristics	SOC* n (%) (n = 924)	Intervention n (%) (n = 967)	*P value*
Female	514 (55.6%)	537 (55.5%)	0.967
Male	410 (44.4%)	430 (44.5%)	0.967
Age (M, SD)	37.3 (9.0)	37.3 (9.0)	0.828
Race/ethnicity			0.053
Black-Zulu	882 (95.6%)	935 (97.3%)	
Black-Xhosa	13 (1.4%)	13 (1.4%)	
Black-Another race	23 (2.5%)	10 (1.0%)	
Indian	2 (0.2%)	0 (0.0%)	
Coloured	1 (0.1%)	3 (0.3%)	
Other	2 (0.2%)	0 (0.0%)	
Education			0.646
No schooling	134 (14.5%)	133 (13.8%)	
Class1/GR1 - STD7/GR9	405 (43.9%)	440 (45.8%)	
STD8/GR10 - STD10/Matric/N3/GR12	373 (40.4%)	381 (39.6%)	
Post-secondary	11 (1.2%)	7 (0.7%)	
Employment and Income			
Currently unemployed	657 (71.2%)	698 (72.2%)	0.629
Household income <R1500/Month (~US $200)	394 (70.7%)	538 (72.6%)	0.354
Relationship and Family			
Married/living with a partner	213 (23.1%)	203 (21.1%)	0.279
Cohabitating with sex partner	475 (51.4%)	449 (46.4%)	0.031
Have one or more children	809 (88.4%)	861 (89.4%)	0.493
Currently trying to have a baby	227 (24.6%)	272 (28.1%)	0.086
Housing			
Housing location = Rural	617 (66.9%)	653 (67.5%)	0.778
Dwelling Type = Informal	509 (55.1%)	532 (55.1%)	0.974
Lives in City or Township	149 (16.1%)	204 (21.1%)	0.006
HIV Diagnosis and Treatment at Study Baseline (Clinical chart extraction)			
HIV positive for 2 or more years	415 (57.6%)	372 (56.8%)	0.752
On ARTs for 2 or more years	304 (35.9%)	277 (33.2%)	0.241
CD4 Count <200	233 (29.9%)	230 (29.7%)	0.920
HIV viral load <=50 copies/mL= Undetectable (±90 days from Baseline†)	367 (78.3%)	364 (74.0%)	0.121
HIV viral load Mdn, IQR copies/mL among those with detectable viral load	[975, 175: 8800]	[545, 134: 3050]	0.087
Meets with a counselor at clinic at least every 3 months	774 (83.8%)	770 (79.6%)	0.020
Self-Reported Physical and Mental Health			
FAHI - Physical Health (possible range=0–40) (M, SD)	28.2 (8.0)	26.9 (8.2)	0.001
Depressed (Modified CESD using 15 as cutoff)	197 (21.3%)	239 (24.7%)	0.080
Reported drinking alcohol weekly or more frequently	48 (5.2%)	16 (1.7%)	0.0001

*Standard-of-care

Percentages are based on the number of participants who indicated a specific response divided by the number of participants who responded to the item in question.

Significant differences presented as adjusted scores using mean substitution for missing values to allow for use of variable in main analyses (2 missing values for living in city or township; 3 missing values for cohabitation; 3 missing values for seeing counselor at least every 3 months; 16 missing values for drinking weekly; and 1 missing value for depression scores). Missingness was unrelated to condition.

Abbreviations: ART - Antiretroviral Medication Therapy; CESD - Centers of Epidemiological Studies- Depression scale; FAHI - Functional Assessment of HIV Infection; GR - Grade level; IQR - Interquartile Range; M - Mean; Mdn - Median; N - National Qualification Framework; n - Number of participants; R - South African Rand; SD - Standard Deviation; STD - Standard

Table 2

ITT generalized linear mixed effects modeling with non-normal outcome distributions (negative binomial) and AR(1) covariance structure comparing intervention to control.

Variable	Estimate	Standard Error	df	t	p
Number of events without condom with any partner					
Intercept	0.6239	0.1891	6	3.30	0.0164
Condition (Intervention)	0.08902	0.2646	6	0.34	0.7480
Time effect in Intervention Arm	−0.4462	0.05162	6628	−8.64	<.0001
Time effect in Control Arm[a]	−0.2210	0.05098	6628	−4.33	<.0001
Time by condition (Intervention)	−0.2241	0.07351	6628	−3.05	0.0023
Number of events without condom with partners perceived to be HIV negative or HIV status unknown partners					
Intercept	0.01043	0.1353	6	0.08	0.9411
Condition (Intervention)	0.2293	0.1895	6	1.21	0.2717
Time effect in Intervention Arm	−0.7212	0.05328	6628	−13.54	<.0001
Time effect in Control Arm[a]	−0.3124	0.04604	6628	−6.79	<.0001
Time by condition (Intervention)	−0.4088	0.07042	6628	−5.81	<.0001

[a]Derived by model where intervention arm served as referent group. Intervention condition=1; Control condition=0.