

## **Behavior Change Interventions to Prevent HIV among Women Living in Low and Middle Income Countries**

**3ie Synthetic Reviews – SR008**  
**Draft Protocol**  
**November 2009**

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**Funding:** 3IE

**NOTE: THIS IS A DRAFT THAT WAS SUBMITTED BUT NOT YET APPROVED  
BY THE CAMPBELL COLLABORATION SOCIAL WELFARE GROUP.**

## 1. Background

### ***Description of the Condition***

Globally, women and girls are exceptionally vulnerable to HIV infection. Although women represent about half of all people living with HIV, in Sub-Saharan Africa where the pandemic is concentrated, women comprise 59 percent of people living with HIV infection (UNAIDS, 2008). Young women become susceptible to HIV at an early age — in some areas the prevalence of infection among women between 15-24 years is more than twice that of young men (Pettifor, Rees, et al., 2005; UNAIDS, 2008). Women living in lower income countries are particularly at risk, as extreme poverty and other structural factors such as gender inequities, lack of education, and violence reduce their ability to control health outcomes or access HIV-related information and services (Krishnan, et al., 2008).

HIV prevention efforts in women have been hampered by the generally disappointing results of biomedical prevention trials. Candidate female-controlled biomedical prevention strategies, such as cervical barriers and microbicides, have not yet shown efficacy in randomized trials (Halpern, et al., 2008; Padian, et al., 2007; Peterson, et al., 2007; Skoler-Karppoff, et al., 2008). Thus, prevention focuses mainly on male-controlled prevention methods such as male circumcision and condoms. Male circumcision, although highly effective at preventing female-to-male sexual transmission, has yet to be shown to directly reduce women's risk of infection (although reductions in HIV prevalence will indirectly benefit women) (Turner, et al., 2007; M. Wawer, et al., 2008). Male and female condoms are effective at preventing sexual transmission of HIV but both require male partner knowledge and consent (French, et al., 2003; National Institute of Allergy and Infectious Diseases, 2000). Finally, although improved diagnosis and treatment of sexually transmitted infections (STI) may be an important strategy to reduce HIV transmission and deleterious effects of other STIs (Grosskurth, et al., 1995), women in the poorest parts of the world may not have access to or utilize sexual and reproductive health services (Kiwanuka, et al., 2008). Thus, in the absence of an effective vaccine or alternative female-controlled biomedical prevention method, HIV prevention efforts for women currently focus on the mainstay of prevention strategies – behavior change (Kalichman, 2008).

### ***Description of the Intervention***

Behavioral strategies to prevent the sexual transmission of HIV include programs that aim to delay age of sexual debut, decrease the number of sexual partners and concurrent partnerships, increase the proportion of protected sexual acts, increase acceptance of voluntary counseling and testing (VCT), and improve adherence to successful biomedical prevention strategies, such as condom use (Coates, Richter, & Caceres, 2008). These interventions can focus on the individual, peer, couple, group, family, institution, or the community. In addition, they vary widely in duration, intensity, and delivery. In order to produce measureable population-level changes in HIV infection, behavioral interventions need to produce change in enough people for a sufficient time to impact transmission dynamics (Coates, et al., 2008). Behavioral interventions targeting men who have sex with men (Herbst, et al., 2005), sexually transmitted disease clinic patients (Crepaz, et al., 2007), heterosexual African Americans (Darbes, Crepaz, Lyles, Kennedy, & Rutherford, 2008), sexually experienced adolescents in the United States (Mullen, Ramirez, Strouse, Hedges, & Sogolow, 2002), and people living

with HIV (Crepaz, et al., 2006) are effective in reducing self-reported sexual risk behaviors. In addition, meta-analytic reviews suggest that interventions that are targeted to specific race or gender groups, include skills training, and that are based on behavioral theory demonstrate efficacy, again, when measured by self-report (for review of meta-analyses, see Noar 2008) (Noar, 2008).

### ***Why Is It Important To Do This Review***

Despite numerous behavior change interventions that have been evaluated since the beginning of the HIV epidemic more than 25 years ago, there is a notable paucity of data on the direct effect of such interventions on HIV incidence. Examining HIV infection as the outcome in efficacy trials is critical for several reasons. Most obviously, because the ultimate objective of such interventions is to prevent new HIV infections, evaluating the effect on HIV incidence is the only way to measure program impact directly. Furthermore, reported sexual behaviors can be subject to reporting and recall bias and may be inconsistent with what is known about population-level HIV infection prevalence (Lagarde, et al., 2001; Plummer, et al., 2004). Although greater resources are often needed to conduct evaluation trials with HIV infection as the endpoint, they are generally acceptable to study participants and have been utilized in several large randomized trials of behavioral interventions (Cowan, et al., 2002; Kamali, et al., 2003; Kamb, et al., 1998; Koblin, Chesney, & Coates, 2004).

## **2. Objectives**

To date, no reviews have been conducted that summarize the effect of behavioral interventions for HIV prevention in women and girls in the developing world. Recently, the results of several large randomized trials of the effect of behavioral interventions on HIV incidence have been published, the data from which now permit a more focused review of these trials for HIV prevention in women (Gregson, et al., 2007; Jewkes, et al., 2008; Pronyk, et al., 2006). Given the increased risk of HIV incidence among women and girls (Krishnan, et al., 2008; Pettifor, Rees, et al., 2005; UNAIDS, 2008) our objective is to systematically review and summarize behavioral change interventions to prevent the sexual transmission of HIV among women and girls living in low- and middle-income countries.

## **3. Methods**

### **3.1 Criteria for considering studies for this review**

#### ***Types of Studies***

Eligible studies are those:

- 1) Published in 1990 or after;
- 2) Using randomized controlled designs (individual or community) or quasi-experimental prospective designs with a control group;
- 3) Evaluating behavioral interventions focusing on sexual transmission of HIV;
- 4) Conducted in low- and middle-income countries as defined by the World Bank;

- 5) Conducted either entirely in women or reporting gender-stratified effect estimates (either in the manuscript or shared by study authors); and
- 6) Reporting HIV incidence or cumulative risk in the intervention and comparison arms or an overall relative measure of effect (e.g., incidence rate ratios (IRR), risk ratios (RR)). Although effect estimates adjusted for confounders are preferred, studies with only unadjusted ("crude") estimates are eligible for inclusion.

Trials will be excluded if they are:

- 1) Conducted in men;
- 2) Conducted in high-income countries;
- 3) Pertain to intravenous transmission;
- 4) Pertain to prevention of mother-to-child transmission; or
- 5) Are inappropriate article types such as a reviews or commentaries.

There will be no language restrictions to the search. For example, three eligible studies are:

- 1) Jewkes R, Nduna M, Levin J, et al. Impact of stepping stones on incidence of HIV and HSV-2 and sexual behaviour in rural South Africa: cluster randomised controlled trial. *Bmj*. 2008;337:a506. This study evaluated the effect of the Stepping Stones participatory learning approach on HIV prevention in South Africa. There was no effect of the program on HIV incidence.
- 2) Pronyk PM, Hargreaves JR, Kim JC, et al. Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomised trial. *Lancet*. Dec 2 2006;368(9551):1973-1983. This study, known as "IMAGE", evaluated the effect of a microfinance program combined with the Sisters for Life (SFL) gender and HIV training program on HIV incidence. The authors found no effect of the program on reducing HIV incidence in program communities.
- 3) Patterson TL, Mausbach B, Lozada R, et al. Efficacy of a brief behavioral intervention to promote condom use among female sex workers in Tijuana and Ciudad Juarez, Mexico. *Am J Public Health*. Nov 2008;98(11):2051-2057. This study evaluated the effect of *Mujer Segura*, an individual counseling program for sex workers in Mexico to improve condom use. The authors found no effect on HIV incidence.

Although qualitative research is critically important in the development, monitoring, and evaluation of behavioral interventions to prevent HIV infection, we will not include qualitative studies in our review.

### **Types of Participants**

Studies must focus on women or girls living in low- and middle-income countries as defined by the World Bank.

### **Types of Interventions**

Studies must evaluate behavioral interventions to prevent the sexual transmission of HIV. Behavioral strategies to prevent the sexual transmission of HIV include programs

that aim to delay age of sexual debut, decrease the number of sexual partners and concurrent partnerships, increase the proportion of protected sexual acts, increase acceptance of voluntary counseling and testing (VCT), and improve adherence to successful biomedical prevention strategies, such as condom use (Coates, Richter, & Caceres, 2008). These interventions can focus on the individual, peer, couple, group, family, institution, or the community.

### ***Types of Outcome Measures***

Primary outcome. Eligible studies must report HIV incidence or cumulative risk in the intervention and comparison arms or an overall relative measure of effect (e.g., incidence rate ratios (IRR), risk ratios (RR)). Although effect estimates adjusted for confounders are preferred, studies with only unadjusted (“crude”) estimates are eligible for inclusion.

Secondary outcomes. To examine the effect of interventions across the causal chain, we also will examine the effect of the interventions on incident STIs as well as the effect of the interventions on HIV-related risk behavior such as number of partners and condom use.

## **3.2 Search Methods for Identification of Studies**

### ***Electronic Searches***

The following electronic databases will be searched for published data:

PubMed/MEDLINE

PsycInfo

The Cochrane Library including the Cochrane Central Register of Controlled Trials (CENTRAL)

Web of Science

Sociological Abstracts

National Library of Medicine Gateway

African Index Medicus

Regional Index for Latin America and the Caribbean (Virtual Health Library)

IndMed (the regional database for Indian biomedical journals)

### ***Reference Lists***

We will conduct a cited reference search with key articles and review scanned reference lists of eligible articles and reviews.

### ***Hand-searching journals***

We will not hand-search journals for this review.

### ***Grey Literature***

Unpublished data will be located by searching the following sources:

Current Controlled Trials Register

The International Clinical Trials Registry Platform Search Portal

clinicaltrials.gov

Computer Retrieval of Information on Scientific Projects (CRISP)

Conference on Retroviruses and Opportunistic Infections Abstracts

International Society for Sexually Transmitted Disease Research Annual Meetings

International AIDS Society Annual Meetings

We will consult with HIV prevention experts to ensure that we have not missed any relevant articles. We will also contact study authors for additional information about potentially eligible trials (including effect estimates among women) (Gregson, et al., 2007; Kamali, et al., 2003).

We will develop a customized search strategy for each database relying on the database's controlled vocabulary or index (e.g., medical subject headings (MeSH)) or free text terms. In most cases, search strategies will combine terms for (1) HIV infection, (2) behavior or counseling, (3) prevention, and (4) study design restrictions (randomized controlled designs or quasi-experimental). In PubMed/MEDLINE, we will search for clinical trials using an adapted version of Cochrane's "Highly Sensitive Search Strategy" for identifying randomized controlled trials (The Cochrane Collaboration, 2008). A detailed description of the search strategy, including keywords, is presented in the **Appendix**.

Relevance decisions will be made on an iterative basis. For example, titles will first be sorted to eliminate obviously ineligible studies, such as those conducted entirely in men. A second filtering process will involve reviewing abstracts of the remaining reports, with special attention placed on identifying the design of the study, country(s) of implementation, and biological outcomes. Abstracts will be specifically searched for mention of a behavioral intervention tested against a control intervention with biological outcomes. Report of any sexually transmitted disease outcome in the abstract such as incident gonorrhea or Chlamydia infections will automatically warrant a full length review of the article to determine if HIV testing was conducted. We will conduct a detailed manual review of full length articles to determine eligibility. Repeated cross-sectional studies (Pettifor, Kleinschmidt, et al., 2005) or studies only reporting prevalence are not considered eligible (The Voluntary HIV-1 Counseling and Testing Efficacy Study Group, 2000).

### 3.3 Data Collection and Analysis

#### ***Selection of Studies***

This systematic review will include studies that report the effect of behavioral change interventions to prevent the sexual transmission of HIV among women and girls living in low- and middle-income countries. Only randomized controlled trials (individual or community) or quasi-experimental designs are eligible for inclusion. Studies that use random allocation of treatment minimize selection bias and reduce confounding by creating a comparison group similar to the treatment group except for the treatment of interest (the “counterfactual” group). In the case of HIV prevention trials, some trials randomly allocate individuals (Patterson, et al., 2006) and others randomly allocate communities or other clusters (Pronyk, et al., 2006). Although both studies measure HIV incidence as an outcome, cluster randomized trials are often measuring HIV incidence in the community at large, rather than among participants in a particular program.

Quasi-experimental designs are also eligible for inclusion. These study designs (such as difference-in-difference, regression discontinuity, or propensity score matching) attempt to simulate a counterfactual group through analysis techniques. Prospective cohort designs with a comparison group are eligible, although the treatment is not randomly allocated. Given the potential for variability in trial design, we will pay special attention to methodological quality in the data abstraction and analysis phase to ensure comparability of results across studies.

The measurement of HIV incidence is an inclusion criterion. Eligible reports must report HIV incidence or cumulative risk in the intervention and comparison arms or an overall relative measure of effect (e.g., incidence rate ratios (IRR), risk ratios (RR)). Although effect estimates adjusted for confounders are preferred, studies with only unadjusted (“crude”) estimates are eligible for inclusion given the small number of expected studies.

Sexual behavior (e.g., condom use) is an important outcome on the causal pathway and we will abstract all data on behavior when it is available. It is expected that the types and definitions of behavior change will vary widely from report to report and this will limit comparison across studies. For example, some studies measure condom use at last sex, whereas others measure condom use over a time period with a Likert scale (“always”, “sometimes”, “never”). For this reason, it is unlikely that we will be able to compare behavioral change outcomes across studies in a quantitative fashion.

Similarly, sexually transmitted infections (STI) *may* be on the causal pathway between behavior change and HIV acquisition (although rigorous randomized controlled trials evaluating the effect of STI treatment for HIV prevention have had mixed results with the majority showing no effect on HIV incidence (Celum, et al., 2008; Celum, et al., 2009; Ghys, et al., 2001; Gregson, et al., 2007; Grosskurth, et al., 1995; Kamali, et al., 2003; Kaul, et al., 2004; Watson-Jones, et al., 2008; M. J. Wawer, et al., 1999)). Furthermore, modeling studies have suggested that behavioral strategies may have different impacts on HIV and STIs – reducing the number of partners may be more important for highly-infectious STIs such as gonorrhea, whereas condom use may be more effective than reducing the number of partners at reducing HIV transmission risk (Pinkerton, Layde, DiFranceisco, & Chesson, 2003). Nevertheless, STI outcomes are often measured in addition to HIV outcomes, and for completeness, we will abstract STI outcomes reported in any eligible report.

For both secondary outcomes (behavior change and STIs), it is important to note that our review will not include all studies of behavioral interventions for women and girls in lower income countries with these two outcomes – only those that measured the effect on HIV incidence will be included. In other words, our review will have a biased sample of studies that measure the effect of behavioral interventions on behavior and (non-HIV) STIs. As we are selecting on the measurement of HIV incidence, attempting to estimate a single effect estimate on behavior change and STIs would be inappropriate. Thus, quantitative summary measure of effects will only be considered for HIV outcomes (see **Statistical Procedures and Conventions**).

### **Data Abstraction and Management**

Data Abstraction. For each eligible article or abstract, a single investigator (S.M.) will abstract the most adjusted measure of effect on the primary outcome of HIV incidence (e.g., IRR, RR). In cases where only the incidence rates in each study arm are presented, we will compute IRRs and 95% confidence intervals using standard methods (K. Rothman, 2002). Although the incidence rate ratio is the preferred measure of effect; we are aware of at least one study which reports a RR (Doyle, et al., 2009; Pronyk, et al., 2006), which we assume will approximate the IRR given the rarity of the outcome and that the “exposure” to the intervention should only negligibly affect the person-time at risk (K. J. Rothman & Greenland, 1998). Alternatively, if the exposure did affect the average time at risk, we would expect the RR to be closer to the null than the IRR in which case the RR would be more conservative (K. J. Rothman & Greenland, 1998). Studies which only report HIV prevalence will not be included. Of course, the final determination of which measures of effect to include will be made based on the studies determined eligible for the review.

We also will examine the effect of the interventions on incident STIs as secondary outcomes as well as the effect of the interventions on HIV-related risk behavior such as number of partners and condom use. In cases where multiple behavioral measurements were assessed in a single study over time, we will examine the effect with the longest follow-up period. As mentioned above, although we consider behavior change and STIs to be secondary outcomes, we expect wide variability in terms of definitions, measurement time periods, and which studies report this information (see **Criteria for Determination of Independent Findings**, above).

We will also abstract data including trial year, location, and population as well as details about the intervention (e.g., type, length, audience, behavioral theory (if specified), and nature of the control group). A list of information to be abstracted is provided below:

<ul style="list-style-type: none"> <li>• Author</li> <li>• Publication year</li> <li>• Study years</li> <li>• Study type (e.g., individual RCT)</li> <li>• Study design</li> <li>• Study population</li> <li>• Population age</li> <li>• Location</li> <li>• Follow-up period</li> <li>• Number of participants</li> <li>• Number of women participants</li> <li>• Percent of women participants</li> <li>• Intervention details, including unit of delivery (e.g. couples, families)</li> <li>• Intervention duration</li> <li>• Behavioral theories guiding work</li> <li>• Control group details</li> </ul>	<ul style="list-style-type: none"> <li>• Whether control group received an attenuated version of the main intervention (e.g. condom promotion)</li> <li>• Allocation method</li> <li>• Participation rate</li> <li>• Retention rate</li> <li>• Whether study was powered for HIV incidence</li> <li>• HIV incidence in all study arms</li> <li>• Measure of effect</li> <li>• 95% confidence intervals</li> <li>• Whether analysis was multivariable</li> <li>• Whether analysis was intent-to-treat</li> <li>• Effect on behavior (abstracted information varies by study)</li> <li>• Effect on STIs (abstracted information varies by study)</li> </ul>
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### 3.4 Assessment of Risk of Bias in Included Studies

We will assess trial quality using a “component approach” after completion of the literature search; to prevent exclusion of potentially valid information study quality will not be part of the inclusion criteria (Egger, Smith, & Altman, 2001). We will assess dimensions of internal validity such as allocation method, type of control group, participation rate, attrition bias, and type and appropriateness of statistical analyses (e.g., intent to treat). We will also consider the role of selection bias for each study.

### 3.5 Measures of Treatment Effect

The primary outcome of interest is HIV incidence which can be presented as an incidence per trials arm a risk ratio (RR), or an incidence rate ratio (IRR). In cases where only the incidence rates in each study arm are presented, we will compute IRRs and 95% confidence intervals using standard methods (K. Rothman, 2002). Although the incidence rate ratio is the preferred measure of effect; we are aware of at least one study which reports a RR (Doyle, et al., 2009; Pronyk, et al., 2006), which we assume will approximate the IRR (see above). Studies which only report HIV prevalence will not be included. Of course, the final determination of which measures of effect to include will be made based on the studies determined eligible for the review.

### 3.6 Unit of Analysis Issues

The unit of analysis may be the individual, family, community, or other cluster. We will not restrict the review to studies with a particular unit of analysis. Based on our preliminary search of the literature, we expect many trials of behavioral interventions for HIV prevention to be community randomized trials.

### 3.7 Dealing with Missing Data

Although we consider behavior change and STIs to be secondary outcomes, we expect wide variability in terms of definitions, measurement time periods, and which studies report this information. We therefore expect there to be a lot of missing data for these outcomes which will determine the level of quantitative synthesis we are able to do.

In terms of other pieces of information which we will collect (see list above), we do not expect there to be significant amounts of missing information as these are standard information to report in HIV prevention trials. If there are pieces missing, we will contact study authors to for this information as well as secondary analysis reports using the same dataset.

Our approach to handling missing data will be consistent with recommendations from Cochrane which include:

- Making explicit the assumptions of any methods used to cope with missing data: for example, that the data are assumed missing at random, or that missing values were assumed to have a particular value such as a poor outcome.
- Performing sensitivity analyses to assess how sensitive results are to reasonable changes in the assumptions that are made.
- Addressing the potential impact of missing data on the findings of the review.

### 3.8 Data Synthesis

Data will be abstracted into a Microsoft Excel file. Subsequent data analysis will be conducted in Excel and STATA software (StataCorp, College Station, TX, USA).

Based on substantive knowledge of the area, we anticipate that few studies will meet the inclusion criteria and that the study populations and interventions will be substantially variable. Studies must share a common quantitative footing for pooled measures to have meaning, so our analysis strategy will be iterative based on aspects of our findings, such as:

- The number of studies meeting the inclusion criteria,
- The types and variability of study populations (e.g., sex workers, adolescents),
- Homogeneity of follow-up periods,
- Intervention types,
- Homogeneity of study quality, and
- Study design types (e.g., individually randomized trials, longitudinal cohort studies).

As mentioned above, quantitative analysis will only be considered for the primary outcome of HIV incidence, as the review sample of reports with STI and behavioral outcomes are only a subset of the universe of studies with STI and behavioral outcomes (see **Criteria for Determination of Independent Findings**, above).

### ***Subgroup Analysis and Investigation of Heterogeneity***

If quantitative analysis is appropriate (based on qualitative assessment, substantive knowledge, statistical tests for effect homogeneity with Cochran's Q test statistic, and the potential for publication bias), we will present incidence rate ratios of HIV infection in a forest plot, along with the summary pooled incidence rate ratio. Other measures of effect (for example, the relative risk) will be considered based on information available in the reports. We will use random-effects models to weigh intervention effects across studies or within each study design or analysis category, using stratified homogeneity tests to examine the consistency of estimates within categories. Second, we will conduct a series of univariable and multivariable random-effects meta-regression analyses, each with the HIV incidence rate ratio as the dependent variable and study design or analysis feature(s) as the independent variable(s).

If we choose not to proceed with a quantitative synthesis of results, we will adopt a systematic approach to presentation of the results, discussing both significant and non-significant results and presenting the same information from each study. We will present descriptive information about each unique intervention as well as a forest plot of measures of effect (without a pooled estimate).

In either case, our final report will include a detailed narrative report about each trial and intervention, its effect on HIV infection, trial quality, and effect on secondary outcomes.

### **3.9 Plans for Updating the Review**

The review will be updated after initial comments from internal and external review (December 2009 – January 2010). We have also established automatic updates for the review in PubMed/MEDLINE, so any new articles generated from our search string will be automatically emailed to us weekly.

## **4. Timeframe**

Searches for published and unpublished studies	2/2009 — 4/2009
Relevance assessments	3/2009 — 5/2009
Pilot testing of study codes and data collection	4/2009
Extraction of data from research reports	4/2009 — 6/2009
Presentation of initial findings at Impact Evaluation meeting in Cairo	3/2009 — 4/2009
Statistical Analysis	6/2009 — 7/2009
Preparation of report	6/2009—11/2009
Report revisions	11/2009—2/2010

## 5. Acknowledgments

We would like to thank 3ie for funding this review.

## 6. The Review Team and Contributions of Authors

**Dr. Nancy Padian** is an internationally recognized expert in the sexual transmission of HIV and other STIs. For the last 20 years, she has developed and directed a range of research and intervention projects on STIs, HIV, and contraception in vulnerable, hard-to-reach populations in the U.S. and internationally as Executive Director of the Women's Global Health Imperative at the University of California, San Francisco (UCSF) and subsequently at RTI International. In 1994, she co-founded the University of Zimbabwe-UCSF Collaborative Research Programme in Women's Health in Zimbabwe. In 1996 Dr. Padian began an ongoing research program on adolescent reproductive health in the Mission District in San Francisco. She is an elected member of the Institute of Medicine, American Epidemiology Society, and the International Society for Sexually Transmitted Disease Research. She frequently consults for UNAIDS, WHO, and the World Bank on programs related to care, treatment, and prevention of HIV.

**Dr. Rugare Abigail Kangwende** is an infectious disease physician in the Department of Health Sciences at Africa University in Mutare, Zimbabwe. Dr. Kangwende is a public health specialist and coordinator of Africa University's insect blanket initiative. Dr. Kangwende has also previously served as a co-investigator on a large HIV vaccine trial in Zimbabwe.

**Dr. Sandra McCoy** is a postdoctoral epidemiologist at RTI International with expertise in the prevention of HIV and sexually transmitted diseases. Dr. McCoy has experience working with a variety of vulnerable populations, including her dissertation work which focused on HIV transmission among the rural poor in the Southeastern United States. She previously worked at the U.S. Centers for Disease Control and has recently begun consulting for UNAIDS on HIV evaluation methodology.

Dr. McCoy will lead the review phase of the project and will be responsible for overseeing the search. She will work closely with Dr. Kangwende and will divide search responsibilities for both reviewers. Dr. McCoy will make the initial relevance decisions, which will be confirmed by Dr. Padian by reviewing full text versions of the potentially eligible reports.

Drs. McCoy and Kangwende will prepare and present a preliminary presentation on the review findings at the Perspectives on Impact Evaluation Conference in April 2009. Dr. McCoy will prepare a first draft of the report, and Dr. Kangwende and Dr. Padian will assist with revisions and incorporating reviewer comments.

## 7. Statement Concerning Conflict of Interest

We have no conflicts of interest to declare.

## 8. Appendix

PubMed/MEDLINE Search Strategy. In most cases, search strategies will combine terms for (1) HIV infection, (2) behavior or counseling, (3) prevention, and (4) study design restrictions (randomized controlled designs or quasi-experimental). In PubMed/MEDLINE, we will search for clinical trials using an adapted version of Cochrane's "Highly Sensitive Search Strategy" for identifying randomized controlled trials (The Cochrane Collaboration, 2008). The search will be conducted with advice from a reference librarian at the University of California, Berkeley.

We will evaluate the following (MeSH) search terms for PubMed (in addition to other keywords identified during the search):

Adolescent

Adult

HIV Infections/prevention & control

Incidence

Unsafe Sex/prevention & control\*

Safe Sex

HIV Infections/psychology

Health education

Health Knowledge, Attitudes, Practice

HIV Infections/transmission

Risk-Taking

Sexual Behavior

Behavior Therapy/methods\*

Sexually Transmitted Diseases/prevention & control\*

Health Education/methods

Prospective Studies

We will consider the use of free text terms such as:

HIV Infections

HIV

Human Immunodeficiency Virus

AIDS

Acquired Immune Deficiency Syndrome

Behavior

Counseling

Unsafe sex

Risk behavior

Prevention and control

Prevention

Primary prevention

Cohort study

We will use the Cochrane Collaboration's Highly Sensitive Search Strategy for identifying randomized controlled trials in PubMed/MEDLINE:

1. randomized controlled trial [pt]
2. controlled clinical trial [pt]
3. randomized [tiab]
4. placebo [tiab]
5. clinical trials as topic [mesh: noexp]
6. randomly [tiab]
7. trial [ti]
8. #1 or #2 or #3 or #4 or #5 or #6 or #7
9. animals [mh] not (humans [mh] and 10. animals [mh])
11. #8 not #9

Our search strategy will likely combine MeSH and free text terms for HIV infection (for example, "HIV Infections OR HIV OR Human Immunodeficiency Virus OR AIDS or Acquired Immune Deficiency Syndrome"), behavior or counseling interventions ("Behavior OR health education OR Health knowledge, attitudes, practice OR Counseling OR unsafe sex OR risk behavior"), prevention ("Prevention and control [sh] OR prevention OR primary prevention") and study design types. We will limit the search to 1990 or afterward.

Cochrane Central Register of Controlled Trials (CENTRAL) Search Strategy. We will use a similar strategy to search CENTRAL. CENTRAL includes files that will be indexed by MeSH terms (those studies also indexed in PubMed) and studies that are only indexed by free text terms (such as those indexed in EMBASE). Since all of the studies in CENTRAL are clinical trials, we will not need to limit the search by study design.

As a starting place, we will employ the same search string as used in PubMed (for example, combining terms HIV infection, behavior or counseling interventions, and prevention). An example search strategy might be:

1. HIV Infections OR HIV OR Human Immunodeficiency Virus OR AIDS or Acquired Immune Deficiency Syndrome
2. Behavior OR health education OR Health knowledge, attitudes, practice OR Counseling OR unsafe sex OR risk behavior
3. Prevention OR primary prevention
4. #1 AND #2 AND #3

We will also evaluate other terms for inclusion in the strategy, and examine the number and quality of “hits” using individual search sequences listed above. The search strategy for other databases will be constructed in a similar way and will be based either on the database’s index system or on free text terms.

## 9. References

- Celum, C., Wald, A., Hughes, J., Sanchez, J., Reid, S., Delany-Moretlwe, S., et al. (2008). Effect of aciclovir on HIV-1 acquisition in herpes simplex virus 2 seropositive women and men who have sex with men: a randomised, double-blind, placebo-controlled trial. *Lancet*, 371(9630), 2109-2119.
- Celum, C., Wald, A., Lingappa, J., Magaret, A., Wang, R., Mugu, N., et al. (2009). *Twice-daily acyclovir to reduce HIV-1 transmission from HIV-1 / HSV-2 co-infected persons within HIV-1 serodiscordant couples: a randomized, double-blind, placebo-controlled trial* Paper presented at the 5th IAS Conference on HIV Pathogenesis, Treatment, and Prevention.
- Coates, T. J., Richter, L., & Caceres, C. (2008). Behavioural strategies to reduce HIV transmission: how to make them work better. *Lancet*, 372(9639), 669-684.
- Cowan, F. M., Langhaug, L. F., Mashungupa, G. P., Nyamurera, T., Hargrove, J., Jaffar, S., et al. (2002). School based HIV prevention in Zimbabwe: feasibility and acceptability of evaluation trials using biological outcomes. *AIDS*, 16(12), 1673-1678.
- Crepaz, N., Horn, A. K., Rama, S. M., Griffin, T., Deluca, J. B., Mullins, M. M., et al. (2007). The efficacy of behavioral interventions in reducing HIV risk sex behaviors and incident sexually transmitted disease in black and Hispanic sexually transmitted disease clinic patients in the United States: a meta-analytic review. *Sex Transm Dis*, 34(6), 319-332.
- Crepaz, N., Lyles, C. M., Wolitski, R. J., Passin, W. F., Rama, S. M., Herbst, J. H., et al. (2006). Do prevention interventions reduce HIV risk behaviours among people living with HIV? A meta-analytic review of controlled trials. *AIDS*, 20(2), 143-157.
- Darbes, L., Crepaz, N., Lyles, C., Kennedy, G., & Rutherford, G. (2008). The efficacy of behavioral interventions in reducing HIV risk behaviors and incident sexually transmitted diseases in heterosexual African Americans. *Aids*, 22(10), 1177-1194.
- Doyle, A., Ross, D. A., Maganja, K., Changalucha, J., Hayes, R., & Team., a. t. M. k. V. T. (2009). *Long-term Impact of a Behavioral Change Intervention on HIV, STI, Knowledge, Attitudes, and Reported Sexual Behaviors among Young People in Rural*

- Mwanza, Tanzania: Results of a Community Randomized Trial*. Paper presented at the 16th Conference on Retroviruses and Opportunistic Infections.
- Egger, M., Smith, G. D., & Altman, D. G. (Eds.). (2001). *Systematic Reviews in Health Care: Meta-Analysis in Context* (2nd ed.). London: BMJ Publishing Group.
- French, P. P., Latka, M., Gollub, E. L., Rogers, C., Hoover, D. R., & Stein, Z. A. (2003). Use-effectiveness of the female versus male condom in preventing sexually transmitted disease in women. *Sex Transm Dis*, 30(5), 433-439.
- Ghys, P. D., Diallo, M. O., Ettiegne-Traore, V., Satten, G. A., Anoma, C. K., Maurice, C., et al. (2001). Effect of interventions to control sexually transmitted disease on the incidence of HIV infection in female sex workers. *AIDS*, 15(11), 1421-1431.
- Gregson, S., Adamson, S., Papaya, S., Mundondo, J., Nyamukapa, C. A., Mason, P. R., et al. (2007). Impact and process evaluation of integrated community and clinic-based HIV-1 control: a cluster-randomised trial in eastern Zimbabwe. *PLoS Med*, 4(3), e102.
- Grosskurth, H., Mosha, F., Todd, J., Mwijarubi, E., Klokke, A., Senkoro, K., et al. (1995). Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet*, 346(8974), 530-536.
- Halpern, V., Ogunsoola, F., Obunge, O., Wang, C. H., Onyejebu, N., Oduyebo, O., et al. (2008). Effectiveness of cellulose sulfate vaginal gel for the prevention of HIV infection: results of a Phase III trial in Nigeria. *PLoS ONE*, 3(11), e3784.
- Herbst, J. H., Sherba, R. T., Crepaz, N., Deluca, J. B., Zohrabyan, L., Stall, R. D., et al. (2005). A meta-analytic review of HIV behavioral interventions for reducing sexual risk behavior of men who have sex with men. *J Acquir Immune Defic Syndr*, 39(2), 228-241.
- Jewkes, R., Nduna, M., Levin, J., Jama, N., Dunkle, K., Puren, A., et al. (2008). Impact of stepping stones on incidence of HIV and HSV-2 and sexual behaviour in rural South Africa: cluster randomised controlled trial. *BMJ*, 337, a506.
- Kalichman, S. C. (2008). Time to take stock in HIV/AIDS prevention. *AIDS Behav*, 12(3), 333-334.
- Kamali, A., Quigley, M., Nakiyingi, J., Kinsman, J., Kengeya-Kayondo, J., Gopal, R., et al. (2003). Syndromic management of sexually-transmitted infections and behaviour change interventions on transmission of HIV-1 in rural Uganda: a community randomised trial. *Lancet*, 361(9358), 645-652.
- Kamb, M. L., Fishbein, M., Douglas, J. M., Jr., Rhodes, F., Rogers, J., Bolan, G., et al. (1998). Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. *JAMA*, 280(13), 1161-1167.
- Kaul, R., Kimani, J., Nagelkerke, N. J., Fonck, K., Ngugi, E. N., Keli, F., et al. (2004). Monthly antibiotic chemoprophylaxis and incidence of sexually transmitted infections

- and HIV-1 infection in Kenyan sex workers: a randomized controlled trial. *JAMA*, 291(21), 2555-2562.
- Kiwanuka, S. N., Ekirapa, E. K., Peterson, S., Okui, O., Rahman, M. H., Peters, D., et al. (2008). Access to and utilisation of health services for the poor in Uganda: a systematic review of available evidence. *Trans R Soc Trop Med Hyg*, 102(11), 1067-1074.
- Koblin, B., Chesney, M., & Coates, T. (2004). Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet*, 364(9428), 41-50.
- Krishnan, S., Dunbar, M. S., Minnis, A. M., Medlin, C. A., Gerdt, C. E., & Padian, N. S. (2008). Poverty, gender inequities, and women's risk of human immunodeficiency virus/AIDS. *Ann N Y Acad Sci*, 1136, 101-110.
- Lagarde, E., Auvert, B., Chege, J., Sukwa, T., Glynn, J. R., Weiss, H. A., et al. (2001). Condom use and its association with HIV/sexually transmitted diseases in four urban communities of sub-Saharan Africa. *AIDS*, 15 Suppl 4, S71-78.
- Mullen, P. D., Ramirez, G., Strouse, D., Hedges, L. V., & Sogolow, E. (2002). Meta-analysis of the effects of behavioral HIV prevention interventions on the sexual risk behavior of sexually experienced adolescents in controlled studies in the United States (Vol. 30, pp. S94-S105).
- National Institute of Allergy and Infectious Diseases. (2000). *Workshop Summary: Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention*.
- Noar, S. M. (2008). Behavioral interventions to reduce HIV-related sexual risk behavior: Review and synthesis of meta-analytic evidence (Vol. 12, pp. 335-353).
- Padian, N. S., van der Straten, A., Ramjee, G., Chipato, T., de Bruyn, G., Blanchard, K., et al. (2007). Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *Lancet*, 370(9583), 251-261.
- Patterson, T. L., Orozovich, P., Semple, S. J., Orozco, H. S. S., Fraga, M., Amaro, H., et al. (2006). A Sexual Risk Reduction Intervention for Female Sex Workers in Mexico: Design and Baseline Characteristics. *Journal of HIV/AIDS & Social Services*, 5(2), 115-137.
- Peterson, L., Nanda, K., Opoku, B. K., Ampofo, W. K., Owusu-Amoako, M., Boakye, A. Y., et al. (2007). SAVVY (C31G) gel for prevention of HIV infection in women: a Phase 3, double-blind, randomized, placebo-controlled trial in Ghana. *PLoS ONE*, 2(12), e1312.
- Pettifor, A. E., Kleinschmidt, I., Levin, J., Rees, H. V., MacPhail, C., Madikizela-Hlongwa, L., et al. (2005). A community-based study to examine the effect of a youth HIV prevention intervention on young people aged 15-24 in South Africa: results of the baseline survey (Vol. 10, pp. 971-980).

- Pettifor, A. E., Rees, H. V., Kleinschmidt, I., Steffenson, A. E., MacPhail, C., Hlongwa-Madikizela, L., et al. (2005). Young people's sexual health in South Africa: HIV prevalence and sexual behaviors from a nationally representative household survey. *AIDS*, 19(14), 1525-1534.
- Pinkerton, S. D., Layde, P. M., DiFranceisco, W., & Chesson, H. W. (2003). All STDs are not created equal: an analysis of the differential effects of sexual behaviour changes on different STDs. *Int J STD AIDS*, 14(5), 320-328.
- Plummer, M. L., Ross, D. A., Wight, D., Chagalucha, J., Mshana, G., Wamoyi, J., et al. (2004). "A bit more truthful": the validity of adolescent sexual behaviour data collected in rural northern Tanzania using five methods. *Sex Transm Infect*, 80 Suppl 2, ii49-56.
- Pronyk, P. M., Hargreaves, J. R., Kim, J. C., Morison, L. A., Phetla, G., Watts, C., et al. (2006). Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomised trial. *Lancet*, 368(9551), 1973-1983.
- Rothman, K. (2002). *Epidemiology, An Introduction*. New York: Oxford University Press.
- Rothman, K. J., & Greenland, S. (1998). *Modern Epidemiology* (2nd ed.). Philadelphia: Lippincott Williams & Wilkins.
- Skoler-Karppoff, S., Ramjee, G., Ahmed, K., Altini, L., Plagianos, M. G., Friedland, B., et al. (2008). Efficacy of Carraguard for prevention of HIV infection in women in South Africa: a randomised, double-blind, placebo-controlled trial. *Lancet*, 372(9654), 1977-1987.
- The Cochrane Collaboration. (2008). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1* [updated September 2008]. from Available from [www.cochrane-handbook.org](http://www.cochrane-handbook.org)
- The Voluntary HIV-1 Counseling and Testing Efficacy Study Group. (2000). Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. *Lancet*, 356(9224), 103-112.
- Turner, A. N., Morrison, C. S., Padian, N. S., Kaufman, J. S., Salata, R. A., Chipato, T., et al. (2007). Men's circumcision status and women's risk of HIV acquisition in Zimbabwe and Uganda. *AIDS*, 21(13), 1779-1789.
- UNAIDS. (2008). *Report on the Global AIDS Epidemic*. Retrieved from [http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008\\_Global\\_report.asp](http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/2008_Global_report.asp).
- Watson-Jones, D., Weiss, H. A., Rusizoka, M., Chagalucha, J., Baisley, K., Mugeye, K., et al. (2008). Effect of herpes simplex suppression on incidence of HIV among women in Tanzania. *N Engl J Med*, 358(15), 1560-1571.
- Wawer, M., Kigozi, G., Serwadda, D., Makumbi, F., Nalugoda, F., Watya, S., et al. (2008). *Trial of Male Circumcision in HIV+ Men, Rakai, Uganda: Effects in HIV+ Men*

*and in Women Partners*. Paper presented at the 15th Conference on Retroviruses and Opportunistic Infections, Boston, MA.

Wawer, M. J., Sewankambo, N. K., Serwadda, D., Quinn, T. C., Paxton, L. A., Kiwanuka, N., et al. (1999). Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Rakai Project Study Group. *Lancet*, 353(9152), 525-535.