Examining the Association between Self-reported Condom Use and Sexually Transmitted Infections

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ABSTRACT

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(Under the direction of Professor Frieda Behets)

Two analyses were performed using data from an 18-month study of a condom promotion intervention among 1000 female sex workers (FSW) in two cities in Madagascar. The first analysis explored whether participating in such a study and being exposed to such an intervention over time would change the strength of the association between self-reported condom use and incident sexually transmitted infections (STI). The analysis found no evidence of a change in the association over time. In addition, there was no indication of a dose-response relationship between the number of reported unprotected sex acts and incidence of STI. The second analysis tested the risk of STI associated with self-reported condom use by partner type. Over the 18 months of the study, participants reported greatly increased rates of condom use with clients, but continued low condom use with personal partners. Participants who reported less than 100% condom use with personal partners, but 100% condom use with clients had no increased odds of STI as compared to those who reported 100% condom use with both partner types (odds ratio (OR) 0.9, 95% confidence interval (CI) 0.5, 1.6). Conversely, participants who reported inconsistent condom use with clients, but consistent condom use with their personal partners had an 8.3 times higher odds of STI (95% CI 0.5, 138.0)

as compared to consistent condom users with both partner types. We conclude that asking study participants to report the actual number of sex acts and the number of those sex acts that were protected by condoms may result in falsely precise estimates of their exposure to risky sex acts. The results indicating that unprotected sex with personal partners does not contribute to risk of STI are contrary to indications from other recent studies in West Africa about the infection status of personal partners of FSW. The relationship should be further explored before programs change the message that FSW should use condoms with all partners.

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LIST OF ABBREVIATIONS

ACASI	audio computer-assisted self-interviews
CDC	Centers for Disease Control
CT	chlamydia (*Chlamydia trachomatis*)
FHI	Family Health International
FSW	female sex worker
FTFI	face-to-face interview
Gc	gonorrhea (Neisseria gonorrhoeae)
GEE	Generalized Estimating Equation
GDP	gross domestic product
HIV	human immunodeficiency virus
LCR	ligase chain reaction
LNR	Laboratoire Nationale de Référence (LNR), the Malagasy national reference laboratory for HIV/AIDS
MCFC-MAD	the Measuring the Impact of Male and Female Condom Promotion among Sex Workers in Madagascar Study ("parent" study)
OR	odds ratio
PE	peer educator
PHSC	Protection of Human Subjects Committee (FHI)
RPR	rapid plasma reagin assay (test for syphilis)
SAQ	self-administered questionnaire
STI	sexually transmitted infection
TV	trichomonas (*Trichomonas vaginalis*)
WHO	World Health Organization

I. INTRODUCTION AND SPECIFIC AIMS

Sexually transmitted infections (STI) continue to be a major public health problem in populations across the world, especially in developing countries.[2, 3] Effective medical treatments for non-viral STI exist and epidemiologists have produced many studies describing how these infections move through populations. Nevertheless, rates of STI incidence, including HIV, remain high.[3]

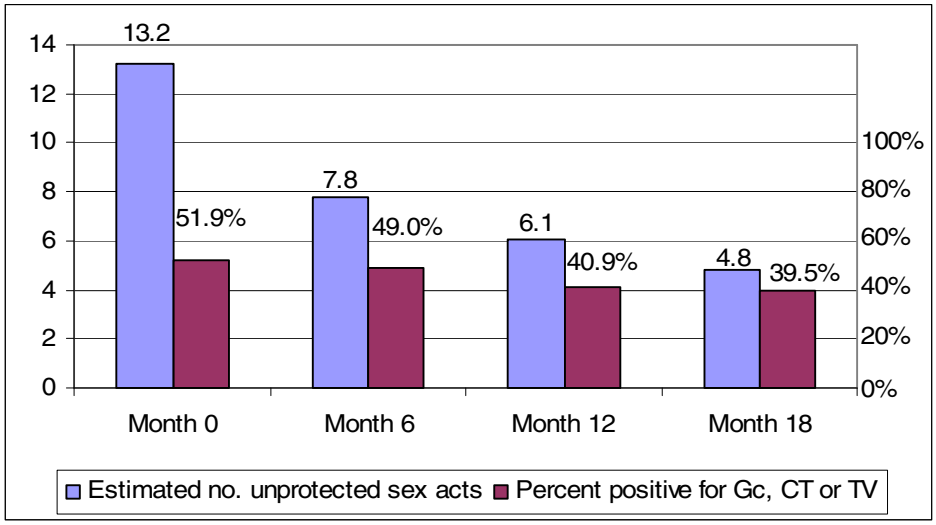
Sexual behavior change is key to STI control and prevention[4] and most public health programs concentrate on changing this behavior, especially the rate of sexual partner acquisition and condom use. The important question then becomes, how do we know if these interventions are successful? Or, how do we measure sexual behavior change? As one might well imagine, measuring sexual behaviors is fraught with difficulties (beyond the normal complications of self-reports of any kind[5]) due to its sensitive and essentially unobservable nature.

A good example of the difficulties of measuring the effects of interventions comes from an 18-month study that followed a cohort of 1000 female sex workers (FSW) in two cities in Madagascar. The Measuring the Impact of Male and Female Condom Promotion among Sex Workers in Madagascar (MCFC-MAD) study tested a clinic-based and peer education intervention to prevent STI and examined whether introducing female condoms would increase the overall number of protected sex acts and decrease the prevalence of STI.

While the intervention appeared to be successful in getting participants to increase their condom use and decrease their number of unprotected sex acts[6], the incidence of curable STIs among the participants did not decrease commensurately. (Figure 1) This

weak association between self-reported condom use and STI has been observed in other studies, however the explanation for it remains elusive.[7-10]

Figure 1: Number of self-reported unprotected sex acts (previous 30 days) and incident cases of curable sexually transmitted infections*



*Gonorrhea (Gc), Chlamydia (CT), Trichomoniasis (TV)

As mentioned above, the question of the relationship between self-reported condom use and STI has been studied in multiple dimensions. Whether this relationship should be strong or weak is still disputed in the literature due to both difficulties in measuring condom use and the variability among the individual organisms that can infect humans and their biological transmissibility.[9, 11, 12] This dissertation explores the association between self-reported condom use and STI, at single time points and longitudinally. I then examine risk of STI associated with two different types of sexual partners (clients and personal partners).

Specific Aim 1

The evidence about whether self-reported condom use and STI are associated is mixed. The data being used for this dissertation provide an opportunity to examine this association in a population with high rates of incident STI and repeated measures of self-reported condom use. Over time research study participants became more familiar with the study personnel and at the same time, were repeatedly receiving messages emphasizing the importance of condom use. This process may have increased the pressure on participants to give what they considered to be socially desirable responses, whether the responses actually reflected their behaviors or not. On the other hand, a longitudinal study could result in increased rapport and trust between interviewer and respondent, eliciting more truthful reporting about undesirable behaviors over time. In either case, an effect over time on the accuracy of self-reporting seems likely, although whether influences in competing directions would cancel each other out is also a possibility.

Objectives: (1) To determine if there is an association between recent self-reported condom use and STI incidence; (2) to determine if the association between self-reported condom use and STI incidence changed as female sex workers spent increasing time as research participants.

Specific Aim 2

Most of the decrease in unprotected sex acts took place as a result of increased condom use with clients. It is easy to assume that increasing condom use with clients

alone can decrease a sex workers' risk of incident STI and too often only non-condom use with clients is seen as a risk factor for sex workers. However, with poor rates of personal partner treatment and probable high rates of personal partners of sex workers who have multiple sexual partners themselves, these personal partners may serve as a reservoir of infection for their sex worker partners. Thus, high self-reported condom use with clients alone may not necessarily predict low incidence of STI.

Objective: To determine if inconsistent condom use with personal partners and 100% consistent condom use with clients was associated with a higher risk of STI compared to FSW who reported consistent condom use with both clients and personal partners.

II. REVIEW OF THE LITERATURE

The literature on the issue of self-reported condom use is voluminous and many questions about the measurement of this important behavior remain. Two key subject areas comprise most of the literature: 1) challenges in measuring a self-reported, non-observable behavior and 2) whether changes in self-reported condom use can serve as a proxy for changes in the risk of acquiring sexually transmitted infections in measuring the impact of prevention intervention and vice-versa. This literature review will begin by reviewing the various forms of mis-measurement and bias in self-reported condom use. Second, I will examine previous attempts to measure the quality of self-reported condom use. Finally, I will discuss the literature on the relationship between self-reported condom use and incident sexually transmitted infections.

Self-reported condom use is subject to multiple forms of mis-measurement and bias.

A number of issues complicate measuring condom use. First, condom use is a private act that cannot be directly observed in most instances. Second, there are no good physiological indications that a condom has been used, as there are for many medications, although tests to identify whether a condom has *not* been used are being examined.[13-16] As will be discussed below, using self-reported condom use as a proxy for STI risk or the reverse is difficult due to a relationship in which increasing condom use will not necessarily correlate with decreased risk of STI.[7, 12, 17, 18] The risk of STI is related to several inter-related factors, including the susceptibility of the uninfected person, the infectiousness of the infected partner, the

> "All measurement is befuddled with error. About this the scientist can and does do something: he ascertains the possible extent of the error, determines whether it is constant (biasing) or variable, or both, and ever strives to improve his instruments and his techniques."
>
> -- McNemar (as quoted in Turner and Miller [1])

transmission efficiency of the type of STI and other variables even more difficult to measure than condom use (see section below for fuller discussion). Thus, most studies and program evaluations rely on self-report of condom use despite it being subject to biases related to recall periods and discomfort in talking about such a sensitive behavior.[19]

Researchers have tested a number of methods to confront these difficulties, which has led to a literature replete with multiple forms of condom use measurement, as noted by two reviews of over 100 studies measuring condom use.[20, 21] The variety of different measurements makes comparisons across studies difficult. This has prompted several calls for creating a standard measure of condom use.[22-25] International organizations like the United Nations have attempted to define standard measures but global agreement is still lacking.[26] However, the literature does give several recommendations for how self-reported condom use should and should not be measured. These best practices in measuring condom use are discussed below.

<u>The most useful response category for self-reported condom use is the number of unprotected sex acts.</u>

Probably the most common method of self-reported condom use measurement is by using an "always-sometimes-never" scale, or a similar ordinal scale. While this type of question is relatively easy for respondents to answer, it only crudely measures condom use. "Always" and "never" are categories meant to denote 100% and 0% condom use, yet research has shown that not everyone interprets them as absolutes.[27] Furthermore, this scale does not allow for observation of increased condom use (between 1-99%) that does not achieve 100 percent.[23] At least one study of different response categories,

among female sex workers (FSW) in the Dominican Republic, concluded that the always-never scale resulted in over reporting of condom use as compared to reporting condom use for the last 5 partners.[28] A study among FSW in Cameroon randomized over 2000 participants to receive questionnaires with condom use questions asked in five different ways. They randomly assigned participants to answer questions using always-never scales with three recall periods (last month, last six months, current use, period unspecified). This study found no association between any of these measures and prevalent HIV infection.[29] The use of a prevalent outcome in this study weakens the findings since the recall periods may or may not have actually captured the period when respondents were engaging in behaviors leading to HIV risk.

Reported condom use at last sex has been advocated as an appropriate, easy-to-obtain measure that minimizes recall bias.[30] However, "last sex" measures will only be useful if the last sexual encounter is representative of the respondent's sexual encounters during the time period of interest – empiric evidence indicates that this is not the case.[25, 29]

To evaluate the effect of an intervention on changes in behavior, a more precise measure of condom use is required. Current practice favors asking respondents the number of sex acts they have had during the reference period and then the number of those acts that were protected by condom use. This figure has often been reported as the percentage of unprotected sex acts. The more appropriate measure is the number of unprotected sex acts, since a higher number of unprotected sex acts will expose the person to greater risk of infection, regardless of what percentage of the total number of sex acts this actually constitutes.[17, 23, 31] A mathematical modeling exercise confirmed

that the number of unprotected sex acts is a better measure of risk for less infectious STIs (e.g. HIV).[32] However, for highly infectious STIs (e.g. gonorrhea, chlamydia), the number of sexual partners was more predictive of STI risk.

To maximize respondent recall, reference periods for sexual behaviors should be chosen with regard to both their frequencies and how memorable they are.

In order to assess the influence of condom use behavior on sexually transmitted infections, or to predict the probability of infection, condom use is often assessed over a considerable period of time. The respondent's ability to accurately recall behaviors depends upon the period for which they are being asked to recall, the format of the question and the frequency of the behavior.[17, 33] Reference periods for sexual behaviors in published studies have varied from the last sex act, to the past week, to a respondent's entire lifetime.[20, 29, 33-43] Longer recall periods are less reliable, however, especially for behaviors that are frequent.[35] For example, a partner study in rural Senegal compared weekly reports of sexual activities with four-week retrospective reports and found that both men and women reported higher numbers of sex acts when retrospectively reporting for the four-week period, suggesting over-reporting as a form of recall bias.[36, 44] Recall of unusual activities seems to be better since they stand out in respondents' minds, but sex acts might not be unusual activities for sex workers.

Research in cognitive psychology has shown that when asked to recall something from too long ago, respondents "resort to inferences that use partial information from memory to construct a numeric answer."[45] In other words, they "guess-timate" if the recall period is too long. On the other hand, a series of studies among FSW in the Dominican Republic and Cameroon concluded that a too-short reference period might

encompass too few sex acts and thus not accurately represent the average level of condom use.[28, 29, 46] In sum, the best recommendation for how to choose a recall period seems to be by taking into account the group being studied. Highly sexually active people may need shorter recall periods to accurately remember their behaviors; general populations in stable unions may be suited to a longer recall period, since their sexual acts tend to fall into the same patterns over time.

Alcohol and drug use impair recall ability, but it is unclear how often FSW in Africa engage in these activities.

Another complication for recall of sexual behaviors may be alcohol and drug consumption. It is clinically well documented that alcohol and drug use impair recall of events that take place after drinking/drug use has begun.[47, 48] Furthermore, a recent systematic review concluded that there is substantial evidence in the literature for the association between alcohol consumption and STI.[49] It is commonly believed that many sex workers engage in drug and/or alcohol use to aid them in tolerating or conducting their work; at the same time, many illicit drug users are believed to be forced into sex work to finance their habits.[50-52] This relationship has been fairly well documented in the Western world, particularly as regards crack cocaine addition.[52] However, alcohol and drug use by sex workers in Africa does not appear to have been systematically studied. A study of sex workers in Madagascar found that between 35-45% of FSW used alcohol at least once a week, but daily alcohol consumption was less common (1.6-10.2%).[53] Another study mentioned in passing that some Zimbabwean sex workers do not use condoms because they are too drunk,[54] but the true prevalence of alcohol and drug use among African sex workers and its effect on their recall of sexual behaviors is

largely unknown. One study in semi-rural towns in Malawi did document that alcohol use by FSW was associated with a 2.6 times greater odds of prevalent STI (95% confidence interval: 1.2-5.5).[55] STI was diagnosed via genital and speculum exam in this study. A study among female bar and hotel workers in Tanzania used rigorous laboratory methods to examine the prevalence of HIV and other STI and found that women with strong indications of problem drinking were 1.92 times more likely to have HIV infection (95% CI: 1.06-3.47) than women who did not drink.[56]

Social desirability bias is likely to prompt over-reporting of socially desirable behaviors, such as condom use.

In some cultures talking about sex is taboo, making it extremely difficult to put respondents at ease when discussing their sexual behaviors. However, even where sex is discussed openly, in today's atmosphere of concern over HIV/AIDS, most people have repeatedly heard messages urging them to use condoms to prevent HIV and other STIs. Regardless of whether respondents have been successful in adopting this behavior, they know that the "right" answer, the socially desirable answer is to say that they have been using condoms. This social desirability pressure is presumed to be one of the major problems in measuring condom use.[11, 22, 33, 57, 58]

The expected direction of social desirability bias (a.k.a. self-report bias, self-presentation bias) is that respondents will over-report condom use, since they believe that condom use is expected of them. This would result in exaggerated conclusions of the success of a project (Type I error). Similarly, most researchers assume that adults underreport most of their sexual behaviors, although some behaviors may be over-reported in some populations.[59] For example, a study among Kenyan adolescents (aged

15-21, N=4366) concluded that boys were over-reporting their sexual experiences as a form of braggadocio, since approximately one-third of the male respondents admitted that they were not "very honest" in their answers.[60] More alarming yet, Turner and Miller hypothesized that social desirability bias creates systematic non-random bias where people reporting "always" condom use are more likely to be misrepresenting their condom use than those who report "never" condom use.[1] This makes estimating the predicted effect of social desirability bias extremely difficult.

Another example of how social desirability might be biasing self-reports is observed in the reporting of number of sexual partners. Numerous studies have found that women report fewer sexual partners than men.[8, 33, 57, 61-64] For example, a population-based longitudinal study in rural Tanzania surveyed 3684 people about how many sexual partners they had in the past year and whether these sexual partners lived within the study area.[64] Since the majority of men and women in the study area were surveyed, the researchers expected that they could quantify how many sexual partnerships there were between residents. However, single women reported only half as many relationships as the men's reports would have predicted. It is not known in this study or the others if women are under-reporting or men are over-reporting, although it is likely that the bias is occurring in both directions. Another possible explanation of the gender differential in number of sex partners is selection bias: it is possible that very sexually active men are more likely to agree to participate in research on sexual topics, while less sexually active women are more likely to participate. If there is a smaller pool of women who have multiple partners and these women are under-represented in surveys,

this might also explain the mismatch in numbers of sexual relationships reported by men and women.[33]

Fishbein and Pequenat suggested techniques for minimizing the amount of intentionally faulty reporting by respondents:

- Assuring confidentiality and ultimate anonymity;
- Stressing the importance of honest answers for the scientific integrity of the project;
- Using methods (e.g., audio computer-assisted self-interviews) that eliminate the need for respondents to report socially undesirable answers face-to-face; and
- Asking respondents to sign a statement that they will give honest answers.[17]

There is some evidence that these techniques work. For example, a qualitative study of women who were former research study participants in Cameroon (N=40) found that while the respondents agreed that others may have exaggerated their condom use for various reasons, many felt an *obligation* to respond honestly for scientific posterity.[65] A U.S. study also found that matching interviewers with respondents on gender and enhancing questions with normalizing, non-judgmental language [1] in questionnaires improved reporting of sensitive sexual behaviors.[59] A qualitative study discussing the best ways to ask questions about sensitive sexual behaviors with Ghanaian and Nigerian women (N=60) at high-risk of acquiring HIV reported that respondents were very preoccupied with the possibility of confidentiality of responses being compromised. [66]

[1] For example, including language before the question such as, "Many people say that they have a hard time getting their boyfriends or husbands to use condoms."

Most respondents preferred a female interviewer and many said they would feel most comfortable with a health care worker conducting the interview.

The magnitude of the effect of socially desirable reporting is unknown.

Only a limited number of studies have tried to measure the impact of social desirability bias on reporting of sensitive behaviors.[67-70] Personality research has identified two relatively independent factors operating on socially desirable reporting: the process of self-deception where one selectively recalls events to give a more positive interpretation of one's own actions and impression management where one actively attempts to deceive the other. Impression management-type tendencies appear to be more easily influenced than self-deceptive practices.[69] A study of injection drug users (N=2885) combined two scales representing the different dimensions of social desirability described above in order to quantify social desirability bias. While the investigators found an association between higher levels of social desirability and lower reported levels of HIV risk taking behaviors, a multiple regression analysis failed to find a significant confounding effect of social desirability on the relationship between self-reported risk factors and HIV status.[67] A study among Canadian university students (N=504), using the same two dimensions of social desirability, found only modest evidence of social desirability influencing sexuality self-reports.[69] A study of FSW in the Philippines (N=1383) used a simpler, validated scale measuring social desirability (the Marlowe-Crown Social Desirability Scale) and found no evidence of an association between the social desirability scale and self-reported condom use.[70] The authors of this study concluded that there was no social desirability bias in the self-reports of

condom use, however other research has indicated that the Marlowe-Crown scale may not be generalizable in non-Western cultures and thus they may not have properly measured social desirability tendencies in their population.[71]

Despite the results described above minimizing the possible effect of social desirability bias, their pertinence to measures of self-reported condom use in high-risk populations in Africa is questionable. This literature review failed to find any studies attempting to measure social desirability bias using these concepts in Africa. One might speculate that the magnitude of susceptibility to social desirability pressures could be strongly mediated by cultural factors. Therefore, while the presence of socially desirable reporting among African populations is probable, the magnitude of its effect seems completely unknown.

<u>The respondent's relationship with the sexual partner appears to be a strong predictor of condom use.</u>

When asking questions of FSW about condom use the *type* of sexual partner the respondent is reporting about must also be taken into account. People tend to have unprotected sex with safe partners and practice safer sex with risky partners. For example, the general population is more likely to use condoms with casual partners and female sex workers are more likely to use condoms with clients.[23, 72-75] Many studies have further delineated condom use between casual clients, regular clients and personal partners, finding that the more intimate the relationship is perceived to be by the FSW, the less likely she is to insist on condom use.[54, 55, 73, 74, 76-84] Female sex workers generally report that they cannot or will not insist on condom use with regular clients

because they depend on them for income or in personal, non-paying relationships because it would damage the sense of trust and affection.[77, 79-83]

A study of FSW in Cameroon (N=2266) found that reported condom use with non-paying partners was more predictive of HIV infection than reported condom use with clients.[29] The study, which had the primary objective of comparing different response categories for self-reported condom use, found that FSW who reported "always" condom use with non-client partners had between a 0.3 and 0.4 times reduced odds of HIV infection (depending on type of response category assigned to; 3 of the 4 odds ratios excluded the null value), as opposed to those women who reported "never" condom use with non-client partners.

A recent study of clients and non-paying partners of FSW in Benin (N=404 clients, 56 boyfriends) showed that boyfriends had higher rates of HIV infection than clients (8.4% prevalence in clients, 16.1% in boyfriends).[78] The Benin study did not have a statistically representative sample; however, both clients and boyfriends were recruited via the same FSW. Given the information about highly differential condom use by partner type and the limited information on infection rates by partner type, it is clear that knowing what kind of sexual partners a FSW is referring to is key in estimating her risk of STI.

Incorrect condom use results in STI risk in an act that would otherwise be protected.

Another often neglected dimension of condom use measurement is *correct* use of condoms.[23] According to Fishbein and Pequegnat, "incorrect condom use almost always equates to unprotected sex" since a broken condom exposes both partners to infection.[17]

A study in the US among STD clinic patients found that reported condom errors were associated with a 1.91 times higher odds (95% CI 1.23, 2.96) of gonorrhea.[85] International studies have shown condom failure rates (condom breakage and slippage) of between 2.0-13.3 per 100 condoms used.[86, 87] Failure rates were higher in Africa than in Asia or the United States.[87] A study of FSW and their clients in Benin (N=314 FSW, 208 men) showed that only 11% of the respondents were able to demonstrate correct condom use.[88]

Another incorrect condom use behavior, initially identified through qualitative research, is the application of the condom after the initial penetration (late application), either because the partners got "carried away" and started penetration before putting the condom on, or because the partners wanted the feel of flesh-on-flesh and so only wore the condom for ejaculation.[89] A study using a convenience sample of university students in Australia found that 13% of condoms were put on late, and that this was more likely with regular partners and if the condom was being used for contraception only, but this phenomenon has not been noted in the literature on FSW and condom use.[90]

A recent study attempting to reduce unmeasured confounding in relationships between self-reported condom use and STD reported that consistent condom use `with any reported condom slippage or breakage was associated with more risk of incident gonorrhea or chlamydia in a cohort of STD clinic patients in the US.[91] This study emphasizes that it is essential to both measure problems in condom usage and control for them in analyses of this relationship.

While face-to-face interviewing may contribute to respondent embarrassment, its advantages may make it preferable for survey research in Africa.

In research involving human subjects, the mode of interview administration may have important effects on the reporting of sensitive information. A common hypothesis states that modes of interview administration that do not require respondents to admit directly to another person a proscribed or embarrassing behavior are probably more likely to elicit accurate self-reports of these behaviors than direct, face-to-face questioning.[57, 92, 93] There are three major modes of interview administration: face-to-face interviews (FTFI) where respondents respond verbally to interviewer questions; self-administered questionnaires (SAQ) where respondents write their answers privately; and audio computer-assisted self-interviews (ACASI) where respondents listen to a recorded voice and then respond to the questions using a computer keyboard, touch screen or mouse. Variants of all of these exist, however I focus here on the three major modes of interview administration. In general, SAQ and ACASI offer more privacy to respondents while FTFI requires respondents to directly give answers to an interviewer and are hypothesized to be problematic for asking sensitive questions.

A wide body of empirical evidence exists on the effects of interview mode on reporting of sensitive behavior, including sexual behaviors. Studies comparing SAQ and FTFI have found few differences in reporting of sensitive behavior among highly literate populations in the US and the UK.[94, 95] Several large, randomized studies in high-risk American populations of sexually transmitted disease clinic patients,[96-98] adolescent males,[93, 99] gay men,[100] and intra-venous drug users,[100-103] found significantly higher rates of sensitive sexual behaviors reported (e.g. unprotected receptive anal intercourse) when respondents used ACASI as compared to FTFI or SAQ. Although the validity of

self-reported sexual behaviors reported via ACASI can not be definitively established, studies have attempted to validate this mode of interview by comparing self-reports of drug use with biological testing. The results are mixed. A study of students in Thailand (N=1725) found that ACASI elicited increased reporting of drug use, but 16% of those who tested positive for methamphetamine denied its use via ACASI, indicating that ACASI did not elicit all sensitive behaviors in this particular population.[104] The only other study in the literature that attempted to validate ACASI with a biological measure is a study of marijuana use by teenagers in the US (N=182).[105] This study actually found that the number of respondents who reported using marijuana via ACASI was *higher* than those that tested positive in urinalysis; however, the argument could be made that marijuana use is not a severely proscribed practice in this population and so is not as subject to mis-reporting as other, more sensitive practices.

Issues of social desirability are tightly bound in cultural traditions, thus comparisons of the different interview modes in the US or UK are probably not applicable in sub-Saharan Africa.[71] There are however only a few studies that examine the issue of interview mode in an African setting; these are discussed below. A 1998 comparison of FTFI and SAQ among in-school adolescents in rural Tanzania (N=4958) concluded that neither mode of administration was clearly superior for eliciting accurate reports of sexual experience.[106] The study also included biological measures of sexual experience (STI, HIV infection, and pregnancy). Among the small subset of male respondents who tested positive for biological markers of sex, 75% reported sex in the SAQ while only 58% of males reported sex in the FTFI. Conversely, 31% of females who tested positive for a biological marker reported sex in the SAQ and 45% reported

sex in the FTFI. The authors of this study report more accurate accounts of sexual behavior were obtained through in-depth interviews and participant observation; however, qualitative methods do not generally produce population prevalence estimates since they are so much more labor-intensive to conduct. In 2000 this study team repeated the SAQ survey with 4424 of the same respondents.[107] Comparing the 1998 FTFI responses to the 2000 SAQ responses, adolescents continued to report sensitive sexual information in the SAQ mode. However, the authors found little reliability between responses in the 1998 and 2000 SAQ surveys, which raises questions about the overall validity of these reports of sexual behavior.

A unique study of a general population in rural Zimbabwe (N=6179) found that an informal confidential voting interview method, a technique blending FTFI and SAQ whereby respondents recorded their own answers to questions on color-coded pieces of paper which were dropped into ballot boxes, elicited more reports of sensitive sexual behaviors such as multiple sexual partners than the standard FTFI method.[108, 109] These results indicate that Africans have similar responses to increased privacy when answering sensitive questions; however, there were significant numbers of inconsistent responses and greater occurrence of item non-response using this new method and it requires numeracy and at least some literacy from respondents, limiting its usefulness in other contexts.

Even fewer published studies have used ACASI in sub-Saharan Africa. Despite the fact that early proponents of ACASI thought it might be uniquely appropriate for developing country settings,[110] the experience in Africa has been mixed. A test of the feasibility of using the method among women of different educational backgrounds in

Zimbabwe found that the vast majority of the women tested (N=221) preferred ACASI to FTFI and thought they could answer more honestly with ACASI.[111] Nevertheless, respondents had considerable difficulty with the ACASI method and over one-third (34.9%) of women in the lowest educational group (which was defined as primary school or less, a category encompassing the majority of women in sub-Saharan Africa) had one or more discrepancies in the basic, non-sensitive information they provided between the ACASI and FTFI modes, suggesting a large incidence of error.

A 1999 study in rural Kenya randomized 4,400 unmarried adolescents to answer questions in face-to-face interviews, via self-administered questionnaires or with ACASI.[60] The study found that ACASI elicited less reporting of sexual activity among boys (the direction they hypothesized given cultural expectations of boys to be highly sexually active). However, while the researchers expected girls to be under-reporting sexual activity in FTFI and thus expected higher reports for girls in ACASI, they found the opposite. Girls reported more sexual activity in FTFI. Furthermore, the introduction of computers in this rural population engendered "hostility and distrust" among community elders, suggesting that ACASI may not be the best mode of interview for resource-poor settings. When the same researchers repeated the experiment in another district of Kenya (N=712), they found that girls reported higher levels of greatly stigmatized sexual behavior (e.g. coerced sex or sex with a relative, stranger or older man) with the ACASI mode.[112] On the other hand, there were considerably higher levels of non-response and much less consistency of response among ACASI respondents, prompting more questions about the suitability of this interview mode in rural Kenya.

Thus despite its possible disadvantages, FTFI may remain a preferred mode of administration for sexual behavior questionnaires in developing countries due to its several advantages. First, face-to-face interviews tend to have lower participation refusal rates than surveys that are sent through the mail or done over the telephone.[113, 114] FTFI also tends to have significantly fewer missing data due to non-responses, since respondents can directly ask the interviewer about questions that confuse them and seem less likely to refuse to answer outright in a face-to-face situation.[98] (However, at least one research team makes the case that high response rates in FTFI are due to respondents feeling pressured to respond to the interviewer.[112]) In addition, interviewers can clarify confusing or contradictory answers within the setting of an FTFI, leading to more consistency in responses, as noted in the Kenya study discussed above. Furthermore, through the interview process a rapport may be generated between the interviewer and respondent that encourages the respondent to be more patient through long interviews and to respond more honestly.[59] Finally, in many settings, especially the developing world, literacy rates are low, making self-administered survey instruments impracticable and infrastructure restrictions make it impractical to conduct surveys by telephone or mail. Furthermore, many people have very limited experience with technology like computers, which may create fear and distrust, as discussed in the Kenya study above. Further evidence of this comes from a qualitative study with women at high-risk of HIV infection in two West African countries (N=60), which reported that many of these women were suspicious of the idea of answering questions on a computer.[66] Their principal concern was that their confidentiality could somehow be compromised by the device.

Participants involved in long-term research may experience an "interviewer effect" that increases their perceived pressure to give socially desirable responses.

Mensch and Kandel (1988) were among the first to discuss the potential disadvantages of face-to-face interviews in longitudinal cohorts.[115] In looking at drug reporting in a cohort of young Americans, they found that people who had seen the same interviewer more than once were less likely to report drug use, especially more socially sanctioned drugs (e.g. cocaine, instead of marijuana). They termed this the "interviewer familiarity" effect. In fact, they found that it was not necessary for respondents to be interviewed by the same person every time for under-reporting to occur. Respondents who had seen an interviewer more than once at any time in the past also under-reported drug use as compared to respondents who had never seen an interviewer more than once. Mensch and Kandel concluded that respondents were affected by social desirability bias of the interviewer familiarity effect whether they had seen the interviewer in the *past* or whether they anticipated seeing the reviewer again in the *future*. A review of the literature did not find any studies relating to this issue and reporting of sensitive behavior or further papers about the effect of interviewer familiarity on reporting of illicit drug use.

Assessing the quality of self-reported condom use remains a challenge.

There are two means of judging how well a test performs. "The reliability of a test is its capacity to give the same results – positive or negative, whether correct or incorrect – on repeated application in a person with a given level of disease."[116] A test can be reliable (e.g. elicit the same information consistently) and still not yield the

"truth". Validity, on the other hand, assesses whether the test is giving the correct information. The reliability of a survey question refers to whether the question administered several times (or to several people) reaps the same information. The validity of a survey question describes whether it elicits an *accurate* report of the frequency/experience of the sexual behavior. Good reliability and validity are both necessary components of a good measure, however good reliability can exist with poor validity, whereas good validity only comes with good reliability. This means that validity is often the more important test of the usefulness of a measure.

Reliability studies have generally found sexual behavior questions to be reliable, although there is considerable variance in their results.

Reliability between two ratios is often assessed using the Kappa statistic, which measures the amount of agreement between two sets of ratings, taking into account agreement by chance. A value of between 0.80 and 1.0 is considered excellent agreement, indicating very good reliability.[117]

Some of the earliest studies on the measurement of self-reported condom use looked at the reliability of the measure. Most commonly, reliability studies examine whether the same question administered to the same person at different times elicits the same information (known as test-retest reliability). For example, an early study examining AIDS-related risk factors among gay men (N=26) found high reliability on sexual history self reports administered 72 hours apart (Pearson correlation coefficients >0.80).[118] A similar study from 1987 (N=116) found "moderate" agreement using the Kappa test (kappa between 0.52 and 0.63) for sexual history on questionnaires completed on average 5 weeks apart.[119] A study of participants in drug rehabilitation facilities

(N=246) found high test-retest reliability for both sexual behavior and drug use variables over (on average) a two-week period. Interestingly, while reliability on the condom use variables was still high (kappa = 0.72), it was lower than for other sexual behavior variables (kappa between 0.83 and 0.91).[120] This type of reliability testing is most useful for assessing recall biases, which can be improved with a variety of recall-enhancing techniques. In general, reliability decreases as the time of recall increases. The reliability of a test is also a function of how the results are measured. A dichotomously measured variable will on average have higher reliability than a scale measure using six categories. The more precisely a concept is measured, the greater the likelihood for recall bias.[120]

A review of the test-retest reliability literature found only one published report of such studies on sexual behavior in Africa.[61] The WHO coordinated a series of 5 small studies (Nigeria N=332, Philippines N=350, Senegal N=51 couples, Uganda N=445, Zimbabwe N=338) looking at the reliability of sexual behavior questions and found mixed results. Test-retest reliability for self-reports of casual sex in the past 12 months ranged from low to acceptable (Nigerian military population kappa=0.12-0.21; Philippines urban kappa=0.78; Ugandan urban population kappa=0.52; Uganda rural population kappa=0.23). However, the Zimbabwe study site found good agreement, with over 75% of men and women agreeing on most sexual behavior questions, indicating good reliability. As with US studies, it appears that reliability of reporting on sexual behavior in Africa is a complex function of memory, population characteristics, the mode of interview administration, and the sensitivity of the questions being asked.

Interpartner reliability studies offer inconsistent conclusions about the external validity and reliability of self-reported sexual behavior.

A second technique used for examining the reliability of sexual self-reports has been to look at the consistency of reporting between sexual partners (interpartner reliability). These studies often use a paired *t*-test to assess reliability, since the two values being compared are not from the same subject, but are still dependent. Studies have found variable consistency in reports of sexual histories within couples.[61] A study of heterosexual couples in urban Baltimore (N=71 couples) found a high degree of agreement in couples' reports of sexual activities, including condom use. Agreement was measured by mean differences in couples' reporting of sexual behaviors in number of days (differences between –0.03 and –1.1) and number of acts (differences between –0.04 and –2.7). Mean differences in this study increased over time of recall.[121] Another study of heterosexual couples (N=363 couples), this one in San Francisco, also found high reliability between couples' reports of number of sex acts (kappa=0.68-0.70) and use of condoms (no condoms: kappa=0.74; condoms $\geq$ 75%: kappa = 0.59-0.86).[122] And a recent study among college students (N=112 couples) in San Francisco found excellent correlations between partners in reporting on different sexual activities over a two-week period (e.g., r=0.88 for frequencies of vaginal intercourse, r=0.86 for condom use).[123] This study, however, found that among women with genito-urinary symptoms of a urinary tract infection, the agreement between partners was less correlated. The women with urinary tract infections generally reported more sex acts than did their partners, implying that people with symptoms are likely to over-report activities they suspect may have caused those symptoms.

In Africa, too, the results have been mixed. A multi-center study in four African countries found poor agreement (Cotonou, Benin: N=212 couples, kendall tau-b value 0.512; Yaounde, Cameroon: N=172, tau-b 0.537; Kisumu, Kenya: N=238, tau-b 0.375; Ndola, Zambia: N=263, tau-b 0.294) between husband's and wives' reports of the number of sex acts they engaged in over a seven-day period.[8] But a study in rural Senegal found high reliability in interpartner reports of number and timing of sex-acts for a five day period (N=52 couples; kappa= 0.82).[36, 44]

In the end, interpartner concordance only measures the consistency of reports between partners but is still subject to the same social desirability and recall biases discussed above. Furthermore, gendered social expectations may cause men and women to bias their reporting in opposite directions. Thus, interpartner reliability studies can be seen as a type of external validity testing that offer further evidence that people tell the truth about their sexual behaviors, but do not offer "proof".

Lack of a gold standard makes validating self-reported condom use difficult.

There is some evidence to show that sexual behavior can be measured accurately by self-report, although this evidence is dated. For example, in their year 2000 review of behavioral and biological measures for AIDS prevention programs Fishbein and Pequegnat cite a study that measured the presence of sperm in daily urine samples with self-reports of sexual activity. That study found almost perfect agreement in its small sample of 15 African-American women. Similarly, the authors cite a larger study (N=571) comparing the self-reported history of STI with medical records for sexually active female adolescents in the US; this study found 93% agreement.[17]

In another review of the literature on the reliability and validity of self-reported sexual behavior, Dare and Cleland acknowledged that "it is extremely difficult to present clear-cut conclusions concerning the trustworthiness of survey information on sexual behavior and related matters."[61] At the same time, these authors conclude that the overall impression of the accuracy of self-reports is reassuring, with little indication that the magnitude of the inevitable biases makes the information without use. Of course, Dare and Cleland were writing in 1994 before several studies (discussed below) reported a lack of association between incident infection and self-reported condom use. Furthermore, there may be more reason to be concerned about self-reports of condom use than reports about other sexual behaviors. Today's world is inundated with messages stressing the importance of condom use, which may increase the pressure a respondent feels to report in a socially desirable manner. In a randomized study of the association between different condom use measurements and HIV infection in a Cameroonian sex worker population (N=2266), Weir, et al. concluded that the way the investigator measures self-reported condom use can greatly influence its association with HIV infection.[29] Thus, it is not necessarily the "self-reported" quality of condom use that makes the measure difficult to use.

Skepticism about the accuracy of self-reported condom use is still wide-spread due to investigators' inability to establish the internal validity of self-reports. Generally, one establishes the internal validity of a measure by comparing it to a gold standard of "truth". The ultimate gold standard for condom use would be direct observation of sexual activity with notation of whether condom use occurred, when, and whether the condom was used correctly. Even if such a study could pass ethical scrutiny, the kind of

people who would agree to such a design would be so self-selected that generalizations would be impossible.

Sexual behavior research has used the presence of semen in urine or vaginal/cervical fluids in the past to validate reports of sexual behavior, however the utility of this kind of testing is limited since the reliable period of detection lasts only approximately 48 hours.[61] A study of HIV discordant couples (N=963) in Zambia was able to effectively use microscopic detection of sperm in vaginal wet-mounted smears to validate reports of condom use.[124] The study asked couples to keep prospective coital diaries for four three-month periods. Every three months the couples reported to the study clinic to turn in the coital diaries and for testing of biological markers, including presence of sperm and STI. Sperm was detected in 15% of the intervals where couples reported 100% condom use, indicating that these respondents were still under-reporting their risky behaviors even when they knew there might be biological traces detected that would prove them wrong.

Another method for biologically validating condom use has recently been developed. The presence of prostate specific antigen (PSA) in a woman's vagina after penile-vaginal intercourse is indicative of incorrect or no condom use. PSA tests were successfully used to test the effectiveness of the female condom as a barrier to semen.[14] More recently, a study using a subset of participants from the MCFC-MAD study tested the validity of self-reported condom use using PSA.[15] The study found that 21% of respondents who reported no sex in the past 48 hours had evidence of PSA in their vaginal vaults and 39% of respondents who said they had only protected sex in the past 48 hours tested positive for PSA, throwing doubt on the validity of their self-reports of

sexual behavior. A second study by the same team among FSW in Kenya found PSA in 11% of FSWs who reported either protected sex only or no sex for the past 48 hours.[16] The team hypothesized that the likelihood of detecting PSA may have been decreased by the common practice of douching in this cohort. PSA is a promising test for establishing the validity of self-reported sexual behavior, but can only measure the *non*-use of condoms and only in the previous 48 hours. Additionally, PSA tests require vaginal swabs from the participants which requires much more intimate cooperation from a participant than simply reporting sexual behavior and laboratory tests are required to conduct the tests for PSA.

STI has been proposed as both a proxy and substitute for self-reported condom use.

Without a biological gold standard for condom use, researchers have looked to different relationships to offer validation of self-reported condom use. Since the ultimate goal of barrier-based prevention interventions is to reduce the incidence of STIs (including HIV), many have argued that rather than using the imprecisely measured self-reported condom use as a proxy for STI, STIs should be measured directly.[22, 61] Practically, however, administering questionnaires to gather self-reported condom use is much easier, more acceptable to respondents, and less expensive than collecting specimens and performing laboratory tests for STI.

Rather than replacing self-reported condom use, STI has also been proposed as a proxy that can be used to validate it. While self-reported condom use has an intrinsic value as a measure of the mechanism of action (behavior change) of most prevention programs, there is much controversy over whether STI incidence can or should serve as a proxy for it, or the reverse.[1, 7, 9, 10, 18, 22, 125, 126] It is tempting to assume that increasing

condom use will automatically lead to decreasing risk of STI. However, the risk of STI for an individual is principally determined by the infection status of the sexual partner. If a person uses condoms 99% of the time, but the one time they do not use a condom, they have sex with an infected person their probability of infection is greater than zero. In fact, this probability can be anywhere from less than 1% to 30-50% depending on other factors, particularly the infectiousness of the pathogen, the infectiousness of the infected partner him/herself, and facilitators of infection (e.g. infection by ulcerative STI) that result in varying susceptibilities of the uninfected partner. On the other hand, if a person never uses condoms, but only has sex with uninfected partners then their individual probability of infection will be zero. Furthermore, the decrease in one risk factor (e.g. increased condom use) may lead to increases in other risks (e.g. increased number of sexual partners due to feeling of safety).[17, 127]

The risk of STI at a population level is also subject to several factors, as described in the model of the reproductive rate for sexually transmitted infections: transmission efficiency per contact (ease with which infectious partners pass on the infection), the exposure of susceptible individuals to infected persons, and the duration of infectivity.[17, 128, 129] In addition, at the population level, the overall prevalence of infection in that population is highly significant. Each of these biological determinants is influenced by other, behavioral factors (called proximate determinants by Boerma and Weir[129]). The proximate determinants are in turn influenced by underlying factors such as social and cultural context and intervention programs.

Condom use affects the rate of STI by decreasing the transmission efficiency of the pathogen. Thus, an increased rate of condom use in a population should correspond

to decreased STI, although the strength of that relationship is dependent on the complicated constellation of proximate and biological determinants affecting individual-level risk. Therefore, in order to observe changes in STI as a result of increased condom use, one would need to look at large numbers of people, over a long time period or in a population with a high prevalence of infection.[130] Consequently, high STI rates are needed to use STIs as biological validators of self-reported condom use.[10, 32]

The complicated relationship between condom use and STI precludes its simple use for analysis of individual risk, but may be valid for aggregated populations.

In sum, biological and self-reported behavioral variables cannot substitute for one another, nor can they be used to validate each other for a single individual. Their relationship may, however be useful for examining change in a population. As Fishbein and Pequegnat conclude: "it is important to investigate and understand the relationships between behavioral and biological measures; in particular, to understand when and under what circumstances one can expect to find a relationship between behavioral and biological outcomes." ([17], p. 106)

As a practical example of these difficulties, Zenilman et al. conducted an analysis to "validate" the accuracy of self-reported condom use in a prospective cohort of sexually transmitted disease clinic attendees in Baltimore (N=598).[10] This influential study used incident sexually transmitted infections as the validating test and found no association between that and self-reported condom use. The study found that the only statistically significant predictor of incident STI at the time of follow up for both men and women was having had an STI at the time of enrollment. The authors attributed the lack of association between STIs and self-reported condom use in large part to misrepresentation

of condom use by participants: "Although the majority of subjects (59%) reported they never used condoms, we suspect that at least some of the remaining subjects over-estimated their actual condom use." (p. 20) In fact, the respondents to the Zenilman survey did report high rates of condom use – at the follow-up visit, 23% of men and 19% of women reported always using condoms during the last 30 days.

Following the furor over Zenilman's conclusion that self-reported condom use could not be used to predict STI, a subsequent re-analysis of the Zenilman data found no good explanations for the lack of association between incident STI and self-reported condom use other than that the quality of condom self-report was poor.[1, 9, 18, 125] Even looking at several alternate explanations (high rates of condom breakage, confounding influence of large number of partners, new partners or prior history of more than average number of STIs), none was found to adequately explain the lack of association between self-reported condom use and incident STI.

Existing analyses of the relationship between self-reported condom use and STI incorporate weaknesses that can be addressed in the MCFC-MAD dataset.

Other analyses examining the association between self-reported condom use and STI and have found mixed results (Table 1). The influential study that initiated this debate about the merits of self-reporting of condom use found no association between self-reported condom use and incident STI in a population of male and female STD clinic attendees in Baltimore (N=598).[10] Indeed, they found that 15% of the men who reported always using condoms and 23.5% of the women who reported always using condoms had an incident STI. Another study among STD clinic attendees in the US (N=2879) also

failed to find an association between self-reported sexual behaviors like condom use and presence of STI.[9]

Among adolescents, one study of US teenage girls (N=484) found that self-reported consistent condom use did not have a protective effect on incident STIs (RR 0.9; 95%CI 0.5-1.6).[131] However, the way that "consistent" was defined (always condom use with the "main partner") leaves open the possibility that the respondent could have had other non-protected exposure to STI, leading her to be misclassified as unexposed. A study of male and female adolescents in Minnesota (N=404), however, found a significant association (Pearson χ^2 = 9.86, p<0.05) between those who reported more frequent condom use with the last two partners and absence of STI.[132] The Minnesota study avoided the problem of defining consistent condom use, but was cross-sectional and thus STIs were prevalent and not incident. Another study among detained adolescent females (N=134) using prevalent STI found a significant association between consistent condom use and STI when adjusting for the number of acts where a condom broke (PR 3.59, 95% CI 1.13-11.38).[133] Finally, a study among low-income adolescents in Birmingham, Alabama found a significant association between self-reported consistent condom use and incident STI (RR 1.69, 95% CI 1.16, 2.46).[134]

The contradictory results of tests of the association between self-reported condom use and STIs argue for more sophisticated measurement of self-reported condom use as a proxy for risk. For example, a study of Mexican Americans and African Americans in the US found a statistically significant association (adjusted OR 1.9 (95% CI 1.1-3.3) between a composite measurement of "unsafe sex", comprising condom use problems and more than 5 unsafe sex acts with casual partners, and STI.[126]

A study of Filipino sex workers (N=1383) found that the mean number of prevalent STIs among those who said they always used condoms was lower than the mean number among those who said they used condoms less than always (0.62 as compared to 0.90, $p<0.01$), however they ignored the fact that there was still STI in the group reporting consistent condom use.[70] This study has other problems, including its crude measurement of condom use (they asked how often the respondents used condoms during vaginal sex without specifying a reference period) and its cross-sectional design which necessitated use of prevalent infections. Furthermore, the authors provided no information about how the STIs were diagnosed, or even which STI were included in their measurements, making it difficult to interpret their results.

In Africa, findings have been less contradictory (and more rigorously conducted) showing little association between self-reported condom use and STI in general and HIV in particular. Some of these studies do point to the importance of partner type in assessing self-reported condom use as a risk factor for STI. For example, a large cross-sectional multi-center general population study in sub-Saharan Africa did not find a significant association between self-reported frequent (always or often) condom use with non-spousal partners in the past 12 months and STI at the population-level.[135] Nor did the study find that frequent condom use was protective for STI at an individual level, except in the case of two STIs (chlamydia and HSV-2) among women in one of the four cities. This study did not, however, assess the association between reported condom use with all partners (spousal and non-spousal), probably because of low reported condom use with spouses. A population-level study in Malawi among women coming to antenatal clinics found that consistent condom use increased over a four year period

(5.8% to 15.0%), but at the same time HIV prevalence also increased (19% to 30%).[136] And a study among HIV discordant couples in Zambia (N=963 couples) detected sperm in 15% of women who said that they always used condoms.

The previously mentioned study among FSW in Cameroon (N=2266) found little association between self-reported condom use (as measured by five different types of questions) and HIV infection.[29] However, the study did find that the association between condom use and HIV was strongest for reported use with non-paying (personal) partners. A large study among FSW in Cote d'Ivoire (N=5218) conducted four cross-sectional studies over a 6 year period and found that a population-level increase in condom use correlated with a decrease in HIV and STD prevalence.[137] This study, however, has all the weaknesses associated with ecological study designs, including an inability to ascribe causality to what it observed.

On the side of no association, a multi-year project among bar and hotel workers in Tanzania (N=519 and 1042) found a statistically insignificant relationship between STI and self-reported condom use during a first phase (N=519) and this lack of association continued through to the baseline of the second phase (N=1042).[56, 138] In addition, as described above two studies among FSW in Africa tested the validity of self-reported condom use using PSA.[15, 16] The studies found significant proportions of respondents who either reported no sex in the past 48 hours or only protected sex in the past 48 hours, but who tested positive for PSA.

To summarize, 17 published studies reporting on the association between self-reported condom use and sexually transmitted infections (STI) showed mixed results: 9/17 found no association, and 8/17 found some association.[9, 10, 15, 16, 29, 70, 91, 124, 126, 131-

[138] In addition, a review of ten studies in Africa reporting both condom use and HIV found that one study showed a protective, significant effect of condom use on HIV infection while the other nine showed no discernable association.[26] In the studies that found a significant association between self-reported condom use and a sexually transmitted infection, five used prevalent measures of STI, which makes it impossible to ascribe a causal association between the reported condom use and presence of infection.[29, 70, 132, 133, 137] By contrast, seven of the nine studies reporting no association used either incident cases of STI or biomarkers,[9, 10, 15, 16, 124, 131, 136] thus appearing to provide stronger evidence for a lack of association. Among the 17 studies, five used populations of FSW in Africa and they were evenly split between finding an association and not.[15, 16, 29, 137, 138]

Table 1: Summary of previous studies that empirically examined association between self-reported condom use and STI

Study location	Population	Condom use measurement	Biological markers	Laboratory tests used	Observed association
Studies that found some association					
St. Paul, MN[132]	Adolescents (ages 13-21) recruited from schools and community-based clinics (N=398)	Consistency (sometimes, usually, always) of reported condom use with the latest partner(s)	Prevalent *Trichomonas vaginalis* (TV), *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (Gc)	TV: culture in STS media; CT: culture in McCoy cells; Gc: Thayer-Martin media	Significant ($p<0.05$) inverse relationship between consistency of reported condom use with the latest partner(s) and the occurrence of an acute STD
Southern Philippines[70]	Female sex workers (N=1383)	"Always" use condoms while engaging in vaginal sex	Unspecified "STI"	Not specified; data obtained from local clinics where FSW are required to undergo examination for STI	The proportion who had STI in the past 6 months and said they always use condoms was 8%, compared with 22% for those who did not always use condoms
Yaoundé and Douala, Cameroon[29]	Female sex workers (N=2266)	Randomized study of different measures: last 10 acts, retrospective coital log, always-sometimes-never scale with recall periods of past 6 months, past month, or current use	Prevalent HIV	HIV: ELISA, confirmed with additional ELISA and western blot	Regardless of type of measure or reference period, the strongest association between condom use and infection was for use with partners who were not clients.
Abidjan, Cote d'Ivoire[137]	Female sex workers (N=5218)	Consistent condom use with all clients during the most recent working day	Prevalent HIV, TV, CT, Gc, syphilis	HIV: ELISA, confirmed with either western blot or combination of monospecific ELISAs; TV: wet mount; CT: enzyme immunoassay (EIA); Gc: culture	Consistent condom use during most recent working day was associated with an increased odds of HIV infection (odds ratio (OR) 1.16, 95% confidence interval (CI): 1.00, 1.36)

Study location	Population	Condom use measurement	Biological markers	Laboratory tests used	Observed association
San Antonio, TX[126]	Mexican American and African American women (N=477)	Composite variable for unsafe sex: never using condoms with one or more casual partners **or** both ≥5 unprotected acts in the past 3 months **and** incorrect or problematic condom use	Incident CT, Gc	CT and Gc: DNA-probe testing of endocervical samples (GenProbe)	Reported unsafe sex was associated with a greater odds of STI (OR 2.9, 95% CI 1.5, 5.6 at 6 months; OR 1.9, 95% CI 1.1, 3.3 at 12 months)
Birmingham, AL[134]	African-American female adolescents (ages 14-18) recruited from medical clinics and schools (N=390)	Consistent condom use during all sexual encounters in the previous 6 months	Incident TV, CT, Gc	TV: culture in InPouch media; CT and Gc: ligase chain reaction (LCR) DNA testing of vaginal swabs	Significant association between self-reported consistent condom use and incident STI (RR 1.69, 95% CI 1.16, 2.46), but 17.8% of "consistent" users had incident infections at follow-up
Georgia, USA[133]	Female adolescents (ages 14-18) in short-term detention facilities (N=134)	Consistent and correct (i.e. no condom failure) condom use with all partners in the previous 2 months	Prevalent CT, Gc	CT and Gc: initially LCR testing of urine specimens, later amplified DNA asses (BCProbeTec)	When adjusting for the number of acts where a condom broke, found a significant association between prevalent STI and self-reported condom use (PR 3.59, 95% CI 1.13, 11.38)
Urban Alabama[91]	Female STD clinic attendees (N=1122)	Consistent condom use without breakage or slippage in previous 6 months	Incident TV, CT, Gc, bacterial vaginosis (BV), syphilis, herpes simplex virus type 1 (HSV-1) and 2 (HSV-2)	TV: wet mount; CT: culture in McCoy cells; Gc: Thayer-Martin media BV: wet mount using Amsel criteria; syphilis: RPR confirmed by VDRL assay; HSV: assay (as described in Macaluso, 1999[139])	In case-crossover analysis, found significantly reduced risk of infection (RR 0.49, 95% CI 0.26, 0.92)

Study location	Population	Condom use measurement	Biological markers	Laboratory tests used	Observed association
Studies that found little or no association					
Baltimore, MD[10]	STD clinic attendees (N=598)	Partner-specific information on the number of unprotected sex acts in the past 30 days	Incident TV, CT, Gc, syphilis	TV: wet mount or culture; CT and Gc: culture; syphilis: rapid plasma reagin (RPR) confirmed by fluorescent treponemal antibody tests (FTA)	15% of men and 23.5% of women who were "always" users of condoms had incident sexually transmitted diseases at follow-up
Blantyre, Malawi[136]	Female antenatal clinic attendees (N=2460)	Consistent condom use in the past 6 months	Incident TV, Gc, syphilis	TV: wet mount; Gc: culture; syphilis: RPR confirmed by FTA tests	Incidence of gonorrhea, trichomoniasis, and syphilis did not decline among women reporting consistent condom use
Large city in the southeastern US[131]	Female urban adolescent (age 14-19) health clinic attendees (N=650)	Consistent ("always") condom use	Incident HSV-2, TV, CT, Gc, syphilis, hepatitis B virus (HBV)	HSV-2: immunoblot test; TV and Gc: culture; CT: polymerase chain reaction (PCR) DNA test or culture in McCoy media; syphilis: RPR and FTA; HBV: antibody tests	Self-reported consistent condom use was not significantly associated with having any incident STD
Baltimore, MD, Newark, NJ; Denver, CO; San Francisco and Long Beach, CA[9]	HIV-negative heterosexuals attending large public STD clinics (N=2879)	Number of episodes of unprotected sex by main vs. occasional partner	Prevalent HIV, CT, GC, syphilis	HIV : repeated ELISA ; CT : PCR; Gc: culture; syphilis: FTA	No association between STD incidence and number of unprotected sex acts with the main partner, but new infection was more common among people who had 6 or more episodes of unprotected sex with occasional partners

Study location	Population	Condom use measurement	Biological markers	Laboratory tests used	Observed association
Cotonou, Benin; Yaoundé, Cameroon; Kisumu, Kenya; Ndola, Zambia[135]	General population randomized household survey (N=7824)	Frequent ("always" or "most of the time") condom use with non-spousal sexual partners in the past 12 months	Prevalent HIV, HSV-2, TV, CT, Gc, syphilis, men's reports of genital pain/discharge and of any genital sores in previous 12 months	HIV: ELISA confirmed with rapid test or HIV 2.2 Blot; HSV-2: ELISA; TV: culture in InPouch media; CT and Gc: DNA amplification on urine samples; syphilis RPR confirmed by TPPA	No significant association between reports of frequent condom use with non-spousal partners and STI, except for the association between chlamydial and HSV-2 infection in Yaoundé
Lusaka, Zambia[124]	HIV discordant couples (N=963 couples)	Number of sexual encounters with and without a condom, with spouse and outside of the marital relationship in the past 3 months	Incident HIV, pregnancy, presence of sperm in vagina	HIV: rapid test confirmed with second rapid test and two ELISAs; sperm: microscopy	Sperm was present in 15.1% of vaginal smears taken when no unprotected sex had been reported
Moshi, Tanzania[56, 138]	Female hotel and bar workers (equivalent to FSW) (N=519)	Always using condoms with partners in the past 5 years	Prevalent HIV, HSV-2, BV, TV, CT, Gc, syphilis, *Candida albicans*	HIV: repeated EIA, confirmed with western blot; HSV-2: EIA; TV: wet mount; CT: antigen detection EIA; Gc: culture on Thayer Martin media; syphilis: RPR confirmed by TPPA; Candidiasis: gram stain	No difference in prevalence of any STI between self-reported consistent condom users vs. never and non-consistent users
Antananarivo and Tamatave, Madagascar[15]	Female sex workers	Any unprotected sex in the past 48 hours	Presence of prostate specific antigen (PSA) in provider-collected vaginal samples	PSA: Abbott IMx assay	Twenty-one percent of women who reported no sex for the prior 48 hours had significant levels of PSA present in vaginal swabs
Mombasa, Kenya[16]	Female sex workers	Any unprotected sex in the past 48 hours	Presence of prostate specific antigen (PSA) in self-collected vaginal samples	PSA: Abbott IMx assay	Eleven percent of women who reported either no sex or only protected sex in the past 48 hours tested positive for PSA

III. OVERVIEW OF DATASET

The data used in this dissertation come from a study conducted by Family Health International (FHI) in 2000 called the Measuring the Impact of Male and Female Condom Promotion among Sex Workers in Madagascar study (MCFC-MAD). This chapter will describe the context of the MCFC-MAD study (also referred to as "the parent study"), the design and execution of the study, and the specific data that pertain to this dissertation. Understanding the data and how they were collected will inform how the reader interprets the analyses and results reported in the following chapters. First, I will discuss the Malagasy context.

The Malagasy context: high burden of STI, low but increasing incidence of HIV

Madagascar is an island nation off the south-eastern coast of Africa with a population of approximately 16 million (Figure 2). It is a poor nation; the World Bank estimates that 70 percent of its population lives in poverty.[140] Less than 10 years ago Madagascar had largely escaped the burden of the HIV pandemic, probably because of its geographic isolation, but this appears to be changing. A 1999 estimate put HIV prevalence in Madagascar at 0.15 percent, as compared to its continental neighbor, Mozambique's estimated 13-15 percent HIV prevalence rate.[141] By 2005 the estimated HIV prevalence among adults in Madagascar had increased to 1.8 percent, although a WHO review of the quality of HIV surveillance systems noted some problems with the surveillance in Madagascar, throwing this figure into some doubt.[3, 142] If the rate of HIV infection is indeed increasing in Madagascar, it may be exacerbated by high rates of syphilis and other curable sexually transmitted infections within sex worker and general populations. For example, a 1996 study by Behets, et al. found 12.1% prevalence of

syphilis (RPR and TPHA positive) among women attending antenatal clinics, and 30.5% prevalence among unregistered female sex workers.[143] A more recent study by the same research team found a prevalence of curable STIs of over 70% among sex workers in Antananarivo and Tamatave.[144] Studies have also shown low rates of condom use in the general population and among sex workers: 6.5% in one cohort of rural men (N=401); 9.5% among relatively highly educated hospitalized men and women in Antananarivo (N=134); 5.7% among women and 16.1% among men in a study of STI (N=643) in a coastal rural community; and less than 50% among sex workers (N=316).[145-148]

Besides the low rates of condom use reported in the studies described above, there may be some cultural factors facilitating the high burden of STI in Madagascar. Men are not generally expected to remain monogamous within their marriages and older men often take younger women as sexual partners.[145, 149-151] For example, an ethnographic study of the role of married and single women in a rural area of Northern Madagascar noted that women are much more likely to divorce a husband for not supporting her properly than they are to divorce a husband for having sexual relations with another woman.[149] The epidemiologic evidence bears out these observations. Two studies of STI in four distinct regions of rural Madagascar found that nearly half of all men (46.4% among 401 rural men in three villages and 46% among 310 rural men in a different region) reported having 2 or more sexual partners in the recent past.[145, 148] Both of these studies recruited household by household in their target communities and so are considered to be representative of behaviors in their communities. A study of adolescent sexual behaviors selected 1915 sexually active young people aged 15-24 (957 male) through multistage stratified sampling in peri-urban areas of Toamasina province

(Tamatave is the capital of this province).[152] Over one-third (37.8%) of the young men in this representative sample reported having had 2 or more sexual partners in the past year. Finally, a convenience sample of 134 hospital patients and visitors in rural Antananarivo (63 male) found that 30.2% of the men reported having more than one sexual partner in the past six months.[146] Beyond this evidence of how common multiple sexual partnerships are, one of the studies of rural men found that people with symptomatic STI often undergo traditional treatments rather than face stigmatization by going to the clinic, or are "prescribed" ineffective regimens of antibiotics by unlicensed personnel in pharmacies or other stores.[148]

Design of MCFC-MAD Study and study procedures

In 2001, 1,000 self-identified, active female sex workers were recruited by peer educators (see below for description) in two cities in Madagascar: the capital, Antananarivo, and a major port city in the northeast, Tamatave (Figure 2).

The parent study used an 18-month time series design and had two objectives: (1) to examine the effect of an intervention on condom use and incident STI; and (2) to examine the effect of introducing female condoms in addition to male condoms on condom use and incident STI. To address the parent study objective of determining the effect introducing female condoms would have on the level of protected sex acts, the study was conducted in two phases: Phase I, the male condom phase and Phase II, the female condom phase. Since the parent FHI investigators were interested in isolating the incremental effect of female condoms, they included the male condom phase (Phase I) to create a baseline situation where sound condom promotion for the male condom was

already taking place. While male and female condoms provide equivalent levels of protection against STI,[153, 154] they are approximately 21 times the price of male condoms.[155, 156] Previous studies that examined making the female condom available in public distribution systems found that the female condom provided only slightly higher levels of protected sex acts, but these studies were either observational or compared a female condom promotion to a status quo where there was no equivalent promotion of male condoms.[157-160] A more rigorous cluster-randomized trial of female condom promotion in Kenya found no increased protection from STI related to female condoms, although it did find an overall reduction of incident STI in both intervention and control sites.[161]

In addition to examining the incremental effect of the female condom on level of protected sex acts, the parent study investigators also sought to determine if success in persuading participants to use the female condom would require a more intensive intervention than typical promotions of male condoms due to the female condom's newness and the fact that it is more complicated to use than male condoms. To address this question, the parent study compared the effects of receiving condom promotion via peer education alone ("peer only") to the effects of receiving peer education in addition to clinic-based education ("peer+clinic").

Recruitment of the MCFC-MAD cohort

About half of the 1000 women who participated in the MCFC-MAD study had been participants in a previous study to identify appropriate and effective STI screening and treatment strategies for female sex workers and to evaluate the feasibility and

acceptability of STI treatment programs for female sex workers that provided services in partnership with the women themselves.[144] The previous study (aka IMPACT study) was coordinated by the IMPACT Project and Behets and colleagues at the University of North Carolina at Chapel Hill. At their final visit for the IMPACT study, participants were invited to participate in the MCFC-MAD study. To supplement those women from the IMPACT cohort who agreed to participate in the study, new participants were recruited by peer health educators for the MCFC-MAD study at places where sex work usually occurs (e.g. known establishments where sex workers work).

Since half of the participants had already been participating in an STI prevention program with the IMPACT project, they may have been more familiar with prevention messages and condom use than the newly recruited women. Indeed, the IMPACT carryover participants were more likely to report 100% condom use with both clients and personal partners at baseline than the newly recruited participants, which may have been a result of having participated in the IMPACT project (Table 2). On the other hand, the IMPACT carryover participants exhibited significantly more risk than the newly recruited participants for some behaviors. For example, they reported more sex acts with clients and a higher number of *unprotected* sex acts with clients than did newly recruited participants. However, in regards to the main outcome variable, STI, there was no difference between the two groups at baseline.

Oral informed consent to participate in the study was given by all study participants in Malagasy. Participants signed or made their mark on the consent form in the presence of study staff and a non-study witness. The MCFC-MAD study was approved by the Protection of Human Subjects Committee (PHSC) at FHI and by the

ethical review board of the National Reference Laboratory for HIV/AIDS (Laboratoire Nationale de Réference VIH/SIDA) in Madagascar.

Randomization procedures

In the parent study, participants were randomized at the beginning of each phase (for a total of two randomizations) to receive condom promotion via either peer education alone ("peer only"), or peer education *and* clinic-based education ("peer+clinic") (Figure 3). A computer generated random allocation list stratified by study site was created by the parent study investigators using a block permuted approach with block sizes of 20, 10, and four. Assignment to study arm was accomplished at the initial clinic visit after interview and examination through use of sequentially numbered sealed, opaque envelopes containing the group assignment. Clinic staff and participants were not blinded to group assignment, but STI testing and reporting were done by laboratory staff blind to group assignment.

The first randomization produced statistical equivalence between the participants in each study arm ("peer only" vs. "peer+clinic"). The second randomization was included in the study design to ensure that while evaluating the incremental effect of female condoms and the effect of "peer only" versus "peer+clinic" interventions in Phase II, there was a randomized distribution of participants who had previously received the more intensive "peer+clinic" intervention. What follows is a detailed description of the study procedures for each of the two study phases.

Phase I: Male condom phase

At the beginning of the six-month male condom phase (Phase I), all participants were individually randomized to one of two study arms, either peer education alone (the "peer only" intervention) or peer education in addition to clinic-based education ("peer+clinic" intervention).

Peer educators underwent two weeks of training before Phase I and one week of additional training before Phase II. During the study, the peer educators met weekly with study staff in the clinic to review their work experiences and participate in continuing education sessions. Peer education encounters consisted of 15 minute participant contacts with peers who were also female sex workers. To maximize attendance at follow-up visits, peer educators visited the residence of each participant on the day she was scheduled to report for a follow-up visit. While walking with the participant to the study clinic for the bi-monthly scheduled visits, the peer educators discussed signs and symptoms of STI and the importance of condom use following a Stages of Change model.[162] These "walking" peer intervention sessions were recorded for each participant by the peer educators when they arrived at the clinic. The records included the peer educator's assessment of which stage of behavior change each participant was at during the time of the walking session. (The length of the interaction was not recorded.) These records were also reviewed in the weekly meetings between the peer educators and the study staff. Study participants were not asked to rate how influential their interactions with the peer educators were. Virtually all (99.9%) participants reported having talked to their peer educator about either the male or female condom at each bi-monthly study visit (Table 3).

Participants in the second study arm received the same peer educator promotion ***in addition to*** clinic-based counseling ("peer+clinic" arm). Participants who were assigned to receive the "peer+clinic" intervention met individually with a trained counselor at each study visit for approximately 15 minutes to discuss the same issues of STI recognition and condom use as were discussed by the peer educators. In addition, counselors demonstrated proper use of condoms and gave participants the opportunity to practice the application of both male and female condoms using penis and pelvic models. In designing Phase I, the parent study investigators hypothesized that the addition of more intensive counseling by a health care provider in the clinic (the "peer+clinic" arm) would lead to more consistent condom use (especially with female condoms), as compared to those women in the "peer only" arm.

In Phase I all participants in both study arms had access to male condoms at a subsidized price (about US $0.03/condom) through the study clinic or peer educators.

Phase II: Female condom phase

At the beginning of the 12-month female condom phase (Phase II), participants were again randomly assigned to one of the two study arms, either "peer only" or "peer+clinic". All participants were given access to both male and female condoms at the same subsidized price (US$0.03/condom) in the same locations during the female condom phase (Phase II).

It should be noted that during conduct of the parent study Madagascar experienced a period of political unrest in 2002 following a contested election (for more information see the BBC News archives[163]). Following a December 2001 election, the

incumbent President Ratsiraka refused to accept results proclaiming the victory of Marc Ravalomanana. The crisis was centered in Tamatave, Ratsiraka's hometown and the location of his loyalist troops, but despite this crisis, study procedures continued. The crisis was resolved when Ravalomanana's forces captured rebel provinces and Ratsiraka fled into exile. Madagascar suffered economically because of the crisis,[164] which may have affected the number of clients FSW had access to, especially in Tamatave. Indeed, during a 2004 visit to Madagascar study participants in Tamatave related anecdotally that finding clients in the past 2-3 years had become more difficult. An anthropological study of transactional sex among youth in Tamatave also noted that this political crisis disrupted the sexual economy.[151] This appears to be demonstrated by the declining number of clients study participants reported in Tamatave (Table 4).

Study visits and interviews

Participants were requested to come to the study clinic in their city every two months (for a total of 10 visits; four in Phase I and six in Phase II) to answer a set of questions about their sexual partners and condom use behaviors. Both clinics were public dispensaries that had previously provided services to FSW and were already familiar to the study participants. At each visit, a female interviewer interviewed each participant individually in a private room in the study clinic using a structured questionnaire. The questionnaires took approximately 30 minutes to administer and collected the following information: demographic information about the participant; the number and types of sexual partners the participant had had in the previous 7 days; condom use with clients and personal partners during the last sex act and in the previous 30 days; factors

influencing the risk of STI re-infection, including problems with condom use; and study participants' reports on the interactions they had with peer educators and clinic-based counselors.

Every six months (for a total of four times), during their regular clinic visits and following the interview, participants were seen by a clinician employed solely by the study for diagnosis and treatment of STI. Study women were tested for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*. Since a previous study had shown that HIV infection was very low in this population (0.2% among FSW in 1995),[143] HIV was not considered as a useful outcome measure in this study. Standardized procedures for specimen collection were followed in each of the two sites.[165] An initial stream urine specimen was collected for gonorrhea and chlamydia testing. A swab sample was collected from the posterior fornix of the vagina for immersion in InPouch (BioMed, San Jose, CA, USA) to test for trichomonads.

After the interview and clinical exam were finished, participants who were randomized to the study arm that received clinic-based counseling met with the counselor.

Laboratory methods

In Tamatave all biological samples were taken to a laboratory adjacent to the study clinic immediately following collection. In Antananarivo the specimens were sent daily to the Laboratoire National de Référence (LNR), the national reference laboratory. Project-dedicated laboratory technicians in both sites were trained at the LNR, which was also responsible for quality control at both laboratories. In addition to standard quality control procedures supervised by the LNR (e.g. repeat testing of a sample of specimens),

the study manager met weekly with laboratory technicians to review procedures for sample collection and processing.

Trichomonas infection was diagnosed on-site in both facilities by specially trained laboratory technicians using direct microscopic examination (wet mount preparation) on the day of collection. If trichomonads were not present on direct examination on the day of collection, the samples were retained for 5 days of incubation at 37°C using InPouch and detected by culture after 3, 4, and 5 days. The InPouch method is associated with good sensitivity (from 69.2% to 72.4% compared to Xeno-strip-TV assay and 86.8% compared to other culture media) and 100% specificity.[166-171] In addition, due to a design that combines the ability to do both wet mount microscopy and culture without handling the specimen, InPouch reduces the risk of specimen contamination compared to other culture methods.[166]

Gonococcal and chlamydial infections were diagnosed by ligase chain reaction (LCR) testing (Abbott LCx Probe System, Abbott Laboratories, Abbott Park, IL, USA). Because LCR technology was not available in Madagascar at the time of the study, technicians aliquoted urine samples into two numbered cryovials for each participant which were then stored at -20°C in designated boxes until shipped on dry ice to the Microbiology Core Laboratory of the North Carolina Sexually Transmitted Infections and Topical Microbicides Cooperative Research Center. The Core Laboratory has extensive expertise in nucleic acid amplification testing for detection of sexually transmitted pathogens including *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. The testing was performed according to the manufacturer's protocol. Among the various nucleic acid

amplification tests (NAAT), LCR has been found to be very sensitive[2] (93.5% sensitivity, 99.8% specificity) in detecting gonorrhea and the most sensitive test for diagnosing chlamydia (90.1% sensitivity, 100% specificity) from urine specimens.[172-174]

Treatment regimens for study participants

The prevalence of curable STI (i.e., non-viral infections) was high in this population; approximately 60% of participants at each study visit had at least one curable sexually transmitted infection (Table 5). Therefore, at the same time that they were tested for STI, all participants were presumptively treated for gonorrhea and chlamydia following World Health Organization (WHO) treatment guidelines for sexually transmitted diseases.[175] Participants received a directly observed single-dose of 500mg ciprofloxacin for gonorrhea and 1g azithromycin for chlamydia. Participants with trichomonas infection (direct identification and/or positive culture) received single-dose directly-observed treatment (2g metronidazole).

All of these treatment regimens are associated with excellent cure rates. A randomized controlled trial of syndromic treatment in South Africa found that a single oral dose of 1g azithromycin achieved 95.8% cure for chlamydia and 98.2% cure for gonorrhea.[176] A meta-analysis summarizing 12 trials of the treatment effectiveness of 1g azithromycin for chlamydial infection found a 97% cure rate.[177] Although there has been documentation of gonorrheal resistance to ciprofloxacin, particularly in Asia, ciprofloxacin is still "considered to be the agent with the greatest activity against *N. gonorrhoeae*," according to the WHO.[175] A 1992 study in Madagascar found that all of

[2] Sensitivity and specificity calculated compared to Gen-Probe PACE 2 assay for chlamydia and culture for gonorrhea.

the 46 gonococcal isolates found were sensitive to ciprofloxacin, confirming that there is not ciprofloxacin resistance in the country.[178]

A review of 18 randomized clinical trials found 100% cure rates for male and female genital gonorrheal infections using a 250mg single dose of ciprofloxacin.[179] The WHO and the U.S. Centers for Disease Control and Prevention (CDC) recommend a dose of 500mg of ciprofloxacin to overcome increasing fluoroquinolone resistance among strains of gonorrhea and this is the dosage that was given to MCFC-MAD study participants.[180] A randomized, double-blind study conducted in a U.S. urban STD clinic found that 2g metronidazole was associated with an 84% cure rate for trichomoniasis.[181] This cure rate is lower than the rates noted for gonorrhea and chlamydia treatments, but is only significantly increased if sexual partners are treated simultaneously.[175] Unfortunately, partner treatment is an unrealistic expectation for a population of FSW. Due to these cure rates, we assumed that STIs diagnosed after baseline (at Months 6, 12 and 18) represented new infections rather than partially treated prevalent infections.

Rationale for excluding syphilis from outcome variable

During their clinical visits, a venous blood sample for syphilis serology was also collected from participants. Using the diagnostic methods described above, one can confidently determine a *new* infection of gonorrhea, chlamydia and trichomonas if the client has received proper medication for any previous infections, as the participants in the MCFC-MAD study did. However, a positive syphilis test six months after treatment may be reflecting the previous infection, rather than a new infection. In fact, some patients with adequately treated syphilis may maintain serologic abnormalities for 1-2

years, even extending to lifetime "positive" RPR tests.[182] Furthermore, since syphilis has a longer incubation period, an infection diagnosed in one six-month period may have been acquired in the previous six months. For that reason, syphilis was excluded from the outcome variables for this dissertation.

Parent study results

Phase I of the trial evaluated the relative effects of the two intervention arms and found that participants in the "peer+clinic" arm reported more self-reported condom use than those in the "peer only" arm.[6] At the end of Phase I the odds ratio for incident gonorrhea, chlamydia and trichomonas infection was 0.7 (95% confidence interval (CI): 0.5, 0.9) for participants in the "peer+clinic" arm, as compared to participants in the "peer only" arm. While the "peer+clinic" arm had a statistically significant lower risk of incident STI as compared to the "peer only" arm, the incidence of STI remained high in both study arms at the end of Phase I. In the "peer+clinic" arm 32.1% of participants had new STI infections at the end of Phase I. In the "peer only" arm 41.4% of participants had new STI infections. The parent study authors concluded that these data provided weak support for the hypothesis that clinic-based counseling would significantly contribute to a successful male condom promotion intervention. Results for Phase II are in press.[183]

Socio-demographic characteristics of the MCFC-MAD cohort

As described above, approximately half of the MCFC-MAD participants were in Antananarivo (a.k.a. Tana) and half in Tamatave. At the end of the six-month male condom phase (Phase I), 90.1% of respondents reported for the study visit with no

differences between study sites or study arms (Table 6). By the end of the female condom phase (Phase II), at Month 18, 81.8% of respondents participated in the last study visit. The rate of participation at the end of the study was significantly lower in Tamatave than Antananarivo (78.7% vs. 84.7%, p=0.003) but there were no differences in study arm, participant age, condom use, or STI incidence between those who completed the last study visit and those who did not (data not shown).

At baseline, participants in the two cities were roughly equivalent (Table 4). The average age was 28.3 with a range of 16 to 64 years at baseline. Women in Antananarivo were very slightly older than women in Tamatave (mean 28.4 in Antananarivo, 28.2 in Tamatave). Most women were unmarried, although over 30 percent of participants reported having a regular partner (steady boyfriend, living with someone, or married) (Table 4). In Antananarivo, more women reported being separated or divorced, and cohabiting was much more common than in Tamatave. The reason for this is unknown. By Month 18 the proportion of women in both sites reporting steady personal partners increased (baseline: 22.1% Antananarivo, 36.3% Tamatave; Month 18: 45.2% Antananarivo, 44.7% Tamatave).

On average, at baseline women reported 7.0 clients with whom they had sexual intercourse in the past seven days (range: 0-60) (Table 4). The average number of clients in Antananarivo (7.9 in the past 7 days) was slightly higher at baseline than in Tamatave (average 6.2 clients in past 7 days). Participants in Antananarivo consistently had a larger average number of clients throughout the study. This could possibly be due to the larger size of Antananarivo in comparison to Tamatave, but data were not collected to explain this difference. The number of clients in Antananarivo remained fairly steady,

while the number of reported clients in Tamatave dropped by half over the study period. The average number of personal partners (defined as "a partner who doesn't have to pay you") in the past 7 days did not change from baseline to Month 18 (0.42 in previous 7 days at baseline and 0.44 in previous 7 days at Month 18) but was consistently marginally higher in Antananarivo than Tamatave (data not shown).

As with the number of clients, the average number of sex acts with clients in the past 30 days (number of sex acts with clients in the past 7 days was not collected) decreased in Tamatave from 18.8 at baseline to 9.7 at Month 18, but remained relatively steady in Antananarivo (24.8 at baseline, 23.0 at Month 18). Overall, however, the pattern of client numbers remained stable throughout the study, although more participants reported no clients in the previous 30 days at Month 18 than they did at baseline (Figure 4).

Socio-demographic characteristics of a similar cohort

Although the MCFC-MAD study did not collect additional demographic information on its participants, a published account of socio-demographic characteristics of the IMPACT cohort of FSW exists, from which approximately half of the MCFC-MAD participants were drawn.[53] Reviewing the characteristics of this cohort can lend a better sense of the context in which the participants of the MCFC-MAD study live. The IMPACT cohort also recruited half its participants from Antananarivo and half from Tamatave and found significant differences between the two cities. As in the MCFC-MAD cohort, women in Antananarivo were more likely to report having a personal partner (Antananarivo 67.3%, Tamatave 10.0%). FSW in Antananarivo had an average

of 1.7 children, while those in Tamatave had an average of 1.1 children. In both cities educational levels were low, but women in Antananarivo were less educated than women in Tamatave. In Antananarivo 38.0% of participants had less than primary education, as compared to 23.1% of participants in Tamatave.

Women in Antananarivo were more likely to report sources of income other than sex work than women in Tamatave (31.4% in Antananarivo, 18.4% in Tamatave), but average fees per sex act were lower in Antananarivo than Tamatave (Antananarivo low/high averages US $1.37-$4.56; Tamatave $2.91-$9.06). The total number of clients in the previous seven days was similar between the two cities (Antananarivo 5.9, Tamatave 6.4) and slightly lower than what was observed in the MCFC-MAD cohort at baseline. The most common clients of the FSW were truck drivers (22.0% of clients in Antananarivo, 17.4% in Tamatave) and taxi drivers (Antananarivo 31.4%, Tamatave 15.3%). Participants in the IMPACT cohort reported that client resistance to condom use was very common (70.7% of FSW in Antananarivo reported at least one occurrence during the previous month of a client refusing to use a condom, 69.6% of FSW in Tamatave reported the same) and the MCFC-MAD study found similar percentages at baseline. However, women in Tamatave were more likely to report using condoms 100% of the time with clients in the past month than women in Antananarivo (12.4% in Antananarivo, 28.5% in Tamatave). At the same time, reports of problems using condoms were more frequent in Tamatave than Antananarivo (13.8% reported slippage or breakage of a condom in the past month in Antananarivo, 25.3% in Tamatave reported the same).

As with other reports about female sex workers in Madagascar, the IMPACT cohort had a high two-month incidence of STI after receiving presumptive treatment.[143, 144, 147] (The MCFC-MAD study used the same treatment algorithm as the IMPACT study.) Rates of gonorrhea, chlamydia, syphilis and candidiasis were similar between Antananarivo, but women in Antananarivo were more likely to have trichomoniasis and women in Tamatave were more likely to have bacterial vaginosis. The MCFC-MAD study also found no significant differences between prevalence or incidence of gonorrhea, chlamydia, and syphilis, and also found that women in Antananarivo were more likely to have trichomoniasis (candidiasis and bacterial vaginosis not reported).

Tables

Table 2: Differences between IMPACT carryover participants and newly recruited participants at baseline

	IMPACT carryover participants (N=516)	Newly recruited participants (N=484)	
	Mean	**Mean**	**p-value of t-test for differences**
Age	26.8	28.2	P=0.01*
Number of clients, past 7 days	6.7	6.2	P=0.33
Number of personal partners, past 7 days	0.3	0.4	P=0.02*
Number of sex acts with clients, past 30 days	21.6	18.3	P=0.003*
Number of sex acts with personal partners, past 12 months	65.5	67.2	P=0.83
Number of unprotected sex acts with clients, past 30 days	12.1	6.2	p<0.0001*
Number of unprotected sex acts with personal partners, past 12 months	61.4	53.8	P=0.19
	Percentage	**Percentage**	**p-value for chi-square**
Reporting 100% condom use with clients	14.3	5.8	p<0.0001*
Reporting 100% condom use with personal partners	7.1	2.6	P=0.005*
Positive for any STI	32.0	30.9	P=0.55
Positive for gonorrhea, chlamydia or trichomoniasis	25.4	26.7	P=0.06

* Statistically significant (p<0.05) difference between groups

Table 3: Participant reports of their interactions with peer educators (PE) about condoms by follow-up visit

	Month 6 (N=901)		Month 12 (N=863)		Month 18 (N=818)	
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**
Spoke with PE about male condoms since last study visit	900	(99.9)	657	(76.1)	760	(92.9)
Spoke with PE about female condoms since last study visit	n/a		862	(99.9)	817	(99.9)
Provider in clinic ever talked with participant about using male condoms	676	(75.0)	707	(82.0)	673	(82.3)
Provider in clinic ever talked with participant about using female condoms	n/a		585	(67.8)	549	(67.1)
Obtained female condoms from PE	n/a		250	(29.0)	339	(41.4)

Table 4: Respondent characteristics at baseline and last study visit, Month 18 by study site

	Baseline (N=1000)				Month 18 (N=818)			
	Tamatave (n=500)		Antananarivo (n=500)		Tamatave (n=391)		Antananarivo (n=427)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Age								
29 years or less	298	(59.6)	303	(60.6)	198	(50.6)	224	(52.5)
30 years or more	200	(40.0)	197	(39.4)	192	(49.1)	203	(47.5)
Age unknown	2	(0.4)	0		1	(0.3)	0	
Mean (Median)	28.2 (27.0)		28.4 (27.0)		30.4 (29.0)		30.2 (29.0)	
Marital status*								
Single, without steady boyfriend	312	(62.9)	59	(11.9)†	215	(55.0)	100	(23.4) †
Single, with steady boyfriend	172	(34.7)	101	(20.3) †	133	(34.0)	177	(41.5)**
Cohabiting	1	(0.2)	99	(19.9) †	1	(0.3)	171	(40.1) †
Married, living with/apart from spouse	8	(1.6)	9	(1.8)	42	(10.7)	16	(3.7) †
Widowed	1	(0.2)	32	(6.4) †	0		41	(9.6) †
Separated/divorced	2	(0.4)	198	(39.8) †	0		306	(71.7) †
No response	4	(0.8)	2	(0.4)	0		0	
Number of clients, past 7 days								
None	14	(2.8)	20	(4.0)	101	(25.8)	8	(1.9) †
1-2	70	(14.0)	59	(11.8)	72	(18.4)	41	(9.6)
3-4	152	(30.4)	108	(21.6)**	94	(24.0)	74	(17.3)**
5-6	101	(20.2)	95	(19.0)	58	(14.8)	74	(17.3)
7-10	84	(16.8)	123	(24.6)**	41	(10.5)	93	(21.8) †
11+	59	(11.8)	94	(18.8)**	11	(2.8)	58	(13.6) †
No response‡	20	(4.0)	1	(0.2) †	14	(3.6)	79	(18.5) †
Mean (Median)	6.2 (5.0)		7.9† (6.0)		3.4 (3.0)		7.3† (6.0)	

* Women could report more than one marital status

† p<0.000; ** p<0.05

‡ Includes women who refused to respond, said they didn't know, or said they were menstruating in the past 7 days

Table 5: STI incidence by STI type

	Month 0 (prevalence) (N=1000)		Month 6 (N=901)		Month 12 (N=863)		Month 18 (N=818)		Test for trend*
	N	(%)	N	(%)	N	(%)	N	(%)	p-value
Gonorrhea	224	(22.5)	164	(18.6)	132	(15.4)	93	(11.5)	0.00**
Chlamydia	147	(14.7)	125	(14.1)	77	(9.0)	85	(10.5)	0.00**
Trichomonas	356	(35.6)	327	(36.3)	248	(28.7)	240	(29.3)	0.00**
Syphilis†	303	(30.3)	363	(40.4)	282	(32.9)	299	(36.6)	0.08

Missing values:
Month 0, Gc=3, CT=3, TV=0, syphilis=1, Any=2
Month 6, Gc=18, CT=16, TV=0, syphilis=3, Any=11
Month 12, Gc=3, CT=3, TV=0, syphilis =7, Any=3
Month 18, Gc=10, CT=10, TV=0, syphilis =1, Any=5
* Cochrane Armitage test for linear trend
† RPR and TPPA positive; note: these may not be incident cases as even successfully treated infections will sometimes test as RPR and TPPA positive
** Statistically significant

Table 6: Number of participants at each follow-up visit

Visit No.	No. Participants			Percentage Lost to Follow-up (from baseline)		
	Tamatave	Antananarivo	Total	Tamatave	Antananarivo	Total
0* (baseline)	500	500	1000	-	-	-
1 (2 mo.)	482	489	971	3.2	2.2	2.9
2 (4 mo.)	468	480	948	6.4	4.0	5.2
3* (6 mo.)	438	463	901	12.4	7.4	9.9
4 (8 mo.)	429	459	888	14.2	8.2	11.2
5 (10 mo.)	425	455	880	15.0	9.0	12.0
6* (12 mo.)	418	445	863	16.4	11.0	13.7
7 (14 mo.)	406	443	849	18.8	11.4	15.1
8 (16 mo.)	394	438	832	21.2	12.4	16.8
9* (18 mo.)	391	427	818	21.8	14.6	18.2

* STI tests & treatment performed

Figures

Figure 2: Map of Madagascar

Figure 3: MCFC-MAD study design, 2001-2003

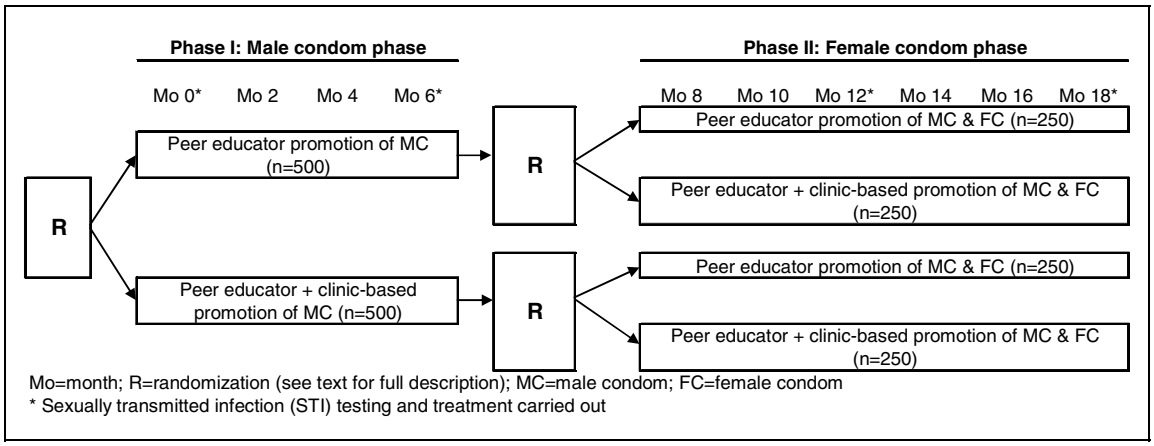
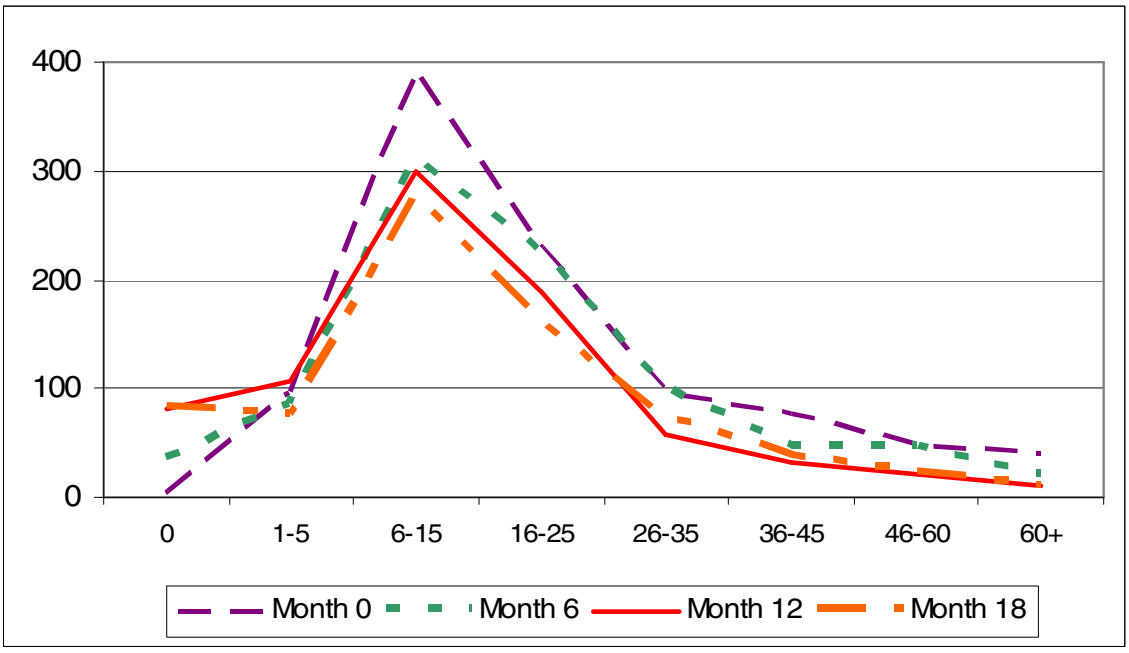


Figure 4: Number of reported sex acts with clients previous 30 days, according to follow-up visit



IV. RESEARCH PLAN AND METHODS

This chapter will focus on the variables of interest in the analyses, discussing how they were measured and how they will be analyzed. It is important to note that paper one and paper two use many of the same variables, but they examine them in different ways and examine different objectives. While both papers used the same outcome measure, STI, the first paper uses STI to examine the validity of self-reported condom use, and the second paper uses STI as an endpoint to explore the risk of unprotected sex with different types of sexual partners. These papers were split in two because the first paper addresses a methodological issue (how confident can we be about self-reported condom use over time?) and the second paper addresses a prevention issue (how important is condom use with personal partners?). The measurement of all the variables used in both papers' analyses will be discussed first. Following this, the analytic approach of each paper will be presented.

Outcome measure: incident sexually transmitted infection

The outcome measure used for both papers is the cumulative six-month incidence of STI. As described above, every six months, during their regular clinic visits, participants were examined and tested for three curable sexually transmitted infections: *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*. Since participants were treated at each six month visit, STIs at visits in Month 6, 12 and 18 were considered incident (new) infections. Because participants were only tested every six months, there is no data on exactly when the new infections were acquired, thus the outcome variable measured a 6-month incidence rate of these three STIs.

At Month 6, the first measurement of incident infection, 51.1% of participants tested positive for at least one of these three STIs. At Month 12, incident STI was 40.9% and at Month 18 it was 39.2 percent (Table 7). Participants in Antananarivo generally had higher rates of STI (particularly trichomonas) than those in Tamatave, although the difference between the two sites decreased over time.

Main exposure of interest: self-reported condom use

Both analyses in this dissertation explore different dimensions of self-reported condom use. Below is a description of how self-reported condom use was measured in the MCFC-MAD study. The particular categorization of self-reported condom use used for each paper is explained in the methods section of that paper.

Sexual History: Numbers and Types of Partners

"In the past 7 days, that is to say since last _____ **(FILL IN DAY OF THE WEEK; SAME DAY AS INTERVIEW)**, with how many different clients have you had sexual intercourse? By 'client,' I mean a sexual partner who has to pay to have sex with you.

In the past 7 days, how many different sexual partners have you had who do not have to pay to have sex with you?"

Every two months peer educators accompanied participants to the clinic, where study clinicians administered a questionnaire on the participants' sexual behaviors. The questionnaire asked the women to report their condom use behaviors with clients and personal partners separately. The first questions respondents were asked were the numbers and types of sexual partners they had had in the previous seven days (see sidebar for exact wording; instructions for the interviewer are bolded). Starting with a shorter recall period and then moving to a longer period may assist respondents in remembering events accurately.[45]

Respondents were next questioned about their condom use with clients. To minimize social desirability pressure on respondents, the interviewers began this section by emphasizing the confidentiality of the respondent's answers, and explained that their honest responses would be most helpful to the study (see sidebar for exact wording). Questions covered the last sex act, decision-making regarding condom use, and the number of protected sex acts with clients in the past 30 days. This continuous measure was calculated by subtracting the number of times the respondents reported using a male or female condom with a client from the total number of sex acts the respondents said they had with clients. If respondents had difficulty determining a number, interviewers were instructed to assist them by recording week-by-week or month-by-month numbers and then computing the sum.

Condom use with clients

"READ: As I have mentioned before, we are looking for ways to help young women like yourself to protect their health. Please think about these questions carefully and respond as honestly as possible. You will help us greatly by sharing accurate information with us. Remember that I will keep your answers private: Your name will not be written on this form, and will never be used in connection with any of the information you tell me.

I would like to continue by asking you questions about your recent sexual experiences with clients. Recall that by "clients," I mean sexual partners who have to pay to have sex with you.

The last time you had sex with a client did you and your client use a condom?

Now I would like you to think about all the times you have had sex with clients over the past 30 days. That would be between today and (**GIVE DATE 1 MONTH PRIOR**). About how many sex acts in total did you have with clients over those past 30 days?

ALLOW THE RESPONDENT TIME TO MAKE THIS ESTIMATE. IF SHE HAS TROUBLE, ASSIST HER IN CONSIDERING THE TOTAL NUMBER OF SEX ACTS WITH CLIENTS WEEK-BY-WEEK, THEN HELP HER TO COMPUTE THE SUM.

Of those (fill in number from Q above) sex acts, about how many times did you use a male condom?

Of those (fill in number from Q above) sex acts, about how many times did you use a female condom?"

Respondents were asked for the same information about personal partners, but for the previous 12 months. The recall periods for clients and personal partners were different following suggestions in the literature current at the time that the study protocol was written that frequent events (such as sex with clients) would be reported more accurately over a shorter period.[34, 35, 46] The longer recall period for personal partners reflected the fact that many of the FSW live away from home and only see their personal partners infrequently.

Overall, self-reported condom use increased over time, primarily with clients. Thus, the total number of unprotected sex acts with clients decreased (Table 9). The average monthly number of unprotected sex acts with personal partners did not change over the 18 months of the study.

At baseline, women in Tamatave were less likely to use condoms with either clients or personal partners than women in Antananarivo. Over time, the difference in condom use with clients between sites decreased (Table 10). The intervention had very little impact on condom use with personal partners, especially for women in Antananarivo. Women in Tamatave were less likely to use condoms with personal partners than women in Antananarivo, and this difference persisted throughout the study (Table 9). Comparing the proportion of respondents who said they used condoms 100% of the time with those who said they used a condom at the last sex act, it appears that last sex act is not a good proxy for consistent condom use and would exaggerate the rate of consistent condom use significantly (Table 9).

Other measured variables of interest

In order to evaluate the association of interest between self-reported condom use and incident STI, several covariates (see below) hypothesized to be related to self-reports, condom use or STI were examined in the analyses. These associations were examined graphically by constructing a directed, acyclic graph (DAG) (Figure 5). Besides age, all variables were measured anew at all of the four time points (Months 0, 6, 12 and 18).

- *Age.* Younger women were more likely to have STI than older women and thus the association between baseline age and STI was not linear on a logit scale. To account for this, it was necessary to categorize the variable rather than use it in its continuous form. Examining the odds ratios for STI by categorized age, it appeared that the risk of STI began to drop after age 25. Therefore, rather than dichotomizing at the median age, the variable was dichotomized at 25 years of age to better capture the risk associated with younger or older age. (The distribution of age is described in the previous chapter.)
- *Personal partner status.* Marital status was dichotomized by whether women reported currently having a personal partner or not. Women who were single with steady boyfriends, were cohabiting with a boyfriend, or were married and living with their spouse, were considered to be coupled. Women who said they were single without a steady boyfriend, or who reported their marital status as married, but living apart, divorced, separated, or widowed and did not report a boyfriend were considered single. At baseline, 61.1% of respondents reported they were single; at Month 18 only 39.5% of respondents said that they were single (data not shown).

- *Total number of clients had sexual intercourse with in the previous 7 days.* Respondents were asked a separate question about their total number of reported clients in the previous seven days.
- *Total number of personal partners with whom had sexual intercourse in the previous 7 days.* Respondents were also asked a separate question about the total number of personal partners with whom they had sex in the previous seven days.
- *Total number of sexual partners in the previous 7 days.* As described above, participants responded separately to a question about the total number of sexual partners they had in the previous 7 days. This variable includes both clients and personal partners. On average at baseline, respondents reported having had 7.3 sexual partners in the previous 7 days (median: 5.0; range: 0-61). This average decreased over time and at Month 18 respondents reported 5.1 total sexual partners in the previous 7 days (median: 4.0; range: 0-51).
- *Problems with condom use.* Problems with condoms were also assessed for the previous 30 days and included condom breakage and significant slippage (e.g. a male condom slipping off the penis or a female condom slipping out of place during intercourse) for both male and female condoms. At baseline nearly a quarter of respondents (22.3%) reported a condom problem in the previous 30 days, but at Month 18 this proportion had decreased to 10.6 percent (Table 10).
- *Client resistance to condom use.* Client resistance to condom use was measured with two direct questions posed to the participants: whether in the previous 30 days a client had offered more money for sex without a condom; and if there had been a time when the participant wanted to use a condom but the client refused. Nearly two-thirds of

respondents (64.6%) reported client resistance to condom use at baseline, but by Month 18, only 27.3% of respondents reported experiencing any client resistance (Table 10).

- *Refusal of unprotected sex.* A participant's willingness to refuse unprotected sex was assessed by asking if she had refused to have sex with a client in the previous 30 days because the client refused to use a condom. At baseline, half of respondents (53.0%) reported at least one instance of refusing unprotected sex with a client in the previous 30 days; this proportion remained essentially unchanged at Month 18 at 49.9 percent (Table 10).
- *Symptoms of interim STI infection.* Signs of STI infection between study visits were assessed by questions about perceived STI symptoms since the last visit or use of medication for STI symptoms since the last visit. These signs decreased over time in the study; at baseline 44.0% of respondents had a sign of an STI since last treatment, whereas at Month 18 only 18.6% had an STI sign between clinic visits.
- *Use of contraception.* Use of contraception includes all modern contraceptives except condoms. Contraceptive use was relatively rare; at baseline 16.8% of respondents reported using a contraceptive method and at Month 18 14.4% reported using a contraceptive.
- *Experience of violence.* Participants' experience of violence was measured by asking if they had been raped, forced to have sex or beaten in the previous 30 days. Reported experience of violence was very rare in this population. At baseline, 3.7% of respondents reported an experience of violence in the previous 30 days. At Month 18, only 0.2% of respondents reported similar experiences.

Finally, the two intervention groups ("peer only" and "peer+clinic") and the two study cities (Tamatave and Antananarivo) were examined as potential confounders and study site was examined as a potential effect modifier.

Analytical approach: Paper One

The objectives of Paper One were (1) to determine if there was an association between recent self-reported condom use and STI incidence; and (2) to determine if the association between self-reported condom use and STI incidence changed as female sex workers spent increasing time as research participants. As with any longitudinal data analysis, the first step of analysis for Paper One was to examine trends using graphs and tables of summary statistics. Then separate analyses were done for each time point and the change from the previous time point calculated. Potential confounders for the multivariate model were identified on the basis of the directed, acyclic graph (DAG) described above (see Figure 5). The analysis in Paper One used three time points, Months 6, 12 and 18, as those were the only visits where incident STI was measured.

Multivariate analysis

Since this cohort of women was measured repeatedly for outcomes and exposures, the data are clustered within subject. This clustering does not meet the standard regression requirement of statistically independent observations, thus calling for regression methods that take into account the correlations in the data. A Generalized Estimating Equation (GEE) model is preferred because it efficiently accounts for the correlated observations, but does not require perfect specification of the structure of these correlations to produce unbiased estimates and standard errors.[117] A GEE model is also

appropriate because it calculates population-averaged estimates. In this analysis, subject-specific correlation was not expected, but rather population-wide concurrence between the two factors of interest.[184]

Some basic assumptions must be met to use a GEE model, although some of them can be relaxed: the number of subjects/clusters must be large (>100); there should be little or no missing data, or the data should be missing completely at random; and the clusters/individual subjects should be independent from each other. The data from the MCFC-MAD study meet the sample size requirement. No pattern-ness in missing values was identified through looking at gaps in follow-up and dropouts and examining whether they were related to either the outcome (e.g. women with STI were more likely to dropout) or the point in time. Non-informative missing does not pose problems for GEE analysis of the data. There was very little missing data in the outcome variable (Table 7); however, there were many missing observations regarding self-reported condom use in the case where respondents did not have any sexual acts in the reporting period. An advantage of GEE analysis is that it does not exclude cases with incomplete data, which makes these missing data less worrisome.[185] Despite the fact that there may be some dependencies in outcome between individual women, it is anticipated that these were small and that the independence of individual subjects can be assumed.

In order to calculate the most efficient and accurate standard errors and variance for the GEE model, a covariance structure of the outcome variables ("working correlation matrix") must also be defined. To do this, an unstructured working correlation matrix was specified and the pairwise correlations estimated by the model examined. A disadvantage of the unstructured matrix is that it requires more parameters than other

matrices; however, this was of little concern in this large sample. An exchangeable working correlation matrix was also a good option for this analysis, since exchangeable matrices assume that the variation between clusters is much stronger than within clusters. This is a good assumption for a study that is making repeated measurements on individuals, since it assumes that measurements within an individual are more correlated than measurements between individuals. Alternatively, an auto-regressive working correlation matrix assumes that measurements of the same individual closer in time are more similar than those more distant in time from each other and may also be a good correlation matrix for longitudinal analyses.[185]

Since the outcome variable was dichotomous, a logistic regression model was used. The principal independent variable was the estimated number of unprotected sex acts in the previous 30 days for both partner types. A variable measuring the time effect and a time interaction term (time x self-reported condom use) was inserted into the GEE regression model to demonstrate the direction and the statistical significance of the association between the predictive ability of self-reports and time. The time effect variable was used to answer the primary question of whether the quality of self-report degenerated or improved over time. The time interaction term is also necessary to produce an odds ratio for time points other than the reference time point.

Covariates were assessed to determine whether they confounded the relationship between self-reported condom use and STI. If the removal of a covariate changed any of the main exposure estimates by more than 0.10 as measured by the natural log of the adjusted estimate divided by the non-adjusted estimate (LN(adjusted / unadjusted)), the covariate was judged to be affecting both the exposure and outcome variables and

confounding their relationship, thus it was retained in the model. Covariates were also examined for possible effect measure modification by comparing stratified odds ratios (OR). For example, effect modification by study site was examined by comparing whether ORs for Tamatave were statistically significantly different than those for Antananarivo.

Analytical approach: Paper Two

The analysis in Paper Two also used STI incidence as its dependent variable. This paper examined the association between STI and self-reported condom use using a different perspective, however. The objective of Paper Two was to determine if unprotected sex with personal partners among FSW is associated with a higher risk of STI compared to FSW who report consistent condom use with personal partners. Thus self-reported condom use was compared between different types of sexual partners.

Although women were interviewed 10 times about their condom use with clients and personal partners, the long recall period for personal partners (12 mos.) resulted in overlapping measurements of condom use with personal partners for the four time points where STI was measured (each 6 months apart). For the analysis in Paper 1, this overlap was ignored to profit from the additional information of the three visits where incident STIs were measured. However, since the principal focus of Paper 2 was the influence of reported condom use with personal partners, it was preferable to use only those measurements that occurred at non-overlapping time points. Therefore, the analysis for Paper 2 used only data from Months 6 and 18.

Because the model included repeated measurements of the same subject, which produces correlated observations, a GEE model was also used for this analysis. An alternative to including 2 measurements in one model is to run two cross-sectional logistic regression models, however this does not allow for the assessment and control of the effect of time itself. A significant time effect would indicate that the odds of infection changed from one time point to the next. Especially if the odds decreased from baseline to the end of the study, this might signify a decrease in the prevalence of infection among the participants' partners. It might also reflect more strategic condom use by sex workers. Time was also examined for any effect modification using interaction variables. The confirmation of time as an effect modifier would indicate that patterns of condom use had different effects on the odds of infection at different time points.

As with the analysis in Paper 1, the possible confounding influence and effect measure modification of several variables were considered for this model, as described in the results section of the manuscript.

Tables

Table 7: Six-month incidence of gonorrhea, chlamydial or trichomonas infection by study site and follow-up visit

	Month 6				Month 12				Month 18			
	Tamatave (N=438)		Antananarivo (N=463)		Tamatave (N=418)		Antananarivo (N=445)		Tamatave (N=391)		Antananarivo (N=427)	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Gonorrhea*	86	(19.6)	78	(16.9)	53	(12.7)	79	(17.8)	45	(11.5)	48	(11.2)
Chlamydia†	45	(10.3)	80	(17.3)	27	(6.5)	50	(11.2)	38	(9.7)	47	(11.0)
Trichomonas**	119	(27.2)	208	(44.9)	85	(20.3)	163	(36.6)	95	(24.3)	145	(34.0)
Total Gc, CT, and TV‡	187	(42.7)	254	(54.9)	141	(33.7)	212	(47.6)	143	(36.6)	178	(41.7)

*Missing: Mo. 6, 18; Mo. 12, 3; Mo. 18, 10
†Missing: Mo. 6, 16; Mo. 12, 3; Mo. 18, 10
**Missing: Mo. 6, 0; Mo. 12, 0;
‡Some clients tested positive for more than one of the three outcome STIs.

Table 8: Number of unprotected sex acts, according to partner type

	Clients*		Personal Partners†	
	Baseline (N=983)	Month 18 (N=683)	Baseline (N=463)	Month 18 (N=444)
25% percentile	1.0	0.0	1.17	1.33
Median	5.0	0.0	4.0	4.0
75% percentile	13.0	2.0	8.0	8.0
Mean	10.5	2.1	5.6	5.5
Range	0-198	0-40	0-32	0-63
Missing values**	17	135	537	374

* Previous 30 days † Average monthly estimate for previous 12 months
** Missing values could be due to non-response, don't know, or did not have sex acts with that partner type in previous 30 days.

Table 9: Condom use with clients and personal partners by site

Percentage of protected sex acts with clients (previous 30 days)

	Baseline (N=1000)				Month 18 (N=818)			
	Tamatave (n=500)		Antananarivo (n=500)		Tamatave (n=391)		Antananarivo (n=427)	
	N	(%)	N	(%)	N	(%)	N	(%)
0%	63	(12.6)	34	(6.8)	6	(1.5)	5	(1.2)
1% - <25%	40	(8.0)	66	(13.2)	6	(1.5)	10	(2.3)
25% - <50%	99	(19.8)	88	(17.6)	14	(3.6)	12	(2.8)
50% - <75%	129	(25.8)	103	(20.6)	43	(11.0)	27	(6.3)
75% - <100%	73	(14.6)	90	(18.0)	42	(10.7)	66	(15.5)
100%	90	(18.0)	108	(21.6)	194	(49.6)	256	(60.0)
No reported sex with clients	2	(0.4)	3	(0.6)	84	(21.5)	0	
Missing*	4	(0.8)	8	(1.6)	2	(0.5)	51	(11.9)

Percentage of protected sex acts with personal partners (previous 30 days)

	N	(%)	N	(%)	N	(%)	N	(%)
0%	111	(22.2)	225	(45.0)	149	(38.1)	188	(44.0)
1% - <25%	26	(5.2)	30	(6.0)	8	(2.1)	56	(13.1)
25% - <50%	10	(2.0)	15	(3.0)	12	(3.1)	22	(5.2)
50% - <75%	11	(2.2)	15	(3.0)	7	(1.8)	29	(6.8)
75% - <100%	4	(0.8)	16	(3.2)	6	(1.5)	21	(4.9)
100%	10	(2.0)	39	(7.8)	26	(6.7)	50	(11.7)
No reported sex with personal partners	318	(63.6)	155	(31.0)	179	(45.8)	3	(0.7)
Missing*	10	(2.0)	5	(1.0)	4	(1.0)	58	(13.6)

Used condom at last sex act with a client

	N	(%)	N	(%)	N	(%)	N	(%)
Yes	239	(47.8)	289	(57.8)	335	(85.7)	388	(90.9)
No	261	(52.2)	210	(42.0)	55	(14.1)	39	(9.1)
Missing†	0		1	(0.2)	1	(0.3)	0	

Used condom at last sex act with a personal partner

	N	(%)	N	(%)	N	(%)	N	(%)
Yes	27	(5.4)	76	(15.2)	45	(11.5)	124	(29.0)
No	158	(31.6)	147	(29.4)	175	(44.8)	302	(70.7)
Missing†	315	(63.0)	277	(55.4)	171	(43.7)	1	(0.2)

* Missing values could be due to non-response, don't know, or did not have sex acts with that partner type in the previous 30 days.

† Missing values could be due to non-response, don't know, or did not have sex acts with that partner type.

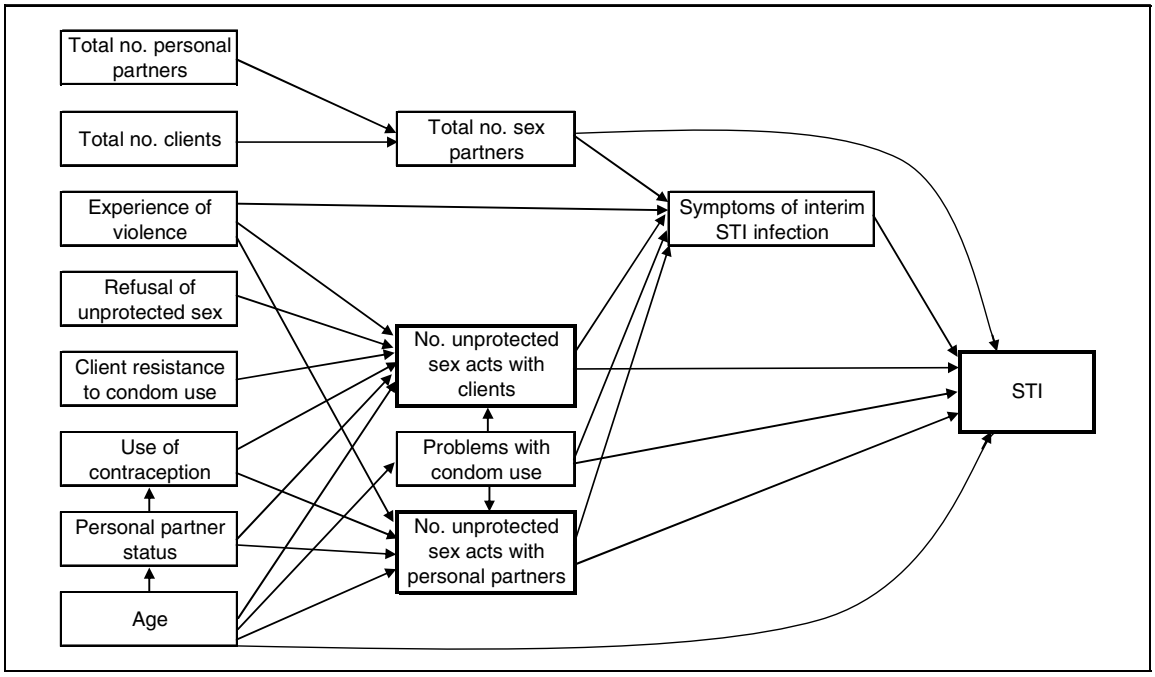
Table 10: Covariates at baseline and last study visit, Month 18 by study site

	Month 0 (N=1000)				Month 18 (N=818)			
	Tamatave (n=500)		Tana (n=500)		Tamatave (n=391)		Tana (n=427)	
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
Had condom break, slip or tear in previous 30 days								
Yes	82	(16.4)	141	(28.2)	34	(8.7)	53	(12.4)
No	416	(83.2)	357	(71.4)	322	(82.4)	355	(83.1)
Missing*	2	(0.4)	2	(0.4)	35	(9.0)	19	(4.5)
Client resistance to condom use in previous 30 days								
Yes	338	(74.9)	308	(61.6)	112	(28.6)	111	(26.0)
No	113	(25.1)	192	(38.4)	194	(49.6)	265	(62.1)
Missing*	49	(9.8)	0		85	(21.7)	51	(11.9)
Refused to have sex unprotected sex with a client in previous 30 days								
Yes	212	(42.4)	318	(63.6)	189	(48.3)	219	(51.3)
No	285	(57.0)	182	(36.4)	118	(30.2)	157	(36.8)
Missing*	3	(0.6)	0		84	(21.5)	51	(11.9)

* Missing may be due to a “don’t know” or no response, or because the respondent reported no sex acts with clients in the past 30 days.

Figures

Figure 5: Directed, acyclic graph (DAG) describing associations between outcome and exposure variables, and possible confounding variables



V. RESULTS: PAPER ONE

Association between self-reported condom use and incident sexually transmitted infections over time in a cohort of female sex workers in Madagascar

Abstract

Background

Self-reported condom use may not be an accurate measure of actual condom use. Evidence surrounding the association between self-reported condom use and sexually transmitted infections (STI) is mixed. We employed data from an 18-month study of 1000 female sex workers (FSW) to examine whether this association changes over time.

Methods

During an 18-month intervention study, every six months, participants were tested and treated for STI, generating data on incident infections across 3 time points. We examined using separate logistic regression models the association between incident STI and self-reported condom use at each time point. Change over 18 months was evaluated using a longitudinal generalized estimating equation (GEE) regression model.

Results

Rates of incident STI decreased by 24.0% over the study period (from 51.9% to 39.5%), while the total number of reported unprotected sex acts decreased by 63.6% (from 13.2 per month to 4.8 per month). Overall, none of the categories of self-reported condom use was significantly associated with incident STI at any time point. No dose-response relationship was observed. An increased number of reported unprotected sex acts was not associated with a greater risk of STI. We found no clear trend between time or level of unprotected sex and increasing number of unprotected sex acts.

Discussion

Self-reported condom use was not significantly associated with STI incidence at any single time point in this cohort, and the association did not change over time, casting doubt on the accuracy of self-reported condom use.

Background

Sexual risk reduction programs often use self-reported condom use as an indicator for measuring success. This measure may not, however, be an accurate measure of actual condom use. Self-reported condom use is subject to biases including recall[29, 35, 45] and social desirability bias[69, 92] associated with reduced validity.[22, 57, 186] Of 17 published studies concerning the association between self-reported condom use and sexually transmitted infections (STI) nine reported no association, and eight reported some association.[9, 10, 15, 16, 29, 70, 91, 124, 126, 131-138] Of studies that found a significant association between self-reported condom use and a sexually transmitted infection, five used prevalent measures of STI, which preclude ascribing a causal association between the reported condom use and the presence of infection.[29, 70, 132, 133, 137] By contrast, six of the nine studies reporting no association used either incident cases of STI or biomarkers,[9, 10, 15, 16, 124, 131, 136] thus appearing to provide stronger evidence supporting a lack of association. Among these 17 studies, five used populations of female sex workers (FSW) in Africa and these studies were evenly split between finding an association and not.[15, 16, 29, 137, 138]

We explored the association between condom use as reported by FSWs and risk of STI using data from a condom promotion intervention in two cities in Madagascar. Our study had two objectives: (1) to determine if there was an association between self-reported condom use and STI incidence; and (2) to determine if the association between self-reported condom use and STI incidence changed as FSW spent greater amounts of time as research participants. We hypothesized that given a high baseline prevalence of

STI in this population, as well as the advantages of measuring incident STI, we would observe a dose-response relationship between lower reports of unprotected sex acts and lower STI incidence.

Over time research study participants became more familiar with the study personnel and at the same time, were repeatedly receiving messages emphasizing the importance of condom use. This process may have increased the pressure on participants to give what they considered to be socially desirable responses, whether the responses actually reflected their behaviors or not. On the other hand, a longitudinal study could result in increased rapport and trust between interviewer and respondent, eliciting more truthful reporting about undesirable behaviors over time. We further explored the hypothesis that this relationship would change over time as a result of changing experiences of social desirability pressure.

Methods

We used data from a randomized controlled trial of condom use promotion conducted from 2001-2003 in Antananarivo, the capital city, and Tamatave, a port city in the northwest of Madagascar.[6] One thousand self-identified, active FSW were followed during an 18-month study, which had two phases: Phase I, the male condom phase, and Phase II, the female condom phase.[183]

Participants were randomized at the beginning of each of the two phases to receive condom promotion via either peer education alone ("peer only"), or peer education *and* clinic-based education ("peer+clinic"). In Phase I all participants in both study arms had access to male condoms at a subsidized price (about US $0.03/condom)

through the study clinics or peer educators. In Phase II, all participants were given access to both male and female condoms at the same subsidized price.

Participants were interviewed every two months to collect demographic and sexual behavior information. Every six months, participants were tested for *Neisseria gonorrhoeae*, and *Chlamydia trachomatis* using ligase chain reaction (LCR) testing (Abbott LCx Probe System, Abbott Laboratories, Abbott Park, IL, USA) and InPouch (BioMed, San Jose, CA, USA) for *Trichomonas vaginalis*. These procedures have been more fully described elsewhere.[6, 183]

Participants were presumptively treated for gonorrhea and chlamydia every six months and based on laboratory diagnosis for trichomoniasis. We assumed that incident STIs represented new infections since the treatment regimens used have excellent cure rates.[176, 177, 179-181]

The outcome measure used for this analysis was the cumulative six-month incidence of STI, defined as the respondent testing positive for gonorrhea, chlamydial or trichomonas infection at any of the six-month follow-up visits, Months 6, 12 and 18.

Male and female condoms provide equivalent levels of protection against STI.[154] Reports of female and male condom use were combined for this analysis after stratified analysis failed to show that self-reported condom use and incident STI was different for women who reported female condom use and women who reported no female condom use.

The exposure variable of self-reported condom use was operationalized as the estimated total number of unprotected sex acts with all partners in the 30 days prior to the interview. Respondents reported separately on partners who had to pay to have sex with

them (clients) and personal partners who did not have to pay to have sex with them (e.g., boyfriends). At each interview, respondents were asked to report the total number of sex acts they had with clients in the previous 30 days, and the total number of those acts where a male or female condom was used. Respondents were asked the same questions about sexual behavior with personal partners, but for the previous 12 months. Participants were asked to recall behaviors with their personal partners over a longer recall period to capture irregular behaviors for women living distant from their personal partners. To make the data about personal partners comparable to that about clients, the personal partner estimates were divided by 12 to represent a monthly average. Women who reported not having had a personal partner in the past 30 days were counted as having had zero unprotected sex acts with personal partners in the previous 30 days, even if a 12 month estimate was available. The estimated exposure measure was then the sum of these two variables. The estimated total *number* of unprotected sex acts was used as the exposure measure because it represents an absolute measure of the risk, giving weight to each individual exposed sex act.[12, 31]

Univariate analysis showed that the number of unprotected sex acts was not normally distributed; therefore the number of unprotected sex acts was analyzed as a categorical rather than a continuous variable. Four categories were defined for the average number of unprotected sex acts in the previous 30 days: Zero=0 unprotected sex acts; Few=1-3 unprotected sex acts; Some=4-10 unprotected sex acts; and Many=10+ unprotected sex acts.

Covariates hypothesized to be related to self-reports, condom use or STI were examined. Besides age and baseline STI status, time-varying covariates examined

included: having a steady personal partner; reported total number of sexual partners in the previous 7 days by partner type; condom breakage or slippage in the previous 30 days; client resistance to condom use in the previous 30 days; refusal of unprotected sex in the previous 30 days because the client refused to use a condom; symptoms of interim STI infection; use of non-barrier contraception; rape, forced to have sex or beaten in the previous 30 days.

Finally, the two intervention groups (*Study arm*) and the two study cities (*Study site*) were examined as potential effect modifiers and confounders.

The data were analyzed using SAS 8.02 (SAS Institute, Inc., Cary, North Carolina). Bivariate comparisons of differences in proportions and means were examined using chi-square tests and t-tests respectively, in COMPARE2 version 1.45, a WIN-PEPI program (available at www.brixtonhealth.com). Missing data were rare and all available data were used for the analyses.

To examine the association between incident STI and self-reported condom use at each individual time point, separate logistic regression models were constructed. To examine any change in this association over time, a longitudinal regression model was completed using all three time points that had data on incident STI. Generalized estimating equation (GEE) analysis (auto-regressive working correlation matrix) was utilized in this multi-time point model to account for the clustering among observations of the same individual. To test the hypothesis that the association changes over time, the model included interaction terms for each level of condom use with each level of time. A statistically significant interaction term ($p<0.05$) would indicate that the association of interest was different at different time points.

To determine if covariates were effect modifiers, stratified analyses were conducted. A variable was considered an effect modifier if the odds ratios were statistically significantly different ($p<0.05$) between the levels of stratification. The fully adjusted model included covariates (i.e. potential confounders) hypothesized to be related to STI, successful condom use and self-report behaviors. Covariates were assessed using backward stepwise elimination to determine whether they confounded the relationship between self-reported condom use and incident STI. If the removal of a covariate changed any of the main exposure estimates by more than 0.10 as measured by the natural log of the adjusted estimate divided by the non-adjusted estimate (LN(adjusted/unadjusted)), it was judged to confound the relationship and was retained in the adjusted model. A test of heterogeneity was used to examine changes over time in the longitudinal model.

The analysis was approved by the ethics committee at the University of North Carolina at Chapel Hill's School of Public Health. The parent study was approved by the ethics committees of the National HIV/AIDS Reference Laboratory in Madagascar, and Family Health International (FHI) in North Carolina, United States.

Results

Over three-quarters of respondents (81.8%) participated in the last study visit. The rate of attrition was higher in Tamatave than Antananarivo (21.3% vs. 15.3%, $p=0.003$) but there were no differences in participant age, condom use, or STI at baseline between those who dropped out of the study and those who completed the last study visit by study site. The mean age of participants at baseline was 28.3 (median 27.0; range, 16-

64). Most women were unmarried. Nearly 40% of participants reported having a personal partner at baseline and this proportion increased over time (Table 11).

At baseline women reported having had sex with a median of 5.0 clients (mean, 7.0; range, 0-60) in the previous 7 days. By Month 18, this number had decreased to 4.0 (mean, 5.3; range, 0-50; t-test for difference in means: t=5.86, p=0.000). Most of this decrease occurred in Tamatave. The number of personal partners remained essentially unchanged (mean at baseline 0.4, mean at Month 18 0.4).

The estimated number of reported unprotected sex acts decreased during the study, largely due to decreases in the number of reported unprotected sex acts with clients (Table 12). At baseline, 65.6% of respondents said they did not use condoms with personal partners and at Month 18 this was reported by 58.7 percent. While rates of incident STI decreased by 24.0% over the study period (Cochrane-Armitage test for linear trend, $p<0.0001$) (Table 13), the total number of reported unprotected sex acts decreased by 63.6% (Mann-Kendall test for trend, $p<0.05$) (Figure 6).

Single time point models

The initial modeling examined the association between self-reported condom use and incident STI at individual time points (Table 14). Overall, none of the categories of self-reported condom use was significantly associated with incident STI at any of the three time points. Furthermore, no dose response relationship was observed between number of reported unprotected sex acts and the estimated risk of incident STI.

Longitudinal model

In the longitudinal analysis, the odds ratios for STI incidence at all time points and all levels of unprotected sex acts were very close to the null value with confidence

intervals that included 1 (Table 15). Furthermore, we evaluated the sets of odds ratios at each level of self-reported condom use to determine if there were any significant variations over time. We found no significant differences across the odds ratios from Month 6, Month 12 and Month 18 for few, some and many unprotected sex acts. The odds ratios by time and level of unprotected sex graphed in Figure 7 illustrate the lack of trend.

Discussion

We failed to find an association between self-reported condom use and incident STI at any single time point in this cohort, and the association did not change over time. Furthermore, we observed no dose-response relationship between reports of unprotected sex acts and incident STI.

While self-reported condom use has an intrinsic value as a measure of the mechanism of action (behavior change) of most STI prevention programs, there is controversy over whether it can serve as a proxy for STI incidence.[1, 7, 9, 10, 18, 22, 125, 126] As mentioned previously, other studies examining this association have yielded mixed results. Our study falls on the side of no observed association. The risk of STI for an individual sex act is principally determined by the prevalence of infection in the sexual network and thus the infection status of individual sexual partners. Increased condom use in a sexual network should in theory result in a lower incidence of STI (e.g. dose response model), although the strength of any would depend on a complicated constellation of factors affecting individual-level risk (including, for example, individual susceptibility). To observe changes in incident STI as a consequence of increased condom use, one would need to look at large numbers of people, over a long time period,

and do so in a population with a high incidence of infection.[130] High STI rates may be necessary for the use of STIs as biological validation of self-reported condom use.[10] Our cohort of FSW was a good population in which to examine this association because they had high numbers of sex partners and high rates of STI.[3]

Our findings illustrating increases in "0" unprotected sex acts and decreases in "1 or more" unprotected sex acts (Table 12) suggest that social desirability pressures may have led participants to report their behaviors inaccurately. Other studies similarly support this notion. For example, female study participants in Cameroon reported that participants often did not give truthful answers to questions about condom use because of a desire to meet the interviewers' expectations (social desirability bias).[65] A countervailing hypothesis is that participants might have felt increasingly more comfortable reporting truthfully to interviewers over time, and been increasingly influenced by the condom promotion messages, which would have presumably resulted in more accurate reporting. A U.S. study among youth found that substance use was under-reported when the respondent was familiar with the interviewer from previous interviews, and that the prospect of a future interview with the same person also affected responses.[115] It is possible that both increased trust and increased pressure resulted in equal effects on reporting and balanced each other out, but unlikely that if either had a strong effect it would be completely balanced by the other. We were not able to examine alternate effects of being interviewed by the same person at every visit or being

[3] Note: we observed a decrease in the mean number of clients seen per week in one of the study cities. The decrease may have been due to civil unrest, a subsequent economic depression centered in this city and a decrease in activity in the local commercial sex industry.[163. BBC News. Madagascar turmoil: BBC News, 2002, 164. afrol News. Poverty deepened in Madagascar. *Article in Economy-Development section*, 2003.)

interviewed by a variety of interviewers because each study site had only one interviewer throughout the study.

There are several possible study-related explanations for the lack of association observed between self-reported condom use and incident STI. An obvious issue is problems in measuring the exposure variable, self-reported condom use. Two different recall periods were combined in the self-reported condom use variable: 30 days (clients) and 12 months (personal partners). Furthermore, since the three time points (Months 6, 12, and 18) used for this analysis are 6 months apart, the 12-month recall period for personal partners overlaps from one time point to another. The longer recall period for personal partner data may make these data subject to more recall bias, but to exclude personal partner data would limit the usefulness of the data since many sexual acts, most of them unprotected, would be unaccounted for. A 30-day recall period may have also been too long for accurate recall; however, using 'last sex' as an alternative might not be representative of typical behaviors and there were no other measures available in this study.

The influence of unmeasured confounding factors might also explain a lack of association. We have no information, for example, about the sexual behaviors and infection status of the participants' clients and personal partners. If a large proportion of the FSW in this study were having unprotected sex with uninfected partners, it could preclude finding the expected association between incident STI and self-reported condom use. Other investigators have found significant associations between incident STI and the total number of clients reported and the duration of sex work, but we did not observe the former relationship and did not have information on the latter.[137] Without knowing

more about the infection status of their partners, it is difficult to know how much risk a woman takes at each unprotected sex act.

These weaknesses are counterbalanced by two strengths of our study. First, we used incident cases of STI as our outcome indicator, which gives greater weight to our conclusions. A second strength is that through the longitudinal nature of the dataset, we were able to test for any changes in the association between self-reported condom use and incident STI over time. Changes over time might have indicated that self-reports became more or less predictive of STI with increasing time as a study participant. This sort of longitudinal association has not been reported on elsewhere in the sexual behavior literature but may have implications for the design of longitudinal studies.

In conclusion, our inability to identify a proxy variable for the incidence of STI is not a new dilemma. Nevertheless, the problematic indicator self-reported condom use continues to be used as a proxy measure of risk of STI. A recent review of evaluations of 16 HIV prevention programs among adolescents in Africa and Latin America attests the continued use of this indicator.[19] Program evaluators working with programs that aim to change sexual behavior should be clear about the objectives of their programs and identify indicators accordingly. *As self-reported condom use does not appear to accurately predict decreasing risk of infection, it should not be used to define the ultimate success of a disease prevention program.* The alternative of instituting laboratory tests as a means for determining incident infections may be more expensive and more complicated than the use of self-reported proxy measures. Yet as our study has suggested, this method may be better than continuing to allocate resources to intervention programs that will have no reliable measure of their success.

Tables

Table 11: Respondent characteristics at baseline and last study visit, Month 18 according to study site

	Baseline (N=1000)				Month 18 (N=818)			
	Tamatave (n=500)		Antananarivo (n=500)		Tamatave (n=391)		Antananarivo (n=427)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Age								
24 years or less	191	(38.2)	196	(39.2)	114	(29.2)	127	(29.7)
25 years or more	307	(61.4)	304	(60.8)	276	(70.6)	300	(70.3)
Age unknown	2	(0.4)	0		1	(0.3)	0	
Mean (years)	28.2		28.4		30.4		30.2	
Personal partner status								
Steady personal partner	178	(35.6)	205	(41.0)	172	(44.0)	323	(75.6) †
No steady personal partner	318	(63.6)	293	(58.6)	219	(56.0)	104	(24.4) †
Missing	4	(0.8)	2	(0.4)	0	--	0	--
Number of clients, past 7 days								
None	14	(2.8)	20	(4.0)	101	(25.8)	8	(1.9) †
1-2	70	(14.0)	59	(11.8)	72	(18.4)	41	(9.6) †
3-4	152	(30.4)	108	(21.6)**	94	(24.0)	74	(17.3)**
5-6	101	(20.2)	95	(19.0)	58	(14.8)	74	(17.3)
7-10	84	(16.8)	123	(24.6)**	41	(10.5)	93	(21.8) †
11+	59	(11.8)	94	(18.8)**	11	(2.8)	58	(13.6) †
No response‡	20	(4.0)	1	(0.2) †	14	(3.6)	79	(18.5) †
Mean	6.2		7.9†		3.4		7.3†	

† p<0.000; ** p<0.05

‡ Includes women who refused to respond, said they didn't know, or said they were menstruating in the past 7 days

Table 12: Unadjusted number of unprotected sex acts, according to partner type

	Clients*				Personal Partners†			
	Month 6 (N=901)		Month 18 (N=818)		Month 6 (N=901)		Month 18 (N=818)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
0 unprotected sex acts	398	(44.2)	450	(55.0)	59	(6.6)	52	(6.4)
1-5 unprotected sex acts	245	(27.2)	148	(18.1)	243	(27.0)	202	(24.7)
6-10 unprotected sex acts	94	(10.4)	52	(6.4)	136	(15.1)	118	(14.4)
11-15 unprotected sex acts	45	(5.0)	14	(1.7)	48	(5.3)	52	(6.4)
16+ unprotected sex acts	63	(7.0)	17	(2.1)	34	(3.8)	19	(2.3)
Did not have sex with that partner type in previous 30 days	37	(4.1)	84	(10.3)	379	(42.1)	373	(45.6)
Missing values**	19	(2.1)	53	(6.5)	2	(0.2)	2	(0.2)
Mean	4.8		2.1		5.6		5.5	
Median	1.0		0.0		4.0		4.0	
Range	0-210		0-40		0-29		0-63	

* Previous 30 days † Average monthly estimate for previous 12 months
** Missing values could be due to non-response or responding “don’t know”.

Table 13: Incidence of gonorrhea, chlamydial or trichomonas infection according to follow-up visit

	Month 0 (N=100)		Month 6 (N=901)		Month 12 (N=863)		Month 18 (N=818)	
	N	%	N	%	N	%	N	%
Positive	519	51.9	441	49.0	353	40.9	321	39.2
Negative	479	47.9	447	49.6	508	58.9	491	60.0
Missing	2	0.2	13	1.4	2	0.2	6	0.7

Table 14. Odds ratios estimating risk of incident sexually transmitted infection for each of three time points in a prospective cohort study of female sex workers in Madagascar, 2001-2003.

	Month 6* (N=830)		Month 12† (N=727)		Month 18† (N=671)	
	Adjusted Odds Ratio	**(95% CI‡)**	**Adjusted Odds Ratio**	**(95% CI‡)**	**Adjusted Odds Ratio**	**(95% CI‡)**
Number of sex acts during previous 30 days unprotected by condoms (self-reported)						
Zero	1.00		1.00		1.00	
1-3 (few)	0.91	(0.54, 1.52)	0.70	(0.40, 1.22)	0.97	(0.58, 1.61)
4-10 (some)	0.76	(0.48, 1.20)	0.95	(0.60, 1.50)	0.97	(0.62, 1.54)
11+ (many)	1.11	(0.65, 1.90)	0.79	(0.45, 1.39)	0.63	(0.35, 1.16)

All estimates calculated from logistic regression models using SAS (v. 8.02).

*****Adjusted for baseline STI, client resistance to condom use, study site, age 29 years or younger, and intervention arm.

† Adjusted for baseline STI, client resistance to condom use and study site.

‡Confidence Interval

Table 15: Odds ratios estimating risk of incident sexually transmitted infection over 12 months for participants in a prospective cohort study of female sex workers in Madagascar, 2001-2003.

	Adjusted Model (N=2232)*	
Covariates	**Odds Ratio**	**(95% CI†)**
Number of sex acts during previous 30 days unprotected by condoms (self-reported) by time		
Zero	1.00	
1-3 (few) at Month 6	0.79	(0.59, 1.07)
1-3 (few) at Month 12	0.79	(0.49, 1.27)
1-3 (few) at Month 18	0.67	(0.41, 1.09)
4-10 (some) at Month 6	0.89	(0.68, 1.16)
4-10 (some) at Month 12	0.68	(0.46, 1.02)
4-10 (some) at Month 18	0.99	(0.67, 1.47)
11+ (many) at Month 6	0.81	(0.57, 1.14)
11+ (many) at Month 12	0.95	(0.61, 1.49)
11+ (many) at Month 18	0.91	(0.57, 1.44)

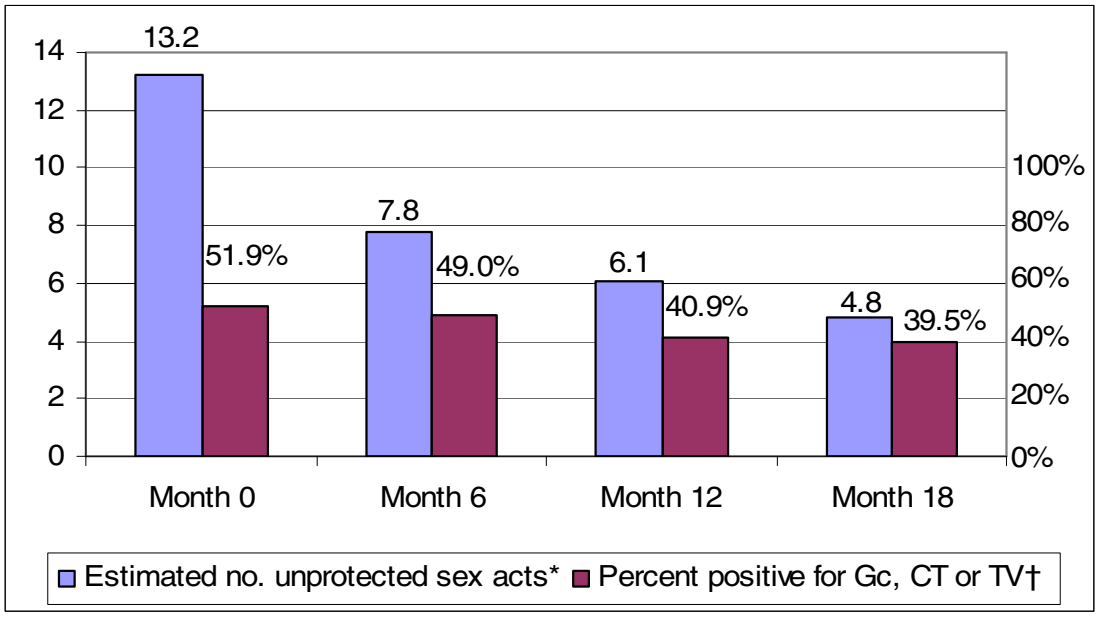
All estimates calculated from GEE logistic regression models using SAS (v. 8.02).

*****Adjusted for baseline STI, client resistance to condom use and study site.

†Confidence Interval

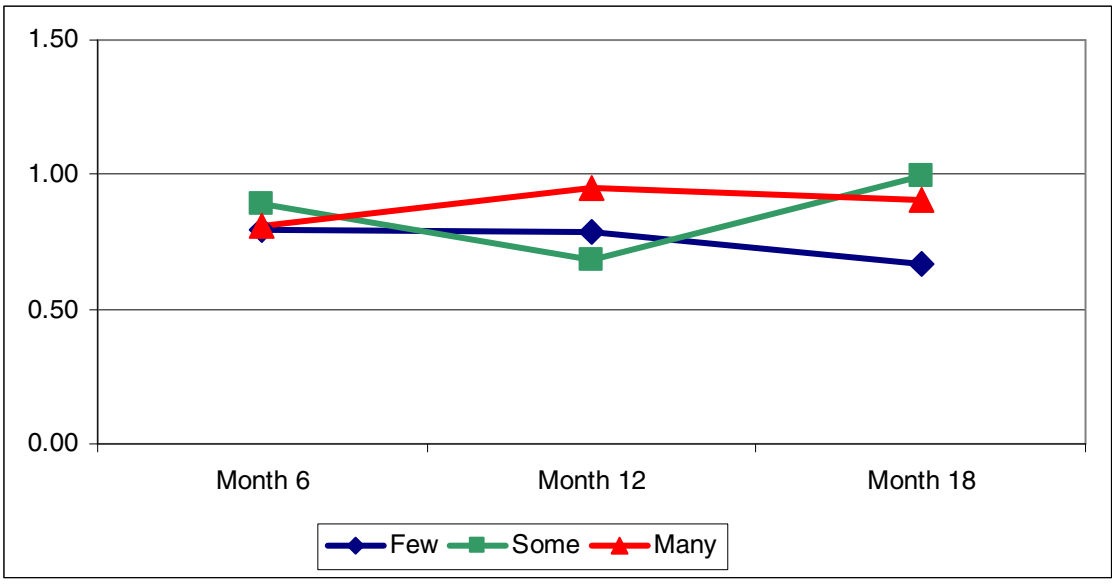
Figures

Figure 6: Number of self-reported unprotected sex acts with all partners (previous 30 days) and incident cases of STI for participants in a prospective cohort study of female sex workers in Madagascar, 2001-2003.



* Estimated number of unprotected sex acts: Mann-Kendall test for trend $p<0.05$
† Percent positive for Gonorrhea (Gc), Chlamydia (CT) or Trichomoniasis (TV): Cochrane-Armitage test for linear trend $p<0.0001$

Figure 7: Odds ratios estimating risk of incident sexually transmitted infection by number of self-reported unprotected sex acts for participants in a prospective cohort study of female sex workers in Madagascar, 2001-2003, adjusting for study site and client resistance to condom use.



VI. RESULTS: PAPER TWO

Infrequent condom use with personal partners and risk of sexually transmitted infections among female sex workers in Madagascar

Abstract

Background

Female sex workers (FSW) often report using condoms infrequently with personal sexual partners who might carry sexually transmitted infections (STI) as well as clients. We evaluated the relationship between self-reported condom use with each partner type and incident STI over 18 months among FSW in Madagascar.

Methods

One-thousand FSW prospectively reported on condom use with clients and personal partners; responses were categorized as follows: (1) 100% consistent condom use with clients and personal partners, (2) consistent condom use with clients but not personal partners, (3) consistent condom use with personal partners but not clients, and (4) inconsistent condom use with both personal partners and clients. The risk of STI acquisition was calculated in a multivariate logistic regression model using generalized estimating equations (GEE) to adjust for clustering of responses.

Results

At study completion, few respondents (6%) reported consistent condom use with personal partners but over half of respondents (55%) reported 0 unprotected sex acts with clients in the past month. Compared to the group that reported consistent condom use with both partner types, the odds ratio (OR) for STI acquisition among respondents who reported consistent condom use with clients and inconsistent use with personal partners

was 0.9 (95% confidence interval (CI): 0.5-1.6). Women who had an STI at baseline had a 3.0 times higher odds (95% CI: 2.2, 4.2) of acquiring a subsequent STI.

Discussion

We found no evidence that inconsistent condom use with personal partners increased risk of STI in this cohort of FSW.

Background

Female sex workers (FSW) have been reported to have higher rates of sexually transmitted infections (STI), including HIV, than the population average in both developing as well as developed countries.[52, 149, 187] STI prevalence rates are higher in sub-Saharan African populations than in developed countries, and African FSW tend to have higher rates still.[2] FSW have an elevated risk of STI due to their greater numbers of sexual partners and are considered to be the "driving force" of at least one HIV epidemic in West Africa.[9, 84, 187, 188] Furthermore, at least two studies have shown that reductions in the burden of STI among FSW are associated with a lower prevalence of STI among men in the general population.[189, 190]

While FSW might report a higher frequency of condom use with clients, they report using condoms much less frequently with personal (non-paying) partners.[55, 74, 76-82, 84] FSW have reported that they cannot or will not insist on condom use in personal relationships because it would damage the trust and affection or endanger the economic support that they might be receiving from these partners.[77, 79-81, 191] Two recent studies in Benin and Ghana showed that personal partners had higher rates of HIV infection than clients of FSW and men in the general population.[78, 84] Another study in Cameroon showed that low self-reported condom use with personal partners was associated with HIV infection.[29] Personal partners may be acquiring STI from their FSW partners but personal partners may *also* be acting as reservoirs, resulting in re-infection of the FSW. This concern has led to several calls for increased targeting of condom promotion interventions to both personal partners and clients of FSW although none have yet been reported in the literature.[53, 78, 80, 84, 188, 191, 192]

We evaluated the relationship between unprotected sex, type of sexual partner and risk of STI using data from a condom promotion intervention study among FSWs previously documented to have high rates of STI.[6, 143] The objective of the present study was to determine if inconsistent condom use with personal partners and 100% consistent condom use with clients was associated with a higher risk of STI compared to FSW who reported consistent condom use with both clients and personal partners.

Methods

We used data from a randomized controlled trial of condom promotion carried out from 2001-2003 in Antananarivo, the capital city and Tamatave, a port city in the northeast of Madagascar.[6] One thousand self-identified, active FSW were followed during an 18-month study, which had two phases: Phase I, the male condom phase, and Phase II, the female condom phase.[183]

Participants were randomized at the beginning of each of the two phases to receive condom promotion via either peer education alone ("peer only"), or peer education *and* clinic-based education ("peer+clinic"). In Phase I all participants in both study arms had access to male condoms at a subsidized price (about US $0.03/condom) through the study clinics or peer educators. In Phase II, all participants were given access to both male and female condoms at the same subsidized price.

Participants were interviewed every two months to collect demographic and sexual behavior information. Every six months, participants were tested for *Neisseria gonorrhoeae*, and *Chlamydia trachomatis* using ligase chain reaction (LCR) testing (Abbott LCx Probe System, Abbott Laboratories, Abbott Park, IL, USA) and InPouch

(BioMed, San Jose, CA, USA) for *Trichomonas vaginalis*. These procedures have been more fully described elsewhere.[6, 183]

Participants were presumptively treated for gonorrhea and chlamydia every six months and based on laboratory diagnosis for trichomoniasis. We assumed that incident STIs represented new infections since the treatment regimens used have excellent cure rates.[176, 177, 179-181]

The outcome measure used for this analysis was the cumulative six-month incidence of STI, defined as the respondent testing positive for gonorrhea, chlamydial or trichomonas infection at any of the six-month follow-up visits, Months 6, 12 and 18.

Male and female condoms provide equivalent levels of protection against STI.[154] Reports of female and male condom use were combined for this analysis after stratified analysis failed to show that self-reported condom use and incident STI were different for women who reported female condom use and women who reported no female condom use.

Respondents reported separately about partners who had to pay to have sex with them (clients) and personal partners who did not have to pay to have sex with them (e.g., boyfriends). At each interview, respondents were asked to report the total number of sex acts they had with clients in the previous 30 days, and the total number of those acts where a male or female condom was used. Respondents were asked the same questions about sexual behavior with personal partners, but for the previous 12 months. This longer recall period was chosen to capture irregular behaviors for women living distant from their personal partners, but resulted in considerable overlap in the reporting on personal partners from one study visit to the next. In this analysis, we use observations

for both partner types at two study visits twelve-months distant from one another, Months 6 and 18. Respondents were also asked to specify the last time they had sex with a personal partner or client. In some cases, respondents reported that their last sex act with one of these partner types was more than 30 days ago and these women were excluded from the primary analysis.

Consistent condom use was defined as reported 100% condom use with both partner types. Anything less than 100% was considered inconsistent condom use. The respondents were divided into four groups for each time period (Months 6 and 18), those who reported: (1) consistent condom use with both personal partners and clients, (2) consistent condom use with clients but not personal partners, (3) consistent condom use with personal partners but not clients, and (4) inconsistent condom use with both partner types. The lowest risk group, those who reported consistent condom use with both partner types, was used as the referent for this analysis.

We conducted a secondary analysis to include some of our "missing" data in the analysis by defining the women who reported no sex acts with a particular partner type as having no unprotected sex acts (Table 16). We defined the exposure variable in this analysis as "no unprotected sex acts" rather than "consistent condom use".

Covariates hypothesized to be related to self-reports, condom use or STI were examined. Besides age and baseline STI status, time-varying variables examined included: having a steady personal partner; reported total number of sexual partners in the previous 7 days according to partner type; condom breakage or slippage in the previous 30 days; client resistance to condom use in the previous 30 days; personal partner resistance to condom use in the previous 12 months; refusal of unprotected sex in the

previous 30 days because the client refused to use a condom; symptoms of interim STI infection; use of non-barrier contraception; and rape, or having been forced to have sex or beaten in the previous 30 days.

Finally, the two intervention groups (*Study arm*) and the two study cities (*Study site*) were examined as potential effect modifiers and confounders.

The data were analyzed using SAS 8.02 (SAS Institute, Inc., Cary, North Carolina). Bivariate comparisons of differences in proportions and means were examined using chi-square tests and t-tests respectively, in COMPARE2 version 1.45, a WIN-PEPI program (available at www.brixtonhealth.com).

Multivariate regression modeling was used to examine the association between STI and self-reported condom use with each particular partner type. A multivariate regression model was constructed using generalized estimating equation (GEE) analysis to account for the clustering between observations (unstructured working correlation matrix).

To test the hypothesis that unprotected sex with personal partners is associated with STI, three indicator variables (inconsistent use with both partners, consistent use with clients but not personal partners, and consistent use with personal partners but not clients) were included in the model with consistent use with both partner types serving as the reference group. Odds ratios for each of the three condom use patterns were compared to the referent group.

The fully adjusted model included potential confounders hypothesized to be related to STI, successful condom use and self-reporting behaviors. Covariates were assessed using a backward stepwise elimination procedure to determine whether they

confounded the relationship between self-reported condom use and STI. If the removal of a covariate changed any of the main exposure estimates by more than 0.10 as measured by the natural log of the adjusted estimate divided by the non-adjusted estimate (LN(adjusted/unadjusted)), it was judged to confound the relationship and was retained in the adjusted model.

The analysis was approved by the institutional review board at the University of North Carolina at Chapel Hill's School of Public Health. The parent study was approved by the ethics committees of the National HIV/AIDS Reference Laboratory in Madagascar, and Family Health International (FHI) in North Carolina, United States.

Results

Over three-quarters of respondents (81.8%) participated in the last study visit. The rate of attrition was higher in Tamatave than Antananarivo (21.3% vs. 15.3%, p=0.003) but there were no differences in participant age, condom use, or STI at baseline between those who dropped out of the study and those who completed the last study visit by study site. The mean age of participants at baseline was 28.3 (median 27.0; range, 16-64). Most women were unmarried. Nearly 40% of participants reported having a regular personal partner at baseline and this proportion increased over time (Table 17). Women in Tamatave were more likely to have a steady personal partner than women in Antananarivo ($p<0.001$ at both Month 6 and 18).

At Month 6, a total of 49.0% of participants in both cities were diagnosed as having an infection of gonorrhea, chlamydia or trichomonas (Table 17). At the end of the study, Month 18, 39.5% of participants in both cities tested positive for one or more new (incident) infections, a 19.4% decrease from Month 6. Compared to participants in

Tamatave, participants in Tana were significantly more likely to have STI at Month 6 ($p<0.001$), but by Month 18 this difference had disappeared ($p=0.135$).

The average number of reported unprotected sex acts with clients decreased by half from Month 6 to Month 18, from 4.8 per month to 2.1 (Table 18). The estimated number of unprotected sex acts with personal partners per month remained steady throughout the study period (5.6 at Month 6, 5.5 at Month 18). There was no difference in rate of condom use according to study site.

Association between STI and condom use by partner type

In the multivariate analysis examining 100% consistent condom use, respondents who reported 100% condom use with clients, but less than 100% with personal partners did not have an increased odds of STI compared to respondents who reported consistent condom use with both partner types (Table 19). Women who reported inconsistent condom use with both clients and personal partners and those who were consistent condom users with their personal partners and inconsistent condom users with their clients had an elevated odds of STI compared to the referent group.

The confidence intervals for parameter estimates for both "inconsistent condom use with clients" categories were broad, indicating a lack of precision consistent with lack of statistical significance. When we added in women reporting no sex acts, the precision of the estimates improved but our conclusions were essentially unchanged (Table 20).

We found that baseline STI status, resistance to condom use by each partner type, the number of clients in the previous 7 days, and the absolute number of unprotected sex acts with clients and personal partners confounded the association between consistent

condom use and STI. Hence we adjusted for these variables in the analyses reported in Tables 4 and 5.

Discussion

For our cohort of FSW, inconsistent condom use with personal partners was not associated with an elevated risk of STI. Our results suggest that participants who reported inconsistent condom use with clients may have an elevated risk of STI, but parameter estimates were imprecise, even when analyses included women reporting no sex acts (an analytic strategy to increase limited statistical power associated with small cell sizes).

A study in West Africa showed that personal partners of sex workers tend to have other FSW and non-FSW partners with whom they do not use condoms and that the personal partners had higher prevalence of HIV than clients.[78] Another study in West Africa showed a protective effect against HIV infection of reported condom use with personal partners.[29] A greater exposure to unprotected sex acts would in theory be expected to correlate more strongly with highly infectious diseases like those examined in this study than with HIV.[193] However, our findings do not support an association between unprotected sex with personal partners and incident STI.

How might our results be interpreted? Lack of evidence for STI risk associated with personal partners might reflect partners also being treated for STI at the same time as their FSW girlfriends. Personal partners might be getting treatment because the FSW told her partner about an infection, although this is unlikely since FSW were presumptively treated for gonorrhea and chlamydia. More plausibly personal partners might have accessed treatment for STI because men tend to be more symptomatic for

some STIs (esp. gonorrhea and chlamydia) or because these men had a higher index of suspicion for STI due to the profession of their FSW partners.

Another possible explanation for our findings could be that the personal partners of these FSW don't have other sexual partners or that they are embedded within sexual networks with a low risk of infection. The low rate of reported condom use with personal partners that we observed in this cohort is consistent with findings from a variety of studies.[54, 77, 79, 80, 82, 191] Other studies have further delineated condom use between casual clients, regular clients and personal partners, finding that the more intimate the relationship is perceived to be by the FSW, the less likely she is to insist on condom use. It may be that personal partners themselves consistently use condoms in sexual relationships outside their relationship with the FSW, especially if they consider their relationship with the FSW to be their primary relationship.

Some might propose that since the rate of sexual encounters with personal partners was so much lower than that for sexual encounters with clients, it only makes sense that unprotected sex with clients is associated with greater risk for STI. However, the reported *number* of unprotected sexual encounters in this cohort was similar for clients and personal partners, indicating that the FSW had as many potentially infectious exposures with personal partners as with clients.

The strongest and only statistically significant predictor of incident STI in this analysis was prevalence of STI at study baseline. Given the directly observed treatment, we assumed that these were indeed new infections. This association between previous STI and new infection has been observed elsewhere.[10, 91, 194] We assumed that baseline STI was an independent predictor because it was a marker of risky behaviors or infected

partners. Programs designed to decrease the burden of STI may want to take this result into account when counseling their clients. Clients who have current infections may need more intensive risk reduction counseling to avoid future re-infection. In addition, this information could be used to make research designs more cost-effective. Researchers conducting studies with STI as an endpoint may want to consider enrolling only people with a current STI, since those people are much more likely to have a subsequent re-infection and may enable them to follow a smaller cohort over time.

A limitation of this analysis is that two different recall periods were compared in the self-reported condom use variable for clients (30 days) and personal partners (12 months). The longer recall period for personal partner data might make these data subject to more recall bias. Due to the nature of the analysis exploring different partner types there was however no alternative to using these data. Research in cognitive psychology has shown that when asked to recall something from the distant past, respondents "resort to inferences" based on typical experience to estimate a numeric answer.[45] Rates of condom use with personal partners remained relatively constant over the duration of the study, suggesting that this measurement is reliable; however, reliability does not imply validity therefore we can only interpret this measure with caution.

Although we started with a large cohort of participants, when we sub-divided them into consistency of condom use by partner type we were left with small numbers in some of the strata. This study therefore had limited power to observe associations between these strata and incident STI.

We relied on self-reported condom use to measure association with STI. The potential for self-presentation bias in self-reported condom use has been extensively discussed.[9, 10, 18, 22] However, if participants were more accurate in reporting on absolute use (i.e., situations where they achieved 100% condom use) versus partial condom use, a correlation between self-reported condom use and STI stronger than previously observed could result. Participants might also be more accurate in their reporting about condom use with personal partners since non-use of condoms in these personal relationships seems to be socially well accepted, unlike social pressures to use condoms with clients.

A major strength of this analysis is its use of incident STI data and self-reported condom use for both partner types collected prospectively over a period of 12 months. This allowed us to examine condom behaviors in light of newly acquired infections, making a stronger case for observed associations. The conclusion that personal partners present little risk of STI to our cohort may not, however, be generalizable to other contexts. Madagascar differs from the rest of sub-Saharan Africa in that it has high rates of curable STI, but a low observed rate of HIV infection.[3]

In order to best target prevention messages to contain the spread of STI, we must learn more about the clients and personal partners of FSW. If other contexts are similar to that observed in the present study, it may be most effective to target condom use prevention to clients of FSW, rather than trying to influence them in the emotional relationships they have with personal partners. Future research should focus on understanding where the risk of STI and HIV is coming from by looking at all male partners of FSW and targeting interventions appropriately.

Table 16: Self-reported consistency of condom use and exposure to unprotected sex by partner type according to incident sexually transmitted infection (STI)

Part A: 100% consistent condom use by partner type

	1: Consistent with both clients and personal partners		2: Consistent with clients, inconsistent with personal partners		3: Inconsistent with clients, consistent with personal partners*		4: Inconsistent with both clients and personal partners		5: No reported sex with clients or personal partners		Missing condom use data	
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
STI at Month 6												
Yes	22	(53.7)	81	(44.8)	10	(71.4)	140	(55.3)	179	(45.8)	9	(42.9)
No	19	(46.3)	99	(55.7)	4	(28.6)	109	(43.1)	204	(52.3)	12	(57.1)
Missing	5	(1.1)	1	(0.6)	0	--	4	(1.6)	8	(2.0)	0	--
STI at Month 18												
Yes	12	(27.3)	69	(35.0)	2	(50.0)	58	(50.4)	160	(39.6)	20	(37.0)
No	32	(72.3)	127	(64.5)	2	(50.0)	57	(49.6)	239	(59.2)	34	(63.0)
Missing	0	--	1	(0.5)	0	--	0	--	4	(0.1)	0	--

Part B: Unprotected sex by partner type

	1: No unprotected sex with either clients or personal partners		2: No unprotected sex with clients, some with personal partners		3: Some unprotected sex with clients, none with personal partners		4: Some unprotected sex with both clients and personal partners		Missing condom use data	
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
STI at Month 6										
Yes	103	(44.4)	86	(42.8)	103	(53.1)	140	(55.3)	9	(42.9)
No	122	(52.6)	113	(56.2)	91	(46.9)	109	(43.1)	12	(57.1)
Missing	7	(3.0)	2	(1.0)	0	--	4	(1.6)	0	--
STI at Month 18										
Yes	96	(33.2)	81	(33.2)	65	(56.5)	58	(50.4)	21	(38.2)
No	190	(65.7)	161	(66.0)	49	(42.6)	57	(49.6)	34	(61.8)
Missing	3	(1.0)	2	(0.8)	1	(0.9)	0	--	0	--

* Of those 14 respondents who said they were consistent condom users with personal partners but consistent with clients at Month 6, only one reported this behavior pattern at Month 18.

Table 17: Respondent characteristics at Month 6 and last study visit, Month 18 according to study site

	Month 6 (N=901)				Month 18 (N=818)			
	Tamatave (n=438)		Antananarivo (n=463)		Tamatave (n=391)		Antananarivo (n=427)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Personal partner status								
Steady personal partner	194	(44.3)	360	(77.8)*	172	(44.0)	323	(75.6)*
No steady personal partner	244	(55.7)	103	(22.3)*	219	(56.0)	104	(24.4)*
Missing	0	--	0	--	0	--	0	--
Diagnosed with curable sexually transmitted infection (gonorrhea, chlamydia, or trichomonas infection)								
Yes	187	(42.7)	254	(54.9)	143	(36.6)	178	(41.7)
No	241	(55.0)	206	(44.5)	242	(61.9)	249	(58.3)
Missing	10	(2.3)	3	(0.7)	6	(1.5)	0	--

* p<0.000

Table 18: Number of unprotected sex acts in previous month, according to partner type

	Clients*				Personal Partners†			
	Month 6 (N=901)		Month 18 (N=818)		Month 6 (N=901)		Month 18 (N=818)	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
0 unprotected sex acts	398	(44.2)	450	(55.0)	59	(6.6)	52	(6.4)
1-5 unprotected sex acts	245	(27.2)	148	(18.1)	243	(27.0)	202	(24.7)
6-10 unprotected sex acts	94	(10.4)	52	(6.4)	136	(15.1)	118	(14.4)
11-15 unprotected sex acts	45	(5.0)	14	(1.7)	48	(5.3)	52	(6.4)
16+ unprotected sex acts	63	(7.0)	17	(2.1)	34	(3.8)	19	(2.3)
Did not have sex with that partner type in previous 30 days	37	(4.1)	84	(10.3)	379	(42.1)	373	(45.6)
Missing values**	19	(2.1)	53	(6.5)	2	(0.2)	2	(0.2)
Mean no. sex acts	19.8		16.2		5.9		6.3	
Mean no. unprotected sex acts	4.8		2.1		5.6		5.5	
Median	1.0		0.0		4.0		4.0	
Range	0-210		0-40		0-29		0-63	

* Previous 30 days † Average monthly estimate for previous 12 months
** Missing values could be due to non-response or responding “don’t know”.

Table 19: Risk of incident sexually transmitted infection by 100% consistent condom use and partner type among female sex workers in Madagascar, 2001-2003.

Covariates	Reduced-Adjusted Model (N=747*) Odds Ratio	(95% CI†)
Consistent condom use by partner type		
Consistent with both clients and personal partners	1.00	
Consistent with clients, inconsistent with personal partners	0.90	(0.50, 1.62)
Inconsistent with clients, consistent with personal partners	8.31	(0.50, 137.96)
Inconsistent with both clients and personal partners	4.44	(0.35, 56.68)
Positive for STI at Month 0 (baseline)		
No	1.00	
Yes	3.00**	(2.15, 4.18)
Client resistance to condom use		
No	1.00	
Yes	0.24	(0.02, 2.97)
Personal partner resistance to condom use		
No	1.00	
Yes	0.93	(0.65, 1.34)
Number of clients in the previous 7 days	1.01	(0.98, 1.04)
Number of unprotected sex acts with clients in the previous 30 days	1.02**	(1.00, 1.05)
Average number of unprotected sex acts with personal partners in the previous 30 days	0.98	(0.95, 1.01)

All estimates calculated from GEE logistic regression models using SAS (v. 8.02).
*Note: there were 901 observations at Month 6 and 818 observations at Month 18. 972 observations were excluded because of missing data or because of no reported sex acts.
†Confidence Interval **Statistically significant at $p<0.05$.

Table 20: Risk of incident sexually transmitted infection by reported exposure to unprotected sex and partner type among female sex workers in Madagascar, 2001-2003.

Covariates	Reduced-Adjusted Model (N=946*) Odds Ratio	(95% CI†)
Exposure to unprotected sex by partner type**		
No unprotected sex with either clients or personal partners	1.00	
No unprotected sex with clients, some unprotected sex with personal partners	0.94	(0.61, 1.43)
Some unprotected sex with clients, no unprotected sex with personal partners	4.37	(0.85, 22.49)
Some unprotected sex with both clients and personal partners	3.45	(0.67, 17.68)
Positive for STI at Month 0 (baseline)		
No	1.00	
Yes	3.20††	(2.37, 4.32)
Client resistance to condom use		
No	1.00	
Yes	0.33	(0.06, 1.65)
Personal partner resistance to condom use		
No	1.00	
Yes	0.93	(0.70, 1.23)
Number of clients in the previous 7 days	1.01	(0.98, 1.03)
Number of unprotected sex acts with clients in the previous 30 days	1.02††	(1.00, 1.04)
Average number of unprotected sex acts with personal partners in the previous 30 days	0.98	(0.95, 1.01)

All estimates calculated from GEE logistic regression models using SAS (v. 8.02).
*Note: there were 901 observations at Month 6 and 818 observations at Month 18. 673 observations were excluded because of missing data at one of the two observation points. 481 of these were missing because they did not answer the question about personal partner resistance to condom use or because they reported no personal partners.
**Respondents reporting no sex acts with a partner type were considered to have no exposure to unprotected sex with that partner type.
†Confidence Interval ††Statistically significant at $p<0.05$.

VII. CONCLUSIONS

This dissertation set out to explore why participants' reports of unprotected sex acts decreased dramatically over the life of the MCFC-MAD study, but STI incidence did not decrease an equivalent amount. Although STI did decrease during the study, the proportion of participants with new infections was still nearly forty percent (39.5%) 18 months after the study promoting condom use commenced. Such a weak association between self-reported condom use and STI has been observed before and the most common conclusion has been that researchers and program evaluators cannot rely on the men and women they are questioning to give correct reports of their sexual behavior.

The first aim of the dissertation was to establish if there was an association between self-reported condom use and STI in this population and to examine the longitudinal association between self-reported condom use and STI for signs of an "interviewer familiarity" effect. Repeatedly hearing condom promotion messages and repeatedly answering the same questions about condom use behaviors might have impacted the social desirability pressures experienced by respondents. We hypothesized that the effect of time could either increase respondents' comfort in answering honestly because of increased trust and rapport with the study interviewers, or it could decrease their comfort in answering accurately because of perceived mounting pressure when their behavior did not adhere to recommended condom use messages. We expected that this longitudinal effect would result in changing strength of association between self-reported condom use and that the magnitude of the change would allow us to draw conclusions about the magnitude of the effect of social desirability in this cohort. In fact, we found no evidence of a changing association over time and concluded that if there is changing accuracy of self-reports, it is either a very small change, or the change occurs in both

directions hypothesized and has no overall effect. We also did not observe the expected relationship of increasing risk of STI associated with reports of more unprotected sex acts, indicating no dose-response relationship.

The second aim of the dissertation was to test the hypothesis that the weak association between self-reported condom use and STI was not due to faulty reporting on the participants' part but because the partners with whom they were not using condoms, largely their personal partners, were likely transmitting STI to them. To examine whether this was the case, we divided the population into groups where respondents reported 100% consistent condom use with clients and personal partners, where respondents reported consistent condom use with one partner type, but not the other, or where respondents reported inconsistent condom use with both partner types. Surprisingly, we found that unprotected sex with personal partners was *not* associated with STI in this cohort. Our data suggest that it was rather unprotected sex with clients that increased the odds of STI.

Strengths

The major strengths of this study were the excellent follow-up rate for 18 months data, and the rigorous measurement of STI and repeated self-reported condom use at several points in time. Furthermore, due to presumptive treatment coinciding with testing for STI, we had information about incident infections over a known period of time. This enabled us to conduct longitudinal analyses of the association of interest, which has not been reported before in the literature. The high prevalence of curable STI in this

population was also an advantage, since it provided many cases within which to observe the association of interest.

Limitations

There were several limitations of the data used for these analyses. First, inconsistent recall periods for sex acts with clients (30 days) and personal partners (12 months) required us to assume that patterns of condom use with personal partners were similar for each month. Making this assumption, we used an estimated average monthly measure of the number of unprotected sex acts with personal partners in order to make the two measures consistent. It may be that this assumption was not appropriate and that we have introduced differential misclassification into the measurement of unprotected sex acts with personal partners. When we repeated the longitudinal analysis using only self-reported condom use with clients, the results did not change.

Another important limitation of these analyses is that we attempted to discuss the validity of the self-reported condom use without the benefit of an available gold standard for establishing conclusive validity. It is possible that the weak associations observed in the papers are actually artifacts of unmeasured confounders. We controlled for all hypothesized confounding factors that were measured in the data set, however one of the most important ones, social desirability pressure, was not assessed. Our attempt to assess social desirability longitudinally produced null findings, thus we cannot draw conclusions about this key dimension of self-reporting.

Finally, the focus of the second paper was on the risk associated with unprotected sex with different partner types, but the only information we had on these partners was reported by the FSW themselves. Without independent information about their male partners, and particularly the infection status of these men, it is difficult to comfortably draw the conclusion that FSW need not attempt to improve their condom use rates with personal partners.

Future directions

The question of whether self-reported condom use is a valid measure of risk for STI remains open following these analyses. The lack of any dose-response relationship in the first paper between self-reported condom use and STI casts doubt on the measurement of condom use as a continuous variable. On the other hand, when we examined risk of STI by 100% consistent condom use and partner type, we found stronger (although imprecise and non-significant) associations. It may be that asking respondents to count the number of unprotected sex acts results in false precision of the measurement of their risk of STI. However, given the poor reliability and validity of always-to-never scales of condom use reported in several studies,[27-29, 46] it may be worthwhile to continue to ask respondents for numerical estimates of the number of protected sex acts, but to rely on a dichotomized measure of 100% consistent condom use versus less than 100% condom use as the measure of decreased risk of STI.

Although many doubts about the usefulness of self-reported condom use as a measure of risk of STI remain, in many low-resource contexts, it continues to be the only practical way to measure prevention intervention success. Recent work using prostate

specific antigen (PSA) to measure the reliability of self-reports has concluded that self-reports may have very poor validity[15, 16]. However, the short 48-hour time period over which PSA is applicable to measuring STI risk makes it an undesirable marker of prevention interventions. Where STI cannot be measured directly, we must continue research into improving the validity of self-reported sexual behavior. For example, the results of paper 2 should be verified in other contexts before we can discount condom use with personal partners as unimportant in prevention efforts with FSW. In addition, developing less expensive (while maintaining sensitivity and specificity) tests for STI may also assist STI control programs in better measuring their progress.

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