Sexually Transmitted Infection (STI) screening, case and contact treatment, and condom promotion resulting in STI Reduction two years later in rural Malawi

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Abstract

As part of a longitudinal cohort study in rural Malawi in 2000, 469 men and 758 women were asked to respond to a series of surveys, were tested for gonorrhea and chlamydia, and received their results and treatment, if applicable, for themselves and up to 2 partners if positive for either sexually transmitted infection (STI). Two years later, in 2002, 328 men and 525 women were again asked to respond to survey questions, tested again for gonorrhea and chlamydia, and were also tested for HIV – of these, 247 men and 453 women had also given urine samples in 2000. In 2000, the gonorrhea and chlamydia prevalence was 6.2% and 5.8% among men, and 3.6% and 4.9% among women. Two years later, prevalence of gonorrhea and chlamydia was 0.7% and 1.4% among men, and 1.3% and 1.1% among women. Although we did not test for HIV in the first round, the HIV prevalence in 2002 was 19.2%. The implications of the findings are discussed in the context of interventions for STI prevention and to reduce HIV transmission in sub-Saharan Africa.

Introduction

Sexually transmitted infections (STIs) are a tremendous health and economic burden in developing countries[1,2]. In Africa, excluding HIV, they are the second largest source of healthy life years lost among women in fertile years (15-44 years old), resulting in a variety of health problems including chronic pelvic inflammatory disease in women, urethral strictures in men, septicemia, and eye infections in newborns that can lead to blindness[1,3]. They are estimated to account for 17% of the economic losses due to ill health in developing countries[1]. Moreover, the presence of STIs increases the likelihood of transmission and acquisition of human immunodeficiency virus (HIV)[3-6]. For example, HIV shedding in semen was six times higher among men with gonococcal urethritis in Malawi than among men without this condition[7].

Various strategies for decreasing STI prevalence in the general population have been proposed and implemented in different settings, including promotion of safer sex, condoms, and early health care seeking behaviors; periodic presumptive treatment; partner notification and treatment; and syndromic management of STIs, among others[5]. There is no strong evidence about the effects of partner notification strategies, though there is some indication that provider-led notification may work better than patient-led notification; however, some question this strategy, particularly in the context of locations where sensitive and specific diagnostic tools are not available and where partner notification may be initiated without a positive diagnosis for an index case[5,8].

The effectiveness of syndromic management and periodic mass treatment have both been rigorously evaluated as a way to decrease STI prevalence within communities, and though there are mixed results, it seems both methods can significantly reduce the prevalence of curable infections[9-12]. Specifically, syndromic management of STIs has been promoted by the WHO for over a decade and subsequently incorporated by many STI control programs[3]. Multiple studies have found this strategy effective in lowering the prevalence of curable STIs in the general population and cost-effective as an intervention[9-11,13,14]. However, syndromic management can only be effective if the patient is experiencing symptoms. Various studies have suggested that syndromic management alone is not an effective STI control strategy, particularly due to the issue of asymptomatic cases[15,16]. For Chlamydia trachomatis (CT) alone, it is estimated that 70-75% of women do not experience symptoms; this percentage is even higher for men[3]. For Neisseria gonorrhoeae (GC), up to 80% of women may be asymptomatic, and approximately 10% of men, and these estimates vary widely[3]. Additionally, some feel that syndromic management can lead to overdiagnosis and treatment of STIs, resulting in increased costs to the system and potential drug resistance, amongst other problems[2]. Due to the costs and, in some countries, unavailability in obtaining laboratory testing for various STIs, improvements in rapid diagnostic testing of STIs should have a profound effect on the implications of syndromic management[3].

Various studies have also examined whether STI treatment and control is an effective strategy to decrease HIV transmission and prevalence. An initial study in Mwanza, Tanzania showed promising evidence that by using an STI prevention strategy that included syndromic treatment, one could expect to decrease HIV prevalence by as much as 40%[9]. Three subsequent randomized controlled trials failed to show a significant effect of STI control on HIV prevalence. These latter studies include a mass STI treatment strategy in Rakai, Uganda, and two syndromic management interventions in Masaka, Uganda and eastern Zimbabwe[10-12]. Lower prevalence of curable STIs due to less risky sexual behavior and the maturity of HIV epidemic have been suggested as possible reasons for lack of observed effect in these studies[17]. Despite the lack of observed association between intervention and HIV prevalence, mathematical models suggest that syndromic management of curable STIs should remain cost-effective in highly HIV endemic areas, specifically where HIV prevalence is higher than 5%[18].

In Malawi, syndromic management was being implemented in all central/district hospitals and rural health centers in 1993[19,20]. However, data from the 2004 Malawi Demographic and Health Survey, conducted soon after this study, revealed that only 27% of women and 29% of men with an STI or STI symptoms in the past 12 months reported seeking advice at a clinic or from a health professional; a larger percentage sought advice that was not from a health professional: 31%

of women and 11% of men reported they would seek advice from a traditional healer, 6% of women and 8% of men would seek advice or medicine from a pharmacy, and 21% of women and 11% of men would seek advice from friends or relatives[21].

Data from the "Malawi Pregnancy and Sexually Transmitted Infection (STI) Risk Perception and Avoidance Study", a prospective cohort study that took place in Mangochi, Malawi in 2000 and 2002, were used to examine the two main objectives of this study: 1) to determine whether gonorrhea (GC) and chlamydia (CT) screening, combined with case and sexual partner treatment, as well as condom promotion, resulted in a reduction in the prevalence of these STIs over 14-22 months; and 2) describe HIV prevalence in this sample[22].

Statement of the Problem

Setting

The study took place in the eastern lakeside region of the Mangochi district, situated in southern Malawi near the border with Mozambique. Mangochi is a predominantly rural district that in 2000 had an approximate population of 600,000[23]. Most of the people living in this district are from the Yao tribe, speak Chiyao and Chichewa, and are of Moslem faith[23]. Within Malawi, one of the poorest countries in the region, Mangochi is one of the poorest districts, with some of the lowest education and health indicators in the country[24]. Mangochi is sub-divided into 11 traditional authorities, three of which were selected for this study using probability proportional to size (PPS) methods[22]. Within each of these three TAs, four enumeration areas were selected[22].

The estimated population in Malawi in 2000 was 11.8 million[25]. HIV prevalence was estimated to be 14.2% of adults at the end of 2003, with an estimated 84,000 deaths due to the disease in the same year[26]. In 1995, 46% of STI clinic patients tested at seven sites outside of the major urban areas were HIV positive; more than half of those tested within the urban areas were diagnosed as HIV positive[26].

Study design

The Malawi Pregnancy and Sexually Transmitted Infection (STI) Risk Perception and Avoidance Study was a prospective cohort study that was conducted in two rounds. A multistage cluster sample design was used to sample households wherein all eligible women and men were selected for interviews. At the first stage, three traditional authorities (TA) were selected from a total of seven TA and two sub-TA using probability proportional to size (PPS). At the second stage, four enumeration areas (EA) within each TA were selected again using PPS. Households for each EA were enumerated. Households were then sampled from the list using a random starting point and a sampling interval that would provide the approximately 125 households per EA that we needed.

The first round consisted of weekly interviews for six consecutive weeks between June and December 2000. Field teams consisting of groups of four to five research assistants were based in housing arranged with the village chief. The surveys included socio-demographic information; knowledge, attitudes and behaviors associated to a variety of reproductive health topics (i.e., fertility, pregnancy, family planning, STIs, abortion, sexual behavior), based on our topics of interest. Due to the sensitive nature of the topic and to build rapport, the same research assistant returned to interview his or her participants week after week. In addition, in the third week, participants were also given the option to provide a urine sample for gonorrhea (GC) and chlamydia (CT) testing. For those who consented to it, urine was collected in urine cups, and kept in coolers with frozen packs during the day. The samples were moved daily to the District Hospital, where it was aliquoted, frozen at -20C, and transported to the University of North Carolina at Chapel Hill (UNC-CH) in the United States for analysis using polymerase chain reaction (PCR)-based testing. Because local capability for the PCR testing was not available at the Lilongwe Central Hospital (LCH) at that time, using funding from a National Institutes of Health Fogarty International Center training grant, two technicians from the LCH lab were trained and conducted these analyses at UNC-CH. Results were available in the field within one month. Those who tested positive for GC were given Ciprofloxacin 500mg or, among pregnant women, Erythromycin 500mg four times a day for seven days. Men who tested positive for CT were given Doxycycline 100mg twice a day for seven days, and women who tested positive for CT were given Erythromycin 500mg four times a day for seven days. The syndromic approach was too non-specific on which to base treatment options, primarily because of the large number of asymptomatic infections found among women. These individuals were also encouraged to inform any sexual partners about this diagnosis and were provided treatment for up to two partners.

The second round took place in March-May of 2002, between 14 and 22 months after the first round. This round consisted of weekly interviews for two consecutive weeks. In the first week, participants were given the option of providing urine samples for GC, CT and HIV testing. Urine collection, transport and testing was similar to that in the first round, except that the testing was now done in Malawi by the two trained LCH personnel. Once again, those who tested positive were provided with treatment for themselves and up to 2 partners. At the time of the study, HIV rapid testing was not available or approved in Malawi, so venipuncture would have been required for HIV ELISA testing with blood. However, the Calypte HIV urine Western Blot (Calypte Biomedical Co., Portland, OR, USA) was available, so we were able to accurately detect HIV from urine samples in Malawi. Pregnant women who were HIV positive were provided with a single dose of nevirapine to be taken at labor and a dose of nevirapine for their newborn at delivery.

While our field teams were in the communities in both rounds, they were adequately supplied with condoms that were handed out indiscriminately to anyone who asked about them or accepted our offer for them, and counseling on their use was provided to those interested. Moreover, while in the field for the study, the team noted that at times the health posts ran out of condoms, and they also made sure, in collaboration with the Mangochi District health office, that condoms were readily available at the health centers.

STATA 11.0 was used for the data analysis[27]. Frequencies for the various outcomes of interest were calculated, and chi-square and Fisher's exact tests were used for comparisons.

Sample

Study respondents were drawn from a self-weighted probability sample of 1,390 households in the three traditional areas (TA) using probability proportional to size (PPS), as described above. All occupants of the sampled households

were enumerated, and all men between the ages of 20 and 44 and all women between the ages of 15 and 34 were provided with information about this prospective cohort study, asked if they were interested in participating, and if so, the full IRB-approved consent process was carried out with each potential participant. This yielded a total sample size of 915 men and 1,192 women, of which 737 men (80.7%) and 1,014 women (85.1%) were successfully interviewed in the first week of contact in round one. Participation dropped every week (from reasons ranging from travel to unavailability to refusal); during week 3, when urine samples were collected, we had 635 men and 895 women participating (86.2 and 88.3% of those who participated in week 1). The second round of interviews and urine sample collections was 14-22 months later: 451 men and 727 women participated at this time (61.2% and 71.7% participation rate, respectively, compared to the first week of the first round of the study). There were a total of 700 individuals, 247 men and 453 women, who were screened in both rounds. Most of the analysis will focus on these 700 individuals for whom we have specimen data for both rounds.

Informed consent was obtained from each study participant and for each of the various components of this study: 1) agreement to participate in the survey portion, 2) agreement to be tested for GC and CT, and 3) agreement to be tested for HIV (only in round 2).

This study was reviewed and approved by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill, as well as the Malawian National Health Research Committee.

Results

During the initial screening period of July 2000 – January 2001, 469/635 (73.9%) men and 758/895 (84.7%) women consented to GC and CT screening, and provided urine samples. During the second round, March – May 2002, 328/451 (72.7%) men and 525/727 (72.2%) women consented to STI screening, of which 247 and 453 were tested during both rounds. All the analyses in this section are based on the 700 individuals who were screened in rounds one and two. A total of 573 individuals, 222 men and 351 women, consented to HIV testing in round two.

The socio-demographic characteristics of the study sample that were screened in rounds one and two, and both rounds, are presented in Table 1. In all rounds, those with a higher education and a higher perceived risk for STI were more likely to give urine than those with 4 years or less of education and low/small perceived risk (not shown in table 1). There were no detectable differences among those who participated in rounds one versus two, particularly examining for differences in demographics, perception of risk for STIs, or STI symptoms or history.

Among those who were tested in both rounds (n=700), prevalence of GC and CT in the first round was 4.7% and 5.7%, respectively, and 10% of those whose urine was sampled were positive for at least one of these (see Table 2). In the first round, GC prevalence was lower among women than men (3.3% and 7.3%, respectively, P = 0.018), and CT prevalence was also slightly lower among women than men, though the difference for CT was not significant (5.1% and 6.9%, respectively). Prevalence for GC and/or CT combined was also slightly lower for women (8.4%) than men (13.0%) (P = 0.054).

Table 1: Socio-Demographic Background and Perceived Risk for STIs Among Individuals Screened for STIs in Rounds One and Two, and in Both Rounds of Malawi Study, 2000 and 2002

Individual Characteristics	**Round One (n=1227)**	**Round Two (n=857)**	**Both Rounds (n=700)**
Age			
15-19 (only women)	**21.9**	**23.3**	**21.6**
20-24	**32.4**	**28.1**	**28.3**
25-29	**28.0**	**28.8**	**30.7**
30-34	**17.4**	**18.9**	**18.4**
35-39 (only men)	**12.8**	**13.9**	**13.4**
40-44 (only men)	**9.8**	**11.5**	**10.9**
Gender			
Male	**38.2**	**38.5**	**35.3**
Female	**61.8**	**61.5**	**64.7**
Education			
None	**38.0**	**39.0**	**38.1**
1-4 years	**26.7**	**27.5**	**26.4**
5+ years	**35.0**	**33.4**	**35.3**
Perceived Risk for STI			
None	38.0	**39.0**	**50.1**
Small-Moderate	22.7	**24.0**	**22.1**
Great	20.8	**23.2**	**25.9**
Occupation			
Farm-related	50.7	**52.9**	**53.7**
Skilled	8.5	**8.2**	**8.7**
Trade	18.5	**18.1**	**16.9**
Other	22.6	**21.2**	**21.0**
Mobility a			
Gone last year (men)	23.9	**22.7**	**23.1**
Partner gone last year (women)	16.4	**13.7**	**14.8**

a Mobility defined as having been gone from home for over a month in the past year. Men were asked if they had been gone for over a month in the past year, whereas women were asked if their male partners had been gone for over a month in the past year.

Table 2. STI Prevalence and Incidence Among Participants Screened in Both Rounds (2000 and 2002) (n=700)

Pathogen	Round 1	Round 2
GC		
Men	7.3 (18)	0.8 (2)
Women	3.3 (15)	1.6 (7)
Total	4.7 (33)	1.3 (9)
CT		
Men	6.9 (17)	1.6 (4)
Women	5.1 (23)	1.3 (6)
Total	5.7 (40)	1.4 (10)
GC and/or CT		
Men	13.0 (32)	2.0 (5)
Women	8.4 (38)	2.4 (11)
Total	10.0 (70)	2.3 (16)
HIV		
Men	NA	15.8 (35) [a]
Women	NA	18.5 (65) [a]
Total	NA	17.5 (133) [a]

a Indeterminate: 3.1 (18/573); men 2.3 (5/222); women 3.7 (13/351)

In the second round, the overall GC prevalence was 1.3% and the overall CT prevalence was 1.4%; an approximately five fold decrease in each, though this difference is not statistically significant. The prevalence of GC was slightly lower for men (0.8%) than women (1.6%), and the prevalence of CT was almost identical among men (1.6%) and women (1.3%) – none of these gender differences were significant. Urine was not tested for HIV in round one, but the overall prevalence in our sample was 17.5% (only 573 individuals accepted being tested for HIV, hence the smaller denominator; there were an additional 3.1% that were indeterminate). HIV prevalence was slightly higher for women (18.5%) than men (15.8%), though the difference was not significant.

None of those who were positive for GC and/or CT in the first round and who were re-screened in the second round were re-infected (not shown). Of the 37 people infected and treated for GC in round one, 33 were re-screened at round two and none were re-infected with GC. Likewise, of the 46 who were infected and treated for CT in round one, 40 were re-screened and none were re-infected with CT.

Within our sample of individuals screened during rounds one and two, self reported condom use increased following the first screening and treatment period from 12.6% to 13.4% (P = 0.000).

The percentage of men and women reporting any STI symptom at round one and two is presented in Table 3. For women, the symptoms included lower abdominal pain, foul smelling discharge, genital sores or ulcers, genital warts, burning pain on urination, redness or inflammation of genitals, or genital itching. For men, the symptoms included urethral discharge, genital sores or ulcers, genital warts, burning on urination, and painful swelling in groin area.

Table 3. Reported STI Symptoms by Gender

Reported STI Symptoms	Men (n=247)		Women (n=453)	
	Round 1	Round 2	Round 1	Round 2
Abdominal pain	NA	NA	4.4 (20)	12.6 (57)
Urethral (men)/Foul smelling (women) discharge	0	2.0 (5)	0.7 (3)	3.8 (17)
Genital sores/ulcers	0.8 (2)	4.5 (11)	1.1 (5)	4.0 (18)
Genital warts	0.4 (1)	0.4 (1)	0.7 (3)	1.3 (6)
Pain at urination	3.6 (9)	8.9 (22)	3.1 (14)	11.5 (52)
Painful swelling (men)/ redness/inflammation in genital area (women)	0.4 (1)	0.4 (1)	0.2 (1)	2.2 (10)
Genital itching	NA	NA	4.4 (20)	14.0 (62)
Reports at least one of the above symptoms	4.9 (12)	11.3 (28)	8.6 (39)	26.0 (118)

There were no significant associations found between any of the reported current symptoms (individual symptoms or reporting at least one symptom) and STI infection for either sex in the first round (not shown in table). In the second round, among men there was a statistically significant association between GC infection and urethral discharge (P = 0.000), as well as pain at urination (P = 0.041). Among women in the second round, abdominal pain (P = 0.015), genital warts (P = 0.003), and pain at urination (P =0.009) were significantly associated with having GC infection. None of the symptoms were significantly associated to being infected with CT.

Discussion

There are significant programmatic and policy implications from our findings. First, one recognized successful intervention for STI prevention[28] - and one of the widely discussed strategies for HIV prevention[29-30], albeit with mixed findings in the literature - is STI screening and treatment. We found an approximately five fold decrease in the GC and CT prevalence in the 14-22 months following a representative population based screening that also involved treatment for cases and up to two contacts, condom promotion, and health education on use of condoms. Though this reduction was not statistically significant, none of the individuals who were GC or CT positive in the first round and who received treatment were re-infected in the second round of the study. In the context of the literature on partner notification, the approach taken in this study – of actually giving out treatment for the positive index case and up to two partners – is different than the strategy examined in various studies consisting of notifying partners whether via patient him/herself or via a health provider and based on reported symptoms, but one that may be worth studying further. Like

any strategy, it will have it pros and cons, one of which is that it could result in other unintentional uses for the treatments if not monitored (i.e., treatment for partners could be sold to others for profit).

More research is also needed to determine if STI screening and case/partner treatment is cost effective and relevant in sub-Saharan African settings to reduce the prevalence of asymptomatic STI for HIV prevention[29-30]. The only way to determine if the STI screening and treatment approach taken in this study has an effect on HIV acquisition/transmission in this setting is to continue to monitor HIV prevalence/incidence while continuing the STI screening and treatment program. In this study, there was only one round of testing for HIV.

Findings from this study regarding the poor association between reported STI symptoms and actual STI infection in both periods are not surprising considering what is known about the large percentage of asymptomatic cases of STIs. Namely, the most likely explanation for the lack of association between reported STI symptoms and testing positive for gonorrhea and chlamydia is that there is simply a large percentage of individuals who are asymptomatic. There are also other possible explanations. Our survey was conducted face-to-face and it is possible people abstained from reporting any symptoms with our study team due to the sensitive nature of the topic or for other reasons. Various studies have revealed that social desirability bias influences what is discussed in face-to-face interviews, particularly as it relates to sexual practices (with the bias working in both directions)[31]. To reduce social desirability bias, the research team ensured that the same research assistant interviewed the same participant throughout all rounds of the study (there was only a small amount of staff turnover) and that questions of a more sensitive nature were asked in later interviews (questions on STI symptoms were in week 2); interestingly, reported STI symptoms were higher in the second round than in the first, despite a lower prevalence of GC and CT infection. The Malawi National Statistical Office uses the same technique used by this study team for self-reporting of STI symptoms; self reported STI symptoms were similar to those observed in the second round of this study: 4% of men and 4.8% of women reported a genital discharge, and 4.4% of men and 8.0% of women reported a genital sore or ulcer[32].

There was also a statistically significant increase in reported condom use between the two rounds. Though it could be due to social desirability bias as well – the participants knew that this practice is valued in general – it might also be the result of health education on condom use that was given out by the research team during the approximately two months that the teams lived in each of the communities during round one, and the team's distribution of condoms to anyone who asked for them.

Conclusion

This longitudinal study in Malawi involved survey and biospecimen collection in 2000 and 2002, with treatment provided to STI cases identified in each round and up to two of their partners. We did not test the partners (unless they were also participants in our study) nor did we supervise the distribution of antibiotics for the partners; it is possible that uninfected individuals were treated or that infected partners did not take their treatment dose. We are not able to confirm if all antibiotics for infected partners were used per our recommendation. However, despite the lack of statistical significance, the five fold decrease in GC and CT between rounds one and two, and lack of re-infection among those treated for GC and CT in the first round, is promising and warrants further exploration.

References

1. World Bank. World development report 1993: investing in health. New York: Oxford University Press for the World Bank; 1993.
2. Mayaud P, Mabey D. Approaches to the control of sexually transmitted infections in developing countries: old problems and modern challenges. Sex Transm Infect 2004; 80: 174-182.
3. World Health Organization. Global prevalence and incidence of selected curable sexually transmitted infections. Geneva, Switzerland: World Health Organization; 2001.
4. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. Lancet 1998; 351(suppl III): 5-7.
5. World Health Organization. Global strategy for the prevention and control of sexually transmitted infections: 2006-2015: breaking the chain of transmission. Geneva, Switzerland: World Health Organization; 2007.
6. Wasserheit JN. Epidemiological synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. STD 1992; 19: 61-77.
7. Cohen MS, Hoffman IF, Royce RA, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. Lancet 1997; 349(9069): 1868-73.
8. Hawkes S, Mabey D, Mayaud P. Partner notification for the control of sexually transmitted infections: effectiveness in resource poor countries is unproved. Letter to the editor. BMJ 2003; 327: 634-635.
9. Grosskurth H, Mosha F, Todd J, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomized controlled trial. Lancet 1995; 346: 530-36.
10. Gregson S, Adamson S, Papaya S, et al. Impact and process evaluation of integrated community and clinic-based HIV-1 control: A cluster-randomised trial in eastern Zimbabwe. PLoS Med. 2007; 4(3): e102. doi:10.1371/journal.pmed.0040102
11. Kamali A, Quigley M, Nakiyingi J, et al. Syndromic management of sexually-transmitted infections and behavior change interventions on transmission of HIV-1 in rural Uganda: a community randomized trial. Lancet 2003; 361(9358): 645-652.
12. Wawer MJ, Sewankambo NK, Serwadda D, et al. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Lancet 1999; 353: 525-535.
13. Colvin M, Bachmann MO, Homan RK, et al. Effectiveness and cost effectiveness of syndromic sexually transmitted infection packages in South African primary care: cluster randomized trial. Sex Transm Infect 2006; 82(4): 290-4. doi: 10.1136/sti.2005.019240
14. Adams EJ, Garcia PJ, Garnett GP, et al. The cost-effectiveness of syndromic managment in pharmacies in Lima, Peru. Sex Transm Dis 2003; 30(5): 379-387.
15. Clark JL, Lescano AG, Konda KA, et al. Syndromic management and STI control in urban Peru. PLoS ONE 2009; 4(9): e7201.
16. Romoren M, Sundby J, Velauthapillai M, et al. Chlamydia and gonorrhoea in pregnant Batswana women: Time to discard the syndromic approach? BMC Infectious Diseases 2007; 7(27). doi: 10.1186/1471-2334-7-27
17. Korenromp EL, White RG, Orroth KK, et al. Determinants of the impact of sexually transmitted infection treatment on prevention of HIV infection: a synthesis of evidence from Mwanza, Rakai, and Masaka intervention trials. JID 2005; 191(Suppl 1): S168-175.
18. White RG, Orroth KK, Glynn JR, et al. Treating curable sexually transmitted infections to prevent HIV in Africa: Still an effective control strategy? JAIDS 2008; 47(3): 346-353.
19. Management of Sexually Transmitted Infections Using Syndromic Management Approach: Guidelines for Service Providers. Lilongwe, Malawi: Malawi Ministry of Health; 2007.
20. Brown LB, Krysiak R, Kamanga G, et al. Neisseria gonorrhoeae Antimicrobial Susceptibility in Lilongwe, Malawi, 2007. Sexually Transmitted Diseases 2010; 37(3): 169-172.
21. National Statistical Office (NSO) [Malawi] and ORC Macro. Malawi Demographic and Health Survey 2004. Calverton, Maryland:

NSO and ORC Macro; 2004.
22. Centre for Social Research, Save the Children Federation USA, Malawi Ministry of Health and Population, MEASURE Evaluation. Avoiding Unwanted Pregnancy and Sexually Transmitted Infections: A Rural Malawi District Study. Chapel Hill, NC: MEASURE Evaluation; 2004.
23. Malawi Government. Mangochi District Profile. Limbe, Malawi: Montfort Press; 1999.
24. National Statistical Office. Malawi: An Atlas of Social Statistics, 2002. Zomba, Malawi: National Statistical Office; 2003.
25. US Census Bureau (2011). International Data Base, Demographic Indicators, Malawi, 2000. (http://www.census.gov/population/international/data/idb/country.php). (July 12, 2011).
26. Joint United Nations Programme on HIV/AIDS (UNAIDS), United Nations Children's Fund (UNICEF), World Health Organization (WHO). Malawi: Epidemiological Fact Sheets on HIV/AIDS and Sexually Transmitted Infections. Geneva, Switzerland: UNAIDS, UNICEF, WHO; 2004. (http://data.unaids.org/Publications/Fact-Sheets01/malawi_en.pdf). (August 3, 2011).
27. Stata Corporation. Stata statistical software, release 11. College Station, TX: Stata Corporation; 2011.
28. Wetmore CM, Manhart LE, Wasserheit JN. Randomized controlled trials of interventions to prevent sexually transmitted infections: learning from the past to plan for the future. Epidemiol Rev 2010; 32(1): 121-136.
29. Ng BE, Butler LM, Horvath T, et al. Population-based biomedical sexually transmitted infection control interventions for reducing HIV infection. Cochrane Database Syst Rev 2011; 3: CD001220.
30. Ward H, Ronn M. Contribution of sexually transmitted infections to the sexual transmission of HIV. Curr Opin HIV AIDS 2010; 5(4): 305-310.
31. Minnis AM, Steiner MJ, Gallo MF. Biomarker validation of reports of recent sexual activity: results of a randomized controlled study in Zimbabwe. Am J Epidemiol 2009; 170(7): 918-924.
32. Damisoni H, Bicego G. Malawi Demographic and Health Survey 2000. Chapter 11: AIDS and Other Sexually Transmitted Infections. Zomba, Malawi: National Statistical Office and Macro International, Inc.; 2000. (http://www.measuredhs.com/pubs/pdf/FR123/11Chapter11.pdf). (Accessed August 3, 2011).