HIV Partner Notification in Malawi: Comparing Methods and Predicting Partner Testing

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ABSTRACT

LILLIAN B. BROWN: HIV Partner Notification in Malawi: Comparing Methods and Predicting Partner Testing
(Under the Direction of William C. Miller)

HIV transmission in sub-Saharan Africa is predominately heterosexual. Sexual partners of persons with newly diagnosed HIV infection require HIV counseling, testing and, if necessary, evaluation for therapy. However, many African countries do not have a standardized protocol for partner notification and the effectiveness of partner notification has not been evaluated in developing countries.

We conducted a randomized trial of HIV partner notification to determine the rates of counseling, testing and new HIV diagnoses among partners. Individuals with newly diagnosed HIV infection presenting to STI clinics in Lilongwe, Malawi were randomized to one of three methods of partner notification: passive referral, contract referral, or provider referral. The passive referral group was responsible for notifying their partners themselves. The contract referral group was given seven days to notify their partners, after which a health care provider contacted partners who had not reported for counseling and testing. In the provider group, a health care provider notified partners immediately. Partners to index patients enrolled in the passive and contract referral arms were used to identify characteristics of partners unlikely to report for counseling and testing.

Overall, 240 index patients named 302 sexual partners and provided locator information for 252. Among locatable partners, 107 returned for HIV counseling and

testing. The proportion of partners returning was 24% (95% CI 15 – 34%) in the passive referral arm, 51% (95% CI 41 – 62%) in the contract referral arm, and 51% (95% CI 40 – 62%) in the provider referral arm ($p<0.001$). Among returning partners (n=107), 67 (64%) were HIV-infected with 54 (81%) newly diagnosed. Partner's failing to report for testing was associated with male partner sex, relationship duration less than 6 months or between 6 and 24 months, and index education greater than primary.

This research is the first to provide evidence on the most effective method of partner notification in sub-Saharan Africa. Active partner notification was feasible, acceptable, and effective among STI clinic patients. Using a risk score to identify partners unlikely to report on their own can reduce the resources required to attempt to locate all partners in the community while increasing the testing yield compared to patient-referral.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
GUD	Genital Ulcer Disease
HIV	Human Immunodeficiency Virus
HTC	HIV Testing and Counseling
KCH	Kamuzu Central Hospital
KSU	Kamuzu Central Hospital STI Unit
RNA	Ribonucleic Acid
STI	Sexually Transmitted Infections
WHO	World Health Organization

CHAPTER 1

SPECIFIC AIMS

The prevalence of HIV infection in sub-Saharan Africa is the highest in the world, yet most infected persons do not know their HIV status[1, 2]. Late diagnosis of HIV infection worsens treatment outcomes, and HIV counseling and testing provides an entry point to ART care, psychosocial support, and basis for behavior change. Increasing counseling and testing rates among high-risk populations represents an opportunity to increase early diagnosis and treatment. Partners of individuals testing positive while seeking treatment for sexually transmitted infections (STIs) are a particularly important population to target for increased counseling and testing as HIV discordance within couples is common in Africa[1, 3], and infectiousness is high in HIV-infected individuals with a concurrent STI. Providing counseling and testing to partners of individuals recently diagnosed with HIV infection is an important way to target prevention strategies and provide early care to a very high risk population.

Partner notification involves informing the sexual partners of HIV-positive persons that they have been exposed and encouraging them to seek counseling, testing and other prevention and treatment services. The effectiveness of partner notification is unknown in low-income countries. However, disclosure of HIV-status by women in

antenatal and post-partum clinics often increases prevention behaviors. In these settings, successful partner notification leads to greater use of antiretroviral drugs to avoid perinatal HIV transmission, greater adherence to advice to avoid breastfeeding, and higher levels of condom use [4]. Despite the potential benefits, very little is known about the process of partner notification by men and non-pregnant women or the best strategy for increasing counseling and testing rates.

The proposed research will compare the three main methods of partner notification in an STI clinic population: passive referral, contract referral, and provider referral. Passive referral requires index patients to notify partners concerning their possible exposure to HIV by themselves. Under contract referral, the index patient is given a period of time to contact and notify sexual partners him/herself; if partners are not notified and tested within this time period, health care providers will complete the process. Under provider referral a health care provider contacts the partners directly. A predictive model will be used to develop a risk score algorithm to identify partners likely to require provider-assisted referral. *My **overarching hypotheses** are that active partner notification (contract referral or provider referral) will result in higher rates of partner HIV counseling and testing than passive referral; active partner notification (contract referral or provider referral) will identify more undiagnosed HIV infections among partners; and predictors of partner testing can be used to develop a risk score algorithm predicting partners unlikely to seek counseling and testing following notification*. This research will be the first to provide important evidence on the most effective method of partner notification in a sub-Saharan African STI clinic patient

population. Information gained through this research will consequently facilitate formation and adoption of appropriate explicit partner notification guidelines.

SPECIFIC AIM 1: To examine the relative effectiveness of three methods of partner notification: patient referral, contract referral, and provider referral, to achieve partner HIV-testing.

SPECIFIC AIM 2: To determine the proportion of newly diagnosed HIV cases, including acute HIV, for each method of partner notification.

SPECIFIC AIM 3: To identify index, partner, and community factors predicting partner testing and counseling and develop a risk score algorithm to target provider assisted referral.

Overview: Patients with newly diagnosed HIV infection in the Kamuzu Central Hospital (KCH) STI clinic in Lilongwe, Malawi will be randomized to passive referral, contract referral, or provider referral methods of partner notification. Endpoints of interest will be the proportion of partners receiving counseling and testing, partner HIV status, and predictors of partner counseling and testing.

CHAPTER TWO

BACKGROUND

HIV in Malawi

HIV prevalence in Malawi is among the highest in the world. AIDS is now the leading cause of death among 15-49 year olds in Malawi. In a population of 11.5 million, an estimated 1 million adults and children are living with HIV/AIDS. Each year another 81,000 become infected [5]. HIV prevalence is highest in urban areas, estimated at 17.1% in a population-based survey (Figure 1) [2]. Despite this high prevalence, only a small proportion of the population reports being tested. In Lilongwe district, only 17% of women and 16.5% of men report receiving an HIV test and approximately 80% of HIV infected individuals have never been tested and do not know their status [2].

HIV and Sexually Transmitted Infections

Persons attending sexually transmitted infections (STI) clinics and their sexual partners are at high risk for HIV infection. STI Clinics in urban areas of sub-Saharan Africa record HIV prevalence rates of 46-50% [6] and as such, provide an excellent opportunity to identify (through HIV testing and counseling) and refer HIV positive patients, notify their partners and provide STI and counseling interventions that help reduce HIV transmission. The STI Unit at Kamuzu Central Hospital (KCH) is a free clinic that

services the general public residing within or passing through Lilongwe district and serves approximately 1100 STI patients per month. Currently individuals seeking treatment at the clinic are tested for HIV under an "opt-out" policy in which they are tested for HIV unless they specifically decline (in contrast to an "opt-in" policy in which a person must explicitly request to be tested). During the first year of opt-out testing, 6602 patients with no previous HIV test were seen. Of these, 4111 (62%) were tested for HIV, and 1127 (27%) new HIV infections were identified. Approximately 5 new infections are identified in the clinic each day. Each of these newly diagnosed individuals has sexual partners who require evaluation for therapy, if they are also infected, or prevention interventions, if they are uninfected.

HIV Testing and Importance of Early Diagnosis

HIV-infected individuals seeking care at an STI clinic are at high risk for onward transmission. STIs can facilitate HIV transmission by invoking more infectious HIV variants[7] and increasing HIV concentrations in genital lesions and semen[8, 9]. The risk of HIV transmission is directly related to viral burden, and increases markedly with increasing concentrations[10]. Partners of these individuals are exposed to high levels of virus and it is therefore imperative to reach them for evaluation for treatment (if they are also infected) or prevention measures (if they are uninfected).

In spite of the high prevalence of infection, many HIV-1-infected in this region of the world continue to go undiagnosed. Even when diagnosis occurs promptly, many persons are lost to the health care system and present for care too late for the benefits

of antiretroviral therapy [11-13]. Late presentation is associated with depleted CD4 counts, and CD4 count at the initiation of therapy predicts survival [14, 15]. Late presenters have significant short-term mortality[16-18] and early diagnosis of HIV infection is increasingly understood as the critical gateway to providing individuals with ART and effective prevention and care. The majority of HIV transmission occurs from persons unaware they are infected [19]; therefore, it is an important public health responsibility to increase the percent of HIV-infected individuals who know their status.

Treatment is currently a reality for HIV infected individuals in Malawi. Malawi began a national scale-up of antiretroviral treatment (ART) in 2004, and has since started over 100,000 people on treatment [5, 20]. Effective partner notification will increase HIV testing rates, providing an opportunity earlier diagnosis and referral for treatment.

HIV Partner Notification

The purpose of HIV partner notification is to increase HIV diagnosis and referral. Partner notification involves informing sexual partners of HIV-positive persons that they have been exposed and encouraging them to seek counseling, testing and other prevention and treatment services. Two important goals of HIV partner notification are to provide earlier diagnosis and referral to appropriate services for those who are infected, and to provide testing and prevention counseling to HIV negative individuals and promote risk reduction [21, 22].

The three main methods of partner notification are passive referral, contract referral, and provider referral[23]. Passive referral is currently the standard of care, in which the patient is encouraged to counsel partners concerning their possible exposure to HIV by themselves. Under contract referral health care providers of the index patient obtain names and locations of the partners, but allow the source patient a period of time to contact and notify sexual partners him/herself. If partners are not notified and tested within this time period, the health care providers will contact and counsel the partners, advising them they have been exposed to HIV while maintaining the anonymity of the index case. Under provider referral, HIV positive people give the names and locations of their sexual partners to a health care provider, who then contacts the partners directly, advising them they have been exposed to HIV while maintaining the anonymity of the index case. In contrast to passive referral where the index patient must notify the partner themselves, the anonymity of the index case is maintained during contact with the partners during contract referral and provider referral. Both contract referral and provider referral demand more resources than passive referral and requires the cooperation of the index case.

Passive notification is currently the standard of care in Malawi. In the KCH STI clinic, newly diagnosed patients are provided notification cards to give to their partners. The notification card instructs the partner to return to the clinic, and allows partners to bypass the regular reception and waiting room to receive priority counseling and testing. This method of passive referral only rarely leads to presentation of the partner. Less than 1% of all clinic visits at KCH are referred partners (for all STI syndromes,

including HIV). The current National Malawi HIV/AIDS Testing and Counseling Policy on disclosure indicates that counselors should 'advise and assist' HIV positive individuals to notify partners (passive notification), but also identified a need to 'develop appropriate and explicit guidelines outlining how, when and to whom beneficial disclosure by a health care worker may be made.'

Evidence on Partner Notification in Developed Countries

Public Health partner notification programs were incorporated into U.S. and British syphilis control efforts in the 1930s and 1940s, and were later expanded to include gonorrhea, chlamydial infection, and HIV. In the United States, partner notification has been required of state and local health departments as a condition for receiving federal HIV prevention funds since the 1980s. Currently, local and state health departments that receive funding from the CDC are required to include partner counseling and referral services (PCRS) in their HIV prevention programs[24]. In American and European settings, approximately 20% of partners tested through partner notification services are new HIV diagnoses. An evaluation of the success of PCRS in North Carolina revealed that 20.5% of tested partners of HIV index patients had HIV infections that were previously undiagnosed[25] and 22% of partners referred through partner notification services in San Francisco were new HIV diagnoses[26]. A review of partner notification in 6 European countries uncovered new HIV infections in 21% of current partners and 10% of ex-partners[27] and 25% of tested partners in Scotland were new HIV infections[28]. The yield of new diagnoses is potentially much greater in the higher prevalence African settings.

Passive referral in developed countries results in few partners seeking counseling and testing. In a small study in the U.S. comparing patient referral with contract referral, partner notification and uptake of HIV testing increased with contract referral [29]. In the contract referral arm, 50% of partners were successfully notified and of those, 46% accepted HIV testing in the contract referral arm. In contrast, only 7% of partners were notified in the passive referral arm. In an evaluation of a public health partner notification only 20% of locatable partners received counseling through patient referral[30]. Similar results with passive notification were observed in the UK. Among 501 newly infected HIV-positive patients, only 27 partners received HIV counseling and testing[31]. Active partner notification services has increased receipt of HIV counseling and testing among sexual partners of patients with new HIV diagnoses, and those who successfully notify their partners are more likely to disclose their HIV status to future sex partners. In addition, relationship dissolution is lower and condom use is higher when partner notification messages successfully reach the partner[32].

Partner Notification and HIV Disclosure in Developing Countries

The effectiveness of HIV partner notification in developing countries is unknown since, to date, partner notification strategies have not been evaluated in developing countries[33]. However, patients in STI clinics report provider-assisted referral would be helpful for STI partner notification and partner referral [34]. HIV partner notification has recently been implemented in Cameroon and to date over 2000 partners have been

evaluated [35], supporting the feasibility of partner notification in Africa. Additionally, descriptive studies demonstrate benefits to partner disclosure in African settings.

Partner disclosure in the antenatal setting led to increased condom use [4, 36-38] and greater use of antiretroviral drugs to avoid perinatal transmission [4]. Partner disclosure in the post-partum setting also appeared to influence decisions regarding breastfeeding [37] and subsequent pregnancies [38], although others observed no effect of disclosure on subsequent reproductive behavior [39]. Partnership dissolution is low after disclosure in the antenatal or postnatal setting [36, 40].

Disclosure to a main partner by women attending HIV Care facilities report safer sexual behaviors, including increased condom use and abstinence[41]. Non-disclosure among men and women accessing HIV services in South Africa was associated with increased multiple partnerships and lower condom use compared to those who had disclosed. In a community sample of South African men and women disclosure to partners was associated with lower risk behavior, including increased condom use and decreased number of sexual partners[42].

These studies demonstrate the potential benefits for partner notification, such as risk behavior change when both partners know their status and making informed reproductive health choices, particularly the more contemporary studies in which treatment options were available. However, all are observational, all rely on self-

reports of disclosure, and none address the efficacy of different methods of partner notification in Sub-Saharan Africa.

Predicting HIV testing

Clinical prediction models are a method to identify individuals at high risk for a medical problem who might benefit from treatment or intensified prevention efforts. Studies have identified characteristics, behaviors, and contexts associated with HIV testing behavior, HIV status and HIV outcomes.

HIV testing is associated with age[43], sex, and education status. In addition, transport difficulties limit the number of people seeking voluntary counseling and testing at established health care settings and stand-alone VCT sites [44]. Among urban Malawians, women are more likely to have tested than men and men and women 20-29 with a secondary education or higher are the most likely to test for HIV[2]. In Malawi rates of HIV infection increase with education, wealth, and high-risk sexual partners (non-marital, non-cohabitating)[2].

Risk scores can be used to efficiently target resources and inform counseling messages. A paper-based risk score algorithm to identify acute HIV infection in Malawi reduces the number of expensive RNA PCR tests required to identify individuals in the highly infectious, acute phase of HIV infection[45]. Men who have sex with men (MSM) at high

risk for HIV acquisition can be identified using a risk score and is used in practice to intensify interventions and follow-up among men at high risk for HIV infection[46]. Risk assessment tools have also attempted to identify individuals at high risk for HIV infection among STD clinic attendees in order to target HIV testing [47], however a highly sensitive tool did not successfully reduce the amount of tests in that high-risk population. Models have also been developed to successfully predict STI infection[48] and target with intensive interventions. Predictive models have also been developed to predict HIV acquisition among injection drug users [49] with the purpose of stratifying participants in clinical trials.

CHAPTER THREE

RESEARCH DESIGN AND METHODS

Overview

We conducted a three arm randomized clinical trial, comparing three methods of HIV partner notification: patient referral, contract referral, and provider referral. Briefly, 240 individuals with newly diagnosed HIV-infection at the Kamuzu Central Hospital STI clinic were randomized to one of the three arms. In the clinical trial, the primary outcome was partner HIV counseling and testing. The secondary outcome was the proportion of partners identified with HIV infection. In addition to the primary analyses of the clinical trial, we assessed predictors of partner HIV counseling and testing and developed a risk score algorithm to identify partners unlikely to present for counseling and testing on their own in order to refer them to immediate provider-assisted referral.

Study Population

The study population comprised newly diagnosed HIV-infected individuals and their sexual partners seeking care at the Kamuzu Central Hospital STI Unit (KSU) and the Bwaila Hosptial outpatient STI unit in Lilongwe, Malawi. Both the STI Unit at Kamuzu Central Hospital and at Bwaila hospital service the general public residing within or passing through Lilongwe district and serves approximately 1100 STI patients per

month. Rapid HIV tests are performed under an opt-out protocol by clinical officers, nurses, and voluntary counseling and testing (VCT) counselors. At KSU individual pre-test counseling is performed and Determine and Unigold rapid HIV tests are run in parallel. The rapid test results are recorded as positive (both positive), discordant (one positive, one negative), or negative (both negative). At Bwaila group pre-test counseling is performed followed by individual testing and post-test counseling. At Bwaila Determine and Unigold rapid HIV tests are performed following the World Health Organization's serial testing protocol [50]. Patients who received a positive HIV test result for the first time were asked about their interest and willingness to participate in the study by the VCT counselor or clinician who gave them the test result. Patients with discordant HIV tests at KSU were advised they were at high risk for being in the window period of HIV infection, and asked if they would like to be screened for a separate ongoing study in the clinic focused on the immunology of acute HIV infection. If they were not interested in being screened for acute HIV infection, they were advised to return for repeat testing in a short period of time, and if positive, were eligible at that point. Limited information was collected about patients who were not interested in participating, including demographics and reasons for refusal, in order to make comparisons between those who do and do not consent.

Study Procedures

Enrollment and randomization

Index patients completed an informed consent process with a nurse or counselor, in which the study procedures were explained and the potential risks and benefits of

participating discussed in the patient's native language (Chichewa). Patients who had a positive HIV test result for the first time, live in Lilongwe, were 18 years or older, had been sexually active in the last 90 days, were willing and able to provide locator information for their sexual partners, and agree to be randomized to a method of partner notification were eligible to participate. All received counseling on the importance of safe sex behavior, staged using WHO clinical staging criteria, and had blood drawn for CD4 counts using flow cytometry. Participants answered a short questionnaire about recent sexual behavior, including the number, type, and names and detailed locations of sexual partners in the past three months. All were provided notification cards to give to their partners, which included instructions for returning to the clinic and an identification number linking the partner to the index patient. Index patients were then randomized to passive, contract, or provider referral using a permuted block design with randomly allocated block sizes of 6, 9, and 12, stratified by sex and study site. Randomization assignment was concealed in a sealed envelope until the end of the enrollment visit (after all partner data and locator information had been collected). A randomization list was generated in advance using Stata version 10 statistical software (College Station, TX). Separate lists were generated for men and women and study site. The study arm allocation for each study number was concealed in a sealed envelope with only the study number on the outside until the end of the enrollment visit (after all partner data and locator information had been collected).

Index patients randomized to the passive referral arm were counseled to refer their partners to visit the clinic for HIV counseling and testing.

Index patients randomized to the contract referral arm were advised that if their partners do not present for counseling and testing within 7 days, community outreach workers would contact and counsel the partners to visit the clinic for counseling and testing, advising them they had been exposed to HIV while maintaining the anonymity of the index case.

Index patients randomized to the provider referral arm were advised that a community outreach worker would then contact the partner(s) directly after 24 hours, advising them they have been exposed to HIV while maintaining index case anonymity, and would encourage them to visit the clinic for counseling and testing.

All community contact with study participants was performed by community outreach workers from the KCH STI clinic. These community outreach workers are trained HTC counselors or nurses who are trained in HTC procedures.

Partner visits

Regardless of study arm and method of notification, all partners of the index patients received referral cards to bring to the clinic so that they could be identified as a partner. All patients visiting the STI clinic during the study period were asked about their receipt of a partner notification card. A log of named partners was maintained during the study period and checked against the KCH clinic log weekly to ensure all partners visiting KCH were captured regardless of whether they brought their partner

notification card. Index patient returning for their 2 week follow-up visit were asked if they know whether or not their partner sought HIV counseling and testing, and if they knew where the partner went for it. If the partner did not visit KCH for counseling and testing, area HTC centers were visited by a community tracer to confirm the visit.

Partners were tested for HIV under the opt-out testing protocol which is standard of care in the clinic. Partner HIV-status was determined in the clinic using Determine and Unigold rapid HIV tests conducted in parallel, and confirmed by western blot. HIV antibody-negative or -indeterminate specimens were screened for the presence of HIV RNA using the ultrasensitive Roche Amplicor Monitor HIV RNA assay. After partners provided consent they completed a questionnaire about their sexual behavior and HIV testing history and had blood drawn for CD4 counts, if the rapid tests were positive, or RNA testing, if the rapid tests were negative or discordant.

Follow-up visits for clinical care

Index patients: Index patients returned to the clinic 2 weeks after their enrollment visit to receive the results from their CD4 test and initiate HIV care. Index patients eligible to receive antiretroviral therapy based on CD4 count were referred to the Lighthouse clinic, an HIV treatment clinic adjacent to KCH, or an ART treatment clinic of their choice. Every reasonable effort was made to retain index patients in clinical care. Detailed locator information was collected about the index patient, and community tracers were employed if the index patient did not return for the follow-up visit.

Additionally, if the participant had a mobile phone study staff called them as soon as they missed their follow-up visit. Other retention methods, such as reminder cards, were not feasible for this population, as mail service to homes is uncommon.

In addition to initiating HIV care, the follow-up visit was used to obtain limited information about the partner notification process. Index patients were asked whether their partners were notified, how their partners were notified, and their knowledge of whether their partners had sought HIV counseling and testing,

Partners: Partners with HIV infection were offered the same clinical care opportunities as the index patients.

Data Analysis

Specific Aim 1

Determine which method of partner notification, patient referral, contract referral, or provider referral, will result in the highest rate of partner referral and partner HIV-testing uptake.

Hypothesis: *Partner HIV counseling and testing will differ between study arms. Specifically, active partner notification (contract referral or provider referral) will result in a higher proportion of partner HIV counseling and testing than passive referral, and provider referral will have higher partner counseling and testing than contract referral.*

Outcome: The primary outcome for Aim 1 was the proportion of named, locatable partners who return to the clinic and receive HIV counseling and testing by study arm. The secondary outcome for Aim 1 is the proportion of named partners who return to the clinic, including those who consent to HIV testing and those who decline HIV testing. There is not likely to be a substantial difference between these two outcomes, as partners who choose to travel to the clinic are likely to agree to be tested for HIV. Subgroup analyses by type of partner will be performed. Index patients will be asked to indicate whether each partner is their main partner (e.g. spouse) or a casual partner (e.g. bargirl).

Statistical Analysis

The two outcomes, proportion of partners agreeing to testing and the proportion of partners returning for counseling and testing, will be evaluated by study arm. Subgroup analyses will be repeated by type of partner (main partner vs. casual partner) and by sex.

It is important to recognize that the units of analysis are the partners, and they may not be fully independent observations. One index case may name more than one partner, although we anticipated that a large majority will name only one partner based on our experience in the STI clinic in Lilongwe. Because of this clustering on the index case, traditional statistical tests are not appropriate. To account for the clustering, we used unconditional logistic regression with a cluster robust variance estimator [51] to compare the proportions of HIV testing uptake in each arm of the study. In this model, the

dependent variable is represented as the natural log of the odds a partner will be tested for HIV:

$$\ln\left(\frac{p}{1-p}\right) = \alpha + \beta_1 contract + \beta_2 provider \qquad \text{(equation 3.1)}$$

Study arm (referral method) is a disjoint indicator variable in this model where passive referral is the reference level, contract=1 if contract referral and 0 if provider or passive referral, and provider=1 if provider referral and 0 if contract or passive referral. With this model without other covariates, the proportions in each study arm were calculated directly from the coefficients:

$$\begin{aligned} P(testing \mid passive\ ref\ erral) &= \frac{e^{\alpha}}{1+e^{\alpha}} \\ P(testing \mid contract\ ref\ erral) &= \frac{e^{\alpha+\beta_1}}{1+e^{\alpha+\beta_1}} \\ P(testing \mid provider\ ref\ erral) &= \frac{e^{\alpha+\beta_2}}{1+e^{\alpha+\beta_2}} \end{aligned} \qquad \text{(equation 3.2)}$$

95% confidence intervals were calculated using robust standard errors, and differences between the referral methods were determined using the Wald p-values associated with each coefficient either directly (β_1 represents test of contract versus passive; β_2 represents test of provider versus passive) or by specification after running the model (H_0 for contract versus provider: $\beta_1 = \beta_2$,). The comparison between contract referral vs. passive referral and provider referral vs. passive referral were treated as two separate confirmatory experiments, each tested at $\alpha = 0.05$. The comparison between provider and contract referral were exploratory in nature as the study was not powered to detect differences between these two active methods of partner notification.

In the subgroup analysis by type of partner separate models were fit for main partners and casual partners. Main partners were defined as spouses and live-in partners, or boyfriend/girlfriend if the index did not name a spouse or live-in partner. Casual partners included regular casual partners, infrequent casual partners, sex workers and boyfriend/girlfriend if the index already had a spouse. In the subgroup analysis by sex separate models were fit for men and women.

Cox Proportional Hazards Regression with robust confidence intervals [52] was used to investigate time to presentation for each partner by method of partner notification. The outcome was defined as the time to HIV counseling and testing, and was calculated as the number of days between the index patient's first visit and the date of presentation. The Wald chi-square test was used to compare the effect of method of partner notification on time to presentation. The proportional hazards assumption was evaluated using the Cox test and visually by plotting the ln(-ln(survival)) against ln(time).

Sensitivity analyses were conducted where unit of analysis was the index case (rather than the named partner of the index case) and the outcome was defined as 'at least one partner visiting the clinic'.

Specific Aim 2

Determine the proportion of newly diagnosed HIV cases, including acute HIV, for each method of partner notification.

Hypothesis: *The proportion of previously undiagnosed HIV cases identified will differ between study arms. Specifically, provider and contract referral will identify a higher proportion of undiagnosed HIV cases than passive referral.*

Outcome: The outcome was the proportion of previously undiagnosed HIV cases, including acute HIV, in each study arm, defined as the number of new HIV cases identified per index case.

Statistical Analysis

Both the proportion of named partners testing HIV positive and the rate of newly diagnosed HIV cases were reported in each study arm. The analysis proceeded as described for Aim 1 using unconditional logistic regression with a cluster robust variance estimator [51] to compare the proportions of HIV infection in each arm of the study. Sub-group analysis by type of partner (main partner vs. casual partner) and sex were performed.

95% confidence intervals were calculated using robust standard errors, and differences between the referral methods were determined using the Wald p-values associated with each coefficient directly (β_1 represents test of contract versus passive; β_2 represents test of provider versus passive).

Specific Aim 3

Identify predictors of HIV counseling and testing uptake among partners and develop a risk score algorithm to target provider-assisted referral.

Hypothesis: *Predictors of partner testing can be used to develop a risk score algorithm predicting partners unlikely to seek counseling and testing following notification*

Identifying characteristics of index patients and their sexual partners who are likely to return for counseling and testing will be useful for refining HIV partner notification and informing the implementation of HIV partner notification in this setting. A predictive model was developed using all partners with locator information provided by the enrolled index patients who were not traced by a community counselor.

Outcome The outcome for the predictive model was partner failing to report to the clinic for counseling and testing.

Statistical Analysis

Data and Variable Selection

Data provided by the index during their enrollment visit during the clinical trial was used to construct the predictive models. The reliability of a logistic predictive model is a function of the prevalence of the outcome in the study population, the total study population, the number of variables fitted in the model, and how well the variables have been measured. To estimate the maximum number of variables a model could support, we used the formula [(3*n1*n2)/N]/10 where n1 is the number of persons with the outcome, n2 is the number of persons without the outcome, and N is the total

population [53]. One-hundred seventy locatable partners were named in the passive and contract referral arms and had the opportunity to report for testing on their own accord and 37 partners reported for testing on their own. Eight predictors could be included in the full model.

Variables hypothesized a priori to be predictors of partner reporting for counseling and testing included index characteristics and partner characteristics. Index characteristics included age of the index, enrollment site (KCH vs. Bwaila STI clinics), diagnosis of genital ulcer disease on physical examination, and index education. Partner characteristics included partner sex, partner type (main partner vs. non-main partner), duration of partnership, and high transport barriers.

Partner testing was hypothesized to differ by sex, as previous analysis of the KSU database demonstrated men were more likely to opt-out of HIV testing than women and experience suggested male partners are less likely to seek counseling and testing. Partner type was also hypothesized to be related to partner HIV counseling and testing and response to partner notification methods. Indexes may be more likely to disclose to and notify main partners, and once notified main partners may be more likely to seek counseling and testing.

Indexes may be more likely to notify partners they have known for longer and less likely to notify new sexual partners. Duration of partnership was categorized at less than 6 months, 6 – 24 months, and greater than 24 months in order to capture new

partners, use information about the dose-response relationship between length of partnership and partner testing, and ensure adequate strata sizes for multivariate modeling.

Age is a risk factor for HIV-infection as sero-prevalence estimates show the prevalence of HIV increases with age. Age is also associated with the acquisition of new partners, with younger patients more likely to acquire new partners and 15-19 year olds and 20-24 year olds reporting the highest rate of risky partnerships [2]. Previous analyses of the KSU database suggested younger patients were more likely to opt-out of HIV testing. Age of the index was dichotomized at age less than 25.

The diagnosis of genital ulcer disease was hypothesized to influence partner testing because the partner may also have genital sores and be motivated to seek treatment for him or herself. GUD is also a know co-factor for HIV transmission, increasing the risk for both transmission and acquisition.

Sentinel surveillance data on HIV infection in Malawi suggests higher education is associated with HIV infection and previous analysis of the KSU database showed individuals with greater than a primary education were less likely to consent to HIV testing (more likely to opt-out). Education was coded as a dichotomous variable with a cut-point at completion of primary education because of the similarity of participants within these binary strata of education. Since primary education is free in Malawi the

greatest difference exists between persons with a primary education or less and persons with any secondary education.

Partner area of residence was described by the index when they provided locator information about the each partner. Lilongwe is organized by discrete, numbered neighborhoods (called area). An indicator term would capture economic, geographic, and unmeasured variables contributing to the probability of partner return. However, the biggest geographical barrier to visiting the clinic for HTC is transport logistics. Distance, transport availability (whether an area is on a main public transport network), and transport cost are highly correlated (areas farther from the hospital don't have public transport and are expensive to travel from) so a single indicator variable for transport barriers was created. Transport barriers were considered high if the partner did not live in an area served by the public transport network in Lilongwe or if the partner would need to pay for more than one mode of transport in order to reach the clinic.

Model building

We first calculated unadjusted odds ratios for partner failing to report and all partner characteristics (male sex, non-main partner, relationship duration less than 6 months and 6-24 months, and transport barriers) and index characteristics (age less than 25 years, enrollment site, STI other than GUD diagnosed, and greater than primary education).

All variables were entered into the full model. We constructed a simplified final model using backwards selection with a predetermined stopping rule of p = 0.10 to maintain predictive ability and reduce the likelihood of omitting important variables. Nested models were compared using likelihood ratio tests. We examined the model for collinearity and overly influential covariate patterns [54].

A risk score algorithm was developed for Model 1 to predict the risk of a partner not reporting for counseling and testing among partner's who were not traced in the community. In order to create a simple instrument that can be applied in the field we assigned each variable in the final Model 1 a predictor score equal to its beta coefficient (natural log of the adjusted odds ratio) rounded to the nearest integer [55]. We summed the risk scores to obtain a risk score for each participant. We assessed model accuracy and risk score accuracy using area under the receiving operator characteristics curves.

We calculated the proportion of partners requiring tracing by a community counselor under each risk score scenario as:

$$P_{traced} = Se \times P_{NR} + (1 - Sp) \times (1 - P_{NR}) \qquad \text{(equation 3.3)}$$

Where P_{traced} = proportion of partners traced, Se = sensitivity, Sp = specificity, and P_{NR}= proportion failing to report

We calculated the proportion of partners traced unnecessarily as:

$$P_{unnecessary} = (1 - Sp) \times (1 - P_{NR}) \qquad \text{(equation 3.4)}$$

Where $P_{unnecessary}$ = proportion of partners traced unnecessarily, Se = sensitivity, Sp = specificity, P_{NR}= proportion failing to report

In the clinical trial, the proportion of partners who tested under universal provider assisted referral was 51%[56]. The estimated proportion of partners tested under each risk score scenario was calculated as:

$$P_{tested} = (0.51 \times P_{traced}) + (Sp \times (1 - P_{NR})) \quad \text{(equation 3.3)}$$

where P_{tested} = estimated proportion of partners tested, Sp = specificity, P_{NR}= proportion failing to report, P_{traced} = number of partners traced

A false positive was a partner who was identified using the risk score algorithm for provider-assisted referral, but would have reported to the clinic on their own. A false negative is a partner who was not identified for provider-assisted referral using the risk score algorithm and did not receive testing. The relative costs of false negatives and false positives were compared at different model cut-points using the formula:

$$Cost = (1 - p) \times \frac{(1 - Sp_1) - (1 - Sp_2)}{p \times [(1 - Se_2) - (1 - Se_1)]} \quad \text{(equation 3.4)}$$

where p is the prevalence of partner testing on their own (21%), Sp_1 and Se_1 are the specificity and sensitivity of universal provider-assisted referral (cut-point=0) and Sp_2 and Se_2 are the specificity and sensitivity of each cut-point.

The cases of HIV missed for each cut-point relative to universal provider-assisted referral was calculated as the prevalence of HIV among tested partners (64%)[56] times the number of false negatives.

We performed internal validation of the modeling strategy and model performance using 1000 bootstrap repetitions [57].

Sample size and power calculations

The sample size of 240 was based on the initial level of funding to conduct the study, which included qualitative and cost-effectiveness endpoints in addition to the analyses outlined. The overall study was designed primarily to demonstrate a difference between patient referral and the two active methods of partner notification (contract and provider referral). Based on the assumption of one partner per index client and 15% of the partners in the passive referral arm presenting, the overall sample size of 240 index patients with 80 index patients in each arm was calculated prior to the start of the study to have 85% power to detect (α=0.05, two-sided test) a 25% difference between passive referral and the two active referral study arms (contract or provider). By assuming only one partner per index patient (when some patients will likely name more than one partner), these calculations provide a conservative estimate of the sample size required to yield 85% power and do not need adjustment for the effect of clustering.

Data Quality

Data was double-entered into an Access database and validated. Missing outcome data are not an issue for the primary analyses because there is no loss to follow-up. An intensive data collection training and the clinic's considerable experience completing case report forms for research studies minimized the missing values for the demographic data included in the predictive analyses.

CHAPTER FOUR

RESULTS: HIV PARTNER NOTIFICATION IS EFFECTIVE AND FEASIBLE IN SUB-SAHARAN AFRICA: OPPORTUNITIES FOR IMPROVED HIV TREATMENT AND PREVENTION

The prevalence of HIV infection in sub-Saharan Africa is the highest in the world, yet most HIV-1-infected persons in this region do not know their infection status[1, 2]. Persons who present late in the course of their HIV disease have significant short-term mortality[16]. Early diagnosis of HIV infection is increasingly understood as a critical gateway to appropriate ART provision and effective prevention. Furthermore, most HIV transmission occurs from persons unaware that they are infected[19]. Early recognition of HIV infection provides enormous personal and public health benefit.

In the United States and Europe, active provider-assisted partner notification has become a key HIV prevention strategy leading to increased HIV counseling and testing among sexual partners of patients with new HIV diagnoses[22, 27, 29]. Generally, three methods of partner notification are available: passive referral, contract referral, and provider referral[23]. With passive referral, the patient is encouraged to disclose the exposure of their partner(s) to HIV by themselves. Under contract referral, health care

providers allow the index patient a short period of time to contact, notify and refer sexual partners, after which a health care provider advises the contact of their exposure while maintaining the anonymity of the index case. Under provider referral, a health care provider contacts the partners immediately and directly, but with anonymity.

In sub-Saharan Africa, the effectiveness of partner notification strategies has not been evaluated[33]. Passive referral, the standard of care in Africa, has had minimal success[58]. Use of active partner notification has been limited by concerns regarding privacy protection and social harm, and apparent lack of community and political support. However, the potential benefit of partner notification is evident. In antenatal and postpartum clinics, disclosure of HIV-status by women has improved prevention behaviors including condom use[4, 37, 38], uptake of prevention of mother to child transmission activities[4, 37], and decision-making regarding subsequent pregnancies[38]. Clearly, the potential public health benefit of partner notification in sub-Saharan Africa is substantial.

We compared patient referral, contract referral, and provider referral among patients with newly diagnosed HIV in a sexually transmitted infections (STI) clinic setting in Malawi. The results suggest that partner notification is feasible, safe, acceptable and can increase the detection of patients with previously unrecognized HIV infection.

Methods

Study population

Persons with newly diagnosed HIV infection at Kamuzu Central Hospital and Bwaila Hospital outpatient STI clinics in Lilongwe, Malawi were recruited. All patients presenting to these STI clinics are tested for HIV under an opt-out protocol that includes group pre-test counseling, rapid tests (Determine HIV-1/2, Abbott Laboratories and Unigold, Trinity Biotech), and individual post-test counseling. Patients from Lilongwe who had a positive HIV test result for the first time, were 18 years or older, had been sexually active in the last 90 days, were willing and able to provide locator information for their sexual partners, and agreed to be randomized to a method of partner notification were eligible to participate.

Study procedures

Index patients provided informed consent and answered a short questionnaire about recent sexual behavior, including the number, type, and locations of sexual partners in the past three months. All were provided referral cards to give to their partners, were counseled on the importance of safe sex behavior, staged using WHO clinical staging criteria, and had blood drawn for CD4 counts using flow cytometry (Epics-XL, Coulter). Index patients were then randomized to passive, contract, or provider referral using a permuted block design with randomly allocated block sizes of six, nine, and twelve, stratified by sex and study site. The passive referral group was responsible for notifying their partners themselves. The contract referral group was given seven days to notify their partners, after which a health care provider contacted partners who had not reported for counseling and testing. Notification in the provider referral group occurred within 48 hours. Randomization assignment was concealed in a sealed envelope until

the end of the enrollment visit (after all partner data and locator information had been collected).

Index patients returned to the clinic two weeks after enrollment to receive CD4 test results and initiate HIV care. Index patients eligible for antiretroviral therapy based on CD4 count or WHO clinical stage were referred to a convenient HIV treatment clinic. Index patients were also asked whether their partners were notified, how their partners were notified, and their knowledge of their partners HIV counseling and testing behavior.

Incoming patients were identified as partners if they presented a partner referral card or their name was found on the log of named partners during cross-checking. Partners were tested for HIV under the opt-out testing protocol that is standard of care in the clinic. HIV antibody-negative or -indeterminate specimens were tested for the presence of HIV RNA using the ultrasensitive Roche Amplicor Monitor HIV RNA assay.

Statistical Analysis

Partners were considered "locatable" if the index was able to provide locator information, including name and where they could be found, during enrollment. Main partners were defined as spouses and live-in partners, or boyfriend/girlfriend if the index did not name a spouse or live-in partner. Casual partners included regular casual partners, infrequent casual partners, sex workers and boyfriend/girlfriend if the index already had a spouse. Partners were considered new HIV diagnoses if they were testing

for the first time or their previous test result had been negative. The primary outcome was partner visit to the clinic during the 30 days following index enrollment.

Based on the assumption of one partner per index client and 15% of the partners in the passive referral arm presenting, the overall sample size of 240 index patients with 80 index patients in each arm was calculated prior to the start of the study to have 85% power to detect (α=0.05, two-sided test) a 25% difference between passive referral and the two active referral study arms (contract or provider).

Unconditional logistic regression with a cluster robust variance estimator[51] was used to calculate 95% confidence intervals for the proportion of locatable partners visiting by arm and risk differences and relative risks of visiting for the two active referral arms versus the passive referral arm. Pre-planned subgroup analyses were performed by sex and type of partner (main partner vs. casual partner). Planned sensitivity analyses where the unit of analysis was the index case (rather than the named partner of an index case) and the primary outcome was defined as at least one partner visiting the clinic were conducted. Time to presentation among all locatable partners was analyzed using Cox Proportional Hazards Regression with robust confidence intervals[52] to account for clustering by index patient. The Wald chi-square test was used to compare the effect of method of partner notification on time to presentation. The proportional hazards assumption was evaluated using the Cox test and visually by plotting the ln(-ln(survival)) against ln(time). We used Stata version 10 (StataCorp, College Station, Texas, USA) for all analyses.

Ethical considerations

The Institutional Review Board at the University of North Carolina, Chapel Hill and the National Health Sciences Research Committee in Malawi approved the protocol. Informed consent was obtained from all participants prior to participation.

Results

We recruited 240 newly diagnosed HIV positive men and women between 2 October 2008 and 2 September 2009. Of 401 persons attending the clinics with a diagnosis of HIV infection, 267 met eligibility criteria. Of these, 240 (89%) enrolled in the study [Figure 4.1]. Reasons for refusal to participate included not having time (26%), did not want to (17%) or afraid (3%) to notify partners, and wanting time to think about it (23%). Refusers were similar in sex (p=0.2), age (p=0.3), and marital status (p=0.8) to participants, but had more median years of education (10 years vs 8 years) (p=0.04).

Among index patients, 58.3% were female and 71.2% were married [Table 4.1]. The median CD4 count at HIV diagnosis was 317.5 cells/mm^3 (range 25-1254). Index patients named 1-11 sexual partners in the previous 3 months, although most named a single partner (86%). Three index patients randomized to the provider referral arm named five, eight, and ten sex workers as partners for whom they could not provide basic locator information. No other index named more than three partners.

Overall, 302 partners were named including 219 (73%) main partners. The index reported planning to have sex again with 220 (73%) of the partners. The median partnership duration was 24 months (IQR: 3-84). Condom use was low; only 15% of index patients reported condom use at last sex and 77% reported never using condoms with any partner [Table 4.2].

Among 302 named partners, locator information was available for 252 (84%). Compared to non-locatable partners, locatable partners were more likely to be spouses (64% vs. 0%), male (56% vs. 10%), and have a duration of the partnership >1 month (79% vs. 7%).

Overall, 107 (35%) partners visited the clinic. Partner presentation, including non-locatable partners, was 22% (95% CI 13 – 30%) in the passive referral arm, 48% (95% CI 38 – 58%) in the contract referral arm, and 37% (95% CI 28 – 45%) in the provider referral arm. Restricting the analysis to locatable partners, the proportion of partners visiting was 24% (95% CI 15 – 34%) in the passive referral arm, 51% (95% CI 41 – 62%) in the contract referral arm, and 51% (95% CI 40 – 62%) in the provider referral arm [Table 4.3]. Among locatable partners, those in the contract and provider referral arms were both 2.1 times as likely to visit the clinic compared to those in the passive referral arm (contract versus passive: RR 2.1; 95% CI 1.4-3.2; $p< 0.001$; provider versus passive: RR 2.1; 95% CI 1.4-3.2; $p<0.001$). The proportion of partners visiting the clinic was 27% higher in both the contract and provider referral arms, as compared to passive referral (contract versus passive: RD 27%; 95% CI 13-41% $p< 0.001$; provider

versus passive: RD 27%; 95% CI 13-41%; p<0.001). The proportion of index patients with at least one partner visiting the clinic for counseling and testing was 26% (95% CI 16 – 35%) in the passive referral arm, 55% (95% CI 44 – 66%) in the contract referral arm, and 51% (95% CI 40 – 62%) in the provider referral arm.

Time to presentation among partners was associated with method of partner notification (p<0.001) [Figure 4.2]. The hazards were not proportional over time so hazard ratios were estimated separately for partner visit in the first seven days and after seven days. Among locatable partners, the hazard ratio for evaluation in the first seven days for partners in the contract referral arm was 1.4 (95% CI 0.7-2.6) and 2.1 (95% CI 1.1-3.7) for partners in the provider referral arm compared to partners in the passive referral arm. After seven days, the hazard ratio for evaluation for partners in the contract referral arm was 6.6 (95% CI 2.3-18.8) and 4.3 (95% CI 1.4-13.0) for partners in the provider referral arm compared to partners in the passive referral arm. The median time between enrollment of the index and partner presentation among those who visited the clinic was three days in the passive referral arm (IQR 2-7 days), seven days in the contract referral arm (IQR 3-11 days), and four days in the provider referral arm (IQR 2-8 days). In the contract referral arm, 30 (67%) partners who reported for counseling and testing were traced by a community counselor.

The acceptance rate for HIV testing among partners seen in the clinic was high. Overall, 104 (97%) of partners accepted HIV testing, and 67 (64%) tested HIV-positive; one partner was identified as acutely infected based on HIV RNA in the blood, lack of HIV

antibodies and subsequent seroconversion. Fifty-four (81%) were new HIV diagnoses by self-report. Twelve partners (15%; 95% CI 7-22%) in the passive referral arm, 21 partners (24%; 95% CI 15-33%) in the contract referral arm, and 21 partners (26%; 95% CI 16-35%) in the provider referral arm were new HIV diagnoses. The median CD4 count among partners was 344 (range: 47 - 940). Twenty-eight percent of partners were eligible to start antiretroviral therapy based on the current Malawi treatment guidelines (CD4 < 250 cells/mm^3) [Table 4.4]. Most partners reported only a single sexual partner, with 85 (82%) reporting one sexual partner in the previous 3 months.

Index patients and partners reported two social harms. In one instance, a female index reported her male partner abandoned her when she disclosed her HIV status. In the other, a female partner called the police when the community counselor visited the home. The situation was quickly resolved and the partner later sought counseling and testing at the clinic.

Discussion

The HIV pandemic in Africa has been unabated for more than 20 years, despite massive prevention efforts[59]. The introduction of ART in recent years has undoubtedly benefited many patients, but frequently patients receive therapy too late for maximal benefit. Currently, access to ART is increasing, and ART as a prevention tool has been supported[60]. However, optimal treatment and prevention require that infected people know their status. To achieve this goal, novel strategies of massive household testing[61]

and couples counseling[62] have been investigated. Partner notification, a logical and potentially critical intervention, has not been evaluated.

In Malawi, we observed that provider-assisted methods of HIV partner notification are feasible, acceptable and effective among STI clinic patients. A high proportion of eligible patients participated and provided accurate partner locator information. Provider-assisted partner notification was implemented without difficulty and was supported by clinic staff. Provider-assisted partner notification resulted in more partners receiving counseling and testing services than passive referral, the current standard of care.

Partner notification increased early referral to care. About one quarter of infected partners were eligible to begin ART based on current Malawian national guidelines and half of all infected partners had a CD4 count of 350 cells/mm^3 or less. Given that mortality is significantly increased in late presenters and baseline CD4 count is a strong predictor of response to antiretroviral therapy and mortality[14], the population of partners identified in this study are highly likely to benefit from knowledge of their status.

Prevention of HIV transmission within serodiscordant partnerships is an important HIV prevention strategy. In our study, 45% of tested partners were in a serodiscordant relationship. Serodiscordant couples receiving couples counseling report increased condom use and lower rates of seroconversion[63, 64]. Partner notification may be an

effective strategy to facilitate both individual behavior change among uninfected individuals and increase couples counseling in the region.

Provider-assisted partner notification is an important method to increase testing among male partners. While 50% of male partners sought evaluation in the contract and provider referral arms, only 15% did in the passive referral arm. Extending provider-assisted notification to antenatal clinic settings may be a novel way to increase male involvement in prevention of mother-to-child transmission programs. To date male involvement in PMTCT has been low in sub-Saharan Africa[65, 66] and continues to be difficult to implement. When male partners are involved or couples counseling is provided during PMTCT, HIV testing uptake is higher and women are more likely to implement PMTCT treatment and care interventions[67].

The potential for social harms is a key concern in partner notification programs. However, the index patients and partners in our study reported only two social harms throughout the entire study period, a 0.5% cumulative incidence. Experience elsewhere in the region suggests social harms are not increased among women in couples antenatal testing compared to women who do not disclose to their partner[68], and in South Africa men and women who disclosed their HIV status reported an increase in social support[42]. Experience in the U.S. suggests partner notification does not increase partnership dissolution[32]. However, prior history of abuse in a relationship following disclosure of HIV status is a strong predictor of reported physical or emotional abuse following disclosure[69]. Screening for intimate partner violence and emotional abuse

could be incorporated into post-test counseling and further operations research will be necessary to investigate the effect of provider assisted partner notification on social harms in a variety of African settings.

The STI clinic population in this study may not be representative of all new HIV diagnoses. Partners may be more motivated to respond to notification messages because of potential for STI treatment. However, partners of persons testing positive while seeking treatment for STIs are important to target for increased counseling and testing, as infectiousness is high in HIV-infected individuals with a concurrent STI. Implementation of HIV partner notification in STI clinics should go along with partner notification for STI treatment.

Successful partner notification is contingent on index patients providing locator information for their partners and community counselors successfully locating partners. In our study population, index patients often did not know the name or location of one-time or short-term partners. These partners are unlikely to be notified by the index and are unable to be traced by community counselors. Unfortunately, this group may represent high transmitter populations. As provider-assisted partner notification techniques are further refined in this setting, techniques to elicit more accurate locator information and find partners will be improved, and a larger proportion will be expected to be located and receive counseling and testing.

Early evaluation of a partner is preferred because of prevention opportunities. Provider referral led to more rapid clinic visits. Partners who visit on their own volition were seen in the first week; most partners who returned in the passive referral arm did so within the first week and a third of partners sought counseling and testing on their own when contract referral was used. Accordingly, provider-assisted referral can be used to improve return after about one week.

This study provides the first evidence of the feasibility and effectiveness of partner notification in sub-Saharan Africa. Partner notification, including provider-assisted strategies, has recently been implemented in Cameroon and more than 2000 partners have been evaluated[35], further supporting the feasibility of partner notification in non-Western settings. The passive referral approach to partner notification has not been successful. Active partner notification strategies, such as contract or provider referral, are required. More aggressive partner notification has the potential to rapidly and efficiently expand HIV treatment and prevention. Active partner notification is an opportunity that cannot continue to be missed.

Table 4.1. Index Patient Demographics by study arm

	Passive referral (n= 77)	Contract referral (n= 82)	Provider referral (n= 81)	Total (n=240)
Sex [n(%)]				
Male	31 (40.3%)	36 (43.9%)	33 (40.8%)	100 (41.7%)
Female	46 (59.7%)	46 (56.1%)	48 (59.3%)	140 (58.3%)
Age [years, median (IQR)]	30 (25-36)	28 (24-33)	28 (24-33)	28 (24-33)
Married [n (%)]	56 (72.7%)	59 (72.0%)	56 (69.1%)	171 (71.2%)
Education [years, median (IQR)]	8 (2-10)	9 (7-11)	8 (5-10)	8 (5-11)
Number sexual partners in last 3 months [median (range)]	1 (1-3)	1 (1-3)	1 (1-11)	1 (1-11)
Total number of partners named	93	94	115	302
Locatable partners named	82	88	82	252
Mean sexual partners in previous 3 months	1.2	1.1	1.4	1.3
CD4 Count [cells/mm3, median (IQR)]	351 (228-466)	301 (187-492)	308 (204-466)	317.5 (206-472)
CD4 <250 [n (%)]	25 (32.5%)	33 (40.2%)	31 (38.3%)	89 (37.1%)

Table 4.2. Named partner characteristics (n=302)

Characteristic	Passive referral (n= 93)	Contract referral (n= 94)	Provider referral (n= 115)	Total
Partner type [n(%)]				
Spouse or live-in partner	50 (53.8%)	60 (63.8%)	56 (48.7%)	166 (54.6%)
Boyfriend/Girlfriend	23 (24.7%)	15 (16.0%)	22 (19.1%)	60 (19.7%)
Regular casual partner	9 (9.7%)	8 (8.5%)	7 (6.1%)	24 (8.6%)
Casual partner, have sex with once or a few times	9 (9.7%)	5 (5.3%)	5 (4.4%)	19 (6.3%)
Sex worker	0	2 (5.3%)	11 (9.6%)	13 (4.3%)
Unknown	2 (2.2%)	4 (4.3%)	14 (12.2%)	22 (7.2%)
Length of partnership [median months (IQR)]	24 (2.5-72)	24 (3-84)	24 (1-84)	24 (3-84)
Plan to have sex with partner again	70 (75.3%)	69 (73.4%)	81 (70.4%)	220 (79.4%)
Used condom at last sex	13 (14.0%)	14 (14.9%)	19 (16.5%)	46 (15.1%)
Never use condoms with partner	60 (64.5%)	62 (66.0%)	59 (51.3%)	234 (77.5%)
Locator information known	82 (88.2%)	88 (93.6%)	82 (71.3%)	252 (83.4%)

Table 4.3: Proportion of locatable partners visiting clinic for counseling and testing by study arm

	Passive Referral (N = 82)		Contract Referral (N = 88)						Provider Referral (N = 82)					
	Percent Return	(95% CI)	Percent Return	(95% CI)	RD	(95% CI)	RR	(95% CI)	Percent Return	(95% CI)	RD	(95% CI)	RR	(95% CI)
Overall	24	(15-34)	51	(41-62)	27	(13-41)	2.1	(1.4-3.2)	51	(40-62)	27	(13-41)	2.1	(1.4-3.2)
Men	16	(5 -26)	52	(38-66)	37	(19-54)	3.4	(1.6-7.0)	51	(37-65)	36	(18-53)	3.3	(1.6-6.9)
Women	35	(20-51)	50	(34-66)	15	(-7-37)	1.4	(0.8-2.4)	51	(35-68)	16	(-6-39)	1.5	(0.9-2.5)
Main Partner	28	(17-38)	55	(43-66)	27	(12-43)	2.0	(1.3-3.1)	54	(43-66)	27	(11-42)	2.0	(1.3-3.0)
Casual Partner	8	(0-22)	33	(9-58)	25	(-3-54)	4.3	(0.6-32.5)	30	(1-59)	22	(-9-54)	3.9	(0.5-32.1)

Notes: a) Abbreviations: CI – confidence interval; RD – risk difference; RR – risk ratio.

b) Percent return reflects the incidence of partners returning to the clinic.

c) Passive referral is the referent for the calculation of the risk difference and risk ratio for both contract and provider referrals. As the referent, the risk difference for passive referral is 0 and the risk ratio is 1.

d) 95% CI are calculated using robust confidence intervals to account for multiple partners per index case.

Table 4.4. Partner HIV test results and CD4 counts (cells/mm^3) (n=107)

Partner Results	N	n	%
Partners tested	107	104	97%
Main partners tested	98	97	99%
Casual partners tested	9	7	92%
Partners with positive test results	104	67	64%
Main partners with positive test results	97	63	64%
Casual partners with positive test results	7	4	57%
Partner CD4 count [median cells/mm3 (IQR)]	344 (225-450)		
CD4 < 250	67	17	29%
CD4 250-350	67	13	22%
CD4 > 350	67	29	49%

Figure 4.1. Study Population

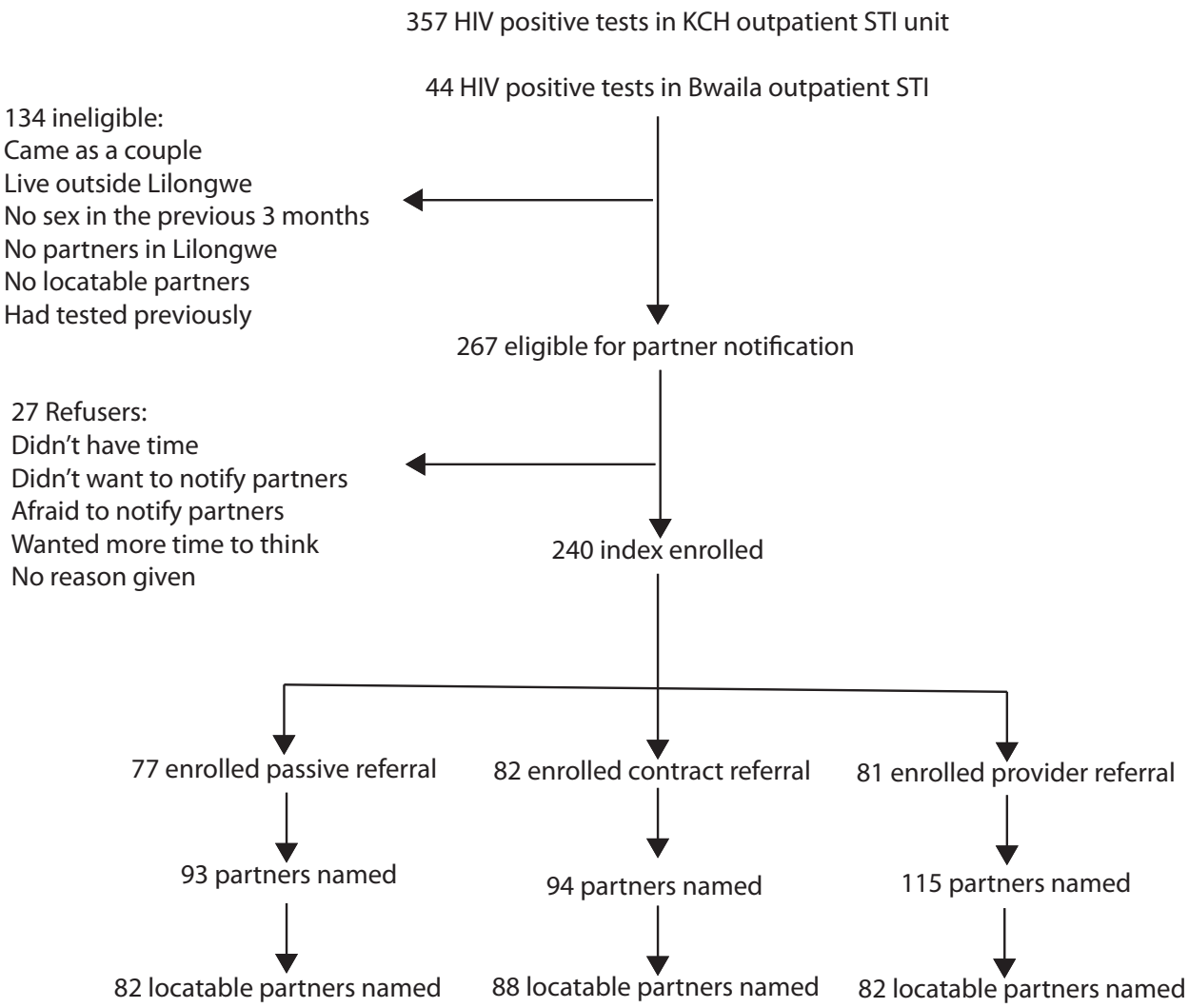
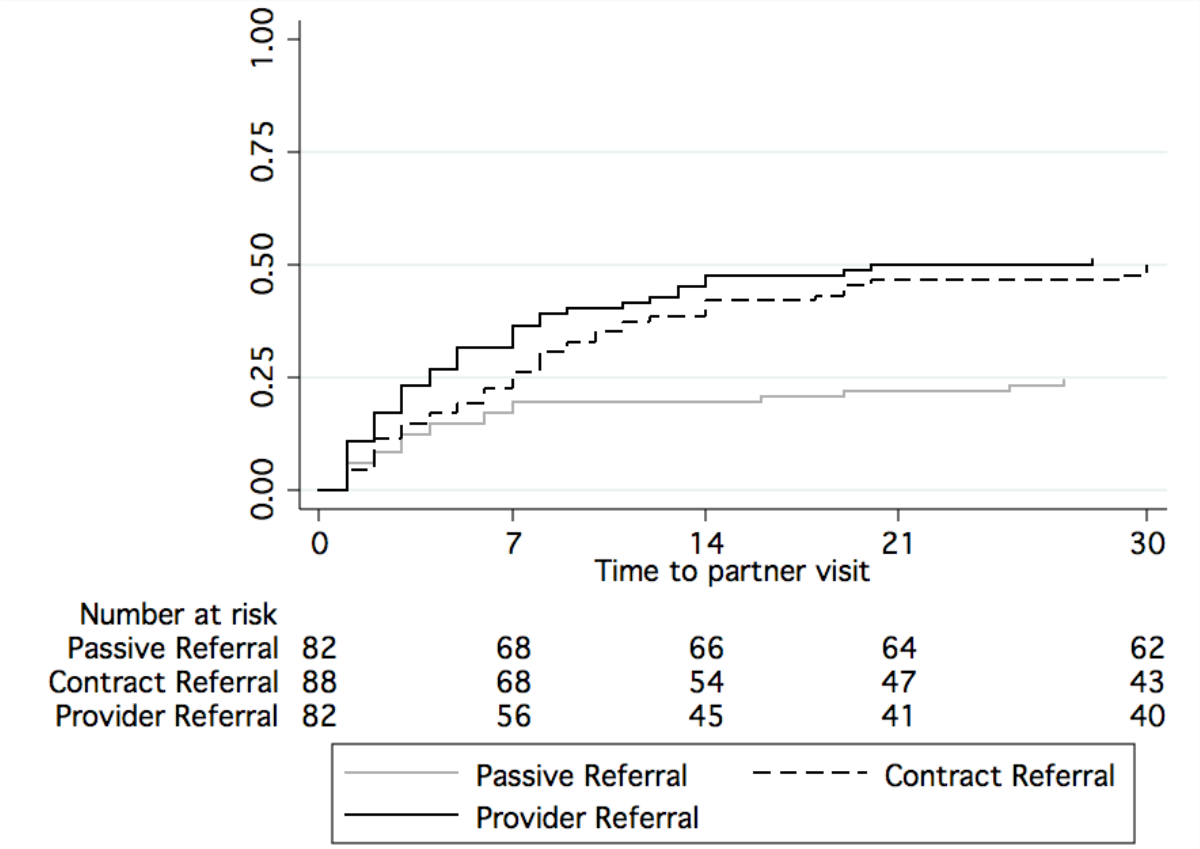


Figure 4.2. Proportion of locatable partners visiting clinic for HIV testing and counseling by method of partner notification (n=252)



CHAPTER 5

RESULTS: PREDICTING PARTNER HIV COUNSELING AND TESTING FOLLOWING A PARTNER NOTIFICATION INTERVENTION

Introduction

HIV counseling and testing provides an opportunity for prevention and an entry point to clinical care. Few infected persons in sub-Saharan Africa know their HIV status [1, 2]. The sexual partners of individuals diagnosed with HIV infection are an important population to target for counseling and testing as HIV serodiscordance within couples is common in Africa [64, 70] and if the partner is infected, they can benefit from evaluation for antiretroviral treatment. Providing counseling and testing to partners of individuals recently diagnosed with HIV infection is an important way to target prevention strategies and provide early care to a very high risk population.

Partner notification is a strategy to increase counseling and testing among sexual partners of HIV-positive persons and involves informing partners that they have been exposed to HIV and encouraging them to seek counseling, testing and other diagnostic and preventive services [23]. Partner notification programs were developed in the 1930s and 1940s as part of the U.S. and British syphilis control efforts, and were later expanded to include gonorrhea, chlamydial infection, and HIV. Partner notification

programs are implemented in every state in the United States, and programs in both the United States and Europe have been found effective in identifying previously undiagnosed HIV infections [26-28, 71]. However, strategies to increase partner testing have not been evaluated in developing countries [33] and little is known about partner testing behavior in these settings. To date, the standard of care for partner notification in sub-Saharan Africa is patient referral.

We conducted a randomized trial in Africa to determine the effectiveness of partner notification strategies to increase partner referral in Lilongwe, Malawi. The overall partner counseling and testing rate was 35% and provider-assisted referral methods of partner notification were twice as effective than when the patient was completely responsible for notification themselves (patient referral) and resulted in the most rapid evaluation of partners[56]. However, provider-assisted methods of referral are resource-intensive and usually require additional counseling and field staff and transportation. Ideally, only those partners who are unlikely to respond to patient referral should be targeted with provider-assisted referral, while partners more likely to report rapidly on their own for counseling and testing should be given the opportunity to do so. Understanding the characteristics of the partners and index patients associated with returning to the clinic for HIV counseling and testing will inform the implementation of partner notification programs in sub-Saharan Africa and suggest sub-populations to be targeted for future provider-assisted partner notification efforts.

We therefore sought to identify index patient and partner characteristics predicting partner uptake of HIV counseling and testing by creating a risk score algorithm to predict partners unlikely to report for counseling and testing on their own.

Methods

Study setting and population

Individuals with newly diagnosed HIV infection at the Kamuzu Central Hospital and the Bwaila Hospital outpatient STI clinics in Lilongwe, Malawi were recruited into a trial of HIV partner notification [56]. Patients from Lilongwe who had a positive HIV test result for the first time, were 18 years or older, report being sexually active in the last 90 days, were willing and able to provide locator information for their sexual partners, and agreed to be randomized to a method of partner notification were eligible to participate. Index patients were randomized to one of three methods of HIV partner notification: patient referral, contract referral, or provider referral. The patient referral group was responsible for notifying their partners themselves. The contract referral group was given 7 days to notify their partners, after which a health care provider contacted partners who had not reported for counseling and testing. In the provider referral group, a community counselor notified partners directly. Partners to index patients enrolled in the passive and contract referral arms were included in this analysis because they were the groups that represented partners who had the opportunity to report to the clinic on their own within 7 days.

Data collection

All index patients answered a short questionnaire that included items related to demographics and recent sexual behavior, including the number, type, and locations of sexual partners in the past three months. Clinical staff performed a physical examination and patients received treatment for STI based on the Malawi Syndromic Management guidelines. All were provided referral cards to give to their partners and had blood drawn for CD4 counts using flow cytometry (Epics-XL, Coulter). Index patients received their randomization assignment at the end of their enrollment visit (after all partner data and locator information had been collected).

Partners were identified when they visited the clinic if they presented a partner referral card or by cross-checking a log of named partners with all incoming patients to the clinic. Partners were tested for HIV under the opt-out testing protocol that is standard of care. HIV antibody-negative or -indeterminate specimens were tested for the presence of HIV RNA using the ultrasensitive Roche Amplicor Monitor HIV RNA assay.

Data was double-entered into a Microsoft Access database and checked for accuracy.

Data analysis

The predictive model includes all partners with locator information provided by the enrolled HIV-positive index patients who had the opportunity to report to the clinic on their own accord (i.e. all partners of index patients enrolled in the patient and contract

referral arms). The outcome for the model was failing to report to the clinic for counseling and testing on their own accord, without tracing by community counselors (for the contract referral arm only after 7 days). Partners of index patients in the contract referral arm who reported to the clinic after contact with a community counselor were considered not returning on their own.

All data was provided by the index during their enrollment visit.

Variables hypothesized a priori to be predictors of partner reporting for counseling and testing included index characteristics and partner characteristics. Index characteristics included age of the index, enrollment site (KCH vs. Bwaila STI clinics), diagnosis of genital ulcer disease on physical examination, and index education. Partner characteristics included partner gender, partner type (main partner vs. non-main partner), duration of partnership, and transportation barriers.

Main partners were defined as spouses and live-in partners, or boyfriend/girlfriend if the index did not name a spouse or live-in partner. Non-main partners included regular casual partners, infrequent casual partners, sex workers and boyfriend/girlfriend if the index already had a spouse. Duration of partnership was categorized at less than 6 months, 6 – 24 months, and greater than 24 months in order to capture new partners, use information about the dose-response relationship between length of partnership and partner testing, and ensure adequate strata sizes for multivariate modeling. Age of the index was dichotomized at age less than 25 since younger age groups (15-19 and

20-24) in Malawi are more likely to report high-risk partnerships. Genital ulcer disease (GUD) of the index was determined during physical examination by a clinician during the enrollment visit. Index education was dichotomized at completed primary education or less compared to greater than primary education. Partner area of residence was described by the index when they provided locator information about the each partner. Transport barriers were considered high if the partner did not live in an area served by the public transport network in Lilongwe or if the partner would need to pay for more than one mode of transport in order to reach the clinic.

We first calculated unadjusted odds ratios for partner failing to report and all partner characteristics (male gender, non-main partner, relationship duration less than 6 months, relationship duration 6 – 24, months and transport barriers) and index characteristics (age less than 25 years, enrollment site, STI other than GUD diagnosed, and greater than primary education).

We used multiple logistic regression to develop a predictive model of the partner failing to report. All variables were entered into the full model. We constructed a simplified final model using backwards selection with a predetermined stopping rule of $p = 0.10$ to maintain predictive ability and reduce the likelihood of omitting important variables. Nested models were compared using likelihood ratio tests. We assessed model accuracy for all using area under the receiving operator characteristics curves.

In order to create a simple instrument that can be applied in the field we assigned each variable in the final model a predictor score equal to its beta coefficient (natural log of the adjusted odds ratio) rounded to the nearest integer [55]. We summed the risk scores to obtain a risk score for each participant. We calculated the proportion of partners requiring tracing by a community counselor under each risk score scenario as:

$$P_{traced} = Se \times P_{NR} + (1 - Sp) \times (1 - P_{NR}) \quad \text{(equation 5.1)}$$

Where P_{traced} = proportion of partners traced, Se = sensitivity, Sp = specificity, and P_{NR}= proportion failing to report

We calculated the proportion of partners traced unnecessarily as:

$$P_{unnecessary} = (1 - Sp) \times (1 - P_{NR}) \quad \text{(equation 5.2)}$$

Where $P_{unnecessary}$ = proportion of partners traced unnecessarily, Se = sensitivity, Sp = specificity, P_{NR}= proportion failing to report

In the clinical trial, the proportion of partners who tested under universal provider assisted referral was 51%[56]. The estimated proportion of partners tested under each risk score scenario was calculated as:

$$P_{tested} = (0.51 \times P_{traced}) + (Sp \times (1 - P_{NR}) \quad \text{(equation 5.3)}$$

where P_{tested} = estimated proportion of partners tested, Sp = specificity, P_{NR}= proportion failing to report, P_{traced} = proportion of partners traced

A false positive was a partner who was identified using the risk score algorithm for provider-assisted referral, but would have reported to the clinic on their own. A false negative is a partner who was not identified for provider-assisted referral using the risk score algorithm and did not receive testing. The relative costs of false negatives and false positives were compared at different model cut-points using the formula:

$$Cost = (1-p) \times \frac{(1-Sp_1)-(1-Sp_2)}{p \times [(1-Se_2)-(1-Se_1)]} \qquad \text{(equation 5.4)}$$

where p is the prevalence of partner testing on their own (21%), Sp_1 and Se_1 are the specificity and sensitivity of universal provider-assisted referral (cut-point=0) and Sp_2 and Se_2 are the specificity and sensitivity of each cut-point.

The cases of HIV missed for each cut-point relative to universal provider-assisted referral was calculated as the prevalence of HIV among tested partners (64%) [56] times the number of false negatives.

We performed internal validation of the modeling strategy and model performance using 1000 bootstrap repetitions [57]. We used Stata v.10 (College Station, Texas) for all analyses.

Ethical considerations

The Institutional Review Board at the University of North Carolina, Chapel Hill and the National Health Sciences Research Committee in Malawi approved the protocol. Informed consent was obtained from all participants prior to participation.

Results

Among 252 partners with locator information provided, 170 partners were in the passive or contract referral arms and had the opportunity to report to the clinic on their own and were included in the analysis. Thirty-seven (21.8%) partners reported to the clinic on their own volition. Slightly more than half of partners were male, most were classified as main partners, and most named only a single partner in the previous three months [Table 5.1].

In bivariable analysis, male partners, being a non-main partner, relationship duration of less than 6 months, and an STI other than GUD diagnosed in the index was associated with a partner not reporting to the clinic without community tracing [Table 5.2]. Partner type was not included in multivariate analysis because of co-linearity with relationship duration. The final model predicting failure to report to the clinic included male partner gender, relationship duration < 6 months, relationship duration 6 - 24 months and greater than primary education in the index. The area under the receiver operator characteristic curve for the final model was 0.76 (95% CI 0.67 – 0.83). Male gender, index education greater than primary, and relationship duration 6 – 24 months were assigned a score of 1 and relationship duration less than 6 months was assigned a

score of 2 in the risk score algorithm [Table 5.2]. The area under this receiver operator characteristic curve for the risk score was 0.76 (95% CI 0.67 – 0.84).

A risk score cut-off of ≥3 has a sensitivity of 29% and a specificity of 94% [Table 5.3, Figure 5.1] for identifying partners unlikely to report to the clinic on their own volition. Under this scenario, only 24% of all partners would be traced by a community counselor and 32% of all partners are expected to be tested [Table 5.3, Figure 5.2].

When the cut-off is ≥2, more partners would be referred for tracing immediately and the specificity still remains high. The sensitivity increases to 68%, with specificity at 77%; 58% of all partners would be traced with provider-assisted notification and 46% of all partners are expected to be tested using a risk score cut-off of ≥2. When the risk score cut-off is ≥2 all new partners in the last 6 months are targeted for provider-assisted referral.

At a risk score cut-off of ≥2, both the false negative and false positive rates are low. When all partners are referred for provider-assisted referral the false positive rate is 21%. If false positives and false negatives are weighted equally, then a cut-off of ≥2 minimizes both, and only misses 3 (9%) diagnoses of HIV relative to universal provider-assisted referral [Table 5.3]. In our setting and using the cutoff of ≥2, the relative costs of false negatives must be 9 times as costly as false positives to justify tracing all partners.

The bootstrapped samples yielded the same predictors following backward elimination. Confidence intervals derived from bootstrap validation were consistent with the original analysis.

Discussion

Reaching the sexual partners of persons testing positive for HIV is critical for both potential treatment and prevention. HIV partner notification is one method to reach this high-risk population. Despite its potential, HIV partner notification has yet to be implemented widely in sub-Saharan Africa [35] and many logistics must still be determined, including how and whom to target with provider-assisted referral.

We have shown that HIV partner notification, including provider-assisted techniques, is feasible in this setting. However, because provider-assisted HIV partner notification will require additional human resources to be effective, it is essential to determine best strategies and practices. Prediction models for HIV acquisition have been used to target counseling messages and interventions [46, 47, 49]. Here, we predict who is unlikely to respond to partner notification by the index patient alone in order to direct provider-assisted referral.

Using a risk score to target provider-assisted referral can reduce the resources required to trace clients in the community compared to universal provider-assisted referral and increase partner testing compared to patient-referral. For example, when the risk score cut-off is ≥2 less than two-thirds of the resources can be used to yield more than 90% of

the partners tested under universal provider-assisted referral. Identifying populations to target provider-assisted referral will inform policy-makers and implementing agencies.

Rapid referral of partners is preferred, and our experience in the field suggests partners are more likely to be located the earlier they are traced. We have also observed that a high proportion of partners who are located and notified of their exposure present for counseling and testing. Urban populations in sub-Saharan Africa are highly mobile. Delay in partner tracing reduces the ability to locate and refer partners for counseling and testing. However, tracing all sexual partners may not be feasible, particularly in resource constrained settings. Given the resources involved in community tracing, the ideal risk score cut-off should have a sufficiently high specificity to minimize tracing partners who are likely to come in on their own, while simultaneously identifying a large proportion of those who would not come in on their own without provider assistance. In the Malawi setting, using an easy to implement risk score with a cut-off of ≥2 would result in almost 70% of partners who are unlikely to report for testing and counseling on their own to be referred to provider-assisted referral immediately and very few partners being traced unnecessarily.

The relative costs of false positives and false negatives need to be considered when determining the optimal cutoff, or whether universal referral should be implemented at all. The costs of a false positive are the resources involved in locating partners in the community and the potential social costs, such as stigma and loss of confidentiality,

which in our Malawi experience were minimal. The costs of a false negative are the partner not receiving testing and perhaps not being notified, necessary prevention, and if the partner were HIV-infected, the costs of not accessing treatment services and the potential for onward transmission related to lack of awareness of one's HIV status. If false negatives and false positives are weighted equally, then the cut-point of 2 minimizes both and the fewest errors are realized. If the costs of missing the opportunity to test a partner and prevent an HIV transmission event are weighted more strongly, then a lower cut-point or universal testing would be preferred. At a cut-point of 2 a false positive must be 9 times more costly than a false negative to justify immediate provider-assisted referral for all partners. The relative costs may differ based on the setting and must consider the HIV prevalence, the availability of prevention and treatment services, and the capacity to follow-up with partners in the community.

Provider-assisted partner notification could be an important tool to increase referral among male partners, who we found are unlikely to be notified and be tested on their own. All female patients who test positive for HIV could be presented the option of provider-assisted referral during post-test counseling. The results of our predictive model suggest provider-assisted partner notification strategies could also help increase the proportion of new partners and casual partners who receive testing earlier.

While the model we developed here may be useful in an STI clinic setting, its generalizability to other settings where partner notification may be implemented may

be limited. Partners of index patients seeking treatment for STIs might be more motivated to respond because of the potential for STI treatment. However, STI diagnosis was not an important predictor in the final model and was not included in the risk score. Future validation in a variety of HIV counseling and testing settings where partner notification is implemented will help refine the algorithm's usefulness.

The small number of events limited our ability to examine additional potential predictors. Also, the ability of a model to predict future events in new populations is reduced when too many parameters are used to estimate for the amount of information in the data. Internal validation using bootstrapping was performed, however the precision and optimism of the model performance may be exaggerated by the over fitting of the model. The model should be refined in future, larger study populations to improve its usefulness as a clinical screening tool. However, very little is currently known about partner testing in sub-Saharan Africa and these characteristics will continue to be refined in practice as partner notification is implemented in the region.

HIV partner notification is new to sub-Saharan Africa. Understanding index and partner responses and who to target with different strategies will guide efficient and effective implementation. All partners are at high risk for HIV infection and contact with a provider greatly increases the probability of partners receiving testing. A simple, easy to calculate risk score may be a useful tool for partner notification programs to target provider referral and increase the yield of partner notification efforts while controlling implementation costs.

Table 5.1. Index and partner characteristics (n = 170)

Characteristic	N	%
Partner Characteristics		
Partner sex		
Male	93	45.3%
Female	77	54.7%
Partner type		
Main partner	142	83.5%
Non-main partner	26	16.5%
Length of partnership		
< 6 months	45	26.5%
6 – 24 months	42	24.7%
> 24 months	83	48.8%
Face transport barriers		
Yes	84	49.1%
No	86	50.9%
Index Characteristics		
Age of index		
< 25 years	52	30.6%
≥ 25 years	118	69.4%
Enrollment site		
Bwaila	21	12.4%
Kamuzu Central Hospital	149	87.7%
GUD diagnosed		
Yes	38	22.4%
No	132	77.6%
Index Education		
≤ Primary education or less	95	55.9%
> Primary education	75	44.1%

Table 5.2. Unadjusted and adjusted odds ratios and risk scores for index and partner characteristics predicting partner HIV counseling and testing (n = 170)

Predictor	OR	95% CI	aOR	95%CI	β	Score
Partner Characteristics						
Sex						
Female	1.0		1.0			
Male	2.3	1.1 – 4.8	3.5	1.6 – 8.3	1.3	1
Type of Partner						
Main partner	1.0					
Non-main partner	8.8	1.2 – 67.4				
Partnership duration						
< 6 months	6.4	1.8 – 22.5	10.5	2.8 – 39.9	2.4	2
6 – 24 months	2.3	0.9 – 5.8	2.6	1.0 – 6.9	0.9	1
> 24 months	1.0		1.0			
Faced transport barriers						
Yes	1.0	0.5 – 2.0				
No	1.0					
Index Characteristics						
Age						
< 25 years	2.6	1.0 – 6.7				
>= 25 years	1.0					
Enrollment site						
Bwaila	0.7	0.2 – 1.8				
Kamuzu Central Hospital	1.0					
STI diagnosed						
GUD	2.1	0.9 – 4.7				
Other	1.0					
Education status						
<= Primary Education	1.0					
> Primary Education	2.1	0.9 – 4.6	2.2	1.0 – 5.2	0.8	1

Table 5.3. Sensitivity and specificity of risk score to predict partners unlikely to report for counseling and testing, proportion of partners traced and tested for each risk score cut-off, and errors in a population of 100 partners

Risk Score Cut-off	Sensitivity*	Specificity†	Proportion of partners traced‡	Proportion of partners traced unnecessarily§	Proportion of partners tested#	False Positives**	False Negatives††	Total Errors‡‡	Cases of HIV missed relative to universal provider-assisted referral§§	Relative cost of false negatives relative to false positives##
0	100%	0%	100%	21%	51%	21	0	21	0	
>=1	94%	25%	84%	17%	51%	16	0	16	0	15.7
>=2	68%	78%	45%	8%	46%	5	5	10	3	9.2
>=3	29%	94%	23%	5%	32%	1	19	20	12	5.0
>=4	5%	97%	15%	14%	23%	1	28	29	18	3.8
No Tracing	0%	100%	0%	0%	21%	0	30	30	19	3.8

* Sensitivity (Se) is the proportion of partners who require tracing (those who fail to report on their own) who are traced under each risk score cut-off

† Specificity (Sp) is the proportion of partners who will report on their own who are not traced (correctly identified as not requiring tracing)

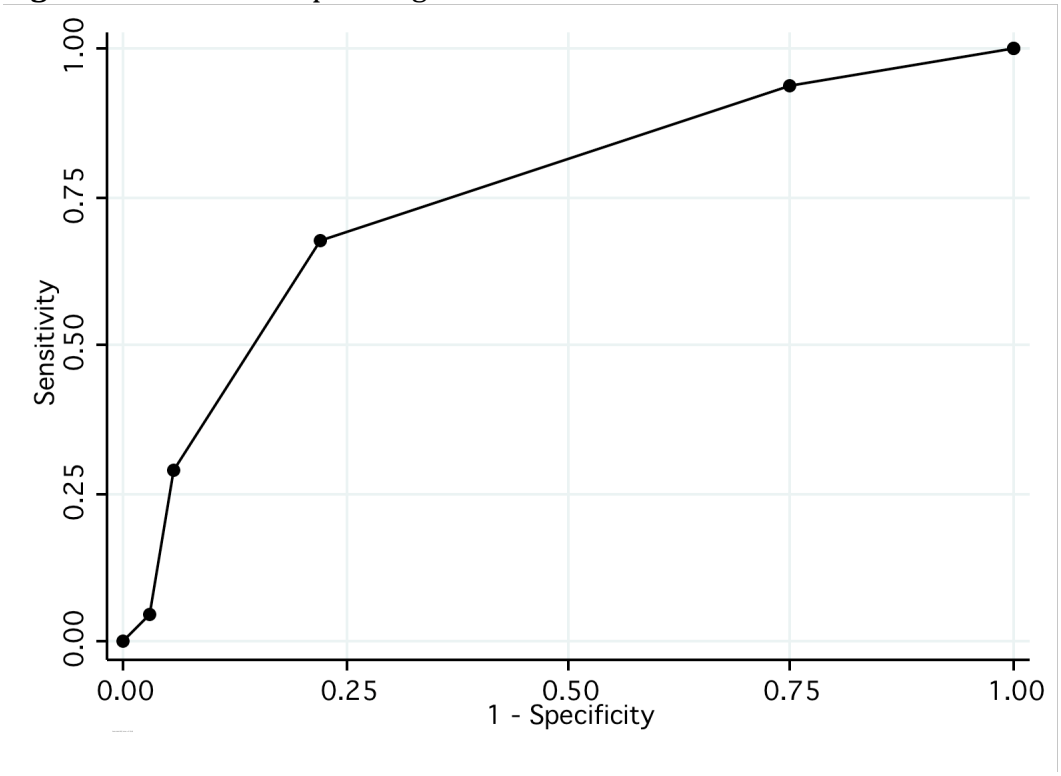
‡ Proportion traced by counselor = $Se*P_{no\ report} + (1-Sp)*(1-P_{no\ report})$, where $P_{no\ report}$ = proportion failing to report

§ Proportion of partners traced unnecessarily = $(1-Sp)*(1-P_{no\ report})$, where Se = sensitivity, Sp = specificity, $P_{no\ report}$ = proportion failing to report

Proportion of partners tested = $0.51*P_{Ttraced} + Sp*(1 - P_{no\ report})$

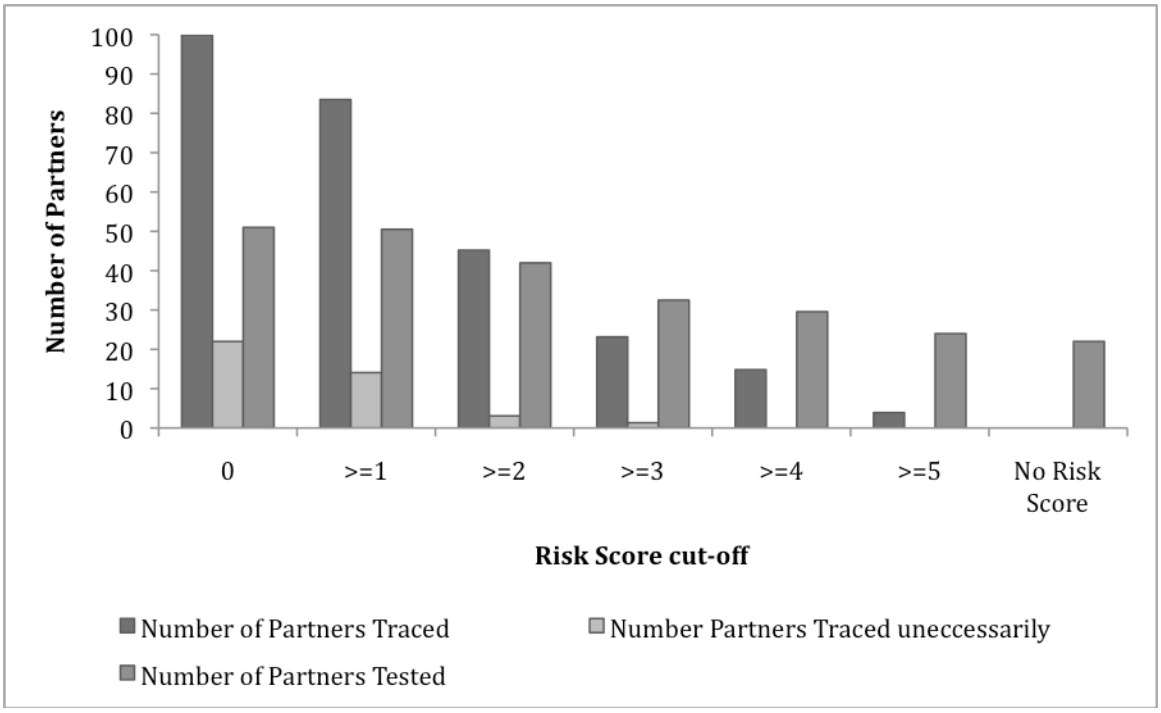
** A false positive was a partner who was identified using the risk score algorithm for provider-assisted referral, but would have reported to the clinic on their own.
††A false negative is a partner who was not identified for provider-assisted referral using the risk score algorithm and did not receive testing.
‡‡Total errors is the number of false positives plus the number of false negatives
§§ The cases of HIV missed for each cut-point relative to universal provider-assisted referral was calculated as the prevalence of HIV among tested partners (64%) [56] times the number of false negatives.
The relative costs of false negatives and false positives were compared at different model cut-points using the formula cost = (1-p)*[(1-Sp1) - (1-Sp2)]/ p*[(1-Se2) - (1-Se1)] where p is the prevalence of partner testing on their own (21%), Sp1 and Se1 are the specificity and sensitivity of universal provider-assisted referral (cut-point=0) and Sp1 and Se1 are the specificity and sensitivity of each cut-point.

Figure 5.1. Receiver Operating Characteristics Curve for different risk score cut-offs.



ROC curves plot sensitivity versus 1 – specificity for all possible cut-offs of an algorithm. A perfect algorithm would arch to the upper left corner; an algorithm with no useful discrimination is a diagonal line connecting the lower left to upper left corners. The Area under the ROC curve for the algorithm is 0.76 (95% CI 0.67 – 0.84).

Figure 5.2. Number of partners traced, number of partners traced uneccessarily, and number of partners tested for different risk score cutoffs in a population of 100 partners



In a population of 100 partners when no partners are traced 21 are expected to report to the clinic on their own and 79 are not expected to report to the clinic on their own volition. When all partners are traced 51% are expected to report for counseling and testing [56]. The number of partners traced is calculated as [sensitivity x 79 partners + (1 – specificity) x 21 partners]. The number of partners traced uneccessarily is the number of partners who are traced but would have reported to the clinic on their own accord and is calculated as (1 – specificity) x 21 partners. The total number of partners tested is calculated as 0.51 x [number of partners traced) + (specificity x 21 partners).

CHAPTER 6

CONCLUSIONS

This research attempted to learn more about the process of HIV partner notification in sub-Saharan Africa, a region of the world greatly affected by HIV but where few know their infection status. The aims of this project were to 1) determine which method of partner notification, passive referral, contract referral, or provide referral, would result in the highest proportion of partners receiving HIV counseling and testing; 2) to describe the HIV prevalence among partners; and 3) to describe partner characteristics associated with partner testing and partner HIV status and to develop an easy to implement risk score algorithm to identify partners to target with immediate provider-assisted referral. We conducted a three-arm randomized trial in which persons with newly diagnosed HIV infection were assigned a method of partner notification. Data from the clinical trial was then used to develop prediction models and a risk score algorithm to be used to target provider-assisted referral.

Provider-assisted methods of partner notification, contract referral and provider referral, were more effective than passive referral and resulted in more than twice as many partners receiving testing. Provider-assisted methods of referral were particularly effective at increasing partner testing among male partners and casual

partners. Immediate provider-assisted referral led to the most rapid evaluation of partners. However, the rate of partner return was similar between contract referral and provider referral after seven days.

Partner notification uncovered many persons with previously unidentified HIV infection. Provider-assisted methods of partner notification resulted in more partners receiving testing, and these methods identified a greater number of new infections per index. Partner notification helped many partners access treatment earlier, as approximately a quarter of all partners were already eligible for treatment based on the Malawi treatment guidelines (CD4 count < 250 cells/mm^3). More than half of tested partners had CD4 counts less than 350 cells/mm^3, the cut point for ART treatment eligibility currently being discussed by the Ministry of Health for revised treatment guidelines.

Among partners given the opportunity to present for testing on their own (partners of indexes assigned to passive and contract referral), male partners, short-term partners, casual partners, and partners of more educated index patients were unlikely to present on their own. Using a risk score algorithm, partners unlikely to present on their own can be referred for immediate provider-assisted referral and very few partners who are likely to present on their own will be traced unnecessarily. All partners are at high risk of HIV infection and it is critical to reach them with testing, prevention, and treatment services.

Partner notification was feasible in a busy clinic setting in an urban area in sub-Saharan Africa. The protocol was implemented quickly and all clinic nurses and counselors were actively involved. Clinic staff supported partner notification and gave positive feedback.

Partner notification was also acceptable to STI clinic patients. A high proportion of those eligible agreed to participate and provide locator information about their partners. Index patients and partners both indicated their support for partner referral, and while most preferred to notify their partners on their own, they also expressed the right of the partner to be informed of their risk and take steps to protect themselves. The high acceptability of partner notification in this setting demonstrates that thorough and high quality counseling enables people to understand the importance of public health programs. HIV affects every facet of life in Malawi and the population accepts and supports HIV programs in the context of appropriate counseling.

Finally, few social harms were observed in our study population. Both indexes and partners were asked repeatedly about personal, legal, and economic harms experienced as a result of partner notification. Only two social harms were reported throughout the course of the study. No partners or index patients reported intimate partner violence and only one instance of relationship dissolution following disclosure of HIV status was observed.

Strengths

Provider-assisted methods of HIV partner notification are new to sub-Saharan Africa. While it has been implemented in a limited area in West Africa[35], the effectiveness has never been evaluated. Our work provides the first data on the effectiveness of different methods of HIV partner notification in a region of the world greatly affected by HIV.

The study design allowed us to directly compare the effectiveness of three different strategies of partner notification. We minimized the potential effects of confounding variables and reduced selection bias by randomizing index participants to a particular method of partner notification rather than allowing them to choose. While some selection bias may still be present, only a small proportion of eligible index patients refused participation.

HIV partner notification is a topic directly relevant to the local population. The vast majority of HIV transmission in Malawi is through heterosexual sex, and the sexual partners of those diagnosed with HIV need to be evaluated for antiretroviral therapy, if infected, or targeted with prevention programs so that they can stay uninfected. There is currently no national policy on HIV partner notification; the HIV counseling and testing guidelines only state that there is a need to provide evidence on when and to whom provider-assisted referral should be made. Providers have long been frustrated by the low rate of partner counseling and testing and are enthusiastic and eager to implement new ways to increase the numbers of partners receiving important

treatment and prevention services. The data generated by our work will be shared with policy makers and directly addresses a stated deficiency in the national strategy.

In addition to local relevance, HIV partner notification is a topic of global public health importance. With more than 1 million new infections annually,[6] novel methods of HIV prevention are urgently needed. Positive prevention (i.e. prevention programs carried out through HIV-infected persons) will become increasingly important. The failure of providers to find and direct treatment and prevention services to the sexual partners of persons with both new and established infection hampers the global response. Partner notification can be a primary prevention activity as the uninfected partner can take immediate actions to protect themselves from further exposure.

Limitations

This study was conducted in an STI clinic so its generalizability to other populations, such as antenatal and the general testing population may be limited. Partners of STI patients may be motivated to respond to partner notification messages because of the potential for STI treatment. However, individuals diagnosed with HIV seeking treatment for sexually transmitted infections are an important population to target as HIV transmission is amplified in the presence of a concurrent infection with STI. Additionally, partner notification is also likely to be at least as effective in other testing populations, such as antenatal and general counseling and testing populations as we observed among STI clinic patients, as there might be more motivation for partner involvement in these groups in the absence of the stigma of STI.

All partner notification activities, including counseling, collecting locator information, and finding partners in the community were conducted by highly experienced providers trained in research methods. They are experienced in collecting locator information from clients and counseling patients about procedures. The effectiveness of provider-assisted partner notification will also reflect the amount of training and skill of the counselors.

Successful partner notification is contingent on index patients being able to provide locator information for their partners and community counselors being able to successfully locate partners. In order to be "locatable" an index must know the partner's name and be able to describe where they live or where they can be found. In our study population, locator information was often unavailable for one-time or short-term partners. These partners are unlikely to be notified by the index and are unable to be traced by community counselors. This is unfortunate because this group likely represents high transmitter populations. Overall, half of locatable partners who received provider-assisted referral sought counseling and testing, suggesting partner notification may be most effective in longer-term, more stable partnerships. Although we do not know the proportion of partners notified in the passive referral arm, in the contract and provider referral arms 72/95 (76%) of partners who were successfully notified by a provider returned to the clinic for counseling and testing. As provider-assisted partner notification techniques are further refined in this setting, techniques to

elicit more accurate locator information and find partners will be improved and a larger proportion will be expected to be located and return for counseling and testing.

While few social harms were observed in our study population, the length of follow-up was limited. Additionally, we do not have social harms data on the partners who did not report for testing and counseling at the clinic. Index patients and partners who reported were counseled extensively to report any experiences of social harms to clinic staff. However, a longer period of follow-up is necessary to thoroughly assess the social impact of partner notification.

The small number of events limits the power of predictive modeling. Only 37 partners reported for counseling and testing on their own, which was used to develop a risk score. Many covariates were hypothesized to influence the probability of a partner returning and partner HIV test result. The ability of a model to predict future events is reduced when too many parameters are used to estimate for the amount of information in the data. Internal validation using bootstrapping was performed. However, the precision and optimism may be exaggerated by the over-fitting of the model. The model should be refined in future, larger studies in order to be useful as a clinical screening tool. The primary objective of the predictive modeling is to elucidate partner characteristics associated with partner testing and to use the risk score to target immediate provider-assisted referral. Very little is known about partner testing in sub-Saharan Africa and these characteristics will continue to be refined in practice as partner notification is implemented in the region.

Finally, the implementation of partner notification on a wider scale requires resources and local support. Many resources, including trained personnel, are required for provider-assisted referral. Many of the regions most affected by HIV also experience shortages of health care workers. Additionally successful implementation requires buy-in from the local population. Partner notification methods that require following up with partners in their community or at their homes will never be feasible without the support of the local community.

Future directions

Provider-assisted partner notification is an effective method to increase partner testing among both new HIV diagnoses and established infections. Many individuals with established infection have not disclosed to their partner and their partner's status remains unknown. Offering partner notification services to individuals with established infection can be a method to increase disclosure and all of the associated benefits, such as increased uptake of PMTCT activities, improved treatment adherence, and safer sexual behavior.

Partner notification can also be a gateway to couples counseling. In our study and in other population-based data across the region, 40-50% of infected individuals have a spouse or partner that is HIV negative[3]. Sero-negative partners in discordant couples are a significant risk group for HIV infection as heterosexual sex within unions or regular partnerships is estimated to account for the majority of incident HIV infections

in a variety of African settings [72, 73]. Therefore, prevention of HIV transmission within sero-discordant partnerships is an important HIV primary prevention strategy. Sero-discordant couples receiving couples counseling report increased condom use and lower rates of seroconversion[64, 74, 75] and modeling suggests couples counseling in sero-discordant couples could reduce transmission rates by up to 60%[76]. Couples counseling helps create a safe environment for disclosure of HIV status among partners and can facilitate communication and cooperation required for risk reduction or treatment and care decisions as well as family planning.

Increasing partner testing is a first step towards increasing prevention and treatment activities. Partner notification could be expanded to offering counseling and testing to households and provide a gateway to high-risk social networks. Index patients and their sexual partners can be asked to identify and refer others in their social networks for HIV counseling, testing, and treatment and prevention services. Social networks strategies have been used successfully to identify undiagnosed cases of syphilis [77] and HIV [78, 79]. Since members of the same social group often display similar sexual risk behaviors, social network strategies have been more effective at identifying new HIV diagnoses than traditional testing and counseling sites. [78] Therefore, extending partner notification to the sexual and social networks of the partner may be an efficient and high yield approach to identifying undiagnosed HIV infection and providing HIV testing and counseling services to high-risk populations.

Barriers to partner testing on a wider scale will include the availability of HTC services. Mobile VCT and household based testing is a way to decrease structural barriers associated with testing and increase access to testing. Door-to-door and household testing reached the largest proportion of previously untested individuals at the lowest cost[80] and home delivery of results increases the utilization of counseling and testing compared to clinic-based settings[44]. Household based testing is also an important strategy to combat the socio-economic inequalities observed with clinic-based testing [81]. However, confidentiality and effective referral are crucial to non-facility based testing.

Our experience with partner notification and experience elsewhere in the region with HIV disclosure suggests social harms will not be increased through partner notification[42, 68]. However, implementation of HIV partner notification needs to incorporate social harms monitoring and include measures to protect index patients and partners from social harms, such as screening for intimate partner violence and emotional abuse during post-test counseling.

For maximum effectiveness on a population level partner notification should be expanded to a variety of setting where HIV testing occurs, including PMTCT settings, Voluntary Counseling and Testing centers, tuberculosis clinics, and other health care settings. The advantages of partner disclosure in PMTCT settings are documented [4, 36, 37] and increased partner disclosure may also improve health outcomes in these other venues.

As partner notification is implemented on a wider scale, predictive models to direct provider-assisted referral should be re-examined and refined. The analyses conducted as part of this clinical trial should be used to guide new models and risk score development. These models should be validated in future populations and a variety of populations receiving partner notification services.

These data have implications for HIV testing policy in Malawi. Currently, provider-assisted partner referral procedures have not been officially developed, although a need for the development of "appropriate and explicit" guidelines has been stated. The effectiveness data were disseminated locally to the Malawi Ministry of Health, including the Testing Advisor and the Director of HIV/AIDS programs. The Ministry's primary interest was the impact of partner notification programs on the national treatment programs. The Ministry also asked questions regarding who they should target with partner notification. Both the effectiveness data from the clinical trial and the predictive model will provide valuable information as HIV testing guidelines are revised in Malawi. Additionally, the cost-effectiveness of the different strategies of partner notification should be examined and continually evaluated as partner notification is implemented on a wider-scale both in Malawi and elsewhere in the region. Continued collaboration with policy-makers will be crucial to ensure the data are used to inform policy.

Despite the push for increased testing, an unacceptably high proportion of infected persons in Africa do not know their status. HIV partner notification is an important

method to increase counseling and testing among high-risk individuals and represents and important component of the UNAIDS call for universal HIV counseling and testing by 2010. HIV partner notification is critical as a link to clinical care, including treatment, and as a primary prevention method.

APPENDIX A

INFORMED CONSENT DOCUMENTS

Consent to Participate in a Research Study
Adult Subjects Biomedical Form
Index Consent

IRB Study #08-0862
Consent Form Version Date: June 24, 2009
Title of Study: Operations Research to Determine the Community Acceptability and Most Effective Method of HIV Partner Notification at Kamuzu Central Hospital STI Clinic, Lilongwe, Malawi

Principal Investigator: Gift Kamanga
UNC Project, Lilongwe Department: STD Clinic Manager
UNC Project, Lilongwe Phone number: 01-755-056
Co-Investigators: Francis Martinson, Clement Mapanje, Lillian Brown, Bill Miller, Audrey Pettifor and Irving Hoffman
Funding Source: Malawi National AIDS Commission and UNC Project, Lilongwe
Study Contact telephone number and email:
Gift Kamanga 01-755-056, gkamanga@unclilongwe.org.mw;
Francis Martinson 01-755-056, fmartinson@unclilongwe.org.mw

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason.

Research studies are designed to obtain new knowledge that may help other people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the UNC Project, Lilongwe. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to learn the best way HIV positive persons should notify their sexual partners that have been exposed to HIV. This is called Partner notification. Partner notification involves informing the sexual partners of HIV-positive persons that they have been exposed and encouraging them to seek HIV counseling, testing and other prevention and treatment services. The Malawi National HIV/AIDS Policy and Testing and Counseling Guidelines state that partner notification methods should be used to help HIV positive persons notify their partners, however we don't know which method is the most effective and acceptable in Malawi.

You are being asked to be in the study because you had a positive HIV test at our clinic today.

Are there any reasons you should not be in this study?
You should not be in this study if you are not willing to provide the names and locations of your sexual partners or if you are not willing to return to the clinic in 2 weeks for a follow-up visit.

How many people will take part in this study?
If you decide to be in this study, you will be one of approximately 240 people in this research study.

How long will your part in this study last?
Your participation in this study will last approximately 2 weeks. Today's visit will last about 1 hour and another final 1 hour visit will be in 2 weeks time.

What will happen if you take part in the study?
Today you will talk to an HIV counselor on the importance of safe sex behavior, will have a brief physical exam, blood will be drawn for a CD4 count to determine if you need HIV treatment, and you will answer a short questionnaire about recent sexual behavior, including the number and type of sexual partners you have had in the past three months.

You will also talk to an HIV counselor about your recent sexual partners, including their names and where they can be found. You will then be assigned by chance, like flipping a coin, to one of three study groups: passive referral, contract referral, or provider referral.

If you are assigned to the passive referral study group you will be given a notification card to give to each of your sexual partners. The partner can then bring the card back to the clinic if they visit for HIV testing and counseling services.

If you are assigned to the contract referral study group you will be given notification cards to help you notify your partners. However, if your partners do not come to the clinic for counseling and testing within 7 days, a community outreach worker will contact your partners. They will advise your partners that they have been exposed to HIV and urge them to visit the clinic for counseling and testing. Your identity will never be disclosed to your partner when they are notified that they have been exposed to HIV.

If you are assigned to the provider referral study group, a community outreach worker will contact the partner(s) directly to assure they have been notified as soon as possible. They will be advised that they have been exposed to HIV and encouraged to visit the clinic for counseling and testing. Your identity will never be disclosed to your partner.

You will be asked to return to the clinic in two weeks to receive your CD4 count results and to answer a short questionnaire about the partner notification process. You will be referred to the Lighthouse clinic if ARV (HIV) treatment is indicated.

What are the possible benefits from being in this study?
The benefits to you from being in this study may be to help you notify your sexual partners that they may have been exposed to HIV. Malawi may benefit from the results of this research by informing policy makers what is the best method of providing partner notification to individuals exposed to HIV.

What are the possible risks or discomforts involved with being in this study?
You may feel embarrassed to answer questions about your sexual behavior. You can refuse to answer any questions asked of you at any time.

We will protect your confidentiality to the greatest extent possible. Your identity is never disclosed to your partner. If your partner must be contacted in the community we will prevent other people (non-partners) from intercepting partner notification messages. Once a partner is located, their identity must be confirmed before continuing and all discussion with the community outreach worker must take place in a private place.

Notifying your sexual partner(s) that have been exposed to HIV may cause you social, economic, legal or physical harm due to the partner notification process. Our team of researchers and counselors will do everything in our power to help you resolve these problems if they arise.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this research study in order to receive care at the STI clinic.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will your privacy be protected?
If you decide to be in this study you will be assigned a study ID number. This number will be linked to your name and medical record at the STI clinic only through a separate log book that will be kept in a separate locked file. Only the study coordinator will be able to link your medical record that has your name on it and your study information that only has your study number on it. At the conclusion of the study, this link between your name and number will be destroyed.

No subjects will be identified in any report or publication about this study. In some cases, your information in this research study could be reviewed by representatives of the

University of North Carolina, research sponsors, or Malawi government agencies for purposes such as quality control or safety.

<u>What will happen if you are injured by this research?</u>
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. If such problems occur, the researchers will help you get medical care or counseling and all costs will be paid by the UNC Project, Lilongwe. By signing this form you do not give up any of your legal rights.

<u>What if you want to stop before your part in the study is complete?</u>
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

<u>Will you receive anything for being in this study?</u>
You will be reimbursed for your transport expenses to and from the research clinic. The average transport reimbursement per visit will be the local equivalent of US$4 at any point in time.

<u>Will it cost you anything to be in this study?</u>
It will not cost you anything to be in this study. All tests, visits or procedures are free of charge.

<u>Who is sponsoring this study?</u>
This research is funded by the Malawi National AIDS Commission and the UNC Project, Lilongwe. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

<u>What if you have questions about this study?</u>
You have the right to ask, and have answered, any questions you may have about this research. If you have questions, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

<u>What if you have questions about your rights as a research subject?</u>
All research on human volunteers is reviewed by the Malawi Health Sciences Research Committee a Committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject you may contact, anonymously if you wish, the chairman, Dr. Charles Mwansambo at 08-826-946.

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Signature Page: Consent Form

Title of Study: Operations Research to Determine the Community Acceptability and Most Effective Method of HIV Partner Notification at Kamuzu Central Hospital STI Clinic, Lilongwe, Malawi

Principal Investigator: Gift Kamanga, STD Clinic Manager

SIGNATURES

If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to the procedures, please sign your name or make your mark below.

_____	_____	_____
Participant Name (print)	Participant Signature	Date
_____	_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date

Participant is ☐ literate ☐ illiterate

Witness name, signature and date are required on this form only when the consenting participant is illiterate/not able to read.

_____	_____
Participant name (print)	Date

Participant name and date written by _____ on _____

(only fill if participant is illiterate)

_____	_____	_____
Witness Name (print)	Witness Signature	Date

Consent to Participate in a Research Study
Adult Subjects Biomedical Form
Partner Consent

IRB Study # 08-0862
Consent Form Version Date: June 24, 2009
Title of Study: Operations Research to Determine the Community Acceptability and Most Effective Method of HIV Partner Notification at Kamuzu Central Hospital STI Clinic, Lilongwe, Malawi

Principal Investigator: Gift Kamanga
UNC Project, Lilongwe Department: STD Clinic Manager
UNC Project, Lilongwe Phone number: 01-755-056
Co-Investigators: Francis Martinson, Clement Mapanje, Lillian Brown, Bill Miller, Audrey Pettifor and Irving Hoffman
Funding Source: Malawi National AIDS Commission and UNC Project, Lilongwe
Study Contact telephone number and email:
Gift Kamanga 08-870-623, gkamanga@unclilongwe.org.mw;
Francis Martinson 01-755-056, fmartinson@unclilongwe.org.mw

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason.

Research studies are designed to obtain new knowledge that may help other people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the UNC Project, Lilongwe. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this research study is to learn the best way HIV positive persons should notify their sexual partners that have been exposed to HIV. This is called partner notification. Partner notification involves informing the sexual partners of HIV-positive persons that they have been exposed and encouraging them to seek HIV counseling, testing and other prevention and treatment services. The Malawi National HIV/AIDS Policy and Testing and Counseling Guidelines state that partner notification methods should be used to help HIV

positive persons notify their partners, however we don't know which method is the most effective and acceptable in Malawi.

You are being asked to be in the study because you are a partner of an HIV infected person and have tested either negative or positive or have an unclear result.

Are there any reasons you should not be in this study?
You should not be in this study if you are not willing to talk about how many persons you have had sex with in the last 3 months.

How many people will take part in this study?
If you decide to be in this study, you will be one of approximately 500 people in this research study.

How long will your part in this study last?
Your participation in this study will last approximately 30 minutes.

What will happen if you take part in the study?
You will be asked a few questions about your sexual history.

If you tested HIV positive today you will talk to an HIV counselor on the importance of safe sex behavior, will have a brief physical exam, and blood (1 teaspoon) will be drawn for a CD4 count to determine if you need HIV treatment

If your HIV test today is negative or unclear, blood will be drawn (1 teaspoon) for another blood test (RNA) to determine your final HIV status , and if this extra test shows you are newly HIV infected, you will be contacted at home with this information. Either way, negative or newly infected you need to protect all sexual acts with condoms. If newly infected, you will have a CD4 test to see if you need to start immediately on treatment.

You will be referred to the Lighthouse clinic if ARV (HIV) treatment is indicated.

What are the possible benefits from being in this study?
The benefits to you from being in this study may be to help you get treatment for HIV if it is indicated. Malawi may benefit from the results of this research by informing policy makers what is the best method of providing partner notification to individuals exposed to HIV.

What are the possible risks or discomforts involved with being in this study?
You may feel discomfort when blood is drawn. You also may feel dizzy or faint, or experience bruising or swelling at the blood drawing site. You also may become worried or anxious while waiting for your HIV test results. Trained counselors will be available to help you deal with these feelings.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this research study in order to receive care at the STI clinic.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will your privacy be protected?
If you decide to be in this study you will be assigned a study ID number. This number will be linked to your name and medical record at the STI clinic only through a separate log book that will be kept in a separate locked file. Only the study coordinator will be able to link your medical record that has your name on it and your study information that only has your study number on it. At the conclusion of the study, this link between your name and number will be destroyed.

No subjects will be identified in any report or publication about this study. In some cases, your information in this research study could be reviewed by representatives of the University of North Carolina, research sponsors, or Malawi government agencies for purposes such as quality control or safety.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. If such problems occur, the researchers will help you get medical care or counseling and all costs will be paid by the UNC Project, Lilongwe. By signing this form you do not give up any of your legal rights.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?
You will be reimbursed for your transport expenses to and from the research clinic. The average transport reimbursement per visit will be the local equivalent of US$4 at any point in time.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study. All tests, visits or procedures are free of charge.

Who is sponsoring this study?
This research is funded by the UNC Project, Lilongwe. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research subject?
All research on human volunteers is reviewed by the Malawi Health Sciences Research Committee a Committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject you may contact, anonymously if you wish, the chairman, Dr. Charles Mwansambo at 08-826-946.

- -

Signature Page: Partner Consent Form

Title of Study: Operations Research to Determine the Community Acceptability and Most Effective Method of HIV Partner Notification at Kamuzu Central Hospital STI Clinic, Lilongwe, Malawi

Principal Investigator: Gift Kamanga, STD Clinic Manager

SIGNATURES

If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to the procedures, please sign your name or make your mark below.

_____	_____	_____
Participant Name (print)	Participant Signature	Date
_____	_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date

Participant is ☐ literate ☐ illiterate

Witness name, signature and date are required on this form only when the consenting participant is illiterate/not able to read.

_____	_____
Participant name (print)	Date

Participant name and date written by _____ on _____
(only fill if participant is illiterate)

_____	_____	_____
Witness Name (print)	Witness Signature	Date

Signature Page: Oral Consent Form for study refusers

Title of Study: Operations Research to Determine the Community Acceptability and Most Effective Method of HIV Partner Notification at Kamuzu Central Hospital STI Clinic, Lilongwe, Malawi

Principal Investigator: Gift Kamanga, STD Clinic Manager

You have decided not to participate in the study but we would like to ask you a few questions about why you didn't want to participate and your feelings about partner notification. Knowing reasons why people like yourself might refuse partner notification will help us understand which method of partner notification is the most effective and acceptable in Malawi.

Answering these questions will take approximately 15 minutes. We will not record your name or any other identifying information about you.

SIGNATURES

If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to the procedures, please mark an 'X' in the appropriate box below:

Participant: ☐ agrees ☐ does not agree

If you have read this consent form and explained it to the participant and they demonstrate they understand the information, and voluntarily agree to the procedures, please sign your name below.

_____	_____	_____
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date

APPENDIX B

STUDY INSTRUMENTS

PARTNER NOTIFICATION STUDY: INDEX PATIENT ELIGIBILITY FORM

To be asked of participant:

1 How old are you? ___ ___ years

2 Is today the first time you had a positive HIV test or someone told you that you were infected with HIV? ☐ Yes ☐No

If No then end of form

3 Have you had sex during the last 3 months? ☐ Yes ☐No

If No then end of form

4 Do you live in Lilongwe City? ☐ Yes ☐No

If No then end of form

5 Are you willing and able to provide information about your sexual partners, including names and locator information? ☐ Yes ☐No

If No then end of form

If participant is less than 18 years old or answered no to any questions above then participant is not eligible

6 Is participant eligible? ☐ Yes ☐No

If No then end of form

To be completed by research staff:

5 Did the participant provide informed consent for study participation? ☐ Yes ☐No

If No then end of form

Initials	Date

PARTNER NOTIFICATION STUDY: INDEX PATIENT ENROLLMENT

KSU ID: ☐☐☐☐☐

Part 1. Demographic Data

Item	Question	Response
1	*Indicate client sex*	☐ [0] Male ☐ [1] Female
2	*Indicate STI diagnosis (from KSU CRF)*	☐ [0] No STI diagnosed ☐ [1] GUD ☐ [2] AVD ☐ [3] BU ☐ [4] UD ☐ [5] PRUD ☐ [6] LAP ☐ [7] SS ☐ [8] BA ☐ [9] GW ☐ [10] OTHER STI
3	What is your date of birth?	___ ___ ___ ___ ___ ___ ___ D D M M M Y Y
4	Age:	___ ___ years
5	What is the highest level of education you have completed?	☐ [0] Never attended school Primary School (Standard): ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4 ☐ [5] 5 ☐ [6] 6 ☐ [7] 7 ☐ [8] 8 Secondary school (Form): ☐ [9] 1 ☐ [10] 2 ☐ [11] 3 ☐ [12] 4 ☐ [13] Above secondary school
6	How well can you read Chichewa?	☐ [0] Very well ☐ [1] Well ☐ [2] Somewhat ☐ [3] Not at all

7	How well can you write Chichewa?	☐ [0] Very well ☐ [1] Well ☐ [2] Somewhat ☐ [3] Not at all
8	How well can you read English?	☐ [0] Very well ☐ [1] Well ☐ [2] Somewhat ☐ [3] Not at all
9	How well can you write English?	☐ [0] Very well ☐ [1] Well ☐ [2] Somewhat ☐ [3] Not at all
10	Was subject able to sign their name on the consent?	☐ [1] Yes ☐ [0] No
11	What is your tribe?	☐ [0] Chewa ☐ [1] Tumbuka ☐ [2] Yao ☐ [3] Sena ☐ [4] Lomwe ☐ [5] Ngoni ☐ [6] Tonga ☐ [7] Nkhonde ☐ [8] Other ☐ [99] Don't know
12	Are you currently earning an income?	☐ [1] Yes ☐ [0] No → **skip to #14**
13	What do you do to earn an income? (*mark all that apply)*	☐ [1] Taxi driver ☐ [2] Truck driver ☐ [3] Street vendor

		☐ [4] Market vendor ☐ [5] Mechanic/petrol station attendant ☐ [6] Bar, tavern, club owner/manager ☐ [7] Bar, tavern, club employee ☐ [8] Hotel owner/manager ☐ [9] Hotel employee ☐ [10] Security guard ☐ [11] Hairdresser, barber ☐ [12] Beer/liquor store owner ☐ [13] CBO/NGO staff ☐ [14] Government staff ☐ [15] Chief/community leader ☐ [16] Health care worker ☐ [17] Teacher ☐ [18] Police/military officer ☐ [19] Agricultural work/farmer ☐ [20] Business/office work ☐ [21] Butcher ☐ [22] Domestic worker/gardener/cleaner ☐ [23] Other (specify):_____[23a]
14	Do you have electricity at your home?	☐ [1] Yes ☐ [0] No

15	Do you have running water at your home?	☐ [1] Yes ☐ [0] No
16	What is your marital status?	☐ [0] Married ☐ [1] Never married ☐ [2] Separated ☐ [3] Divorced ☐ [4] Widowed
17	How many living children do you have?	___ ___
18a	What area do you live in?	_____
18b	If no area, please indicate Village and nearest area:	_____

Part 2. Sexual Behavior

19	Thinking back to the last month (four weeks), how many different partners did you have sex with?	___ ___ partners
20	Now thinking back to the last three months (12 weeks), including those you just named, how many different partners did you have sex with?	___ ___ partners
21	How many times during the last week did you have sex?	___ ___
22	How many times during the last month did you have sex?	___ ___
23	How old were you the first time you had sex?	___ ___ years
24	Have you ever had a negative HIV test?	☐ [1] Yes ☐ [0] No → **end of form**
25	If yes, when was your last HIV test?	_____ weeks ago *or* _____ Months ago *or* _____ Years ago

PARTNER NOTIFICATION STUDY: PARTNER DATA

To be asked of index patient
Complete a separate form for each named partner

Partner ID: ____ ____ ____ ____ - ____ ____

Part I. Partner Demographics

1	Partner age	___ ___ years
2	Sex of partner	☐ [0] Male ☐ [1] Female
3	How would you describe your relationship to this partner?	☐ [0] Husband/Wife ☐ [1] Live-in partner, not married ☐ [2] Boyfriend/Girlfriend ☐ [3] Regular casual partner – have sex with on an ongoing basis ☐ [4] Non-regular casual partner – have sex with only once or a few times ☐ [5] Sex worker/prostitute/bargirl/freelancer
4	When was the first time you had sex with this partner?	___ ___ days ago *or* ___ ___ months ago *or* ___ ___ years ago
5	When was the last time you had sex with this partner?	___ ___ days ago *Must be less than 90 days ago*
6	How many times in the month (4 weeks) before that did you have sex with this partner?	___ ___ times
7	Do you plan to have sex with this partner again?	☐ [1] Yes ☐ [0] No
8	Did you use a condom the last time you had sex with this partner?	☐ [1] Yes ☐ [0] No

9	Think back to the last 5 times you had sex with this partner. Of those 5 times, how many times did you use a condom?	☐ [0] 0 ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4 ☐ [5] 5 ☐ [9] Index has had sex with this partner less than 5 times → Go to item 10
10		10a. Total number of times you have had sex with this partner? ☐ [0] 0 ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4 10b. Number of times you used a condom with this partner? ☐ [0] 0 ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4
11	What is the HIV status of this partner?	☐ [1] Positive ☐ [0] Negative ☐ [2] Don't Know HIV status of partner
12	Have you ever experienced violence or physical harm by this partner?	☐ [1] Yes ☐ [0] No
13	Have you ever been violent or physical harmful to this partner?	☐ [1] Yes ☐ [0] No

Part II. Partner Locator Data

14	Is index able to provide locator information on this partner?	☐ [1] Yes ☐ [0] No

Complete Partner Locator Form

PARTNER NOTIFICATION STUDY

PARTNER LOCATOR - MAP FORM

Partner: Home ☐ Work ☐	
tel	visit

2. PARTNER DETAILS

Name:		Alias:	

Age: Sex: M / F Religion: Marital status:
Education:

Home
Area: House #: Landlord name: Tel (home):
email:

Important landmarks

Origin Home:	District: TA: Village:
Going away: Y ☐ N ☐	Where: When: How long: Contact address:

Work
Occupation: Employer name:

Work address: Tel: email:

Best time of day to find them:
Partner description (what does partner look like):
Additional Information:

3. OTHER CONTACT DETAILS *(Is there another person who may know where to find them?)*

Name:		Alias:	

Home

Area: House#: Landlord name:

Important landmarks

PARTNER NOTIFICATION STUDY: INDEX PATIENT RANDOMIZATION

1	How many partners did index patient name? *(Item 20 from INDEX PATIENT ENROLLMENT)*	___ ___
2	Was a partner data form completed for each partner?	☐ [1] Yes ☐ [0] No
3	Number of locator forms completed?	___ ___
	If YES to 2, open randomization assignment envelope	
4	Assigned partner notification method	☐ [0] **Passive referral** ☐ [1] **Contract referral** ☐ [2] **Provider referral**
5	If randomized to **contract referral arm**, enter date one week from enrollment date	___ ___ ___ ___ ___ ___ ___ ___ D D M M M Y Y

Partner Notification Study: Index Patient Follow-up

1	*To be completed by research staff:* Number of partners named by index patient:	___ ___

For each partner:

2a	Partner ID	____ ____ ____ ____ - ____ ____
2b	Did you notify partner 01?	☐ [1] Yes ☐ [0] No
2c	How many days after your first visit did you notify them?	___ ___ days
2d	To your knowledge, has partner 01 sought HIV counseling and testing?	☐ [1] Yes ☐ [0] No ☐ [2] Don't Know
2e	If yes, where did they go for HIV counseling and testing?	☐ [0] KCH STD (7c) ☐ [1] Other location ☐ [2] Don't Know *If other location*, name of location: _____
3a	Partner ID	____ ____ ____ ____ - ____ ____
3b	Did you notify partner 02?	☐ [1] Yes ☐ [0] No
3c	How many days after your first visit did you notify them?	___ ___ days
3d	To your knowledge, has partner 02 sought HIV counseling and testing?	☐ [1] Yes ☐ [0] No ☐ [2] Don't Know
3e	If yes, where did they go for HIV counseling and testing?	☐ [0] KCH STD (7c) ☐ [1] Other location ☐ [2] Don't Know *If other location*, name of location: _____

Use next page for additional partners

Index Patient Clinical Data

4a	WHO clinical stage	☐ [1] Stage I ☐ [2] Stage II ☐ [3] Stage III ☐ [4] Stage IV
4b	CD4 Count	_____ cells/mm^3

If CD4 <250 or WHO Stage III-IV then refer to Lighthouse Clinic ☐ [1] Yes ☐ [0] No

Additional Partner Information

5a	Partner 3 ID	____ ____ ____ ____ - ____ ____
5b	Did you notify partner 03?	☐ [1] Yes ☐ [0] No
5d	How many days after your first visit did you notify them?	___ ___ days
5e	To your knowledge, has partner 03 sought HIV counseling and testing?	☐ [1] Yes ☐ [0] No ☐ [2] Don't Know
5f	If yes, where did they go for HIV counseling and testing?	☐ [0] KCH STD (7c) ☐ [1] Other location ☐ [2] Don't Know *If other location*, name of location: _____
6a	Partner 4 ID	____ ____ ____ ____ - ____ ____
6b	Did you notify partner 04?	☐ [1] Yes ☐ [0] No
6d	How many days after your first visit did you notify them?	___ ___ days
6e	To your knowledge, has partner 04 sought HIV counseling and testing?	☐ [1] Yes ☐ [0] No ☐ [2] Don't Know
6f	If yes, where did they go for HIV counseling and testing?	☐ [0] KCH STD (7c) ☐ [1] Other location ☐ [2] Don't Know *If other location*, name of location: _____
7a	Partner 5 ID	____ ____ ____ ____ - ____ ____
7b	Did you notify partner 05?	☐ [1] Yes ☐ [0] No
7d	How many days after your first visit did you notify them?	___ ___ days
7e	To your knowledge, has partner 05 sought HIV counseling and testing?	☐ [1] Yes ☐ [0] No ☐ [2] Don't Know
7f	If yes, where did they go for HIV counseling and testing?	☐ [0] KCH STD (7c) ☐ [1] Other location ☐ [2] Don't Know *If other location*, name of location: _____

PARTNER NOTIFICATION STUDY: SOCIAL HARMS TO INDEX

Item	Question	Response
1	Since your last study visit, have you experienced any problems with the following people as a result of being in this study:	
1a	Your spouse or partner?	☐ [1] Yes ☐ [0] No
1b	People at home/family?	☐ [1] Yes ☐ [0] No
1c	Your friends?	☐ [1] Yes ☐ [0] No
1d	People at work?	☐ [1] Yes ☐ [0] No
1e	People at school?	☐ [1] Yes ☐ [0] No
1f	Your landlord or property owner?	☐ [1] Yes ☐ [0] No
1g	The police?	☐ [1] Yes ☐ [0] No
1h	Other people? Specify:	☐ [1] Yes ☐ [0] No
	If no to all, end of form	
2.	Please describe the problem:	
3.	Has this problem, or any of these problems resulted in:	
3a.	Emotional harm to you? By emotional harm, I mean feeling increased stress, anxiety, worry, or depression as a result of this problem. If Yes, please describe the problem:	☐ [1] Yes ☐ [0] No

3b.	Economic/financial harm to you? For example, has this problem resulted in the removal/loss of your home, property, or ability to earn income? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No
3c.	Legal harm to you? For example, has this problem resulted in legal charges, lawyers, or incarceration? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No
3d.	Physical harm to you? For example, has anyone physically hurt you as a result of this problem? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No

PARTNER NOTIFICATION STUDY: PARTNER ELIGIBILITY FORM

1	Did participant provide a partner notification card or was identity as a partner of an enrolled index confirmed by study staff?	☐ Yes ☐No *If No then end of form*
2	Partner ID *(from notification card and verified with Partner Name Form)*	___ ___ ___ ___ - ___ ___
	To be asked of participant:	
3	How old are you?	___ ___ years *If less than 18 then end of form*

If participant is less than 18 years old or answered no to question 1 above then participant is not eligible

4	Is partner eligible?	☐ Yes ☐No *If No then end of form*
	To be completed by research staff:	
5	Did the partner provide informed consent for study participation?	☐ Yes ☐No *If No then end of form*

Initials	Date

HIV Partner Notification Study: Partner Visit Form

KSU ID: ☐☐☐☐☐

Part I. Partner Demographics

1	Partner ID	____ ____ ____ ____ - ____ ____
2	Date partner attended clinic:	__ __ __ __ __ __ __ __ D D M M M Y Y
3	Partner Sex	☐ [0] Male ☐ [1] Female
4	Partner date of birth	__ __ __ __ __ __ __ __ D D M M M Y Y
5	Partner age	___ ___ years (*partner must be at least 18 years old)*
6	Partner highest level of education you have completed?	☐ [0] Never attended school Primary School (Standard): ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4 ☐ [5] 5 ☐ [6] 6 ☐ [7] 7 ☐ [8] 8 Secondary school (Form): ☐ [9] 1 ☐ [10] 2 ☐ [11] 3 ☐ [12] 4 ☐ [13] Above secondary school
7	What is your marital status?	☐ [0] Married ☐ [1] Never married ☐ [2] Separated ☐ [3] Divorced ☐ [4] Widowed

8	What area do you live in?	_____
9	If no area, please indicate Village	_____

Part II. Sexual Behavior

10	Thinking back to the last month (4 weeks), how many different partners did you have sex with?	___ ___ partners
11	Now thinking back to the last three months (12 weeks), including those you just named, how many different partners did you have sex with?	___ ___ partners
12	How would you describe your relationship to each of these partners?	
12a	Partner 1	☐ [0] Husband/Wife ☐ [1] Live-in partner, not married ☐ [2] Boyfriend/Girlfriend ☐ [3] Regular casual partner – have sex with on an ongoing basis ☐ [4] Non-regular casual partner – have sex with only once or a few times ☐ [5] Sex worker/prostitute/bargirl/freelancer ***→ If only 1 partner in #11, skip to 13***
12b	Partner 2	☐ [0] Husband/Wife ☐ [1] Live-in partner, not married ☐ [2] Boyfriend/Girlfriend ☐ [3] Regular casual partner – have sex with on an ongoing basis ☐ [4] Non-regular casual partner – have sex with only once or a few times ☐ [5] Sex worker/prostitute/bargirl/freelancer ***→ If only 2 partners in #11, skip to 13***

12c	Partner 3	☐ [0] Husband/Wife ☐ [1] Live-in partner, not married ☐ [2] Boyfriend/Girlfriend ☐ [3] Regular casual partner – have sex with on an ongoing basis ☐ [4] Non-regular casual partner – have sex with only once or a few times ☐ [5] Sex worker/prostitute/bargirl/freelancer ***→ If only 3 partners in #11, skip to 13***
12d	Partner 4	☐ [0] Husband/Wife ☐ [1] Live-in partner, not married ☐ [2] Boyfriend/Girlfriend ☐ [3] Regular casual partner – have sex with on an ongoing basis ☐ [4] Non-regular casual partner – have sex with only once or a few times ☐ [5] Sex worker/prostitute/bargirl/freelancer
13	Have you ever had an HIV test?	☐ [1] Yes ☐ [0] No → ***if no skip 14 & 15 and go straight to 16***
14	When was your last HIV test?	_____ weeks ago *or* _____ Months ago *or* _____ Years ago
15	What was the result of your last HIV test?	☐ [1] Reactive ☐ [0] Non-reactive ☐ [2] Discordant

Part III. HIV Testing and STI symptoms

To be completed by nurse in exam room

16	Did partner experience any of the following symptoms is the previous 2 weeks:	Itch?	☐ [1] Yes	☐ [0] No
		Ulcer?	☐ [1] Yes	☐ [0] No
		Dysuria?	☐ [1] Yes	☐ [0] No
		Discharge?	☐ [1] Yes	☐ [0] No
		Rash?	☐ [1] Yes	☐ [0] No
		LAP?	☐ [1] Yes	☐ [0] No
		Bubo?	☐ [1] Yes	☐ [0] No
		Other?	☐ [1] Yes	☐ [0] No
		No symptoms	☐ [1] Yes	☐ [0] No

17	Did partner accept HIV testing?	☐ [1] Yes ☐ [0] No
18	HIV Rapid test result	☐ [1] Reactive ☐ [0] Non-reactive ☐ [2] Discordant
IF Rapid Test is reactive complete item 19 and item 20		
19	WHO clinical stage	☐ [1] Stage I ☐ [2] Stage II ☐ [3] Stage III ☐ [4] Stage IV
20	CD4 Count	_____cells/mm^3

PARTNER NOTIFICATION STUDY: SOCIAL HARMS TO PARTNER

Item	Question	Response
1	Have you experienced any problems with the following people as a result of partner notification:	
1a	Your spouse or partner?	☐ [1] Yes ☐ [0] No
1b	People at home/family?	☐ [1] Yes ☐ [0] No
1c	Your friends?	☐ [1] Yes ☐ [0] No
1d	People at work?	☐ [1] Yes ☐ [0] No
1e	People at school?	☐ [1] Yes ☐ [0] No
1f	Your landlord or property owner?	☐ [1] Yes ☐ [0] No
1g	The police?	☐ [1] Yes ☐ [0] No
1h	Other people? Specify:	☐ [1] Yes ☐ [0] No
	If no to all, end of form	
2.	Please describe the problem:	
3.	Has this problem, or any of these problems resulted in:	
3a.	Emotional harm to you? By emotional harm, I mean feeling increased stress, anxiety, worry, or depression as a result of this problem. If Yes, please describe the problem:	☐ [1] Yes ☐ [0] No

3b.	Economic/financial harm to you? For example, has this problem resulted in the removal/loss of your home, property, or ability to earn income? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No
3c.	Legal harm to you? For example, has this problem resulted in legal charges, lawyers, or incarceration? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No
3d.	Physical harm to you? For example, has anyone physically hurt you as a result of this problem? If yes, please describe the problem:	☐ [1] Yes ☐ [0] No

PARTNER NOTIFICATION STUDY: REFUSERS

Item	Question	Response
1	*Indicate client sex*	☐ [0] Male ☐ [1] Female
2	What is your date of birth?	___ ___ ___ ___ ___ ___ ___ D D M M M Y Y
3	What is your age?	___ ___ years
4	What is the highest level of education you have completed?	☐ [0] Never attended school Primary School (Standard): ☐ [1] 1 ☐ [2] 2 ☐ [3] 3 ☐ [4] 4 ☐ [5] 5 ☐ [6] 6 ☐ [7] 7 ☐ [8] 8 Secondary school (Form): ☐ [9] 1 ☐ [10] 2 ☐ [11] 3 ☐ [12] 4 ☐ [13] Above secondary school
5	What is your marital status?	☐ [0] Married ☐ [1] Never married ☐ [2] Separated ☐ [3] Divorced ☐ [4] Widowed
6a	What area do you live in?	
6b	If no area, please indicate Village:	
7	Why did you choose not to participate in this research study:	☐ [0] Don't have time today ☐ [1] Don't want to notify my partner(s) ☐ [2] Afraid to notify my partner(s) ☐ [3] Don't want provider to contact my partner(s) ☐ [4] Need more time to think about it ☐ [5] Other: _____

Use back of form if additional space for 7 is required

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