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HIV partner notification is effective and feasible in sub-Saharan Africa: Opportunities for HIV treatment and prevention

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Abstract

Background—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.

Methods—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 referral group, a health care provider notified partners directly.

Results—240 index patients named 302 sexual partners and provided locator information for 252. Among locatable partners, 107 returned for HIV counseling and testing; 20/82 (24%; 95% CI 15 – 34%) partners returned in the passive referral arm, 45/88 (51%; 95% CI 41 – 62%) in the contract referral arm, and 42/82 (51%; 95% CI 40 – 62%) in the provider referral arm (p<0·001). Among returning partners (n=107), 67 (64%) of were HIV-infected with 54 (81%) newly diagnosed.

Discussion—This study provides the first evidence of the effectiveness of partner notification in sub-Saharan Africa. Active partner notification was feasible, acceptable, and effective among STI clinic patients. Partner notification will increase early referral to care and facilitate risk reduction among high-risk uninfected partners.

Keywords

Partner notification; HIV counseling and testing; sub-Saharan Africa

Introduction

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

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present late in the course of their HIV disease have significant short-term mortality[3]. 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[4]. 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[5-7]. Generally, three methods of partner notification are available: passive referral, contract referral, and provider referral[8]. 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[9]. Passive referral, the standard of care in Africa, has had minimal success[10]. 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[11-13], uptake of prevention of mother to child transmission activities[12, 13], and decision-making regarding subsequent pregnancies[11]. 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.

Methods

Study population

Persons with newly diagnosed HIV infection at Kamuzu Central Hospital and Bwaila Hospital outpatient STI clinics in Lilongwe, Malawi were recruited. Lilongwe is the capital city of Malawi with a population of approximately 900,000. 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 and counseled them to visit the clinic while maintaining the anonymity of the index case. Notification in the provider referral group occurred within 48 hours. Community outreach workers who are trained HIV testing counselors or nurses performed notification. A standard protocol for community contact was followed. 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) an absolute difference of 25% between passive referral and the two active referral study arms (contract or provider).

Unconditional logistic regression with a cluster robust variance estimator[14] 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[15] 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. Reasons for ineligibility included living outside Lilongwe, no sexual partners in the previous 3 months, no sexual partners in Lilongwe, they came for testing as a couple, or had tested positive previously. Of those eligible, 240 (89%) enrolled in the study. 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 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 76% reported never using condoms with their partner [Table 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 20/93 (22%; 95% CI 13 – 30%) in the passive referral arm, 45/94 (48%; 95% CI 38 – 58%) in the contract referral arm, and 42/115 (37%; 95% CI 28 – 45%) in the provider referral arm. Restricting the analysis to locatable partners, the proportion of partners visiting was 20/82 (24%; 95% CI 15 – 34%) in the passive referral arm, 45/88 (51%; 95% CI 41 – 62%) in the contract referral arm, and 42/82 (51%; 95% CI 40 – 62%) in the provider referral arm [Table 3]. None of the partners classified as non-locatable returned. 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 1]. 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. In the first seven days, locatable partners in the contract referral arm returned at a similar rate to the passive referral arm (hazard ratio 1.4 (95% CI 0.7-2.6)), but locatable partners in the provider referral arm returned at a higher rate (HR 2.1 (95% CI 1.1-3.7) compared to partners in the passive referral arm. After seven days, locatable partners in both the contract referral (HR 6.6 (95% CI 2.3-18.8)) and provider referral arms (HR 4.3 (95% CI 1.4-13.0)) returned at a higher rate than 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. 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 and 13 partners had previously tested positive. 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]. 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 (spouse) 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[16]. 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[17]. However, optimal treatment and prevention require that infected people know their status. To achieve this goal, novel strategies of massive household testing[18] and couples counseling[19] 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[20], 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[21, 22]. 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[23, 24] 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[25].

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[26], and in South Africa men and women who disclosed their HIV status reported an increase in social support[27]. Experience in the U.S. suggests partner notification does not increase partnership dissolution[28]. 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[29]. 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.

The 50% partner return rate compares favorably with other evaluations of HIV partner notification in developed countries[6] and is a conservative estimate of the number of partners who received testing services as it is possible partners may have tested elsewhere. Counseling index patients to advise their partners to visit the study clinics minimized partners testing elsewhere, and the partner cards clearly described the location of the study

clinics. Partner cards also included instructions for area testing centers to return the cards to the study clinics if partners presented the cards at those locations and study staff periodically visited other major testing sites in Lilongwe to determine if partners had tested there. No index patients reported partners who tested at other sites.

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 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[30], 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.

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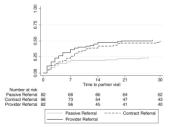

Figure 1. Time to presentation among partners was associated with method of partner notification

Table 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 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	71 (76.3%)	71 (75.5%)	88 (76.5%)	230 (76.1%)
Locator information known	82 (88.2%)	88 (93.6%)	82 (71.3%)	252 (83.4%)

Table 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	(0-37)	1.4	(0.8-2.4)	51	(35-68)	16	(0-39)	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	(0-54)	4.3	(0.6-32.5)	30	(1-59)	22	(0-54)	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

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

Partner Results	n	N	%
Partners tested	104	107	97%
Main partners tested	97	98	99%
Casual partners tested	7	9	92%
Partners with positive test results	67	104	64%
Main partners with positive test results	63	97	64%
Casual partners with positive test results	4	7	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%