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Active HIV Case Finding in the City of Kigali, Rwanda: Assessment of Voluntary Assisted Partner Notification Modalities to Detect Undiagnosed HIV Infections

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Background: Voluntary assisted partner notification (VAPN) services that use contract, provider, or dual referral modalities may be efficient to identify individuals with undiagnosed HIV infection. We aimed to assess the relative effectiveness of VAPN modalities in identifying undiagnosed HIV infections.

Setting: VAPN was piloted in 23 health facilities in Kigali, Rwanda.

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Methods: We identified individuals with a new HIV diagnosis before antiretroviral therapy initiation or individuals on antiretroviral therapy (index cases), who reported having had sexual partners with unknown HIV status, to assess the association between referral modalities and the odds of identifying HIV-positive partners using a Bayesian hierarchical logistic regression model. We adjusted our model for important factors identified through a Bayesian variable selection.

Results: Between October 2018 and December 2019, 6336 index cases were recruited, leading to the testing of 7690 partners. HIV positivity rate was 7.1% (546/7690). We found no association between the different referral modalities and the odds of identifying HIV-positive partners. Notified partners of male individuals (adjusted odds ratio 1.84; 95% credible interval: 1.50 to 2.28) and index cases with a new HIV diagnosis (adjusted odds ratio 1.82; 95% credible interval: 1.45 to 2.30) were more likely to be infected with HIV.

Conclusion: All 3 VAPN modalities were comparable in identifying partners with HIV. Male individuals and newly diagnosed index cases were more likely to have partners with HIV. HIV-positive yield from index testing was higher than the national average and should be scaled up to reach the first UNAIDS-95 target by 2030.

Key Words: voluntary assisted partner notification, HIV-positive yield, index case, Rwanda

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BACKGROUND

Rwanda has a strong national HIV programmatic response, leading to a stable national HIV prevalence of approximately 3%, ¹⁻³ and is on track to achieve the UNAIDS 95-95-95 target by 2030. The Rwanda Population-based HIV Impact Assessment of 2018–2019 estimated that 84% of all people living with HIV (PLHIV) know their status, 97% of whom are on antiretroviral therapy (ART), and of them, 90% are virally supressed. ⁴ The study also estimated the HIV annual incidence among adults to be 0.08%, ⁵ corresponding to approximately 5400 new infections per year. ⁵ The scale-up of HIV services is characterized by diverse HIV testing

modalities, resulting in a decrease in positivity rates from 11% in 2004 to 0.5% in 2020.⁶ With a low HIV testing yield, traditional passive means of providing HIV testing may be insufficient in reaching undiagnosed PLHIV.

Recent World Health Organization guidelines recommend active HIV case finding through voluntary assisted partner notification (VAPN) services through index cases. Partner notification includes passive approaches, where index cases are encouraged to notify the partner(s), or active approaches, where the initiative is entirely with the index case. The latter includes contract referral, where index cases enter into a contract with health care providers to disclose their HIV status to partner(s) and refer them for testing, and providers may contact the partner(s) if the case fails to do so. Provider referral is another modality where the provider confidentially contacts the partner(s) for testing, and dual referral occurs when the provider accompanies the index case in disclosure. Rwanda is the first African country to implement all 3 notification approaches.

Active case-finding approaches showed benefits over passive referral modalities in some countries. Rwanda introduced assisted partner notification in 2018–2019, but no study has evaluated the comparative performance of different partner notification modalities. In this study, we compared partner notification approaches to assess their effectiveness in detecting undiagnosed PLHIV in Kigali, Rwanda.

METHODS

Study Population

This is an analysis of data from a public health program, which include index cases with a new HIV diagnosis and PLHIV on ART who reported sexual partners of unknown HIV status. Data were collected from 23 of 59 health facilities in Kigali, supported by the US President's Emergency Plan for AIDS Relief, offering a pilot contact tracing program. The Rwandan national HIV guidelines recommend clinical visits every 3 or 6 months for unstable or stable patients, respectively. During each clinical visit, every adult patient on ART (including those who reengage in HIV care) is routinely asked about sexual encounters with partners with unknown HIV status since the last visit. Individuals confirming such encounters during the past 12 months before clinical visits and newly identified individuals who initiate ART were considered as index cases and were then asked to consent for participation in the study for partner notification. Index cases were explained the notification modalities, and they could choose any of the 3 modalities (contract, provider, or dual referral). This study excluded index cases and sexual partners younger than 18 years and index cases at risk of intimate partner violence, as assessed by the health care provider conducting the screening.

Study Variables and Source

The primary outcome is the HIV status (positive/negative) of the partner invited through the assisted case-finding program. HIV testing followed the Rwandan national

HIV guidelines. Among the 19 variables collected by the HIV program, a panel of local expert selected the following 12 factors that were believed to be potentially associated with our outcome partner relationship with the index case (spouse/ husband/cohabitant, boyfriend/girlfriend, occasional/ commercial sex worker/client of commercial sex worker, and others) and index case characteristics including age (younger than 25, 25-34, 35-44, and older than 45 years), sex (male/ female), type of index case (new HIV diagnosis or already on ART), recent viral load (< or ≥1000 copies/mL within the 12month time point), >1 sexual partner in the last 3 months (yes/ no), vaginal or anal sex act without condoms in the last 12 months (yes/no), paid sex act in the last 12 months (yes/no), or received money or goods in exchange for sex act in the last 12 months (yes/no). In addition, information on the facility where the index case was diagnosed or cared for was collected such as the number of patients on ART at the health facility (<1000, 1000-2000, and >2000 patients), the number of health care practitioners per 10,000 populations at the health facility (<3, 3–6, and >6 practitioners), and health facility location (rural/ urban). Data were extracted from the case reporting form by 1 nurse and keyed into the District Health Information System-2, a free, open-source health management data platform.

Statistical Analysis

We used a Bayesian hierarchical logistic regression model to assess the association of each referral modality on the HIV status after adjusting for index and health facility-related characteristics and while accounting for residual variability at the level of the index case and the health facility. Adjusting factors were selected within a Gibbs variable selection approach¹⁰ among a set of 12 potential factors as mentioned earlier. The model with the highest posterior probability was chosen to select the covariates and build a final model. The Markov chain Monte Carlo simulation was used to estimate model parameters. We reported posterior distribution with 95% credible interval (CI). Detailed model formulation and implementation are given in the Appendix (see Supplemental Digital Content 1, http://links.lww.com/QAI/B768). Analyses were completed using R software, version 3.6.1 and OpenBUGS software, version 3.2.3 rev 1012.

Ethical Consideration

Informed consent was obtained from each participant before inclusion in the study. The Rwanda National Ethics Committee approved the protocol for implementation.

RESULTS

Between October 1, 2018, and December 30, 2019, 6336 index cases who reported to have had sex act with a partner of unknown HIV status were identified. These individuals disclosed 11,633 partners (ratio of 1.8 partners per index case) of whom 89.7% (10,432/11,633) could be invited for testing at health facilities. Respondents to the invitation were 79.3% (8276/10,432) individuals, of whom 92.9% (7690/8276) accepted HIV testing. These identified partners related to

TABLE 1. Characteristics of Index Cases, Notified Partners, and Number of Identified HIV-Positive Partners

	No. of Notified Partners Tested for HIV	No. of HIV-Positive Partners Detected from Partne Notification (%)
Overall	7690	546 (7.1)
Characteristics of partners		` '
Used partner notification		
Contract referral	2605	217 (8.3)
Provider referral	3394	238 (7.0)
Dual referral	1691	91 (5.4)
Relationship between index and partner	1051)
Spouse/husband/cohabitant	1545	132 (8.5)
Boyfriend/girlfriend	728	75 (10.3)
Occasional/FSW or client of FSW	4602	272 (5.9)
Others	776	64 (8.2)
Characteristics of index cases with partners who were notified and tested for HIV	,,,	01 (0.2)
Age category, yrs		
Younger than 25	648	44 (6.8)
25–34	2660	200 (7.5)
35–44	2637	195 (7.4)
Older than 45	1668	99 (5.9)
Sex		
Male	2934	277 (9.4)
Female	4756	269 (5.7)
Type of index case		
New HIV diagnosis	2192	230 (10.5)
Already on ART	5498	316 (5.7)
Viral load suppression (recent)		
No viral load suppression (≥1000 copies/mL)	608	40 (6.6)
Viral load suppression (<1000 copies/mL)	7082	506 (7.1)
More than 1 sexual partner in the last 3 mo		
No	7060	506 (7.2)
Yes	630	40 (6.3)
Vaginal or anal sex act without condoms in the last 12 mo		
No	5907	433 (7.3)
Yes	1783	113 (6.3)
Paid sex act in the last 12 mo		
No	6950	483 (6.9)
Yes	740	63 (8.5)
Received money or goods in exchange for sex act in the last 12 mo		
No	6897	502 (7.3)
Yes	793	44 (5.5)
No. of patients on ART at health facility		
<1000	3172	148 (4.7)
1000–2000	1630	126 (7.7)
>2000	2888	272 (9.4)
No. of health practitioners per 10,000 population within health facility		
<3	1388	105 (7.6)
3–6	5102	397 (7.8)
>6	1200	44 (3.7)
Health facility location		
Rural	959	42 (4.4)
Urban	6731	504 (7.5)

TABLE 2. Bivariate and Multivariable Bayesian Logistic Regression Analyses for the Identification of Undiagnosed HIV-Positive Partners

	N	Bivariate Analysis, OR (95% CI)	Multivariable Analysis, AOR (95% CI)
Type of partner notification			
Contract referral	2605	1.00	1.00
Provider referral	3394	0.83 (0.68 to 1.01)	0.96 (0.74 to 1.25)
Dual referral	1691	0.62 (0.48 to 0.80)	0.92 (0.63 to 1.33)
Index case sex			
Female	2909	1.00	1.00
Male	1796	1.74 (1.46 to 2.07)*	1.84 (1.50 to 2.28)*
Type of index case			
HIV-positive on ART	3397	1.00	1.00
New HIV diagnosis	1308	1.92 (1.61 to 2.29)*	1.82 (1.45 to 2.30)*
Variance			Median (95% CI)
Index case level			1.14 (0.62 to 1.90)
Health facility level			0.70 (0.33 to 1.39)

^{*}Significant based on 95% CI.

4507 index cases, of which 26.5% (1308/4507) were newly diagnosed and 73.5% (3.397/4507) were on ART. Among notified and tested partners, 33.9% (2605/7690) were contacted through contract referral, 44.1% (3394/7690) through provider referral, and 22.0% (1691/7690) through dual referral. Overall, 7.1% (546/7690) of the partners were newly tested positive for HIV. The percentage of HIV-positive partners detected from partner notification was 8.3% (217/2605) when notified through contract referral, 7.0% (238/3394) when notified through provider referral, and 5.4% (91/1691) when notified through dual referral. Higher rates of HIV-positive partners were seen when index cases were male individuals (9.4%), had a new HIV diagnosis (10.5%), or when index cases were cared for by larger health facilities (9.4%) or health facilities in urban areas (7.5%) (Table 1).

Sex and the type of index case were the 2 factors identified by the Bayesian Gibbs variable selection as important for the risk of diagnosing an HIV-positive partner with a posterior probability of 41.9% (see Appendix, Table A1, Supplemental Digital Content 1, http://links.lww.com/QAI/B768) and were carried over to build the bivariate and final model. Compared with contract referral modality, provider referral and dual referral methods did not show any significant association with the identification of undiagnosed partners, with an adjusted odds ratio (AOR) of 0.96 (95% CI: 0.74 to 1.25) and AOR of 0.92 (95% CI: 0.63 to 1.33), respectively. Male index cases and newly diagnosed HIV-positive individuals were more likely to disclose new HIV-positive partners, with AOR 1.84 (95% CI: 1.50 to 2.28) and AOR 1.82 (95% CI: 1.45 to 2.30), respectively (Table 2).

DISCUSSION

This study has demonstrated that the 3 VAPN modalities (contract, provider, and dual referral) were comparable regarding identifying new HIV cases in Rwanda. The recruitment rate of HIV-positive partners was found to be higher for male individuals and newly diagnosed index cases initiating ART. The overall positivity yield was estimated at 7.1%, which is more than 10 times higher than the positivity rate provided by traditional passive testing modalities,6 confirming that VAPN approaches are effective methods to target and identify undiagnosed PLHIV who may be unaware of their HIV status. Our study showed the feasibility, acceptability, and effectiveness of partner notification in the diagnosis of remaining undiagnosed PLHIV in Rwanda and further supports similar conclusion of previous studies conducted in sub-Saharan Africa (SSA) that have applied the 2016 World Health Organization guidelines for active HIV case finding is SSA.11-15 The absence of a significant association between positive yield and disclosure methods is an important finding because it allows national programs to determine which referral modality might be most effective in a given country context or based on available health care worker manpower.

Compared with female individuals, male index cases showed a higher probability to identify positive partners. This finding could be explained by a combination of several factors. First, HIV transmission efficiency differs across sexes, where male-to-female transmission is known to be higher than female-to-male transmission^{16,17} and partially attributed to high rates of male circumcision (72.4%) in Kigali.⁴ Moreover, men are less likely to have a higher viral load suppression on ART (84.4% men versus 93.2% women) and are more likely to have multiple sexual partners.4 However, in this study population, there were no differences regarding the mean number of disclosed sexual partners (2.4) for men and 2.3 for women, P < 0.001). Second, it may be easier for male index cases to identify their partners. A Tanzanian study reported 6.2 times higher likelihood for male index cases to list more than 1 sexual partner compared with female index cases. 18 Especially in SSA, women can face more barriers than men in partner notification, fueled by fear of abandonment or relationship ending, of experiencing physical or emotional violence, and of being undervalued for not having a child. 18-20 It is therefore important to consider differences between male and female behaviors and roles and their consequences on testing, partner notification, and disclosure of HIV status. Furthermore, men (and male partners) are harder to reach by HIV testing services²¹ due to stigma.²²⁻²⁴ Only 38.2% of index cases in our study were men, and a study conducted in Rwanda has shown a low uptake of HIV testing services among men.25 In Tanzania. male index cases had a 2.2 times higher likelihood of successfully referring a partner than female index cases, 18 meaning that male partners of female index cases were less likely to present for testing. This suggests that men may need additional support to motivate testing.

The strength of our study is its novelty as the first evaluation of active case finding in Rwanda using a large cohort of index cases with a high notification rate of 66%. However, our study has several limitations. First, because our study was conducted only in the major Kigali metropolitan area (urban with a higher HIV prevalence, incidence, and volume of patients compared with other provinces), generalizability to the whole country may be limited. There may be differences in HIV testing, status disclosure, and partner notification between urban and rural areas because the population of rural areas has often lower access to testing facilities and faces a higher rate of stigma and discrimination. Second, we cannot exclude differences regarding disclosure between males and females due to cultural barriers and the type of sexual encounter (eg, with a sex worker). Third, VAPN was introduced at ART enrollment, and participation was voluntary. Patients not linked to care and patients who refused to participate were therefore excluded from the analysis. However, we expect this bias to be minimal because linkage to ART in Rwanda is greater than 95%,25 and participation refusal was low with less than 3% of indexes refusing consent. Fourth, we did not know the directionality of HIV infection among partners, particularly among newly infected and suboptimally treated index cases. Finally, approximately one-third of partners did not undergo testing, and information on their HIV status was not available.

In conclusion, this study shows that VAPN modalities are not associated with the probability of identifying undiagnosed PLHIV. Contract referral, provider referral, or dual referral could be equally implemented and scaled up as component interventions to reach the first UNAIDS-95 by 2030. Further studies are recommended to assess the acceptability and uptake of each modality, including investigations in both rural and urban populations.

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REFERENCES

- Institut National de la Statistique du Rwanda (INSR) and ORC Macro. Rwanda Demographic and Health Survey 2005. Calverton, MD: INSR and ORC Macro; 2006.
- National Institute of Statistics of Rwanda (NISR) [Rwanda], Ministry of Health (MOH) [Rwanda], and ICF International. Rwanda Demographic and Health Survey 2010. Calverton, MD: NISR, MOH, and ICF International; 2011.
- National Institute of Statistics of Rwanda (NISR) [Rwanda], Ministry of Health (Rwanda), ICF International (Rockville, MD): Rwanda Demographic and Health Survey 2014–15. Rockville, MD: NISR, MOH, and ICF International.
- 4. Rwanda Biomedical Centre (RBC), National Institute of Statistics of Rwanda (NISR), The United States President's Emergency Plan for AIDS Relief (PEPFAR), The United States Centers for Disease Control and Prevention (CDC), Westat, ICAP at Columbia University. Rwanda Population-Based HIV Impact Assessment (RPHIA) 2018–2019: Final

- Report. 2020. Available at: https://phia.icap.columbia.edu/wp-content/uploads/2020/11/RPHIA-Final-Report_web.pdf. Accessed December 30, 2020
- Ministry of Health (Rwanda), International Center for AIDS Care and Treatment Programs (ICAP). Rwanda Population Based HIV Impact Assessment. 2019. Available at: https://phia.icap.columbia.edu/wpcontent/uploads/2019/10/RPHIA-Summary-Sheet_Oct-2019.pdf. Accessed May 17, 2021.
- Rwanda Biomedical Centre. National HIV and Viral Hepatitis Annual Report 2019–2020. Kigali, Rwanda: Rwanda Biomedical Centre; 2020. Available at https://www.rbc.gov.rw/fileadmin/user_upload/report2019/ 53059%20RPHIA_Report_V9_Web.pdf.
- World Health Organization (WHO). Guidelines on HIV self-testing and partner notification. Supplement to consolidated guidelines on HIV testing services. 2016. Available at: http://apps.who.int/iris/bitstream/ handle/10665/251655/9789241549868-eng.pdf; jsessionid=6D620F3520A65BEBAB09CB2D6CFFBA24?sequence=1. Accessed May 19, 2021.
- Rwanda Ministry of Health. Rwanda Biomedical Centre. National HIV and Viral Hepatitis Annual Report 2017–2018. Kigali- Rwanda; 2018.
- Rwanda Biomedical Centre. National Guidelines for Prevention and Management of HIV and STIs. Kigali- Rwanda; 2017.
- Dellaportas P, Forster JJ, Ntzoufras I. On Bayesian model and variable selection using MCMC. Stat Comput. 2002;12:27–36.
- Buhikire K, Voss J, Kigozi J, et al. Reaching the first 90 in Uganda: predictors of success in contacting and testing the named sexual partners of HIV+ index clients in Kiboga District. AIDS Behav. 2018;22:2458–2467.
- Kahabuka C, Plotkin M, Christensen A, et al. Addressing the first 90: a highly effective partner notification approach reaches previously undiagnosed sexual partners in Tanzania. AIDS Behav. 2017;21:2551–2560.
- Joseph Davey D, Wall KM, Serrao C, et al. HIV positivity and referral to treatment following testing of partners and children of PLHIV index patients in public sector facilities in South Africa. *J Acquir Immune Defic* Syndr. 2019;81:365–370.
- Masyuko SJ, Cherutich PK, Contesse MG, et al. Index participant characteristics and HIV assisted partner services efficacy in Kenya: results of a cluster randomized trial. J Int AIDS Soc. 2019;22(suppl 3):e25305.
- Mahachi N, Muchedzi A, Tafuma TA, et al. Sustained high case-finding through index testing and partner notification services: experiences from three provinces in Zimbabwe. J Int AIDS Soc. 2019;22(suppl 3):e25321.
- Comparison of female to male and male to female transmission of HIV in 563 stable couples. European Study Group on Heterosexual Transmission of HIV. BMJ. 1992;304:809–813.
- Padian NS. Female-to-male transmission of human immunodeficiency virus. JAMA. 1991;266:1664.
- Plotkin M, Kahabuka C, Christensen A, et al. Outcomes and experiences of men and women with partner notification for HIV testing in Tanzania: results from a mixed method study. AIDS Behav. 2018:22:102–116.
- Obermeyer CM, Osborn M. The utilization of testing and counseling for HIV: a review of the social and behavioral evidence. Am J Public Health. 2007:97:1762–1774.
- Maman S, Medley A; World Health Organization, Department of Gender and Women's Health. Gender Dimensions of HIV Status Disclosure to Sexual Partners: Rates, Barriers, and Outcomes: A Review Paper. Geneva, Switzerland: Dept. of Gender and Women's Health (GWH), Family and Community Health (FCH), World Health Organization; 2003
- UNAIDS. Blind Spot—Reaching Out to Men and Boys Addressing a Blind Spot in the Response to HIV. Geneva, Switzerland: UNAIDS;
 Available at: https://www.unaids.org/sites/default/files/media_asset/blind_spot_en.pdf. Accessed May 17, 2021.
- DiCarlo AL, Mantell JE, Remien RH, et al. 'Men usually say that HIV testing is for women': gender dynamics and perceptions of HIV testing in Lesotho. *Cult Health Sex.* 2014;16:867–882.
- Skovdal M, Campbell C, Madanhire C, et al. Masculinity as a barrier to men's use of HIV services in Zimbabwe. Glob Health. 2011;7:13.
- Siu GE, Wight D, Seeley JA. Masculinity, social context and HIV testing: an ethnographic study of men in Busia district, rural eastern Uganda. BMC Public Health. 2014;14:33.
- Ross J, Sinayobye d'Amour J, Yotebieng M, et al. Early outcomes after implementation of treat all in Rwanda: an interrupted time series study. J Int AIDS Soc. 2019;22:e25279.