Ethiopian Medical Journal 2023, 61(1)
Open access articles distributed in terms of

ISSN 0014-1755 eISSN 2415-2420

Original Article

Validation of HIV risk screening tool to identify infected adults and adolescents greater than 14 years at community level in Tanzania and Zambia

Kesetebirhan Delele Yirdaw*[1], Justin Mandala[2]

[1]Family Health International, Addis Ababa, Ethiopia
[2]Global Health, Population and Nutrition, Family Health International, Washington DC, USA

Corresponding author*: kesetebirhan@gmail.com

Abstract
Introduction: *There are several risk factors being used to identify undiagnosed HIV-infected adults. As the number of undiagnosed people gets less and less, it is important to know if existing risk factors and risk assessment tools are valid for use.*
Methods: *Data from the Tanzania and Zambia Population-Based HIV Impact Assessment (PHIA) household surveys which were conducted during 2016 was used. We first included 12 risk factors (being divorced, separated or widowed; having an HIV+ spouse; having one of the following within 12-months of the survey: paid work, slept away from home for ≥1-month, having multiple sexual partners, clients of sex workers, sexually transmitted infection, being tuberculosis suspect, being very sick for ≥3-months; ever sold sex; diagnosed with cervical cancer; and had TB disease into a risk assessment tool and assessed its validity by comparing it against HIV test result. Sensitivity, specificity and predictive value of the tool were assessed. Receiver Operating Characteristic (ROC) curve comparison statistics was also used to determine which risk assessment tool was better.*
Results: *HIV prevalence was 2.3% (2.0%-2.6%) (n=14,820). For the tool containing all risk factors, HIV prevalence was 1.0% when none of the risk factors were present (Score 0) compared to 3.2% when at least one factor (Score ≥1) was present and 8.0% when ≥4 risk factors were present. Sensitivity, specificity, PPV, and NPV were 82.3% (78.6%-85.9%), 41.9%(41.1%-42.7%), 3.2%(2.8%-3.6%), and 99.0%(98.8%-99.3%), respectively. The use of a tool containing conventional risk factors (all except those related with working and sleeping away) was found to have higher AUC (0.65 vs 0.61) compared to the use of all risk factors (p value <0.001).*
Conclusions: *The use of a screening tool containing conventional risk factors improved HIV testing yield compared to doing universal testing. Prioritizing people who fulfill multiple risk factors should be explored further to improve HIV testing yield.*

Keywords: *Adult HIV risk assessment tool; Undiagnosed HIV; Never tested for HIV; HIV testing yield, Tanzania, Zambia*
Citation : *Yirdaw KD, Mandala* J, *Validation of HIV Risk Screening Tool to Identify Infected Adults and Adolescents greater than 14 years at Community Level in Tanzania and Zambia .Ethiop Med J 61 (1) 37—49*
Submission date : *18 October 2022 Accepted: 26 December 2022 Published: 1 January 2023*

Introduction

HIV testing is the gateway for case finding, care, and treatment, as well as prevention services for high-risk individuals (1-3). Over the years, remarkable progress has been made in diagnosing infected people and putting them on treatment. To date, Eastern and Southern African countries have coverage of 87% (77%-95%) compared to the 90% UNAID's target of diagnosing 90% of all estimated HIV infected people by 2020, while the coverage is 68% (54%-87%) for Central and Western African countries (4). This correlates with the high uptake of HIV testing across these countries. Prior HIV testing among surveyed men and women 15-49 years was 62% and 74%, respectively for Eastern, Southern, and Central African countries, respectively, from 2015-2018. It was much lower for Western African countries at 31% for women and 16% for men (5, 6).

Maintaining such high testing coverage or conducting door-to-door testing in high-risk communities is not feasible because of the limited funding available for HIV programs considering the flattening of global support for HIV programs, especially that of PEPFAR over the past 10 years (7, 8). As a result of that, a strategic shift has been made to implement targeted HIV testing with the aim of getting high testing yield per dollar spent on HIV test kit in many country HIV programs, including high-burden countries to put as many infected people on treatment and reduce new infection and mortality in the process (9).

A number of HIV risk factors have been identified and in use to effect targeted HIV testing of at-risk people. The World Health Organization (WHO) recommends HIV testing for clients having sexually transmitted infection (STI), viral hepatitis, tuberculosis (TB); key populations including commercial sex workers, men having sex with men, and IV drug users; clients with symptoms or medical conditions that could indicate HIV infection, including presumed and confirmed TB cases (1, 2). Other factors known to increase the risk of HIV infection include having multiple sexual partners (10, 11), being divorced, separated or widowed (DSW) (12), history of being a client of a sex worker (13), having cervical Cancer (14), being partners with known infected person (15).

A number of HIV risk assessment tools were validated in different settings in an effort to determine best options to identify HIV infected adults (10, 16,17). These tools often don't include risk factors recommended by the WHO and in use in high prevalence countries. Knowing the performance and limitation of a risk screening tool containing all common HIV risk factors is crucial to determine case finding strategies that better fit routine implementation setting and assess quality of testing services both in clinical and community settings. This study aims to:

1. determine the performance of a hypothetical HIV risk assessment tool that contains conventional HIV risk factors to identify undiagnosed HIV+ adults and adolescents >14 years,
2. determine the performance of a hypothetical HIV risk assessment tool that contains all potential HIV risk factors to identify undiagnosed HIV+ adults and adolescents >14 years,
3. determine the performance of a hypothetical HIV risk assessment tool that contains only statistically significant HIV risk factors to identify undiagnosed HIV positive adults and adolescents >14 years
4. determine which of the above three tools is better in terms of overall performance to identify undiagnosed HIV positive adults and adolescents >14 years
5. determine if the presence of multiple HIV risk factors in one person improves performance of risk assessment tool to identify undiagnosed HIV positive adults and adolescents >14 years.

Materials and Methods

Study setting and design: This is a cross-sectional study based on secondary analysis of data from two community-based household surveys that were conducted in Zambia (2016) and Tanzania (2016-2017). These surveys were Population-Based HIV Impact Assessment (PHIA) studies conducted with PEPFAR support. These study countries are high burden countries providing donor driven (PEPFAR and Global Fund) HIV program. HIV response is mostly facility based where diagnostic and treatment services are provided with community component mainly focusing on prevention and care aspect. PHIA surveys are cross-sectional nationally representative, household-based surveys. The main objectives of the surveys are to measure national HIV prevalence and viral suppression, nationally and sub-nationally, to assess the impact of HIV treatment and prevention programs in each country. Participants were selected using two-stage, stratified cluster sampling. Participants who provided written consent undergo interview based on a structured questionnaire and a biomarker for HIV testing (18, 19).

Inclusion criteria: adolescents and adults >14 years who had matching interview and biomarker datasets (HIV testing result) and who had never tested for HIV prior the survey was included.

Sample size: was calculated to allow comparison between areas under receiver operating characteristic (ROC) curves between two different risk assessment tools. Sample size was calculated to be 1,363 assuming AUC1=0.65, AUC2=0.6, alpha=0.05, power= 80%, correlation in positive group=0.4, and correlation in negative group=0.4 (21).

HIV risk factors: the following variables were considered in different HIV risk assessment tools to generate a tool with better sensitivity, specificity, and positive predictive value (PPV+): being divorced, separated or widowed (DSW) (12), having an HIV+ spouse (15), having paid work within 12 months of the survey, slept away from home for at least a month within 12 months of the survey, having multiple sexual partners (10, 11)within 12 months of the survey, had ever sold sex (13),clients of sex workers within 12 months of the survey, had sexually transmitted infection (STI) within 12 months of the survey(1, 2), diagnosed with cervical cancer (14), being a tuberculosis (TB) suspect within 12 months of the survey which meant having any of the following symptoms: cough, fever, night sweats or weight loss, had TB disease, past or present, and being very sick for at least 3 months within 12 months of the survey, that is being too sick to work or do normal activities (1, 2).

HIV risk assessment tools examined:

Four different hypothetical tools were considered in the validation:

Tool 1: A tool that contained all conventional and any newly identified statistically significant risk factors that predicted HIV infection status in individuals never tested for HIV,

Tool 2: A tool that contained only statistically significant risk factors associated HIV infection,

Tool 3: A tool that contained conventional

Tool 4: A tool that contained conventional risk factors and a combination of newly identified risk factors.

HIV testing: was offered for everyone in the survey and performed for all consenting adults and adolescents >14 years during the survey. Known HIV+ status was further confirmed through the use of antiretroviral markers within the blood. Those with antiretroviral markers were excluded from the study.

Data analysis

Data were obtained from the public domain of PHIA website (22) and analyzed using Stata 14.0 statistical software. First, risk factors that had association with HIV infection among those who never tested for HIV were identified using Chi Square test. To develop scores for a risk assessment tool, appropriate screening items were selected and coded one when the risk factor was present and zero when it was not and the total score calculated for each individual as the sum of the numerical values of the screening items included within a tool. For instance, for the first screening tool where all risk factors were included, the minimum score was 0 while the potential maximum was 12.Chi Square test was also done to examine if having risk screening score of ≥1, ≥2, ≥3, or ≥4 was associated with HIV infection. Sampling weights were used to adjust statistical values taking into account complex sampling design used in PHIA surveys (20).
To determine the optimal cut-off for the screening tool that will enable identification of people at risk of HIV infection, a receiver operating characteristic (ROC) curve was plotted. The area under the ROC (Receiver Operating Characteristic) curve, Area Under the Curve (AUC) and corresponding sensitivity, specificity, positive predictive (PPV) and negative predictive values (NPV) using the screening tool at different levels of scores were determined. ROC comparison statistics was used to statistically test equality between AUC of the different scores. For the score selected to be having the best combination of sensitivity, specificity, PPV, NPV and AUC, similar analysis was conducted to see if age, gender, and residence affected AUC. This was done by doing stratified analysis of AUC using the stated variables.
Finally, to compare and select between the different risk assessment tools, test of quality of AUC was done. Number needed to test to identify one HIV infected person (NNT+) was also calculated to see if risk assessment tools reduced this number compared to universal testing. To select appropriate variables for the second tool, logistic regression was used. Variables with p- value <0.25 during bi-variable analysis were included in the final model. Variables with p-value <0.05 in the final model were included in the making of Tool 2.

Ethical considerations: Both PHIA surveys had written informed consent, both for interview and blood collection for all participating adults. Parents consented for adolescents. All datasets don't have individual identifiers like names or addresses that can be used to identify people. In addition, the study got a non-human subject determination from the Office of International Research Ethics of Family Health International (FHI360).

Results

Selection of study participants

Of 68,564 adults and adolescents >14 years included in the Tanzania and Zambia PHIA studies, 55,340 had a matching interview and biomarker (including HIV testing) datasets. Of these, 39,103 (70.7%), had previously been tested for HIV and 181 (0.3%) had missing previous HIV testing data, and hence excluded from the analysis. Of the remaining 16,056, 15160 (94.4%) were tested for HIV. Excluding those who didn't have sampling weights, the final study sample was 14,820. (Figure 1)

Compared to individuals who were eligible for inclusion in this study but had missing HIV testing result, those who were tested for HIV during the survey were likely to be older, male, from urban area. They were also less likely to have multiple sexual partners or sexually transmitted infection in the past 12 months. (Table 1)

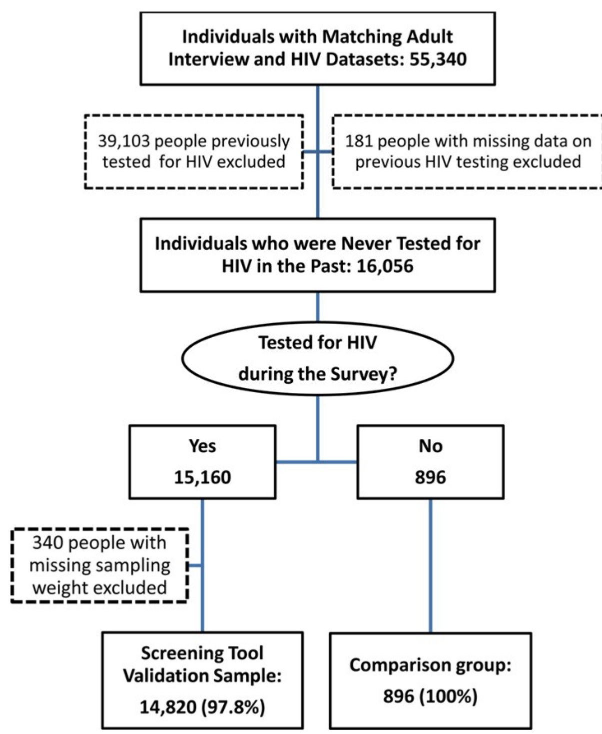


Figure 1. Selection of Study Sample

Table 1. Comparison between Study Participants and non-Participants based on Socio-demographic Characteristics and HIV Risk Factors

Variable	Response	Total, n	Study Participants (Tested for HIV during survey), n (%)	Non-participants (Not tested for HIV during Survey), n (%)	P value
Age	15-24	8,297	7868 (53.1%)	429 (47.9%)	<0.001
	25-49	3,789	3507 (23.7%)	282 (31.5%)	
	50+	3,630	3445 (23.2%)	185 (20.6%)	
Gender	Male	8,488	7945 (53.6%)	543 (60.6%)	<0.001
	Female	7,228	6875 (46.4%)	353 (39.4%)	
Residence	Urban	4,817	4461 (30.1%)	356 (39.7%)	<0.001
	Rural	10,899	10359 (69.9%)	540 (60.3%)	
Education	No education	2,887	2753 (18.6%)	134 (15.0%)	<0.001
	Primary	8,243	7792 (52.6%)	451 (50.3%)	
	Secondary	4,372	4096 (27.6%)	276 (30.8%)	
	Tertiary	214	179 (1.2%)	35 (3.9%)	
Wealth Quintile	Lowest	3,785	3587 (24.2%)	198 (22.1%)	<0.001
	Secondary	3,613	3442 (23.2%)	171 (19.1%)	
	Middle	3,336	3168 (21.4%)	168 (18.8%)	
	Fourth	2,460	2291 (15.5%)	169 (18.9%)	
	Highest	2,522	2332 (15.7%)	190 (21.2%)	
Marital status	Single, Married	13,772	12981 (87.6%)	791 (88.3%)	0.542
	DSW$	1,944	1839 (12.4%)	105 (11.7%)	
Spouse is Known to have HIV	No	15,673	14777 (99.7%)	896 (100.0%)	0.106
	Yes	43	43 (0.3%)	0 (0.0%)	
Having Paid Work*	No	10,842	10212 (68.9%)	630 (70.3%)	0.377
	Yes	4,874	4608 (31.1%)	266 (29.7%)	
Slept Away from Home for >1 month*	No	13,708	12916 (87.2%)	792 (88.4%)	0.280
	Yes	2,008	1904 (12.8%)	104 (11.6%)	
Multiple Sexual Partners*	No	14,125	13292 (89.7%)	833 (93.0%)	0.002
	Yes	1,591	1528 (10.3%)	63 (7.0%)	
Ever Sold Sex	No	14,125	13292 (89.7%)	833 (93%)	0.428
	Yes	1,591	1528 (10.3%)	63 (7.0%)	
Clients of Sex Workers*	No	14,962	14107 (95.2%)	855 (95.4%)	0.749
	Yes	754	713 (4.8%)	41 (4.6%)	

Characteristics of study participants

Variable	Response	Total, n	Study Participants (Tested for HIV during survey), n (%)	Non-participants (Not tested for HIV during Survey), n (%)	P value
Sexually transmitted infection*	No	14,382	13522 (91.2%)	860 (96.0%)	**<0.001**
	Yes	1,334	1298 (8.8%)	36 (4.0%)	
Has Cervical Cancer	No	15,632	14741 (99.5%)	891 (99.4%)	0.921
	Yes	84	79 (0.5%)	5 (0.6%)	
Presumptive TB#*	No	15,356	14479 (97.7%)	877 (97.9%)	0.726
	Yes	360	341 (2.3%)	19 (2.1%)	
TB disease, current or past	No	15,547	14657 (98.9%)	890 (99.3%)	0.225
	Yes	169	163 (1.1%)	6 (0.7%)	
Sick for the past 3 months*	No	15,073	14214 (95.9%)	859 (95.9%)	0.953
	Yes	643	606 (4.1%)	37 (4.1%)	
Total		15,716	896 (100%)	14,820 (100%)	

$Divorced, Separated, or Widowed, *within the last 12 months of the survey,
#Cough, fever, night sweats, or weight loss

Characteristics of study participants
Of 14,820 study participants, 57.8% were men, and had a median age of 30 (IQR: 21-24). HIV prevalence was 2.3% (95% (CI): 2.0-2.6). HIV prevalence was higher for the age category 25-49, among women, and in urban settings, while it was lowest for those with secondary education and those in the highest wealth quintile. (Table 2)

Table 2 Socio-demographic Factors Associated with HIV Infection among adults and adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

Variable	Response	Total, n	HIV+, n (%)	P value
Age	15-24	8,114	49 (0.6%)	**<0.001**
	25-49	3,443	196 (5.7%)	
	50+	3,263	95 (2.9%)	
Gender	Male	8,567	162 (1.9%)	**0.002**
	Female	6,253	176 (2.8%)	
Residence	Urban	4,707	130 (2.8%)	**0.026**
	Rural	10,113	207 (2.1%)	
Education	No education	2,647	82 (3.1%)	**0.001**
	Primary	8,182	197 (2.4%)	
	Secondary	3,859	55 (1.4%)	
	Tertiary	132	4 (3.1%)	
Wealth Quintile	Lowest	3,398	73 (2.1%)	**0.038**
	Secondary	3,412	70 (2.0%)	
	Middle	3,081	73 (2.4%)	
	Fourth	2,432	79 (3.2%)	
	Highest	2,496	43 (1.7%)	
Total		14,820	338 (2.3%)	

$Divorced, Separated, or Widowed; *within the last 12 months of the survey, #Cough, fever, night sweats, or weight loss

Statistically significant predictors of HIV infection

Table 3 summarizes predictors of HIV infection by including only factors being examined in the development of factors included in the development of risk assessment tool. Accordingly, all factors were predictors of infection except for the following variables: Presumptive TB, TB disease, and being sick in the past 3 months.

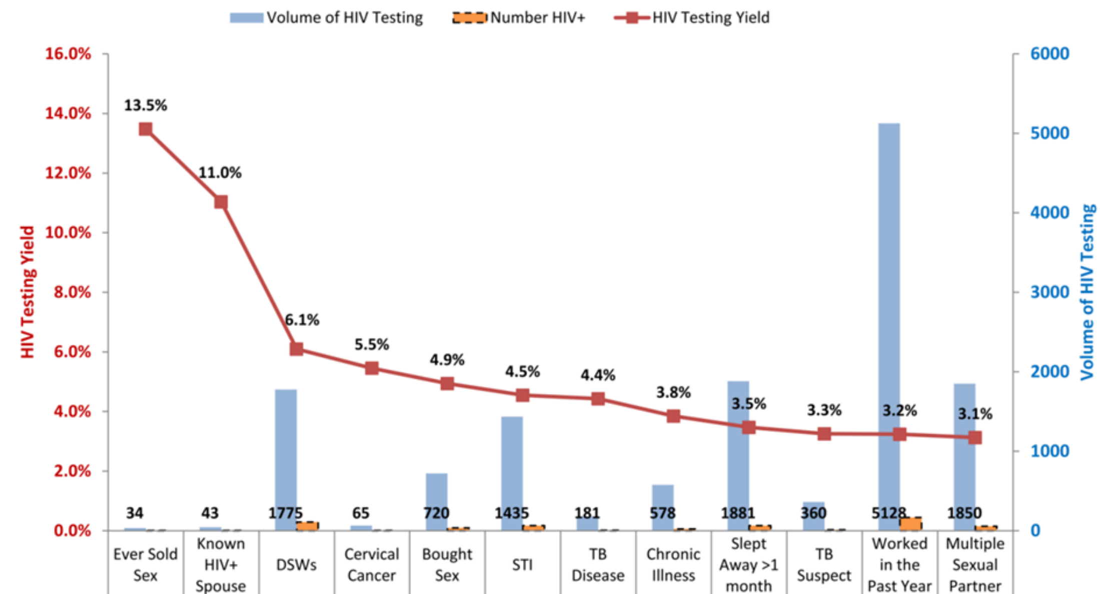
Table 3. Predictors of HIV Infection among adults and adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

Variable	Response	Total, n	HIV+, n (%)	Crude Odds Ratio	P value	Adjusted Odds Ratio	P value
Marital status	Single, Married	13,045	230 (1.8%)	1		1	
	DSW$	1,775	108 (6.1%)	3.6 (2.7-4.8)	<0.001	3.7 (2.7-5)	<0.001
Spouse is Known to have HIV	No	14,777	333 (2.3%)	1		1	
	Yes	43	5 (11.0%)	5.3 (1.8-15.6)	0.004	5.7 (1.8-18.2)	0.005
Having Paid Work*	No	9,692	172 (1.8%)	1		1	
	Yes	5,128	166 (3.2%)	1.8 (1.4-2.4)	<0.001	1.7 (1.3-2.2)	0.001
Slept Away from Home for >1 month*	No	12,939	273 (2.1%)	1		1	
	Yes	1,881	65 (3.5%)	1.7 (1.1-2.5)	0.016	1.4 (0.9-2.2)	0.089
Multiple Sexual Partners*	No	12,970	282 (2.2%)	1		1	
	Yes	1,850	58 (3.1%)	1.4 (1.0-2.0)	0.042	1 (0.6-1.5)	0.889
Ever Sold Sex	No	14,786	333 (2.3%)	1		1	
	Yes	34	5 (13.5%)	6.8 (3.2-14.5)	<0.001	6.8 (3.1-14.9)	<0.001
Clients of Sex Workers*	No	14,100	304 (2.2%)	1		1	
	Yes	720	36 (4.9%)	2.3 (1.5-3.5)	<0.001	1.5 (0.9-2.5)	0.127
Sexually transmitted infection*	No	13,385	274 (2.0%)	1		1	
	Yes	1,435	65 (4.5%)	2.3 (1.6-3.2)	<0.001	1.9 (1.3-2.9)	0.004
Has Cervical Cancer	No	14,755	335 (2.3%)	1		1	
	Yes	65	4 (5.5%)	2.6 (1.1-5.9)	0.029	2 (0.8-5.1)	0.152
Presumptive TB#*	No	14,460	326 (2.3%)	1		1	
	Yes	360	12 (3.3%)	1.5 (0.8-2.8)	0.231	0.7 (0.2-2.6)	0.616
TB disease, current or past	No	14,639	330 (2.3%)	1		1	
	Yes	181	8 (4.4%)	2.0 (0.9-4.2)	0.07	2.2 (0.5-9.1)	0.264

Variable	Response	Total, n	HIV+, n (%)	Crude Odds Ratio	P value	Adjusted Odds Ratio	P value
Sick for the past 3 months*	No	14,242	317 (2.2%)	1		1	
	Yes	578	22 (3.8%)	1.7 (0.9-3.1)	0.086	1.4 (0.7-2.6)	0.347
Total		14,820	338 (2.3%)				

[$]Divorced, Separated, or Widowed; *within the last 12 months of the survey, [#]Cough, fever, night sweats, or weight loss

HIV Prevalence by Risk Factors
Figure 2 summarizes HIV prevalence by risk factor. The highest was recorded for people who sold sex (13.5%), followed by spouses of HIV-infected adults (11%) and those who were divorced, separated, or widowed (6.1%). The presence of other risk factors had HIV testing yield ranging from 3.1%-5.5%. TB in the past 10 years had a testing yield of 33.3% for Zambia compared to 3.7% for those without TB in the past 10 years, p value <0.001 (data not shown).



	Ever Sold Sex	Known HIV+ Spouse	DSWs	Cervical Cancer	Bought Sex	STI	TB Disease	Chronic Illness	Slept Away >1 month	TB Suspect	Worked in the Past Year	Multiple Sexual Partner
Volume of HIV Testing	34	43	1775	65	720	1435	181	578	1881	360	5128	1850
Number HIV+	5	5	108	4	36	65	8	22	65	12	166	58
HIV Testing Yield	13.5%	11.0%	6.1%	5.5%	4.9%	4.5%	4.4%	3.8%	3.5%	3.3%	3.2%	3.1%

Figure 2. HIV Testing Yield by Risk Factors among Adults and Adolescents >14 years who were never tested

Determining cut off (risk score) for risk assessment tools
Looking at the performance of Tool 1 at different risk score levels, those individuals having one or more risk factors were found to have an HIV prevalence of 3.2% which increased with increasing cut-off: 4.4%, 5.6%, 7.9% HIV prevalence for two, three, and four cut-off scores respectively (Table 4). Area under the curve (AUC) can be seen to reduce as the risk assessment cut-off increases. A score of ≥1 was found to have the highest sensitivity at 82.3% (95% CI: 78.6% -85.9%) with the next score of ≥2 having nearly half the sensitivity at 46.8% (42.0%-51.6%). The specificity was higher for a higher cut-off. Positive predictive value was higher for a higher cut-off point while negative predictive value was comparable between all cut-off scores (Figure 3).

Table 4. Association of HIV Risk Scores with HIV Infection using a tool that contains all HIV Risk Factors for Adults and Adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

Risk Score	Response	Total, n	HIV+, n (%)	P value
Score≥1	No	6,122	59 (1.0%)	**<0.001**
	Yes	8,698	279 (3.2%)	
Score≥2	No	11,238	179 (1.6%)	**<0.001**
	Yes	3,582	159 (4.4%)	
Score≥3	No	13,556	267 (2.0%)	**<0.001**
	Yes	1,264	71 (5.6%)	
Score≥4	No	14,445	308 (2.1%)	**<0.001**
	Yes	375	30 (7.9%)	

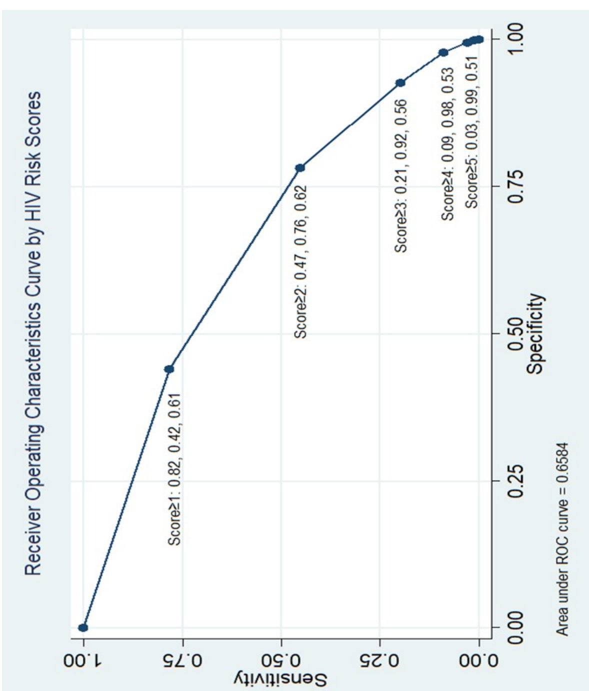


Figure 3. Receiver Operating Characteristics Curve by HIV Risk Scores for Adults and Adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017).

The sensitivity, specificity, and area under the curve are indicated for each cut-off. Compared to a cut-off score of ≥1, AUC was comparable with a cut-off score of ≥2, while it was lower for those with higher cut-off scores (p value <0.001). (Table 5) The AUC was comparable by age, gender, and residence. (Table 6)

Table 5. Sensitivity, Specificity, Positive Predictive Value (PPV+), and Negative Predictive Value (NPV-) for HIV Risk Screening Tool Containing Various Combinations of All Risk Factors
* Score≥1 means an individual who has one or more risk factors for HIV; ** AUC= Area under the Curve of a Receiver Operating Curve;

Screening Tool Score*	Sensitivity	Specificity	PPV	NPV	AUC **	P Value ***
Score≥1	82.3% (78.6%-85.9%)	41.9% (41.1%-42.7%)	3.2% (2.8%-3.6%)	99.0% (98.8%-99.3%)	0.612	
Score≥2	46.8% (42.0%-51.6%)	76.4% (75.7%-77.1%)	4.4% (3.7%-5.1%)	98.4% (98.2%-98.6%)	0.615	0.7137
Score≥3	21.0% (17.1%-24.9%)	91.8% (91.3%-92.2%)	5.6% (4.3%-7.0%)	98.0% (97.8%-98.3%)	0.560	<0.001
Score≥4	8.9% (6.2%-11.6%)	97.6% (97.4%-97.9%)	8.0% (5.1%-10.9%)	97.9% (97.6%-98.1%)	0.533	<0.001

*** P value compares AUC for a given score with the reference Score≥1

Table 6. Comparison of Receiver Operating Characteristics Curve for HIV Risk Screening Tool (Score≥1) by Age, Gender, and Residence for Adults and Adolescents > 14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

Variable	Response	Observation	Area Under ROC Curve	P value
Age	15-24	7,868	0.5756	0.6033
	25-49	3,507	0.5705	
	50+	3,445	0.5478	
Gender	Male	7,945	0.6119	0.6448
	Female	6,875	0.6212	
Residence	Urban	4,461	0.6070	0.7531
	Rural	10,359	0.6137	

Figure 4 summarizes relationship between eligibility, sensitivity, and PPV or HIV testing yield. Eligibility for HIV test decreased with increasing risk score cut-offs: 56% would be eligible with a cut-off score of ≥1, while it was 2% for a cut-off score of ≥4. HIV testing positivity (PPV) and sensitivity or eligibility was negatively correlated with both going down with increasing cut-off score, while PPV increased.

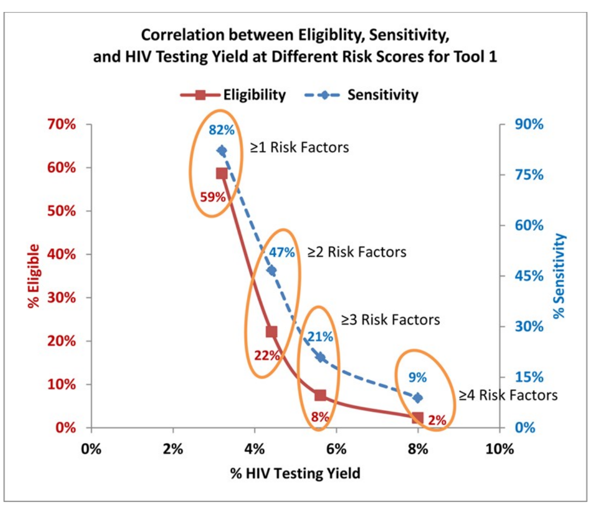


Figure 4. Relationship between Eligibility, Sensitivity, and HIV Testing Yield for a Risk Assessment Tool that contains all Risk Factors for Adults and Adolescents > 14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

In the tool that contained only statistically significant risk factors from the final logistic regression model (Table 3) (Tool 2), being DSW (odds ratio (OR): 3.9 (95% CI: 2.9-5.2); being spouse of a known HIV+ person (OR: 6.1 (95% CI:2.0-19.1)); having history of selling sex for money (OR: 7.7 (95% CI:3.6-16.3)); having sexually transmitted infections in the past 12 months (OR: 2.1 (95% CI:1.4-3)), and having a paid work in the past 12 months (OR: 2.1 (95% CI:1.4-3)); were included in the final model. Tool 4 which contained customized risk factors, the combination of risk factors having paid work in the past year and sleeping away from home for more than a month in the past 12 months were combined as predictors in addition to conventional risk factors. Having a paid work and sleeping away from home were statistically significant predictors of undiagnosed HIV infection (OR: 1.8 (95% CI: 1.1-3.0)).

Comparison of risk assessment tools

Looking at the different risk assessment tools, all were statistically significant predictors of HIV infection with p-value <0.001. For all tools, if none of the risk factors was present, HIV prevalence would be low in the range of 1.0-1.3%. (Table 7) Sensitivity was better for Tool 1 but the corresponding specificity was the lowest. AUC was better for all other tools as compared to this tool, and the difference was much higher for Tools 3 and 4 (p-value<0.001). (Table 8) PPV or HIV testing yield was highest for Tools 3 and 4 at 4.2% and 4.0%, respectively, if at least one risk factor was present. Tool 3 had the lowest proportion of people eligible for testing at 34%the highest being for tool 1 at 59%. (Table 7) Number needed to test (NNT+) was 24 for Tool 3, while it was 43 if universal testing was used.

Table 7. of Risk Scores with HIV Infection using a tool that contains all HIV Risk Factors for Adults and Adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017**)**

Risk Assessment Tool	Response	Total, n	HIV+, n (%)	P value
Tool 1: All Risk Factors: Score≥1	No	6,122	59 (1.0%)	**<0.001**
	Yes	8,698	279 (3.2%)	
Tool 2: Statistically Significant Risk Factors in final model: Score≥1#	No	7,850	90 (1.2%)	**<0.001**
	Yes	6,970	247 (3.6%)	
Tool 3: Conventional Risk Factors: Score≥1	No	9,717	123 (1.3%)	**<0.001**
	Yes	5,103	215 (4.2%)	
Tool 4: Customized Tool: Score≥1*	No	9,294	117 (1.3%)	**<0.001**
	Yes	5,526	221 (4.0%)	

#Only those included in the final model were considered; *Customized tool=Conventional risk factors + Working for a payment in the past 12 months and sleeping away from home for at least 1 month in the past 12 months of the survey.

Table 8. Sensitivity, Specificity, Positive Predictive Value (PPV+), and Negative Predictive Value (NPV-) for each potential HIV Risk Screening Tool for Adults and Adolescents >14 years who were never tested for HIV before PHIA Surveys conducted in Zambia (2016) and Tanzania (2016-2017)

Risk Factor Selection Strategy	Sensitivity	Specificity	PPV	NPV	AUC**	P value***
Tool 1: All risk factors	82.3% (78.6%-85.9%)	41.9% (41.1%-42.7%)	3.2% (2.8%-3.6%)	99.0% (98.8%-99.3%)	0.6116	
Tool 2: Statistically significant only#	73.4% (69.1%-77.6%)	53.6% (52.8%-54.4%)	3.6% (3.1%-4.0%)	98.9% (98.6%-99.1%)	0.6267	0.035
Tool 3: Conventional risk factors	63.5% (58.9%-68.1%)	66.2% (65.5%-67.0%)	4.2% (3.6%-4.8%)	98.7% (98.5%-98.9%)	0.6469	<0.001
Tool 4: Customized tool*	65.5% (61.0%-70.1%)	63.4% (62.6%-64.2%)	4.0% (3.5%-4.5%)	98.7% (98.5%-99.0%)	0.6412	<0.001

#Only those included in the final model were considered; *Customized tool=Conventional risk factors + Working for a payment in the past 12 months and sleeping away from home for at least 1 month in the past 12 months of the survey. **AUC= Area under the Curve of a Receiver Operating Curve;
*** P value compares AUC for a given risk assessment tool with the reference tool that contains all risk factors.

Discussion

We set out to validate HIV risk assessment tool used for adults. In this process, we tried various combinations of risk factors in different tools for best possible outcome. The final tool we recommend for use contains conventional risk factors. This screening tool showed a moderate sensitivity and specificity for identifying infected adults at household level. Using this screening tool, the number needed to test to diagnose one HIV infected adult would be 24 down from 43 if universal testing was used.

Looking at individual risk factors, the prevalence of HIV in those who never tested for HIV remained to be high compared to those without risk factors except for TB related risk factors and chronic illness. Two risk factors that stood out with having testing yield of >10% were selling sex for money and having an HIV+ spouse. This is comparable to reported prevalence of 12-20% among FSWs in the study countries (23). ICT for spouses records even higher testing yield at 32% in program settings (24). Marital status is an important risk factor. Being divorced widowed or separated was found to be the third highest risk factor with a yield of 6.1%. DSWs are easily identifiable at community level and can be used to identify at risk people at community or facility level. It is already a risk factor in many countries (25, 26).Cervical cancer is an important risk factor since Human Papiloma Virus, which is a sexually transmitted viral infection, is the causative agent (27). Co-infection with HIV was 5.5% in this study. Having multiple sexual partners was found to have a relatively lower prevalence at 3.1%. This may be due to the higher condom use during casual sex with a non-regular partner (28, 29).

Lifetime TB disease was not statistically significant at the 0.05 cut-off. This should not be misinterpreted as TB not being a risk factor. Data on year of TB diagnosis were present only for Zambia and when we did analysis comparing TB diagnosed in the past 10 years to those who never had TB, or who had TB before 10 years, TB prevalence was much higher at 33.3% prevalence. This should be used in practice instead of lifetime TB disease.

Presumptive TB was not predictor of HIV infection because probably it was defined broadly especially for cough. A definition of cough > 2 weeks may make improve the positivity. In studies where the later definition was used, the positivity was found to be higher (30, 31).

Adults having multiple risk factors were found to have high testing yield and were a small fraction of the total assessed. This should be explored to further identify additional risk factors. A very good example in current use by different case finding and prevention programs is being long distance truck driver, who are likely to sleep away from home, and have multiple sexual partners including sex workers (32, 33).

This study also provides some form of reference for the percentage of people who are potentially eligible for HIV testing fulfilling at least one of the conventional risk factors among those who never tested for HIV. In this study, 34.4% adults who never tested for HIV would be eligible for testing. That is around 9.1% of the initial number of adults interviewed. This provides a reference value with which to compare community HIV case finding interventions when such risk factors are used. However, it would not be advisable to test this much adults as it wouldn't be cost effective. A more targeted approach focusing on sex workers and their clients, partners of known HIV+ index cases, DSWs, and TB cases would be important starting points (2).

Eliciting some of the risk factors especially those related to sexual history may need some experience especially when implementing the risk assessment tool at community level. The use of health extension workers or community health workers who formally do health interventions may help. At facility level where these risk factors are often used maintaining quality of counselling needs to be ensured through ongoing training and on job coaching. Some of the risk factors are treated in speciality clinics like TB in TB clinic, or STI and cervical cancer in gynaecology clinics for women. This will make it easier to implement universal testing for these groups by providing integrated testing services.

The large number of study participants was one of the strengths of the study. Missing data was minimal and was not related to the risk factors being studied. The performance of the final tool was found to be independent of age, gender, and residence making the use of the tool applicable in different scenarios. Some of the risk factors were captured a little different from what is used in actual settings. All parameters of screening tool are likely to improve if the presence of the following risk factors was determined for the past 10 years just like what we did with TB instead of just the past 12 months: multiple sexual partners, STI, and clients of sex workers.

Conclusion

Use of a screening tool containing conventional risk factors improved HIV testing yield compared to doing universal testing. The use of multiple risk factors to improve HIV testing yield should be explored further.

Declarations

Consent for publication

Not applicable

Conflict of interest

The authors declare that they have no competing interests.

Author contribution

KDY originated the research idea, and collected and analyzed the data; KDY & JM contributed to data analysis and writing the manuscript; All authors read and approved the final manuscript.

Funding information

No funding

Acknowledgements

Not applicable.

References

1. World Health Organization: WHO Guidelines on HIV Testing. 2015.
2. World Health Organization: Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment And Care For Key Populations. 2016.
3. World Health Organization: Consolidated HIV Prevention, Care and Treatment Guideline. 2016.
4. UNAIDS: AIDS Info: Progress towards 90-90-90 targets (https://aidsinfo.unaids.org/). 2020.
5. ICF: The DHS Program STATcompiler. http://www.statcompiler.com. August 6 2020. 2020.
6. Maheu-Giroux M, Marsh K, Doyle CM, Godin A, Delaunay CL, Johnson LF, Jahn A, Abo K, Mbofana F, Boily M-C: National HIV testing and diagnosis coverage in sub-Saharan Africa: a new modeling tool for estimating the 'first 90'from program and survey data. AIDS (London, England) 2019, 33(Suppl 3):S255.
7. KFF: U.S. Federal Funding for HIV/AIDS: Trends Over Time (from: https://www.kff.org/hivaids/fact-sheet/u-s-federal-funding-for-hivaids-trends-over-time/). Accessed on August 7, 2020. 2020.
8. Shanaube K, Schaap A, Floyd S, Phiri M, Griffith S, Chaila J, Bock P, Hayes R, Fidler S, Ayles H: What works–reaching universal HIV testing: lessons from HPTN 071 (PopART) trial in Zambia. AIDS (London, England) 2017, 31(11):1555.
9. PEPFAR: Annual Report to Congress. 2019.
10. Balkus JE, Brown E, Palanee T, Nair G, Gafoor Z, Zhang J, Richardson BA, Chirenje ZM, Marrazzo JM, Baeten JM: An empiric HIV risk scoring tool to predict HIV-1 acquisition in African women. Journal of acquired immune deficiency syndromes (1999) 2016, 72(3):333.
11. Birri Makota RB, Musenge E: Factors associated with HIV infection in Zimbabwe over a decade from 2005 to 2015: an interval-censoring survival analysis approach. Frontiers in public health 2019, 7:262.
12. Ba DM, Ssentongo AE, Traore M, Ssentongo P: Prevalence of Human Immunodeficiency Virus and Its Sociodemographic, Knowledge and Behavioral Predictors among Women: A Cross-Sectional Population-Based Survey in Ivory Coast. of 2018, 6:2011-2012.
13. Fauk NK, Kustanti CY, Wulandari R, Damayani AD, Mwanri L: Societal determinants of HIV vulnerability among clients of female commercial sex workers in Indonesia. PloS one 2018, 13(11):e0207647.
14. Wu ES, Urban RR, Krantz EM, Mugisha NM, Nakisige C, Schwartz SM, Gray HJ, Casper C: The association between HIV infection and cervical cancer presentation and survival in Uganda. Gynecologic oncology reports 2020, 31:100516.
15. Dalal S, Johnson C, Fonner V, Kennedy CE, Siegfried N, Figueroa C, Baggaley R: Reaching people with undiagnosed HIV infection through assisted partner notification. AIDS (London, England) 2017, 31(17):2436.
16. Smith DK, Pan Y, Rose CE, Pals SL, Mehta SH, Kirk GD, Herbst JH: A brief screening tool to assess the risk of contracting HIV infection among active injection drug users. Journal of addiction medicine 2015, 9(3):226.
17. Haukoos JS, Hopkins E, Bucossi MM, Lyons MS, Rothman RE, White DA, Al-Tayyib AA, Bradley-Springer L, Campbell JD, Sabel AL: Validation of a quantitative HIV risk prediction tool using a national HIV testing cohort. Journal of acquired immune deficiency syndromes (1999) 2015, 68(5):599.
18. Ministry of Health Z: Zambia Population-based HIV Impact Assessment (ZAMPHIA) 2016: Final Report. Lusaka. 2019.
19. (ZAC). TCfATZAC: Tanzania HIV Impact Survey (THIS) 2016-2017: Final Report. Dar es Salaam, Tanzania. 2018.
20. Population-based HIV Impact Assessment (PHIA) Data Use Manual. NewYork NJ.
21. MedCalcStatisticalSoftwareversion19.4.1(MedCalcSoftware Ltd -O, -Belgium; https://www.medcalc.org;2020).
22. The PHIA Project: Population-Based HIV Impact Assessment Datasets (accessed from: https://phia-data.icap.columbia.edu/files). 2020.
23. Chanda MM, Ortblad KF, Mwale M, Chongo S, Kanchele C, Kamungoma N, Fullem A, Dunn C, Barresi LG, Harling G: HIV self-testing among female sex workers in Zambia: a cluster randomized controlled trial. PLoS medicine 2017, 14(11):e1002442.
24. Mwango L, Mujansi M, Chipukuma J, Phiri B, Sakala H, Nyirongo N, Sivile S, Sinjani M, Lavoie M-C, Claassen C: Reaching the unreachable: early results from index testing in Zambia in the CIRKUITS project. In: JOURNAL OF THE INTERNATIONAL AIDS SOCIETY: 2019: JOHN WILEY & SONS LTD THE ATRIUM, SOUTHERN GATE, CHICHESTER PO19 8SQ, W …; 2019: 13-14.
25. Ministry of Health: National Comprehensive HIV Prevention, Care and Treatment Training for Health care Providers. 2017.
26. Ministry of Health: The Kenya HIV Testing Services Guidelines (from http://www.hivst.org/files1/kenyahtsguidelines20151-160119080906.pdf). 2015.

27. Mayo Foundation for Medical Education and Research: Cervical cancer: symptoms and cause (from: https://www.mayoclinic.org/diseases-conditions/cervical-cancer/symptoms-causes/syc-20352501). 2020.
28. Zambia Statistics Agency - ZSA, Ministry of Health - MOH, University Teaching Hospital Virology Laboratory - UTH-VL, ICF: Zambia Demographic and Health Survey 2018. In. Lusaka, Zambia: ZSA, MOH, UTH-VL and ICF; 2020.
29. Ministry of Health CD, Gender, Elderly, Children - MoH CDGEC/Tanzania Mainland, Ministry of Health - MoH/Zanzibar, National Bureau of Statistics - NBS/Tanzania, Office of Chief Government Statistician - OCGS/Zanzibar, ICF: Tanzania Demographic and Health Survey and Malaria Indicator Survey 2015-2016. In. Dar es Salaam, Tanzania: MoH CDGEC, MoH, NBS, OCGS, and ICF; 2016.
30. Yotebieng M, Wenzi LK, Basaki E, Batumbula ML, Tabala M, Mungoyo E, Mangala R, Behets F: Provider-Initiated HIV testing and counseling among patients with presumptive tuberculosis in Democratic Republic of Congo. The Pan African Medical Journal 2016, 25.
31. Kyaw KWY, Kyaw NTT, Kyi MS, Aye S, Harries AD, Kumar AM, Oo NL, Satyanarayana S, Aung ST: HIV testing uptake and HIV positivity among presumptive tuberculosis patients in Mandalay, Myanmar, 2014-2017. PloS one 2020, 15(6):e0234429.
32. Delany-Moretlwe S, Bello B, Kinross P, Oliff M, Chersich M, Kleinschmidt I, Rees H: HIV prevalence and risk in long-distance truck drivers in South Africa: a national cross-sectional survey. International journal of STD & AIDS 2014, 25(6):428-438.
33. Botão C, Horth RZ, Frank H, Cummings B, Inguane C, Sathane I, McFarland W, Raymond HF, Young PW: Prevalence of HIV and associated risk factors among long distance truck drivers in Inchope, Mozambique, 2012. AIDS and Behavior 2016, 20(4):811-820.