Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_1/5/2022___

Stephen Gurley

Date

Application of a Testing History-Based HIV-1 Incidence Estimator in 12 Sub-Saharan African Nations

By

Stephen Gurley Master of Public Health

Department of Global Epidemiology

Andrew Voetsch, MPH, PhD

Field Advisor

Patrick Sullivan, DVM, PhD

Departmental Advisor

Application of a Testing History-Based HIV-1 Incidence Estimator in 12 Sub-Saharan African Nations

By

Stephen Gurley

Bachelor of Science College of William & Mary 2017

Advisors: Andrew Voetsch, MPH, PhD, and Patrick Sullivan DVM, PhD

An abstract of

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of Master of Public Health in Global Epidemiology

2022

Abstract

Application of a Testing History-Based HIV-1 Incidence Estimator in 12 Sub-Saharan African Nations

By Stephen Gurley

Estimating HIV incidence is essential to monitoring progress in sub-Saharan African nations toward the Joint United Nations Programme on HIV/AIDS (UNAIDS)' 90-90-90 goals. One commonly used method for incidence estimation is to test samples from nationally representative, cross-sectional surveys using laboratory-based incidence assays. However, this approach has several limitations. A proposed alternative method based on reported HIV testing history and the proportion of undiagnosed infections has recently been described that may generate more precise incidence estimates with smaller sample size. Here, we apply this alternative method to nationally representative cross-sectional data from 12 sub-Saharan African nations with varying country-specific HIV prevalence. The testing history-based method consistently produced results that are comparable and strongly correlated with estimates produced using a laboratorybased HIV incidence assay ($R^2=0.96$). Moreover, the testing history-based method estimates are more precise and can produce age- and sex-specific incidence estimates that are informative for programmatic decisions. The method also allows for comparisons of the transmission rate of HIV as well as the drivers of HIV incidence among and within countries. Thus, the testing history-based method is a useful tool for estimating HIV incidence using cross-sectional survey data in the sub-Saharan African region.

Application of a Testing History-Based HIV-1 Incidence Estimator in 12 Sub-Saharan African Nations

By

Stephen Gurley

Bachelor of Science College of William & Mary 2017

Advisors: Andrew Voetsch, MPH, PhD, and Patrick Sullivan DVM, PhD

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Global Epidemiology

2022

Application of a Testing History-Based HIV-1 Incidence Estimator in 12 Sub-Saharan African Nations

Gurley, SA^{1, 2}; Stupp, P³; Fellows, I^{3,4}; Parekh, BS³; Sullivan, PS¹; Voetsch, AC^{1,3*}

¹ Rollins School of Public Health, Emory University, Atlanta, GA
² Emory University School of Medicine, Atlanta, GA
³ Division of Global HIV&TB, United States Centers for Disease Control and Prevention, Atlanta, GA
⁴ Fellows Statistics Inc., San Diego, CA

*Corresponding author and reprints

Dr. Andrew C. Voetsch Mailstop US 1-2 1 Corp Sq Blvd Atlanta, GA 30329 Phone: 404-639-8420 Email: aav6@cdc.gov

This research has been supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention (CDC) under the terms of cooperative agreements #U2GGH001271 and #U2GGH001226. The findings and conclusions of this document are those of the authors and do not necessarily represent the official position of the funding agencies.

Running head: HIV incidence estimation by testing history

Word Count: 189 (Abstract); (Text)

Abstract:

Background: Estimating HIV incidence is essential to monitoring progress in sub-Saharan African nations toward the Joint United Nations Programme on HIV/AIDS (UNAIDS)' 90-90-90 goals. One commonly used method for incidence estimation is to test samples from nationally representative, cross-sectional surveys using laboratorybased incidence assays. However, this approach has several limitations. A proposed alternative method based on reported HIV testing history and the proportion of undiagnosed infections has recently been described that may generate more precise incidence estimates with smaller sample size.

Methods: Here, we apply this alternative method to nationally representative crosssectional data from 12 sub-Saharan African nations with varying country-specific HIV prevalence.

Results: The testing history-based method consistently produced results that are comparable and strongly correlated with estimates produced using a laboratory-based HIV incidence assay (R²=0.96). Moreover, the testing history-based method estimates are more precise and can produce age- and sex-specific incidence estimates that are informative for programmatic decisions. The method also allows for comparisons of the transmission rate of HIV as well as the drivers of HIV incidence among and within countries.

Conclusion: Thus, the testing history-based method is a useful tool for estimating HIV incidence using cross-sectional survey data in the sub-Saharan African region.

Words: 193/350

Background

Since the start of the HIV epidemic, an estimated 79.3 million individuals have been infected worldwide, with over 1.5 million new infection in 2020 and over 36.3 million cumulative deaths (UNAIDS, 2021). In 2014, UNAIDS set 3 ambitious global targets: 1) 90% of all persons living with HIV (PLWH) being aware of their HIV status, 2) 90% of those receiving antiretroviral therapy (ART), and 3) 90% of those achieving viral suppression (90-90-90 goals). Achievement of these were projected to reduce HIV incidence and mortality rates globally by up to 90% by 2030 (UNAIDS, 2014). To monitor progress toward achieving these goals, the President's Emergency Plan for AIDS Relief (PEPFAR) and the United States' Centers for Disease Control and Prevention (CDC), and participating ministries of health conducted nationally representative, population-based HIV impact assessment (PHIA) surveys in 12 sub-Saharan African countries (Porter et al., 2021). Data from these surveys produced estimates of progress toward the 90-90-90 goals; the estimates are used to monitor progress and impact of national HIV treatment and prevention programs (Porter et al., 2021; Justman et al., 2018).

One key impact measure of the 90-90-90 goals is the incidence of new HIV infections. Incidence is not only an important metric itself; it is also required for many other important epidemic metrics, such as the incidence:prevalence and incidence:mortality ratios (Ghys et al., 2018). Ideally, incidence is directly measured by determining the number of new cases among a representative population that is followed over time. However, this would be impractical to measure directly in many settings due to the size, cost, and complicated logistics of incidence studies. Thus, incidence of HIV must instead be estimated using one of several estimation methods. One commonly used method recommended by the World Health Organization (WHO) for estimating incidence of HIV using large cross-sectional surveys is to use incidence assays to distinguish recent infections from long-term infections (UNAIDS & World Health Organization (WHO), 2015; Kassanjee et al., 2012; Brookmeyer et al., 2013). This approach has several limitations. These limitations include the requirement for additional laboratory testing for the biomarker assays, the logistical complexity of these studies and the large sample sizes required in order to generate precise estimates. The large sample size requirement can prevent the generation of robust sub-group or regional estimates. National estimates for sub-groups (e.g., women, young adults) and sub-national regional estimates are of particular interest to HIV prevention and treatment programs because such estimates are used to prioritize specific groups or regions for interventions.

Another limitation is that assay-based incidence estimation requires several *a priori* parameters; these parameters, in turn, require assay calibration and performance

evaluation for different specific populations (UNAIDS, 2018) One parameter is the mean duration of recent infections (MDRI), which is defined as the average length of time that PLWH are classified by assay as having recently acquired infection (Duong et al., 2012). This parameter is dependent on various local, population-specific factors, such as the distribution of HIV subtypes and sensitivity of the local screening program. Recency assays will incorrectly classify some fraction of cases as recent, and this fraction is termed the false recency rate (FRR). Both MDRI and FRR can vary between populations, which can make it difficult to compare population incidence estimates across countries. Assay-based incidence estimation assumes that the epidemic is in a steady state, i.e., that the incidence rate is constant at least for the duration of the recent period(Brookmeyer & Goedert, 1989; Brookmeyer et al., 2013). It also assumes that the HIV biomarkers only progress in one direction as individuals exit the recent period. This assumption is violated when individuals take antiretroviral therapy (ART), as this may alter the natural progression of these biomarkers. Since 2015, the WHO has recommended a "Test-and-Start" strategy, whereby treatment with ART is recommended immediately upon diagnosis, without consideration for CD4 cell count or HIV viral load (World Health Organization, 2016). As such, a greater number of recently diagnosed individuals are on ART, requiring adjustment to estimates through the application of a recent infection testing algorithm (RITA) (Voetsch et al., 2021).

Given these limitations, several alternative methods for incidence estimation have been proposed, including modeling national incidence based on routine HIV surveillance testing programs (Godin et al., 2021) and local population-level viremia dynamics (Farahani et al., 2021).

This paper will focus on evaluating a method utilizing self-reported history of HIV testing (Fellows et al., 2020). It is useful to categorize the population into 3 compartments: uninfected individuals, undiagnosed infections, and diagnosed infections. The incidence rate is defined as the rate at which uninfected individuals enter the undiagnosed infection compartment. The size of the diagnosed plus undiagnosed infection compartments (i.e., prevalence of HIV) is directly estimated in cross-sectional datasets. Among those with prevalent HIV infections, the size of the undiagnosed compartment is estimated using self-reported history of prior diagnosis. Misclassification of self-reported HIV status is corrected using viral load and ART biomarkers. The time from infection to diagnosis (i.e., the time spent in the undiagnosed compartment) is estimated prevalence of HIV, the estimated size of the undiagnosed compartment, and the estimated time from infection to diagnosis. This method has been validated using data from household surveys conducted in Kenya during 2007 and 2012 (Fellows et al., 2020; Waruiru et al., 2014).

Biomarker-based incidence estimation utilizes the transition from recent to nonrecent HIV infection to estimate incidence. Because this recency period is relatively short, biomarker-based incidence estimates are reflective of a short time window, which may make them more subject to stochastic variation in new infections. Additionally, these estimates often have broad confidence intervals, because a relatively small number of infections in the recency window are typically observed, even in large samples. By contrast, the testing history method utilizes the transition from undiagnosed to diagnosed to estimate incidence. Because the average time spent in the undiagnosed compartment is comparatively longer than the time spent as a recent infection, testing history-based estimates may be less subject to stochastic variation. Incidence estimation based on testing history has an additional advantage in that the required inputs for the testing history method are inexpensive to collect and are often already included in many HIV surveys, allowing incidence estimation in the absence of additional laboratory-based incidence assay testing and additional laboratory costs. The testing history-based method also generates estimates of the transmission rate of HIV, defined as the average number of new infections per infected individual per unit time, which allows another means of comparing the HIV epidemic between different nations.

Although the testing history-based method was developed and validated using data from the Kenya AIDS Indicator Survey (KAIS), it remains unclear if the method can be generalized to produce robust estimates of incidence across the sub-Saharan African region given the variation in HIV prevalence and incidence among countries. Here, we describe the results of the application of the testing history-based method to generate national, regional, and sub-group HIV incidence estimates for 12 sub-Saharan African countries and to compare these estimates to those estimates generated using a recency biomarker method.

Methods

PHIA Methods

We used data from nationally representative Population-based HIV Impact Assessment (PHIA) surveys conducted by the US CDC and participating ministries of health in Cameroon, Cote d'Ivoire, Eswatini, Ethiopia, Lesotho, Malawi, Namibia, Rwanda, Tanzania, Uganda, Zambia, and Zimbabwe as previously described (Justman et al., 2018; Sachathep et al., 2021). The PHIA surveys were approved by Institutional Review Boards at CDC, Columbia University, Westat, and in respective countries. Analysis was limited to adults aged 15-59 years. Eligible, consenting participants were asked if they had ever received an HIV test and the month, year, and result of their most recent test. Participants who reported a positive HIV test result were asked the month and year of ART initiation, if applicable. Sociodemographic data about the participants were also recorded. Specific methods for viral load (VL) testing varied by country.

HIV recency testing for confirmed HIV-seropositive participants with plasma samples was conducted using the HIV-1 LAg-Avidity EIA (Sedia Biosciences Corporation, Portland, OR), or if plasma was not available, with DBS using the Maxim HIV-1 LAg DBS EIA (Maxim Biomedical, Bethesda, MD) in a central reference laboratory by laboratorians trained by CDC(Patel et al., 2021). Staff from the Division of Clinical Pharmacology of the Department of Medicine at the University of Cape Town used qualitative high-performance liquid chromatography and tandem mass spectrometry assay to detect country-specific first line and second-line ARV in DBS samples.

Testing History Incidence Calculation

Incidence estimates were calculated using the following formula described by Fellows: $\lambda = \frac{P(U|H)P(H)}{E(TID)(1-P(H))}$, where, λ , is the incidence of HIV, P(H) is the proportion of those infected with HIV among the total population, P(U/H) is the proportion of those who are undiagnosed among the total of those with HIV infection, and E(TID) is the estimated time between infection and diagnosis(Fellows et al., 2020). Among study participants, P(H) is directly calculated using individual results of an assay for HIV seropositivity. Those identified as seropositive that report never having been diagnosed with HIV are considered undiagnosed infections. P(U/H) can be estimated using seroassay results and self-reported diagnosis status for each respondent. Some proportion of respondents will misreport their HIV status: however, this can be accounted for by using ART biomarker and HIV VL data on a small proportion of respondents (Fellows et al., 2020). This method further defines transmission rate, τ , (i.e., the number of infections per unit time per infected individual) as $\tau = \frac{P(U|H)}{E(TID)}$ (Fellows et al., 2020). Confidence intervals were generated using the Jackknife method (Hesterberg et al., 1997).

Biomarker Incidence Calculation

Biomarker-derived incidence estimates were generated using a RITA on stored specimens (Voetsch et al., 2021). In all 12 PHIA surveys analyzed, recent infection was defined as testing recent on the limiting antigen (LAg) Avidity Enzyme Immunoassay with HIV-1 RNA concentration at 1,000 copies/mL or higher and no ART use (Voetsch et al., 2021). ART use was defined as either self-reported ART use or presence of ART biomarkers in specimens.

Incidence estimates were calculated using the formula recommended by the WHO Incidence Working group and Consortium for Evaluation and Performance of

Incidence Assays (Kassanjee et al., 2012). These calculations used the following parameters: MDRI for all nations except Uganda – 130 days; MDRI for Uganda – 153 days (this is to account for subtypes A and D distribution in the population); FRR – 0.00; and time cutoff -- 1 year. Biomarker HIV estimates were calculated in SAS 9.4 (SAS Institute Inc., Cary, NC) using a SAS incidence macro available in the PHIA data use manual (PHIA Collaborating Institutions, 2019). Confidence intervals were generated using the Jackknife variance estimation method.

Linear Regression and Comparison

We applied both incidence estimation methods to all 13 datasets to calculate national incidence estimates. We then used simple linear regression to assess the presence and strength of a correlation. We also applied each incidence estimation method to specific sub-groups based on age category (15-29, 30-59), sex, and geographic location in either an urban or rural community. Of note, the Ethiopia 2017 PHIA survey included only participants living in urban areas, so urban/rural stratum-specific estimates were not calculated for Ethiopia. Differences between incidence estimates were non-overlapping between two categories of the same characteristic.

Results

HIV Incidence and Transmission Rate Estimates by Country:

The overall HIV incidence estimates for each survey using both the testing history-based and biomarker-based methods are shown in **Table 1**. The biomarker-based method incidence estimates ranged from 0.03% in Cote d'Ivoire to 1.14% in Eswatini. In the testing history-based method, these estimates ranged from 0.06% in Cote d'Ivoire to 1.92% in Lesotho. Overall, the testing history-based method produced similar results to the biomarker-based methods (correlation coefficient, $R^2 = 0.96$) (**Figure 1**) (Walker et al., 1989). The largest differences between the two methods estimates were for Lesotho (42% difference), a nation with an extremely high HIV prevalence, and Uganda (32% difference), a nation with a lower HIV prevalence. The 95% confidence intervals for the testing history-based method. The HIV transmission ratios generated by the testing history-based method are shown in **Table 2**. The HIV transmission rate ranged from 1.90% in Namibia to 5.64% in Tanzania.

HIV Incidence Estimates by Country, by Age, Sex, and Location

Incidence estimates among females ranged from 0.03% in Cote d'Ivoire and 1.42% in Eswatini using the biomarker-based method, and from 0.11% in Cote d'Ivoire and 2.83% in Lesotho using the testing history-based method (**Figure 2**). Among males,

incidence estimates ranged from 1.01% and 1.26% in Lesotho and 0.03% and 0.02% in Cote d'Ivoire using the biomarker-based and testing history-based methods, respectively (**Figure 3**). The testing history method was highly correlated with the biomarker-based method among females (R² =0.94) and males (R² = 0.76). Analysis with the biomarker-based estimates resulted in a significant sex-specific difference in HIV incidence only in Zambia, but the testing history-based method resulted in significant sex-specific differences in HIV incidence in 8 out of 12 countries (Lesotho, Zambia, Zimbabwe, Malawi, Tanzania, Namibia, Uganda, and Cameroon).

Among participants aged 15-29 years, the age-specific HIV incidence ranged from 0.03% and 0.04% in Ethiopia to 0.98% and 1.40% in Lesotho using the biomarker and testing history-based methods, respectively (**Figure 4**). Among participants aged 15-29 year, the two methods' incidence estimates correlated well ($R^2 = 0.72$). Among participants aged 30-59 years, age-specific incidence of HIV ranged from 0.017% and 0.073% in Cote d'Ivoire to 1.29% and 2.88% in Lesotho, using the biomarker- and testing-history based methods respectively (**Figure 5**). The testing history-based and biomarker-based age-specific estimates were highly correlated ($R^2 = 0.83$). Analysis with the biomarker-based estimates resulted in age group-specific differences in HIV incidence only in Tanzania, but the testing history-based method resulted in significant age group-specific differences in HIV incidence in 9 out of 12 countries (Lesotho, Eswatini, Zambia, Zimbabwe, Malawi, Tanzania, Namibia, Uganda, and Cameroon).

Among those living in urban areas, the estimates of the incidence of HIV derived using biomarker-based and testing-history based method, respectively were 0.04% and 0.09% in Cote d'Ivoire, 0.96%% and 1.99% in Eswatini and 1.24% and 2.34% in Lesotho (**Figure 6**). Among those living in rural areas, estimates of the incidence of HIV by biomarker-based and testing history-based methods, respectively, were 0.01% and 0.03% in Cote d'Ivoire, and were 0.99% and 1.62% in Lesotho (**Figure 7**). The testing history method was mildly correlated with the biomarker-based method among urban participants (R² =0.45) and strongly correlated among rural participants (R² =0.90). Of note, the 95% confidence intervals for the testing history estimate were larger than the biomarker-based estimates for the high prevalence nations of Eswatini and Lesotho. Analysis with the biomarker-based estimates did not result in significant urban/rural group differences in HIV incidence in any country studied, but the testing history-based estimates suggested urban/rural group differences in HIV incidence in 6 (Lesotho, Zambia, Malawi, Tanzania, Uganda, and Cameroon) out of the 11 countries that stratified data by urban/rural status.

Component Analysis of Incidence Estimates

Comparing the components of the testing history-based incidence estimates can reveal differences in the state of the HIV epidemic across the region (**Figure 8**).

Generally, component analysis revealed that incidence of HIV in countries with the largest incidence rates, such as Eswatini and Lesotho, were largely driven by their high prevalence of HIV (P(H)). Other countries with lower prevalences of HIV, such as Rwanda, Cote d'Ivoire, Ethiopia, and Cameroon, had incidence rates driven by long time between infection and diagnosis. Namibia and Uganda were found to have similar incidence rate estimates to one another, however component analysis revealed that in Namibia this was driven by a larger HIV prevalence, while in Uganda this was driven by a larger undiagnosed proportion.

Discussion

Self-reported testing history modeling produced HIV incidence estimates that correlated well with biomarker-based incidence assay derived estimates. Across the 12 countries studied, the testing history method produced both estimates larger than the biomarker-based method (varying from 8% to 46% in 8 of 12 countries) and estimates smaller than the biomarker-based method (varying from 3% to 47% in 4 of 12 countries), indicating no obvious trend in over- or underestimating incidence. Moreover, the testing history-based method produced estimates that were more precise than the biomarker-based method. This added precision allowed for the detection of significant differences in HIV incidence by sex, age-category, and urban/rural status for many countries that the biomarker-based method would have failed to detect (ranging from 6-9 out of 12 countries). This may allow more precise and localized estimates of the number of new infections and may result in less uncertainty in global HIV modeling efforts through Spectrum. This feature may make this estimation method more useful for national HIV prevention and screening programs wishing to target their interventions and programs to specific sub-populations or regions that have the highest incidence rates of HIV.

The components used to generate incidence estimates in the testing history-based method may provide additional information useful for evaluating national HIV prevention and screening programs. An additional benefit of the testing history-based method is that it can more directly allow us to attribute differences in HIV incidence to other characteristics of the HIV epidemic in each nation. Knowledge of these characteristics may inform nations and programs seeking to curb the incidence of HIV. Although the prevalence of those who are living with HIV is unlikely to decrease (and, in fact, can be expected to grow as PWLH live longer), interventions can alter both the proportion of PWLH who are undiagnosed and the time between infection and diagnosis. For example, although the nations of Namibia and Uganda have similar incidence rates of HIV, component analysis reveals the nations may have different drivers of that incidence. Nations like Namibia with a relatively small proportion of undiagnosed PLWH may already have a robust screening program, but their relatively

large time between infection and diagnosis may indicate that certain incident infections, in certain subgroup populations are more likely to be missed by the current screening apparatus. Conversely, nations like Uganda with a relatively small time between infection and diagnosis may already have programs that successfully screen high-risk groups, but their relatively large proportion of undiagnosed PLWH may indicate that there may be other sub-groups that are being missed by the extant screening program.

This testing history-based method and our analysis have several key limitations. The testing history-based method assumes that the disease and total population are in a steady state (Fellows et al., 2020). The impact of this limitation may be mitigated by comparing testing history-based incidence estimates in each country over time as repeated PHIA surveys are conducted; repeated surveys have thus far been conducted in Eswatini, Lesotho, Malawi, Uganda, Zimbabwe, and Zambia. Forecasting modeling efforts, like UNAIDS' Spectrum, could also be used to minimize the effect of this limitation. Additionally, it assumes that there is no relationship between HIV risk and testing behavior (i.e., high risk groups are not more or less likely to have tested previously). Indeed, those with lower self-perceived risk of HIV report lower rates of uptake of HIV testing (Ajayi et al., 2019; De Paoli et al., 2004). The method also assumes that self-reported testing history is accurate; misclassification of testing history might introduce information bias, and that bias might be differential among countries and population subgroups. Perhaps most importantly, the method assumes that those individuals with laboratory detected evidence of ARV use (i.e., those on treatment) misreport their diagnosis status at the same rate as those without detectable evidence of ARV use (i.e., those not on treatment). It is likely that this misclassification is differential in different nations or sub-groups. Further sensitivity analysis regarding these assumptions in different regions and sub-groups may be needed.

Conclusion

Estimating the incidence of HIV is crucially important as sub-Saharan African nations work towards achievement of UNAIDS 90-90-90 goals. Here, we have applied a recently described HIV incidence estimator in 12 sub-Saharan African nations. These estimates are highly correlated with estimates from the biomarker method across multiple African nations and have greater precision than biomarker-based estimated but require much smaller sample sizes than population surveys. Testing history-based estimates also allow the generation of robust sub-group and sub-national incidence estimates, and such stratified estimates will likely prove useful for countries and local HIV prevention programs. Testing history-based incidence estimation is a useful tool to guide program evaluation and to monitor progress towards UNAIDS goals.

	Testing History Estimate		Biomarker Estimate		Percent
	HIV Incidence (95% CI)	CIR	HIV Incidence (95% CI)	CIR	difference
Lesotho 2016	1.92 (1.74, 2.10)	1.2	1.11 (0.68, 1.52)	2.2	42.1%
Eswatini 2016	1.24 (1.00, 1.48)	1.5	1.14 (0.73, 1.53)	2.1	8.4%
Zambia 2016	0.59 (0.52, 0.66)	1.3	0.61 (0.40, 0.81)	2.0	-3.6%
Zimbabwe 2015	0.55 (0.48, 0.63)	1.3	0.40 (0.24, 0.56)	2.3	27.6%
Malawi 2015	0.43 (0.38, 0.49)	1.3	0.37 (0.20, 0.54)	2.7	15.2%
Tanzania 2016	0.36 (0.32, 0.41)	1.3	0.26 (0.15, 0.36)	2.3	29.7%
Namibia 2017	0.32 (0.26, 0.38)	1.5	0.37 (0.18, 0.55)	3.1	-14.1%
Uganda 2016	0.28 (0.23, 0.32)	1.4	0.41 (0.25, 0.56)	2.2	-47.3%
Cameroon 2017	0.18 (0.15, 0.22)	1.5	0.24 (0.12, 0.36)	3.1	-31.2%
Rwanda 2018	0.07 (0.05, 0.09)	1.8	0.08 (0.02, 0.14)	6.4	-11.5%
Ethiopia 2017	0.07 (0.04, 0.09)	2.1	0.05 (0, 0.10)	15.8	35.3%
Cote d'Ivoire 2017	0.06 (0.02, 0.09)	4.2	0.03 (0, 0.07)	0.6	46.3%

Table 1: Estimated HIV Incidence by Country and Estimate Method, and Percent Difference between Methods,Population-Based HIV Impact Assessments, 2015-19

NOTE: Incidence expressed as a percent, 95% confidence interval (CI) generated using jackknife method. CIR: Confidence interval ratio (upper / lower). Percent difference is the testing history estimate minus biomarker estimate, divided by the testing history estimate. Negative percent change indicates that the biomarker estimate is larger than the testing history estimate.

	Percent Transmission		
Country (Year)	Rate (95% CI)		
Lesotho 2016	5.11 (5.07, 5.14)		
Eswatini 2016	3.02 (2.97, 3.06)		
Zambia 2016	3.97 (3.95, 4.00)		
Zimbabwe 2015	2.81 (2.78, 2.83)		
Malawi 2015	2.92 (2.90, 2.95)		
Tanzania 2016	5.64 (5.59, 5.68)		
Namibia 2017	1.90 (1.87, 1.92)		
Uganda 2016	4.26 (4.22, 4.30)		
Cameroon 2017	4.73 (4.69, 4.78)		
Rwanda 2018	2.30 (1.67, 2.35)		
Ethiopia 2017	2.12 (2.07, 2.93)		
Cote d'Ivoire 2017	2.30 (1.18, 3.42)		

Table 2: Estimated Transmission Rate of HIV by Nation in 12 Sub-Saharan African Nations

Figure 1: Simple Linear Regression Between Methods' Estimates of HIV Incidence in 12 Sub-Saharan African Nations



Legend: Linear regression line-of-best-fit. Axis units: %.



Figure 2: Estimated Female-Specific Incidence of HIV by Nation and Estimate Method in 12 Sub-Saharan African Nations

Figure 3: Estimated Male-Specific Incidence of HIV, by Nation and Estimate Method in 12 Sub-Saharan African Nations





Figure 4: Estimated Age-Specific Incidence of HIV for 15-29 year olds, by Nation and Estimation Method in 12 Sub-Saharan African Nations



Figure 5: Estimated Age-Specific Incidence of HIV for 30-59 year olds, by Nation and Estimation Method in 12 Sub-Saharan African Nations

Figure 6: Estimated Incidence of HIV among those who live in Urban Areas, by Nation and Estimation Method and 12 Sub-Saharan African Nations



Legend: Note – the Ethiopia PHIA survey did not stratify by urban/rural, and all included participants were urban.



Figure 7:Estimated Incidence of HIV among those who live in Rural Areas, by Nation and Estimation Method in 12 Sub-Saharan African Nations

Legend: Note – the 2017 Ethiopia survey did not stratify by urban/rural, and all included participants were urban



Figure 8: Estimated Odds of HIV, Time Between Infection and Diagnosis, and Proportion Undiagnosed by Nation in 12 Sub-Saharan African Nations.

Legend: Components of Testing History-based HIV incidence estimate shown for each nation: Estimated Odds of HIV (i.e. Prevalence of HIV, Blue bar, Right Axis), Proportion of PLWH who are Undiagnosed (Orange bar, Right Axis), and Time between infection and diagnosis in years (Grey bar, left axis).

References:

Ajayi, A. I., Abioye, A. O., Adeniyi, O. V., & Akpan, W. (2019). Concerns about contracting HIV, knowing partners' HIV sero-status and discussion of HIV/STI with sexual partners as determinants of uptake of HIV testing. *Journal of Biosocial Science*, *51*(4), 549–561. https://doi.org/10.1017/S0021932018000330

Brookmeyer, Ron; Goedert, J. J. (1989). Censoring in an Epidemic with an Application to Hemophilia-Associated AIDS. *Biometrics*, *45*(1), 325–335.

Brookmeyer, R., Konikoff, J., Laeyendecker, O., & Eshleman, S. H. (2013). Estimation of HIV incidence using multiple biomarkers. *American Journal of Epidemiology*, *177*(3), 264–272. https://doi.org/10.1093/aje/kws436

- De Paoli, M. M., Manongi, R., & Klepp, K. I. (2004). Factors influencing acceptability of voluntary counselling and HIV-testing among pregnant women in Northern Tanzania. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*, *16*(4), 411–425. https://doi.org/10.1080/09540120410001683358
- Duong, Y. T., Qiu, M., De, A. K., Jackson, K., Dobbs, T., Kim, A. A., Nkengasong, J. N., & Parekh, B. S. (2012). Detection of recent HIV-1 infection using a new limitingantigen avidity assay: Potential for HIV-1 incidence estimates and avidity maturation studies. *PLoS ONE*, 7(3), 1–9. https://doi.org/10.1371/journal.pone.0033328
- Farahani, M., Radin, E., Saito, S., Sachathep, K. K., Hladik, W., Voetsch, D., Auld, A. F., Balachandra, S., Tippett Barr, B. A., Low, A., Smart, T. F., Musuka, G., Jonnalagadda, S., Hakim, A. J., Wadonda-Kabondo, N. W., Jahn, A., Mugurungi, O., Williams, D. B., Barradas, D. T., ... Justman, J. E. (2021). Population Viral Load, Viremia, and Recent HIV-1 Infections: Findings From Population-Based HIV Impact Assessments (PHIAs) in Zimbabwe, Malawi, and Zambia. *Journal of Acquired Immune Deficiency Syndromes (1999), 87*, S81–S88. https://doi.org/10.1097/QAI.0000000002637
- Fellows, I. E., Shiraishi, R. W., Cherutich, P., Achia, T., Young, P. W., & Kim, A. A. (2020). A new method for estimating HIV incidence from a single cross-sectional survey. *PLoS ONE*, *15*(8 August), 1–12. https://doi.org/10.1371/journal.pone.0237221
- *Github Fellstat: Testing History Incidence*. (2020). Github. https://github.com/fellstat/TestingHistoryIncidence
- Godin, A., Eaton, J. W., Giguère, K., Marsh, K., Johnson, L. F., Jahn, A., Mbofana, F., Ehui, E., & Maheu-Giroux, M. (2021). Inferring population HIV incidence trends from surveillance data of recent HIV infection among HIV testing clients. *Aids*, *35*(14), 2383–2388. https://doi.org/10.1097/qad.00000000003021

Hesterberg, T., Shao, J., & Tu, D. (1997). The Jackknife and Bootstrap. In Technometrics

(Vol. 39, Issue 4). https://doi.org/10.2307/1271515

- Joint United Nations Programme on HIV/AIDS (UNAIDS). (2018). *Recent infection testing algorithm technical update*.
- Justman, J., Mugurungi, O., & El-Sadr, W. (2018). HIV Population Surveys Bringing Precision to the Global Response. New England Journal of Medicine, 378(20), 1857– 1859. https://doi.org/10.1056/nejmp1800861
- Kassanjee, R., McWalter, T. A., Bärnighausen, T., & Welte, A. (2012). A new general biomarker-based incidence estimator. *Epidemiology*, *23*(5), 721–728. https://doi.org/10.1097/EDE.0b013e3182576c07
- Patel, H. K., Duong, Y. T., Birhanu, S., Dobbs, T., Lupoli, K., Moore, C., Detorio, M., Sleeman, K., Manjengwa, J., Wray-Gordon, F., Yavo, D., Jackson, K., Domaoal, R. A., Yufenyuy, E. L., Vedapuri, S., Ndongmo, C. B., Ogollah, F. M., Dzinamarira, T., Rubinstein, P., ... Parekh, B. S. (2021). A Comprehensive Approach to Assuring Quality of Laboratory Testing in HIV Surveys: Lessons Learned From the Population-Based HIV Impact Assessment Project. *Journal of Acquired Immune Deficiency Syndromes (1999), 87*, S17–S27. https://doi.org/10.1097/QAI.00000000002702

PHIA Collaborating Institutions. (2019). PHIA Data Use Manual (Issue July).

- Porter, L., Bello, G., Nkambule, R., & Justman, J. (2021). HIV General Population Surveys: Shedding Light on the Status of HIV Epidemics and Informing Future Actions. *Journal of Acquired Immune Deficiency Syndromes (1999), 87*, 2–5. https://doi.org/10.1097/QAI.00000000002701
- Sachathep, K., Radin, E., Hladik, W., Hakim, A., Saito, S., Burnett, J., Brown, K., Phillip, N., Jonnalagadda, S., Low, A., Williams, D., Patel, H., Herman-Roloff, A., Musuka, G., Barr, B., Wadondo-Kabonda, N., Chipungu, G., Duong, Y., Delgado, S., ... Justman, J. (2021). Population-Based HIV Impact Assessments Survey Methods, Response, and Quality in Zimbabwe, Malawi, and Zambia. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *87*, S6–S16. https://doi.org/10.1097/QAI.00000000002710
- UNAIDS. (2014). *To help end the AIDS epidemic*. http://www.unaids.org/sites/default/files/media_asset/90-90_en.pdf
- UNAIDS. (2021). FACT SHEET 2021 Global Hiv Statistics (Issue June).
- UNAIDS, & World Health Organization (WHO). (2015). *Monitoring HIV Impact Using Population-Based Surveys*.
- Voetsch, A. C., Duong, Y. T., Stupp, P., Saito, S., McCracken, S., Dobbs, T., Winterhalter, F. S., Williams, D. B., Mengistu, A., Mugurungi, O., Chikwanda, P., Musuka, G., Ndongmo, C. B., Dlamini, S., Nuwagaba-Biribonwoha, H., Pasipamire, M.,

Tegbaru, B., Eshetu, F., Biraro, S., … Parekh, B. S. (2021). HIV-1 Recent Infection Testing Algorithm With Antiretroviral Drug Detection to Improve Accuracy of Incidence Estimates. *Journal of Acquired Immune Deficiency Syndromes (1999), 87*, S73–S80. https://doi.org/10.1097/QAI.00000000002707

- Walker, E., Kleinbaum, D., Kupper, L., & Muller, K. (1989). Applied Regression Analysis and Other Multivariable Methods. In *Technometrics* (Vol. 31, Issue 1). https://doi.org/10.2307/1270375
- Waruiru, W., Kim, A. A., Kimanga, D. O., Ng'ang'a, J., Schwarcz, S., Kimondo, L., Ng'ang'a, A., Umuro, M., Mwangi, M., Ojwang, J. K., & Maina, W. K. (2014). The Kenya AIDS indicator survey 2012: Rationale, methods, description of participants, and response rates. *Journal of Acquired Immune Deficiency Syndromes, 66*(SUPPL. 1), 1–19. https://doi.org/10.1097/QAI.00000000000114
- World Health Organization, & WHO. (2016). *Progress Report 2016 Prevent HIV, test and treat all*.