CONCISE COMMUNICATION

Inferring population HIV incidence trends from surveillance data of recent HIV infection among HIV testing clients

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Background: Measuring recent HIV infections from routine surveillance systems could allow timely and granular monitoring of HIV incidence patterns. We evaluated the relationship of two recent infection indicators with alternative denominators to true incidence patterns.

Methods: We used a mathematical model of HIV testing behaviours, calibrated to population-based surveys and HIV testing services programme data, to estimate the number of recent infections diagnosed annually from 2010 to 2019 in Côte d'Ivoire, Malawi, and Mozambique. We compared two different denominators to interpret recency data: those at risk of HIV acquisition (HIV-negative tests and recent infections) and all people testing HIV positive. Sex and age-specific longitudinal trends in both interpretations were then compared with modelled trends in HIV incidence, testing efforts and HIV positivity among HIV testing services clients.

Results: Over 2010–2019, the annual proportion of the eligible population tested increased in all countries, while positivity decreased. The proportion of recent infections among those at risk of HIV acquisition decreased, similar to declines in HIV incidence among adults ($\geq$15 years old). Conversely, the proportion of recent infections among HIV-positive tests increased. The female-to-male ratio of the proportion testing recent among those at risk was closer to 1 than the true incidence sex ratio.

Conclusion: The proportion of recent infections among those at risk of HIV acquisition is more indicative of HIV incidence than the proportion among HIV-positive tests. However, interpreting the observed patterns as surrogate measures for incidence patterns may still be confounded by different HIV testing rates between population groups or over time.

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Introduction

Monitoring HIV incidence allows identifying priority populations at high risk of HIV acquisition, essential information for planning interventions and evaluating public health programmes [1]. Biomarker-based assays that detect recent HIV seroconversions, defined as those that have occurred within 4–6 months of HIV infection, are increasingly used to identify ongoing transmission, monitor incidence changes, and identify population groups and geographic areas with higher relative infection levels [1–7]. These assays are often employed in recent infection testing algorithms (RITAs) that reclassify false-recent infections based on additional diagnostics, such as viral load, antiretroviral metabolites or other epidemiological information [1,8–11]. RITAs are now commonly applied to estimate HIV incidence in national household surveys in sub-Saharan Africa [12–15].

Tests for recent infection among people diagnosed with HIV have been implemented as part of routine surveillance systems in several resource-rich countries [16–20]. In sub-Saharan Africa, they have recently been implemented in countries with support from the *President's Emergency Plan for AIDS Relief* (PEPFAR), wherein HIV testing is more widespread and uniquely identifying new diagnoses is a major challenge [12,15]. In such contexts, detecting recent infections supports contact tracing activities to curtail onward community transmission [10,21]. RITAs implemented in routine surveillance systems could additionally contribute to HIV incidence estimation and identifying populations with high risk of acquiring HIV [12,22,23]. There are multiple options to interpret recency data as a surrogate measure for HIV incidence, such as the proportion of recent infections among new diagnoses (HIV-positive tests) or the proportion of recent infections among people at risk of acquiring HIV (HIV-negative tests and recent infections). Although measurable, interpretation of recent infections among persons testing for HIV is challenging because levels of recency among new diagnoses may depend on HIV testing efforts and healthcare seeking patterns across population groups [16,17].

We aimed to characterize the relationship between recent infection among HIV testing services (HTS) clients and population-level incidence, and consider the interpretation of two different indicators for recent infections in routine surveillance systems. We used a mathematical model of HIV testing behaviors and examined trends in the proportion of recent infections among the population at risk of HIV acquisition and the proportion of recent infections among HIV-positive tests (new diagnoses). These were compared with modeled trends in HIV incidence, the proportion tested among the adult population (testing effort), and positivity among HTS clients in Côte d'Ivoire, Malawi and Mozambique over 2010–2019.

Materials and methods

We used *Shiny90*, a mathematical model of HIV testing behaviors developed to estimate HIV status awareness and the number of people being diagnosed through routine HTS with recent HIV infection. Details on model structure, parameterization and calibration have been presented elsewhere [24,25]. Briefly, the model uses as inputs UNAIDS estimates of HIV incidence, prevalence, mortality and ART coverage produced by the *Spectrum/EPP* model (2019 projections files were used) [26,27]. The model estimates rates of HIV testing over time using the proportion of adults ever tested for HIV measured in population-based surveys, and the total annual numbers of tests and of HIV positive tests obtained from HTS programme data.

Shiny90 produces annual estimates of HIV testing rates among adults that vary by age, sex, previous HIV testing history, awareness and treatment status, and $CD4^+$ cell count category. Using these rates, we calculated the probability of an incident infection being diagnosed within 6 months of HIV acquisition [25]. This period was chosen as it roughly corresponds to the setting-specific mean duration of recent infection (MDRI) value used to classify infections as recent or long-standing. To account for the imperfect sensitivity of the HIV testing algorithm during the window period of detection, we assumed that only people with HIV tested 4 weeks after HIV acquisition would be detected [2].

The steps outlined above enabled us to calculate the annual number of recent infections, the number of adults tested for HIV by serostatus and the number tested that are classified as recent infections. We then compared 2010–2019 trends in the proportion of recent infections among persons at risk of HIV acquisition (HIV-negative tests and recent infections) and the proportion of recent infections diagnosed among HIV-positive tests in Côte d'Ivoire, Malawi and Mozambique; three countries with several high-quality population-based surveys and HTS programme data. We examined time trends for these two metrics stratified by sex (male and female) and by broad age groups (15–24 and 25+). We compared these trends to the modelled trends in HIV incidence, the proportion tested among the adult population (testing effort) and the

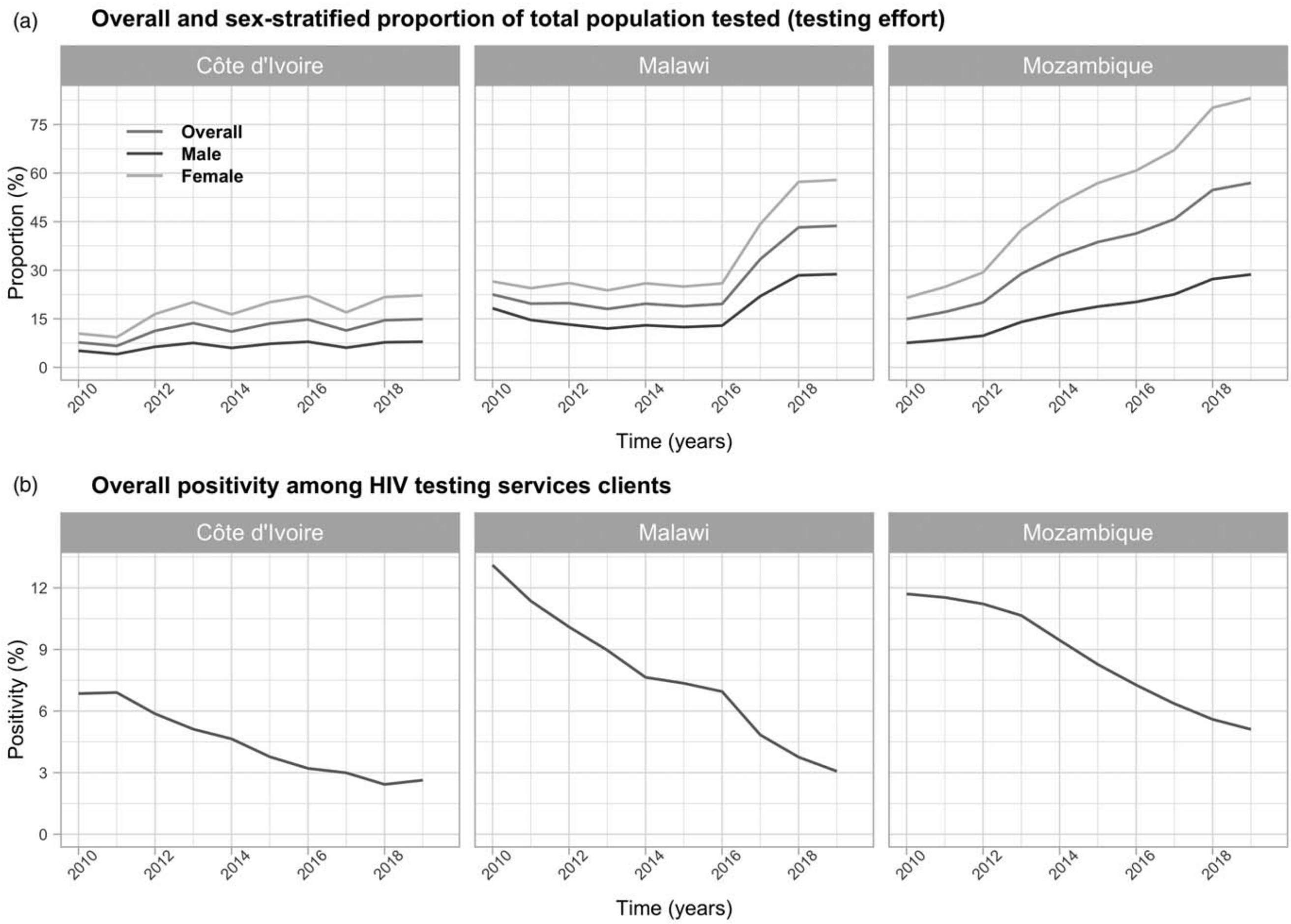

Fig. 1. Modelled trends in HIV testing effort and positivity. (a) Overall and sex-stratified modelled trends in testing effort (defined as the annual number of individual tested for HIV/total population) among people aged ≥15 years from 2010 to 2019 in Côte d'Ivoire, Malawi and Mozambique. (b) Overall modeled trends in positivity among HIV testing services clients aged ≥15 years from 2010 to 2019 in Côte d'Ivoire, Malawi and Mozambique.

proportion HIV-positive among HTS clients (positivity). Total adult population annual estimates were obtained from *Spectrum/EPP.*

Ethics

Ethics approval was granted by the *McGill Institutional Review Board* (A10−E72−17A).

Results

There was good agreement between the model and empirical data in all three countries (Figure S1, http://links.lww.com/QAD/C241). Testing rates increased in all three countries between 2010 and 2019. The annual proportion of adults tested for HIV (number of tests/total population) increased twofold in Malawi and fourfold in Mozambique (Fig. 1a). Increases were larger among women than men over the same period (Fig. 1a). Meanwhile, HIV positivity among HTS clients declined from 6.8 to 2.6% in Côte d'Ivoire, 13.1 to 3.0% in Malawi and 11.7 to 5.1% in Mozambique (Fig. 1b).

Modelled annual HIV incidence was higher than the proportion of recent infections among persons at risk of HIV acquisition in all countries, but both measures declined similarly over the period (Fig. 2a). The proportion of recent infections among those at risk of HIV acquisition declined from 0.12 to 0.06% in Côte d'Ivoire, from 0.41 to 0.22% in Malawi and from 0.81 to 0.45% in Mozambique over 2010−2019. Meanwhile, HIV incidence declined from 0.17 per 100 person-years (PY) to 0.09 per 100 PY in Côte d'Ivoire, 0.62 per 100 PY to 0.36 per 100 PY in Malawi, and 1.14 per 100 PY to 0.89 per 100 PY in Mozambique. In contrast, the proportion of recent infections among HIV-positive tests increased from 1.8 to 2.3% in Côte d'Ivoire, 3.2 to 7.0% in Malawi and 7.0 to 8.9% in Mozambique (Fig. 2b).

The proportion of recent infections among those at risk of HIV acquisition declined for both men and women,

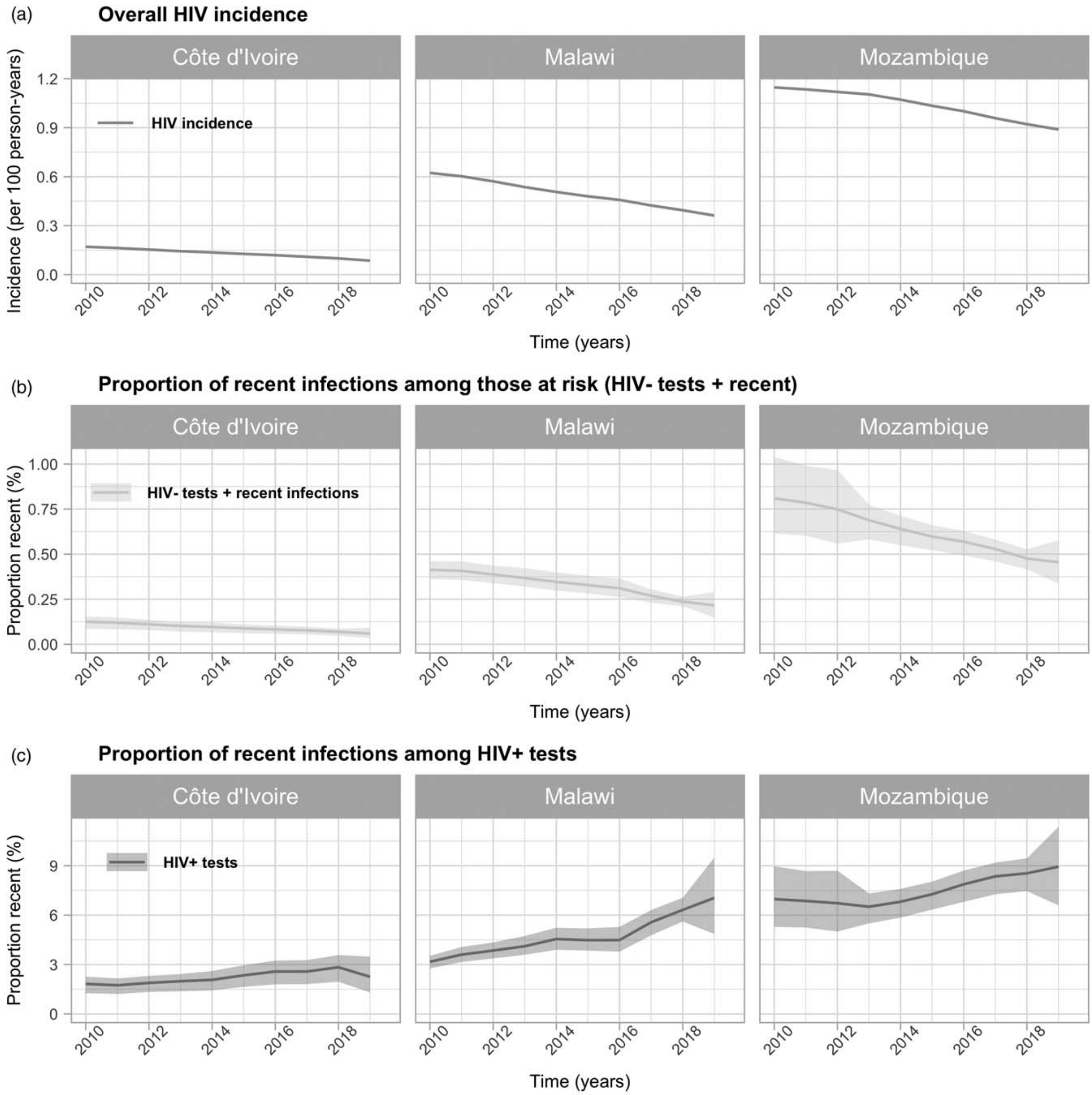

Fig. 2. HIV incidence and recent infections expressed as proportions of HIV tests. (a) HIV incidence (estimated from Spectrum/EPP); (b) proportion of recent infections among those at risk of HIV acquisition (HIV-negative tests and recent infections); and (c) proportion of recent infection among HIV-positive (HIV+) tests in Côte d'Ivoire, Malawi and Mozambique among people aged ≥15 years from 2010 to 2019.

concomitant with reductions in sex-stratified HIV incidence (Figure S2, http://links.lww.com/QAD/C241). The proportion of recent infections among those at risk of HIV acquisition declined more among women than men: 55 versus 49% in Côte d'Ivoire, 50 versus 44% in Malawi, and 47 versus 33% in Mozambique. In contrast, modeled reductions in HIV incidence were the same for both sexes – 49% in Côte d'Ivoire, 42% in Malawi and 22% in Mozambique (Figure S2, http://links.lww.com/QAD/C241) – but rates of HIV testing increased more for women than men (Fig. 1a) resulting in disproportionately larger reductions in the proportion recent among those testing positive.

In Côte d'Ivoire and Malawi, the relative change in the proportion of recent infections among those at risk of HIV acquisition by age groups 15–24 years and 25 and older mirrored trends in HIV incidence. (Figure S2, http://links.lww.com/QAD/C241). The difference was somewhat larger in Mozambique, where the proportion of recent infections among people at risk of HIV aquisition decreased 11% more among those aged 15–24 years than among those aged at least 25 years. In the three countries, younger people had a greater proportion of recent infection among HIV-positive tests, which increased faster than among people aged at least 25 years (Figure S2, http://links.lww.com/QAD/C241).

Discussion

The use of recency assays among people newly diagnosed with HIV has been promoted to enhance real-time HIV surveillance [7,12,23]. Implementing these assays in routine surveillance systems could also improve the timeliness and granularity of efforts to monitor HIV incidence trends and identifying population groups with higher infection risk. However, the interpretation of recency assays from routine surveillance systems should consider both denominators and testing efforts.

We compared two interpretations of data on recent infections among persons testing for HIV in Côte d'Ivoire, Malawi and Mozambique over the 2010–2019 period. Our modelling results strongly suggest that the proportion of recent infections diagnosed among people at risk of HIV acquisition provides a better indication of incidence trends and relative levels than the proportion recently infected among those testing HIV-positive. The proportion of recent infections among those diagnosed with HIV, which mostly increased in all countries, did not mirror trends in incidence. This was likely due to increases in testing effort and diagnosis coverage (Fig. 1a). Further, sex-specific trends in this metric were inconsistent in some countries, which could be attributed to reductions in the proportion of undiagnosed infections and changes in testing efforts or test-seeking behaviours, rather than shifts in active transmission.

However, we also found that sex-stratified trends in the proportion of recently infected among those at risk of HIV acquistion was not reflective of the true sex-stratified trends for HIV incidence. This was due to differences in testing rates by sex. Women tend to seek testing earlier in the course of their infection and test more frequently due to their engagement in antenatal care and other targeted testing activities [10,28]. This conclusion also implies caution when using the proportion of recent infections among those at risk of HIV acquisition to characterize other risk groups or relative incidence patterns where apparent differences may be confounded by different testing patterns. Interpreting programmatic recency data within a framework that explicitly represents differences in testing behaviors, such as the model analysed here, may help to address these limitations.

Our results must be interpreted in light of some limitations. First, we assumed perfect sensitivity and specifity of HIV infection detection, such that there are no false-positive or false-negative. The accuracy and precision of RITA in routine programmatic settings is a distinct and important area of ongoing research that could further compound interpretation of trends [3]. Second, modelled rates of testing were identical for people with recent infection and those with long-standing infections in the model at high $CD4^+$ cell counts ($\geq$350 $CD4^+$). This assumption implies that our results could slightly underestimate the proportions of recent infections, as people with recent infection might engage in at-risk behaviours or experience acute HIV symptoms that motivate seeking healthcare and HIV testing [29,30]. Last, our results should be carefully interpreted in the context of large-scale routine surveillance systems rather than at local levels.

This work is an effort to examine under which circumstances recency data represent an accurate indicator of active HIV transmission and incidence trends. Strengths of our work include, firstly, the integration of routinely collected HTS programme data, population-based surveys and standardized statistical estimates of the HIV epidemic in a coherent modeling framework. Second, we considered sex and age-specific patterns of HIV testing and stratified our results by age and sex. Third, we systematically compared and contrasted our different metrics to incidence estimates, testing efforts and positivity.

Conclusions

Our analysis showed that the proportion of adults recently infected among those at risk of HIV acquisition will more accurately identify areas or groups of individuals at high risk of HIV acquisition and trends in HIV incidence. This denominator should be preferred over HIV-positive tests. However, patterns in this proportion may be a biased reflection of relative HIV incidence patterns in populations with different HIV testing behaviours, such as among men versus women or geographically targeted testing campaigns. Data from routine recent infection testing must be interpreted in the context of patterns and changes in HIV testing.

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A.G., K.G., J.W.E. and M.M.G. conceptualized the study. J.W.E., K.M. and M.M.-G. conceived and designed the model. A.G., K.G., A.J., F.M., E.E., J.W.E., K.M. and M.M.-G. obtained, administered and processed the different databases. A.G., K.G., A.J., J.W.E., K.M. and M.M.-G. contributed to model development and/or revisions. A.G., K.G., J.W.E. and M.M.-G. performed the analyses and all authors contributed to results interpretation. A.G. drafted the manuscript and all authors critically reviewed it for important intellectual content. All authors approved the final version.

Conflicts of interest

There are no conflicts of interest.

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