
Article:
Stevens, O. orcid.org/0000-0001-6842-9434, Anderson, R., Stover, J. et al. (23 more authors) (2024) Comparison of empirically derived and model-based estimates of key population HIV incidence and the distribution of new infections by population group in sub-Saharan Africa. Journal of Acquired Immune Deficiency Syndromes, 95 (1S). e46-e58. ISSN 1525-4135

https://doi.org/10.1097/qai.0000000000003321

OPEN

Comparison of Empirically Derived and Model-Based Estimates of Key Population HIV Incidence and the Distribution of New Infections by Population Group in Sub-Saharan Africa

Oliver Stevens, MPH,[a] Rebecca Anderson, BSc,[a] John Stover, MS,[b] Yu Teng, PhD,[b] James Stannah, MPH,[c] Romain Silhol, PhD,[a,d] Harriet Jones, MSc,[e] Ross D. Booton, PhD,[f] Rowan Martin-Hughes, PhD,[g] Leigh Johnson, PhD,[h] Mathieu Maheu-Giroux, PhD,[c] Sharmistha Mishra, MD, PhD,[i,j] Jack Stone, PhD,[k] Anna Bershteyn, PhD,[l] Hae-Young Kim, PhD,[l] Keith Sabin, PhD,[m] Kate M. Mitchell, PhD,[a,n] Dobromir Dimitrov, PhD,[d,o] Stefan Baral, MD,[p] Deborah Donnell, PhD,[o] Eline Korenromp, PhD,[m] Brian Rice, PhD,[q] James R. Hargreaves, PhD,[e] Peter Vickerman, DPhil,[k] Marie-Claude Boily, PhD,[a,d] and Jeffrey W. Imai-Eaton, PhD[a,r]

Background: The distribution of new HIV infections among key populations, including female sex workers (FSWs), gay men and other men who have sex with men (MSM), and people who inject drugs (PWID) are essential information to guide an HIV response, but data are limited in sub-Saharan Africa (SSA). We analyzed empirically derived and mathematical model-based estimates of HIV incidence among key populations and compared with the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates.

Methods: We estimated HIV incidence among FSW and MSM in SSA by combining meta-analyses of empirical key population HIV incidence relative to the total population incidence with key population size estimates (KPSE) and HIV prevalence. Dynamic HIV transmission model estimates of HIV incidence and percentage of new infections among key populations were extracted from 94 country applications of 9 mathematical models. We compared these with UNAIDS-reported distribution of new infections, implied key population HIV incidence and incidence-to-prevalence ratios.

From the [a]MRC Centre for Global Infectious Disease Analysis, School of Public Health, Imperial College London, London, United Kingdom; [b]Center for Modeling, Planning and Policy Analysis, Avenir Health, Glastonbury, CT; [c]Department of Epidemiology and Biostatistics, School of Population and Global Health, McGill University, Montréal, Canada; [d]HIV Prevention Trials Network Modelling Centre, Imperial College London, London, United Kingdom; [e]Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom; [f]United Kingdom Heath Security Agency, London, United Kingdom; [g]Macfarlane Burnet Institute for Medical Research and Public Health, Melbourne, Australia; [h]Centre for Infectious Disease Epidemiology and Research, University of Cape Town, Cape Town, South Africa; [i]Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [j]MAP Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, Unity Health Toronto, Toronto, Canada; [k]Population Health Sciences, University of Bristol, Bristol, United Kingdom; [l]Department of Population Health, New York University Grossman School of Medicine, New York, NY; [m]Data for Impact, The Joint United Nations Program on HIV/AIDS (UNAIDS), Geneva, Switzerland; [n]Department of Nursing and Community Health, Glasgow Caledonian University London, London, United Kingdom; [o]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center, Seattle, WA; [p]Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD; [q]School of Health and Related Research (SchARR), University of Sheffield, Sheffield, United Kingdom; and [r]Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA.

O.S., R.A., and J.W.I.-E. were funded by UNAIDS. O.S., R.A., R.S., R.D.B., K.M.M., D. Dimitrov, D. Donnell, and M.-C.B. were supported by the HIV Prevention Trial Network (HPTN) Modelling Centre, which is funded by the US National Institutes of Health (grant number UM1-AI068617) through the HPTN Statistical and Data Management Center. J.W.I.-E. was funded by the Bill and Melinda Gates Foundation (OPP1190661) and the National Institute of Allergy and Infectious Disease of the National Institutes of Health under the award number R01AI152721. O.S., R.A., R.S., K.M.M., M.-C.B., and J.W.I.-E. were funded by the MRC Centre for Global Infectious Disease Analysis (reference MR/R015600/1), jointly funded by the UK Medical Research Council (MRC) and the UK Foreign, Commonwealth, & Development Office (FCDO), under the MRC/FCDO Concordat agreement, and is also part of the EDCTP2 programme supported by the European Union. J.S., P.V., M.C.B., and M.M.G. acknowledge funding from the Wellcome Trust (WT 226619/Z/22/Z). H.J., J.R.H., and B.R. were supported by the MeSH Consortium. This work was supported in whole or in part by the Bill & Melinda Gates Foundation (#INV-007055). S.M. and S.B. were funded in part by the National Institutes of Allergy and Infectious Diseases (R01AI170249) at the National Institute of Health for the modeling conducted in this study. S.M. and M.M.G. research programs supported Tier 2 Canada Research Chairs.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

K.M.M. reports payments from Pfizer for teaching, outside the submitted work.

Correspondence to: Oliver Stevens, MPH, St. Mary's Hospital Campus, Norfolk Place, London W2 1PG, United Kingdom (e-mail: o.stevens@imperial.ac.uk).

Results: Across SSA, empirical FSW HIV incidence was 8.6-fold (95% confidence interval: 5.7 to 12.9) higher than total population female 15–39 year incidence, and MSM HIV incidence was 41.8-fold (95% confidence interval: 21.9 to 79.6) male 15–29 year incidence. Combined with KPSE, these implied 12% of new HIV infections in 2021 were among FSW and MSM (5% and 7% respectively). In sensitivity analysis varying KPSE proportions within 95% uncertainty range, the proportion of new infections among FSW and MSM was between 9% and 19%. Insufficient data were available to estimate PWID incidence rate ratios. Across 94 models, median proportion of new infections among FSW, MSM, and PWID was 6.4% (interquartile range 3.2%–11.7%), both much lower than the 25% reported by UNAIDS.

Conclusion: Empirically derived and model-based estimates of HIV incidence confirm dramatically higher HIV risk among key populations in SSA. Estimated proportions of new infections among key populations in 2021 were sensitive to population size assumptions and were substantially lower than estimates reported by UNAIDS.

Key Words: africa, key population, incidence, new infections, female sex workers, men who have sex with men, people who inject drugs

(*J Acquir Immune Defic Syndr* 2024;95:S46–S58)

INTRODUCTION

HIV incidence and the number of new infections are key indicators for tracking progress in the HIV epidemic response.[1] Estimates among key populations, including female sex workers (FSW), gay men and other men who have sex with men (MSM), and people who inject drugs (PWID), guide priorities on where to focus HIV prevention and treatment programming to ensure effective and equitable HIV programmes.[2]

Cohort studies measuring HIV seroconversion of seronegative individuals, while the gold standard method for estimating HIV incidence, are costly and challenging to implement.[3] Conducting incidence cohorts among key populations is further hindered by small study populations, high mobility and transient living arrangements, nondisclosure of risk, and societal marginalisation.[4–6] Systematic reviews and meta-analyses of empirically measured HIV incidence among key populations in sub-Saharan Africa (SSA) have been conducted for FSW and MSM.[7,8] These analyses find that HIV incidence among MSM has not declined over time, and although HIV incidence in FSW has declined since the 1990s, it remains higher than population incidence among all women. Estimates of HIV incidence among transgender women[9,10] and PWID[11,12] exist, but data are insufficient for SSA regional-level meta-analyses. No empirical estimates of HIV incidence exist for transgender men or partners of key populations in SSA.

Given the challenges and scarcity of empirically measuring HIV incidence among key populations, estimates of HIV incidence derived from mathematical models have been used within national HIV program decision-making, policy planning, and HIV advocacy. The modes of transmission model, a simple cross-sectional model that disaggregated the total number of adult infections by the risk group using key population size estimates (KPSE) and sexual behavior data, was widely used in SSA to understand differential HIV risk by the population group.[13,14] Although useful for understanding the epidemic in the short term, the modes of transmission model poorly captured the wider epidemic impacts of effective HIV interventions among key populations[15] and has been succeeded by transmission dynamic models which better capture risk over time. These include goals,[16] optima,[17] and several country-specific models (for South Africa,[18–21] Eswatini,[21] Lesotho,[21] Côte d'Ivoire,[22,23] Cameroon,[24] Senegal,[23] Mali,[23] Kenya,[25] and Tanzania[26]).

Since 2014, as part of its global HIV estimates, the Joint United Nations Programme on HIV/AIDS (UNAIDS) has published estimates of the percentage of new adult HIV infections acquired by key populations. The 2022 Global AIDS Update reported that, in Eastern and Southern Africa (ESA) in 2021, an estimated 21% of new acquired HIV infections were among key populations and a further 25% among their sexual partners and clients. In Western and Central Africa (WCA), 44% of new adult HIV infections were among key populations and 28% among their sexual partners and clients.[1] These were derived by combining results from previous applications of the Incidence Patterns Model,[27] Goals,[28] or Optima models[17] or imputed based on estimates from other countries in the region. These percentages have tended to increase over recent reports. The 2018 Global AIDS Update estimated that 9% and 24% of adult infections in ESA and WCA, respectively, were among key populations.[29] In ESA between the 2018 and 2022 reports, the estimated proportion of infections among FSW increased from 2% to 13% and among their clients and other sexual partners of key populations from 8% to 26%. The reports do not present time trends or country-specific changes, but the increasing proportions reflect changes in sources or assumptions year-to-year and UNAIDS caution against interpreting updated estimates as a trend.

Considering the large and increasing prominence of the UNAIDS-reported estimates for global HIV policy and advocacy, we sought to compare the UNAIDS estimates to empirical data on HIV incidence among key populations and population sizes and results from other mathematical models.[7,30] This analysis addresses the following questions: (1) Are 2021 UNAIDS regional estimates of key population HIV incidence and the percentage of new infections among key populations consistent with empirically derived and model-based estimates? (2) Are estimates of key population HIV prevalence and population size similar across mathematical models, and how do these relate to model-estimated percentage of new infections? (3) Are HIV incidence rates implied by UNAIDS-reported estimates for the percentage of infections among key populations consistent with observed HIV prevalence from key population surveys?

METHODS

We compared estimates of the HIV incidence rate and percentage of new adult HIV infections among key populations between studies empirically measuring HIV incidence among key populations in SSA,[7] mathematical models of HIV transmission dynamics stratified by key population calibrated to sub-Saharan African settings, and estimates reported in the UNAIDS 2022 Global AIDS Update.[1]

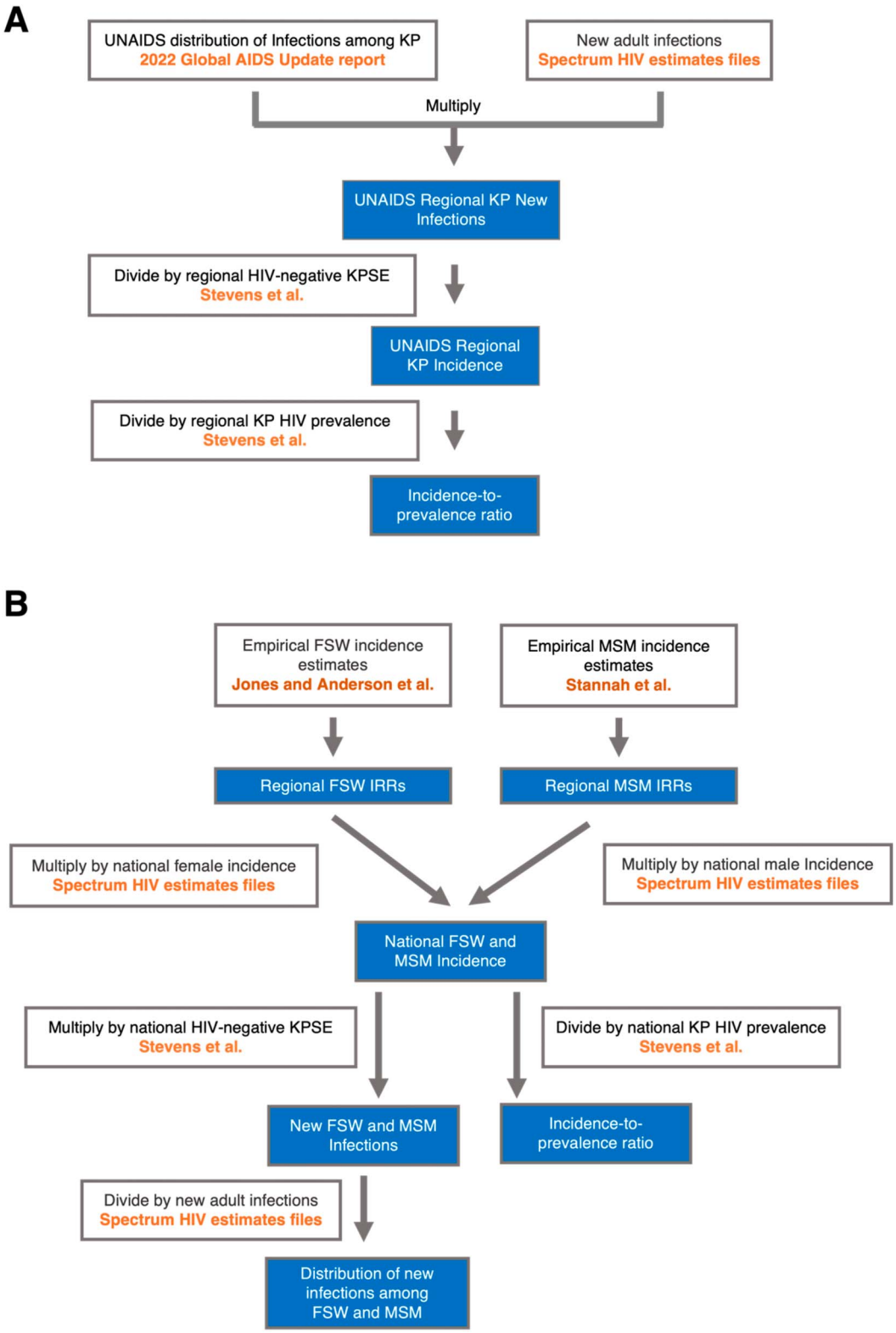

FIGURE 1. Data workflow for estimating the proportion of new infections and the incidence-to-prevalence ratio. A, UNAIDS regional estimates of the distribution of new infections. B, FSW and MSM[7] empirical incidence studies. KP = key population. Data included from UNAIDS Global AIDS Update report,[1] Spectrum,[31] Jones and Anderson et al,[8] Stannah et al,[7] and Stevens et al.[30]

For each source, we combined data from different settings to derive regional (ESA and WCA) estimates for the (1) key population HIV incidence rate, (2) number of new key population infections and their percentage of all new adult HIV infections, (3) ratio of key population HIV incidence to sex-matched total population incidence [incidence rate ratios (IRR)], and (4) ratio of key population HIV incidence to key population HIV prevalence. Analyses were conducted at the regional level because empirical incidence data were insufficient for country-level analyses. This consisted of 2 distinct workflows: incidence metrics were derived from the UNAIDS proportion of new infections among key population and the proportion of new infections among key population were derived from the empirical incidence measures (Fig. 1).

UNAIDS Estimated Proportions of New Infections Among Key Populations and Derived Key Population Incidence Rates

UNAIDS only published estimates for the proportion of adult new infections among key population and their partners[1] and not for the number of new infections, HIV incidence rates, or population size estimates. To derive estimates for the HIV incidence rate by key population, we combined the UNAIDS-reported proportion of infections by key population with UNAIDS estimates for the total number of infections among adults (aged 15–49) in 2021[31] and national estimates for KPSE and HIV prevalence from a collation and pooled analysis of key population survey data in SSA by Stevens et al[30] (Fig. 1A; see Tables S1 and S2, Supplemental Digital Content, http://links.lww.com/QAI/C146).

We aggregated UNAIDS country estimates for the number of infections in 2021 by region (r: ESA or WCA) and multiplied these by the regional key population infection proportions for each key population (FSW, MSM, or PWID) to calculate the UNAIDS-implied number of infections by key population:

$$\text{UNAIDS new infections}_{\text{KP,r}} = \text{UNAIDS proportion of new infections}_{\text{KP,r}} \times \text{Adult infections}_{\text{r}}$$

We then aggregated the national KPSE and HIV prevalence estimates from Stevens et al[30] to obtain the estimated number of HIV-negative key population members by region, used as a denominator for the implied HIV incidence rate:

$$\text{UNAIDS HIV incidence rate}_{\text{KP,r}} = \frac{\text{UNAIDS New infections}_{\text{KP,r}}}{\text{HIV-negative population size}_{\text{KP,r}}}$$

The UNAIDS-derived key population HIV incidence rate was divided by the sex-matched region HIV incidence rate to estimate UNAIDS key population incidence rate ratios (UNAIDS-IRR). We used total population incidence 15–49 years to calculate UNAIDS-IRRs (female incidence for FSW, male for MSM, and both sexes for PWID), as the UNAIDS 2022 Global AIDS Update used the total number of new infections among 15–49 year olds as the denominator to calculate proportions of new infections among key populations.

Empirically Derived IRR and Implied Infections Distribution

We reanalyzed data from a systematic review of studies that empirically measured HIV incidence among MSM from Stannah et al[7] to estimate IRRs relative to modeled estimates of male total population incidence [empirically-derived IRR (E-IRR)]. For each key population incidence study, we calculated the IRR relative to district-age-year–matched total population incidence. District-level incidence for 2022 was extracted from UNAIDS district HIV estimates created with the Naomi model,[32] a small-area estimation model that produces cross-sectional district-level estimates using nationally-representative household survey and routine antiretroviral therapy and antenatal health system data.[33] District-level estimates for 1985–2021 were created by extrapolating 2022 estimates parallel to UNAIDS sex-matched national-level incidence trajectories.[31] MSM incidence studies were commonly restricted to recently sexually active MSM and primarily recruited young MSM.[7] Therefore, we divided the total population male incidence denominator by the proportion of all men who were sexually active[34] at the median age of the MSM study or age 22 in the absence of age information. For MSM incidence studies that did not report the study participants age range, we assumed 15–29 years. Study IRRs were pooled by mixed-effects meta-analysis[28] with a region fixed effect for ESA and WCA and study-country-district–nested random effects. Meta-analysis was conducted using the *metafor* package in R.[35] We conducted sensitivity analysis using national incidence estimates over time from Spectrum in place of 2022 district-level incidence estimates extrapolated backward over time.

E-IRRs for FSW in ESA and WCA were directly available from Jones and Anderson et al.[8] Insufficient data were available to estimate E-IRRs for PWID.

We estimated FSW and MSM incidence rates for each country, c, by multiplying the regional E-IRR times the sex-matched total population HIV incidence for 2021 from UNAIDS estimates (Fig. 1B):

$$\text{Empirical FSW HIV incidence}_{\text{c,r}} = \text{FSW E-IRR}_{\text{r}} \times \text{National female HIV incidence}_{\text{c}}$$

$$\text{Empirical MSM HIV incidence}_{c,r} = \text{MSM E-IRR}_r \times \text{National male HIV incidence}_c$$

Numbers of new infections were calculated by multiplying key population HIV incidence rates times the national number of HIV-negative key population members from Stevens et al.[30] The proportion of new HIV acquisitions among FSW and MSM by country was calculated by dividing the number of new HIV acquisitions among FSW and MSM by the total number of adult infections (15–49 years) from UNAIDS national HIV estimates.[31,36]

$$\text{Empirical new infections}_{KP,c} = \text{HIV incidence}_{KP,c} \times \text{HIV-negative population size}_{KP,c}$$

To assess the sensitivity of new infection proportion estimates to KPSE assumptions, we repeated analysis using the lower and upper 95% credible intervals around the regional KPSE proportion by key population from Stevens et al.[30]

$$\text{Empirical proportion of new infections}_{KP,c} = \frac{\text{New infections}_{KP,c}}{\text{Adult new infections}_c}$$

Mathematical Model Estimates for the Distribution of Infections by the Population Group

We collated outputs from mathematical models that represented HIV transmission dynamics among key population calibrated to settings in SSA. Population size, the number of new HIV infections, and HIV prevalence were extracted for ages 15+ years in 2020 by key population and for the total population. In total, 9 mathematical models provided results for 94 settings (see Table S1, Supplemental Digital Content, http://links.lww.com/QAI/C146). The Goals model[16,28] provided 2 versions reflecting alternative population size assumptions for all 38 SSA countries (76/94 model results). Optima[17] reported results for 15 SSA countries. Thembisa,[18] Stone et al,[17] EMOD,[20] and Mishra et al[21] reported results for South Africa, with Mishra also reporting Eswatini and Lesotho. Maheu-Giroux et al[37] and 2 models by Silhol et al[23,24] reported results for selected West African settings. All models reported estimates for FSW. All except EMOD and Mishra reported estimates for MSM. Only Goals and selected Optima applications reported estimates for PWID.

Analysis

We compared regional estimates of UNAIDS-IRR, E-IRR, and the proportion of new infections by key population derived from UNAIDS estimates, empirical incidence data, and transmission dynamic mathematical models. To assess whether the relationship between HIV incidence and HIV prevalence was similar in model-based estimates (which reconciled prevalence and incidence within a transmission framework) and empirical or UNAIDS-derived estimates, we calculated the ratio of HIV incidence to prevalence by the key population group.

For model results, we assessed how key population HIV prevalence and KPSE assumptions influenced new infection distribution estimates. We compared key population HIV prevalence and KPSEs as a proportion of the total adult population size (both sexes) in countries with 3 or more transmission model estimates. For model results for Eswatini, Lesotho, and South Africa (countries with similar, high prevalence HIV epidemics; 32 total results from 7 models), we calculated the correlation coefficient between KPSE proportion for a key population and the percentage of new infections among key populations to quantify the association between the percentage of new infections to population size.

RESULTS

Key Population HIV IRR From UNAIDS Estimates and Empirical Incidence Studies

UNAIDS 2022 Global AIDS Update estimates of new infection proportions implied HIV incidence rates of 5.9 per 100 person-years (py) for FSW, 2.3/100 py for MSM, and 7.1/100 py for PWID in ESA, and 2.5/100 py for FSW, 3.7/100 py for MSM, and 0.8/100 py for PWID in WCA in 2021 (Table 1). Across SSA, compared with sex-matched total population HIV incidence estimates, incidence was 24 times higher among FSW (ESA: 20 times; WCA: 40 times), 35 times higher among MSM (ESA: 15 times; WCA: 120 times), and 27 times higher among PWID (ESA: 32 times; WCA: 17 times).

By comparison, meta-analysis of directly measured key population HIV incidence relative to matched total population incidence estimated that among FSW in ESA HIV incidence was 5.3 times higher [95% confidence interval (CI): 3.7 to 7.6; Table 2] than in matched total population women, and, in WCA, was 22.4 times higher (95% CI: 11.3 to 44.3). Applying these E-IRRs to UNAIDS, total national incidence estimates implied FSW HIV incidence rates of 1.6/100 py in ESA and 1.4/100 py in WCA (Fig. 2A; Table 2).

Across SSA, empirical incidence estimates among MSM were 41.8 times higher than in matched total population men (95% CI: 21.9 to 79.6; Table 2, see Figure S1, Supplemental Digital Content, http://links.lww.com/QAI/C145). Incidence rates were 141.7 times higher in WCA

TABLE 1. Derived Regional KP HIV Incidence Rates From UNAIDS-Reported Proportions of New Infections

KP	Region	UNAIDS % of New Infections*	Total Population New Infections†	KP New Infections‡	KPSE Count§	KP HIV Prevalence§	Implied Incidence Rate/ 100 py¦	UNAIDS-IRR¶	KP Incidence to Prevalence Ratio#
FSW	ESA	13%	507,000	65,900	1,610,000	31%	5.9	19.8	0.19
	WCA	24%	124,000	29,800	1,400,000	13%	2.5	40.3	0.18
	SSA	**15%**	**631,000**	**94,700**	**3,070,000**	**23%**	**4.0**	**23.7**	**0.18**
MSM	ESA	3%	507,000	15,200	789,000	15%	2.3	15.1	0.15
	WCA	18%	124,000	22,400	721,000	16%	3.7	123.2	0.23
	SSA	**6%**	**631,000**	**37,900**	**1,530,000**	**16%**	**2.9**	**34.7**	**0.19**
PWID	ESA	3%	507,000	15,200	275,000	22%	7.1	31.8	0.32
	WCA	2%	124,000	2490	339,000	4%	0.8	17.0	0.18
	SSA	**3%**	**631,000**	**18,900**	**632,000**	**13%**	**3.4**	**27.2**	**0.27**

*Source: UNAIDS Global HIV Estimates 2022, UNAIDS special analysis.[1]
†Source: UNAIDS Global HIV Estimates 2022, National Spectrum estimates for ages 15–49 in 2021.[31]
‡Calculated as the proportion of new infections times total new adult infections.
§Source: Stevens et al.[30] collation and pooled analysis of KP surveys.
¦Calculated as the number of new KP infections divided by the number of HIV-negative KP members [KPSE × (1 − HIV prevalence)].
¶Calculated as the implied KP incidence rate divided by the sex-specific total population incidence rate (FSW matched to incidence in women aged 15–49, MSM matched incidence in men aged 15–49, and PWID matched to incidence in both sexes aged 15–49).
#Calculated as the implied incidence rate divided by KP HIV prevalence.

(95% CI: 52.2 to 384.7) and 22 times in higher in ESA (95% CI: 14.1 to 34.3). MSM HIV incidence rates calculated using regional E-IRR were 3.3/100 py in ESA and 4.3/100 py in WCA (Fig. 2A; Table 2). Sensitivity analysis matching to national-level total population male incidence, instead of subnational, increased SSA IRR to 50.2 (95% CI: 27.4 to 92.1; see Figure S2, Supplemental Digital Content, http://links.lww.com/QAI/C145) and the associated MSM HIV incidence rate to 4.0/100 py.

Proportion of New Infections Acquired by FSW and MSM

E-IRRs and mathematical model studies implied a smaller proportion of new infections among FSW than UNAIDS regional estimates (Fig. 2B). Using extrapolated incidence rates, 3% and 13% of new HIV infections were acquired by FSW in ESA and WCA, respectively, and 4% and 21% by MSM in ESA and WCA (Fig. 2B; Table 2; see Tables S4 and S5, Supplemental Digital Content, http://links.lww.com/QAI/C146). Together, E-IRR–based estimates implied 12% of new infections in SSA were among MSM and FSW. Estimates of the proportion of new infections among key population using E-IRRs were sensitive to KPSE assumptions. KPSE sensitivity analysis using the lower and upper 95% CI from Stevens et al indicated between 9% and 19% of new infections occur among FSW and MSM in SSA (see Table S7, Supplemental Digital Content, http://links.lww.com/QAI/C146).

Figure 3 reports the proportion of infections among key population groups from mathematical models. Across 94 country estimates from 9 models, 3% of new infections in SSA occurred in FSW [median estimates weighted by national HIV-positive population size; interquartile range (IQR) 2%–6%, 2% (IQR 0%–4%) in MSM, and 1% (IQR 0%–2%)] in PWID. The percentage of new infections differed by region among FSW (ESA: 3% IQR 2%–5%; WCA: 7% IQR 4%–10%) and MSM (ESA: 1% IQR 0%–3%; WCA: 5% IQR 3%–16%), but not for PWID.

TABLE 2. Empirical KP Incidence Studies—Derived Regional KP HIV Incidence Rates

KP	Region	E-IRR*	Sex-Specific Total Population Incidence/100 py†	KP Incidence/ 100 py‡	KP New Infections§	Total New Infections†	% of New Infections¦	Incidence to Prevalence Ratio¶
FSW	ESA	5.3	0.30	1.59	17,700	507,000	3%	0.05
	WCA	22.4	0.06	1.36	16,600	124,000	13%	0.10
	SSA	**8.6**	**0.17**	**1.44**	**34,200**	**631,000**	**5%**	**0.06**
MSM	ESA	22.0	0.15	3.30	22,100	507,000	4%	0.22
	WCA	141.7	0.03	4.25	25,700	124,000	21%	0.27
	SSA	**41.8**	**0.08**	**3.53**	**45,500**	**631,000**	**7%**	**0.23**

*Source: FSW IRR from Jones and Anderson et al,[8] MSM IRR from Stannah et al.[7]
†Source: UNAIDS Global HIV Estimates 2022, National Spectrum estimates for ages 15–49 in 2021.[31]
‡Calculated as IRR times sex-specific total population incidence rate.
§Calculated as the KP incidence rate multiplied the number of HIV-negative KP members [KPSE × (1 − HIV prevalence)] from Stevens et al.[30]
¦Calculated as the number of new KP infections divided by the total number of new infections.
¶Calculated as the KP incidence rate divided by the KP prevalence from Stevens et al.[30]

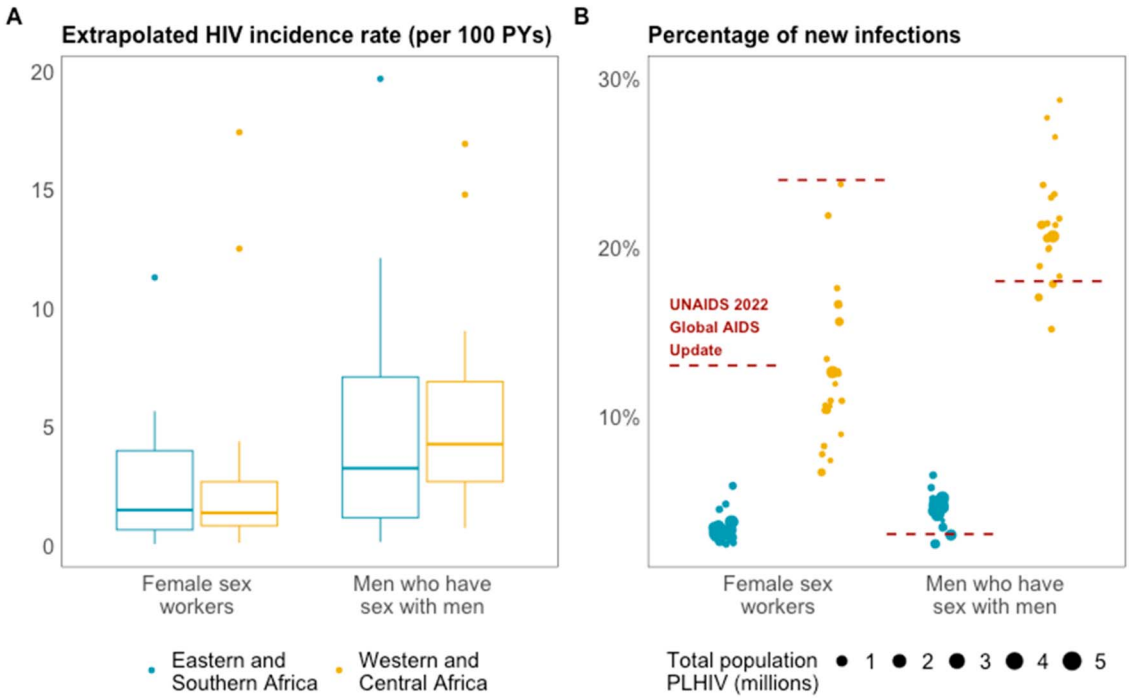

FIGURE 2. Extrapolated HIV incidence rates and proportion of new infections among FSW and MSM derived from E-IRR from systematic review. A, National-level extrapolated HIV incidence rates in FSW and MSM in 2021 in ESA and WCA. Box plots summarize range of national HIV incidence for 39 countries calculated by multiplying IRR from Jones & Anderson et al[8] (FSW) and Stannah et al[7] (MSM) times sex-matched adult HIV incidence from UNAIDS 2022 HIV estimates. B, The percentage of new adult infections in 2021 that were among FSW and MSM as a proportion of total adult HIV infections from UNAIDS 2021 HIV estimates resulting from combining extrapolated HIV incidence rates in A with KP size and HIV prevalence estimates from Stevens et al.[30] The horizontal dashed line represents the regional UNAIDS estimate of the percentage of new infections by the population group from the 2022 UNAIDS Global AIDS Update. py, person-years.

Model Estimates of HIV Prevalence and Population Size and Association With the Distribution of New Infections

Modeled HIV prevalence and population size proportions for the same country commonly varied by more than 2-fold across models in 8 countries with 3 or more models (Fig. 4). Across 7 models representing the South African epidemic, FSW KPSE proportions varied 4-fold (0.2%–0.9%) and MSM KPSE proportions 2-fold (0.4%–1.0%). Restricted to models for South Africa, Lesotho, and Eswatini, the percentage of new infections was strongly correlated with the population size for FSW ($R^2 = 0.69$; Fig. 4C) and PWID ($R^2 = 0.94$) and only weakly correlated for MSM ($R^2 = 0.21$; Fig. 4C).

Incidence to Prevalence Ratio

Among FSW in SSA, UNAIDS infection distribution estimates implied an incidence-to-prevalence ratio of 0.19 (ie, HIV prevalence among FSW was 5 times higher than annual incidence) and similar between regions (ESA: 0.19 and WCA 0.18). Incidence-to-prevalence ratios derived from empirical FSW incidence and prevalence estimates (SSA: 0.06, ESA: 0.05, and WCA: 0.10) or from mathematical models (SSA median 0.10, ESA 0.12, and WCA 0.09) were 2 to 3 times lower than the UNAIDS-implied ratio (Fig. 5A, see Table S6, Supplemental Digital Content, http://links.lww.com/QAI/C146).

Among MSM, UNAIDS estimates implied an incidence-to-prevalence ratio of 0.19 for SSA (ESA: 0.15 and WCA: 0.23) which is similar to the empirically based MSM ratio (SSA: 0.23, ESA: 0.22, and WCA: 0.27) and much higher than the MSM ratio from mathematical models (SSA median ratio: 0.03, ESA median: 0.02, and WCA median: 0.05; Fig. 5B).

UNAIDS incidence-to-prevalence ratios estimates implied very high ratios for PWID (SSA: 0.27, ESA: 0.32, and WCA: 0.18), 5 times higher than model estimates from the Optima and Goals models (SSA median ratio: 0.05, ESA: 0.04, and WCA: 0.07, Fig. 5C).

DISCUSSION

Empirical HIV incidence data and mathematical models calibrated to data on HIV prevalence by population group across SSA confirmed that key populations are disproportionately vulnerable to acquiring HIV. Through systematically triangulating available HIV incidence, HIV prevalence, and population size data from SSA, we estimated that around 12% of all new HIV infections in SSA were among FSW and MSM,

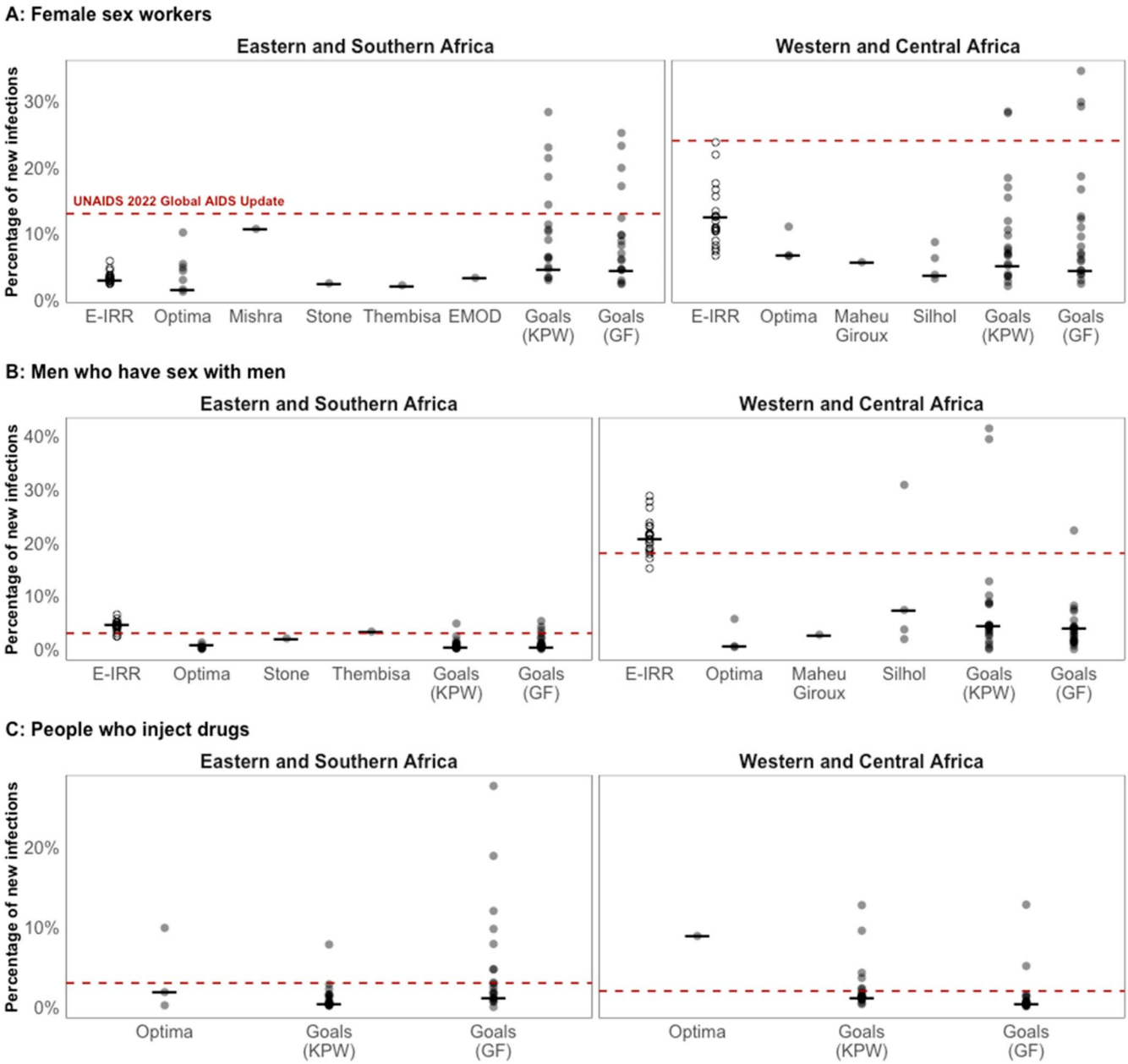

FIGURE 3. Comparison of percentage of new adult infections among each KP group in SSA across mathematical models and empirical sources. A, FSW, (B) MSM, and (C) PWID. Each circle represents 1 country estimate. UNAIDS 2021 regional estimates for FSW, MSM, and PWID are represented by the horizontal dashed line. Estimates from E-IRR calculated from IRR (Stannah et al[7] for MSM and Jones and Anderson et al[8] for FSW) and population size estimates (Stevens et al[30]) are represented by open circles and model-based estimates by filled circles. Within each source, the solid red line is the median weighted by national HIV-positive population size. GF, The Global Fund; KPW, Key Population Workbook.

despite comprising only around 1% of adults at risk. In ESA, where HIV is more prevalent, FSW and MSM accounted for around 7% of new infections. In WCA, FSW and MSM accounted for around 34% of new infections. Across mathematical models of HIV transmission dynamics, MSM, FSW, and PWID constituted 6% of all new infections but with variation across models and settings. The disproportionate share of new infections among these populations further underscores the importance of appropriate and effective treatment and prevention interventions for these populations to reduce inequalities and end HIV/AIDS as a public health threat by 2030.

Although key populations were disproportionately vulnerable to HIV, estimates for the distribution of HIV infections among FSW, MSM, and PWID in SSA from mathematical models and those derived from empirical

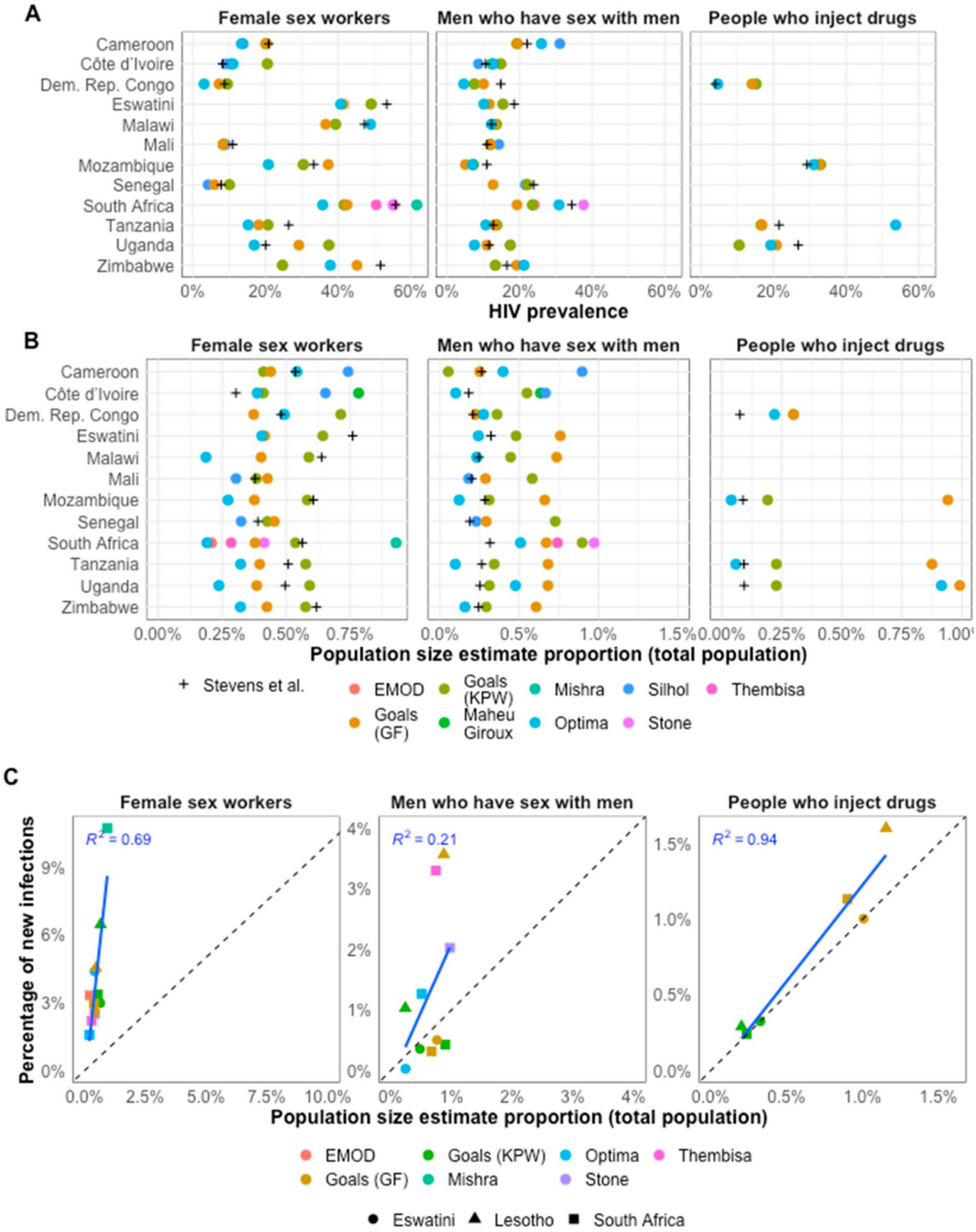

FIGURE 4. Heterogeneous model-based KP estimates. Comparison of model-based estimates of HIV prevalence (A) and population size estimate proportions (B) in 2020 countries selected were those with 3 or more models available. Synthesized surveillance data from Stevens et al[30] represented by black crosses to differentiate from model inputs. KP KPSE proportions are calculated relative to the total adult population size (both sexes) used in each model. C, Comparison of population size estimate proportion and the distribution of new infections in models calibrated to Eswatini, Lesotho, and South Africa. Countries selected as they are neighboring countries with comparable, high prevalence HIV epidemics. Blue line represents the line of best fit and the dotted line represents the line of equality.

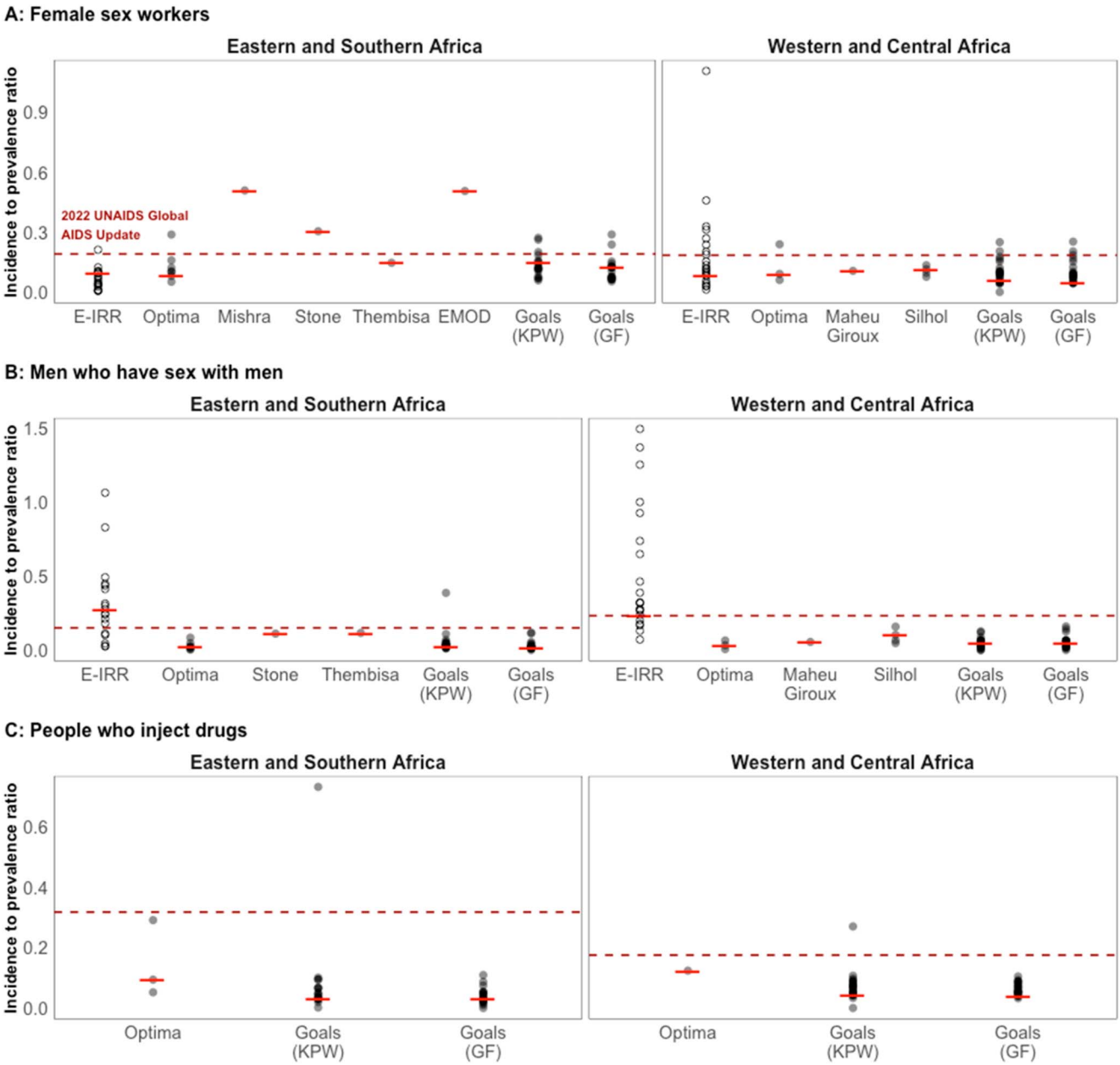

FIGURE 5. Ratio of KP group HIV incidence rate to HIV prevalence in SSA. Each circle represents 1 country estimate. The incidence to prevalence ratio derived from the UNAIDS regional estimates of the percentage of new infections occurring in FSW, MSM, and PWID are represented by the red dotted line. Estimates from E-IRR are represented by open circles and model-based estimates by filled circles. Within each model, the red line is the median weighted by the national HIV population size. GF, The Global Fund; KPW, Key Population Workbook.

incidence and cross-sectional key population surveys were substantially lower than the combined 25% reported in the 2022 UNAIDS Global AIDS Update.[1] Our estimates were particularly lower for FSW, among whom UNAIDS reported 15% of new infections, compared with 5% from our analysis. Identifying the main reasons for these differences is challenging due to multiple differences in approaches. Owing to data sparsity about key populations in SSA, previous UNAIDS estimates had compiled information from disparate sources for each population group and extrapolated infection proportions across many countries, without country-specific nationally adequate information about population sizes, prevalence, or incidence. Our approach here to analyze and extrapolate data on the constituent components driving infections (incidence, prevalence, and population size) in statistical meta-analyses and mathematical models may provide an attractive basis for more systematic approaches in future analyses.[38]

Mathematical model-based estimates of key population HIV incidence were calibrated to HIV prevalence but did not

incorporate empirical incidence estimates in model fitting (but may have been used as model validation[19]). Empirically derived FSW IRR was broadly consistent with model-based estimates of FSW incidence. However, empirical MSM IRR was higher than estimated by mathematical models fitted to prevalence data. Annual incidence rates derived from E-IRR among MSM were similar to or exceeded matched cross-sectional MSM HIV prevalence from biobehavioral surveys, which represent cumulative HIV incidence for the full duration at-risk. There are several potential explanations for this discrepancy. First, MSM surveys disproportionately recruit young MSM, who may experience higher infection risk but shorter duration at risk, resulting in higher observed incidence-to-prevalence ratios than among MSM across all ages represented by mathematical models.[7,39] Second, cohort studies measuring incidence may disproportionately recruit or retain higher-risk MSM than those reached in cross-sectional HIV prevalence or KPSE studies. Third, mathematical models that represent MSM by a single adult age or risk compartment, implicitly interpreting MSM surveys which disproportionately capture young MSM population as representative of all MSM are likely to misrepresent HIV infections, current burden, or both. Models that estimate age-specific and duration-specific force of infection and formally reconcile seroprevalence and incidence data may be required to estimate HIV incidence and prevent underestimation of HIV prevention needs for young key population members or recent risk initiates.[38,40]

Model-based estimates of the proportion of new infections among key population were highly correlated with KPSE proportions, underscoring the importance of KPSE assumptions. Compared with surveillance methods for HIV prevalence and antiretroviral therapy coverage, KPSE methods are poorly standardized, of varying quality, and produce highly heterogeneous estimates.[6,30,41–43] Calibrating models at national level requires extrapolation of local (eg, city level) population size estimates to areas lacking key population surveillance data.[44] This is particularly challenging given spatial and temporal heterogeneity in size estimate proportions among FSW[45] and further increases uncertainty around size estimates.[43,45,46] Adopting consensus national-level KPSE developed through country-led processes by HIV estimates and key population surveillance teams will be important for overall model appraisal and consensus estimates for the distribution of new infections by key population.

Our analysis has focused on estimating the distribution of annual infections across population groups, similar to UNAIDS-reported statistics. Substantial research has demonstrated that this cross-sectional representation of HIV acquisition poorly quantifies the epidemiological impacts of effective prevention among key populations by not reflecting network effects and the potential to avoid onward transmission.[15,19,47,48] Counterfactual-based metrics such as the transmission preventable attributable fraction or intervention scenario analysis, whose counterfactual scenario accounts for projected cumulative incidence in all population groups over a longer time horizon, better reflect the benefits of HIV prevention efforts among key populations.[17,39–41] Our finding that mathematical models indicated a lower proportion of infections among key populations than assumed by UNAIDS does not undermine modeling evidence for prioritized interventions among these populations; the same models reporting results in this analysis have consistently found large epidemiologic impact and cost-effectiveness for interventions averting transmission among key populations.[19,21–23]

This analysis has several limitations. First, 76 of the 94 modeled scenarios used in this analysis were derived from the Goals model, which was, therefore, disproportionately represented in the results. However, Goals estimates for the proportion of infections among FSW and MSM were similar to models developed to study key population transmission dynamics in specific settings. Second, E-IRRs used subnational total population incidence denominators extrapolated over time. The extrapolation assumed the proportional change in incidence at the district level was the same as that at the national level, and historical subnational estimates may be highly uncertain. More generally, studies measuring HIV incidence, prevalence, and population size among key populations used heterogeneous methods and were usually in specific urban populations which increased uncertainty in extrapolating to national estimates. Sensitivity analysis of MSM E-IRRs (see Figure S2, Supplemental Digital Content, http://links.lww.com/QAI/C145) and FSW E-IRRs[8] using national-level incidence estimates, informed by surveillance data over time, indicates that this is unlikely to have significantly distorted our analysis. Third, to increase comparability with UNAIDS-derived and model-based estimates, we used denominators aged 15–49 to calculate the number of new infections among key populations. Key population survey participants typically have a younger age distribution compared with the total population. Fourth, our derived estimates for HIV incidence from empirical incidence meta-analyses and the UNAIDS distribution of new infections (Fig. 1) relied on national estimates of KPSE and HIV prevalence from Stevens et al,[30] which involved regression model extrapolations in many countries lacking local key population surveillance data. Misspecification of these national estimates, particularly of KPSE, would cause misestimation of the percentage of new infections and the incidence to prevalence ratio. However, we found that when using the 95% credible range of KPSE assumptions in combination with E-IRR, the proportions of new infections among FSW and MSM were still smaller than those published in the 2022 UNAIDS Global AIDS Update (see Table S7, Supplemental Digital Content, http://links.lww.com/QAI/C146).

CONCLUSION

Empirical incidence data and mathematical models confirm dramatically higher HIV acquisition risk among key populations in SSA and a larger proportion of total new infections occur among in WCA than ESA. Proportion of new infections among key populations were sensitive to population size assumptions. However, triangulation of model-based estimates and empirical HIV incidence studies suggests the proportion of new adult infections occurring among key populations is substantially lower than reported in the UNAIDS 2022 Global AIDS Update. Model estimates of the constituent components used to determine infections (incidence, prevalence, and KPSE) vary widely. Systematic

data analysis and extrapolation and using transmission dynamic modeling frameworks that reconcile all available key population surveillance data may improve the empirical basis for estimates of new infections among key populations.[38,40] Improved HIV surveillance among key populations could help to reduce variability and improve robustness of estimates of the contribution of key population to the HIV epidemic in SSA.

ACKNOWLEDGMENTS

The authors thank Sonia Arias-Garcia (UNAIDS) for her comments and critical review of this manuscript.

REFERENCES

1. UNAIDS. *Danger: UNAIDS Global AIDS Update 2022*. 2022. Available at: moz-extension://6cb2a390-95ae-5049-93bc-b6e44134ef78/enhanced-reader.html?openApp&pdf=https%3A%2F%2Fwww.unaids.org%2Fsites%2Fdefault%2Ffiles%2Fmedia_asset%2F2022-global-aids-update_en.pdf. Accessed January 31, 2023
2. United Nations. *End Inequalities. End AIDS. Global AIDS Strategy 2021-2026 | UNAIDS*; 2021. Available at: https://www.unaids.org/en/resources/documents/2021/2021-2026-global-AIDS-strategy. Accessed May 5, 2021.
3. Hallett TB, Zaba B, Todd J, et al. Estimating incidence from prevalence in generalised HIV epidemics: methods and validation. *PLoS Med.* 2008; 5:e80–e0622.
4. Jin H, Restar A, Beyrer C. Overview of the epidemiological conditions of HIV among key populations in Africa. *J Int AIDS Soc.* 2021;24(suppl 3): e25716.
5. Hakim AJ, MacDonald V, Hladik W, et al. Gaps and opportunities: measuring the key population cascade through surveys and services to guide the HIV response. *J Int AIDS Soc.* 2018;21(suppl 5):e25119.
6. Sabin K, Zhao J, Garcia Calleja JM, et al. Availability and quality of size estimations of female sex workers, men who have sex with men, people who inject drugs and transgender women in low- and middle-income countries. *PLoS One*. 2016;11:e0155150.
7. Stannah J, Soni N, Keng J, et al. Trends in HIV testing, the treatment cascade, and HIV incidence among men who have sex with men in Africa: a systematic review and meta-regression analysis. *Lancet HIV*. 2023;10:528.
8. Jones HS, Anderson R, Cust H, et al. HIV incidence among women engaging in sex work in sub-Saharan Africa: a systematic review and meta-analysis. *medRxiv*. 2023. Available at: https://www.medrxiv.org/content/10.1101/2023.10.17.23297108v2
9. Sullivan PS, Phaswana-Mafuya N, Baral SD, et al. HIV prevalence and incidence in a cohort of South African men and transgender women who have sex with men: the Sibanye Methods for Prevention Packages Programme (MP3) project. *J Int AIDS Soc.* 2020;23(suppl 6):e25591.
10. Sandfort TGM, Mbilizi Y, Sanders EJ, et al. HIV incidence in a multinational cohort of men and transgender women who have sex with men in sub-Saharan Africa: findings from HPTN 075. *PLoS One* 2021; 16(2):e0247195.
11. Kurth AE, Cleland CM, Des Jarlais DC, et al. HIV prevalence, estimated incidence, and risk behaviors among people who inject drugs in Kenya. *J Acquir Immune Defic Syndr*. 2015;70:420–427.
12. Perry R, Artenie A, McNaughton AL, et al. *Characterising HIV Incidence Among People Who Inject Drugs Engaged with Harm-Reduction Programs in Four Provinces in South Africa*. IAS; 2023. Available at: https://programme.ias2023.org/Abstract/Abstract/?abstractid=4919
13. Gouws E, Cuchi P; International Collaboration on Estimating HIV Incidence by Modes of Transmission. Focusing the HIV response through estimating the major modes of HIV transmission: a multi-country analysis. *Sex Transm Infect.* 2012;88(suppl l_2):i76–i85.
14. Shubber Z, Mishra S, Vesga JF, et al. The HIV modes of transmission model: a systematic review of its findings and adherence to guidelines. *J Int AIDS Soc.* 2014;17:18928.
15. Mishra S, Pickles M, Blanchard JF, et al. Validation of the modes of transmission model as a tool to prioritize HIV prevention targets: a comparative modelling analysis. *PLoS One*. 2014;9:e101690.
16. Stover J, Glaubius R, Teng Y, et al. Modeling the epidemiological impact of the UNAIDS 2025 targets to end AIDS as a public health threat by 2030. *PLoS Med.* 2021;18:e1003831.
17. Kerr CC, Stuart RM, Gray RT, et al. Optima: a model for HIV epidemic analysis, program prioritization, and resource optimization. *J Acquir Immune Defic Syndr.* 2015;69:365–376.
18. Johnson LF, May MT, Dorrington RE, et al. Estimating the impact of antiretroviral treatment on adult mortality trends in South Africa: a mathematical modelling study. *PLoS Med.* 2017;14:e1002468.
19. Stone J, Mukandavire C, Boily M, et al. Estimating the contribution of key populations towards HIV transmission in South Africa. *J Int AIDS Soc.* 2021;24:e25650.
20. Bershteyn A, Klein DJ, Wenger E, et al. *Description of the EMOD-HIV Model v0.7*. arXiv; 2012.
21. Mishra S, Huiting M, Schwartz S, et al. Epidemic impact of sustained viraemia among female sex workers in Southern Africa. Croi 2019. 2016: 34.
22. Maheu-Giroux M, Vesga JF, Diabaté S, et al. Changing dynamics of HIV transmission in Côte d'Ivoire: modeling who acquired and transmitted infections and estimating the impact of past HIV interventions (1976-2015). *J Acquir Immune Defic Syndr*. 2017;75:517–527.
23. Silhol R, Maheu-Giroux M, Soni N, et al; For the ATLAS Team. Assessing the potential population-level impacts of HIV self-testing distribution among key populations in Côte d'Ivoire, Mali, and Senegal: a mathematical modelling analysis. *medrXiv*. 2023. Available at: https://www.medrxiv.org/content/10.1101/2023.08.23.23294498v2.
24. Silhol R, Baral S, Bowring AL, et al. Quantifying the evolving contribution of HIV interventions and key populations to the HIV epidemic in Yaoundé, Cameroon. *J Acquir Immune Defic Syndr.* 2021; 86:396–405. doi.
25. Stone J, Fraser H, Walker JG, et al. Modelling the impact of HIV and hepatitis C virus prevention and treatment interventions among people who inject drugs in Kenya. *AIDS*. 2022;36:2191–2201.
26. Fraser H, Stone J, Wisse E, et al. Modelling the impact of HIV and HCV prevention and treatment interventions for people who inject drugs in Dares Salaam, Tanzania. *J Int AIDS Soc.* 2021;24:e25817.
27. Bórquez A, Cori A, Pufall EL, et al. The incidence patterns model to estimate the distribution of new HIV infections in sub-Saharan Africa: development and validation of a mathematical model. *PLoS Med.* 2016;13:e1002121.
28. Stover J, Hallett TB, Wu Z, et al. How can we get close to zero? The potential contribution of biomedical prevention and the investment Framework towards an effective response to HIV. *PLoS One*. 2014;9:e111956.
29. UNAIDS. *Miles To Go*. 2018;11:1119–1120.
30. Stevens O. Key population size, HIV prevalence, and ART coverage in Sub-Saharan Africa: systematic collation and synthesis of survey data. *medrXiv*. 2022. Available at: https://www.medrxiv.org/content/10.1101/2022.07.27.22278071v1
31. UNAIDS. Spectrum file request—UNAIDS HIV Tools. Available at: https://hivtools.unaids.org/spectrum-file-request/. Accessed August 30, 2022.
32. UNAIDS. HIV sub-national estimates viewer; 2021. Available at: https://naomi-spectrum.unaids.org/. Accessed May 12, 2022.
33. Eaton JW, Dwyer-Lindgren L, Gutreuter S, et al. Naomi: a new modelling tool for estimating HIV epidemic indicators at the district level in sub-Saharan Africa. *J Int AIDS Soc.* 2021;24(suppl 5):e25788.
34. Nguyen VK, Eaton JW. Trends and country-level variation in age at first sex in sub-Saharan Africa among birth cohorts entering adulthood between 1985 and 2020. *BMC Public Health*. 2022;22:1120.
35. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw*. 2010;36:1–48.
36. Stover J, Glaubius R, Mofenson L, et al. Updates to the Spectrum/AIM model for estimating key HIV indicators at national and subnational levels. *AIDS*. 2019;33(suppl 3):S227–S234.
37. Maheu-Giroux M, Vesga JF, Diabaté S, et al. Population-level impact of an accelerated HIV response plan to reach the UNAIDS 90-90-90 target in Côte d'Ivoire: insights from mathematical modeling. *PLoS Med.* 2017; 14:e1002321.
38. Korenromp EL, Sabin K, Stover J, et al. *New HIV Infections Among Key Populations and Their Partners in 2010 and 2022, by World Region—A Multi-Sources Estimation*. JAIDS; 2023. In this issue.

39. Stannah J, Dale E, Elmes J, et al. HIV testing and engagement with the HIV treatment cascade among men who have sex with men in Africa: a systematic review and meta-analysis. *Lancet HIV*. 2019;6:e769–e787.
40. Silhol R, Anderson RL, Stevens O, et al. Fractions of HIV infections acquired among sexual partners of key populations: estimates from HIV transmission-dynamic models. *JAIDS*. 2023;1–26. In this issue.
41. Neal JJ, Prybylski D, Sanchez T, et al. Population size estimation methods: searching for the holy grail. *JMIR Public Health Surveill.* 2020;6:e25076.
42. Johnston LG, Nguyen VK, Balakrishnan S, et al. Deriving and interpreting population size estimates for adolescent and young key populations at higher risk of HIV transmission: men who have sex with men and females who sell sex. *PLoS One*. 2022;17:e0269780.
43. Laga I, Niu X, Rucinski K, et al. Mapping the number of female sex workers in countries across sub-Saharan Africa. *Proc Natl Acad Sci USA*. 2023;120:e2200633120.
44. Edwards JK, Hileman S, Donastorg Y, et al. Estimating sizes of key populations at the national level: considerations for study design and analysis. *Epidemiology*. 2018;29:795–803.
45. Fearon E, Chabata ST, Magutshwa S, et al. Estimating the population size of female sex workers in Zimbabwe: comparison of estimates obtained using different methods in twenty sites and development of a national-level estimate. *J Acquir Immune Defic Syndr*. 2020;85:30–38.
46. Datta A, Lin W, Rao A, et al. Bayesian estimation of MSM population size in Côte d'Ivoire. *Stat Public Policy*. 2019;6:1–13.
47. Mishra S, Silhol R, Knight J, et al. Estimating the epidemic consequences of HIV prevention gaps among key populations. *J Int AIDS Soc.* 2021; 24(suppl 3):e25739.
48. Mishra S, Boily MC, Schwartz S, et al. Data and methods to characterize the role of sex work and to inform sex work programs in generalized HIV epidemics: evidence to challenge assumptions. *Ann Epidemiol.* 2016;26:557–569.