Key population HIV estimates in sub-Saharan Africa

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Statement of originality

All work contained in this thesis is my own, and all else is appropriately referenced.

Abstract

Key populations experience disproportionate HIV burden in sub-Saharan Africa, but their inclusion in national HIV estimates has been constrained by fragmented surveillance and limited analytical capacity. At the outset of this thesis, no system collated and validated key population surveillance data; reviews had weak indicator and population coverage; UNAIDS estimates of new infections by population group were poorly substantiated; national programmes had limited ownership and use of data; and methods for translating surveillance data into programme-actionable estimates, including HIV incidence, were unavailable outside data-rich settings. This thesis aimed to lay the foundations for country-specific key-population-stratified estimates of comparable rigour to total population estimates within the UNAIDS estimates process.

In Chapter 2, I collated and validated key population size (KPSE), HIV prevalence, and antiretroviral therapy coverage data collected across sub-Saharan Africa during 2010–2023, incorporating grey literature omitted from reviews and databases, and produced national estimates for all mainland countries in the region. Chapter 3, detailed the success and failures of the UNAIDS Key Population Workbook, developed to enable national teams to review observation-level data and create nationally-owned key population estimates. Chapter 4 estimated HIV prevalence was 50% higher among transgender women than cis-gender men who have sex with men in sub-Saharan Africa. Chapter 5 triangulated triangulated empirical incidence observations, mathematical models, and surveillance data and indicated that 12% of new HIV acquisitions occurred among key populations, much lower than UNAIDS' estimate of 25%. Chapter 6 developed a statistical model estimated HIV incidence among female sex workers in Cotonou, Benin, from age- and duration-stratified cross-sectional prevalence data without requiring client surveillance or sexual-mixing data.

Acknowledgements

Principally to Jeff who endured an unyielding quantity of moaning and whining over the last four years. I think I have become fractionally less of a toddler through this process. Perhaps. Your advice to do a PhD or get a different job was – as ever – correct. I think I mostly enjoyed it, or, at minimum, it provided an excellent source of material to complain about. None of this would have been possible without your teaching and patience – I am deeply grateful. Beyond the statistics and the debugging and all of that, it is your philosophy of how science should be conducted that has been most rewarding.

To Rebecca without whom the slog through reams of surveillance data would not have been possible. Working with you has been extremely fun. I'm sorry the participant-level data work has not flourished into what it could have been; that is partially my fault. I hope it was still worth it.

The thesis has my name in big letters on the front which does a disservice to all who contributed to it: I find the use of "I" in a thesis distasteful. I have been fortunate to work with many colleagues across academia, government, and international organisations during this work, in particular my co-authors on the manuscripts detailed below and those detailed in advance of each chapter. The UNAIDS Reference Group on Estimates, Modelling, and Projections was a fascinating group to be parachuted into, to make a career from, and I learnt a great deal from all its members. Thanks to Jeff, Leigh, and Tim for being fooled by the gift of the gab despite absolutely no knowledge to back it up.

Finally, though not an acknowledgement, it feels as if this thesis was planned and largely conducted in a different world. We plow forward into a world championed by inward-looking fascists, indifferent to the needs of others. I suspect much of this work is now of little relevance, but I hope someone will need it one day.

“In a concentrated HIV epidemic, the bulk of infections are among people who engage in especially high-risk drug-taking or sexual practices, principally injection drug users, men who have sex with other men, and sex workers and their clients. These groups usually exist on the margins of society, and their activities are often illegal. This makes HIV surveillance extraordinarily difficult, both ethically and practically. Where people are subject to imprisonment or systematic discrimination for their HIV-related behaviors, there must be serious doubts about the wisdom of even trying to identify populations and individuals for HIV surveillance. The validity of self-reported behavioral information gathered from people whose risk behaviors are illegal is also open to question.”

Pisani *et al.*, HIV Surveillance: A Global Perspective (2003) [emphasis mine]

“I don't want you to be impressed. I want you to understand. This is not sophistry. And this is not hypocrisy. This is reality. I have sex with men. But unlike nearly every other man of whom this is true, I bring the guy I'm screwing to the White House and President Reagan smiles at us and shakes his hand. Because *what* I am is defined entirely by *who* I am. Roy Cohn is not a homosexual. Roy Cohn is a heterosexual man, Henry, who fucks around with guys.”

Roy Cohn, Angels in America: A Gay Fantasia on National Themes (1991)

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1. Introduction

1.1 Emergence

At some point in the early twentieth century, a man was bushmeat hunting in south-eastern Cameroon.[1,2] As he was gutting the carcass, or cleaning his blade, he nicked his finger and his blood mingled with that of his primate catch. Tragically for him, and for millions that followed, the simian immunodeficiency virus (SIV) circulating within the primate had acquired sufficient mutation to survive and replicate within a human host.[1,3,4] This was probably one of many zoonotic jumps that SIV had made over centuries, but it was this moment that initiated one of the most successful pandemics in human history. He went home, and had sex with a wife or a girlfriend, or floated his catch down the Sanga river to sell at the nearby market.[1,4] Perhaps he bought sex from a woman plying her trade in and around the market, benefitting from men travelling beyond the gaze of their partners. Some would be dead within a decade, their immune systems rendered defenceless to opportunistic infection.[5] But the now-human immunodeficiency virus (HIV) lived on, navigating its 500 mile journey down the Sanga and Congo rivers from sexual partnership to sexual partnership, from husband to wife, from trader to sex worker, until it reached the capital of Belgian Congo: Leopoldville.[3]

Interwar Leopoldville provided what previously-failed zoonoses of SIV had sorely needed: a growing urban centre, fuelled by the discovery of mineral wealth and rapid urbanisation by the miners and workers that accompanied it.[6] This resulted in a large gender disparity: two men for every woman, and informal sex work provided by “les femmes libres” blossomed.[7] Over the next thirty years, despite these ideal conditions for the explosive spread of a sexually transmitted disease, HIV expanded proportionally with total population growth.[3,6] Les femmes libres provided a form of integrated social care for the wife-less labourers: meals would be cooked, clothes would be washed, and sex would be had.[7] They had a couple of men on their books at any one time, and were renumerated for the time they spent, not on a per sex-act basis. By 1940, HIV had

extended its reach to the southern Congo mining cities of Lubumbashi and Mbuji-Mayi, through the railway network built to ferry diamonds and ore to the coast, and ten years later it had penetrated the densely forested north.[3] None of this seemed to suggest a particularly auspicious future for HIV, or to distinguish it from becoming yet another endemic sexually transmitted infection.

The Belgian colonialists were fully aware that a workforce widely suffering from sexually transmitted infections emanating from sex work would slow the wholesale extraction of rubber, minerals, and diamonds, and responded surprisingly pragmatically: a tax levied on sex work, the establishment of free testing and treatment, and mandatory monthly check-ups for registered femmes libres.[7] Low sensitivity syphilis testing and poorly efficacious treatments requiring multiple injections per course led to a rising number of intravenous injections throughout the 1940s with little ability to sterilise syringes between uses.[7,8] Following the end of World War II, Leopoldville's population grew dramatically.[6,7] A gonorrhoea outbreak soon followed, with a commensurate rise in intravenous injections, reaching 150,000 per year in 1953 in a city that totalled no more than 250,000 people.[7] An iatrogenic outbreak of Hepatitis B was traced to a major hospital in Leopoldville, and iatrogenic transmission of HIV may have been widespread, increasing the transmission rate and prevalence beyond what was possible from concurrent sexual partnerships of les femmes libres alone.[8–10]

In 1960, the Republic of Congo declared independence from Belgium and much of the country fell into civil war. The prosperous mining provinces of Katanga and South Kasai declared independence and many fled towards the capital as Belgian restrictions on internal migration ceased to exist. The new government was penniless and unemployment and economic destitution were commonplace within Leopoldville. Men could not afford to buy the time of les femmes libres beyond buying sex itself, and women could not afford to turn away any prospective buyer. Episodic informal sex work with a handful of clients faded, and commercial sex work with hundreds or thousands of

clients a year took its place.[7] The growth rate of HIV-1 increased almost threefold and finally, after decades of lingering transmission, the pandemic had begun.[3]

Much of this reconstructed narrative is conjecture. The early history of HIV relies on scant phylogenetic data from a small number of preserved specimens[1,3,6] and circumstantial evidence of other sexually transmitted infections and/or iatrogenic transmission. Some assert that unsterilised needles could not cause such rapid epidemic growth and genital ulcer disease was the primary driver of transmission[8,11], while others refute this.[3,7] Despite strong evidence that HIV had been widely circulating within Leopoldville for decades,[6] there exist few accounts of widespread excess mortality from a mystery immunosuppressive disease.[12] The Belgian Congo experienced high all-cause mortality, and adult life expectancy was low.[13] While late-stage HIV infection and mother-to-child transmission were likely responsible for deaths among sex workers and their children, the precise aetiology of pandemic HIV will never be known. What is agreed upon, however, is that sex work and their itinerant clients were central to its emergence.

1.2 Gay Related Immune Deficiency

To stabilise the political and economic vacuum in post-colonial West Africa, and prevent the establishment of Communist states arising from large working classes that had been denied the right to form a political class, the United Nations sought to recruit a French-speaking middle class from across the global Black African diaspora.[14] By the early 1960s, over 7,000 Haitian professionals had volunteered, working across recently-declared independent Francophone West African states, most notably in Leopoldville. Some returned home, and HIV accompanied them, with the first introduction estimated around 1966, whereupon heterosexual transmission continued.[15,16] Haiti was a major sex tourism destination, particularly for American gay men.[17] A single introduction of HIV from Haiti to New York is estimated to have occurred in 1971 (whether it was a Haitian immigrant or a returning American sex tourist is unknown), whose infection is

the origin of the majority of global HIV infections outside sub-Saharan Africa.[15] It spread silently throughout sexual networks of 1970s gay America, buoyed by the gay liberation movement, taking root in particular in San Francisco (HIV prevalence among gay men was 4.5% in 1978) and New York (6.6% in 1978).[15,18,19] The first clinical observations were reported in July 1981 in a seminal Morbidity and Mortality Weekly Report from the US Centres for Disease Control and Prevention (CDC) reporting: “Kaposi's sarcoma, an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men”.[20] Presciently, it also noted “an endemic belt across equatorial Africa, where Kaposi's sarcoma commonly affects children and young adults and accounts for up to 9% of all cancers”. Clinicians soon linked Kaposi’s sarcoma, and other opportunistic infections including pneumonia, oral candidiasis, and toxoplasmosis, now recognised as AIDS-defining illnesses, to immunosuppression and low CD4 T cell counts as hallmarks of the condition.[21,22] It became known as *Gay Related Immune Deficiency* (GRID), and was misattributed variably to a range of causes including the use of alkyl nitrites (poppers), psychedelics including LSD, infectious agents, righteous punishment, or a combination thereof.[23–26] In 1982, recognising the broader aetiology reported by clinicians and the stigmatising damage that “GRID” might cause the gay community, CDC renamed the immunodeficiency *Acquired Immunodeficiency Syndrome - AIDS* (though not before transiting through *4H Syndrome*: *Homosexuals, Heroin addicts, Haemophiliacs, and Haitians*).[27–29] Two years later, HIV was discovered as the infectious agent underlying AIDS (then called human T-lymphotropic virus type III), by which time HIV prevalence among gay men in San Francisco had risen from 4.5% in 1978 to 67.4%.[18,30]

1.3 Recognition of the African epidemic and the emergence of “generalised epidemics”

Evidence for an HIV epidemic in Africa, and specifically one transmitted by heterosexual contact, accumulated through the early 1980s. AIDS deaths and prevalent immunodeficiency was characterised among heterosexual Congolese immigrants living

in Belgium 1979-1983.[31] In 1986, high HIV prevalence was documented among sex workers and their sexual contacts in Nairobi which indicated regional transmission beyond Central Africa.[32] The epidemic spread rapidly, initially to East Africa along road networks and subsequently to Southern Africa, buoyed by political instability, civil wars, and the migration that accompanied them.[2,33–36] Though the epidemic originated in Central Africa, the first characterised cases on the continent were in 1982 among two white gay men in Cape Town, with recent sexual contacts in the United States.[37] HIV was conceptualised as a gay, Western disease, and pan-African action was delayed until 1988 when the-then Organization of African Unity (now African Union) passed its first resolution on AIDS, which keen to include "Stressing the fact the HIV Virus has no know [sic] geographical origin".[38]

By the late 1980s, the East African epidemic was mature enough no longer to be strictly associated with female sex workers and their clients, and, by 1986, 37 of 47 African countries reported AIDS deaths or HIV infection.[39] HIV rapidly spilled over into the total population: in the early 1990s, HIV prevalence among pregnant women attending antenatal clinics routinely exceeded 25% in Kenya and Uganda.[40,41] Southern African epidemics developed later; HIV prevalence among migrant miners was under 0.5% in Botswana, South Africa, Lesotho, eSwatini, and Mozambique in 1986.[39] By the early 2000s, antenatal prevalence exceeded 40% in KwaZulu-Natal and eSwatini, and generalised epidemics had established throughout sub-Saharan Africa.[42]

1.4 Defining key populations

Generalised epidemics set sub-Saharan Africa apart from HIV epidemics in the rest of the world, and the region has shouldered an overwhelming proportion of global HIV morbidity and mortality.[43] There are many hypotheses and refutations as to why transmission among 'groups at high risk', now known as key populations, spread into the total population only in sub-Saharan Africa. Despite emergence of generalised transmission in sub-Saharan Africa, today key populations hold a central position in HIV

decisionmaking. There are many definitions of what constitutes a key population with no clear consensus. The United Nations Joint Programme on HIV/AIDS (UNAIDS) considers:

> "gay men and other men who have sex with men, sex workers, transgender people, people who inject drugs, and people in prisons and other closed settings as the five main key populations that are particularly vulnerable to HIV and frequently lack adequate access to services. Key populations can also include women and gender-diverse people who are also people who inject drugs, and/or incarcerated, and/or engage in sex work. In all countries, key populations also include people living with HIV."[44]

This is a broad definition which encompasses all people living with HIV and gives insufficient space to biological risk associated with specific behaviour. Others make specific mention of other populations at high risk of HIV acquisition, adolescent girls and young women, or clients of female sex workers.[44,45] This thesis will focus on the first four of UNAIDS' key populations: female sex workers (FSW), men who have sex with men (MSM), people who inject drugs (PWID), and transgender people – principally transgender women (TGW).

The Global Fund to Fight AIDS, Tuberculosis, and Malaria defines key populations as [46]:

> Epidemiologically, [a key population] faces increased risk, vulnerability and/or burden due to biological, socioeconomic and structural factors. Access to relevant services is significantly lower for the group than for the rest of the population. Dedicated efforts and strategic investments are required to expand coverage, equity and accessibility. The group faces frequent human rights violations, systematic disenfranchisement, social and economic marginalization

and/or criminalization, increasing vulnerability and risk and reducing access to services.

I prefer this definition as it gives primacy to biological risk, which is linked to specific behaviours associated with each key population. [47,48] As supported by widespread transition towards person-centred language, a definition that centres behaviour rather than identity is important. These behaviours are primarily unprotected sex with multiple sexual partners for female sex workers, unprotected anal sex for MSM and TGW (particularly receptive anal sex), and sharing needles and injecting equipment for PWID. Individuals may also engage in multiple risk behaviours (e.g. TGW may also sell sex), though this is not a focus of this thesis.[49] Secondarily, additional HIV risk is exerted on key populations due to structural factors that impede ability to engage in behaviours that protect against HIV acquisition or transmission, which may be experienced at the individual-level (e.g. power dynamics preventing a sex worker from negotiating condom use with a client), community-level (e.g. avoiding HIV prevention services for fear of verbal abuse from staff), or societal-level (e.g. arrest and imprisonment for same-sex behaviour).[50] An individual experiencing either significant biological or structural risk should not be considered a key population; coincident risk is required. This distinction is important to ensure that all 'populations of interest in the HIV response' are not termed 'key populations', and why we should or should not prioritise them in the HIV response.

There is also no clear consensus on what defines each of the four key populations. HIV risk is a continuum and imposing categories upon it is artificial. If one sells sex for a month each year when agricultural income has dried up, are you a sex worker? If one has a friend with whom they have sex and he buys food in exchange, are you sex worker? Definitions such as 'transactional sex work', a broader definition often defined as the exchange of sex for money, gifts, or favours, and 'commercial sex work' (earning all or most of one's income from sex work) try to address this, but each still encompasses a breadth of HIV risk.[44,51–53] The term "gay men", which describes a

population by an identity, has been superseded “men who have sex with men” which describes a population by a risk behaviour. This recognises that heterosexual men can engage in anal sex with men, but remains insufficient to capture heterogeneity in HIV risk across sexual preference and insertive role.[44,54–56] Mathematical modelling and policymaking require people to fall into neatly partitioned boxes, while the reality of fluid self-identity and exposure to HIV risk is much more complex. The struggle clearly to define key population identity and periods of risk is repeatedly revisited throughout this thesis.

1.5 Legal status and social attitudes towards key populations in sub-Saharan Africa

Behaviours and identities associated with key populations are both widely criminalised and marginalised in sub-Saharan Africa.[57–60] These legally and socially punitive environments are underpinned by religious and social conservatism, inherited colonial-era legislation, and widespread social stigma. Some countries enforce explicit criminalisation and prosecution of key populations (whether outlawing their behaviour or their identities), while others may rely on municipal by-laws and public order legislation to criminalise key populations indirectly. Across all African settings, including those that do not criminalise key populations, qualitative accounts of physical and sexual violence, financial extortion, and false imprisonment by police and criminal justice services are commonplace.[59–61] The UNAIDS National Commitments and Policies Instrument (NCPI) surveys both national authorities and civil society across a range of legal and stigma-related indicators. The results are often contradictory.[62] This heterogeneity in regulation, enforcement, and their reporting is well illustrated in the Namibian sex work environment:

- The Combating of Immoral Practices Act (1980), inherited from the South African Sexual Offences Act (1957), does not prohibit selling sex but does criminalise associated activities including public solicitation and running a brothel;[63]

- Sex workers are detained under municipal street regulations prohibiting loitering in Windhoek, while both street- and brothel-based sex work is tolerated in Walvis Bay and Swakopmund;[63,64]
- NCPI reporting from national authorities indicate that sex work is criminalised and that there are no legal protections for sex workers, while civil society report that sex workers are not arrested or prosecuted for selling sex;[62] and
- Sex workers surveilled during the 2012 and 2019 Biological and Biobehavioural Surveys report high prevalence of physical, sexual, and verbal abuse, and qualitative studies report assault by police during detention.[63,65,66]

A 2022 data mapping exercise to measure country-specific stigma against key population over time concluded that structural indicators (e.g. those monitoring criminalisation and non-discrimination laws) were the only indicators available with sufficient coverage over space and time, while those relating to social norms and attitudes were "not identified as having sufficient data to use in a summary measure at present despite their importance".[58] Accordingly, summaries of statute alone may paint an inaccurate picture of the lived experience of key populations seeking to engage with criminal justice and healthcare services. These limitations notwithstanding, 2024 national authority submissions to NCPI in sub-Saharan Africa report:

Sex work

- Three countries (Angola, Sierra Leone, and Mozambique) do not criminalise sex work;
- A further seven "do not subject sex work to punitive regulation";

Same-sex behaviour/identity and transgender identity

- Eighteen countries do not criminalise same-sex sexual acts in private;
- Twenty-nine countries do not criminalise transgender identity;

Drug possession and harm reduction

- No countries have decriminalised drug possession;

- Eleven countries operate needle and syringe programmes; and
- Nine countries offer opioid substitution therapy.

While same-sex behaviour is decriminalised in half of sub-Saharan African countries and transgender identity in nearly all countries this is generally due to a lack of legislation rather than widespread permissive attitudes.[67] Sub-Saharan African political and religious leaders and their citizens have often espoused intensely homophobic values over the course of the epidemic. [67–69] Only South Africa, Botswana, Namibia, Mozambique, and Angola have actively sought to decriminalise same-sex behaviour and enshrine constitutional protection against discrimination on the basis of sexual orientation, and attitudes towards MSM outside of Southern Africa remain dire.[69] Though increasing urbanisation and education among young adults holds promise for liberalising attitudes towards MSM, there is no guarantee of progress as Ghana, Uganda, Niger, Nigeria, and Kenya have all recently prepared or passed legislation to increase legal restriction on same-sex behaviour.[69]

These legally and socially punitive environments have hindered the provision of effective public health responses to the HIV epidemic among key populations through two principal mechanisms: [58,59,70]

1) Preventing key population members from engaging with HIV prevention and treatment programmes; and
2) Weakening HIV surveillance and strategic information among key populations, in turn weakening the evidence base for resource allocation and intervention planning among key populations.

1.6 A loss of focus on key populations in sub-Saharan Africa

Risk and spatial heterogeneity was integrated into the international AIDS response from its earliest beginnings. [31,32] In 1989, the International Commission of Jurists (ICJ)

partitioned the epidemic into Pattern 1 countries where infections "occur among homosexual or bisexual males and urban intravenous drug users" and Pattern 2 where "most cases occur among heterosexuals … [in countries where] intravenous drug use and homosexual transmission are either non-existent or occur at a very low level", noting that HIV prevalence had reached 1% in some Pattern 2 countries.[71] Key populations featured prominently in the *Intervention Priorities for the 1990s* from the United Nations' precursor to UNAIDS, the World Health Organization (WHO) Global Programme on AIDS (GPA): peer education, outreach, and condom provision for commercial sex workers (including specific mention of transgender sex workers); designing interventions for targeting MSM in developing countries; and promoting harm reduction interventions including needle and syringe programmes.[72]

The prominence of sex work in international guidance was aligned with the prevalent understanding of epidemic spread and the development of community transmission in Africa: (1) migrant men, including miners and truck drivers, some of whom are HIV-positive, enter an area of low HIV prevalence and buy sex; (2) HIV prevalence among sex workers rises rapidly to near-saturation[32,73–75]; and (3) HIV is transmitted widely through clients of female sex workers whose bridging sexual networks facilitate the transmission of HIV into lower risk women, forming a disseminated epidemic.[53,76–79] Indeed, throughout the late 1980s and 1990s the formation of clinics and HIV prevention programmes specifically targeting female sex workers were not only a central part of the epidemic response, but had been shown to be successful at reducing HIV/STI transmission among both sex workers and the wider community:

- Cote d'Ivoire: *Clinique de Confiance*, Abidjan engaged over 5000 FSW from 1992-1998, delivering health education interventions and condom provision. HIV prevalence declined from 89% to 32% 1992-1998, and notably from 86% to 19% among those who had sold sex for less than one year;[73,80]

- Benin: *Project Sida-2,* Cotonou offered a free testing and condom distribution programme. HIV prevalence decreased from 53% to 41% 1993-1999 while increasing in other cities not covered by the intervention;[74,81]
- Democratic Republic of Congo: Health education and condom distribution programme decreased HIV incidence among FSW from 11.7/100 person-years (py) to 4.4/100py 1988-1991; [82]
- Kenya and Zimbabwe: Peer education programme increased condom usage "from virtually nil in 1986 to ~80% of all reported sexual contacts [among Nairobi FSW] by 1989", leading to a decline in STIs among both men and women and an estimated 10,000 averted HIV infections per year in Nairobi at ~$10/averted infection.[53,83]

While intervention and surveillance among PWID and MSM were recommended by the WHO GPA, this had little traction in African states and there are no studies among PWID in sub-Saharan Africa in the 1980s. Overlooking PWID may have been a justifiable epidemiological reality; or, akin to MSM, it may have been motivated by stigma and denial. Rapid assessments of drug use in Ethiopia (1995) reported no injecting drug use and in Cameroon (1994) only 2% of those using cocaine reported injecting, while it was occasionally observed in Kenya (1994).[84–86]

Except for South Africa, the existence of homosexual behaviour was widely denied and state-sanctioned homophobia prevented the design and implementation of research studies among MSM throughout the 1990s.[60,87,88] State positions denying the existence of MSM were effective in shaping multilateral documents, including a key report in 1997 from the World Bank, the European Union, and UNAIDS which near-omits mention of MSM from the African epidemic, while delineating epidemic designations which would shape the response for decades to come.[89] Three years later in 2000, WHO and UNAIDS formalised these epidemic designations around a 1% HIV prevalence threshold into two principal states:[90]

1. Concentrated: HIV prevalence consistently over five percent in at least one defined sub-population. HIV prevalence below one percent in pregnant women in urban areas.
2. Generalised: HIV prevalence consistently over one percent in pregnant women.

All of mainland sub-Saharan Africa was categorised as a generalised epidemic: at first glance a logical progression from the ICJ Pattern 2 definition, supported by HIV serosurveillance among pregnant women engaging with antenatal care. Despite the early successes of prevention programmes targeting sex workers, the prevailing opinion was that the epidemic response should focus on generalised transmission as further investment in key population-directed programming was shutting the stable door after the horse had bolted.[91] Undoubtedly, many epidemics had grown beyond that which could be controlled with HIV prevention programmes targeted at sex workers and their clients alone. At their peaks in the early 1990s, Kenyan and Ugandan epidemics reported HIV prevalence among pregnant women above 25%, and as the 2000 guidance was being issued, South Africa and Zimbabwe were experiencing similarly severe epidemics.[92–94] "HIV serosurveillance in groups considered at high risk (e.g. sex workers and their clients)" (p39) was to be viewed as an optional additional extra within a generalised epidemic surveillance portfolio because "small changes in prevalence in the general population are likely to have a more significant effect on the overall impact of the epidemic ... simply because the sheer numbers in the general population are so much larger" (p32).[90]

Though modelling studies in the early 2000s continued to support the role that sex work and bridging networks played in maintenance of high prevalence generalised HIV epidemics[95–99], international guidance including the 2000 WHO/UNAIDS Surveillance Guidelines aligned perceptions of FSW with those of MSM and PWID: minor players

rather than as key drivers of heterosexual generalised epidemics. This was a shift in attitude and policy, which accelerated the marginalisation of key populations in generalised epidemic discourse and surveillance.

1.7 HIV epidemiology among key populations

This thesis focuses on four indicators: population size estimates (PSE), HIV prevalence, ART coverage/viral load suppression, and HIV incidence. Here I briefly summarise the thirteen systematic reviews of data collated in sub-Saharan Africa published since 2000, of which eight have been published since the start of this thesis in 2021, reflecting the increasing momentum behind key population epidemiology in recent years (Table 1.1). In 2021, there were profound gaps in the peer-reviewed literature: over a decade since any systematic collation of data among female sex workers, and several population-indicator combinations that had not been reviewed, including all indicators among transgender women. These gaps motivated the research in this thesis.

Table 1.1: Systematic reviews among key populations in sub-Saharan Africa 2000-present

Decreasing data availability →

	FSW	MSM	PWID	TGW
Population size estimates	Vandepitte (2006)[100] Mishra (2014)* [101] Laga (2023)Δ [102]	-	Mathers (2008)[103] Degenhardt (2017)[104] Degenhardt (2023) Δ [105]	-
HIV prevalence	Baral (2012) [106] Papworth (2013)[107]	Baral (2007)[88] Papworth (2013)[107] Hessou (2019)[108]	Mathers (2008)[103] Degenhardt (2017)[104] Degenhardt (2023) Δ [105]	Kloek (2023) Δ [109]
ART coverage	Mountain (2014)[110]	Stannah (2019)[111] Stannah (2023) Δ [112]	-	-

HIV incidence	Mishra (2014)* [101] Jones & Anderson (2023) Δ [113]	Stannah (2023) Δ [112]	Artenie (2023) Δ [114]	-

* Doctoral thesis review, unpublished in peer-reviewed literature

Δ Published since the start of this thesis

1.7.1 Female sex workers

Regarding population size estimates for female sex workers, Vandepitte et al. (2006) reviewed 17 studies in nine countries 1997-2004. All were conducted using venue-based mapping methods and estimated that median 1.1% (range 0.4-4.3%) of the adult female population sold sex and remains widely cited.[100] Mishra (2014; Imperial College London PhD Thesis) included fifty studies, including responses to nationally-representative household surveys, with median 1.8% (range 0.25-13%) of adult women selling sex.[101] Recently, Laga et al. (2023) collated and modelled subnational population size proportions, estimating 1.1% (95%CI 0.8-1.3%) of adult women aged 15-49 sold sex.[102]

Regarding HIV prevalence, following the UNAIDS/WHO Second Generation Surveillance Guidelines few key population surveys were conducted between 2000-2007.[107] HIV prevalence among female sex workers was meta-analysed by Baral et al. (2012) including studies 2007-2011 from sixteen countries. The odds of HIV infection was 12 times higher in FSW than in nationally-matched adult women aged 15+. HIV prevalence exceeding 30% was found throughout sub-Saharan Africa which, while high, represented a steep decline from studies in the early epidemic.[106,107] ART coverage data among FSW was sparse; four studies in the early treatment era (2007-2010) from Kenya, Zimbabwe, and Burkina Faso report 20-70% of FSW were currently on treatment.[110] Jones & Anderson (2023) estimated that HIV incidence among FSW was eight times higher than in matched total population women (N studies = 32). Incidence

among FSW has declined steeply since 2000, parallel to incidence declines among matched total population women.[113]

1.7.2 Men who have sex with men

MSM population size estimates in sub-Saharan Africa have not been systematically compiled. The first studies recording HIV prevalence among MSM were published in the mid 2000s, almost 20 years after serosurveillance began among FSW.[88,115,116] Progress of MSM surveillance remained slow: by 2016 only 17 countries had HIV prevalence observations (N=17; median 15.8%), where HIV prevalence exceeds that among total population men by five-fold.[108] Stannah et al. (2023) reviewed ART status among all MSM living with HIV (N=26) and estimated 73% ART coverage in 2020, a significant increase from 10% in 2010.[112] Unlike declining HIV incidence among FSW, HIV incidence among MSM (N=39) has remained high in sub-Saharan Africa with the latest studies reporting in excess of 5 seroconversions/100py.[112]

1.7.3 People who inject drugs

Rolling reviews of global data on PWID conducted by Mathers and Degenhardt in 2008, 2017, and 2023 constitute all collated data among PWID in sub-Saharan Africa.[103–105] The latest review identified 23 countries with PWID PSEs and estimated that 0.21% (95%CI 0.11, 0.38) of adults inject drugs (0.05% of women, 0.38% of men). While the number of sub-Saharan African countries with evidence of injecting drug use rose from 13 in 2007 to 23 in 2023, the region remains the weakest globally for surveillance among PWID. Regional pooled HIV prevalence was 11.2% (95%CI 5.4, 19.0), with significantly higher HIV prevalence among women compared to men.[105] Artenie et al.[114] identified a single unpublished HIV incidence observation among PWID (2.6/100py) and ART coverage has not yet been reviewed.

1.7.4 Transgender women

HIV surveillance data among transgender women are particularly sparse. Cisgender MSM (cis-MSM) and transgender women (TGW) have historically been conflated within HIV surveillance in sub-Saharan Africa.[117,118] Up to one-third of respondents to surveys 2011-2016 in Western and Central Africa seeking to recruit cis-MSM using "individuals assigned male at birth who have reported recent sex with men" as study inclusion criteria identified as female or transgender.[119] HIV prevalence among TGW recruited as part of these eight cis-MSM surveys indicate high HIV prevalence (median 25%) and significantly higher than cis-MSM within the same survey.[119] Dedicated surveillance for transgender women has only emerged within the last 10 years: Baral *et al.* (2013)[120] and Poteat *et al.* (2016)[121] reviewed HIV prevalence among transgender populations globally but found no studies in sub-Saharan Africa. Kloek *et al.* (2023) identified ten HIV prevalence studies among TGW and found high HIV burden: eight-fold and two-fold higher than total population in WCA and ESA respectively.[109] There are no reviews available for PSE, ART coverage, or HIV incidence among TGW.

1.8 HIV surveillance

1.8.1 Evolution of HIV surveillance in African settings

AIDS case reporting using a clinical case definition, the presence of AIDS-defining illnesses, and subsequently an HIV diagnosis, formed the backbone of early HIV surveillance in the United States and Western Europe.[122] Reliant on widespread health clinic access and laboratory testing, this approach was unimplementable in sub-Saharan Africa.[122–124] Instead, in 1985, the WHO established a clinical definition for AIDS, applicable for clinical use in Africa with regionally prevalent AIDS-defining illnesses—the Bangui definition.[125] At the Bangui meeting, it was also recognised that due to a lack of laboratory capacity the creation of serological surveillance alongside

clinical reporting was paramount which should include “one or more serological and epidemiological surveys on the groups at high risk, such as prostitutes”.[125]

Serosurveillance among sentinel groups, including pregnant women, blood donors[78,126,127], the military, and STI clinic attendees[128,129], using unlinked anonymous testing (UAT) was rapidly scaled up across the continent.[126,130] UAT tested for HIV using blood drawn for a pre-existing purpose and, as the results were not linked or communicated back to the patient, did not require informed consent and results unaffected by participation bias relating to HIV stigma.[122,130] While well suited to epidemiological surveillance, UAT required easily accessible sentinel populations (i.e not key populations). As HIV epidemics matured, with HIV knowledge and testing more commonplace, surveillance from STI clinics and blood donors became increasingly challenging to interpret as population representative, and, by 1990, antenatal sentinel surveillance (ANC-SS) became the primary source of HIV surveillance data in the region, collected from a small number of clinics in each country that were often disproportionately in urban areas.[124,127,131] Interpretation of sentinel surveillance data focused whether sentinel data among pregnant women was generalisable. A significant body of research was dedicated to interpretation of ANC data, including characteristics of women not attending ANC clinics, fertility patterns of ANC attendees by HIV status, the age distribution of pregnant women, generalisability to men, and urban/rural heterogeneity.[132–136] Though the Bangui meeting sought to entrench surveillance among sex workers within national surveillance portfolios, key population surveillance was not attempted as part of sentinel surveillance, nor would it have been possible to generalise ANC data to the epidemics among key populations.

Throughout the 1990s, the generalised HIV epidemic response was guided primarily by ANC-SS data which was known to differ systematically from population-representative sources.[137–140] In 2000, to strengthen HIV surveillance among adults, particularly among men and in rural areas and to mitigate the biases associated ANC-SS data,

UNAIDS/WHO recommended that countries collect nationally-representative HIV prevalence data sampled using population-representative household surveys.[90,141–143] Demographic and Health Surveys (DHS) containing HIV testing were recommended to be conducted every 5 years and, as population-representative, were quickly considered the 'gold-standard' surveillance method.[142,144–146] Rich, participant-level data on sociodemographic characteristics, risk behaviour (including those associated with key population status), and spatial information, improved the assessment of the epidemic by age, sex, and geographic area. While ANC-SS has been superseded by routine testing at antenatal clinics (ANC-RT), ensuring that all pregnant women are tested for HIV and receive their results, and antiretroviral (ARV) metabolite and viral load testing have become available in Population-Based HIV Impact Assessments (PHIA) surveys, this surveillance paradigm has remained broadly unchanged since 2000.[147–152]

1.8.2 HIV surveillance among key populations

HIV surveillance among key populations differs substantially to that among the total population. There exists no accessible sentinel population through which we may monitor key population epidemics, nor is there a sampling frame through which we may conduct representative surveillance. Household surveys are inappropriate tools for key population surveillance for two reasons: (1) Questions on stigmatised identities and behaviours are met with high levels of non-response. DHS surveys commonly included questions regarding sex work and recent or lifetime sexual partners, and men could be asked whether they had a recent male sexual partner. [153,154] PHIA surveys conducted since 2016 asked the gender of three recent sexual partners and whether the respondent had received or given money or gifts for sex in the past twelve months.[153] Questions pertaining to key populations and stigmatised behaviours, however, are either routinely omitted by survey implementors, or experienced high levels of non-response from participants due to social desirability bias.[153,155] Further, studies which compared face-to-face interviewing (as is conducted for DHS and PHIA surveys) with

anonymised survey methods found significant underreporting of stigmatised behaviours, including engaging in commercial sex, injecting drug use, and homosexual sex;[156,157] and (2) Key populations are poorly captured by household-based sampling frames. Sex workers are mobile populations and move between urban centres for a renewed client base, and associated with trucking routes and transport networks.[158–161] Brothel- and bar-based sex workers may also live in-venue and not in sampled households. One-quarter of people who inject drugs in sub-Saharan Africa report recent homelessness and unstable housing.[104,105,162]

1.8.2.1 Sampling and recruitment methods

In the absence of a formal sampling frame for key populations which impedes the ability to conduct probability-based sampling, key population surveillance relies on non-probability sampling methods which fall into two categories: venue-based hotspot sampling and network-based sampling through peer recruitment.[163]

Venue-based sampling seeks to recruit key population members at known 'hotspots' such as brothels, bars, gay clubs, and harm reduction venues. Methodological approaches for venue-based sampling range in complexity from those that draw convenience samples of individuals who have attended a given venue, those that incorporate sample weights of venue attendance (e.g. Time Location Sampling[164]), to those that create a sampling frame of all known venues which can then be randomly sampled (e.g. Priorities for Local AIDS Control [PLACE][165]).

Network-based sampling, including snowball sampling and Respondent Driven Sampling (RDS), leverage social and sexual networks to access populations otherwise hidden to conventional or venue-based surveillance.[166] Chain referral uses a small number of "seed" participants chosen by study implementors recruit eligible individuals into the study, who in turn act as recruiters for the next wave of participants. The quality

of crude snowball sampling data is dependent on the choice of seed participants and whether they are within representative and generalisable networks. RDS builds on snowball sampling by controlling the distribution of recruitment coupons within each seed's network. By recording the sequence of participant recruitment, surveyed indicators may be statistically adjusted such that that a probability sample may be approximated with formal statistical properties.[167–170]

Significantly different samples are recruited by venue- and network-based sampling methods, with RDS reaching individuals at higher HIV risk: those with weaker social networks, not reached by HIV prevention and treatment services, and with lower educational attainment.[171–174] Accordingly, RDS has become the preferred gold-standard method for sampling hard-to-reach populations when seeking to describe the entire population. [175,176] Its correct implementation remains challenging, with careful formative assessment required as its probability sample approximation relies on several assumptions which are often breached by poorly implemented surveys.[177,178] While venue-based sampling will only sample visible individuals who attend venues, these methods have remained in use as they are quicker and cheaper to implement than RDS.[179–181]

Independent of sampling and recruitment method, surveys among key populations have been conducted predominately in urban areas where it is believed that most key populations may be found.[182–184] When rural locations are sampled, these are usually known sex work hotspots including border towns, mining sites, highways, and truck stops, and are unlikely to be representative of all rural areas.[185,186] This highly biased sampling strategy presents significant challenges for national- and district-level estimates requested by programmes, further discussed in Chapters 2 and 3.

1.8.2.2 Population size estimates

In addition to conducting biobehavioural surveys, key population surveillance portfolios are recommended additionally to include population size estimates (PSE) that quantify the total hidden population size as census-based denominators are unavailable.[182] Many methods exist for estimating population size with no consensus on a gold-standard method.[187,188]

Non-empirical methods

Population size may be estimated by educated guesswork including individual opinions of experts in the field, the Wisdom of the Crowds of key population members, or structured Delphi processes.[189,190] Literature estimates of population size estimate proportion (e.g. 1% of women aged 15-49 are FSW) from other settings can be combined with local census denominators.[190] These methods were historically prevalent within population size estimation, but are not recommended for use by UNAIDS and have since been superseded by more systematic methods, detailed below.[182]

Venue-based methods

Venue-based population size estimation, often referred to as mapping, enumerates the number of key population members in attendance. Crude enumeration of individuals is considered a non-empirical method by UNAIDS, while more complex methods adjust for the share of the population who attend selected venues, the proportion of individuals who attend multiple venues, and peak time variation.[182,191,192] Venue-based population size methods are unable to estimate statistical uncertainty, except those estimated within PLACE sampling.[165] Though the venue-based population size estimates will underestimate total key population size, they are widely used as proxies for the 'reachable' programmatic population when seeking to ascertain programmatic targets and unmet need.[179,191]

Capture recapture-based methods

Two-source capture recapture (2S-CRC) was originally used in ecological studies to estimate population size of plaice in the Atlantic in the 19th century. A sample of individuals is recruited ('captured') and released, and then a second sample recruited. A PSE can be calculated as the number sampled in the first capture divided by the proportion of individuals in the second capture who were sampled in both first and second rounds ('recaptured'). If the total population size is large, the proportion recaptured will be small.

This logic underpins all 'multiplier' PSE methods which constitute most key population PSEs in sub-Saharan Africa. These can be conducted as standalone surveillance exercises or twinned with an RDS survey, which is preferred as the proportion recaptured can be adjusted for network effects,[193] for example:

1) Object multiplier: Surveyors attend a bar known to be frequented by MSM and distribute a unique object (e.g. a bracelet) to all MSM who participate in the study (n1). Two weeks later they visit a similar, nearby bar and survey eligible MSM (n2) and record how many MSM received a bracelet two weeks earlier (n3);
2) Service multiplier: An RDS survey is conducted and respondents are asked if they are members of a named community organisation or attend a named key population programme (n3). The total roster of the organisation or programme acts as a sample, as does those recruited into the survey;
3) Event multiplier: Surveyors convene an event for female sex workers in the weeks preceding an RDS survey. Survey respondents are then asked if they attended the event.

The methodological assumptions required for 2S-CRC are frequently violated for key population size estimation, particularly that (1) the population is static between the two captures; (2) the two captures are independent of one another.[187] Captures cannot be

conducted on the same day as there would be no population mixing, but the further apart the captures in time and space the more severely Assumption 1 is violated. Adding a further capture – “three-source”, 3S-CRC – is a recent development in population size estimation methodology, which relaxes the requirement of capture independence and is viewed by some funders and survey implementors as the best available method.[194–196]

Network-based methods

Successive sampling population size estimation (SS-PSE) is a method for estimating population size from key population RDS survey chain data. Individuals with larger social networks are more likely to be recruited earlier in RDS chain referral as they have higher visibility, and total population size can be estimated from the sequence of referral and self-reported network size.[197]

The network scale up method (NSUM), distinct from all other PSE methods, uses total population respondents of nationally-representative household surveys to estimate key population size. Respondents are asked how many individuals they know belonging to benchmark populations (e.g. university students, butchers, furniture makers) and also each key population. Using the known, true number of benchmark populations from national census counts, respondent network size and the nationally-representative PSE proportion for each key population can be calculated.[198,199]

1.9 HIV estimation

1.9.1 UNAIDS-supported national estimates

Since early in the epidemic, mathematical models have been used to interpret HIV surveillance data and estimate current HIV burden and short-term projections of HIV prevalence and AIDS deaths. Initial WHO models were calibrated at the regional level[200] using two or more ANC-SS HIV prevalence observations over time, census populations, and HIV natural history. Country-specific estimates were first developed in 1997, delineated by concentrated or generalised epidemic status.[131] In concentrated epidemics, national estimates were calculated by summing separate epidemic curves fit to surveillance data and population size estimates among each sub-population; in generalised epidemics models were fit to ANC-SS data alone. In the absence of both size estimates and HIV prevalence data for key populations, adjustment and generalisability of ANC-SS-derived models to represent key populations was impossible.

Much has changed in the HIV epidemic response and its surveillance since these early models, most notably the development of antiretroviral treatment and HIV serosurveillance within nationally-representative household surveys. Estimates are now created annually by national HIV estimates teams and reported to UNAIDS for global reporting. Despite these changes, the modelling paradigm remains similar. The Estimates and Projection Package (EPP), the core HIV incidence estimation model used by national governments in Africa to create HIV estimates today, exists in two configurations: (i) EPP-concentrated, used in North African and some West African countries that experience low prevalence epidemics, accepts key population-stratified demographic and HIV surveillance inputs, and (ii) EPP-generalised, used throughout high prevalence epidemics in sub-Saharan Africa does not.[201–204] Within this paradigm, UNAIDS-supported incidence models for high prevalence HIV epidemics (EPP-generalised and its predecessors) have undergone continuous development: capturing changes in HIV dynamics after sharp declines in HIV incidence of the early 2000s[202,205,206], incorporating nationally-representative household survey data[203], demographic shifts in age patterns of HIV prevalence and treatment scale-up[202], ANC-

RT superseding ANC-SS data,[147,149,151] and the disaggregation of adult infections by age and sex calibrated to pooled, and subsequently country-specific, household survey HIV prevalence data[203,207–210]. Early versions of EPP estimated rural and urban areas as separate epidemics, capturing crude spatial dynamics, followed by more sophisticated modelling approaches to produce provincial and district-level HIV estimates.[201,211–214] These developments to UNAIDS-supported models have supported increasingly granular HIV estimates, but have been directed towards the dimensions of age, sex, and space. Key population-stratified estimates remain absent from the annual country-owned HIV estimates process in sub-Saharan Africa.

1.9.2 Key populations

1.9.2.1 Static models

Despite their omission from the annual estimates process, epidemic appraisals that sought to reflect key populations were conducted by many countries in sub-Saharan Africa from the late 2000s.[215] As part of UNAIDS' *Know Your Epidemic, Know Your Response* initiative, the Modes of Transmission (MoT) Model was developed to assist countries in understanding the distribution of new HIV infections.[216] The model stratified the population into total population groups, including low-risk heterosexual sex and casual heterosexual sex, and key population groups, including sex workers and their clients, and MSM and PWID and their partners. For each subpopulation, a single year projection of the number of new infections was derived using a population size estimate, partner contact rate and associated transmission risk, and partner HIV and STI prevalence. Though the model was easy to understand, it did not calibrate to subgroup HIV prevalence nor produce estimates with uncertainty, and was sensitive to uncertain model assumptions, including population size.[215,217,218] The MoT model was credited with raising the prominence of MSM and PWID within high prevalence epidemics in

Africa[215,216], previously thought to play little to no transmission role in these settings, but has since been critiqued as inappropriate for accurately communicating the role of key population transmission. As a 'static' model, one that produces estimates of single-year risk, the MoT results in sub-Saharan African settings concluded (correctly) that most new infections occurred within the total population.[215,218] Among 18 countries designated to have generalised epidemics, median 2% of new infections were estimated to occur in female sex workers and 7% among their clients.[217] As key populations comprise a very small proportion of the population, the maximum number of annual HIV acquisitions they could experience was always going to be a small fraction of the total, no matter how high their HIV acquisition risk. Subsequent analyses indicate that acquisition-based indicators and those that consider single-year estimation fail to identify populations among whom HIV prevention efforts should be focused.[219,220]

The Incidence Patterns Model (IPM), developed as a successor to the MoT, addressed some of these issues, introducing formal calibration to surveillance data and statistical uncertainty.[221] The MoT's single low risk total population group was stratified by marital, circumcision, treatment, and seroconcordancy status into seventeen groups better to reflect the proportion of new infections among those at lower risk, and in turn among key populations. In addition to HIV acquisitions per subgroup, the number of HIV transmissions per subgroup could also be calculated; an indicator that favours small population groups with weak access to HIV services. While these improvements were motivated by a desire to improve representation of key population transmission, a central reliance on DHS data to parameterise the seventeen total population groups, the omission of clients of female sex workers and partners of MSM and PWID, and the retention of MoT's single-year projection approach meant that the IPM remained an unsuitable model for key population estimation.[222]

1.9.2.2 Transmission dynamic models

Transmission dynamic models compartmentalise the population by demographic, risk, disease, and treatment statuses and reconstruct the complete epidemic, rather than conducting single-year disaggregation as above.

The Goals Risk Structured Model (Goals-RSM) and Optima models were designed to guide intervention planning and resource optimisation, and have been used globally to inform international stakeholder investment cases and target setting.[223–225] Accordingly, HIV interventions and their costings are represented in both models at high resolution, including behavioural interventions, condom distribution and promotion, school and workplace programmes, and HIV testing and treatment. FSW, MSM, and PWID are represented centrally in Optima, including compartments for clients of female sex work and injecting drug use disaggregated by gender, and additionally can reflect multiple risk behaviours (e.g. men who inject drugs can also buy sex). Though Goals-RSM includes compartments for FSW, CFSW, MSM, and PWID, it was not principally designed as a key population estimation model. Most importantly, it models adults as sex-stratified 15-49 age compartments which poorly reflects epidemic dynamics among key populations.[224] Neither model includes compartments for transgender people.

Where Goals-RSM and Optima were designed as targeting and intervention planning models, many country/city/population-specific models have also been developed as epidemic appraisal models. These generally represent epidemics including key population dynamics at the highest resolution, have a commensurately intensive data requirement, and are only applicable to the setting in question e.g.:

- PWID in Kenya [226] and Tanzania[227]: incorporating routine programme data on needle and syringe programmes and opioid substitution therapy, and requiring estimates of sexual mixing patterns by injecting status;
- Stratifying FSW and clients into repeat and occasional practice in eSwatini and Cote d'Ivoire[228,229];

- Stratifying MSM and sexual behaviour data by main and casual partners in South Africa and Cote d'Ivoire; and [229,230]
- FSW in Cotonou, Benin: varying adherence to HIV prevention[231]

Regardless of their parameterisation and epidemic setting, transmission dynamic models are preferred for appraising the role of key populations and potential epidemiologic impacts of prevention interventions reaching key populations as they can capture onward transmission and wider network effects of HIV infection among key populations. They can answer an important question: what is the future 'epidemic potential' of an HIV infection in each subpopulation group?[232,233] These questions underlie the "transmission population attributable fraction" (tPAF) indicator.[233] Where the classical PAF indicator calculates a proportion of cases associated with an exposure (e.g. lung cancer and smoking), tPAF applies the same process to a cumulative number of infections associated with an exposure (e.g. how many total infections can be attributed to sex between men, including all subsequent infections among MSM, bridging infections to women from bisexual men, and any vertical infections from those women etc). Calculation of tPAF requires a dynamically modelled counterfactual scenario (i.e. setting the HIV transmission risk of unprotected anal sex to zero) which enables the historical and future consequences of inadequately meeting the HIV prevention and treatment needs of key populations. Studies that have estimated the proportion of new infections over 10 years in generalised epidemics since 2005 identify wholly different intervention priorities compared to static models, particularly for FSW: 19-40% of new infections are associated with sex work and 4-35% associated with men having sex with men.[229,234–236]

1.10 Rekindling interest in key populations in SSA

1.10.1 Risk heterogeneity and treatment as prevention

The seminal HPTN 052 study among serodiscordant couples showed that ART not only prevented disease progression among PLHIV, but also prevented onward transmission, heralding the “treatment as prevention” era.[237] An influential modelling study by Granich and colleagues concluded that “universal voluntary HIV testing once a year of all people older than 15 years, combined with immediate ART after diagnosis” could eliminate a South Africa-like epidemic to <1 infection/1000py within a decade.[238] In 2014, building on this study, UNAIDS published the 90-90-90 targets to end the AIDS epidemic: that by 2020 90% of people living with HIV (PLHIV) should know their status, of whom 90% should be on treatment, of whom 90% should be virally suppressed.[239] While a useful proof of concept, the Granich model was highly simplistic, lacking strata for age, gender, or risk heterogeneity, and subsequent modelling exercises suggested a less optimistic future.[240,241] Their relation to reality notwithstanding, the targets were highly effective at shaping national HIV strategic planning, mobilising donor funding, and coordinating advocacy efforts, and were an essential component of the remarkable rise in ART coverage across high prevalence epidemics which now exceeds 90% in 10 countries.[242–244]

Though the individual-level benefits of ART have been unequivocally demonstrated, the results of the Universal Test and Treat (UTT) trials and slower-than-desired population level HIV incidence declines paint a more complex picture. [245–250] The UTT trials sought to generalise the findings of treatment as prevention on the individual-level to the population-level and show that HIV treatment reduced community HIV incidence. While the trial communities achieved high levels of viral load suppression and, in some settings, reduced HIV incidence relative to control communities, the expected HIV elimination threshold was not reached. The assumption that attaining population-level 90-90-90 would lead to proportionate declines in HIV incidence or even elimination relied on uniform risk within a population. Marginalised key populations among whom

HIV transmission is disproportionately concentrated may be more likely to be within the 27% who remain unsuppressed at 90-90-90, sustaining community transmission at very low population-level viremia.[251]

A recent review of transmission models quantifying the effect of treatment as prevention in sub-Saharan Africa found that zero of forty models considered lower ART coverage among key populations, including the Goals model used for UNAIDS Fast Track modelling and other international stakeholder analyses.[224,252,253] Leaving behind key populations, who constitute a small fraction of the total number of PLHIV and experience systematic barriers to engaging with care, in the epidemic response or its quantification could jeopardise a treatment-focused strategy to eliminating HIV.[228,254,255]

1.10.2 Equity in the HIV response

Equity and human rights have been core components of the HIV response since the 1980s.[72,256] Language on punitive laws, policies, and practices, stigma, and access to services is commonplace within UNAIDS/WHO guidance and member state-agreed text.[253,257–260] As it has become evident that there is significant heterogeneity in the success of the epidemic response, equity and key populations have become increasingly central within United Nations Global AIDS Strategies, annual UNAIDS Global AIDS Reports, and international donor strategies.[253,259,261,262] The 2021-2016 Strategy *End Inequalities. End AIDS* calls to “maximise equitable and equal access to HIV services and solutions”, including primary HIV prevention for key populations and that key populations “know their HIV status and are immediately offered and retained in quality, integrated HIV treatment and care that optimize health and well-being”.[259] Within the 2021 United Nations Political Declaration on HIV/AIDS, member states agreed the 10-10-10 targets by 2025: fewer than 10% of countries should have punitive legal and policy environments that deny or limit access to services, fewer than 10% of PLHIV and key populations will experience stigma and discrimination, and less than 10% of

women, girls, PLHIV, and key populations will experience gender inequality and violence.[260,263]

1.10.3 International donor funding and National Strategic Planning

Key populations rose in prominence in National Strategic Plans (NSPs) through the 2010s. A majority of funding proposals received between 2007-2010 by The Global Fund and the US President's Emergency Plan for AIDS Relief (PEPFAR) proposed routine HIV programming for FSW, but only a quarter proposed programmes among MSM, and 10% among PWID.[264] MSM and PWID did not appear in any proposals before 2007. By 2012, two-thirds of NSPs mentioned MSM as a priority population, despite a near-absence of population size and HIV prevalence data contained within them.[265] In 2013, The Global Fund mandated inclusion of key populations within funding requests, with particular focus on provision of harm reduction interventions and population size estimation.[46,266] PEPFAR 3.0 (2014) and Global Fund's 2012-2016 and 2017-2022 strategies continued to support routine programme services for key populations but also expanded support for biobehavioural surveillance and population size estimation.[176,262,267] A 2018 WHO review of NSPs in sub-Saharan Africa found a changed landscape: all mentioned FSW (two-thirds included HIV prevalence data, fewer than 10% included population size); 92% mentioned MSM (of which half included HIV prevalence data, fewer than 10% included population size); 84% mentioned PWID (one-third included HIV prevalence, fewer than 10% included population size); and 23% mentioned TGW (HIV prevalence data from Sierra Leone only).[268] While policy pertaining to key populations had become increasingly visible, data use remained weak with population size estimates particularly overlooked in programme planning and funding requests.[269]

1.11 The ecosystem of HIV data reporting and the UNAIDS estimates process

1.11.1 HIV data reporting

Global HIV data reporting is centred around UNAIDS Global AIDS Monitoring [118,270], an annual process through which countries are invited to submit an array of quantitative and qualitative epidemic information. These include modelled epidemic estimates, information on financing the response, laws and policies (including NCPI data), and dedicated sections on inequalities and key populations. Many data elements concerning epidemic monitoring are created during the UNAIDS estimates and, to minimise the reporting burden on countries, are extracted directly from its modelling tools. All data are made publicly available at aidsinfo.unaids.org and are used within UNAIDS Global AIDS Update reports. Though countries are strongly encouraged to engage annually with GAM reporting, there is no obligation to do so, nor are any data elements considered mandatory to finalise a GAM submission.

1.11.2 The annual UNAIDS process and Spectrum: creating total population estimates

UNAIDS supports a year-end process through which national HIV estimates teams create HIV estimates on which to base the following year's policymaking and programming using the Spectrum suite of modelling tools.[271] Spectrum is a cohort-component demographic model with disease-specific modules, including HIV, that sit on top of the demographic engine. Each year, the Spectrum models receive incremental methodological updates to improve existing estimates and add new indicators or models. Week-long in-person estimates workshops are convened biennially to train HIV estimates teams on the software and its latest changes, with remote support guiding

teams in non-workshop years. HIV estimates teams consist of six to ten representatives usually from the Ministry of Health, National AIDS Councils, National Statistics Office, UNAIDS Country Office, and US Government country staff from CDC, USAID, and PEPFAR. Workshop facilitators support national teams to recalibrate the epidemic models using the latest ART, ANC, HIV testing, and – if available – household survey data to create HIV estimates for the year ahead. This can be an arduous task. Treatment programmes have reached high levels of attainment, and small differences in programme enumeration can tip ART or PMTCT coverage above 100%. District-level epidemic models can require thousands of rows of data and can fail to calibrate if given implausible calibration data. Each issue requires careful consideration of data, discussion with programme teams, and consultation with technical experts. As the models have grown in complexity, estimates workshops become increasingly focused on data review and validation. To reduce transcription errors, routine health service data are automatically extracted from health information systems into data repositories, and data review is facilitated by visualisation tools integrated into modelling software.[272,273] This culminates in epidemic estimates for the total population stratified by district, sex, and age group, with a headline package of estimates including adult HIV prevalence, the treatment cascade, HIV incidence, and mother-to-child transmission rate signed off by the Minister of Health. These estimates are widely consumed by national programmes and international stakeholders and funders. They are finalised and submitted to UNAIDS in the Spring, and, providing they receive assent from both the Ministry of Health and UNAIDS, published in the UNAIDS Global AIDS Update report in the Summer.

1.11.3 Global reporting of key population surveillance data

The UNAIDS workflow for key population data and estimates differs considerably from the total population estimates process. Key population surveillance studies fall into two categories: (1) Surveillance studies conducted by national public health authorities (e.g.

biobehavioural surveys), primarily disseminated as grey literature reports and (2) studies conducted by academic institutions and research groups, primarily disseminated in peer-reviewed journals. Biobehavioural survey data constitute the majority of key population surveillance data submitted to GAM while academic studies are rarely drawn upon as strategic information by HIV estimates teams or submitted to GAM.[182,269] Dissimilar to nationally-representative household surveys, there exists no systematically collated database of key population surveillance, nor are estimates teams provided with tools with which to manage or interrogate key population surveillance data.

UNAIDS and The Global Fund reviewed coverage of population size estimates 2010-2014[182] and HIV prevalence data 2001-2017 [184] collated in SSA within GAM or submitted to The Global Fund within funding requests or grant monitoring. Two-thirds (26/39) of countries had a PSE for FSW, half had a PSE for MSM (22/39), and a fifth for PWID (7/39). HIV prevalence data were more widely available: nearly all countries had data among FSW, though most were outdated observations without trends; three-quarters had data among MSM; one-third among PWID; and 10% among TGW. The UNAIDS and Global Fund reviews focused on data coverage and availability: neither the estimates themselves nor their methods were published. PSE data were designated "nationally adequate" if derived using an empirical method, conducted in three or more locations, and extrapolated to national level, and HIV prevalence data if more than half of provinces had data no older than 2015. Only one quarter of countries (10/39) received this designation for PSE within a key population, none of which were highest burden Southern African countries. Niger, Benin, and Cameroon were denoted nationally adequate for HIV prevalence among FSW, while no countries had nationally adequate data among MSM, PWID, and TGW.

Population size estimates submitted to GAM have been published in UNAIDS Global AIDS Update reports[274–276], and presented as the proportion of the national population aged 15-49 among countries for which GAM reported estimates were designated

nationally adequate. In 2020, UNAIDS/WHO recommended that MSM size estimates should be larger than 1% of the 15-49 total male population and that the reporting of national-level estimates that do not meet this threshold would be suppressed.[277] Nineteen national-level PSEs have been published within UNAIDS Global AIDS Update reports:

- FSW (N=7): median 0.87% of 15-49 women, range 0.41-1.49%;
- MSM (N=7): median 1.25% of 15-49 men, range 0.82-1.90%;
- PWID (N=4): median 0.36% of 15-49 men, range 0.02-0.79%; and
- TGW (South Africa only): 1.06% of 15-49 women

HIV prevalence submitted to GAM has been included in Global AIDS Update reports since 2018, with each report containing data from the four years preceding it. HIV prevalence among FSW from 2014-2021 was between 30-40% in ESA and around 10% in WCA, 3-4fold higher than total population women in both regions (Figure 1.2). MSM HIV prevalence was similar across ESA and WCA around 12%, twice total male prevalence in ESA and 10fold higher in WCA. PWID HIV prevalence was 3-4fold higher than total male prevalence (~20% in ESA, ~4% in WCA). TGW HIV prevalence was ~25% in ESA and ~15% in WCA, though data across the region were sparse.

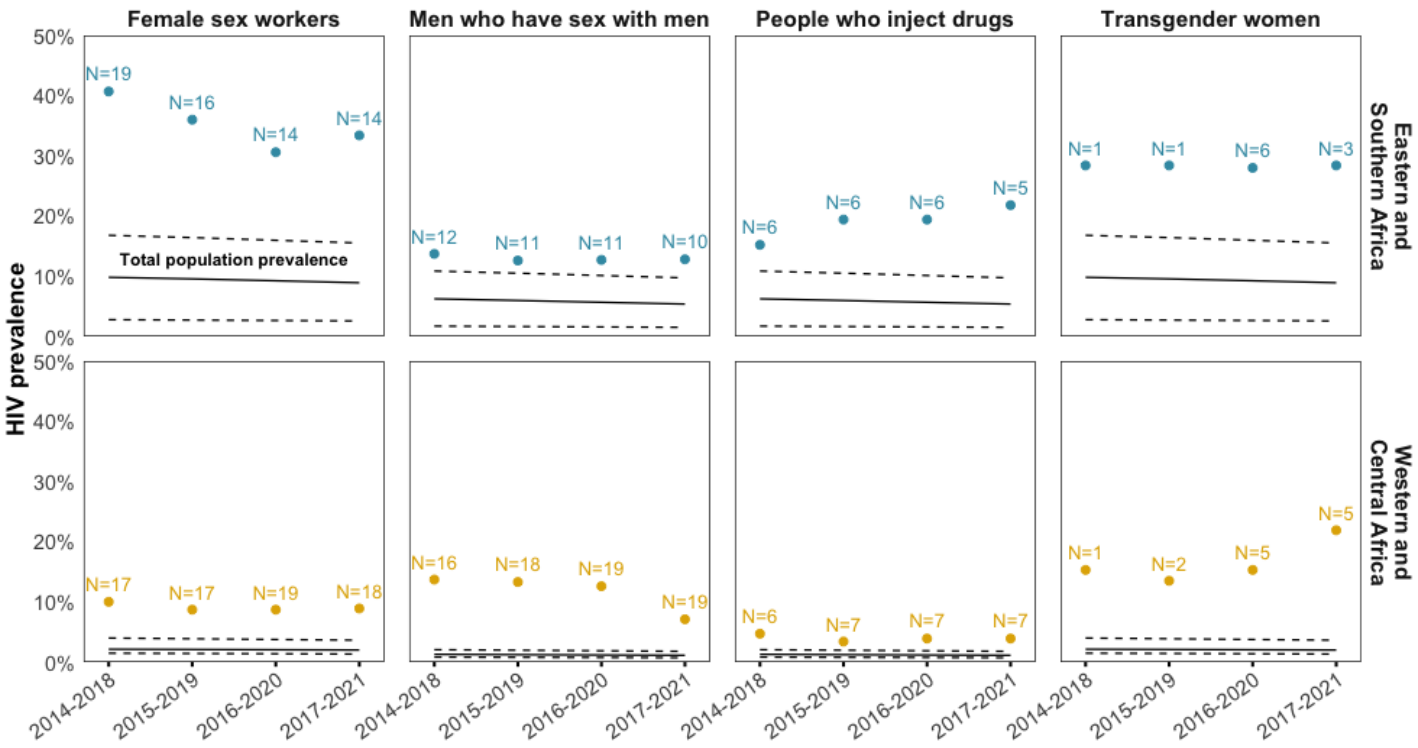


Figure 1.2: Key population HIV prevalence published in UNAIDS Global AIDS Update reports.
Coloured points represent mean key population HIV prevalence during a four-year window from UNAIDS Global AIDS reports 2018-2021[275,276,278,279]. Points should not be interpreted as a trend due to changing country composition of the mean. Annotated numbers denote number of countries contributing to the mean estimate. Grey line represents the gender-matched median national total population HIV prevalence and interquartile range (dashed line) extracted from national HIV estimate Spectrum files.[280] FSW and TGW matched to women, MSM and PWID matched to men.

1.11.4 UNAIDS key population estimates in sub-Saharan Africa

Since 2014, UNAIDS has produced regional estimates of the distribution of new HIV infections by population subgroup using 'nationally adequate' data submitted to GAM and a synthesis of model-based estimates. The methods are not publicly available and as the national composition of data—and undisclosed methods and assumptions—changes each year, estimates over time should not be interpreted as trends. These

estimates are created centrally in Geneva and are considered an interim approach on the road towards country-specific estimates of new HIV infections by subpopulation group. Unlike total population estimates, they are created without involvement of country HIV estimates teams, nor are they used within national planning or receive ministerial signoff. In sub-Saharan Africa in 2021, UNAIDS reported that 50% of new acquired HIV infections were among key populations (24%) and their sexual partners and clients (26%; Figure 1.1), compared to around 15-20% in UNAIDS reports published in 2015-2017. Further consideration to these estimates are given in Chapter 5.

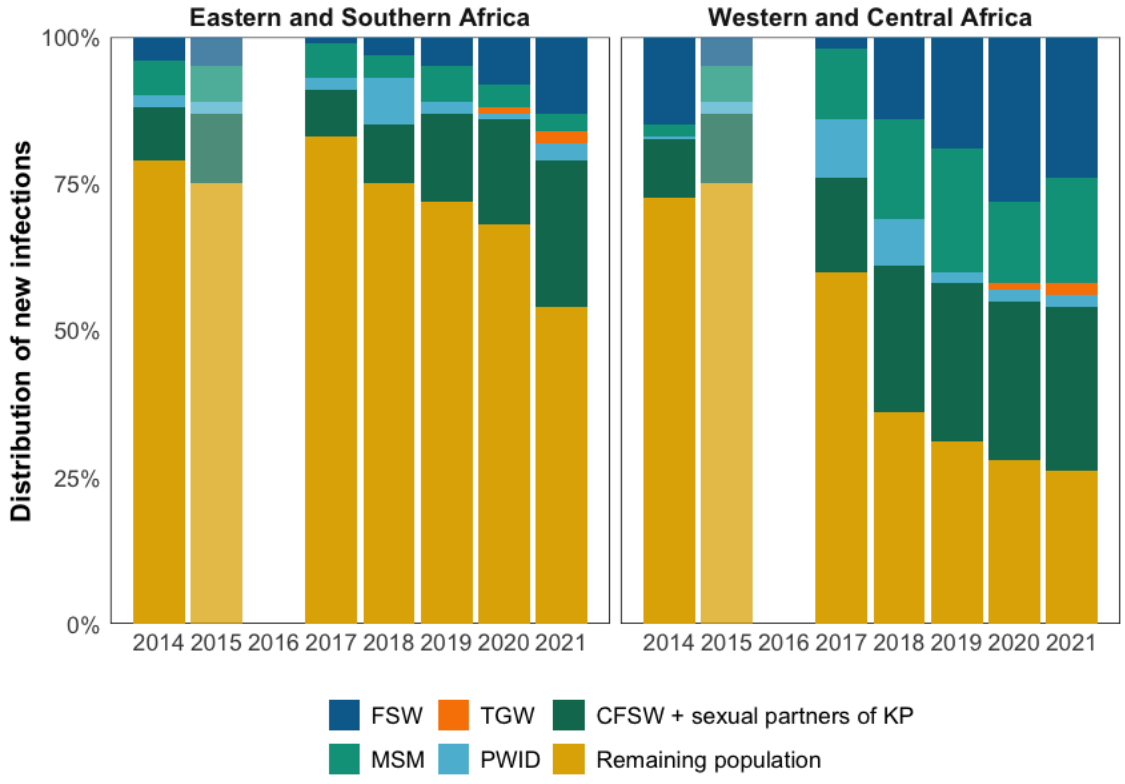


Figure 1.1: The distribution of new infections by population group in Eastern and Southern Africa (ESA) and Western and Central Africa (WCA) published by UNAIDS. Data extracted from UNAIDS Global AIDS Reports.[242,274–276,278,279,281] Pooled estimates for sub-Saharan Africa shown for 2015 (pale shading) as estimates disaggregated by ESA and WCA

unavailable. No estimates available for 2016. Estimates for transgender women available from 2020 onwards.

1.12 Thesis

Data systems in sub-Saharan Africa have strengthened and the generalised/concentrated epidemic dichotomy has became increasingly blurred. In this context, the delineation of UNAIDS incidence models by data availability and epidemic type was expected to fail to meet the future strategic information needs of national HIV estimates teams. The long-term UNAIDS model development strategy seeks to integrate global incidence approaches into a single model which could ingest all types of surveillance data and produce estimates for all population groups.

The UNAIDS Reference Group on Estimates, Modelling, and Projections, through which this work was supported, provides technical advice and model development to UNAIDS in support of the annual HIV estimates process. In April 2021, in line with the aims of the recently published Global AIDS Strategy 2021-2026, the Reference Group sought to:

1. Develop an appropriate modelling tool and workflow for key population stratified estimates for as part of 2022 estimates in sub-Saharan Africa.
2. Review key population data sources and analytical methods in sub-Saharan Africa and develop a consensus guidance and checklist for key population data and assumptions into key population-stratified estimates.
3. Reach recommendations about indicator definitions and programmatic use cases to guide model develop priorities for key population stratified estimation models.

However, the state of play was: (1) no data system that systematically collated and validated key population surveillance data; (2) outdated systematic reviews with weak indicator and population coverage (with many population-indicator combinations wholly absent); (3) weak key population data ownership and use within national programmes;

and (4) poor or non-availability of methods and tools to translate surveillance data into programme-actionable estimates outside the most data-rich settings, particularly for HIV incidence. Accordingly, the overarching objective for this thesis was to lay the foundations for introducing country-specific key population stratified estimates of equal rigour to the total population HIV estimates within the UNAIDS estimates process.

The first half of the thesis focuses on data: what exists, where is it, how can we facilitate estimates teams to engage with it, and to encourage a data-driven approach to key population policymaking. Chapter 2 collates available data on key population size estimates, HIV prevalence, and ART coverage data in sub-Saharan Africa from 2010-2023, and estimates these three indicators at national-level for all mainland countries in the region. In Chapter 3, I introduce and critically review the UNAIDS Key Population Workbook, the tool I created for use within the annual UNAIDS estimates cycle. In Chapter 4, I estimate relative HIV prevalence among transgender women and cis-gender men who have sex with men.

The second half considers HIV incidence; how may systematically collated surveillance data improve estimates of HIV incidence, ensure internal consistency between indicators, and expanding total population-based methods to estimate incidence from cross-sectional prevalence. In Chapter 5, I compare empirical and model-based estimates of HIV incidence among key populations with prevailing UNAIDS estimates. In Chapter 6, I estimate HIV incidence among female sex workers in Cotonou from individual-level survey data. In Chapter 7, I discuss the thesis findings in the context of recent profound funding cuts to the HIV response and consider future directions.

2. Population size, HIV prevalence, and antiretroviral therapy coverage among key populations in sub-Saharan Africa: collation and synthesis of survey data 2010-2023

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- Dr. Jinkou Zhao (The Global Fund surveillance database);
- Dr. Kalai Willis (Global.HIV);
- Dr. James Stannah (McGill University; 2019 and 2023 systematic reviews among MSM); and
- Prof. Louisa Degenhardt (University of New South Wales; 2017 and 2023 systematic reviews among PWID)

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Participants of the UNAIDS Reference Group and my co-authors on the Lancet Global Health manuscript detailed below provided close review and thoughtful feedback on the analysis and manuscript.

I led on data extraction, conceptualising analysis, model development, and manuscript drafting with advice and support from Drs. Jeff Imai-Eaton, Mary Mahy, and Keith Sabin.

Dissemination

The analysis was presented at UNAIDS Reference Group meetings in May 2022 (Glion, Switzerland) and October 2022 (virtual). Some results from this chapter were presented at AIDS2022 in Montreal as a poster presentation (Disproportionate HIV burden among key populations in sub-Saharan Africa: national estimates of population size, HIV prevalence, and ART coverage; abstract number PESCUC18). The manuscript was made available as a pre-print in 2022 (https://doi.org/10.1101/2022.07.27.22278071) and subsequently published in The Lancet Global Health in 2024:

Stevens, O., Sabin, K., Garcia, S. A., Anderson, R., Willis, K., Rao, A., McIntyre, A., Fearon, E., Grard, E., Stuart-Brown, A., Cowan, F., Degenhardt, L., Zhao, J., Hakim, A., Rucinski, K., Sathane, I., Boothe, M., Atuhaire, L., Nyasulu, P., … Imai-Eaton, J. W. (2024). Key population size, HIV prevalence, and ART coverage in sub-Saharan Africa: systematic collation and synthesis of survey data, 2010-23. *Lancet Global Health*, *12*. https://doi.org/10.1016/S2214-109X(24)00236-5

2.1 Introduction

Key populations, including female sex workers (FSW), gay men and other men who have sex with men (MSM), people who inject drugs (PWID), and transgender people, experience higher risk of acquiring and transmitting HIV due to a combination of biological and sociostructural factors, including stigma and criminalisation.[282–284] The Global AIDS Strategy 2021-2026 calls for "equitable and equal access" to HIV prevention and treatment to reduce HIV incidence and end HIV/AIDS as a public health threat by 2030.[285] Delivering evidence-based HIV services for key populations and monitoring attainment of an equitable HIV response requires robust epidemiologic and service engagement indicators, including key population size, HIV prevalence and incidence, treatment and prevention cascades. For this reason, key population surveys, including population size estimation and bio-behavioural surveys, are a standard component of comprehensive national HIV surveillance.

Key population survey data are sparse and less representative of their target population than common general population sampling approaches such as national household surveys or sentinel surveillance. Key population surveys often rely on respondent-driven and venue-based sampling methods[286,287] which require strong assumptions to interpret as population-representative. Household survey sampling frames are inappropriate for reaching populations that are mobile and unlikely to disclose risk behaviour due to societal marginalisation and discrimination.[288–290] Key population surveys are often infrequent and commonly restricted to, or disproportionately conducted in, urban areas.

Systematic reviews and meta-analyses of population size, HIV prevalence, or antiretroviral therapy (ART) coverage encompassing sub-Saharan Africa (SSA) have been conducted for FSW,[291,292] MSM,[293,294] PWID,[295,296] and transgender women (TGW).[297,298] These studies have tended to focus on specific outcomes or population groups of interest, and primarily comprise an appraisal of peer-reviewed literature.

Several complementary ongoing initiatives consolidate HIV data on key populations to support programme planning and implementation, global advocacy, and research. These include the Key Population Atlas and Global AIDS Monitoring (Joint United Nations Programme on HIV/AIDS [UNAIDS]), databases maintained by the US Centers for Disease Control and Prevention (CDC) and The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund), and the Global.HIV initiative (Johns Hopkins University).[299–302] These efforts aim to monitor the state of the epidemic, evaluate programmes, and make recommendations on key population data reporting and quality thresholds. These include similar data sources, but vary in scope, inclusion criteria, data elements recorded, and linkage to and validation against primary source reports. Incomplete recording of key methodological details limits appraisal and formal evidence synthesis, and therefore utility of data for strategic planning.

I consolidated and harmonised key population size estimates (KPSE), HIV prevalence, and ART coverage data from existing databases and described data availability across countries and over time for each key population. I characterised the relationship between key population and total population HIV indicators and extrapolated KPSE, HIV prevalence, and ART coverage data to national-level estimates for mainland countries in SSA.

2.2 Methods

2.2.1 Data sources and extraction

I consolidated data from studies conducted 2010-2023 from four existing databases and two systematic reviews among FSW, MSM, PWID, and transgender people.[294,303] Data among incarcerated people were not included as part of this review. The existing databases were the Joint United Nations Programme on HIV/AIDS (UNAIDS) Global AIDS Monitoring submissions,[304] UNAIDS Key Population Atlas,[305] the Global Fund to

Fight AIDS, Tuberculosis and Malaria (the Global Fund) surveillance database, and a dataset maintained by the US Centers for Disease Control and Prevention (CDC) Division of Global HIV & TB Key Population Surveillance Team (Supplementary Table S2.1). For each observation, I extracted information about the study methodology, study location (country, subnational location), study population gender and age group, central estimate, sample size, standard error, and primary source or reference (e.g., survey report) (Supplementary Table S2.2).

Source documents were compiled from archives accompanying each database, the Johns Hopkins University Global.HIV document repository,[306] Medline, and Google Scholar, following which I contacted UNAIDS Strategic Information advisors and other HIV programme contacts in each country to seek missing reports. I reviewed source documents to deduplicate observations recorded in multiple databases, validate against sources, and extract missing data elements. During source review, I added observations when additional relevant data were reported, or additional sources were ascertained that were not in the initial databases.

Observations were excluded if: key population definition, year, or study area were missing; the study area was non-specific (e.g., ‘urban areas’ or ‘5 provinces’); estimates were modelled or extrapolated; or data could not be confirmed by primary source review. There were no age group eligibility criteria for inclusion in analysis. Studies were not excluded or differentiated in this analysis according to study-specific population group definitions based on engaging in risk behaviours or time periods (e.g. sold sex in the last 6 months versus last 12 months; Supplementary Text S2.1). Transgender men (TGM) were not analysed or reported here due to insufficient data, but available observations are included in supplementary datasets (https://zenodo.org/records/10838438).

2.2.2 Data processing

To facilitate comparison of population sizes across settings, KPSE reported as counts were converted to population proportions. Each KPSE was matched to the total population denominator by age, gender, year, and area. String matching was used to assign each survey area to geographic boundaries from the Global Rural/Urban Mapping Project (GRUMP) or UNAIDS Naomi subnational district populations. Where string matches were found for both GRUMP and Naomi subnational district populations, GRUMP populations were used. Each KPSE was matched to the total population denominator[307–309] by age, gender, year, and area, and assigned to one of seven method categories:[310]

- 2S-CRC: two-source capture-recapture methods included object, service, and event multiplier methods.
- 3S-CRC: three-source capture-recapture.
- PLACE/mapping: consisted of estimates using the Priorities for Local AIDS Control Efforts (PLACE) methodology and other programmatic/hotspot mapping derived estimates.
- NSUM: network scale-up methods.
- SS-PSE: successive sampling population size estimates, e.g. respondent-driven or snowball sampling.

Within a single survey, multiple size estimation methods were commonly conducted and combined into a final consensus KPSE; where possible, separate estimates for each method were extracted. For cases where only a final estimate of multiple methods was reported, two further categories were defined: “Multiple methods – empirical” or “Multiple methods – mixture”. The former contained estimates derived from multiple of the five methods above, while the latter were derived from both empirical and non-empirical methods (enumeration, wisdom of the crowds, key informant interviews, and

the Delphi method). KPSEs derived by solely non-empirical methods were excluded from analyses.

Age stratified data were missing from nearly all key population reports; missing age ranges were assigned as age 15-49 years. Unless gender was specified, PWID were assumed to be men as 90% of people who inject drugs in sub-Saharan Africa are men.[303] Surveys among transgender people which did not report gender were assumed to be among transgender women because respondents often reported high prevalence of male partners and receptive anal intercourse, and surveys among TGM in SSA remain rare.[298]

Key population HIV prevalence and ART coverage observations were compared to total population HIV prevalence or ART coverage, respectively, matched by age, gender, year, and first administrative level (henceforth 'province'). Provincial age/gender-specific HIV prevalence and ART coverage were extracted from UNAIDS Naomi subnational estimates for 2022 and projected backwards 2000-2021 parallel to national HIV prevalence and ART coverage trajectories among adults 15-49 years.[311] Only serologically-determined HIV prevalence observations were included in analysis.

Key population ART coverage observations derived from populations with self-reported HIV-positive status or clinic-based recruitment were excluded. ART usage was determined through either self-report or laboratory methods via antiretroviral (ARV) metabolite biomarker or viral load (VL) testing. Viral load suppression (VLS) observations were standardised using a reporting threshold of 1000 copies/ml.[312] In cases where surveys measured both ARV biomarker and VL, ARV biomarker was used. VLS observations were converted to estimates of ART coverage assuming a logit difference of -0.32, the average difference from studies that measured both viral load and metabolite-confirmed ARV status (Supplementary Text S2.3).

2.2.3 Analysis

2.2.3.1 Key population size

I modelled urban key population sizes as a proportion of the total adult population aged 15-49 with a Bayesian spatial mixed-effects logistic regression model. FSW and TGW were matched to women total population size denominator, and MSM and PWID to men. Spatial smoothing allowed population proportions to be correlated between geographically neighbouring provinces. Each key population was modelled with separate regression models. Logit population proportion was assumed to be normally distributed with mean $\mu_{i,x}$ (province $i \in 1,2,\dots n_{provinces}$ and country $x \in 1,2,\dots,39$) and standard deviation σ. The mean $\mu_{i,x}$ was modelled as a linear function including an intercept β_0, a fixed effect for study method, X_m for $m \in$ {Empirical, PLACE/Mapping} using empirical methods as the reference category, an independent and identically distributed (iid) random effect for study method, δ_j for $j \in$ {2S-CRC, 3S-CRC, network scaleup, SS-PSE, multiple methods (empirical), multiple methods (mixed)}, an intrinsic conditional autoregressive (ICAR) spatial smoothing random effect at the provincial and national levels, θ_i and η_x, respectively, and a study iid random effect, ϵ_s for $s \in 1,2,\dots,n_{studies}$.

$$\text{logit}\left(p_{i,x,M,j,s}\right) \sim N\left(\mu_{i,x,M,j,s}, \sigma\right)$$

$$\mu_{i,x,M,j,s} = \beta_0 + \beta_1 X_m + \delta_j + \theta_i + \eta_x + \epsilon_s$$

$$\beta_0, \beta_1 \sim N(0,5)$$

$$\theta_i \sim ICAR(\sigma_\theta)$$

$$\eta_x \sim ICAR\left(\sigma_\eta\right)$$

$$\delta_j \sim \text{N}(0, \sigma_\delta)$$

$$\epsilon_s \sim N(0, \sigma_\epsilon)$$

National KPSE counts were extrapolated using urban KPSE proportions, the proportion of the population living in urban areas,[313] and the assumed rural-to-urban ratio of key population size.

$$PSE_{i,urban} = p_i \times population_i \times urban\%_i$$

$$PSE_{i,rural} = (p_i \times R{:}U\ ratio) \times population_i \times (1 - urban\%_i)$$

$$PSE_i = PSE_{i,urban} + PSE_{i,rural}$$

The rural-to-urban ratio was assumed to be a $Beta(5,3)$ distribution, which had mean ratio of 0.6 and 80% of the mass between 0.4 and 0.8, allowing wide uncertainty to be propagated into the estimates of $PSE_{i,rural}$. Qualitative data indicate that KPSE proportions are higher in urban areas than rural areas, but no empirical data were available to quantify the rural-to-urban ratio.[314–316] The rural-to-urban ratio was assumed to be a $Beta(5,3)$ distribution, which had mean ratio of 0.6 and 80% of the mass between 0.4 and 0.8, allowing wide uncertainty to be propagated into the estimates of $PSE_{i,rural}$.

2.2.3.2 *Key population HIV prevalence*

I modelled the relationship between key population HIV prevalence and sex-matched total population HIV prevalence (age 15-49 years) in the same province region separately for FSW and PWID, and together for MSM and TGW.

The number of key population members living with HIV, $X_{i,t,x,R}$, is assumed to follow a beta-binomial distribution with expected HIV prevalence, $p_{i,t,x,R}$ for a given province i, year t, country x, and region $R \in \{\text{ESA}, \text{WCA}\}$. Logit transformed prevalence $logit(p_{i,t,x,R})$ is expressed in a linear model with an intercept β_0, fixed effects for matched total population HIV prevalence $logit(\rho_{i,t,x,R})$; region $R \in ESA, WCA$; an interaction between matched total population HIV prevalence and region; an intrinsic conditional autoregressive (ICAR) spatial smoothing random effect at the provincial and national

levels, θ_i for $i \in 1,2,\ldots n_{provinces}$ and η_x for $x \in 1,2 \ldots 39$ respectively, and a study *iid* random effect, ϵ_s for $s \in 1,2, \ldots, n$.

$$X_{t,i,x,R,s} \sim BetaBinomial(n, p_{t,i,x,R,s})$$

$$logit(p_{t,i,x,R,s}) = \beta_0 + \beta_1 logit(\rho_{t,i,x,R}) + \beta_2 R + \beta_3 logit(\rho_{t,i,x,R}) \times R + \theta_i + \eta_x + \epsilon_s$$

HIV prevalence among TGW and MSM were modelled in a single regression. A fixed effect for KP $KP \in \{MSM, TGW\}$ and two interaction terms were added (matched total population HIV prevalence and key population; and region and key population) to permit KP-specific trends:

$$logit(p_{KP,t,i,x,R,s}) = \beta_0 + \beta_1 logit(\rho_{t,i,x,R}) + \beta_2 R + \beta_3 logit(\rho_{t,i,x,R}) \times R + \theta_i + \eta_x + \epsilon_s + \beta_4 KP + \beta_5 logit(\rho_{t,i,x,R}) \times KP + \beta_6 \mathrm{KP} \times R$$

$$\beta_{0:6} \sim N(0,5)$$
$$\theta_i \sim ICAR(\sigma_\theta)$$
$$\eta_x \sim ICAR(\sigma_\eta)$$
$$\epsilon_s \sim N(0, \sigma_\epsilon)$$

2.2.3.3 Key population ART coverage

I modelled key population ART coverage as a function of total population ART coverage, analogously to HIV prevalence. All key populations were modelled together. The observed number on ART, $A_{KP,t,x,i}$, was assumed to have a beta-binomial distribution with the probability of being on treatment, $p_{KP,a,t,x,i}$, for a given key population KP, year t, country x, and province i. $logit(p_{KP,t,x,i})$ was modelled as a linear equation with intercept β_0, fixed effect for matched total population ART coverage, random intercept for each key population $KP \in \{FSW, MSM, PWID, TGW\}$, random slopes matched total population ART coverage by key population, an intrinsic conditional autoregressive (ICAR) spatial smoothing random effect at the provincial and national levels, θ_i for $i \in 1,2, \ldots, n_{provinces}$ and η_x for $x \in 1,2, \ldots,39$ respectively, and a

study *iid* random effect, ϵ_s for $s \in 1,2,\ldots,n$. Insufficient data were available to estimate region-specific trends.

$$A_{KP,t,x,i,s} \sim BetaBinomial(n, p_{KP,t,x,i,s})$$
$$logit(p_{KP,t,x,i,s}) = \beta_0 + \beta_1 logit(\alpha_{t,x,i}) + u_{0KP} + u_{1KP} logit(\alpha_{t,x,i}) + \theta_i + \eta_x + \epsilon_s$$
$$\beta_0, \beta_1 \sim N(0,5)$$
$$u_{0KP} \sim N(0, \sigma_{u_0})$$
$$u_1 \sim N(0, \sigma_{u_1})$$
$$\theta_i \sim ICAR(\sigma_\theta)$$
$$\eta_x \sim ICAR(\sigma_\eta)$$
$$\epsilon_s \sim N(0, \sigma_\epsilon)$$

In sensitivity analysis, I added a fixed effect for study method, M where $M = 0$ for laboratory confirmed ART and $M = 1$ for self-reported ART usage.

I conducted sensitivity analyses in which self-reported ART coverage data were also included. For all three models (KPSE, prevalence, ART coverage) in sensitivity analysis I used ages 15-29 years as the matched total population denominator for MSM and TGW regression analyses, and 15-39 years for FSW, reflecting the younger median age of survey respondents.[317,318]

I combined national KPSE, HIV prevalence, and ART coverage estimates to calculate the number of KPLHIV and on ART. Ninety-five percent credible intervals were generated by combining 1000 posterior samples for each outcome. I calculated 1000 regional median KPSE differences from each of the posterior samples of national KPSE proportions, and calculated 95% credible intervals by combining the 1000 regional median differences. KPLHIV estimates were divided by estimates of the total PLHIV

aged 15-49 years from 2022 national UNAIDS estimates to calculate the proportion of all PLHIV associated with each key population.[319]

Data were extracted, deduplicated, and validated in Microsoft Excel. Statistical analyses were conducted in R version 4.2.0 using the R-INLA package (v23.4.24). [316]

This study received ethical approval from the Imperial College Research Integrity and Governance Team (ICREC #6412027). Regulatory bodies providing ethical approvals or other ethics considerations for included studies are reported in Supplementary File S2.3.

2.3 Results

4542 KPSE conducted between 2010 to 2023 were compiled (Figure 2.1). Following data cleaning, source document review, and area matching, 2065 observations were extracted from 126 studies (Table 2.1; Supplementary Figure S2.1). Data were most available for FSW (n=972, data from 35/39 countries; Supplementary Table S2.3), followed by MSM (n=647, 33/39 countries), PWID (n=329, 23/39 countries), TGW (n=117, 13/39 countries), and TGM (n=16, 2/39 countries). Sixty-nine percent (445/647) of urban MSM population proportion observations were below 1% of the male adult (15-49 years) population (Supplementary Figure S2.2).

I identified 2732 key population HIV prevalence estimates, from which 1183 were extracted from 217 studies after processing. Denominators were reported for 98% (1154/1183) of observations. Most data were available for FSW (n=559, 36/39 countries), followed by MSM (n=370, 34/39 countries), PWID (n=159 21/39 countries), TGW (n=95, 23/39 countries), and TGM (n=5, 5/39 countries).

For ART coverage, 621 observations were identified. After processing, 259 observations were extracted from 62 studies. Denominators were available for 98% (254/259). Data were most available for FSW (n=135, 27/39 countries), followed by MSM (n=92, 24/39), TGW (n=17, 10/39 countries), and PWID (n=15, 8/39 countries). No data were available for TGM. Fifty-nine percent of observations were VLS [152/259], 9% ART metabolite testing [24/259], and 32% self-reported ART usage [83/259].

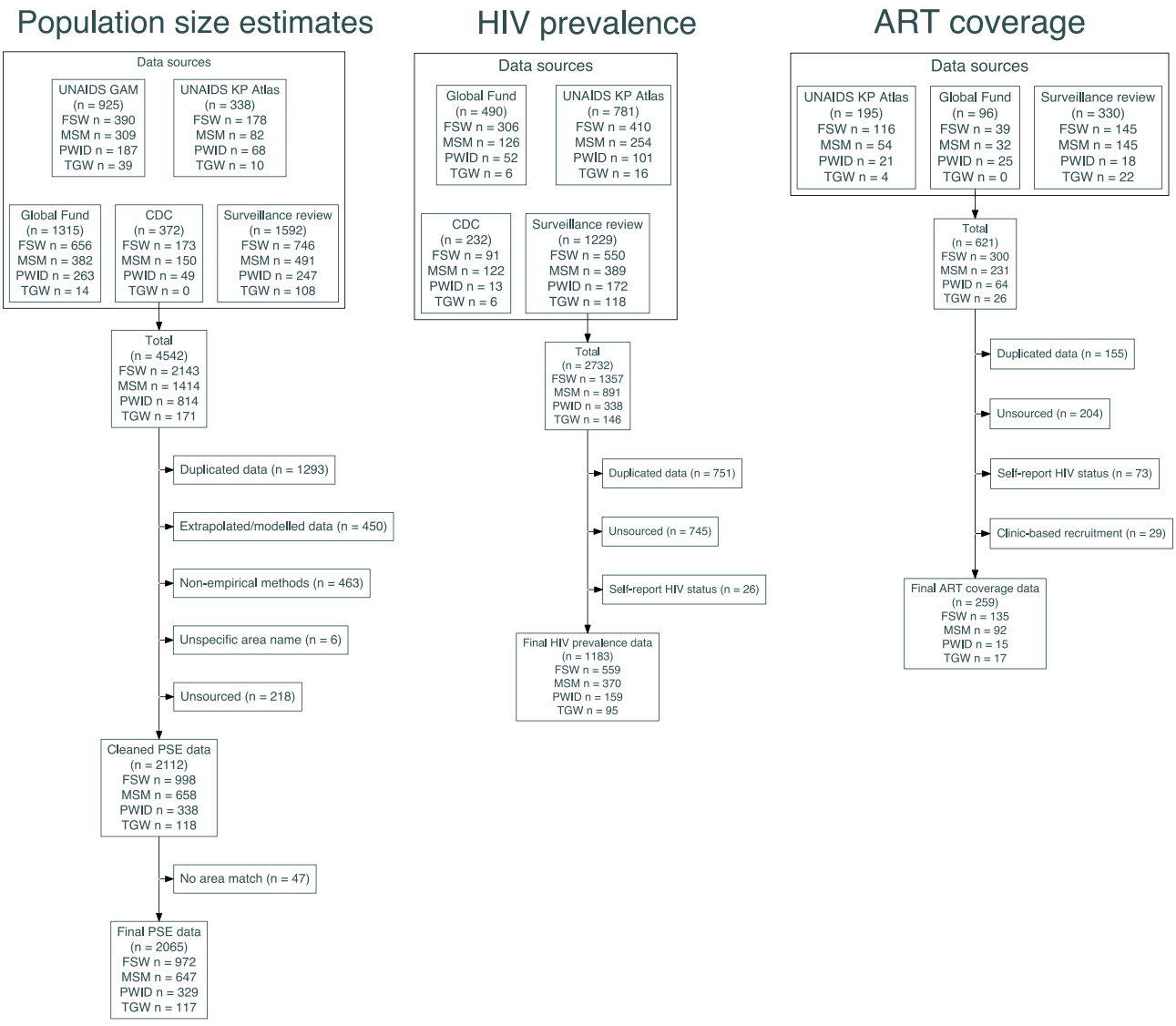


Figure 2.1: Flow diagrams describing identified data for key population size estimates, HIV prevalence data, and key population ART coverage. Each *n* represents number of population/method/location observations, with potentially observations for multiple subnational locations from the same study in same country. ART: Antiretroviral therapy coverage; FSW: Female sex worker; MSM: Men who have sex with men; PWID: People who inject drugs; TGW: Transgender women; KP: Key Population; GAM: Global AIDS Monitoring; CDC: US Centers for Disease Control and Prevention; PSE: Population size estimate.

Table 2.1: Availability of population size, HIV prevalence, and ART coverage data by key population and region during period 2010-2023.

Region	Key population	Size Estimates		HIV prevalence		ART coverage	
		Data-points	Countries with data (n; %)	Data-points	Countries with data (n; %)	Data-points	Countries with data (n; %)
SSA (39 countries)	FSW	972	35 (90)	559	36 (92)	135	27 (69)
	MSM	647	33 (85)	370	34 (87)	92	24 (62)
	PWID	329	23 (59)	159	21 (54)	15	8 (21)
	TGW	117	13 (33)	95	23 (59)	17	10 (26)
	TGM	16	2 (5)	5	5 (13)	0	0 (0)
ESA (18 countries)	FSW	450	17 (94)	236	18 (100)	85	14 (78)
	MSM	291	15 (83)	127	15 (83)	45	12 (67)
	PWID	156	8 (44)	52	9 (50)	10	5 (28)
	TGW	65	7 (39)	38	12 (67)	13	7 (39)
	TGM	16	2 (11)	2	2 (11)	0	0 (0)
WCA (21 countries)	FSW	522	18 (86)	323	18 (86)	50	13 (62)
	MSM	356	18 (86)	243	19 (90)	47	12 (57)
	PWID	173	15 (71)	107	12 (57)	5	3 (14)
	TGW	52	6 (29)	57	11 (52)	4	3 (14)
	TGM	0	0 (0)	3	3 (14)	0	0 (0)

SSA: Sub-Saharan Africa; ESA: East and Southern Africa; WCA: Western and Central Africa; FSW: female sex workers; MSM: men who have sex with men; PWID: people who inject drugs; TGW: transgender women; TGM: transgender men; ART: antiretroviral therapy

I estimated that, across countries, a median 1.65% of urban cisgender women aged 15-49 years were FSW (interquartile range [IQR] 1.35-1.91), 0.89% of men had sex with men (IQR 0.77-0.95), 0.32% of men injected drugs (IQR 0.31-0.34), and 0.10% of women were transgender (IQR 0.06-0.12; Figure 2.2). Incorporating the rural-to-urban ratio, median proportions of national total populations were 1.19% FSW, 0.66% MSM, 0.25% PWID, and 0.08% TGW. In sensitivity analysis using age 15-29 years as a denominator for MSM PSEs and 15-39 years for FSW PSEs, median urban proportions for MSM were 1.36% (IQR 1.15-1.42) and for FSW were 1.82% (IQR 1.60-2.13) (Supplementary Figure S2.3).

Urban KPSE proportions were higher in ESA than WCA among FSW (median difference +0.3%; 95% credible interval [CrI] -0.3, 1.0) and MSM (+0.2%; 95%CrI -0.2, 0.5) but uncertainty ranges contained zero. Proportions were similar between regions among PWID and TGW, but KPSE data were sparse overall. PSE proportions derived from PLACE and mapping studies were significantly lower than those derived from other methods among FSW (odds ratio 0.58; 95%CrI 0.40, 0.83), MSM (0.26; 95%CrI 0.17, 0.41), and PWID (0.31; 95%CrI 0.19, 0.53), and lower among TGW (0.27; 95%CrI 0.07, 1.11) but for TGW the 95% credible interval contained 1 (Supplementary Table S2.4; Supplementary Figure S2.4; Supplementary Tables S2.9-S2.12).

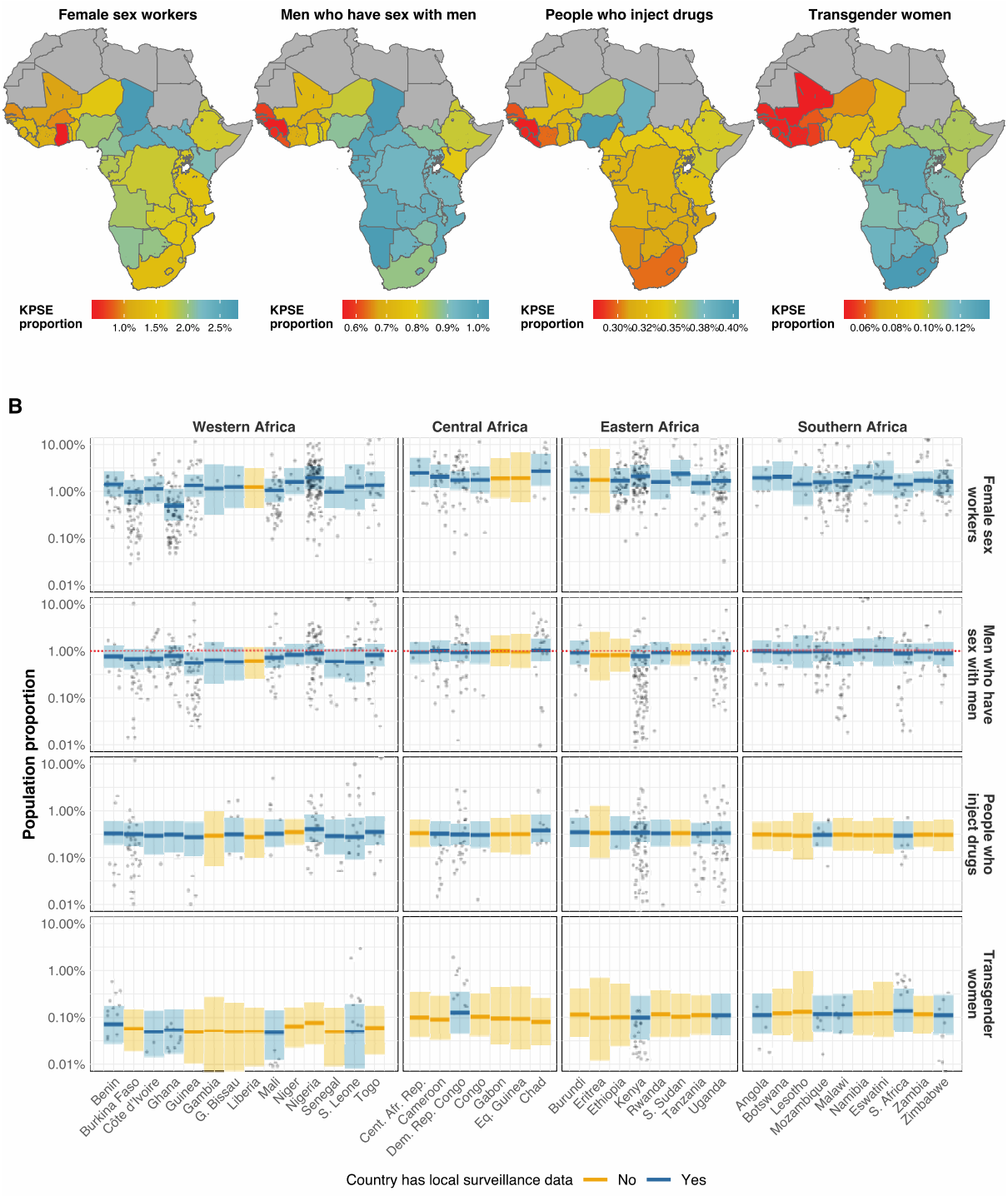


Figure 2.2: Model estimated urban key population size estimate (KPSE) proportions for female sex workers, men who have sex with men, people who inject drugs, and transgender women as a proportion of gender-matched 15-49 years adult total population. (A) Posterior median estimate for each country. Note: colour range is different for each key population chloropleth. (B) Posterior median estimate and 95% credible intervals for each country. Points represent observations of subnational KPSE proportions that used empirical methods. Countries that had local surveillance data are shown in blue, and countries informed only by spatial smoothing from neighbouring countries in yellow. Vertical axis shown on log-scale.

Observed HIV prevalence among key populations was consistently higher than area-matched total population HIV prevalence. Logit key population HIV prevalence in ESA was more strongly correlated with matched logit total population HIV prevalence than in WCA (Figure 2.3). In ESA, 15% population prevalence corresponded to 53% (95%CrI 45, 62) HIV prevalence among FSW, 21% (95%CrI 12, 31) among MSM, 28% (95%CrI 15, 45) among PWID, and 22% (95%CrI 14, 34) among TGW. In WCA, relative patterns were similar, but key population HIV prevalence varied less with total population HIV prevalence than in ESA. HIV prevalence differentials between key population and total population were larger when population prevalence was lower (Figure 2.3C). Supplementary Table S2.5-S2.7 report regression results, Supplementary Table S2.13 reports country-specific estimates, and Supplementary Figure S2.5 reports sensitivity analysis of imputed tested denominators.

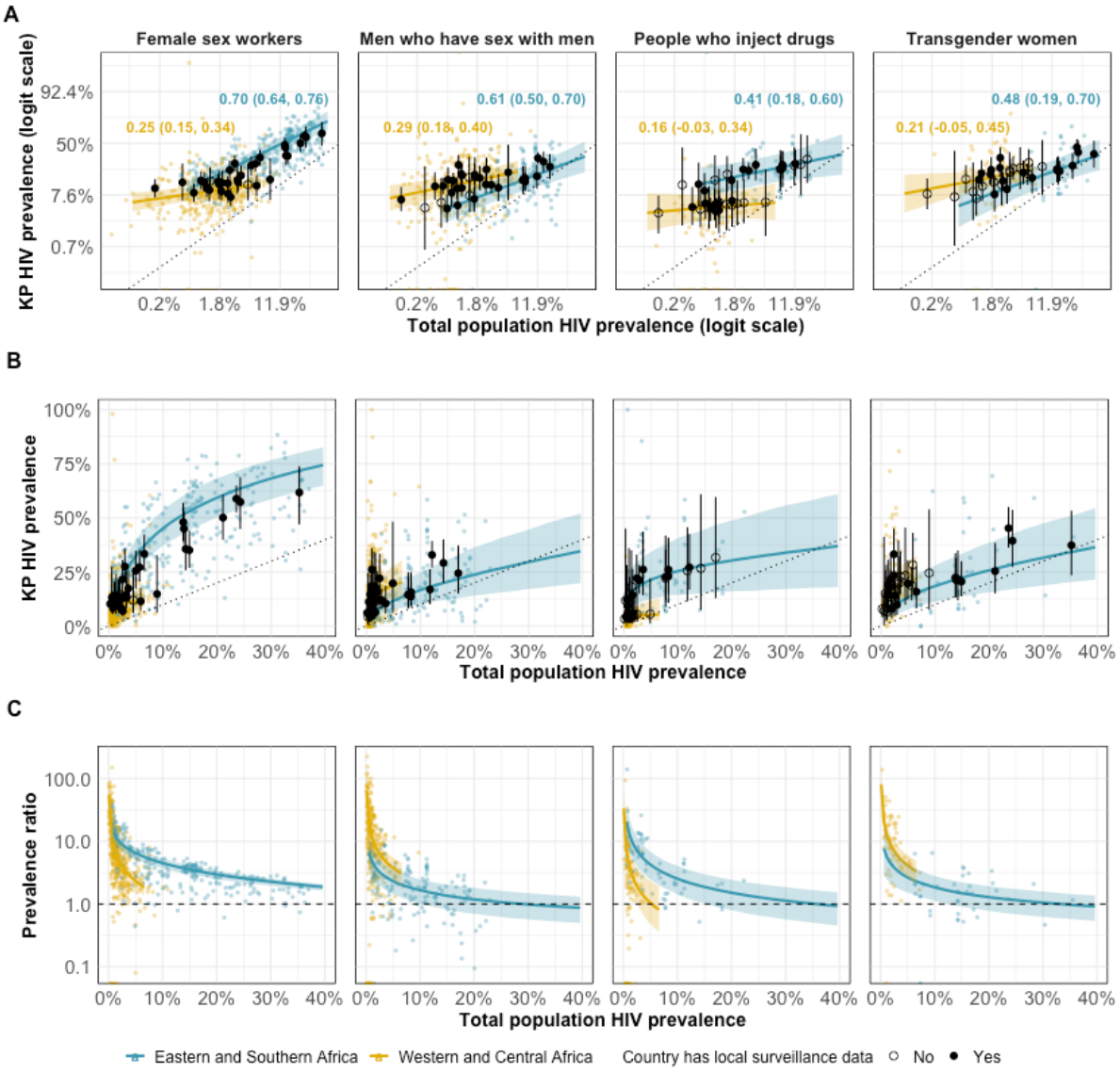


Figure 2.3: Key population and total population HIV prevalence on the logit scale (A), natural scale (B), and expressed as a ratio of key population and total population prevalence (C) for female sex workers, men who have sex with men, people who inject drugs, and transgender women. Coloured points indicate observed key population prevalence plotted against gender/year/province-matched total population prevalence. Logit-scale regional correlation coefficients and 95%CrI uncertainty intervals shown in coloured text in panel A. Coloured lines and shading represent regional estimate and 95% uncertainty results. Points represent country estimates [filled for countries with HIV prevalence data and empty for countries without HIV prevalence data] and 95% uncertainty ranges. Dotted line represents line of equality.

ART coverage among FSW, MSM, PWID, and TGW was correlated with gender-matched population ART coverage, but with wide heterogeneity in relative ART

coverage across studies (Figure 2.4). At 80% population coverage, predicted ART coverage among FSW was 11% lower (95%CrI 19, 4%), 19% lower (30, 10%) among MSM, 25% lower (41, 11%) among PWID, 13% lower (43, 18%) among TGW. Supplementary Table S2.8 reports regression results and S2.14 reports country-specific estimates.

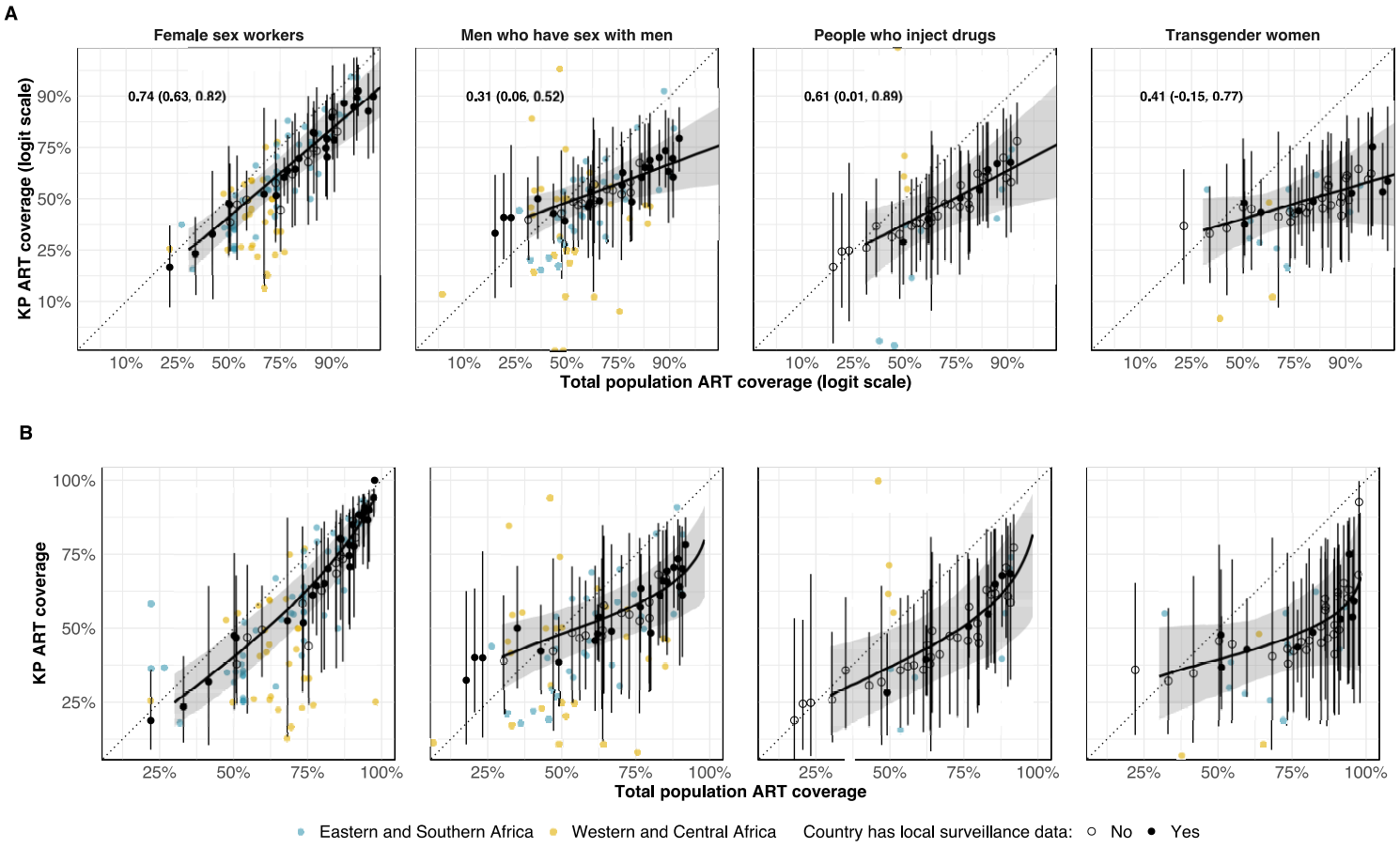


Figure 2.4: Estimated key population ART coverage as a function of total population ART coverage on the estimated logit scale (upper) and natural scale (lower). Coloured points indicate observed key population prevalence plotted against gender/year/province-matched total population ART coverage. Logit-scale correlation coefficients and 95%CrI uncertainty intervals shown in panel A. Black line and shading represent estimate for sub-Saharan Africa and 95% uncertainty results. Black points represent country estimates and 95% uncertainty ranges. Dotted line represents line of equality.

In sensitivity analysis including a fixed effect for ART measurement method, self-reported ART coverage was lower than lab-determined ART, but with wide 95%

credible interval spanning no difference (odds ratio 0.73, 95%CrI 0.47, 1.15; Supplementary Figure S2.6, Table S2.8). Assuming MSM surveys represented MSM aged 15-29 years or FSW surveys represented FSW aged 15-39 years minimally affected HIV prevalence or ART coverage estimates (Supplementary Table S2.16).

Across SSA, FSW, MSM, PWID, and TGW combined were 1.2% (95%CrI 0.9, 1.6) of the population aged 15-49 years (3.7m FSW, 1.9m MSM, 770,000 PWID, and 230,000 TGW), but 6.1% (95%CrI 4.5, 8.2) of PLHIV aged 15-49 years. In ESA this was 4.9% (95%CrI 3.4, 6.9) of PLHIV compared to 1.3% (95%CrI 0.9, 1.8) of the population and, in WCA, 11.7% (95%CrI 8.3, 16.5) of PLHIV compared to 1.2% (95%CrI 0.9, 1.7) of the population. FSW were 4.0% (95%CrI 2.7, 5.7) of PLHIV in SSA (750,000 PLHIV; 95%CrI 520,000, 1,100,000), MSM were 1.4% (95%CrI 0.9, 2.0) or 250,000 PLHIV (95%CrI 170,000, 380,000), PWID were 0.5% (95%CrI 0.3, 0.8) or 89,000 PLHIV (95%CrI 50,000, 150,000), and TGW were 0.2% (95%CrI 0.1, 0.5) or 44,000 PLHIV (95%CrI 20,000, 100,000) (Figure 2.5).

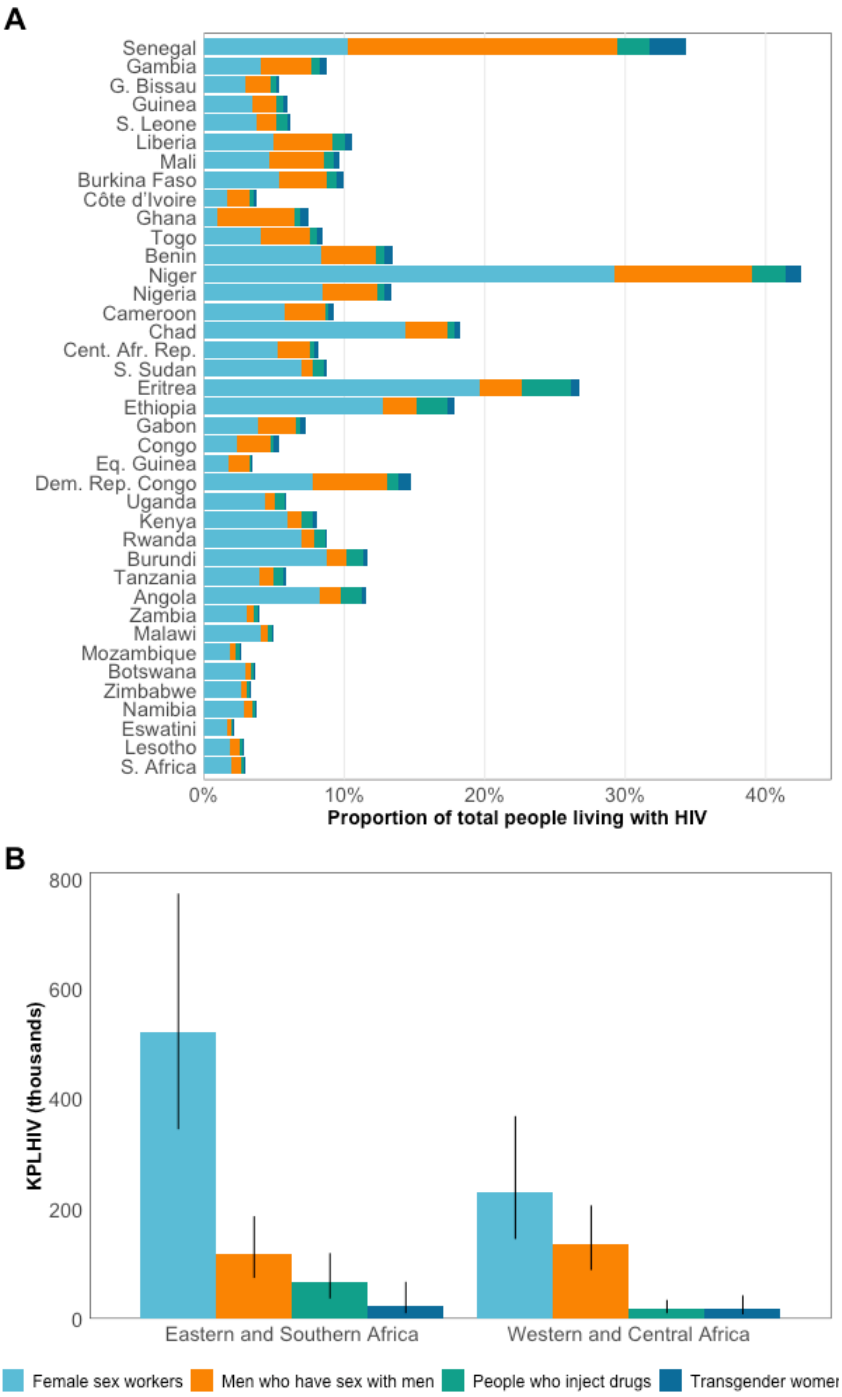


Figure 2.5: (A) HIV positive key population members as a proportion of all PLHIV aged 15-49 years. Countries are ordered geographically. (B) Estimated number of key populations living with HIV (KPLHIV) in Eastern and Southern Africa and Western and Central Africa.

2.4 Discussion

Data from 273 key population surveys provided consistent evidence across sub-Saharan Africa of higher HIV prevalence and lower ART coverage among key populations. I estimated there are 3.7 million FSW, 1.9 million MSM, 770,000 PWID, and 230,000 TGW in SSA who require comprehensive HIV prevention or treatment services. HIV prevalence was estimated to be 21% among FSW, 14% among MSM, 11% among PWID, and 20% among TGW. These were 4.6, 5.9, 4.6, and 4.4 times higher than adult population prevalence, respectively, with larger relative differences when population prevalence was lower. Together, key populations constituted 1.2% of the adult population in SSA but 6.1% of PLHIV. ART coverage among key populations increased with total population coverage, but lagged behind at high population ART coverage levels. However, there was wide uncertainty about estimates aggregated within countries and across SSA.

This exercise highlighted major data gaps and challenges interpreting existing data. Across the twelve combinations of three indicators and four key populations analysed here, on average countries had data for seven combinations (Supplementary Table S2.3). Data gaps are larger when restricting to the highest quality and most recent data. These gaps impede planning for equitable and universal access to HIV services and will persist without firm commitments to collect key population survey data. Implementation of high-quality surveys will also require addressing entrenched discriminatory practices and punitive laws and policies against key populations[284,320–322] In settings lacking or with limited data, these extrapolated estimates can be a foundation with which to guide future surveillance priorities, stimulate in-country data review and use, and estimate HIV epidemic indicators. Future efforts should especially focus on strengthening surveillance for MSM, PWID, and transgender people, and supporting use of HIV service delivery data for all key populations, while ensuring the safety and protection of marginalised individuals and their communities.[284]

Previous key population reviews and meta-analyses[292,323–325] relied on systematic searches of peer-reviewed literature. My initial sources were existing databases, primarily populated by surveillance teams in each country or implementing organisations. This resulted in including a larger grey literature body, such as survey reports, which are infrequently indexed by peer-reviewed databases.[326] However, many observations from initial databases could not be validated in source documents and were excluded from analysis, which in some countries excluded the only reported data. Demand for total population HIV estimates in SSA has promoted high-quality comparable surveillance methods, documentation, and dissemination. Review of key population data by national HIV surveillance teams was introduced into the UNAIDS sub-Saharan African estimates process in 2022, providing context for existing surveys, identifying missing sources and adding new data. This, alongside ongoing key population data initiatives and concerted advocacy efforts that ensure public dissemination, will improve the foundation for HIV surveillance among key populations and promote parity for key populations within national HIV data and strategic information.

Systematically collated data on key population size, HIV prevalence, and ART coverage are critical inputs for mathematical modelling analyses that guide optimal HIV resource allocation. Such studies consistently demonstrate that fully meeting the HIV prevention and treatment needs of key populations would be impactful on reducing overall population incidence due to network effects of averting further onward transmission over time and to non-key population partners.[327,328] Model-based counterfactual indicators that capture these impacts, such as the transmission preventable attributable fraction, are a better basis for intervention prioritisation than simple population proportions reported in survey data.[327,329,330]

My estimate of 0.29% of men in SSA injected drugs was lower than recent estimates from Degenhardt *et al.* of 0.38%, though uncertainty ranges overlapped.[303] This may reflect incorporating the urban-to-rural ratio in national PSE extrapolation in this analysis. I estimated that 1.2% of women aged 15-49 years sold sex, similar to the 1.1% estimated by Laga *et al.*[331] The finding of heterogeneous HIV prevalence ratios

between MSM and the total population was consistent with Hessou *et al.*,[332] particularly in WCA where HIV burden in neighbouring countries can vary considerably. My estimate of 57% ART coverage among MSM in 2022 was lower than 73% from a meta-analysis by Stannah *et al.*[333] of studies conducted up to 2022, with overlapping uncertainty. This may be due to exclusion of ART coverage using self-reported HIV status in this analysis.

Population size estimates measured in the same population at different times or with multiple methods were highly heterogenous, limiting data use for establishing meaningful programmatic targets or monitoring temporal trends. Very large uncertainty ranges around population size and PLHIV modelled estimates were consistent with findings of other statistically summarised and extrapolated PSE from multiple sources.[334–337] Non-existence of rural KPSE studies to empirically inform rural-urban population proportions contributed to five-fold or greater relative uncertainty in extrapolated national estimates. Moreover, quality assessments of individual KPSE studies were not conducted as part of this analysis. Both systematically improving and evaluating study-specific implementation quality and methodological assumptions may reduce heterogeneity and increase the utility of KPSE data.[338–342]

Seventy-two percent of MSM KPSE observations and 38/39 modelled urban MSM estimates were below 1% of the male adult (15-49 years) population which UNAIDS and WHO recommended in 2020 as a minimum MSM population proportion.[343] The minimum threshold was specified to ensure that MSM were not overlooked due to lack of data. Variation in MSM proportions measured in PSE studies may reflect ability to engage in sexual behaviours or surveys, affected by legal and social environment and other factors, rather than differences in distribution of sexual preference. It is also uncertain whether MSM recruited in surveys, who are disproportionately young,[293,294] are representative of the total MSM population. Specifying a minimum 1% threshold for MSM population could result in unrealistic MSM-focused service targets. The threshold should be reconsidered with the wider range of population size and stigma data now available, aligned with risk-based

approaches to quantifying sex work and injecting drug use. Study-specific quality assessments will be important to producing accurate KPSE given stigma experienced by MSM in many settings.

Integrating key population programme data within key population estimates should be a priority to improve utility of surveillance data to guide programmatic response and monitor trends and subnational variation.[344] Triangulating routine HIV testing and treatment data with biobehavioural survey data may help disentangle programmatic double counting, coverage of key population-specific services, and accounting for linkage to care in the estimation of ART coverage and viral load suppression.[345–347] Future surveillance should consider moving beyond strictly defined key population definitions accurately to reflect heterogenous risks among individuals in overlapping risk environments including cisgender MSM and transgender women who sell sex, and FSW and MSM who inject drugs.[348–350]

Several limitations should be considered when interpretating these data and estimates. Firstly, surveys used a range of key population definitions and inclusion criteria which limited comparability, though there was sufficient overlap (Supplementary Text S2.2). Second, lack of explicit geographic survey sampling frames made it challenging to reflect the catchment population for a given survey in matched denominators, particularly given the mobility of key populations.[351] This likely exacerbates the observed heterogeneity in KPSE proportions (Figure 2.2B), and is a major limitation for extrapolating KPSE proportions for programmatic planning. Going forward, specification of population catchments and careful data quality assessments to determine study inclusion and interpretation will improve future data use. Third, sample size or standard errors and age ranges were omitted from most population size data entries, gender was not specified for most observations among PWID, and a small number of observations were missing denominators for number tested. This limited ability to statistically weight, age-standardise, or gender-match data in model extrapolations, though sensitivity analyses indicate little impact on analysis conclusions. Fourth, data were insufficient and too heterogeneous to estimate time trends in population proportions, HIV

prevalence, or ART coverage. Application of standardised recruitment methods, population definitions, and indicator reporting in consistent locations will improve monitoring of trends. Finally, this analysis did not include prisoners and other incarcerated people and future studies should look to expand data synthesis and analysis to this key population.

In conclusion, key populations across SSA experience disproportionate HIV burden and have lower antiretroviral therapy coverage. Consolidated key population data and synthesised estimates provide a basis for key population programming in all countries, including those with limited locally available data. Despite increasing focus on key populations in HIV/AIDS strategies in SSA, large data gaps remain and estimates are highly uncertain. New surveillance strategies, improved use of routine data, and more consistent surveillance implementation are required to furnish more precise estimates and trends for programme planning and support the monitoring of equitable and equal access to HIV prevention and treatment programmes outlined in the Global AIDS Strategy 2021-2026.

3. The Key Population Workbook: enabling HIV estimates teams to engage with and validate key population surveillance data

Acknowledgements

The Workbook was developed in collaboration with UNAIDS, the UNAIDS Reference Group, colleagues from the US CDC, USAID, and PEPFAR, and members of the Mozambique HIV estimates team. Though many perspectives helped develop the Workbook, particular thanks go to Dr. Tim Brown and his expertise from developing the AIDS Epidemic Model interfaces and the close review of key population surveillance data that entailed.

French versions of the Workbook and its guidance material were prepared by UNAIDS and – as ever – Rebecca Anderson.

Dissemination

The Key Population Workbook and its guidance documents were disseminated during the 2022, 2023, and 2025 UNAIDS Estimates processes. Guidance documents may be found at https://hivtools.unaids.org/hiv-estimates-training-material-en/ in English and French.

3.2 Overview and objectives

This chapter considers the Key Population Workbook, an Excel-based tool I created for use by national HIV estimates teams to appraise key population surveillance data within the UNAIDS estimates processes since 2021. The research and data review reported in Chapter 2 was conducted to create a surveillance database that underpins the contents and function of the Key Population Workbook. An example workbook for Mozambique is available as a supplementary file to this thesis and may aid interpretation of this chapter.

Prior to the creation of the Key Population Workbook, UNAIDS collated key population information from country teams using Global AIDS Monitoring. Using the template spreadsheet,[352] teams could submit site-level surveillance observations from primary surveillance, programme data, or modelled estimates. Metadata such as sampling/recruitment methods and source material could also be specified. UNAIDS then assessed submissions for population size and HIV prevalence and placed them into one of three methodological categories: nationally adequate, locally adequate, or inadequate. Nationally adequate estimates are those calculated using "a combination of multiple sites with a clear approach to extrapolating to a national estimate" as described in section 1.8.5. Few countries' estimates attained nationally adequate status, which are the only submissions published in Global AIDS Updates and used within UNAIDS analyses.[277] More information on UNAIDS' adequacy categories can be found in Sabin et al.[353]

As noted in section 1, the overarching objective was to create key population estimates of equal rigour to those among the total population. Estimates teams are intimately familiar with the total population surveillance and programme data used to calibrate EPP/Spectrum. The remarkable scale-up of national programmes across sub-Saharan Africa and the quality and fidelity of routine health system data are rightly considered matters of national pride by many teams. Interpretation of these data and its use within estimation tools would be impossible without teams'

knowledge of data quality issues and other idiosyncrasies, and the same level of familiarity was sought with key population data. The objectives of the Key Population Workbook were to facilitate all country teams to:

- Familiarise themselves with national key population surveillance data;
- Differentiate surveillance data from modelled or extrapolated estimates and programme data;
- Review and validate local surveillance data using simple metrics and visualisations;
- Approve a collection of data for future modelling work;
- Create consensus estimates of population size, HIV prevalence, and ART coverage by key population for use in national programme planning exercises and modelling and global reporting; and
- Produce agreed estimates of new HIV infections by key population using Goals-RSM, or another preferred transmission dynamic model used for national programme purposes.

3.3 Methods

The Workbook was an interactive Microsoft Excel workbook that walked HIV estimates teams through reviewing and validating key population data over five sequential worksheets. The data in the workbook was a combination of pre-populated data and user inputted data, which was then interactively visualised to highlight data quality issues and methodological differences. Users could exclude data, record data cleaning decisions, and create summary metrics for population size, HIV prevalence, and ART coverage. Country-specific workbooks were distributed to HIV estimates teams and its completion was supported during the UNAIDS estimates workshops. Completed workbooks were uploaded to Spectrum which visualised key population indicators in comparison to total population HIV estimates and subsequently submitted to UNAIDS for review and integration with GAM.

3.3.1 Structure of the Excel workbook

The workbook consisted of five core sheets:

Sheet 1: Data input - observation-level data entry for population size, HIV prevalence, and ART coverage/VLS. A pre-populated dataset using the collated data from Chapter 2, which included data elements for surveillance method, age group, surveillance area, year, estimate and uncertainty bounds, and, as appropriate, a sample size or total population denominator. Users could add any missing data from pre-existing studies and append data from newly conducted studies. Population size estimates were required to be converted to a population size estimate proportion using an area-gender-age-year matched total population denominator (pre-populated from Chapter 2.2.3.1). Primary source documents (e.g. a survey report) were required for all observations to be used in downstream analysis.

Sheet 2: Validation - observation-level inclusion or exclusion of data for further analysis.

Users were guided by:

1) Automatically generated “traffic light” quality ratings based on each observation’s surveillance method and sample size. Non-empirical population size estimation methods (Wisdom of the Crowds, simple enumeration, literature methods) were designated “red” [Do not use], PLACE/mapping PSEs and self-reported HIV prevalence/ART coverage were designated “yellow” [Caution], and empirical PSEs and serologically or laboratory-confirmed HIV prevalence/ART coverage designated “green” [Good]. HIV prevalence and ART coverage observations with tested denominators <50 also generated a warning message; and
2) Three plots showing national key population surveillance data compared to all data from across sub-Saharan Africa: population size estimate proportions, HIV prevalence ratio, and ART coverage ratio (Figure 3.1).

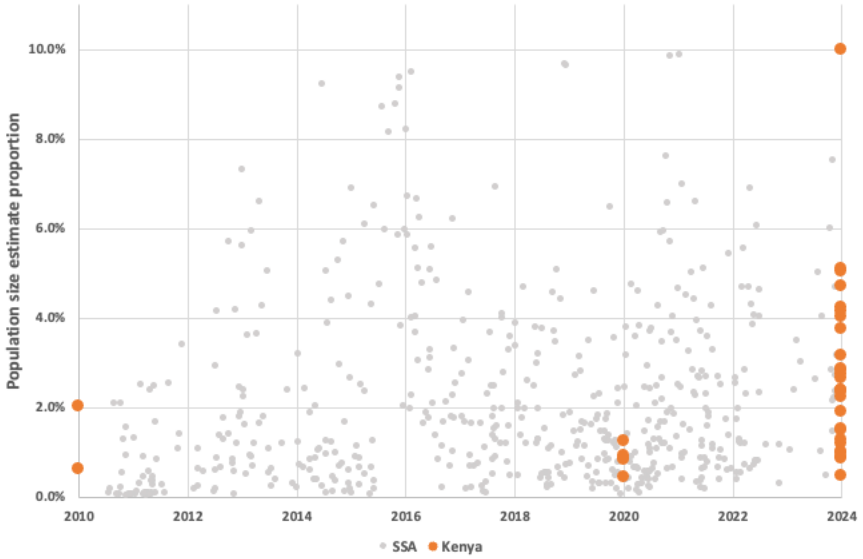


Figure 3.1: Kenya key population workbook comparison plot for population size estimates. Kenyan data shown in orange and data from across sub-Saharan Africa in grey. Similar plots were made available for HIV prevalence and ART coverage ratios.

National data was shown in orange and compared to all data from sub-Saharan Africa in grey. Plots enabled identification of errant data points and directed users to review the surveillance observation, and in the case of key population size estimates, review the matched count denominator.

Each key population observation required a user decision on its inclusion or exclusion to be used in further analysis.

Sheet 3: Creating consensus estimates - consolidation of subnational, longitudinal surveillance data into a single, current year national-level consensus estimate for each indicator and key population. Validated observations were eligible for inclusion in consensus estimates. Population size estimate proportions, assumed to be representative of urban areas, were extrapolated to national-level using assumptions about the urban:rural distribution of key populations and the proportion of the total population living in urban areas. In 2024, the Workbook was linked with the Triangulator model which offered improved methods for extrapolating PSEs to national-level (https://triangulator.unaids.org/).

Using validated observations of HIV prevalence and ART coverage, users calculated average HIV prevalence and ART coverage ratios relative to the total population multiplied by Spectrum estimates for gender-matched 15-49 adults to produce estimates for the current year. If limited or no data were available, the Workbook suggested that country teams adopt modelled estimates for PSE and HIV prevalence derived in Chapter 2.

Sheet 4: District-level population size estimates (optional) - alignment of national-level consensus PSE with a pre-existing district-level PSE distribution. District-level PSE may have been created for other national strategic planning purposes (e.g. PrEP programming) or for international stakeholder exercises (e.g. PEPFAR Country Operational Plans and Global Fund submissions). To ensure alignment between national and district-level estimates, and between inputs to different modelling tools, the workbook either (1) scaled district-level estimates to match national-level consensus PSE or (2) directed users to revise the national consensus estimate to match district-level distribution.

Sheet 5: Estimating new HIV infections - comparing newly created consensus estimates for PSE, HIV prevalence, and ART coverage with inputs to transmission dynamic models. If consensus estimates for population size and HIV prevalence were similar to existing inputs to a transmission dynamic model, the estimated number of new infections from that model could be used. All countries had pre-existing calibrations of Goals-RSM, and some countries additionally had Optima and Incidence Patterns Model calibrations. If consensus estimates differed to model inputs, Goals-RSM would be re-calibrated using new inputs generating an estimate of new HIV infections.

3.4 Results

3.4.1 Production and dissemination of the workbook

Thirty-eight country-specific workbooks (22 in English, 16 in French) were created in each of 2022, 2023, and 2025 UNAIDS estimates rounds, and disseminated by

UNAIDS in 2022 and 2023 estimates rounds. Workbooks were pre-populated with key population surveillance data updated over the course of each year, and with the latest UNAIDS subnational total population estimates from the Naomi model. Workbooks were uploaded to each country's AIDS Data Repository, the central data hub for UNAIDS HIV estimates data and tools, and accompanied by guidance documentation in English and French.

The Workbook was first used in the 2022 UNAIDS estimates round (December 2021) which UNAIDS and country facilitators supported remotely due to the COVID-19 pandemic. Step-by-step instructions and guidance were provided to country facilitators during the UNAIDS "Train the Trainers" workshops, and subsequently to estimates teams during remote workshops. The 2023 UNAIDS estimates round was conducted in-person, where I gave training to facilitators and estimates teams at workshops in Johannesburg (English speaking countries) and Abidjan (French speaking countries).

3.4.2 Completion of the workbook

In 2022, three of 38 countries submitted a Workbook (Rwanda, Malawi, Zimbabwe), none of which had completed the workflow through to estimates of new infections by key population. The very low completion rate was attributed to launching a new tool during the COVID-19 pandemic, without in-person technical support. In 2023, following in-person workshops, thirteen further countries submitted a Workbook as part of their Spectrum file, and an estimated ten further countries completed data input and review but did not submit a Workbook. Fifteen of eighteen submitted Workbook files had consensus estimates for one or more indicator/population combinations.

During 2022 and 2023 estimates round, the majority of users reported significant challenges in understanding and completing the Workbook. Common scientific issues were:

- Criteria by which evaluate observations that were dissimilar to regional averages;
- Validating survey catchment areas and total population denominators for PSE proportions;
- Whether to include or exclude observations based on methodological quality;
- How to determine the urban:rural ratio for key population size; and
- How to weight studies when creating national-level consensus estimates

While users also reported process issues regarding the perceived complexity and overwhelming nature of the Workbook, these were resolved with one-on-one support.

3.4.3 Review of workbooks and use of results

Workbooks submitted during the 2023 estimates process were reviewed by UNAIDS in 2025, but feedback was never relayed back to country teams. I am only aware of Zimbabwe and Malawi using results from the Workbook within national estimate reporting. No consensus estimates created by national estimates teams were incorporated into downstream key population modelling tools (see section 3.5.2.4 below). The surveillance dataset collated during Chapter 2 has not been updated to remove observations that were marked for removal by country teams, and it remains in use in its entirely as calibration data for Goals-RSM.

3.5 Discussion

3.5.1 Successes

The Workbook was an Excel-based interactive platform that allowed national estimates teams, some of whom do not have strong technical skills, to interrogate large quantities of observation-level surveillance data. It prioritised data quality review and offered users simple visualisations that allowed for rapid identification of implausible surveillance data.

3.5.1.1 Ensuring data fidelity

Prior to the Workbook, key population surveillance data that was considered nationally-approved had been restricted to UNAIDS GAM submissions. These data were used to inform key population estimates from desk modelling exercises of Goals, but had never been reviewed by estimates teams. [224] Careful data review in the Workbook by estimate teams, in concert with the desk review in Chapter 2, identified a body of key population surveillance data that was previously unknown to teams (in several cases entire surveys), omitted from or erroneously entered into international stakeholder databases, or entered with unknown sources or methods. Observation-level review of unsourced data often led to these being identified as routine programme data which had been incorrectly regarded as key population surveillance, most commonly of HIV test positivity as HIV prevalence.

3.5.1.2 The importance of metadata

In a field of heterogeneous surveillance methods and methodological quality, the Workbook encouraged a holistic view of data interpretation that prioritised metadata on an equal footing to the data observation itself. Amongst the richest discussion that the Workbook generated concerned the generalisability of venue-based population size estimates, site selection for surveillance, and the value of self-reported vs laboratory-confirmed data. Users were required to specify “confidence scores” (regression weights) for PSE extrapolation which many found challenging to complete, but which also generated thoughtful discussion on the relative quality of PSE methods, in particular implementation and quality of capture-recapture studies.

3.5.1.3 Data in context

Throughout the estimates process – including the creation of the total population estimates – country teams work essentially in isolation from one another, receiving support from UNAIDS and modellers as requested, but with limited knowledge of

shared challenges and issues. This is felt acutely with key population data and estimates: surveys are conducted infrequently, methods and estimates can vary widely, and countries have little ability to triangulate estimates without a shared repository of data.

The Workbook moved away from absolute measures (e.g. PSE counts, HIV prevalence) in favour of indicators expressed relative to the total population (e.g. PSE proportions, HIV prevalence ratios). Users were required to specify population size estimate denominators to calculate proportions, while HIV prevalence and ART coverage ratios were automatically generated by the workbook, matching observations to UNAIDS subnational total population estimates by year, gender, province, and age group. Relative indicators which can be compared across settings were visualised alongside all data in the region (Figure 3.1). These plots enabled teams to easily identify outlier observations, address data input issues, supported discussions of study implementation quality, and were the most positively reviewed section of the Workbook by teams.

3.5.2 Failings

3.5.2.1 "How are I meant to know/do this?"

The Workbook was developed with feedback from UNAIDS, the participants of the UNAIDS Reference Group, and the Mozambique HIV estimates team. Given substantial heterogeneity in surveillance methods and estimates of new HIV infections from transmission dynamic models, uncertainty in key assumptions, and competing voices on what should constitute "a gold standard", the Workbook was developed to be highly flexible. It did not proscribe surveillance methods, provide strict guidance on how to weight or exclude observations, nor mandate a model or method by which an estimate of new HIV infections could be reached. Instead, the Workbook was to be a led by users' domain experience, with the focus on data review and documentation of process. Though this was intended to be a strength of the workbook, the flexibility and lack of concrete guidance frustrated teams when they themselves required instruction on how to proceed.

Estimates teams had a deep understanding of total population surveillance data, but it was rare that they included individuals with strong knowledge of key population surveillance and routine data. Though nearly all observations had been validated against primary sources as part of Chapter 2, the Workbook appeared a daunting task and several teams did not progress past data input. Estimates teams were inappropriately placed to address questions on study-specific implementation, sources of bias, or bring expert domain knowledge as to how key population epidemics had changed over time.

3.5.2.2 "Why am I doing this?"

The needs of UNAIDS and modellers were at odds with the needs of estimates and programme teams. The benefits of completing the workbook were communicated poorly (in particular when an integrated incidence model using the validated data would become available), several aims were conflated into a single tool, and the workbook strategy failed to recognise that its immediate results were of little use or, in some cases, actively contrary to existing national processes. I believe that collating a country-approved and validated set of surveillance data was a justified ask of teams with tangible future benefits to national HIV modelling and HIV programmes (i.e. the first two sheets of the workbook), but neither extrapolation of subnational data to national-level nor the estimation of new HIV infections benefitted country teams.

Countries did not seek national-level key population estimates as key population programmes were usually restricted to a selection of districts, nor did they need key population estimates for the history of the epidemic for which historical data review was required. We sought an estimate of new HIV infections by key population derived from a transmission dynamic model to improve the methods underpinning the distribution of new infections published by UNAIDS. In turn, this required national-level model inputs for which we forced teams through a weakly evidenced extrapolation process that relied on strong assumptions which they felt unqualified to complete. This generated significant frustration, lost the goodwill of several estimates teams, and damaged the credibility and viability of the workbook as a whole.

3.5.2.3 "Not another tool"

There is continual demand from country teams through UNAIDS for additional indicators within the estimates process. Most model development has historically been contained within Spectrum, the software that houses the core demographic, incidence estimation, and epidemic projection models.[354] In recent years, there has been a transition towards a "hub and spoke" modelling structure: Spectrum acts as the hub and standalone modelling tools at the periphery read epidemic information from it and return specialised estimates to it. These include first90[355] (knowledge of HIV status), Naomi[213] (district-level HIV estimates), and the sub-national HIV Estimates in Priority Populations (SHIPP; HIV incidence and population size by behavioural risk category). Each is exposed to national estimates teams through a bespoke interface, whether online[272,356] or within an Excel workbook.[357] The hub and spoke model has permitted rapid model development by several teams in parallel but has created a sprawling and fragmented ecosystem that teams rightly reported as difficult to navigate and unintelligible to new users. The Key Population Workbook added to this confusion and it was commonly held among teams that they were unable to complete the main estimates workflow in the time allotted, let alone a seemingly-continuous flow of new models and interfaces.

3.5.2.4 A lack of strategic direction

The Workbook was beset by a lack of strategic leadership from UNAIDS. Despite key populations featuring centrally within the Global AIDS Strategy, systematically producing epidemiologic estimates on key populations was not afforded the required attention required to create estimates on equal footing to those among the total population. Key population estimates were held to lower standards, both in terms of scientific rigour and process, including not centrally reviewing the submitted Workbooks to ensure the decisions taken were justified and the results credible, nor returned any feedback to countries. In 2023, responding to the workload concerns outlined above, the Reference Group recommended that the Workbook be completed outside the intense December estimates workshops and by national key

population surveillance and routine data experts and representatives from key population community groups, instead of the regular estimates teams.[358] No progress has been made on this in three years.

Confused communication from UNAIDS to country teams and modelling teams betrayed a lack of understanding of the Spectrum “hub on a spoke” model that had been created, leading to internally inconsistent and epidemiologically impossible modelling results between tools (Figure 3.2). Countries repeatedly sought clarification from UNAIDS on the Workbook including when it would become available, whether staff time should be allocated to its completion, how it could be aligned with ongoing national processes, or whether it existed at all.

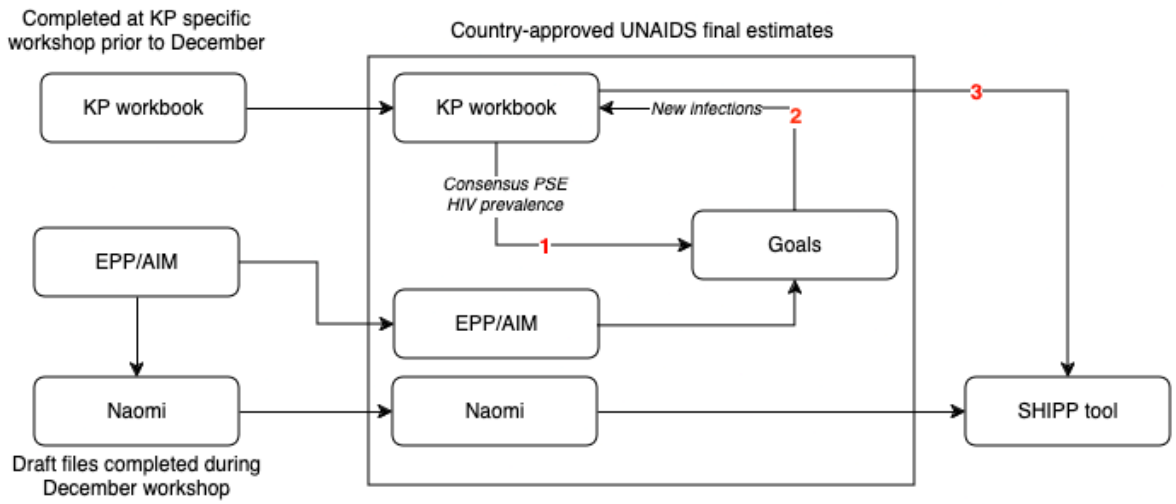


Figure 3.2: A proposed process workflow for key population modelling components within the UNAIDS estimates. Figure created by Rachel Esra and reproduced here with permission. SHIPP: Sub-national HIV Estimates in Priority Populations tool

UNAIDS declined to include key population estimates in the package of strategic information requiring final approval from Ministries of Health and UNAIDS, and country teams quickly realised there was little motivation to engage with the Workbook. UNAIDS withholding publication of estimates on grounds of data quality is considered a serious event by Ministries of Health and cause for reflection and close examination of surveillance data[271] (e.g. Mozambique in 2022[274], and Nigeria

in 2023[42]). This would have been a powerful lever to ensure that key population data were taken seriously, in parity with other HIV epidemic strategic information.

3.5.3 Summary and future directions

The Workbook's failings outnumbered its successes. It was perceived as an overcomplicated tool for which teams received inadequate support and whose results did not justify its workload. Accordingly, it was weakly utilised by overburdened country estimates teams and few completed it over three annual estimates cycles. These failures are underpinned by both the structure of the tool and by the process elements that surrounded it.

Estimates teams and donors continue to require district-level key population strategic information for programme planning, in particular for HIV prevention programming, which are being fulfilled by UNAIDS with weakly informed estimates derived from Chapter 2 without country involvement or oversight. The Workbook has not been used in 2025 or 2026 estimates processes and may not be used again. However, creating a nationally-recognised set of key population surveillance data is still required—further discussed in section 7.3.4—and will need to be completed if the UNAIDS key population estimates are to improve.

4. HIV prevalence in transgender women and cisgender men who have sex with men in sub-Saharan Africa 2010-2022: a meta-analysis

Acknowledgements

The data analysed as part of this chapter were collated under Chapter 2 and the same acknowledgements apply. Additionally, Drs. Mathieu Maheu-Giroux, Trevor Crowell, Anne McIntyre, and Prof. Theo Sandfort provided particular feedback and review which strengthened the analysis throughout.

Dissemination

Work in this chapter was made available as a pre-print in 2023 and has been accepted for publication at *AIDS*:

Stevens, O., Anderson, R. L., Sabin, K., Garcia, S. A., Fearon, E., Manda, K., Dikobe, W., Crowell, T. A., Tally, L., Mulenga, L., Philip, N. M., Maheu-Giroux, M., McIntyre, A., Hladik, W., Zhao, J., Mahy, M., & Eaton, J. W. (2023). HIV prevalence in transgender populations and cisgender men who have sex with men in sub-Saharan Africa 2010-2022: a meta-analysis. *MedRxiv*, 2023.11.09.23298289. https://doi.org/10.1101/2023.11.09.23298289

4.2 Introduction

Transgender people experience a HIV risk environment wherein the combination of high biological HIV risk and sociostructural risk factors result in disproportionate HIV burden.[350,359–361] Societal marginalisation, criminalisation, and stigma have impeded collection of robust HIV surveillance data in sub-Saharan Africa.[293,362,363] HIV strategic information among transgender people has become a necessary component of HIV estimates portfolios to guide decision making. Accordingly, HIV surveillance among transgender people in SSA is increasingly available.[349,364,365] However, as detailed in Chapter 2, data are insufficient to estimate key HIV epidemic indicators for transgender people in all sub-Saharan African countries, with global systematic reviews of HIV epidemiology relying on data from high-income countries, Latin America, and Southeast Asia[350,361]. Data collated under Chapter 2 identified only thirteen countries in SSA with population size estimates for transgender women, 23 countries have surveillance data on HIV prevalence, and ten have ART coverage data (Table 2.1)[366]. National estimates using these data (Supplementary Table S2.12, S2.13, and S2.14) are highly uncertain and, with little country-specific data to inform country random effects, sit close to the global posterior mean. During the completion of the Key Population Workbook, few countries that did have surveillance data among transgender people met the data availability adequacy threshold set by UNAIDS to produce consensus estimates. Surveillance data among transgender men is rarer still, consisting of a single size estimation study in South Africa [367] and five countries with HIV prevalence observations [366].

HIV prevalence data for men who have sex with men (MSM) in SSA are more widely available. I identified 370 HIV prevalence estimates among MSM across 34 of 38 SSA countries. While cis-MSM and transgender women have distinct vulnerabilities to HIV[368,369], studies in SSA indicate that HIV epidemiology in these two populations is linked: transgender women are recruited by cis-MSM into surveys using social and sexual network recruitment[349,370]; transgender women most often report male sexual partners and receptive anal sex[349,364,371]; phylogenetic analysis indicates HIV transmission clustering between transgender women and cis-MSM[372,373]; and

qualitative data indicate that some transgender people associate with belonging to the gay community [374]. Many surveillance studies primarily collecting data among cis-MSM have also included transgender people, providing a source of data in the absence of studies explicitly aiming to recruit transgender people.[117,375] I sought to meta-analyse relative HIV prevalence between cis-MSM and transgender women and assess whether there is a consistent relationship. This may be used to highlight the potentially high HIV burden among transgender women in settings that lack surveillance data among this key population.

4.3 Methods

Data on HIV prevalence among transgender people and cis-MSM between 2010-2022 in sub-Saharan Africa were extracted from UNAIDS Global AIDS Monitoring[299], UNAIDS Key Population Atlas[376], The Global Fund to Fight AIDS, TB, and Malaria surveillance database, US Centers for Disease Control and Prevention key population surveillance databases, and literature searches[366]. Studies that reported estimates of HIV prevalence for cis-MSM and any transgender population (as defined by study authors; see Table 1) in the same study were considered for inclusion. Additional tabulations not reported in previous study publications were shared by the authors of Fearon et al.[370], Keshinro et al. [377], and Malawi 2019/20, Botswana 2017 and Zambia 2021 Biobehavioural Surveys[378–380].

HIV prevalence data were pooled and weighted relative to the number of individuals tested. Where only age-specific HIV prevalence was available, data were pooled to produce a single adult prevalence. Where studies reported HIV prevalence for more than one transgender population, HIV prevalence among transgender women only was included in the meta-analysis. Log-normal random-effects meta-analysis was used to calculate pooled prevalence ratios (PRs) for HIV prevalence among transgender women compared to cis-MSM. Estimates were calculated separately for Eastern and Southern Africa (ESA) and Western and Central Africa (WCA) regions, and across all sub-Saharan Africa using nested study, country, and area random effects. Analyses were conducted in R 4.1.2[381], using the *metafor* package[382].

Province-level cross-sectional estimates of sex-specific total population HIV prevalence were extracted from UNAIDS subnational HIV estimates for 2020 created using the UNAIDS Naomi model[307]. For each country, province-level estimates were projected back in time 2000-2020 parallel to the national-level HIV prevalence trajectory as estimated by the Estimation and Projections Package in Spectrum[311,383]. Four additional observations of HIV prevalence among transgender women[371,384–386] were included in correlation analysis with total population HIV prevalence, which had been excluded from cis-MSM prevalence ratios meta-analysis because they lacked matching cis-MSM HIV prevalence estimates. This study received ethical approval from the Imperial College Research and Ethics Committee (#6473559).

4.4 Results

Twenty-one studies with data from twenty countries (11 in ESA and 10 in WCA) were included in the analysis, encompassing 8,476 transgender women and 24,102 cis-MSM (Table 4.1). Eleven studies were from journal publications, and ten were identified from grey literature including biobehavioural surveys (BBS)[302] and PLACE studies[387]. The median denominator for HIV prevalence among transgender women was 89 (IQR 35-235) and for cis-MSM 368 (IQR 198-426). HIV status was ascertained by serological assays in all studies. HIV prevalence among transgender women ranged from 6.0-69.4% in ESA and 1.9-71.6% in WCA. Cis-MSM HIV prevalence ranged from 1.0-43.7% in ESA and 0.1-55.7% in WCA.

Pooling data across sub-Saharan Africa, HIV prevalence in transgender women was 50% higher than in cis-MSM (Figure 4.1; PR 1.48, 95CI 1.25-1.76). In ESA, prevalence among transgender women was 1.49 times higher than cis-MSM (95CI 1.26-1.75) and in WCA 1.38 times higher (95CI 0.92-2.07).

Table 4.2: Studies included in meta-analysis of HIV prevalence in transgender women (TGW) and cis-gendered men who have sex with men (cis-MSM)

Study	Year of publication	Country	Year of data collection	Recruitment method	Transgender women inclusion criterion	TGW prevalence (%; n/N)	cis-MSM prevalence (%; n/N)
Stahlman et al. [364]	2016	Burkina Faso	2013	RDS	Identified as female or transgender, assigned male sex at birth, and reported having had insertive or receptive anal sex with a man in the past 12 months	0.0% (0/5)	4.5% (1/22)
		Côte d'Ivoire	2015			23.5% (16/68)	7.3% (4/55)
		Togo	2013			22.2% (2/9)	7.1% (3/42)
Keshinro et al. [377]	2016	Nigeria	2016	RDS	Identified as female, assigned male sex at birth, and reported having had insertive or receptive anal sex with a man in the past 12 months	51.5% (123/239)	40.7% (786/1929)
Botswana MoH [379]	2017	Botswana	2017	RDS	Identified as a woman, formerly or currently biologically male	50.0% (6/12)	14.9% (110/736)
Ghana MoH [388]	2017	Ghana	2017	RDS	Identified as a woman, biologically male, and have had anal or oral sex with another man in the last 12 months	28.1% (9/31)	17.4% (650/3723)
Mozambique MoH [389]	2018	Mozambique	2017	PLACE	Identified as a woman or transgender, assigned male at birth	12.7% (15/118)	9.9% (51/517)
Poteat et al. [349]	2017	Burkina Faso	2013	RDS		2.8% (3/108)	3.3% (18/552)
		Côte d'Ivoire	2016			25.5% (76/298)	8.0% (61/766)

Study	Year of publication	Country	Year of data collection	Recruitment method	Transgender women inclusion criterion	TGW prevalence (%; n/N)	cis-MSM prevalence (%; n/N)
		Gambia	2011		Self-identified as transgender or female/woman, and assigned male sex at birth	50.0% (2/4)	9.0% (18/200)
		Lesotho	2014			59.2% (42/71)	28.6% (130/455)
		Malawi	2012			16.0% (12/75)	15.2% (40/263)
		Senegal	2015			37.2% (74/199)	27.8% (147/528)
		Eswatini	2011			14.2% (17/120)	18.6% (38/204)
		Togo	2013			17.6% (9/51)	8.5% (53/626)
Angola MoH [390]	2018	Angola	2017	PLACE	Identified as a woman, and assigned male at birth	9.0% (8/89)	2.0% (20/1016)
Hakim et al. [391]	2018	Mali	2015	RDS	Identified as a woman, assigned male sex at birth, and reported having had insertive or receptive anal sex with a man in the past 6 months	24.3% (9/37)	9.7% (12/124)
Jobson et al. [392]	2018	South Africa	2017	Snowball	Self-identified as female or transgender, biologically male, and as having sex with men	57.1% (12/21)	31.3% (47/150)
Sandfort et al. [393]	2019	Kenya	2016	Convenience	Did not identify as male, assigned male sex at birth, and ever had sex with a man	25.0% (8/32)	14.6% (20/137)
		Malawi	2016			31.6% (12/38)	17.9% (15/84)
		South Africa	2016			57.6% (38/66)	36.9% (90/244)
Liberia MoH [394]	2019	Liberia	2018	RDS	No inclusion criterion provided	27.6% (80/290)	37.9% (240/633)
Fearon et al. [370]	2020	South Africa	2017	RDS	Assigned male at birth and current identity was female or transgender. Sex with a man in last 12 months	44.6% (20/44)	38.6% (90/233)

Study	Year of publication	Country	Year of data collection	Recruitment method	Transgender women inclusion criterion	TGW prevalence (%; n/N)	cis-MSM prevalence (%; n/N)
Malawi MoH [378]	2020	Malawi	2020	RDS	Self-identified as female or transgender. Engaged in sexual activities with other men in the past 12 months	13.5% (73/540)	12.5% (178/1425)
Nigeria MoH [395]	2020	Nigeria	2020	Venue-based	Identifies him/herself as a transsexual and undertakes sexual activity with a man	18.5% (775/4190)	21.1% (926/4397)
Rwema et al. [396]	2020	Rwanda	2018	RDS	Self-identified as transgender or a woman, assigned male sex at birth, and reported having had insertive or receptive anal sex with a man in the past 12 months	9.4% (10/106)	10.2% (64/630)
eSwatini MoH [397]	2021	Eswatini	2020	RDS	Identified as female. Report have insertive or receptive anal sex with a man in the past 12 months	41.2% (7/17)	20.2% (84/415)
Smith et al. [398]	2021	Kenya	2017	RDS	Male sex assignment at birth, self-identify as female or transgender, and having had consensual anal or oral sexual activity with a man in the previous 12 months	40.0% (28/70)	28.9% (151/522)
Sullivan et al. [399]	2021	South Africa	2016	Convenience	Male sex at birth and current gender identity as female or transgender, and report having had insertive or receptive anal sex with a man in the past 12 months	59.1% (13/22)	41.8% (110/263)

Study	Year of publication	Country	Year of data collection	Recruitment method	Transgender women inclusion criterion	TGW prevalence (%; n/N)	cis-MSM prevalence (%; n/N)
Harris et al. [400]	2022	Zimbabwe	2019	RDS	Born biologically male; self-identifed as a woman, transgender, or genderqueer, and engaged in anal or oral sex with a man in the past 12 months	27.5% (92/335)	21.1% (248/1176)
Sierra Leone MoH [401]	2022	Sierra Leone	2021	RDS	A woman who had a gender identity that is different from her sex at birth	4.7% (23/487)	4.2% (18/430)
Zambia MoH [402]	2023	Zambia	2021	RDS	Self-identified as a woman, biologically male at birth and self-reported anal or oral sex with biological male in past 6 months	17% (77/453)	13.5% (147/1088)

RDS=respondent driven sampling [302]; PLACE=Priorities for Local AIDS Control Efforts [387]

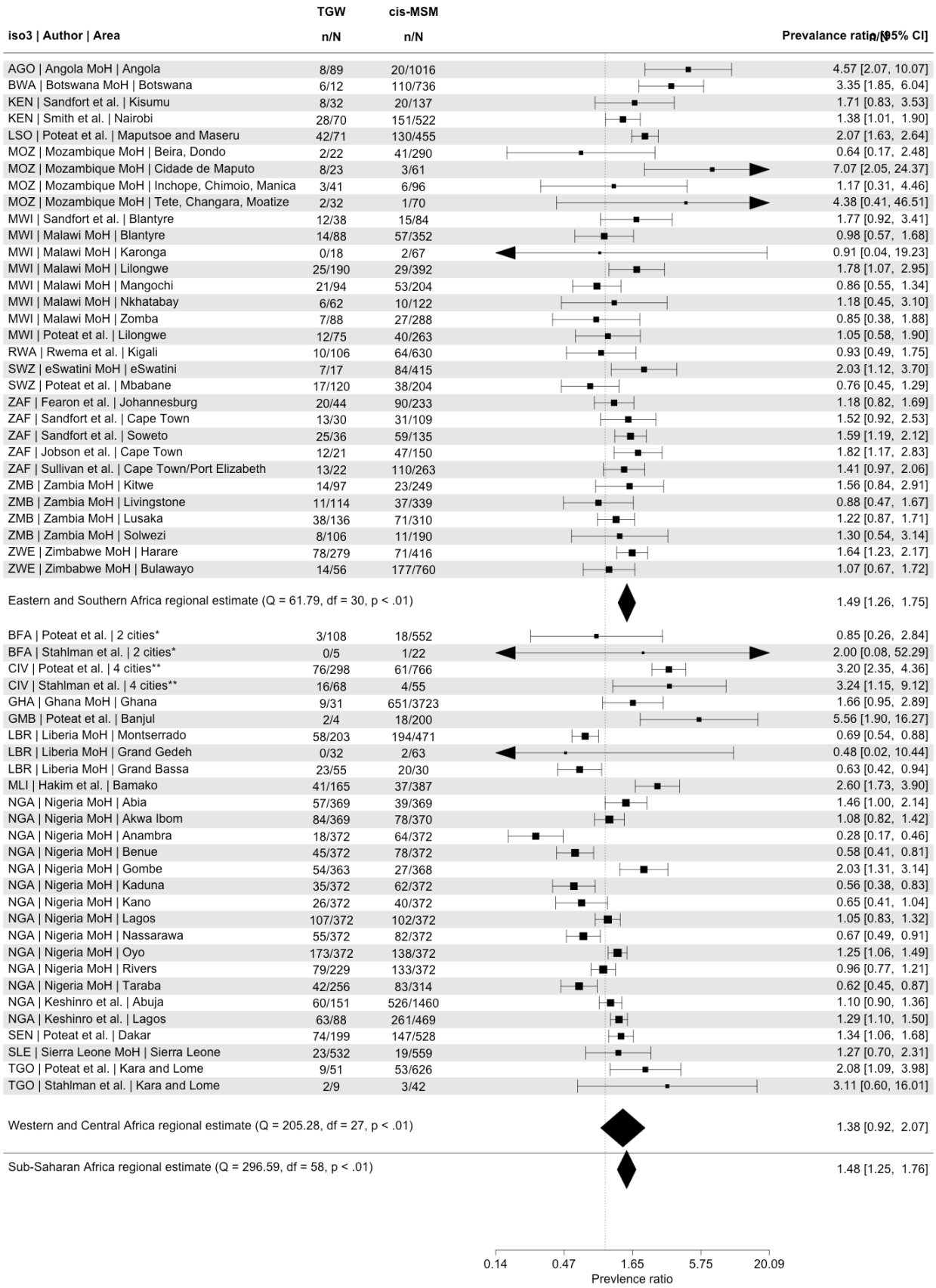

iso3 | Author | Area
TGW n/N
cis-MSM n/N
Prevalance ratio [95% CI]
AGO | Angola MoH | Angola 8/89 20/1016 4.57 [2.07, 10.07]
BWA | Botswana MoH | Botswana 6/12 110/736 3.35 [1.85, 6.04]
KEN | Sandfort et al. | Kisumu 8/32 20/137 1.71 [0.83, 3.53]
KEN | Smith et al. | Nairobi 28/70 151/522 1.38 [1.01, 1.90]
LSO | Poteat et al. | Maputsoe and Maseru 42/71 130/455 2.07 [1.63, 2.64]
MOZ | Mozambique MoH | Beira, Dondo 2/22 41/290 0.64 [0.17, 2.48]
MOZ | Mozambique MoH | Cidade de Maputo 8/23 3/61 7.07 [2.05, 24.37]
MOZ | Mozambique MoH | Inchope, Chimoio, Manica 3/41 6/96 1.17 [0.31, 4.46]
MOZ | Mozambique MoH | Tete, Changara, Moatize 2/32 1/70 4.38 [0.41, 46.51]
MWI | Sandfort et al. | Blantyre 12/38 15/84 1.77 [0.92, 3.41]
MWI | Malawi MoH | Blantyre 14/88 57/352 0.98 [0.57, 1.68]
MWI | Malawi MoH | Karonga 0/18 2/67 0.91 [0.04, 19.23]
MWI | Malawi MoH | Lilongwe 25/190 29/392 1.78 [1.07, 2.95]
MWI | Malawi MoH | Mangochi 21/94 53/204 0.86 [0.55, 1.34]
MWI | Malawi MoH | Nkhatabay 6/62 10/122 1.18 [0.45, 3.10]
MWI | Malawi MoH | Zomba 7/88 27/288 0.85 [0.38, 1.88]
MWI | Poteat et al. | Lilongwe 12/75 40/263 1.05 [0.58, 1.90]
RWA | Rwema et al. | Kigali 10/106 64/630 0.93 [0.49, 1.75]
SWZ | eSwatini MoH | eSwatini 7/17 84/415 2.03 [1.12, 3.70]
SWZ | Poteat et al. | Mbabane 17/120 38/204 0.76 [0.45, 1.29]
ZAF | Fearon et al. | Johannesburg 20/44 90/233 1.18 [0.82, 1.69]
ZAF | Sandfort et al. | Cape Town 13/30 31/109 1.52 [0.92, 2.53]
ZAF | Sandfort et al. | Soweto 25/36 59/135 1.59 [1.19, 2.12]
ZAF | Jobson et al. | Cape Town 12/21 47/150 1.82 [1.17, 2.83]
ZAF | Sullivan et al. | Cape Town/Port Elizabeth 13/22 110/263 1.41 [0.97, 2.06]
ZMB | Zambia MoH | Kitwe 14/97 23/249 1.56 [0.84, 2.91]
ZMB | Zambia MoH | Livingstone 11/114 37/339 0.88 [0.47, 1.67]
ZMB | Zambia MoH | Lusaka 38/136 71/310 1.22 [0.87, 1.71]
ZMB | Zambia MoH | Solwezi 8/106 11/190 1.30 [0.54, 3.14]
ZWE | Zimbabwe MoH | Harare 78/279 71/416 1.64 [1.23, 2.17]
ZWE | Zimbabwe MoH | Bulawayo 14/56 177/760 1.07 [0.67, 1.72]
Eastern and Southern Africa regional estimate (Q = 61.79, df = 30, p < .01) 1.49 [1.26, 1.75]
BFA | Poteat et al. | 2 cities* 3/108 18/552 0.85 [0.26, 2.84]
BFA | Stahlman et al. | 2 cities* 0/5 1/22 2.00 [0.08, 52.29]
CIV | Poteat et al. | 4 cities** 76/298 61/766 3.20 [2.35, 4.36]
CIV | Stahlman et al. | 4 cities** 16/68 4/55 3.24 [1.15, 9.12]
GHA | Ghana MoH | Ghana 9/31 651/3723 1.66 [0.95, 2.89]
GMB | Poteat et al. | Banjul 2/4 18/200 5.56 [1.90, 16.27]
LBR | Liberia MoH | Montserrado 58/203 194/471 0.69 [0.54, 0.88]
LBR | Liberia MoH | Grand Gedeh 0/32 2/63 0.48 [0.02, 10.44]
LBR | Liberia MoH | Grand Bassa 23/55 20/30 0.63 [0.42, 0.94]
MLI | Hakim et al. | Bamako 41/165 37/387 2.60 [1.73, 3.90]
NGA | Nigeria MoH | Abia 57/369 39/369 1.46 [1.00, 2.14]
NGA | Nigeria MoH | Akwa Ibom 84/369 78/370 1.08 [0.82, 1.42]
NGA | Nigeria MoH | Anambra 18/372 64/372 0.28 [0.17, 0.46]
NGA | Nigeria MoH | Benue 45/372 78/372 0.58 [0.41, 0.81]
NGA | Nigeria MoH | Gombe 54/363 27/368 2.03 [1.31, 3.14]
NGA | Nigeria MoH | Kaduna 35/372 62/372 0.56 [0.38, 0.83]
NGA | Nigeria MoH | Kano 26/372 40/372 0.65 [0.41, 1.04]
NGA | Nigeria MoH | Lagos 107/372 102/372 1.05 [0.83, 1.32]
NGA | Nigeria MoH | Nassarawa 55/372 82/372 0.67 [0.49, 0.91]
NGA | Nigeria MoH | Oyo 173/372 138/372 1.25 [1.06, 1.49]
NGA | Nigeria MoH | Rivers 79/229 133/372 0.96 [0.77, 1.21]
NGA | Nigeria MoH | Taraba 42/256 83/314 0.62 [0.45, 0.87]
NGA | Keshinro et al. | Abuja 60/151 526/1460 1.10 [0.90, 1.36]
NGA | Keshinro et al. | Lagos 63/88 261/469 1.29 [1.10, 1.50]
SEN | Poteat et al. | Dakar 74/199 147/528 1.34 [1.06, 1.68]
SLE | Sierra Leone MoH | Sierra Leone 23/532 19/559 1.27 [0.70, 2.31]
TGO | Poteat et al. | Kara and Lome 9/51 53/626 2.08 [1.09, 3.98]
TGO | Stahlman et al. | Kara and Lome 2/9 3/42 3.11 [0.60, 16.01]
Western and Central Africa regional estimate (Q = 205.28, df = 27, p < .01) 1.38 [0.92, 2.07]
Sub-Saharan Africa regional estimate (Q = 296.59, df = 58, p < .01) 1.48 [1.25, 1.76]
0.14
0.47
1.65
5.75
20.09
Prevlence ratio

Figure 4.1: Forest plot comparing HIV prevalence ratios in transgender women (TGW) and cis-gendered men-who-have-sex-with-men (cis-MSM).

* Bobo-Dioulasso and Ouagadougou ** Abidjan, Bouake, Gagnoa, and Yamoussoukro

HIV prevalence among transgender women was highly correlated with study-matched cis-MSM HIV prevalence (Figure 4.2; R^2=0.60) and poorly correlated with UNAIDS province/year-matched total population HIV prevalence (R^2=0.01). Relative to venue- and convenience-based sampling methods, studies using network-sampling methods did not estimate a significantly different pooled HIV prevalence ratio (Table 4.1; PR 1.06 95CI 0.72-1.56).

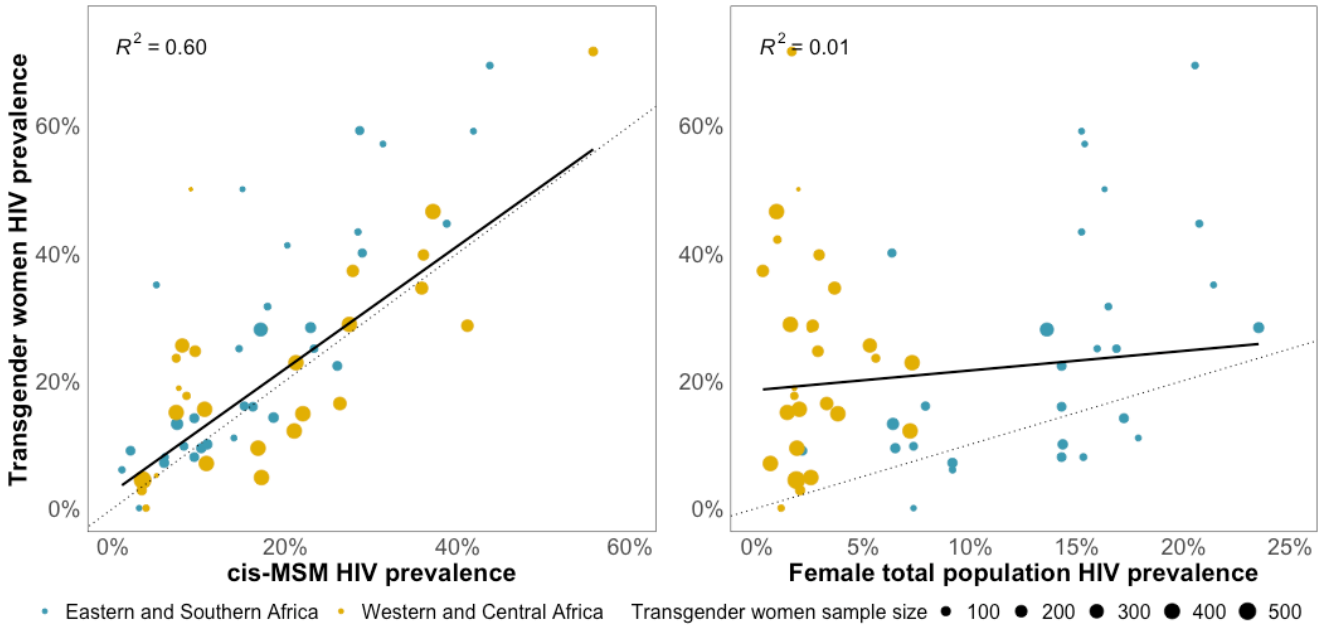


Figure 4.2: Comparison of HIV prevalence among transgender women and cis-gender men-who-have-sex-with men (cis-MSM) (left) and HIV prevalence among transgender women compared to HIV prevalence among all women aged 15-49 years (right). The dotted line represents the line of equality is (y=x). Colour of data points represents the UNAIDS region of the study country.

One-third of studies (6/21) included, or did not specifically exclude, transgender men in the sampled transgender population. Of these six studies, five were BBS or PLACE study reports [378,379,395,397,401]. One study[401] provided disaggregated sample sizes for transgender women and men, but reported aggregated HIV prevalence for all transgender people; three studies did not provide disaggregated sample sizes or HIV prevalence[378,395,397]. Two studies reported HIV prevalence for non-binary populations[370,377]. These data were not included in meta-analysis. In sensitivity analysis excluding the four studies that reported HIV prevalence for transgender women and men combined, the estimated prevalence ratio was slightly higher (SSA PR: 1.63, 95CI 1.36-1.96).

Five studies reported HIV prevalence estimates for transgender men: 10% (4/42) in Benin[386]; 7% (3/44) in Botswana[379]; 4% (2/49) in Uganda[403]; 24% (9/65) in Malawi[404]; and 1% (1/30) in Sierra Leone[401] (Table 4.2). Comparison and interpretation of these estimates is challenging due to small number of studies and sample sizes. From these limited data, transgender men may have a lower risk of HIV infection than transgender women.

Study	Area	Year	HIV prevalence (%)				
			TGM	TGW	cis-MSM	15-49 women	15-49 men
Benin MoH [36]	Benin	2020	9.5	26.4	7 [49]	1.1	0.5
Mujugira et al. [42]	Kampala, Uganda	2020	4.1	20.0 [17]	12.7 [63]	7.4	4.8
Botswana MoH [27]	Botswana	2017	6.8	45.5	14.9	26.2	16
Malawi MoH [43]	Malawi	2021	23.9	62.3	12.5 [26]	9.3	5.6
Sierra Leone [40]	Sierra Leone	2021	1.11	4.36	3.4	1.8	1

Table 4.3: Estimates of HIV prevalence among transgender men (TGM) compared with transgender women (TGW), cis-gendered men who have sex with men (cis-MSM), and 15-49 total population. In each row, estimates in bold are from the same study indicated in the 'Study' column. Transgender women and cis-MSM estimates in italics are the best available comparator estimates from other studies. Total population HIV prevalence estimates are from UNAIDS estimates derived using Spectrum and Naomi models.

4.5 Discussion

Twenty-five studies have measured HIV prevalence among transgender women, a large increase from ten African studies included in a recent systematic review[297]. HIV prevalence was substantially higher among transgender women than cis-MSM in sub-Saharan Africa, providing further evidence of HIV vulnerability distinct from cis-MSM. Previous studies[297,350,361] have identified substantial HIV burden in transgender people, which this meta-analysis supports both in absolute terms and relative to cis-MSM, already a vulnerable and high-risk population sub-Saharan Africa. HIV service needs for transgender women are increasingly recognised in HIV programmes in sub-Saharan Africa. A 2021 review found that transgender people are identified in the National Strategic HIV/AIDS Plans of sixteen countries[405], increasing from ten in 2018[406].

Pooled estimates of HIV prevalence among transgender women or relative risk of HIV infection compared to that in the total population as presented in previous studies have been avoided[350,361]. Firstly, the relative risk of HIV infection in key populations varies with total population HIV prevalence in SSA. Summarising a single relative risk of infection decouples the key population epidemiology in a given country from the HIV epidemic in the total population. In WCA, cis-MSM HIV prevalence can be 100-fold higher than male total population prevalence, while in ESA it may be similar to, or lower than that in the total population[366]. Second, total population HIV prevalence is poorly correlated with cis-MSM HIV prevalence, particularly in WCA where neighbouring countries with similar generalised HIV epidemics can have disparate key population epidemics[323,366]. Instead, I found a consistently higher risk of HIV infection in transgender women compared to cis-MSM. These estimates should be viewed as interim estimates to support programme planning in settings that lack dedicated HIV surveillance, and should not obviate the need for transgender-specific surveillance nor to further discourse that the programmatic needs of transgender people can be wholly met through cis-MSM programmes.[407] Recognising the additional HIV burden experienced by transgender women and their specific health needs (e.g. gender-affirming hormone therapy),

while identifying common needs among sexual and gender minorities (e.g. stigma and gender-based violence interventions) is an important strategy to ensure effective services reach those who need them in an era of constrained resources for key population programmes.

I was unable to estimate the relative HIV prevalence between transgender men and other populations, though limited data indicated that transgender men may have a lower risk of HIV infection than transgender women or cis-MSM. Two studies recruited too few transgender men to estimate HIV prevalence[370,398]. Transgender men remain an understudied population in SSA, and have been the primary focus of only two serological testing studies to date[386,403]. Of six studies in this analysis that did not exclude transgender men, four included recent oral or anal sex with a man as an inclusion criterion. Though data across SSA are limited, they indicate that cis-women are more likely to be partners of transgender men than cis-MSM or other transgender men[379,403,408]. Transgender men are likely, therefore, to be excluded from biological surveillance if all transgender populations are associated with the same HIV risk behaviours as cis-MSM.

Three studies were retained that did not specify which transgender population(s) were recruited in the main analysis[378,395,397]. Sexual behaviour data collected in each study indicated that transgender participants overwhelmingly reported male sexual partners and receptive anal intercourse. All three studies were recent, published since 2020, and with large sample sizes. Sensitivity analysis indicates that their inclusion had only a marginal impact on the estimated relative risk of HIV infection, and I feel that their inclusion alongside studies that explicitly recruited transgender women is justified. Survey data on gender identity were often ambiguous, necessitating its removal from analysis further reducing sample sizes. Consistently adopting the ‘two-step’ method, in which survey participants are first asked their assigned sex at birth followed by their gender today, would improve gender identification in key population surveys and enhance comparability across studies [403,409].

Few studies have measured treatment coverage or viral load suppression among transgender people, and only a subset are laboratory confirmed[366]. While I identified that transgender women are at increased risk of HIV infection, it was not possible to estimate ART coverage or access to treatment services either in absolute terms or relative to cis-MSM. This remains a key data gap in monitoring the objectives laid out by the Global AIDS Strategy.

Interpretation of this analysis is subject to several limitations. Firstly, I did not differentiate between studies whose primary objective was transgender surveillance[349,364,377,380,389–391,395,396,398–401], and those that reported transgender participants alongside the primary objective of cis-MSM surveillance[370,378,379,388,392,393,397]. The latter studies may disproportionately recruit transgender people who socialise with cis-MSM. These data may overstate the similarities between the two populations as phylogenetic clustering studies indicate extensive transmission between cis-MSM/TGW and the heterosexual-identifying population[410]. Second, insufficient age-specific HIV prevalence data were available to estimate age-adjusted prevalence risk ratios which may lead to underestimated prevalence ratios.

4.6 Conclusion

Transgender women have 50% higher HIV prevalence than cis-MSM in SSA and, therefore, transgender women and cis-MSM should not be considered as a single risk population. HIV prevalence among transgender women is highly correlated with cis-MSM prevalence, and cis-MSM HIV prevalence may help inform assessment of HIV prevalence among transgender women in settings that lack dedicated surveillance. Studies estimating the treatment cascade among transgender women and men are a priority to quantify progress towards equitable HIV service access and enable HIV programmes to meet the prevention and treatment needs of transgender people.

5. 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

Acknowledgements

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Empirical data from previous systematic reviews on HIV incidence among MSM[112] were provided by Dr. James Stannah (McGill University) and among FSW[113] by Dr. Harriet Jones (LSHTM) and Rebecca Anderson.

Dissemination

This analysis was presented and refined at the October 2023 UNAIDS Reference Group meeting, and work contained within this chapter was published in *JAIDS*:

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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 (1999)*, *95*(1S), E46–E58. https://doi.org/10.1097/QAI.0000000000003321

5.2 Introduction

As detailed in Section 1.11.4, UNAIDS has published estimates of the percentage of new adult HIV infections acquired by key populations since 2014. 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.[411] 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 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.[412] Though headline estimates within UNAIDS Global AIDS Reports, the methods underpinning them did not use a systematic approach, and instead combined results from previous applications of the Modes of Transmission Model[215,413], Incidence Patterns Model,[414] Goals model,[415] or Optima model,[416] *ad hoc* estimates of population size, or imputed based on estimates from other countries in the region. 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.

HIV incidence and the number of new infections are key indicators for tracking progress in the HIV epidemic response.[412] Estimates among key populations, including female sex workers (FSW), 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.[285] Cohort studies measuring HIV seroconversion of seronegative individuals, while the gold standard method for estimating HIV incidence, are costly and challenging to implement. [417] Conducting incidence cohorts among key populations is further hindered by small study populations, high mobility and transient living arrangements,

non-disclosure of risk behaviour, and societal marginalisation.[288–290] 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.[294,418] These analyses find that HIV incidence among MSM has not declined over time, and, while 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[399,419] and PWID[420,421] 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 programme 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 risk group using key population size and sexual behaviour data, was widely used in sub-Saharan Africa to understand differential HIV risk by population group.[330,422] While 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,[329] and has been succeeded by transmission dynamic models which better capture risk over time. These include Goals[423], Optima[416], and several country-specific models (for South Africa[327,424–426], Eswatini[427], Lesotho[427], Côte d'Ivoire[428,429], Cameroon[430], Senegal[431], Mali[431], Kenya[432], and Tanzania[433]).

Considering the large and increasing prominence of the UNAIDS-reported estimates for global HIV policy and advocacy, I sought to compare the UNAIDS estimates to empirical data on HIV incidence among key populations and population sizes and results from other mathematical models.[294,434] 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?; and (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?

5.3 Methods

I 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 sub-Saharan Africa,[294] 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.[412] For each source, I 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 (IRR), and (4) ratio of key population HIV incidence to key population HIV prevalence. Analyses were conducted at regional level because empirical incidence data were insufficient for country-level analyses. This consisted of two distinct workflows: incidence metrics were derived from the UNAIDS proportion of new infections among key populations; and the proportion of new infections among key populations were derived from the empirical incidence measures (Figure 5.1).

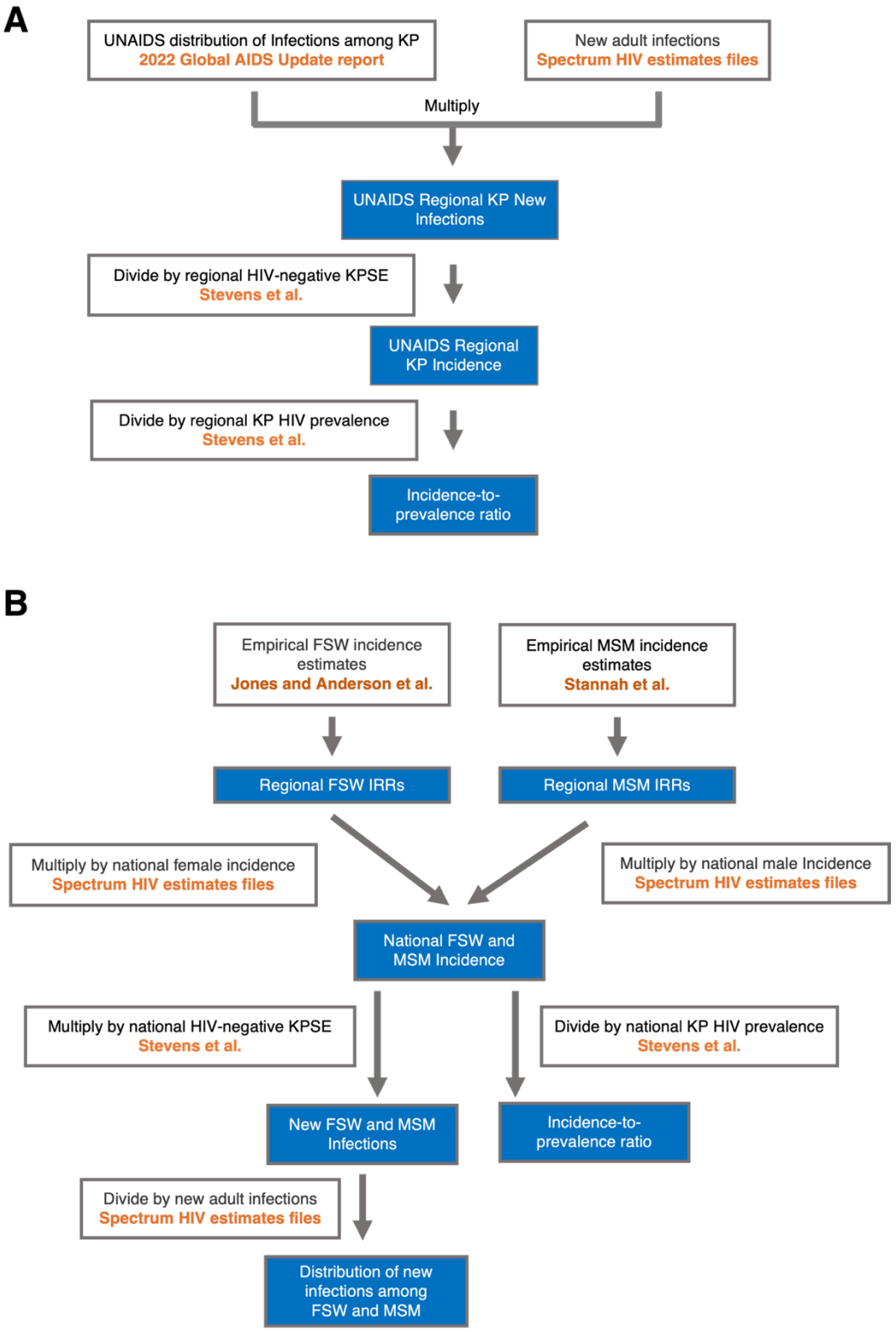


Figure 5.1: Data workflow for estimating the proportion of new infections and the incidence-to-prevalence ratio. (A) UNAIDS regional estimates of the distribution of new infections. (B) Female sex worker (FSW) and men who have sex with men[294] (MSM)

empirical incidence studies. KP = key population; KPSE = key population size stimate. Data included from UNAIDS Global AIDS Update report[412], Spectrum[435], Jones and Anderson et al.[418], Stannah et al.[294], and Chapter 2.

5.3.1 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 populations and their partners[412], and not for the number of new infections, HIV incidence rates, or population size estimates. To derive estimates for HIV incidence rate by key population, I 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[435] and national estimates for key population size estimates (KPSE) and HIV prevalence from Chapter 2 (Figure 5.1A; Supplementary Tables S5.1 and S5.2).

I 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:

$$\text{UNAIDS new infections}_{KP,r} = \text{UNAIDS proportion of new infections}_{KP,r} \times \text{Adult infections}_{r} \quad (1)$$

I then aggregated the national key population size and HIV prevalence estimates from Chapter 2 to obtain the estimated number of HIV-negative key population members by region, used as a denominator for the implied HIV incidence rate:

$$\text{UNAIDS HIV incidence rate}_{KP,r} = \frac{\text{UNAIDS New infections}_{KP,r}}{\text{HIV-negative population size}_{KP,r}} \quad (2)$$

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). I 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.

5.3.2 Empirically-derived incidence rate ratios and implied infections distribution

I reanalysed data from a systematic review of studies that empirically measured HIV incidence among MSM from Stannah *et al.*[294] to estimate IRRs relative to modelled estimates of male total population incidence (E-IRR). For each key population incidence study, I 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,[307] a small-area estimation model that produces cross-sectional district-level estimates using nationally-representative household survey and routine ART and antenatal health system data.[308] District-level estimates for 1985-2021 were created by extrapolating 2022 estimates parallel to UNAIDS sex-matched national-level incidence trajectories.[435] MSM incidence studies were commonly restricted to recently sexually active MSM and primarily recruited young MSM.[294] Therefore, I divided the total population male incidence denominator by the proportion of all men who were sexually active[436] 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, I assumed 15-29 years. Study IRRs were pooled via mixed-effects meta-analysis[30] 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[382]. I conducted sensitivity analysis using national incidence estimates over time from Spectrum in place of 2022 district-level incidence estimates extrapolated backward over time.

Empirically-derived IRRs for FSW in ESA and WCA were directly available from Jones and Anderson *et al.*[113] Insufficient data were available to estimate E-IRRs for PWID. I 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 (Figure 5.1B):

$$\text{Empirical FSW HIV incidence}_{c,\,r} = \text{FSW E-IRR}_r \times \text{National female HIV incidence}_c \quad (3)$$

$$\text{Empirical MSM HIV incidence}_{c,\,r} = \text{MSM E-IRR}_r \times \text{National male HIV incidence}_c \quad (4)$$

Numbers of new infections were calculated by multiplying key population HIV incidence rates times the national number of HIV-negative key population members from Chapter 2. 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.[383,435]

$$\text{Empirical new infections}_{KP,\,c} = \text{HIV incidence}_{KP,\,c} \times \text{HIV-negative population size}_{KP,\,c} \quad (5)$$

$$\text{Empirical proportion of new infections}_{KP,\,c} = \frac{\text{New infections}_{KP,\,c}}{\text{Adult new infections}_c} \quad (6)$$

To assess the sensitivity of new infection proportion estimates to KPSE assumptions, I repeated analysis using the lower and upper 95% credible intervals around the regional KPSE proportion by key population from Chapter 2.

5.3.3 Mathematical model estimates for the distribution of infections by population group

I collated outputs from mathematical models that represented HIV transmission dynamics among key populations calibrated to settings in sub-Saharan Africa. 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, nine mathematical models provided results for 94 settings (Supplementary Table S5.1). The Goals model[423,437] provided two versions reflecting alternative population size assumptions for all 38 SSA countries (76/94 model results). Optima[416] reported results for 15 SSA countries. Thembisa[424], Stone *et al.*[17], EMOD[438], and Mishra *et al.*[427] reported results for South Africa, with Mishra also reporting Eswatini and Lesotho. Maheu-Giroux *et al*.[439] and two models by Silhol *et al.*[429,430] 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.

5.4 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, the ratio of HIV incidence to prevalence was calculated by key population group.

For model results, I assessed how key population HIV prevalence and KPSE assumptions influenced new infection distribution estimates. Key population HIV prevalence and KPSEs as a proportion of the total adult population size (both sexes) was compared in countries with three 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), I 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.

5.5 Results

5.5.1 Key population HIV incidence rate ratios 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, 2.3/100py for MSM, and 7.1/100py for PWID in ESA, and 2.5/100py for FSW, 3.7/100py for MSM, and 0.8/100py for PWID in WCA in 2021 (Table 5.1). Across sub-Saharan Africa, compared to 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% CI: 3.7-7.6; Table 5.2) than in matched total population women, and, in WCA, was 22.4 times higher (95%CI 11.3-44.3). Applying these E-IRRs to UNAIDS total national incidence estimates implied FSW HIV incidence rates of 1.6/100py in ESA and 1.4/100py in WCA (Figure 5.2A; Table 5.2).

Across SSA, empirical incidence estimates among MSM were 41.8 times higher than in matched total population men (95% CI: 21.9-79.6); Table 3, Supplementary Figure S5.1). Incidence rates were 141.7 times higher in WCA (95%CI: 52.2-384.7) and 22 times in higher in ESA (95%CI: 14.1-34.3). MSM HIV incidence rates calculated using regional E-IRR were 3.3/100py in ESA and 4.3/100py in WCA (Figure 5.2A; Table 5.2). Sensitivity analysis matching to national-level total population male incidence, instead of subnational, increased SSA IRR to 50.2 (95%CI 27.4-92.1; Supplementary Figure S5.2) and the associated MSM HIV incidence rate to 4.0/100py.

Table 5.1: Derived regional key population HIV incidence rates from UNAIDS-reported proportions of new infections

KP	Region	UNAIDS% of new infections[a]	Total population new infections[b]	KP new infections[c]	KPSE count[d]	KP HIV prevalence[d]	Implied incidence rate/100py[e]	UNAIDS-IRR[f]	KP incidence to prevalence ratio[g]
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	2,490	339,000	4%	0.8	17.0	0.18
	SSA	3%	631,000	18,900	632,000	13%	3.4	27.2	0.27

[a] Source: UNAIDS Global HIV Estimates 2022, UNAIDS special analysis[412]
[b] Source: UNAIDS Global HIV Estimates 2022, National Spectrum estimates for ages 15-49 in 2021.[435]
[c] Calculated as proportion of new infections times total new adult infections.
[d] Source: Chapter 2
[e] Calculated as the number of new key population infections divided by the number of HIV-negative key population members [KPSE x (1-HIV prevalence)]
[f] Calculated as the implied key population 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)
[g] Calculated as the implied incidence rate divided by key population HIV prevalence
Abbreviations: FSW = female sex workers, MSM = men who have sex with men, PWID = people who inject drugs, ESA = Eastern and Southern Africa, WCA = Western and Central Africa, SSA = sub-Saharan Africa, py = person-years, KPSE = population size estimate.

Table 5.2: Empirical key population incidence studies—derived regional key population HIV incidence rates

KP	Region	Empirically-derived IRR[a]	Sex-specific total population incidence/100py[b]	KP incidence /100 py[c]	KP new infections[d]	Total new infections[b]	% of new infections[e]	Incidence to prevalence ratio[f]
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

[a] Source: FSW incidence rate ratios from Jones and Anderson et al.[418], MSM incidence rate ratios from Stannah et al.[294]
[b] Source: UNAIDS Global HIV Estimates 2022, National Spectrum estimates for ages 15-49 in 2021.[435]
[c] Calculated as IRR times sex-specific total population incidence rate
[d] Calculated as the key population incidence rate multiplied the number of HIV-negative key population members [KPSE x (1-HIV prevalence)] from Chapter 2
[e] Calculated as the number of new key population infections divided by the total number of new infections
[f] Calculated as the key population incidence rate divided by the key population prevalence from Chapter 2
Abbreviations: FSW = female sex workers, MSM = men who have sex with men, PWID = people who inject drugs, ESA = Eastern and Southern Africa, WCA = Western and Central Africa, SSA = sub-Saharan Africa, py = person-years, KPSE = population size estimate, E-IRR: Empirically-derived incidence rate ratio

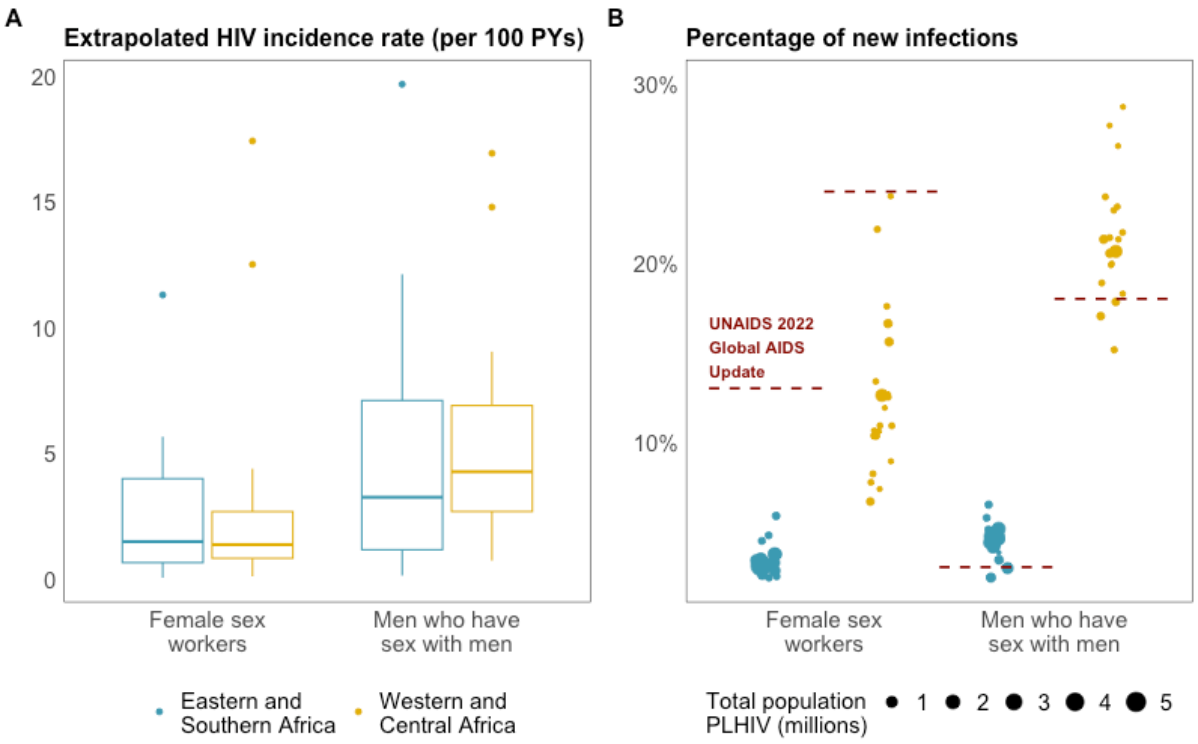


Figure 5.2: Extrapolated HIV incidence rates and proportion of new infections among female sex worker (FSW) and men who have sex with men (MSM) derived from empirically-derived incidence rate ratios (E-IRR) from systematic review. (A) National-level extrapolated HIV incidence rates in female sex workers (FSW) and men who have sex with men (MSM) in 2021 in Eastern and Southern Africa (ESA) and Western and Central Africa (WCA). Boxplots summarise range of national HIV incidence for 39 countries calculated by multiplying incidence rate ratios from Jones & Anderson *et al.*[418] (FSW) and Stannah *et al.*[294] (MSM) times sex-matched adult HIV incidence from UNAIDS 2021 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 panel (A) with key population size and HIV prevalence estimates from Chapter 2. The horizontal dashed line represents the regional UNAIDS estimate of the percentage of new infections by population group from the 2022 UNAIDS Global AIDS Update. PY = person-years

5.5.2 Proportion of new infections acquired by female sex workers and men who have sex with men

E-IRRs and mathematical model studies implied a smaller proportion of new infections among FSW than UNAIDS regional estimates (Figure 5.2B). 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 (Figure 5.2B; Table 5.2; Supplementary Tables S5.4 and S5.5). 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% confidence interval from Chapter 2 indicated between 9 and 19% of new infections occur among FSW and MSM in SSA (Supplementary Table S5.7).

Figure 5.3 reports the proportion of infections among key population groups from mathematical models. Across 94 country estimates from nine models, 3% of new infections in SSA occurred in FSW (median estimates weighted by national PLHIV population size; 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.

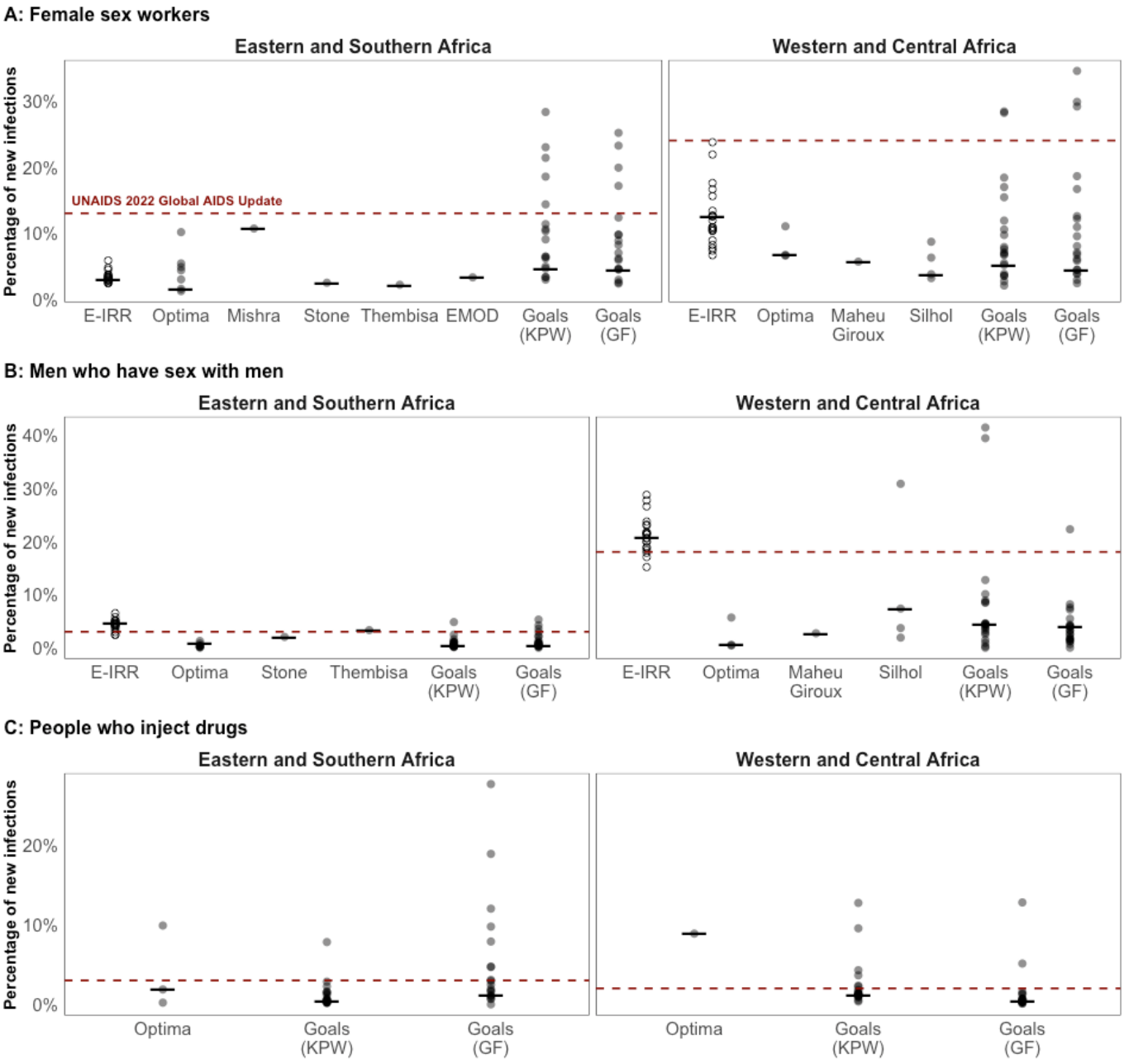


Figure 5.3: Comparison of percentage of new adult infections among each key population group in sub-Saharan Africa across mathematical models and empirical sources. (A) Female sex workers (FSW), (B) Men who have sex with men (MSM), (C) People who inject drugs (PWID). Each circle represents one country estimate. UNAIDS 2021 regional estimates for FSW, MSM, and PWID are represented by the horizontal dashed line. Estimates from empirically-derived incidence rate ratios (E-IRR) calculated from incidence rate ratios (Stannah *et al.*[294] for MSM and Jones and Anderson *et al.*[418] for FSW) and population size estimates (Chapter 2) 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. KPW = Key population workbook; GF = Global Fund

5.5.3 Model estimates of HIV prevalence and population size and association with the distribution of new infections

Modelled HIV prevalence and population size proportions for the same country commonly varied by more than two-fold across models in eight countries with three or more models (Figure 5.4). Across seven models representing the South African epidemic, FSW KPSE proportions varied four-fold (0.2-0.9%) and MSM KPSE proportions two-fold (0.4-1.0%). Restricted to models for South Africa, Lesotho, and eSwatini, the percentage of new infections was strongly correlated with population size for FSW (R^2 = 0.69; Figure 5.4C) and PWID (R^2 = 0.90) and only weakly correlated for MSM (R^2 = 0.21; Figure 5.4C).

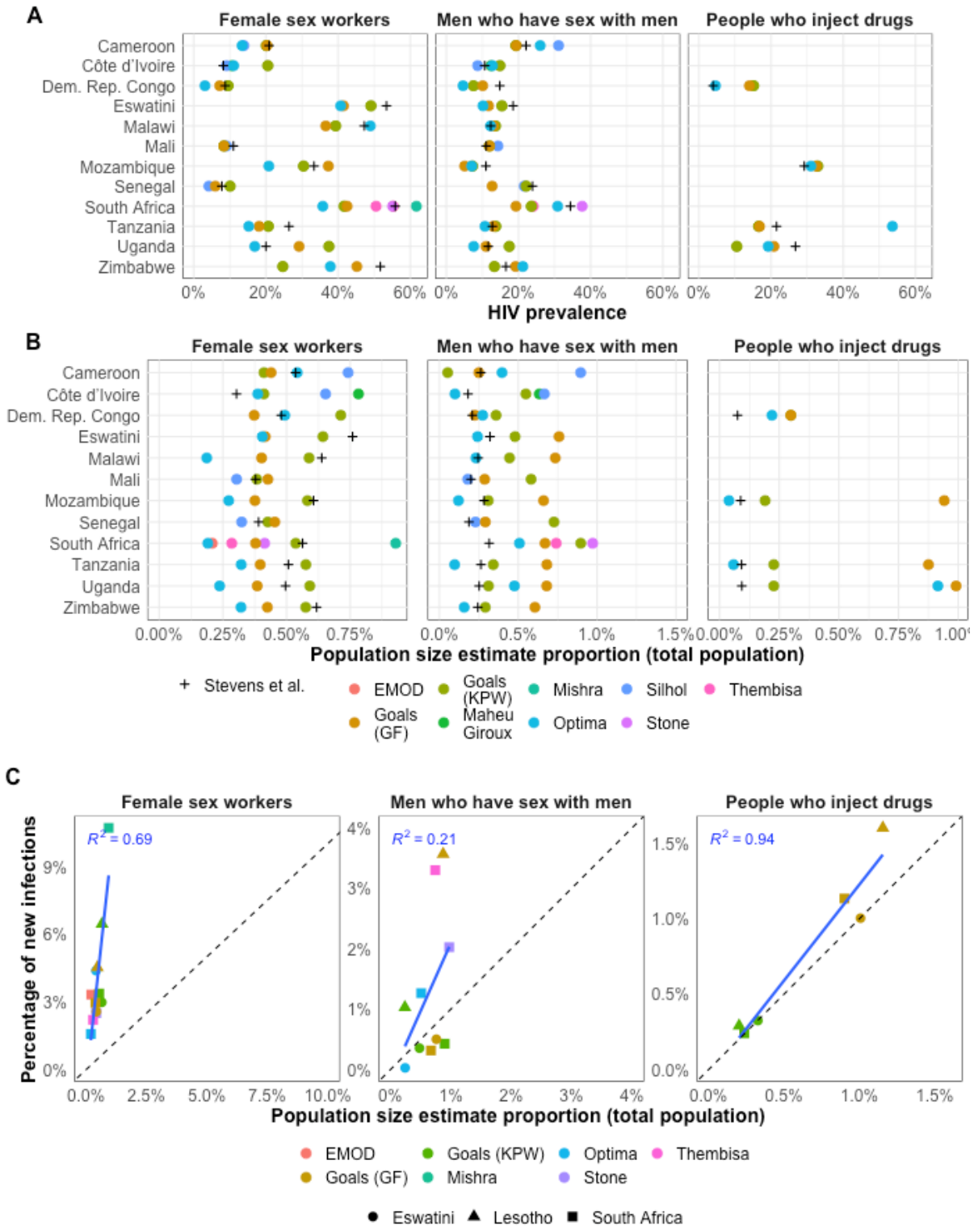


Figure 5.4: Heterogeneous model-based key population estimates. Comparison of model-based estimates of HIV prevalence (A) and population size estimate proportions (B) in 2020 Countries selected were those with three or more models available. Synthesised surveillance data from Chapter 2 represented by black crosses to differentiate from model inputs. Key population 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 neighbouring countries with comparable, high prevalence HIV epidemics. Blue line represents the line of best fit and the dotted line represents the line of equality.

5.5.4 Incidence to prevalence ratio

Among FSW in SSA, UNAIDS infection distribution estimates implied an incidence-to-prevalence ratio of 0.19 (i.e. HIV prevalence among FSW was 5 times higher than annual incidence), and similar between regions (ESA: 0.19; WCA 0.18). Incidence-to-prevalence ratios derived from empirical FSW incidence and prevalence estimates (SSA: 0.06; ESA: 0.05; WCA: 0.10) or from mathematical models (SSA median 0.10; ESA 0.12; WCA 0.09) were two to three times lower than the UNAIDS-implied ratio (Figure 5.5A, Supplementary Table S5.6).

Among MSM, UNAIDS estimates implied an incidence-to-prevalence ratio of 0.19 for SSA (ESA: 0.15; WCA: 0.23) which is similar to the empirically based MSM ratio (SSA: 0.23; ESA: 0.22; WCA: 0.27) and much higher than the MSM ratio from mathematical models (SSA median ratio: 0.03; ESA median: 0.02; WCA median: 0.05; Figure 5.5B).

UNAIDS incidence-to-prevalence ratios estimates implied very high ratios for PWID (SSA: 0.27; ESA: 0.32; WCA: 0.18), five times higher than model estimates from the Optima and Goals models (SSA median ratio: 0.05; ESA: 0.04: WCA: 0.07; Figure 5.5C).

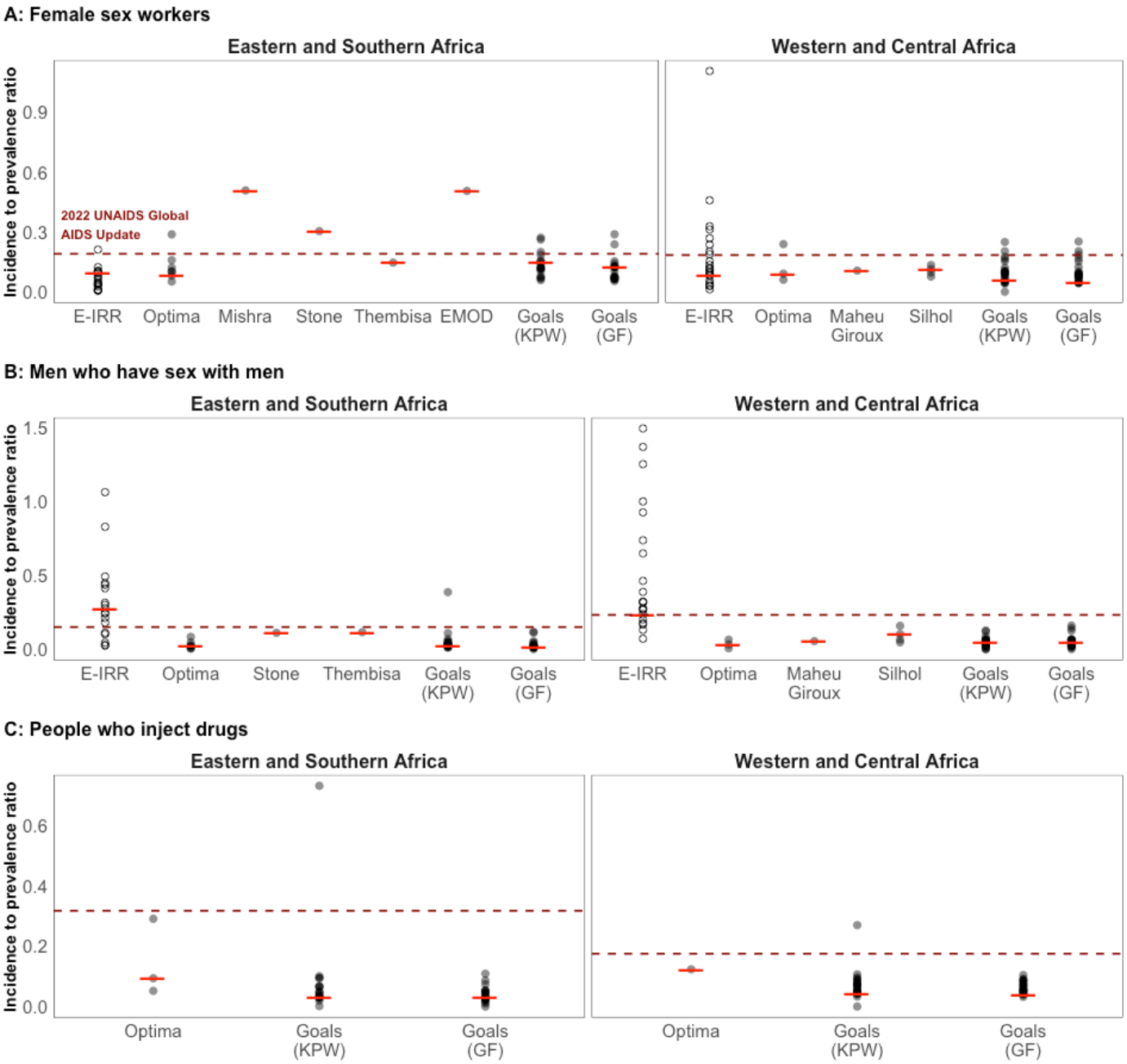


Figure 5.5: Ratio of key population group HIV incidence rate to HIV prevalence in sub-Saharan Africa. Each circle represents one country estimate. The incidence to prevalence ratio derived from the UNAIDS regional estimates of the percentage of new infections occurring in female sex workers, men who have sex with men, and people who inject drugs are represented by red dotted line. Estimates from empirically-derived incidence rate ratios (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 national HIV population size. KPW = Key Population Workbook, GF = Global Fund.

5.6 Discussion

Empirical HIV incidence data and mathematical models calibrated to data on HIV prevalence by population group across sub-Saharan Africa confirmed that key populations are disproportionately vulnerable to acquiring HIV. Through systematically triangulating available HIV incidence, HIV prevalence, and population size data from sub-Saharan Africa, I estimated that around 12% of all new HIV infections in sub-Saharan Africa were among FSW and MSM, despite comprising only around 1% of adults at risk. In Eastern and Southern Africa, where HIV is more prevalent, FSW and MSM accounted for around 7% of new infections. In Western and Central Africa, 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.

While 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 incidence and cross-sectional key population surveys were substantially lower than the combined 25% reported in the 2022 UNAIDS Global AIDS Update.[412] Our estimates were particularly lower for FSW, among whom UNAIDS reported 15% of new infections, compared to 5% from our analysis. Identifying the main reasons for these differences is challenging due to multiple differences in approaches. Due 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 analyse 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.[440]

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[327]). Empirically-derived FSW IRR were broadly consistent with model-based estimates of FSW incidence. However, empirical MSM incidence rate ratios were 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 biobehavioural 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.[293,294] 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 burdenburden, or both. Models that estimate age- 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.[440,441]

Model-based estimates of the proportion of new infections among key populations were highly correlated with KPSE proportions, underscoring the importance of KPSE assumptions. Compared to surveillance methods for HIV prevalence and ART coverage, KPSE methods are poorly standardised, of varying quality, and produce highly heterogeneous estimates.[290,310,331,434,442] Calibrating models at national level requires extrapolation of local (e.g. city-level) population size estimates to areas

lacking key population surveillance data. This is particularly challenging given spatial and temporal heterogeneity in size estimate proportions among FSW[336] and further increases uncertainty around size estimates.[337,443,444] Adopting consensus 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.

This 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.[327,329,445,446] 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 amongst key populations[17,43–45]. The finding that mathematical models indicated a lower proportion of infections among key populations than assumed by UNAIDS does not undermine modelling evidence for prioritised 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.[327,427–429]

This analysis has several limitations. First, 76 of the 94 modelled 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, empirically-derived IRRs used subnational total population incidence denominators extrapolated over time. The extrapolation assumed the proportional change in incidence at district-level was the same as that at 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 (Supplementary Figure S5.3) and FSW E-IRRs[418] using national-level incidence estimates, informed by surveillance data over time, indicates that this is unlikely to have significantly distorted this analysis. Third, to increase comparability with UNAIDS-derived and model-based estimates, I 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 to the total population. Consequently, I are likely to have overstated the proportion of new adult infections among key populations. Fourth, derived estimates for HIV incidence from empirical incidence meta-analyses and the UNAIDS distribution of new infections (Figure 5.1) relied on national estimates of KPSE and HIV prevalence from Chapter 2 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, I 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 (Supplementary Table S5.7).

5.7 Conclusion

Empirical incidence data and mathematical models confirm dramatically higher HIV acquisition risk among key populations in sub-Saharan Africa, and a larger proportion of total new infections occur among key populations in WCA than ESA. 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 modelling frameworks that reconcile

all available key population surveillance data may improve the empirical basis for estimates of new infections among key populations.[440,441] Improved HIV surveillance among key populations could help to reduce variability and improve robustness of estimates of the contribution of key populations to the HIV epidemic in SSA.

6. Estimating HIV incidence among female sex workers from serial cross-sectional surveys in Cotonou, Benin

Acknowledgements

To Prof. Michel Alary for conducting HIV surveillance among female sex workers in West Africa since the earliest days of the epidemic and to his collaborators at Université Laval, Drs. Souleymane Diabaté and Myrto Mondor, who have continued his work, supported this analysis and shared its data, and provided useful feedback on the contemporary dynamics of sex work in Benin.

Estimates of HIV incidence are key to monitoring the HIV epidemic, have formed central components of strategic information portfolios since the early epidemic, and are now urgently required among key populations to target limited provision of long-acting HIV prophylaxis. Empirical incidence studies, mostly commonly prospective cohort studies, require longitudinal follow-up and accordingly are expensive and logistically challenging to implement. Implementation is further complicated among sex workers as criminalisation and frequently moving for work hamper follow-up and introduce heterogeneity into cohorts that may lead to biased estimates of incidence.[113] Our recent systematic review identified only 32 incidence studies among female sex workers conducted in sub-Saharan Africa across the entire epidemic.[113] Meta-analysis of these incidence studies estimated incidence among sex workers was 8 times higher than among subnational location and age matched total population women. Instead, as outlined in Section 1.9.2, model-based estimates calibrated to cross-sectional behavioural and HIV surveillance data are commonly used to estimate HIV incidence.[202,447,448]

Transmission dynamic models that seek to reconstruct the complete epidemic history among all subpopulations are necessarily data demanding.[226,227,229,231] In the case of key populations, where data are sparse, this either restricts their application to the most data rich settings or results in assumption-heavy approaches. Model representations of sex work behaviour are often granular and may incorporate both paying and non-paying partners and their HIV prevalence; frequency of clients, vaginal, and anal sex; and all associated HIV prevention and treatment strata. The absence of direct client population size estimates from most settings is a large source of uncertainty in such models and must be inferred from FSW sexual partner data.[229] Estimates of the proportion of men who buy sex from total population surveys vary widely and are assumed to be under-estimated.[154,229]

Instead, this chapter presents a statistical model that estimates HIV incidence among female sex workers using single-year age- and duration-stratified cross-sectional survey data. Several methods have sought to reconstruct incidence from serial cross-sectional measures of prevalence among the total population in sub-

Saharan Africa where, setting aside migration, mortality is the only opportunity for individuals to leave the population. Catalytic-based approaches calculate incidence from age-specific prevalence under equilibrium conditions. As the age pattern of prevalence is assumed to be constant, prevalence reflects the cumulative exposure to incidence. Gregson et al. detail a catalytic method which fits a functional incidence form to age-specific ANC prevalence data under the assumption of steady state conditions.[449] Several elaborations on this catalytic model have been developed for application in sub-Saharan Africa. Williams et al. specified a separable force of infection which could change over time but maintained a constant age pattern to estimate incidence in South Africa's growing epidemic.[450] Mossong et al. jointly estimated HIV incidence and survival since seroconversion from HIV prevalence alone applied to the same serial prevalence data in Williams et al.

Gregson et al. also detail a simple cohort-based approach comparing prevalence among neighbouring age groups at a single point in time, estimating incidence as the number of infections required to obtain the change in cohort prevalence. This produced similar incidence estimates to their catalytic model. However, both Gregson methods and the catalytic models assume constant age patterns of prevalence over time, an unrealistic assumption for much of the epidemic, nor link serial measures of prevalence as a longitudinal cohort. Instead, using serial cross-sectional measures of prevalence that track hypothetical cohorts over time allows us to estimate incidence in non-steady state conditions: comparing prevalence at time t in age group (a_0, a_1) with prevalence at time $(t + x)$ in age group $(a_0 + x,\ a_1 + x)$. This produces an incidence estimate for each inter-survey period. Hallett et al. detail these longitudinal 'demographic accounting' methods, accounting for the depleting effect of HIV and non-HIV mortality among prevalent PLHIV between surveys.[447,448] This method may be applied in any epidemic state and yields comparable incidence estimates to empirical observations from population-based cohort studies.

Finally, transmission dynamic models fit a continuous transmission or incidence rates within a compartmental model framework and optimise for best fit to observed prevalence data. As detailed in section 1.9.2.2, these include a wide range of models

including EPP-ASM [202], the incidence model used within the UNAIDS HIV estimates in sub-Saharan Africa which uses a basic epidemic structure, to finely behaviourally stratified models that have been used for key population estimation. All methods require external estimates of mortality or survival since seroconversion, which represent the least certain model inputs: routine mortality surveillance in sub-Saharan Africa is very rare, estimates of survival since seroconversion are derived from studies in the pre-treatment era, and mortality estimates among those on ART confounded by CD4 count eligibility changes and treatment interruption.[451–453]

Calculating incidence among sex workers from changes in cross-sectional prevalence over time is complicated by the additional dynamic of initiating and ceasing risk behaviour, often referred to as 'turnover'.[454] If women sell sex for, on average, five years, 20% of the population exit sex work each year. Younger women with lower HIV prevalence initiate sex work and experience high risk of HIV seroconversion during their sex work career. Older women, now with higher HIV prevalence, cease selling sex and re-enter the total population. As the population outflow has higher prevalence than the inflow, HIV incidence can remain high over time despite HIV prevalence remaining constant or declining. In settings where HIV prevalence among sex workers is declining over time, estimating HIV incidence without accounting for population turnover leads to implausibly low, or even negative, estimates.[455] Including duration at-risk (d) within demographic accounting methods acts as an additional dimension by which we may estimate incidence among sex workers: we can compare prevalence at a_0 and $(a_0 + x)$ as in Hallett et al., and additionally and jointly compare prevalence at d_0 and $(d_0 + x)$.

This analysis seeks to create a statistical model that directly estimates annual HIV incidence among sex workers from data on HIV prevalence by sex worker cohort in successive surveys, without relying on assumptions about transmission dynamics or sexual mixing.

6.2 Data and methods

Participant-level data were available from twelve cross-sectional surveys among female sex workers conducted in Cotonou, Benin from 1993-2023 that measured age, HIV prevalence, and reported duration in sex work, among other information. A compartmental model was created representing women transitioning in and out of sex work and acquiring HIV infection. Excess HIV mortality was calculated using a hybrid approach of survival since seroconversion and age-specific mortality rates. HIV incidence was stratified by calendar year and single-year of age and sex work duration. The average duration of sex work was estimated and allowed to vary over time. The model was calibrated to HIV prevalence by age and duration, and the count distribution of women selling sex by age and duration.

6.2.1 Data

The Benin National AIDS Council, in collaboration with a Canadian development and research partnership, has supported *Projet Sida-2* and *Dispensaire IST*, a clinic in Cotonou since the early 1990s. *Dispensaire IST* provides HIV services, including prevention, testing, and treatment, to female sex workers. The programme routinely implemented cross-sectional surveys to monitor the epidemic among sex workers (Table 6.1). Surveys initially recruited using convenience samples of programme attendees, in conjunction with outreach to known sex work hotspots to encourage programme attendance (1993, 1995, 1998, and 2008). Later surveys used hotspot-based sampling (2002, 2005, 2011, 2015, 2017, and 2022), and from 2011 sampling was expanded to cities throughout Benin. This analysis is restricted to data collected in Cotonou.

Table 6.1: Surveillance studies among female sex workers in Cotonou, Benin

Year	Author	Sample size	Recruitment method	Inclusion criteria	Sex work duration	Completeness of recording		
						Age	HIV status	Duration
1993		374			-	96%	98%	-
1995	Alary	388	Convenience sample of clinic attendees	Attended STD screening at clinic dedicated to FSW	Asked as question	87%	100%	79%
1998		593			Asked as question	100%	100%	99%
2002	MoH	473	Convenience sample at hotspots	Self-identify as FSW, 15+	Asked as question	100%	40%	99%
2005	MoH	495	Convenience sample at hotspots	Women formally or informally working as sex workers	Calculated from age and age at first paid sex	100%	80%	89%
2008	MoH	351	Unknown	Unknown	Calculated from age and age at first paid sex	100%	93%	92%
2008	Diabate	319	Convenience sample of clinic attendees	Attended STD screening at clinic dedicated to FSW; 18+	Asked as question	100%	100%	97%
2011	MoH	345	Convenience sample at hotspots	-	Calculated from age and age at first paid sex	100%	96%	98%
2015	MoH	533	Convenience sample at hotspots	Women formally or informally working as sex workers; 15+	Asked as question	99%	97%	90%
2017	Perrault-Sullivan	314	Convenience sample of clinic attendees	Receive money in exchange for sex; 18+; sold sex ≥6mo	Calculated from age and age at first paid sex	99%	-	85%
2017	MoH	395	Convenience sample at hotspots	Identify as FSW; 15+	Calculated from age and age at first paid sex	100%	84%	93%
2022	MoH	385	Convenience sample at hotspots	Identify as FSW; assigned female at birth; 15+	Asked as question	100%	100%	99%

MoH: Ministry of Health, Benin

6.2.2 Compartmental model structure

HIV-negative female sex workers were stratified by calendar year $\{t \in 1993{:}\,2022\}$, single year of age $\{a \in 15, 16\,..\,59, 60+\}$, and single year of duration selling sex $\{d \in <1, 1, 2\,..\,19, 20+\}$ (Figure 6.2). HIV-positive sex workers were further stratified by single year since seroconversion $\{s \in <1, 1, 2\,..\,14, 15+\}$. The minimum age that sex workers could begin selling sex was age 15, therefore 15 year olds must all be in the first year of selling sex, 16 year olds in the first two years etc.

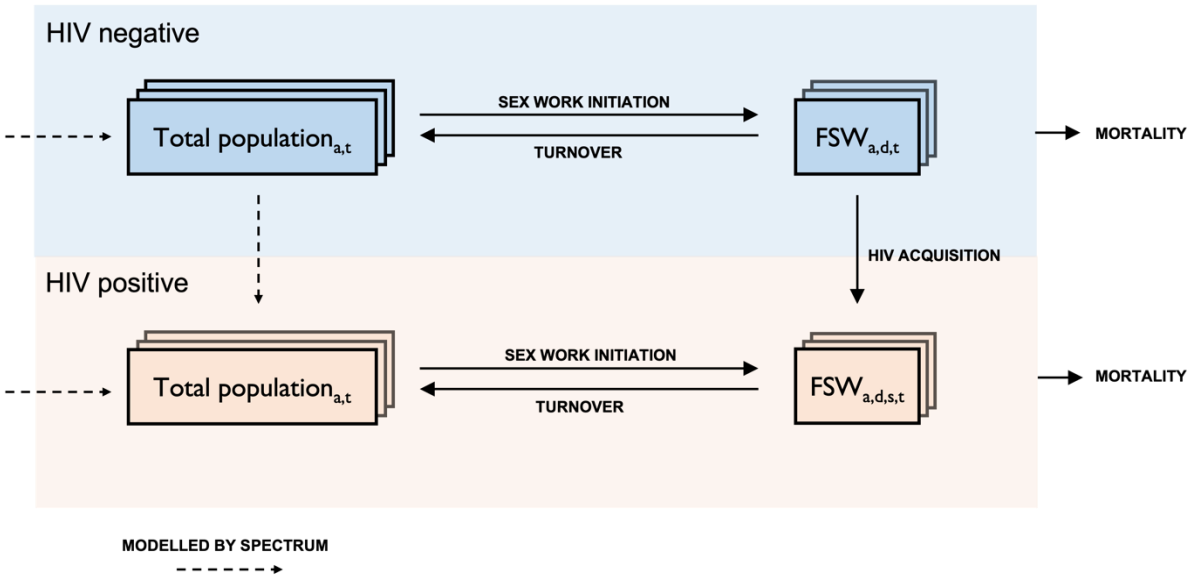


Figure 6.2: Compartmental model schematic diagram

6.2.2.1 Demographic progression, turnover, and mortality

Each year, a proportion of female sex workers cease to sell sex, $\frac{1}{\delta}$ where δ is the mean duration of sex work. The log mean duration of selling sex over time was modelled with an intercept representing the average duration ($\beta_{\delta 0}$) and smooth temporal effect ($\gamma_{\delta t}$). The temporal component was modelled as a cubic B-spline with $K = 7$ knots equally spaced every five calendar years from $t \in \{1993, 1998 \ldots 2022\}$. The spline coefficients were penalised with a first-order

autoregression model, with the autocorrelation parameter fixed at $\phi = 0.95$ to enforce smoothness.

$$\log \delta_t = \beta_{\delta 0} + \gamma_{\delta t}$$

$$\gamma_{\delta t} = \sum_{k=1}^{7} \tilde{\gamma}_{\delta k} B_k(t)$$

$$\gamma_{\delta_t} \sim AR1(\sigma_{\delta_t}, 0.95)$$

A further proportion die each year (μ). Non-HIV mortality among sex workers was assumed to be the same as that among age-matched women, and was extracted from the Benin Spectrum file by five-year age group and year. It was interpolated to single year of age using Beers ordinary interpolation $(\mu^{-}_{a,t})$. All-cause mortality rates among people living with HIV stratified by age and year since HIV seroconversion in the pre-treatment era were estimated by Todd et al.[456] (Figure 6.3A). Non-HIV mortality was subtracted from the Todd rates to estimate excess AIDS mortality by infection duration in the pre-treatment era $(\mu^{+}_{a,s})$. To estimate AIDS mortality in the treatment era without an estimate of the number of sex workers on ART, an ART mortality rate ratio by age and year $\left(MRR_{a,t}\right)$ since treatment became available (ART_t) was calculated by dividing total population AIDS mortality rates relative to rates in the year that treatment became available $(ART_t = 0)$ for all countries in sub-Saharan Africa (Figure 6.3B). Excess AIDS mortality rates stratified by age, time since seroconversion, and year were calculated by multiplying $\mu^{+}_{a,s}$ and the mortality rate ratio (Figure 6.3C):

$$\mu^{+}_{a,s,t} = \begin{cases} \mu^{+}_{a,s} & ART_t < 0 \\ MRR_{a,t} \times \mu^{+}_{a,s} & ART_t \geq 0 \end{cases}$$

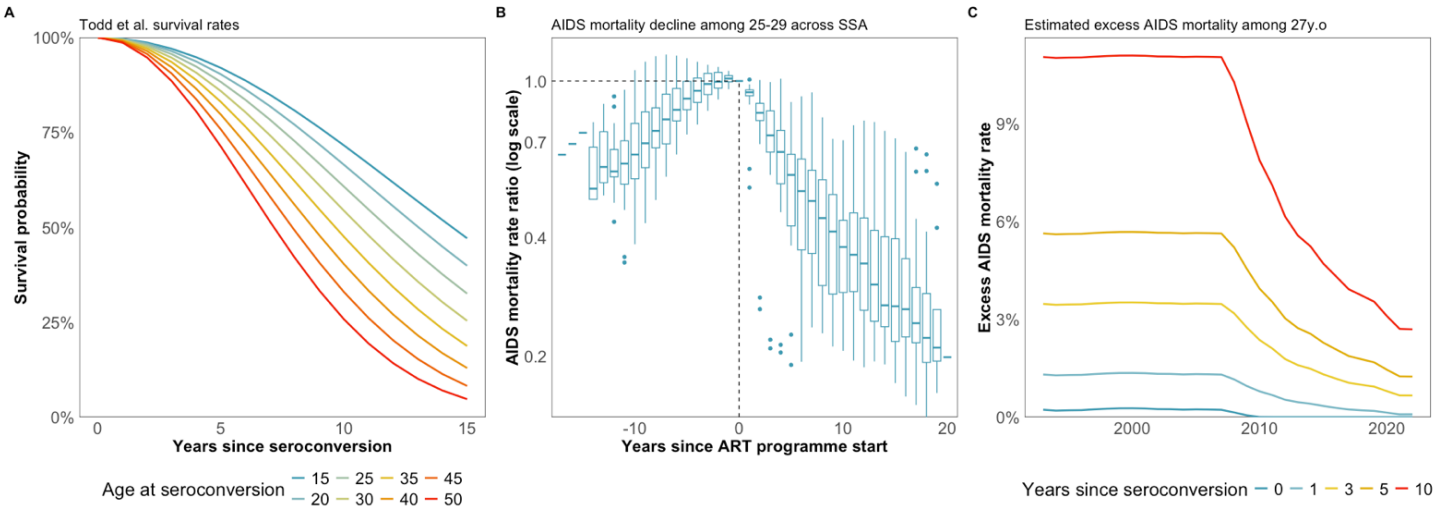


Figure 6.3: Estimating mortality rates among female sex workers in the ART era – an example for 27 year olds. (A) Mortality rates by age and year since seroconversion in the pre-treatment era from analysis by Todd et al. (B) Decline in AIDS mortality among 25-29 year olds in all Spectrum files in sub-Saharan Africa relative to the year since ART became available in each country (C) Estimated mortality rates since seroconversion among 27 year old sex workers.

Surviving sex workers age by one year, increase one year of duration selling sex, and HIV-positive sex workers increase one year since HIV seroconversion (only demographic transitions shown):

$$FSW^{-}_{a,t,d} = FSW^{-}_{a-1,t-1,d-1} \times \left(1 - \frac{1}{\delta_t}\right) \times (1 - \mu^{-}_{a,t})$$

$$FSW^{+}_{a,t,d,s} = FSW^{+}_{a-1,t-1,d-1,s-1} \times \left(1 - \frac{1}{\delta_t}\right) \times (1 - (\mu^{-}_{a,t} + \mu^{+}_{a,s,t}))$$

The final age, duration, and seroconversion indices are cumulative and represent those aged ≥60, selling sex for ≥20 years, or having seroconverted ≥15 years ago.

6.2.2.2 Recruitment of new sex workers

Total population women initiate sex work at rate ψ given by an intercept and a smooth AR1-penalised B-spline pattern over time:

$$logit(\psi_t) = \beta_{\psi 0} + \gamma_{\psi t}$$

$$\gamma_{\psi t} = \sum_{k=1}^{7} \tilde{\gamma}_{\psi k} B_k(t)$$

$$\tilde{\gamma}_{\psi_t} \sim AR1(\sigma_{\psi_t}, 0.95)$$

The annual sex worker population size is calculated fixed at 1% of the total 15-49 female population), and the appropriate number of sex workers is recruited into duration group $d = 0$ to reach this population size (X). Demographic progression or HIV dynamics among the total population were not modelled. Instead, the total number of women by year, age, and HIV status were extracted from the Spectrum file for Benin from which new sex workers were recruited. The proportion π_a entering sex work at each age a was modelled as a gamma distribution and is estimated from the data and allowed to change over time:

$$\pi_{a,t} \sim \Gamma(\alpha_t, \theta_t)$$

The gamma distribution was paramaterised in terms of a mean (μ) and a standard deviation (σ):

$$\alpha_t = \left(\frac{\mu_t}{\sigma}\right)^2$$

$$\theta_t = \frac{\sigma^2}{\mu_t}$$

Where the log mean age of entering sex work was specified with an intercept and a smooth AR1-penalised B-spline temporal effect:

$$\log \mu_t = \beta_{\mu 0} + \gamma_{\mu t}$$

$$\gamma_{\mu t} = \sum_{k=1}^{7} \tilde{\gamma}_{\mu k} B_k(t)$$

$$\tilde{\gamma}_{\mu t} \sim AR1(\sigma_{\mu_t}, 0.95)$$

$X_{a.t}$ (the number of women initiating sex work) is given by the initiation rate (ψ) multiplied by the total female population size and the age distribution of new sex workers (π):

$$X_{a,t} = \psi_t \times \text{15-49 female population size}_t \times \pi_{a,t}$$

The annual initiation rate is identified by summing HIV-negative, HIV-positive, and newly recruited FSW and applying a soft constraint against the target population size, fixed at 1% of the total female population:

$$\sum_{a,d} FSW^{-}_{a,d,t} + \sum_{a,d,s} FSW^{+}_{a,d,s,t} + \sum_{a} X_{a,t} \sim N(1\% \times \text{15-49 female population size}_t, 1)$$

To reflect that women initiating sex work were likely at higher risk of HIV acquisition before formal entry into sex work[457], the prevalence of women entering sex work is adjusted from the total population prevalence by age and time. The age-specific odds of being HIV-positive was multiplied by an odds ratio that varies over time which is estimated from the data (ι_t). This odds ratio was constrained to be between 1 and 5.

$$\text{Odds of being HIV positive at sex work entry} = \frac{\rho_{a,t}}{1 - \rho_{a,t}} \times \iota_t$$

No data exist in Benin on the time since seroconversion for women who are HIV-positive at sex work entry. A recent phylogenetic study in Kenya estimated that

prevalent sex workers seroconverted on average 1.5 years before formal entry into sex work.[457] This model assumes a fixed distribution of $X_s^+ \sim \text{Weibull}(2, 1.4)$ across age and time, which assumes prevalent positives have recently seroconverted (80% of the mass <2 years).

6.2.2.3 Modelling HIV incidence

HIV incidence (λ) was then applied to the HIV-negative FSW population, and new infections added to the HIV-positive population at $s = 0$.

Incidence was assumed to vary smoothly over time, age, and duration. Additional flexibility permitted incidence to vary differentially and smoothly by age over time. The logit annual probability of acquiring HIV infection by time, age, and duration was modelled with an intercept ($\beta_{\lambda 0}$) and AR1-penalised B-splines with K knots over age ($\gamma_{\lambda a}; K = 12$), time ($\gamma_{\lambda t}; K = 9$), duration of selling sex ($\gamma_{\lambda d}; K = 7$), and an interaction between age and time ($\eta_{\lambda a,t}$).

$$\text{logit}\,\lambda_{t,a,d} = \beta_{\lambda 0} + \gamma_{\lambda a} + \gamma_{\lambda t} + \gamma_{\lambda d} + \eta_{\lambda a,t}$$

$$\gamma_{\lambda a} = \sum_{k=1}^{12} \tilde{\gamma}_{\lambda k} B_k(a)$$

$$\gamma_{\lambda t} = \sum_{k=1}^{9} \tilde{\gamma}_{\lambda k} B_k(t)$$

$$\gamma_{\lambda d} = \sum_{k=1}^{7} \tilde{\gamma}_{\lambda k} B_k(d)$$

Incidence rate by duration of sex work was enforced to decline monotonically:

$$\tilde{\gamma}_{\lambda d} = \begin{cases} 0, & d = 0 \\ \tilde{\gamma}_{\lambda d-1} - \exp(\Delta_d), & d > 0 \end{cases}$$

where the log-differences between duration knots (Δ_d) were penalised with an AR1 process.

$$\tilde{\gamma}_{\lambda a}, \tilde{\gamma}_{\lambda t}, \Delta_d \sim AR1(\sigma_{\lambda a,} \sigma_{\lambda t,} \sigma_{\Delta d}, 0.95)$$

The age-time interaction was specified as a separable interaction of the smooth main age and time effects to permit differential age patterns of HIV incidence over time:

$$\eta_{\lambda a,t} = \sum_{k=1}^{12} \tilde{\eta}_{\lambda a,t} B_k(a) \sum_{k=1}^{9} \tilde{\eta}_{\lambda a,t} B_k(t)$$

$$\tilde{\eta}_{\lambda a,t} \sim AR1 \otimes AR1\left(\sigma_{\lambda a,t}, 0.95, 0.95\right)$$

6.2.2.4 Initialising the model

The model did not estimate the entire epidemic; the female sex worker population was initialised in 1993 by age, duration and HIV prevalence. The initial age distribution of sex workers was given by a gamma distribution with shape and scale parameters estimated from the data: $a_{init} \sim \Gamma(\alpha, \theta)$. Sex workers at each age were distributed by duration selling sex such that:

$$X_{a,d} \sim Exp(\lambda_a)$$
$$logit(\lambda_a) = \beta_0 + \beta_1 age$$

Finally, sex workers by age and duration were distributed by HIV status. To achieve HIV prevalence patterns consistent with HIV incidence trajectories, initial prevalence in 1993 was calculated from HIV incidence and mortality in the first year of the

simulation under the assumption of steady-state conditions. The prevalence at age $(a+1)$ and duration $(d+1)$ is the prevalence at age a and duration d less mortality:

$$\rho_{a+1,d+1} = \left(\rho_{a,d} \times \mathrm{e}^{-(\mu_a^- + \mu_a^+))}\right)$$

plus those who seroconvert and avoid HIV-negative mortality:

$$\rho_{a+1,\mathrm{d}+1} = \left(\rho_{a,d} \times \mathrm{e}^{-(\mu_a^- + \mu_a^+))}\right) + \left(\left(1-\rho_{a,d}\right) \times \frac{\lambda_{a,d}}{\lambda_{a,d}+\mu_a^-} \times \left(1 - e^{-(\lambda_{a,d}+\mu_a^-)}\right)\right)$$

6.2.3 Priors and constraints

Fixed effects had weakly informative priors: $\beta \sim N(0, 31.6)$

Standard deviations of random effects had half normal priors: $\sigma \sim N(0, 2.5)$

All smoothing random effects were given soft sum-to-zero constraints to aid identifiability.

6.2.4 Likelihood for FSW survey prevalence and duration data

1. Prevalence

The number of HIV-positive FSW by age and duration was calibrated survey-observed (x) prevalence ($\rho_{a,d,x,t}$):

$$FSW_{a,d,t}^{+} \sim Binom\left(N_{a,d,x,t}, \rho_{a,d,x,t}\right)$$

Survey respondents who did not report a duration of sex work were incorporated into calibration by aggregating over all duration categories, assuming that the missing durations were missing at random:

$$\sum_{d=0}^{20} FSW^{+}_{a,d,t} \sim Binom(N_{a,d=NA,x,t}, \rho_{a,d=NA,x,t})$$

2. Age-duration distribution

The modelled proportion of FSW within each age-duration category was calculated in each year:

$$\alpha_{a,d,t} = \frac{FSW^{-}_{a,d,t} + \sum_s FSW^{+}_{a,d,s,t}}{\sum_{a,d} FSW^{-}_{a,d,t} + \sum_{a,d,s} FSW^{+}_{a,d,s,t}}$$

An observation model adjusted for under-recruitment of FSW at short durations of selling sex (<1 and 1-2 years), relating the true age-duration distribution to that observed in each survey ($\tilde{\alpha}$). Underenumeration (θ) was estimated as a multiplicative factor on the natural scale. Fixed effects at $d = 0$ and $d = 1$ captured the average global under-enumeration at short durations, and survey iid effects ω_x permitted survey-specific deviation from each global average. Underenumeration at $d = 0$ was enforced to be more severe than at $d = 1$ such that:

$$logit(\theta_{x,d=1}) = \beta_{d=1} + \omega_{x,d=1}$$

$$logit(\theta_{x,d=0}) = \theta_{x,d=1} - \exp(\beta_{d=0} + \omega_{x,d=0})$$

$$\omega_{x,d} \sim N(0, \sigma_\omega)$$

$$\tilde{\alpha}_{a,d,x,t} = \alpha_{a,d,t} \times \sum_{d' \in \{0,1\}} (\theta_{x,d'}) \chi_{[d=d']}$$

The bias-adjusted proportions were normalised, converted back to counts, and calibrated to the age-duration distribution in each survey:

$$\widetilde{\alpha'}_{a,d,x,t} = \frac{\tilde{\alpha}_{a,d,x,t}}{\sum \tilde{\alpha}_{a,d,x,t}}$$

$$\tilde{n}_{a,d,x,t} = \widetilde{\alpha'}_{a,d,x,t} \times \left(\sum_{a,d} FSW^{-}_{a,d,t} + \sum\nolimits_{a,d,s} FSW^{+}_{a,d,s,t} \right)$$

$$\tilde{n}_{a,d,x,t} \sim Multinomial(N_{x,t}, p_{a,d,x,t})$$

6.2.5 Validation

Empirical observations of HIV incidence among female sex workers in Benin were available from two studies. Van Damme et al.[458] observed 10 new infections from 1998-2002 (8.3/100py 95%CI 3.4, 13.2) and Diabaté et al.[81] observed 6 new infections from 2008-2012 (1.4/100py 95%CI 0.3, 2.5). Both studies recruited women aged 18 or over. Incidence estimates for ages 18+ in 2000 and 2010, the study midpoints, were compared to empirical observations.

6.2.6 Sensitivity analysis

Several sensitivity analyses were conducted:

1) Removing the under-enumeration observation model when calibrating to the age-duration distribution;
2) Increasing the population size estimate proportion to 2% in 2020, and 1.5% in 2021, returning to 1% in 2022 to simulate a COVID-19 pandemic shock growth in sex work. Fixed effects were added into the incidence and initiation models, estimated only in years 2020 and 2021:

$$\text{logit}\, \lambda_{t,a,d} = \beta_{\lambda 0} + \gamma_{\lambda a} + \gamma_{\lambda t} + \gamma_{\lambda d} + \eta_{\lambda a,t} + \beta_{\lambda,COVID}$$

$$logit(\psi_t) = \beta_{\psi 0} + \gamma_{\psi t} + \beta_{\psi,COVID}$$

$$\boldsymbol{X}\beta_{COVID} = \begin{cases} 0, & t \notin 2020, 2021 \\ 1, & t \in 2020, 2021 \end{cases}$$

3) Alternative specifications for the odds ratio that increases HIV prevalence at sex work initiation (ι_t): constant over time at $\iota_t \in \{1,3,5,10\}$ and varying over time with no upper bound (main results constrain ι_t between 1 and 5);
4) An additional fixed effect in the incidence model to capture very high incidence at $d = 0$:

$$\text{logit}\,\lambda_{t,a,d} = \beta_{\lambda 0} + \gamma_{\lambda a} + \gamma_{\lambda t} + \gamma_{\lambda d} + \beta_1 + \eta_{\lambda a,t}$$

$$\boldsymbol{X}\beta_1 = \begin{cases} 0, & d \notin 0 \\ 1, & d \in 1 \end{cases}$$

6.2.7 Model implementation

Data preparation was conducted in R and the model was implemented in C++ via the R package Template Model Builder (TMB). One thousand samples were drawn from the joint posterior distribution, from which the posterior mean, standard deviation, and quantile-based 95% CI were calculated for each output indicator.

6.3 Results

Descriptive data statistics

4,966 female sex workers participated in 12 surveys conducted between 1993-2022 that measured serological HIV status (N surveys = 11; median completeness 96.6%, interquartile range [IQR] 88.5-99.5%), age (N=12; 99.5% IQR 99.3-100%), and duration of selling sex (N = 11; 92.7% IQR 89.7-98.4; Table 6.1). Six surveys included a question on duration of sex work, while duration was calculated for five surveys using current age and reported age at first paid sex. All surveys used convenience-based sampling, of which five used clinic-based recruitment. HIV status

data from the 1993 survey was excluded from model calibration due to implausible trends in HIV prevalence by age.

Modelled HIV prevalence estimates

HIV prevalence among all sex workers declined consistently from its peak in 1995 at 44.9% (95CrI 41.2-48.9) to 8.6% (95CrI 6.4-11.8%) in 2022 (Figure 6.1A). Prevalence has declined among all age groups, with largest relative declines among the younger age groups (approximately eight-fold decline in 15-19 and 20-24 year olds; Figure 6.1B). In 2022, HIV prevalence remains strongly correlated with age, increasing by *circa* 50% in each successive five-year age group between ages 15 and 49. Trends in HIV prevalence by sex work duration were less consistent (Figure 6.1C). HIV burden increased in the first 3-5 years of sex work and then plateaued, though estimates at long durations of sex work were weakly informed by data, particularly in the pre-treatment era.

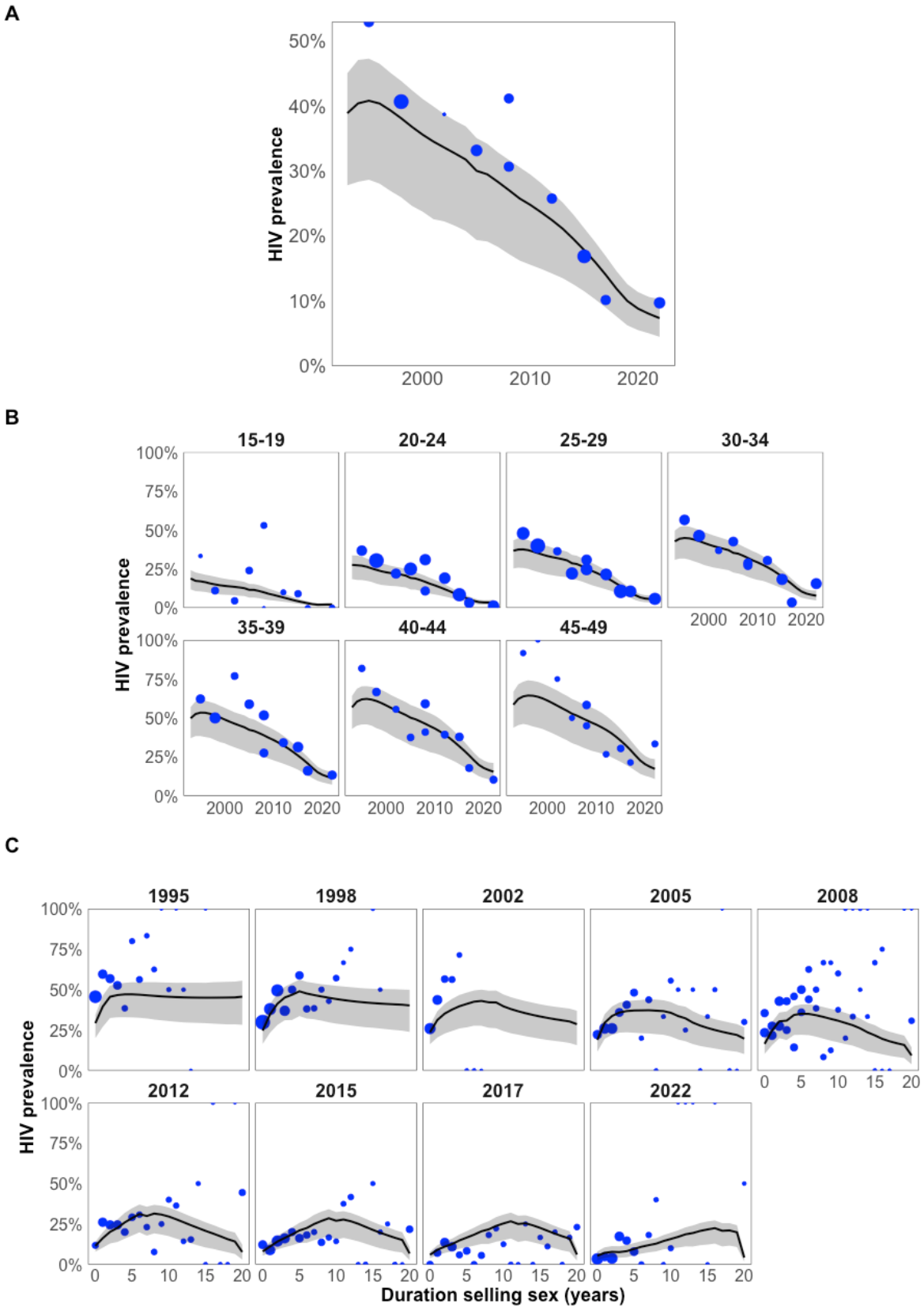


Figure 6.1: HIV prevalence (A) All sex workers over time; (B) By five-year age group over time; (C) All sex workers by duration of selling sex, shown for years of survey. Model

estimates represented by black line with 95% uncertainty range in grey shading. Survey data shown in blue points, sized by sample size.

Modelled HIV incidence estimates

HIV incidence among sex workers aged 15-49 has declined from 19.7/100py (95CrI 9.5-26.9) in 1994 to 2.5/100py (1.2-3.5) in 2013 where it has remained relatively stable 2014-2022 (Figure 6.2A). HIV incidence was concentrated at the lowest durations, with half of cumulative incidence and 81% of new infections occurring within the first two years of selling sex (Figure 6.2B and C). Incidence among 15-29 has converged over time to around 1.5/100py in 2022 (Figure 6.2D), but remains higher in older age groups (Figure 6.2E). In 2022, 60% of new infections occurred among those aged 20-34 (Figure 6.2F).

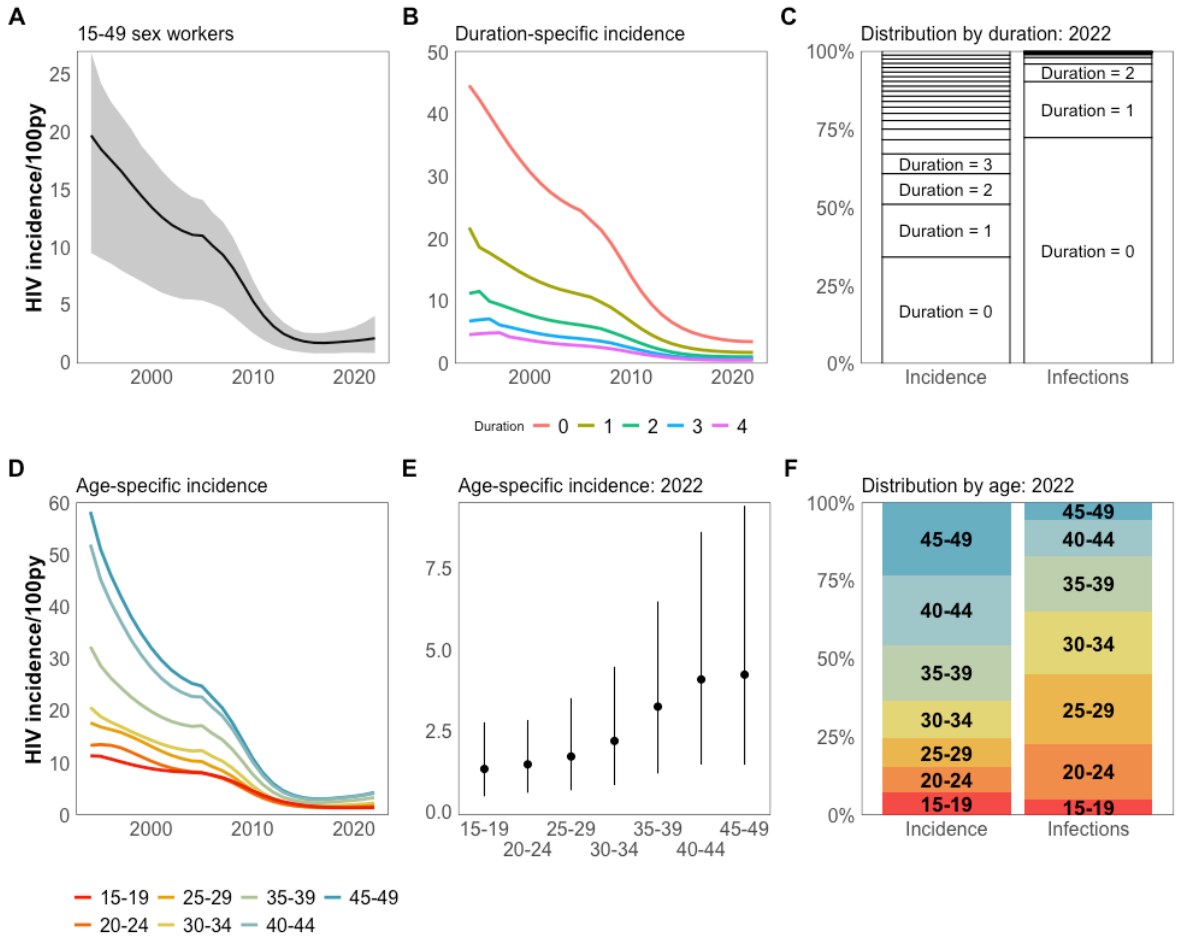


Figure 6.2: Estimates of HIV incidence (A) Among 15-49 sex workers over time; (B) By duration for the first five years of sex work over time; (C) Distribution of incidence and new

infections by duration in 2022; (D) Age-specific incidence over time; (E) Age-specific incidence in 2022; (F) Distribution of incidence and new infections by five-year age group in 2022. 95% credible interval omitted from (B) and (D) for clarity.

HIV incidence sensitivity analysis

Compared to empirical HIV incidence observations among sex workers aged 18+ (not used in model calibration), I estimated a much higher HIV incidence in 2000 (model: 16.7/100py [6.9-19.1] vs study 8.3/100py [3.4-13.2]) and in 2010 (model: 6.2/100py [2.7-7.2] vs study 1.4/100py [0.3-2.5]). In sensitivity analysis, altering the odds ratio that controls HIV prevalence at sex work initiation (ι_t) had a large impact on estimated incidence level and trend (Figure 6.3). Fixing ι_t at 1, 3, 5, or 10 over time all produce similar results that are a poor fit to HIV prevalence data and estimate fluctuating incidence trends that reach very high levels of incidence (30/100py). Empirical incidence may be reconciled with cross-sectional HIV prevalence data by removing the upper bound on ι_t and recruiting women with 30-50% prevalence. Removing the under-enumeration observation model had little effect on HIV incidence trajectories before 2015 whereupon they began to diverge. In 2020, removing the duration observation model decreased HIV incidence by 27% in 2020 (1.4/100py vs 1.9/100py). Simulating an increase in population size to 2% of 15-49 women in 2020 increased incidence by 83% in 2020 (3.4/100py vs 1.9/100py).

Age and duration distributions

The mean duration of sex work was constant between 3 and 3.5 years from 1993-2008, rose to 5 years by 2015, and then fell to 2.5 years by 2022 (Figure 6.3A). Survey under-enumeration of sex workers at short sex work durations was detected in all surveys since 2005. Sex workers in their first year of selling sex were estimated to be under-enumerated by median 60% (IQR 24-71%) and in their second year of selling sex by 19% (IQR 2-39%; Figure 6.3B). Adjusted for under-enumeration, mean duration decreased by 0.5 years (IQR 0.2-1). The mean age of sex workers has remained unchanged between 1995-2022 at 29.5 $\pm$ 1 years (Figure 6.4). The mean age at sex work initiation declined from 28 years old in 1993 to 26 in 2012, and returned to 28 years old by 2019.

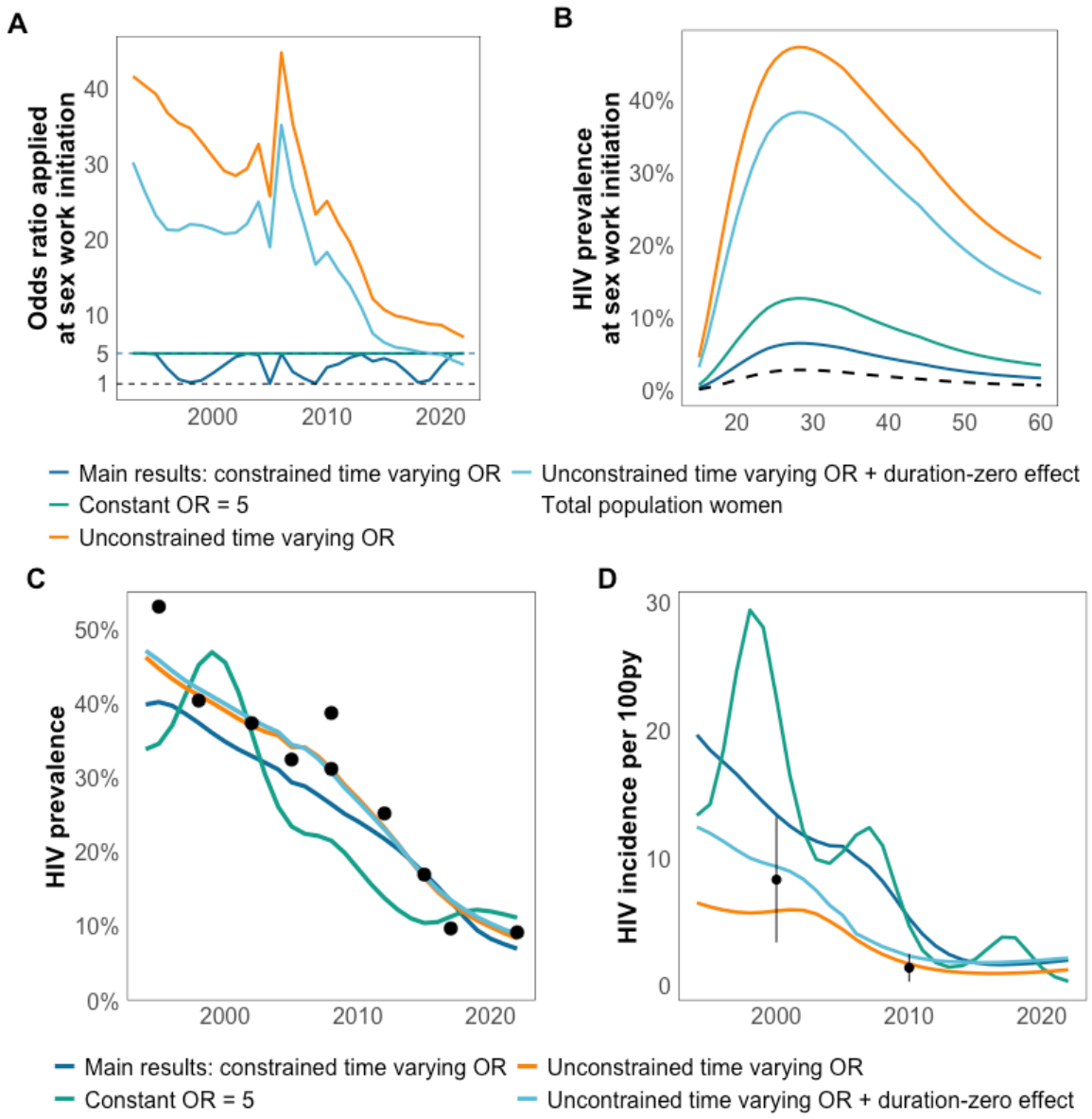


Figure 6.3: HIV incidence sensitivity analysis. (A) Estimated odds ratio (OR) applied to HIV burden at sex work initiation. OR in all sensitivity models has a minimum bound at OR=1 (black dashed line) and main results (blue) have an upper bound at OR=5. (B) HIV prevalence at sex work initiation in 2000 from each model, compared to HIV prevalence among total population women (black dashed line). (C) Estimated HIV prevalence among ages 15-49 compared to survey data (black points). (D) Estimated HIV incidence compared to empirical observations of HIV incidence (not included in model calibration). Results for constant OR=1, 3, and 10 were similar to constant OR=5 and are not plotted.

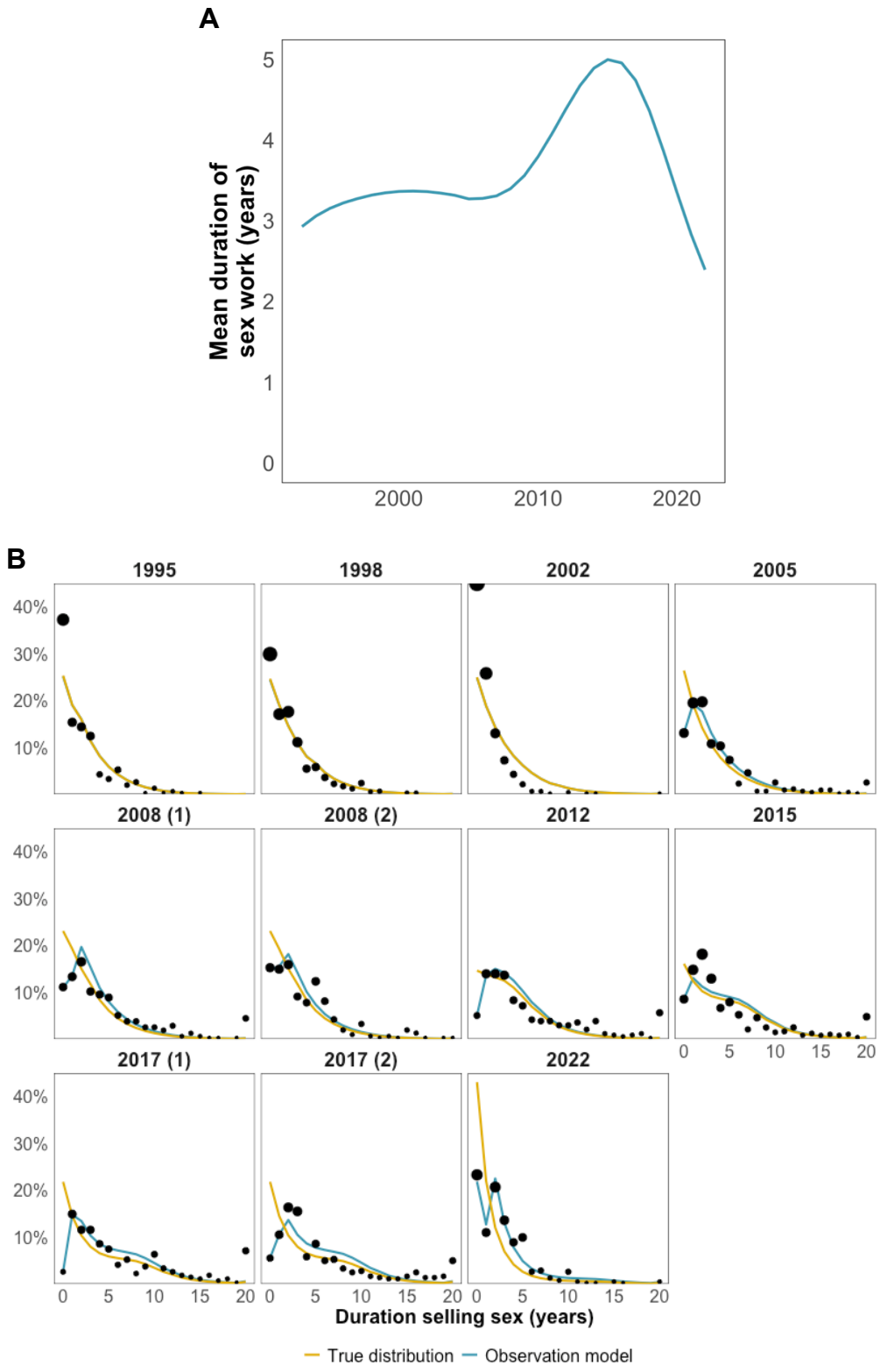


Figure 6.4: Distribution of duration selling sex. (A) Mean duration of sex work over time. (B) The observation model (blue) includes effects to estimate under-enumeration in the first two years of sex work. Accounting for under-enumeration yields the true distribution (yellow). Estimates shown for survey years.

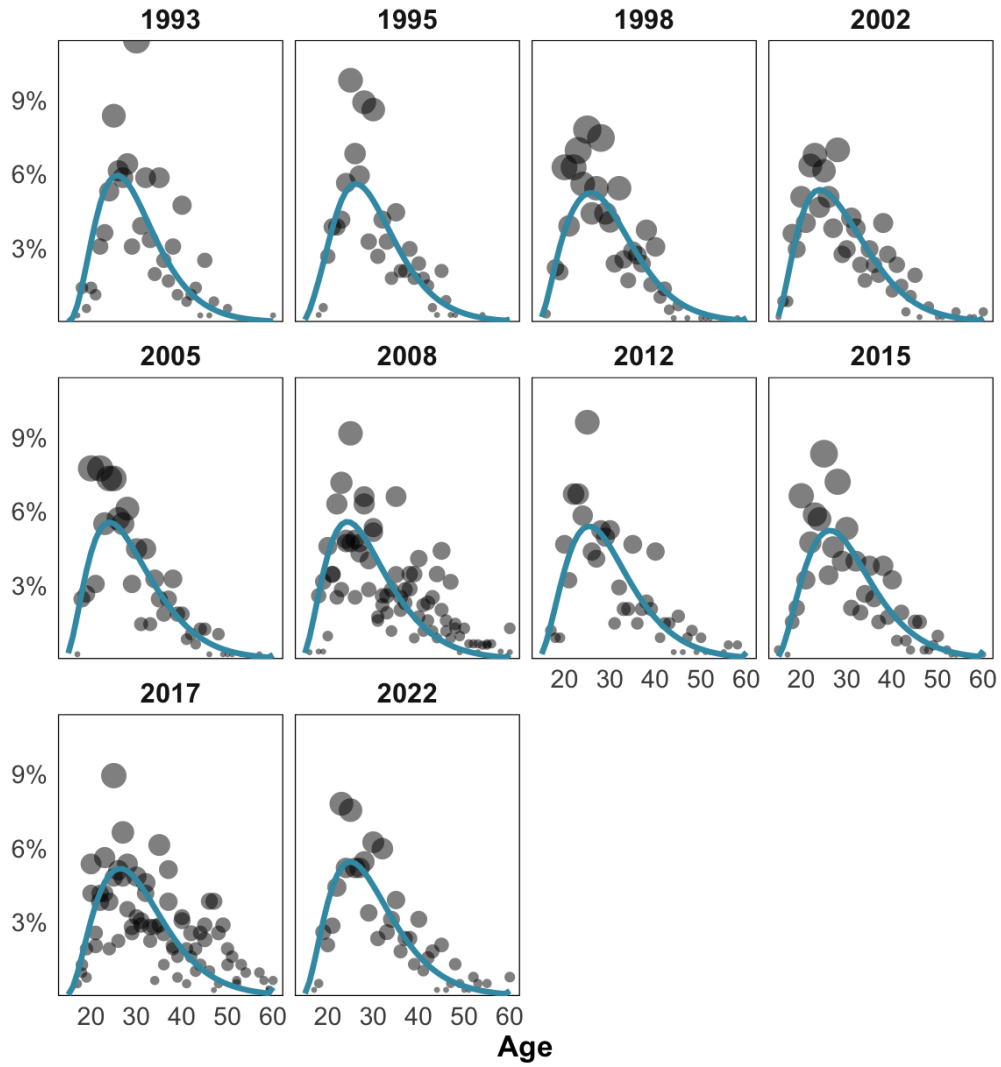


Figure 6.5: Sex worker age distribution. Estimates (blue) shown in year of survey compared to survey data (black points)

6.4 Discussion

I created a statistical model that estimated HIV incidence among female sex workers from serial cross-sectional survey data. It does so without data on CFSW or behavioural parameters of sex work required by full transmission dynamic models. This model could be applied in any setting with one or more surveys among female sex workers. In the Beninese setting, I estimated HIV incidence has declined ten-fold since 1993 to around 2/100py in 2013, whereupon it has plateaued through 2022 (2.6/100py). Incidence in 2022 was 37-fold higher than HIV incidence among total

population women aged 15-39 in Western and Central Africa, compared to 20-fold higher as estimated in a recent meta-analysis of empirical observations of HIV incidence among sex workers.[113]

The model fits well to a diverse range of data, including HIV prevalence by age and duration, age and age at sex work initiation, and duration of sex work. Despite this, estimated HIV incidence was much higher than empirical incidence observations not included in model calibration: 2fold higher in 2000 and 4.5fold higher in 2010.[81,113,458] This is principally driven by survey data that indicate high HIV prevalence among those selling sex for less than 1 year, and little HIV prevalence gradient by duration of sex work. Estimated HIV incidence can be only be aligned with empirical observations if women are recruited at very high HIV prevalence (30-40%) which is is unrealistic in a low prevalence HIV epidemic. Here I will discuss sex work dynamics and biases in surveillance data that may give rise to this difference, and their consequences for interpreting both modelled incidence estimates and empirical incidence observations.

6.4.1 Episodic engagement in sex work

As outlined in section 1.4, sex work is commonly stratified into ‘commercial’ sex work (selling sex for money only and earning all/most of one’s income from sex work) and ‘transactional’ sex work (selling sex for money, or exchanging for gifts or favours). Transactional sex workers may sell sex episodically, driven by transient conditions (e.g. school holidays, poor harvest), see fewer clients, and experience lower HIV incidence risk. Episodic serial entry and exit from sex work are documented in qualitative accounts, but little quantitative data are available to parameterise this behaviour, and existing model-based approaches have required strong assumptions.[459,460] This model did not track former sex workers, instead returning sex workers to the total population upon cessation of sex work. If serial engagement and prevalent infection at sex work entry is common, incidence may be lower and less concentrated at short durations than estimated. Model development should look to utilise survey data on client frequency and proportion of income derived from sex

work to stratify sex work by non-commercial and commercial sex work, with non-commercial sex workers selling sex for shorter durations with a higher rate of serial cessation and initiation. Granular data on episodic sex work should be viewed as a priority within future surveillance or routine data collection.

6.4.2 What is 'duration' really measuring?

In this analysis, duration of sex work was directly available from 6 surveys ("for how long have you sold sex?"), and calculated from current age and age at first paid sex in 5 surveys. In the context of episodic sex work, it is unknown whether survey respondents report total duration of sex work or duration of current episode, though it is widely interpreted in secondary analysis and modelling studies as total duration. Of seventeen surveys among female sex workers in SSA that included both a direct question on duration and asked about age at first paid sex, sixteen reported longer durations using age at first paid sex. There is circumstantial evidence from the 2022 survey that total duration may be being misreported in Benin. Benin is a low prevalence epidemic, and we assume that the majority of HIV-positive sex workers acquired HIV within sex work. The 2022 survey conducted viral load testing and found high levels of viral load suppression (VLS) among sex workers selling sex for <1 year. As it would be challenging to initiate sex work, seroconvert, be diagnosed and linked to care, and reach viral load suppression within, on average, six months, it is likely that some of these women had prevalent infections from previous episodes of sex work. Accordingly, their total duration of sex work would be higher than <1 year and HIV prevalence among those truly at <1 year of sex work be lower than that currently observed in survey data.

Average duration from aggregate data is commonly used to parameterise turnover in key population-stratified models, including in Goals-RSM.[224] HIV incidence estimates are sensitive to sex work duration assumptions: duration determines the rate at which high HIV prevalence FSW are 'diluted' by entrants from the low HIV prevalence total population, and in turn, the incidence required to restore observed prevalence. If estimates of total duration are under-estimated, HIV incidence will be

over-estimated and as absolute durations of sex work are small, single year changes in average duration could lead to large changes in incidence estimates.

6.4.3 Missing women at highest incidence risk

I found evidence for under-enumeration of women selling sex for <1 and 1-2 years from 2005 onwards. Adjusted proportions for women selling sex for <1 year were commonly double survey-observed proportions. Surveys were sampled using hotspot sampling from a peer-generated sampling frame of most-frequented sex work locations, or by clinic-based recruitment. New sex workers may be unaware of these hotspots early in their sex work careers or may have started selling sex informally without attending commercial hotspots. Clinic-based recruitment (including the proposed BBS-Lite[461,462]) and network-based (e.g. RDS) may be further susceptible to under-enumerating individuals at short durations. I estimated that incidence risk declines steeply with duration, similar to incidence estimates among Kenyan sex workers[463], and programmes may be missing individuals at highest risk soon after, or even before[457], sex work initiation. Empirical studies may underestimate incidence by under-recruiting women at <1-2 years of sex work where I estimate half of cumulative incidence occurs.

6.4.4 Sensitivity to population size assumptions

Sensitivity analysis that doubled population size estimate proportion during the COVID-19 pandemic increased 2020 HIV incidence by 83%. There remains a lack of accurate longitudinal estimates of population size which hinders the production of credible count scale estimates, required for programme planning and commodity purchasing, and impacts on our ability accurately to estimate incidence. This analysis assumed a constant population size proportion. The 2022 survey – conducted shortly after the COVID-19 pandemic - reports a shorter average duration than those preceding it. If the population size proportion is held at 1%, the model obtains a short duration distribution by increasing turnover with a modest increase in

incidence to replace the lost prevalence. However, if there is a concomitant increase in population size, the short observed duration is satisfied by an inflow of new entrants with low HIV prevalence, and a large incidence spike is required to reach observed prevalence among those who have sold sex for one year. The limitations of population size estimates are further discussed in section 7.3.1.

6.4.5 Mortality estimates and ART coverage

As in the catalytic and cohort prevalence methods outlined in the introduction, the use of external mortality estimates remains a weakness in estimating incidence from cross-sectional prevalence. EPP-ASM stratifies PLHIV by CD4 category to reflect the concentration of AIDS mortality at low CD4 counts, and additionally tracks the number of PLHIV on treatment by CD4 count at initiation and duration on treatment. Data on CD4 count distribution among sex workers are absent from nearly all settings in sub-Saharan Africa. While programme counts of sex workers on treatment are becoming more widely available from key population programmes, interpretation of these data is impaired by programmatic double-counting due to high levels of mobility and multiple service providers, and an unknown fraction of sex workers receiving treatment from total population services.

Without CD4 data and reliable treatment data, sex workers in this model were tracked by time since seroconversion such that estimates of survival could be used in the pre-treatment era. In the treatment era, mortality rates were derived from the average AIDS mortality decline among the total population. Estimates of ART coverage and VLS were available in 2008 and 2022 surveys, 38% and 68% respectively, indicating that FSW had benefitted from the national ART programme similarly to total population women. These could have been used to calibrate the model and inform mortality rates, though the 2008 survey used clinic-based recruitment where ART coverage would be expected to be higher than among all sex workers and conceptually the aim was a parsimonious model that could be applied in settings with weaker surveillance data. Despite evidence of strong programme engagement among FSW, it is possible that approximating mortality among FSW

from average decline in AIDS mortality has overstated mortality among FSW and thereby overestimated HIV incidence.

6.5 Conclusion

HIV incidence among sex workers in Benin has declined ten-fold since 1993 to around 2.5/100py. Reconciling abundant HIV prevalence data by age and duration should be used to create estimates of HIV incidence in all settings with survey data. These should be used alongside empirical observations and transmission dynamic model estimates of HIV incidence to support HIV prevention programming and targeted provision of pre-exposure prophylaxis.

7. Discussion

7.2 Overview

The overarching objective of this thesis was to lay the foundations for introducing country-specific key population stratified estimates of equal rigour to the total population HIV estimates within the UNAIDS estimates process. As detailed in section 1.12, the landscape at the start of this thesis in 2021 was:

- No data system that systematically collated and validated key population surveillance data;
- Outdated systematic reviews with weak indicator and population coverage (with many population-indicator combinations wholly absent);
- Unsubstantiated UNAIDS estimates of new infections by key population group;
- Weak key population data ownership and use within national programmes; and
- Poor or non-availability of methods and tools to translate surveillance data into programme-actionable estimates outside the most data-rich settings, particularly for HIV incidence.

Data collated and estimates created under this thesis have improved the surveillance data landscape in sub-Saharan Africa, have been used widely within UNAIDS processes, and continues to inform modelling analyses and policymaking.

Key changes to estimates and mathematical models resulting from this thesis

- In 2023, UNAIDS transitioned to a more **systematic modelling approach** for global estimates of the distribution of new infections by sub-population, using transmission dynamic models that **formally reconciled HIV prevalence and population size** with estimates of new infections (consistent with methods in Chatper 5);
- In 2025, UNAIDS revised the distribution of new infections methodology again, **integrating surveillance data from Chapter 2** as calibration data and using relative prevalence among TGW:cis-MSM from Chapter 4 to inform **incidence estimates among TGW;**
- In 2022, national Goals-RSM models used for UNAIDS Global Strategy, Global Fund applications, and PrEP strategy **replaced data from UNAIDS Key Population Atlas/GAM** with population size and HIV prevalence data from Chapter 2;
- In 2025, UNAIDS dropped the **weakly evidenced position** for nationally-adequate population size estimates among MSM to exceed 1% (Chapter 2);
- In 2024, South Africa and the Thembisa model incorporated the results from Chapter 4 to estimate **distinct and disproportionate burden among TGW**;
- Since 2022, the Subnational HIV Estimates in Priority Populations tool (SHIPP) used for **HIV prevention planning among key populations**, including the PrEP-it model and ongoing lenacapavir allocation planning, has used population size estimates from Chapter 2; and
- In 2025, data from Chapter 2 have been used to estimate the impact of PEPFAR cuts on PrEP provision among key populations

In Chapter 2, I collated key population surveillance data and validated existing surveillance databases in sub-Saharan Africa 2010-2024. Much of the collated data were derived from grey literature, and had been omitted by peer-reviewed systematic reviews and international stakeholder databases. I created national-level estimates for population size, HIV prevalence, and ART coverage for all countries in mainland sub-Saharan Africa, which in several settings were the first key population estimates available. Building on the collated surveillance data, I created the Key Population Workbook, for use by country teams within the UNAIDS estimates process. The

Workbook enabled observation-level review of large volumes of key population data and created nationally owned and national-level key population estimates. Despite a few country teams extracting full utility from the Workbook, it remains an underutilised and undersupported tool within the UNAIDS estimates process. In Chapter 4, I estimated that HIV prevalence among TGW was strongly correlated with, and 50% higher than HIV prevalence among cis-MSM. This relationship may be used to support HIV programmes in the absence of dedicated surveillance among TGW. In Chapter 5, I triangulated empirical incidence observations and modelled incidence estimates among key populations with UNAIDS estimates of the distribution of new infections by population group. I estimated that 12% of new HIV acquisitions occurred among key populations, compared to UNAIDS' estimate of 25%. The variation in model-based estimates of the proportion of new infections was primarily explained by large differences in population size assumptions between models. In Chapter 6, I created a statistical model that does not require CFSW surveillance data or data on sexual mixing to estimate HIV incidence among female sex workers in Benin from age- and duration-stratified HIV prevalence data.

The work contained with this thesis was conceived, and largely conducted, before the second Trump presidency. Much of its outputs were designed to inform and interact with a growing key population surveillance, programme, and modelling environment. This reality now seems unlikely to materialise. In the eyes of the United States, the sole funder of PEPFAR and the largest individual funder of UNAIDS, WHO, and the Global Fund, key populations have been deprioritised or find their identities actively denied. At the time of writing, it appears that PEPFAR will be funded until mid-2026, albeit at a dramatically reduced scope that completely omits key populations. Planned biobehavioural surveys are on hold and key population programmes face an uncertain future across sub-Saharan Africa. The end of American altruism in the HIV space has much wider ramifications than key populations: 50% of total HIV spending in sub-Saharan Africa in 2024 was US derived, rising to 60% if domestic funds from South Africa are omitted.[464] If PEPFAR and US contributions to Global Fund cease to exist, national HIV programmes will struggle to contain the HIV epidemic, returning to an era of rising HIV incidence and

mortality among the total population.[465] The future of UNAIDS, its estimates process, and multilateral engagement and support for the HIV response is similarly under threat.[466,467] This discussion seeks to address the current state and future of key population data, what role key populations should play within national surveillance and programme portfolios under severely restricted budgets, and what multilateral organisations can do to facilitate this.

7.3 Assessing contribution of key populations to the HIV epidemic in sub-Saharan Africa

The HIV response has been one of the most expensive public health initiatives in history. In sub-Saharan Africa alone, $174bn has been spent between 2010-2024[464], dwarfing other global priorities (malaria 2003-2023 $60bn[468]; smallpox eradication $1bn[469]), primarily directed towards testing and treatment programmes among the total population.[464] Many other interventions also received significant donor financial support, all of which were linked to reducing HIV incidence/burden but often lead by other ethical and moral priorities. These included targeting structural drivers of HIV transmission (e.g. the DREAMS initiative among adolescent girls and young women[470], and interventions seeking to reduce stigma and gender-based violence) and prioritising health equity in the HIV response, including key populations. Over the last 10 years, tireless advocacy efforts by community organisations, NGOs, and international stakeholders have raised the profile of key populations in an often hostile social and political environment. In my opinion, an inappropriate blurring between advocacy and epidemiological evidence developed in parallel. It was insufficient justification to care about key populations because they were people: quantitative data showing their epidemic importance were required to reinforce funding proposals. Prioritising key populations in the HIV response, principally a consideration of human rights and health equity, slowly morphed into an epidemiological priority whose contribution to total transmission was paramount, even in high prevalence HIV epidemics. Central to this narrative was UNAIDS' year-on-year increasing estimates of the distribution of new infections among key

populations – the “donuts”. These proved a highly effective advocacy tool for additional investment in key population surveillance and programming.

The 2022 UNAIDS Report *In Danger* reported that 25% of new HIV acquisitions in sub-Saharan Africa occurred among key populations, and a further 26% among their sexual partners.[274] This motivated the work for Chapter 5: it was challenging to reconcile the population size estimates and HIV prevalence collated in Chapter 2 with crude duration at-risk assumptions and reach the incidence that the UNAIDS estimates required. Using results from existing transmission dynamic models, empirical incidence data, and the data collated in Chapter 2, I found that the UNAIDS incidence estimates were incompatible with surveillance data. Instead, the consensus estimate from models and empirical data suggested that around 12% of new HIV infections were among key populations in 2022, half that estimated by UNAIDS. Alongside analysis on key population partner transmission rates by Silhol et al.[471], Chapter 5 prompted UNAIDS to revise its methodology in favour of an approach that formally reconciled population size and HIV prevalence for the 2024 Global Report.[117,472] This reduced the proportion of new infections among key populations by 14 percentage points in sub-Saharan Africa to 12% (45-60% reduction among FSW, MSM, PWID, and a 90% reduction for TGW). The principal concerns about this change from several stakeholders were advocacy, communication, and reputation. This was deeply disappointing. Raising funding on an incorrect evidence base in times of plenty was viable, but now risks an unethical future: will trying to maintain key population programmes – having attained ‘essential’ status - result in a net loss of life?

Evidence from transmission dynamic models that estimate tPAF, the preferred indicator to assess the contribution of key populations to the epidemic over time, may inform a way forward. tPAF captures onward secondary transmission through sexual networks and is more appropriate for communicating the epidemic contribution of small populations with dense sexual networks, compared to cross sectional measures of new HIV infections. A recent review from Silhol et al.[220]

compared tPAF estimates from nine epidemic models that included strata for FSW and their clients. From 2020-2029, median 9.2% (IQR 7.3-12.3%) of transmission was associated with female sex workers, and 24.8% (IQR 14.1-45.3%) with their clients. As touched on in section 1.9, that sex work retains its importance after the development of a disseminated, generalised epidemic has been discussed by several modelling studies[95,101,233,235,473], but has not brought about a reframing of 'generalised transmission' within national strategic planning. Estimates of transmission linked to sex work are reliant on assumptions about clients of female sex workers, a population neglected by HIV surveillance and excluded from the scope of Chapter 2, which in retrospect was a mistake. These data remain under-curated: a systematic review on HIV prevalence among CFSW by Xi et al. was presented at the 2022 AIDS conference but has not yet been published.[474] Clients have been routinely omitted from biobehavioural surveillance: ten surveys since 2010 have been conducted, and only Benin and Togo have longitudinal estimates. Focusing surveillance on sex workers without describing their sexual partners was sufficient to meet basic monitoring requirements among sex workers (e.g. HIV prevalence over time), but has presented a major source of uncertainty for holistic epidemic assessments, including predicting the potential impact of targeted lenacapavir provision. Population size estimates of clients are absent from almost all settings (and their quality subject to the same criticism as above). Using DHS data Hodgins *et al.* estimated that 8.5% of men have ever bought sex and 2.7% in the last 12 months.[154] The authors note this is likely to be an underestimate as a client base consisting of 2.7% of men would struggle to support 1-3% of women who sell sex. Some modelling exercises use partner balancing estimates from sexual behaviour data reported by sex workers and clients to estimate client population size.[229] In the models reviewed in Silhol *et al.* calibrated to the South African epidemic alone, client population size varied eight-fold between 1.8-16.2% of the male population. Future analytical work should seek to consolidate partner information in existing surveys without the need for further surveillance.

Transmission dynamic models consistently identify that even in the highest prevalence and "most generalised" Southern African countries decades into the

epidemic, sex work is a major epidemic driver.[220] Planning the distribution of limited stocks of long-acting pre-exposure prophylaxis is currently underway. This is a critical opportunity to avoid an allocation scheme based on HIV incidence alone, consider long-term transmission based metrics, and bring about maximum epidemic impact. In Chapter 4, FSW incidence rates derived from empirical incidence rate ratios were under the proposed 5/100py threshold for lenacapavir targeting in all except four countries, and in Chapter 6, HIV incidence among FSW in Benin was ~2.5/100py. All key populations may be vulnerable, stigmatised, and criminalised, but sex workers' continuing role in wider transmission in sub-Saharan Africa must be recognised, and their HIV prevention and treatment needs prioritised.

Estimates of tPAF among PWID and TGW were not included in the Silhol review, with some groups noting that their population size was too small meaningfully to contribute to the epidemic. [229,235,475] Programmes targeting small and marginalised populations engage individuals at high relative cost. For example, within the Mozambique 2024-2026 funding request to Global Fund for HIV prevention programming, $22m was requested for FSW/CFSW, $8.4m for MSM, $6.4m for PWID, $2m for transgender people, and $32m for adolescent girls and young women (AGYW).[476] Using the population size and HIV prevalence included in the request, this translates into around $125/MSM, $1300/PWID, $300/transgender person, and only $10/AGYW. Relative costs are high, and absolute totals are also large. The budgeted cost of surveillance and services among PWID and TGW in Mozambique is equivalent to conducting a nationally-representative household survey every three years, the gold-standard surveillance method that would bring widespread benefits to all PLHIV. While choosing between allocative efficiency and equity is a policy rather than epidemiological decision, it will be challenging to advocate for the continuation of solely state-funded surveillance and programming among such populations.

7.4 Taking stock of the UNAIDS key population estimates

In a review of the UNAIDS total population HIV estimates, Mahy et al. describe three requirements for modelled estimates and the process by which they are made (emphasis mine):[271]

> "Some simple, logical rules apply to modelled estimates. The **data must be of good enough quality** to allow program managers at the relevant level to act on the results. The estimates must be available at a frequency that allows **timely action to redirect programs**. The owners of the estimates should be **the public health managers** who will act on those estimates … The development of HIV estimates by countries around the world has been considered a good model of health estimates processes **because of the ownership of the estimates by country teams**, the frequency of the estimates and the comparability of the results." (p59)

Since 2016, the UNAIDS key population estimates in sub-Saharan Africa have consisted of single-year estimates of new infections acquired by each population – "the donuts". These have been created within a centralised Geneva-based process and published at the regional level, and at national level since 2024.[117] Since 2023, countries could create national-level consensus estimates of population size, HV prevalence, and new HIV infections using the Key Population Workbook twinned with Goals-RSM. Over the last ten years, little progress has been made on improving the utility and quality of UNAIDS key population estimates in sub-Saharan Africa, which continue to meet none of the above criteria. I consider improvements that could be made to future estimates processes to meet the Mahy requirements.

7.4.1 "The data must be of good enough quality": Improving data standards

In Chapter 2 I collated key population surveillance data 2010-2023, with a focus on validating data contained within existing databases against primary sources. Locating primary sources was a significant undertaking and, particularly for grey literature unavailable online, would not have been possible without the support of Ministries of Health and UNAIDS Country Offices. While select results from some

biobehavioural surveys are published in peer-reviewed literature, it is an arduous process that is not a priority for many Ministries of Health. Most biobehavioural surveys remain as grey literature reports, and may be missed by future systematic reviews. UNAIDS Global AIDS Monitoring and The Global Fund maintain a shared key population surveillance database which has been the preferred vehicle for collating biobehavioural survey data using annual submissions from national teams.[118,270] However, data standards are below those applied to total population surveillance data and in its current form it is an inadequate data collation tool: (1) it is not known when new surveys are conducted and whole surveys are routinely omitted; (2) primary source documents are not required; and (3) submitted data are not validated and/or additional unsubmitted data are not checked for in source documents. Though unvalidated and often unsourced, these data have been used widely within modelling, in particular within Goals-RSM, whose results inform global target setting and policymaking.

This is in sharp contrast to the total population estimates: survey data are carefully curated, country teams have strong knowledge of their results, and their availability and accuracy are central to the production of HIV estimates. As noted in Chapter 2, this is partially due to the estimates process: as HIV modelling tools and their data requirements have proliferated, data standards have risen. The Spectrum modelling tools have become data curation tools in their own right, are used to populate Global AIDS Monitoring, and have been integrated with data repositories without which management of thousands of data observations at high age/sex/spatial resolution would become unworkable.[273] In the absence of a systematic key population modelling strategy within the UNAIDS estimates and the perceived absence of a need for high quality data standards, no such offering exists for key population data. Minimum data standards should: (1) Omit unverified data from modelling analyses; (2) Develop a data collation tool, whether part of Spectrum, GAM, or another platform, for countries to enter specified, mandatory data elements from key population surveys that includes primary sources; and (3) Ensure that submitted data match that in primary source material.

7.4.1.1 Facilitating data use and transitioning away from aggregate data

The dataset and estimates from Chapters 2 and 4 have been used to inform UNAIDS Global Reports and estimates tools, modelling analyses, and programme strategies including the nascent lenacapavir rollout. [153,357,472,477] Its utility has been the most rewarding part of work conducted under this thesis and ensuring data access and use became a central objective (data explorer: https://shiny.dide.ic.ac.uk/kp-data/ and permanent archive: https://doi.org/10.5281/zenodo.10838437). Estimates teams drew most utility from the comparative data plots in the Key Population Workbook (e.g. Figure 3.1) and so too has the data explorer received positive feedback from teams seeking to navigate unwieldy datasets. This is a start.

Total population survey datasets are derived from standardised survey instruments and participant-level data are made available for research use.[152,478–480] Their data is integral to the HIV estimation workflow, from informing fertility rates in demographic projection models to district-level resolution estimates of ART coverage.[354] Data explorers (e.g. StatCompiler, IPUMS[481,482]) further facilitate access to those who lack the technical ability to engage with raw datasets. By comparison, secondary analysis of key population data, including almost all mathematical modelling, relies on aggregate data at whichever strata were made available in survey reports. This inhibits high resolution modelling akin to that implemented for the total population. While the data from total population surveys are seen as true product, the perceived utility of biobehavioural surveys ends at the survey report and its selection of aggregate indicators. This is an unacceptable status quo. Standardising and cleaning datasets for public release should be considered a mandatory requirement of the survey, the onus for which cannot fall under existing workloads of national staff and instead be included as an additional cost of survey implementation. This additional work would likely be cost-saving in the long-run as hundreds of millions of dollars are presently spent on weak and uncertain key population estimates, the best that aggregate data may support. Chapter 6 details the potential of using participant-level data to develop granular methods for incidence estimation from cross-sectional

data, and to encourage the implementation of finely stratified compartmental models across all settings. Though without this thesis, I have led a collaborative effort which has collated and partially harmonised over 220 participant-level key population survey datasets 1993-present, of which the Benin data are a small part. These data had been intended to support a broad research agenda and to parameterise the next generation of the Goals model – Goals-ARM[483] – which would have addressed many of the fundamental flaws in the use of the current Goals-RSM model for key population estimates. Both the development of Goals-ARM and the participant-level data work are presently on hold due to the funding crisis.

7.4.2 Estimates "that allow timely action to redirect programs": what are we estimating and for whom?

As discussed in Chapter 3, estimates teams expressed limited desire for national-level estimates produced by the Workbook: (1) key population surveillance has been overwhelmingly conducted in urban areas from which complex and strongly assumption-based extrapolations are required to reach national estimates; and (2) key population programmes are often limited to select districts where key populations are perceived to be in greatest number.

The intention first to introduce key populations into the Spectrum models at the national-level was informed by historical model development for the total population estimates, which were developed from least to most strata (i.e. easiest to hardest). First EPP/Spectrum national-level estimates were created, stratified by urban/rural location, followed by provincial-level Spectrum files in some settings, and finally district-level estimates from Naomi. District-level estimates are challenging because data are sparse and noisy, and require structured models to produce estimates with credible uncertainty (e.g. spatial smoothing). The same principle was applied to key population estimates and, though programmes and data were subnationally restricted, creating district-level key population estimates without a national epidemic model was considered running before walking. Second, Goals-RSM—a national-level model with key population strata—already existed. It was a convenient off-the-

shelf solution that could be applied to all sub-Saharan African settings and produced estimates of new infections within a modelling framework which formally reconciled epidemic dynamics, population size, and HIV prevalence. Using Goals-RSM was intended as an interim step towards improved mathematical modelling despite national-level estimates being of little use for subnational programme planning, nor do nationally-representative data exist in most settings with which to create its inputs. While its estimates would have been useful to improve the UNAIDS distribution of new infections by subpopulation group, the preoccupation with the UNAIDS donuts was a weak motivation for pursuing national-level estimates and led to a loss of focus on the actual goal: data collation, review, and validation.

Instead, estimates should be re-orientated around programme needs, principally subnational planning. These may be methodologically simpler than previously envisaged and closer resemble monitoring and evaluation of routine data. If currently available data and modelling techniques are unable to furnish teams with credible estimates, none should be created. In future, UNAIDS and modelling teams must feel more empowered to refuse to make estimates. While researchers and modelling teams may be familiar with the weaknesses associated with methods and uncertainty in estimates, once released mathematically modelled estimates can be stripped of nuance. It is poorly understood that a model can be fit to almost no data and produce estimates at fine age/space disaggregation. For example, since the 2023 estimates process, modelled provincial population size and HIV prevalence from Chapter 2 have been disaggregated to estimate the number of HIV-negative key population members stratified by district and age group.[357] These have been used to guide district-level PrEP programming and received by programme teams as very useful estimates. Unfortunately, they have little basis in reality and result in programme targeting no better than guesswork. Second, such estimates are liable to fluctuate dramatically over time given their weak grounding in data and over-reliance on modelling assumptions. Both undermine the credibility and utility of mathematical modelling to direct programmes and do more harm than good.[271]

7.4.3 "The owners of the estimates should be the public health managers": transitioning away from centralised estimates

Since 2016, UNAIDS has created regional – and since 2024, country-level - estimates of the distribution of new infections.[117] This is at odds with the participatory HIV total population estimates process that has put national input and expertise at its core since its inception in 2003.[271] Not only did this build capacity within national programmes, but created ownership of estimates for a stigmatised disease where Geneva-created estimates may have been ignored. This set the HIV process apart from other UN health estimates (e.g. under 5 mortality[484,485]) which remain centralised processes. To be made public under this participatory framework, HIV estimates must be agreed upon by both country teams and UNAIDS following technical review – a crucial step missing from the Workbook process. This ensures "country ownership of the estimates and … that senior country HIV program managers are reviewing the results". Mahy et al. further note that the "country review and signoff process has led to increased reflection on the data entered into the models and has subsequently improved the quality of surveillance systems over time and increased the likelihood of acting on it".[271]

Increased country ownership of the key population estimates would address many of the issues encountered to date. Involvement of teams in the production of estimates would strengthen appraisal of surveillance data and consideration of whether estimates desired by key population programmes for planning may be supported by existing data. In turn this leads to directed surveillance that may address these strategic information gaps. Such ownership is particularly important for key populations: expecting centrally-created estimates to spur action among domestically marginalised and criminalised populations may be ineffectual.

The Key Population Workbook was intended to be the first step towards a standardised surveillance dataset. This would begin the transition away from centrally-produced regional estimates towards a country-led process and create a nationally agreed-upon dataset to be used for model development and integrating

key populations into Spectrum. Regardless of whether the Workbook is used in future, creation of such a dataset is essential for the UNAIDS key population estimates to improve, and if the estimates process is to remain a country participatory process.

7.5 Is key population HIV surveillance supporting programmes?

Ideal surveillance produces an unbiased and representative assessment of the epidemic in a population to guide a maximally efficient programme response. It does so affordably and produces estimates with programmatically-usable uncertainty. In practical terms this means assessing trends over time in key indicators, providing count-scale estimates to support commodity purchasing and, in a donor-driven epidemic response, target setting. Each data element collected (survey question, biological test etc.) should be linked to a programmatic action. This should be mutually beneficial: data are collected in support of programmes, and surveys are structured to strengthen the estimates that programmes rely on. Despite biobehavioural surveys having been conducted for over thirty years, I contend that in most settings surveys fail to produce strategic information that were better than prior assumptions or justify the cost of surveillance. This is not a critique of study teams or their implementation, rather a need for a tighter relationship between surveillance, estimates, and programme needs.

Biobehavioural surveys may include two hundred questions, but, in most settings, we remain unable to characterise dynamics that underpin indicators commonly requested by country teams.[176] There are several examples contained within this thesis, e.g. not reporting catchment area or population denominator for population size estimates, preventing their comparability over time or between settings; or inability to parameterise serial cessation and initiation of sex work. This further includes district-level estimates, the treatment cascade (particularly knowledge of status), trends in key indicators over time, and population size. A ‘hotspot only’ sampling strategy for surveillance, comprising major urban areas and selected rural hotspots (e.g. border towns or mining sites) has created data unable to support the

need for subnational district-level key population strategic information. This is akin to the use of urban-only ANC sentinel surveillance in the early epidemic which dramatically overestimated epidemic burden.[144,486]

Strictly pared-down surveys that are better designed to meet estimation and programme needs could replace bloated surveys that contain detailed sexual, behavioural, and structural factor data, many of which are either never published nor used to inform programme action. The newly-developed BBS-Lite protocol makes good steps towards this: a short, cheap, and fast survey with a focus on biological testing and core sociodemographic and behavioural variables.[462] It recruits from programmes and, while described by UNAIDS as a "methodology for monitoring programmes", is being discussed as the future of key population surveillance.[461] This is concerning given its non-representative sampling: an expanded BBS-Lite protocol in South Africa which used both programme-based and PLACE-style hotspot sampling revealed large differences in HIV prevalence, VLS, and other core indicators by sampling strategy.[487] If RDS surveys are viewed as too expensive and onerous, convenience sampling at hotspots should be prioritised as a surveillance strategy over programme-based methods.

Whichever methods are selected, they must be implemented consistently and stably. Continually changing sampling strategy and where surveillance is conducted needlessly increases uncertainty in key population data. Nesting linked or anonymous key population surveillance (e.g. polling booth surveys[488]) within total population routine programmes; including antenatal clinics, HIV testing programmes, and STI clinics, would be a useful addition to surveillance portfolios. All or a randomly selected sample of attendees could complete a short behavioural survey, offering a relatively consistent sampling frame, large sample sizes over time for little additional cost, and, if available, complement data sourced from key population programmes.

7.6 Population size estimates

Population size estimates are required to convert proportion- and rate-scale estimates into count-scale estimates. Their estimation is considered an essential component of key population surveillance portfolios and their impact is felt throughout this thesis. In Chapter 2, I concluded that statistically-summarised population size estimates were too uncertain to be programmatically useful, with upper bounds commonly 5- or 10-fold larger than lower bounds. In Chapter 5, I found that the proportion of new infections among key populations as estimated by transmission dynamic models was strongly correlated to population size assumptions. In Chapter 6, I refrained from presenting count-scale estimates of new infections among female sex workers in Benin as population size is unknown.

There now exists a plethora of population size estimation methods and no agreement on which should be considered a 'gold-standard' method.[188] Population size estimation exercises usually include multiple methods which, though they should measure the same population, frequently give rise to substantively differing estimates. I illustrate this using two recent PSE studies using the latest available methods. The first a 2020 study from Ghana using 3S-CRC highlights the methodological weakness of population size estimation[196]; and the second, a 2024 study from Malawi using 3S-CRC and SS-PSE, highlights the challenges this poses to estimates teams.

All 3S-CRC studies—a three-body Venn diagram— contain three two-source captures within them. Figure 7.1 shows the ratio of each of the three 2S-CRC sizes relative to the final 3S-CRC. The orange study is reasonably close to the 3S-CRC estimate (though commonly exceeding +/- 30%), while the green and blue studies are systematically larger, in some regions reaching 10fold higher. This raises several questions: (1) if we believe 3S-CRC to be a methodological improvement, how do we interpret 2S-CRC estimates that constitute most observations in sub-Saharan Africa? (2) are these studies measuring the same population and should they be consolidated into a single estimate? and (3) if observations at the same point in time are so disparate, what do longitudinal estimates represent?

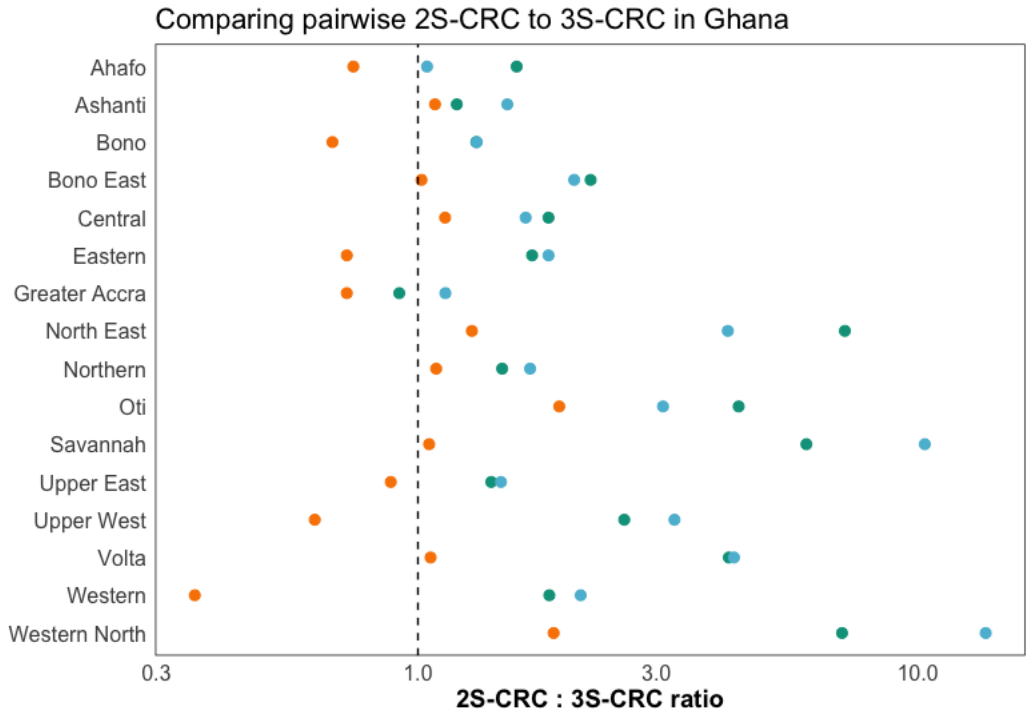


Figure 7.1: Comparing nested 2S-CRC with final 3S-CRC population size estimates. Each 2S-CRC is represented by a colour and population size estimates expressed as a ratio relative to the final 3S-CRC estimate (represented by the dotted line).

The study in Malawi measured population size using 3S-CRC and SS-PSE in thirteen districts (Table 7.1). SS-PSE estimated very large population proportions with wide uncertainty which were irreconcilable with those from 3S-CRC. 3S-CRC estimated 0.5-0.7% in most districts, bar the two largest cities (Lilongwe and Blantyre) and two rural districts (Karonga and Nkhatabay).

Table 7.1: Population size estimates from 2024 BBS in Malawi

	3S-CRC (95%CI)	SS-PSE (95%CI)
Karonga	2.50% (1.73, 4.37%)	
Mzimba	1.40% (0.80, 1.98%)	8.00% (0.76, 15.25%)
Nkhata Bay	2.30% (1.62, 3.87%)	
Dedza	0.70% (0.45, 0.94%)	3.70% (0.33, 7.09%)
Kasungu	0.50% (0.33, 0.70%)	2.70% (0.90, 4.50%)
Lilongwe	2.50% (1.40, 3.52%)	6.20% (0.89, 22.41%)
Salima	0.70% (0.56, 3.50%)	
Blantyre City	2.00% (1.11, 2.83%)	7.90% (0.57, 25.84%)
Chikwawa	0.70% (0.50, 0.94%)	5.80% (2.25, 9.30%)
Machinga	0.70% (0.37, 0.96%)	5.10% (1.51, 8.71%)

Mangochi	0.70% (0.47, 0.91%)	3.90% (0.70, 7.08%)
Mulanje	0.70% (0.45, 0.95%)	2.70% (0.15, 5.32%)
Zomba	0.70% (0.42, 0.98%)	5.20% (2.01, 8.37%)

There are several methods to reach a single “consensus” population size estimate from a qualitative evaluation of studies by domain experts to model-based approaches that weight the final consolidated size estimate by observation uncertainty.[187,489] While the formal reflection of uncertainty in the statistical methods is appealing, they add complexity and require additional user input (e.g. specification of priors). The team sought to reach consensus estimates using the Triangulator model[489], a meta-analysis style model that uses statistical uncertainty, an observation-level user-specified “confidence score” to represent non-sampling uncertainty, and user-specified priors for population size to produce an average weighted estimate. This proved very difficult and the team was surprised that, despite conducting a survey at significant expense, subjective beliefs on population size were still required to reach a consensus estimate: was it possible that rural districts had such high PSE? was it possible that PSE proportions were that much higher in cities? which method do you think is right?

In most districts, Triangulator estimates were around double those derived from the 2019/20 survey, and remained two or three-fold smaller than the number reached by programmes in 2024. Population size models have been developed to reach consensus size estimates with methodological rigour, and teams expect them to produce unequivocal answers of use to programmes, particularly when recent data are available. When this is not the case, their utility is rightly questioned. Because size estimation methods are weak and inconsistent and the resulting estimates disparate, increasingly complex models have been created to reconcile them. Rather than aiding teams to navigate a challenging data landscape, mathematical models and statistical language have obfuscated the process by which consensus estimates were derived. Teams are left worse off than before, disempowered to disagree with a “modelled estimate” as irreconcilable with reality.

Multilateral surveillance guidelines and solicited requests for population size estimation exercises from funders cemented PSEs within surveillance portfolios. This was a logical idea: accurate denominators are required to make count-scale estimates and have been considered essential for programmatic planning. When population size estimates produced varying results, the focus was on collecting more data to increase precision and to create methods to reconcile them. Money was available to conduct more surveillance, and additional studies raised the profile of marginalised populations. In doing so, we stopped asking whether population size was actually measurable, and whether the estimates were of use to programmes. Consensus estimates continue to confirm what teams thought before: about 1-3% of women sell sex, 0.5-1.5% of men have sex with men, not many people inject drugs, and fewer still are transgender, with broad enough uncertainty to encompass any credible scenario. The number of individuals engaged by programmes commonly exceeds size estimates and little is done in response: when PSEs exceed programme counts, this is viewed as evidence of unmet need and targets are set; and when programme counts exceed PSEs, it is assumed that programmatic double counting or incorrect PSEs are masking unmet need, and targets are set exceeding attainment in the previous year. I hope that the data and analyses within this thesis may be used to review the utility of population size estimation studies and to advocate for their discontinuation in sub-Saharan Africa.

As suggested in section 7.4.2, there should instead be renewed focus on estimating population size from routine service data, specifically towards supporting district-level denominators. Programme targets for the number individuals engaged currently inhibit or wholly prevent their use in estimation frameworks as targets are rarely missed. Methodological development should look to analysis of recruitment rates and programme saturation (e.g. ‘microplanning’ studies developed by FSW programmes in Zimbabwe) in combination with hotspot-based surveillance where available to estimate coverage and unmet service need directly.

7.7 Recommendations for key population surveillance and programmes

Key population surveillance and programmes are likely to be gutted, if not fully terminated, across much of sub-Saharan Africa within the next 24 months. Here, I make some recommendations for more sustainable key population surveillance, monitoring, and programmes. As best as can be achieved, surveillance should be integrated within routine programming at minimal cost and healthcare worker time.

Of relevance to national surveillance and programming:

1) Make key population surveillance more sustainable

    - Integrate key population surveillance within routine health programmes, including lightweight behavioural and risk surveys on all or a random sample of clinic attendees. Unlinked anonymous Polling Booth-style surveys that reduce survey bias could produce estimates of population size by directly surveilling programme-attending populations;
    - Re-instate biological and behavioural sentinel surveillance of clients of female sex workers within STI programmes; and
    - Implement small surveys that seek to minimise cost but maximise generalisability and utility by: (1) focusing on biological testing (HIV serostatus, viral load, PrEP plasma concentration) and core behavioural variables; (2) using consistent sampling methods over time, preferably convenience sampling from hotspots; (3) designing surveys to meet strategic information needs of programmes; and (4) conducting surveys annually to provide a credible evidence base for programme direction.

2) Cease to conduct population size estimation studies prioritise routine data-based measures of service use

- Current population size methods are unable to produce credible estimates and do not provide value for money. Where count estimates are required, simple assumptions (e.g. 1.5% of women sell sex) may be inaccurate, but no less wrong than current 'empirical' data;
- Remove programme targets for the number of individuals engaged by programmes as (1) population size estimates informing targets are weak and (2) the existence of targets makes it challenging to use the programme-reported number of individuals as data; and
- Seek to use routine data to estimate population size (e.g. saturation and recruitment rates of new programme attendees, Polling Booth Surveys).

3) Recognise sex work as a core driver of mature, generalised epidemics

- National HIV strategic planning and international guidelines should recognise the epidemic consequences of failing to meeting the HIV prevention and treatment needs of female sex workers; and
- Prioritise programmes and surveillance for sex workers above those for other key populations, and prioritise their access for novel long-acting HIV prevention and treatment therapeutics.

Of relevance to international stakeholders, funders, and future estimates processes:

4) Transition to country-led key population estimates

- Increase utility and quality of key population estimates by ensuring they are created and recognised by national estimates teams;
- Prioritise development of key population estimates that are aligned with the strategic needs of programme teams; and
- Create estimates only in settings where data credibly exist to support them.

5) Raise data standards and improve data use

- Adopt minimum data standards for key population data within reporting and modelling tools, similar to those expected and attained for total population surveillance data; and
- Develop a data repository for participant-level key population data with standardised schema.

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