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Data and methods to characterize the role of sex work and to inform sex work programmes 1 2 in generalized HIV epidemics: evidence to challenge assumptions

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- 8 SB conceived of the paper and provided leadership throughout the review and writing. SM and
- 9 SB wrote the manuscript. SM conducted the data syntheses. SB, SM, MCB, SS, JFB, and SM
- 10 developed and designed the paper and provided critical intellectual input, ideas, edits, data
- 11 synthesis, and writing. All authors contributed significantly to the ideas expressed in the
- 12 manuscript and edited the manuscript.

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1 Summary

In the context of generalized HIV epidemics, there has been limited recent investment in HIV surveillance and prevention programming for key populations including female sex workers (FSWs). Often implicit in the decision to limit investment in these epidemic settings are assumptions including that commercial sex is not significant to the sustained transmission of HIV, and HIV interventions designed to reach 'all segments of society' will reach FSWs and clients. Emerging empiric and model-based evidence is challenging these assumptions. This paper highlights the frameworks and estimates used to characterize the role of sex work in HIV epidemics as well as the relevant empiric data landscape on sex work in generalized HIV epidemics and their strengths and limitations. Traditional approaches to estimate the contribution of sex work to HIV epidemics do not capture the potential for upstream and downstream sexual and vertical HIV transmission. Emerging approaches such as the transmission population attributable fraction from dynamic mathematical models can address this gap. To move forward, the HIV scientific community must begin by replacing assumptions about the epidemiology of generalized HIV epidemics with data and more appropriate methods of estimating the contribution of unprotected sex in the context of sex work.

1 Characterizing the Role of Sex Work in Generalized HIV Epidemics

2 Early in the HIV pandemic, HIV surveillance and prevention focused on high risk, and high

3 burden populations including female sex workers (FSWs), men who have sex with men (MSM)

4 and people who inject drugs (PWID) [1-3]. However, for the last 15 years, the total and relative

- investments in HIV surveillance and programmatic efforts for FSWs declined markedly in many
 countries with generalized HIV epidemics, especially across Sub-Saharan Africa (SSA)[4].
- 7 National expenditure data on HIV suggest that in 17 SSA countries reporting HIV expenditure
- a data after 2007, a median of 0.35% (range, 0.0 to 3.3%) of HIV prevention budgets were
- allocated to HIV prevention for FSWs and clients [5], and 17 of 22 countries estimated that
- between 0.01 to 3.1% of HIV funding including HIV care expenditure benefits FSWs and clients
- 11 [5]. There are also few biological and behavioral data on Key Populations (KPs) in generalized
- 12 HIV epidemics due to challenges in their representative sampling via traditional surveillance
- 13 systems [6]. This has limited our understanding of KPs, and of their vulnerabilities to HIV, in
- 14 most generalized HIV epidemics and limits comprehensive HIV prevention, treatment, and
- 15 care responses.[7, 8] While we focus here on female sex work, these issues have relevance for
- 16 other KP in generalized HIV epidemics.

17 The role of sex work in HIV epidemics refers to the extent to which unprotected sex (condomless

18 and in the absence of antiretroviral-based pre-exposure prophylaxis and treatment) in the context

- 19 of sex work leads to new HIV infections in a given region. Region-specific knowledge on the
- 20 role of sex work can inform the design of HIV prevention programs to ensure that they meet the
- 21 needs of those most vulnerable for HIV acquisition and transmission; achieve maximal and
- sustained HIV prevention benefits at population-levels; optimize resource allocation; and help
- reduce inequities in the HIV care continuum (Box 1). Appropriately characterizing the role of
- sex work in Benin [9], for example, resulted in increases in protective behaviors and reductions
- 25 in HIV incidence and prevalence among FSWs [10], with important impacts on the wider
- 26 population[11-13].

27 Optimizing the preventive potential of different combinations of behavioural, biomedical, and

- structural interventions raises questions about their mix, delivery, and models of implementation to optimize health benefits at affordable costs [14]. Chief among these questions is whether, and
- 30 to what extent, focused HIV programmes are needed for FSWs and clients. Yet often implicit
- 31 within generalized epidemic responses are assumptions that (1) sex work is no longer significant
- to the sustained transmission of HIV, and (2) HIV interventions designed to reach 'all segments
- 32 of society' will reach FSWs and clients [15]. Emerging empiric and model-based evidence is
- 34 challenging these assumptions. This paper draws on systematic reviews and highlights the
- current frameworks and estimates of the role of sex work in HIV epidemics; and the relevant
- 36 empiric data landscape and its strengths and limitations.
- 37

38 Frameworks for Characterizing the Role of Sex Work in HIV Epidemics

- 39 Five frameworks have been used to estimate the contribution of sex work to overall HIV
- 40 transmission (Table 1). Traditional approaches include the numerical proxy [15], the UNAIDS
- 41 HIV Modes of Transmission (MOT) models [16], and the classic population attributable fraction
- 42 (PAF). [17-22]. Emerging approaches include the "transmission" PAF (T-PAF) [13, 23-26] and a
- 43 re-definition of epidemic types on the basis of their behavioral epidemic drivers [20, 27-29]. The

- 1 term *behavioral epidemic driver* refers to risk factors (such as unprotected sex in the context of
- 2 sex work) such that a failure to address the risk factor would undermine all other efforts at HIV
- 3 epidemic control and thus, the risk factor can sustain HIV epidemics Estimates of the
- 4 contribution of sex work to overall transmission vary greatly by methods and the time-horizon of
- 5 measurement. The advantages and disadvantages of each of these frameworks are outlined in
- 6 Table 1. Estimates are summarized in Table 2.
- 7 The numerical proxy approach to defining HIV epidemics and inferring role of sex work
- 8 By the late 1990's, tailored HIV surveillance and prevention policies were grounded in the user
- 9 friendly numerical proxy approach -defining HIV epidemics as concentrated or generalized
- 10 based on HIV prevalence thresholds across risk-groups[15]. This framework drew on the theory
- of epidemic phase for the role of unprotected sex work in sustaining HIV epidemics [30-36]. It suggested that in the early phase of an HIV epidemic, infections entered a population through
- suggested that in the early phase of an HIV epidemic, infections entered a population through
 KP, like FSW, and spread via 'bridge populations,' such as clients, to wider populations. The
- size of these epidemics depended on a maintenance (or general population) network, and the
- extent to which the two networks overlapped [31]. Epidemics were 'concentrated' in the early
- 16 phase, became 'generalized' and were sustained by maintenance networks[31]. The numerical
- proxy emerged when the epidemic phase constructs of 'concentrated' and 'generalized' HIV
- 18 epidemics were assigned HIV prevalence thresholds [15]. Epidemics were classified based on
- 19 whether HIV prevalence exceeded 1% in the general population.) [15, 37, 38]. If overall HIV
- 20 prevalence remained below 1% while HIV burden exceeded 5% in a KP the epidemic was
- 21 deemed concentrated and focused HIV strategies recommended [15, 37, 38]. If HIV prevalence
- surpassed 1% in the general population, the epidemic was generalized and HIV efforts were to
- reach all segments of society [15, 37, 38]. The numerical proxy approach was originally
- 24 developed to guide HIV surveillance, [15] however, in practice often guided resource allocation
- and programmatic design [37, 38].
- 26 Overall HIV prevalence in 39 SSA countries exceeds 1%, with considerable variability as
- 27 defined by the numerical proxy within countries [39]. A limitation of the approach is that
- 28 prevalence thresholds have not been validated for inferring the contribution of specific behaviors
- among KPs including unprotected sex work to overall HIV transmission. [20]. Dynamic
- 30 mathematical modelling studies of SSA regions with >1% HIV prevalence such as in Cotonou,
- 31 Benin and across Kenya, suggest that unprotected sex work can be an important risk for onward
- 32 HIV transmission [9, 13, 24, 29], and challenge the assumption that sex work is not important in
- 33 these epidemics.

Short-term estimates of the distribution of new HIV infections and classic PAF of sex work on prevalent/incident HIV infections

- 36 Allocation of resources is also informed by estimates of the relative burden of new annual HIV
- 37 infections acquired in different risk such as those obtained from the UNAIDS HIV MOT model
- 38 [16, 40]), or the classic PAF on HIV prevalence or incidence [17-19, 41]. The current MOT
- 39 model uses data on HIV prevalence across risk-groups, population size estimates of different risk
- 40 groups including KPs and clients, and sexual behaviors such as number of sexual partners [42].
- 41 The classic PAF is estimated using point prevalence or within-population incidence data, as well
- 42 as estimates of the size of different risk groups.

- 1 Half of the 39 SSA countries with generalized epidemics have estimated the fraction of annual
- 2 new HIV infections acquired by FSWs/clients using the MOT [40, 43], while the classical PAF
- 3 of sex work on prevalent HIV infections in males and females has been estimated in 25 and 27
- 4 countries respectively [22, 44]. These measures often suggest a small role for sex work in current
- 5 generalized HIV epidemics (Table 2), but have been shown to underestimate the medium- to
- long-term contribution of sex work [29, 44]. Both approaches ignore a central feature of HIV
 spread: the propagation of HIV infections via onward HIV transmission (Table 1). Onward
- 8 transmission refers to the chain of transmission from a single (direct) transmission during
- 9 unprotected sex work that leads to another infection between the infected individual and their
- subsequent partners, which in turn, leads to another infection between the newly infected partner
- to their other partners. The MOT and classic PAF capture the single, direct transmission, but not
- 12 the chain of transmission.
- Emerging approaches: the "transmission" PAF and re-defining HIV epidemic typology by
 behavioral epidemic drivers
- 15 The implications of underestimating the contribution of sex work to HIV spread are important
- 16 because they can lead to misallocation of resources. From a program perspective, we may
- 17 erroneously assume that because few infections arise among FSWs/clients, there is little to gain
- 18 from targeted efforts. Two emerging frameworks may address the limitations of the traditional
- 19 approaches by accounting for behaviors which potentiate HIV epidemics.
- 20 The 'transmission PAF' (T-PAF) of sex work accounts for transmission chains over time the
- 21 extent to which the cumulative number of new HIV infections are due directly or indirectly to
- unprotected sex work [9, 23, 25, 26, 29, 44]. The T-PAF is particularly useful because it tells us
- about the potential fraction of infections that may be prevented if we can add to existing
- 24 interventions and protect all FSWs and clients from HIV during sex work. It provides
- 25 information on the potential impact on the total or wider population of a 'perfect' intervention
- 26 for FSWs and clients, without changes in the sexual network or displacement of sex acts As a
- 27 result, the T-PAF provides a clearer picture of the role of unprotected sex work as a driver of
- HIV epidemics with implications for the design, delivery, and scale of HIV prevention. The T PAF is estimated from dynamic mathematical models over different periods of time. Dynamic
- PAF is estimated from dynamic mathematical models over different periods of time. Dynamic
 models are used to predict cumulative infections with and without transmission within
- 31 commercial sex)[9, 25, 26, 29]. Like the numerical proxy, MOT, and classic PAF, the T-PAF
- 32 depends on inputs from the best available empiric data.. Other counterfactuals to describe the
- 33 influence of sex work itself may include displacement of sex acts or changes in the sexual
- 34 network but are distinguished from the T-PAF.
- 35 To date, the T-PAF over different time-periods has been estimated for three SSA countries;
- 36 Benin, Burkina Faso, and Kenya [13, 24, 29, 45]. Estimates of the long term transmission PAF in
- 37 each suggest that even in the presence of sustained existing FSW interventions and medium to
- 38 high-levels of condom use, 13.5-37.6% of all new HIV infections over the next 20 years could be
- 39 due directly and indirectly to sex work [13, 44, 45]. Without FSW interventions, this figure of
- 40 new infections attributable to sex work is estimated to be 58.3-88.9% over the same time-period
- 41 [13, 45, 46]. Direct comparisons of the MOT estimates and classic PAF with the transmission
- 42 PAF where all are derived from simulated HIV epidemics via dynamic mathematical models
- have shown that the MOT and classic PAF are similar to the transmission PAF of sex work in the
 short-term (1 year) but the former are much smaller in the medium- to long-term [29, 46]. This
 - 6

- 1 discrepancy occurs because the transmission-PAF captures onward transmission. Onward
- 2 transmission is particularly important with behavioral epidemic drivers such as unprotected sex
- 3 work associated with high frequency of sexual partnerships and mixing between risk groups [47].
- 4 A systematic review of dynamic mathematical modelling studies summarized the potential
- 5 impact of sex work interventions on onward transmission within the wider community in SSA
- (Table 3)[13, 24, 48, 49] i.e. HIV in the overall population and beyond FSWs and their clients.
 Most models were calibrated to observed HIV prevalence in FSWs [13, 24, 49-52]. They suggest
- that across a range of interventions, focused FSW programming could avert up to 85% of new
- 9 HIV infections in the total population over 15 years[9], and reduce HIV incidence by up to 35%
- 10 over 10 years in the general population [53]. Reaching clients could also provide large
- 11 incremental benefits [54].
- 12 Finally, there has been growing momentum to re-define HIV epidemics on the basis of their
- 13 underlying transmission dynamics and the role of FSW/clients in the emergence and
- 14 persistence of HIV spread [19, 20, 27-29]. In this new classification system, HIV epidemics are
- 15 classified as 'generalized' if they are entirely driven by non-KP sexual networks and 'mixed' if
- 16 epidemic control requires preventing transmission within KP and non-KP networks (preventing
- 17 infections among KP are insufficient to control the epidemic, and likewise if only preventing
- 18 infections among non-KP networks). A growing number of countries are adopting this new
- nomenclature particularly the use of the term 'mixed' epidemic [19, 55]. In practice, this re definition of epidemic types remains dependent on testing via dynamic mathematical models
- definition of epidemic types remains dependent on testing via dynamic mathematical n[29].
- 22

Existing Data Available for the Transmission PAF, Re-Defining HIV Epidemics, and Informing the Design of Sex Work Programs across SSA

25 Dynamic mathematical models can be used to estimate the T-PAF and to help classify epidemics

based on behavioral drivers, but require the best available data on sex work, clear definitions of

who is a sex worker, HIV burdens across risk-groups including clients of FSWs, population size
 of FSWs and clients, mediators of individual-level HIV acquisition and HIV transmission risks,

sexual partnerships and networks, and HIV prevention and treatment coverage. The data needs

- 30 overlap with the programmatic needs to inform the content and scale of sex work programs
- 31 (Table 4). Recent reviews shed light on the current FSW/client data landscape, how data are
- 32 being collected, where, and limitations of the data (Table 5). Stigma and criminalization can pose
- 33 barriers to data collection; working with FSW communities in the design and implementation of
- 34 surveillance and research tools can help ensure data collection is rights-based, appropriate, and
- 35 reflects the diversity of the population.

36 Epidemiologically and Programmatically Meaningful Definitions of Sex Work

- 37 Clear definitions of sex work are needed to (a) ensure FSW/client interventions are reaching
- them and to (b) design intervention packages that meet their needs. [56-60] There is no current
- 39 consensus on the surveillance definition of sex work. Some define sex work as any exchange of 40 sex for money, favors, or goods [61]. Others limit definitions to only the exchange of money.
- sex for money, favors, or goods [61]. Others limit definitions to only the exchange of money,
 large client volumes, self-identification, or reference to sexual partners as FSW/client, when
- 41 money was negotiated [56, 62-64]. Terms such as informal, part-time, clandestine, or
- 43 transactional sex permeate the discourse yet their distinction from formal, high-volume sex work,

remains unclear. [59, 62, 63, 65]. It is important to distinguish sex work within this spectrum
even if individuals engage in more than one type or transition between types [66].

3 Formal sex work with large client volumes in highly-connected and high-risk sexual networks

4 has different implications for HIV spread than casual, or long-term, concurrent partnerships that

5 may be financially motivated [67]. Without clear definitions of sex work, T-PAF analyses to

6 estimate the contribution of sex work to HIV epidemics may use conflated FSW/client size

7 estimations, risk-behaviors, and HIV burdens, thereby under or over-estimating the role of sex

8 work – and limit all approaches, including dynamic modeling. Client volume and percent
9 income from sex work has been associated with HIV in a number of generalized HIV epidemics

ranging from Nigeria to Swaziland[68, 69]. Thus, we suggest a strategy that defines sex work

based on client numbers and on a pragmatic basis for focused HIV prevention efforts.

12 **Population Size Estimation of FSWs and Their Clients**

13 Size estimates and the duration of sex work are central to understanding the contribution of sex

14 work to HIV epidemics. Every framework (Table 1) needs this information - as direct inputs into

15 mathematical models or as the bases for representative sampling for bio-behavioral surveys. Size

16 estimates also are critical for programs to provide services at scale and to monitor coverage, and

are increasingly being used by funders to support allocation of HIV expenditures[70, 71].

18 FSW/client population size estimation are not routinely collected as part of traditional HIV

19 surveillance. However, guidelines on different approaches exist, and several countries have

20 started to enumerate FSWs [71, 72]. Size estimation methods include network-size analyses of

21 respondent driven sampling surveys, and multi-staged key informant and geographic mapping

and enumeration of KP hotspots [71, 73, 74]. Geographic mapping with enumeration has the

added benefit of providing program "catchment areas" for better intervention delivery [75, 76].

24 Size estimations conducted in 29 SSA countries to date suggest that about one to three percent of

adult women are engaged in active formal sex work [44], whereas estimates of client population size range widely from a median of 3% using direct surveys methods to 7-30% using indirect

size range widely from a median of 3% using direct surveys methods to 7-30% using indirect
 methods [46]. The indirect method of client population size estimation was first described by

28 Cote *et al.* to calculate a plausible match from the adult male population to the number and

frequency of clients reported by FSWs, and the frequency of repeat FSW visits reported by

30 clients [17]. These indirect SSA size estimates are similar to those reported in concentrated HIV

31 epidemics characteristic of India [20]. The indirect method requires FSW-specific and client-

32 specific behavioral surveys and FSW size estimations; absence of client surveys has been the

33 limiting factor for estimating client population size. While the value of size estimation cannot be

34 overstated, it is important to note that a number of biases limit each size estimation method for

35 KPs [70, 72], and the indirect method for client size estimation depends on several data from

36 FSW and client-specific surveys. Where possible, triangulating estimates from different methods

- 37 may be helpful[74].
- 38 Size estimations are often conducted once, and rarely repeated using the same approach. Thus,

39 the stability or temporal dynamics of FSW/client size (relative to the general population) remains

40 unknown. Rates of entry and exit from engaging in sex work ("turn over") and thus, duration in

41 sex work, may be important when estimating downstream HIV transmission from unprotected

42 sex work [77] during the career-span of FSW or after retiring from sex work [78]. Sex work

43 population dynamics and how it may influence the T-PAF remain unexplored.

1 **Representative Estimates of Relative HIV Burden**

2 Representative estimates of HIV prevalence, incidence, and, potentially, superinfection data

3 among FSW and clients can be used to estimate the role of sex work in HIV epidemics (Table

4 1)[79]. Obtaining unbiased empirical estimates of HIV incidence is challenging so most dynamic

5 mathematical models will use HIV prevalence data to support model calibration. Optimal

6 estimates can help allocate for HIV care, further risk-stratify FSW and clients, and monitor

- 7 program impacts..
- 8 FSWs/client HIV prevalence data in generalized HIV epidemics comes from household surveys

9 such as the Demographic Health Surveys, and from FSW/client- bio-behavioral surveys. General

10 population surveys are limited by willingness to report sex work.[80]. Household surveys also

tend to under-sample mobile or migrant populations, including truckers, miners, fisher-folk and 11 12

refugees, who may be more likely to be clients or SWs.[81, 82]. While some of these biases are

13 addressed with direct surveys of FSWs and clients, participants in these studies may not be 14 representative of the underlying FSW/client population. For example, two-thirds of FSW HIV

15 data in generalized epidemics of SSA come from convenience sampling of sexually transmitted

- infection (STI) clinics or FSW venues [44]. Despite these limitations, the available data suggest 16
- 17 a disproportionate burden of HIV among FSW in generalized epidemics (Table 5) - and variability in the magnitude of inequity is not fully explained by differences in study design. 18

Three recent systematic reviews of HIV among FSW in the generalized epidemics of SSA 19

20 suggest a 9 to 14-fold greater HIV burden compared to all women of reproductive age [22, 46,

21 83]. Meanwhile, client-specific studies across six SSA countries suggest a 4-fold greater odds of

HIV prevalence among self-reported male clients compared to non-client males [44] [18, 19, 84, 22

23 85].

24 Thus, the next phase in HIV surveillance in generalized HIV epidemics should include FSW and 25 client HIV prevalence estimates. Where possible, HIV prevalence estimates should be obtained via representative sampling [86] using pre-sampling size estimations or venue assessments to 26 inform sampling frames [72]. Where size estimations are not possible, using respondent-driven 27

sampling as a chain-referral strategy may support the calculation of less biased estimates of HIV 28

- 29 burdens [87].
- 30

31 HIV Acquisition and Transmission Risks and Protective Behaviors Among FSW/clients

32 Dynamic models of HIV epidemics that include sex work need to parameterize the heterogeneity

33 in HIV acquisition and transmission risk associated with sex work in order to capture the

'mechanistic' processes that underpin transmission events. There is an extensive body of 34

literature that outlines the proximal and distal determinants of HIV acquisition among FSWs and 35

36 clients [57, 88, 89]. Proximal determinants include differential patterns of condom use by partner

37 type (regular, new, and non-paying), numbers of partners, frequency of sexual acts by partners

and type of sex (vaginal vs. anal), concomitant STIs, , anal and vaginal douching and use of 38

39 drying agents and spermicides[90-92]. Proximal determinants are important for estimating the

40 transmission PAF and re-defining HIV epidemics on the basis of behavioral drivers; whilst

proximal and distal factors such as laws, policies, or health-system factors are each critical to the 41

42 design of HIV programs.

- 1 Currently, the only FSW risk-factor data routinely requested and reported in the UNAIDS
- 2 country reports is condom use at last sex [93]. The majority of studies on HIV factors among
- 3 FSWs have focused on assessing individual, proximal risks. Yet distal factors are increasingly
- 4 recognized as predictors of HIV acquisition and for the coverage of services for FSWs [88, 94,
- 5 95]. In Swaziland, there were significant relationships between increased measures of social
- capital and condom use and uptake of HIV testing in FSWs [96]. Recent modelling of a potential
 causal pathway from history of sexual violence and current condom-use among FSWs suggests
- important population-level effects of sexual violence mediated through individual-level sexual
- 9 practices [97].
- 10 Taken together, these findings suggest the utility of comprehensive risk assessments and causal
- 11 pathways of HIV risk and/or protective behaviors when characterizing HIV- risks among
- 12 FSW/clients. An understanding of proximal determinants is needed to reproduce HIV epidemics
- 13 with dynamic models, and thus, estimate the T-PAF. Estimating the T-PAF of distal
- 14 determinants requires a strong empirical basis for the full causal pathway. However, developing
- 15 indicators to measure the full scope of structural and social factors and relating each to
- 16 individual-level proximal determinants is a challenging and emerging area of research in
- 17 dynamic modeling. Nonetheless, HIV programs are implemented within structural determinants
- 18 such as human rights violations, criminalization, sexual and physical violence, condom
- 19 accessibility and perceived and experienced stigma and discrimination [88]. Programs need to
- 20 address determinants along the full casual pathway to HIV acquisition and transmission during
- 21 sex work.

Characterizing HIV Transmission Networks of FSWs, Clients, and the Wider Community 23

- 24 Key to the transmission PAF is data on how partnerships are formed within sex work and
- 25 between FSW/clients and individuals not directly engaged in sex work, including those involved
- 26 in other financially-motivated partnerships, concurrent or serial multiple partnerships, and the
- 27 'lower-risk' general population. To date, these have only included sexual partnerships but can
- 28 (and should) be extended to include other risks.
- 29
- 30 For the transmission PAF, we usually infer 'who has sex with whom' from available data by
- 31 fitting these data to observed data on HIV prevalence/incidence across risk groups. Such data are
- not routinely collected as part of HIV surveillance, but can come from individual surveys of
- FSWs and clients with questions about the number, type, age, etc. of sexual partners by the type
- of partnership or sexual network surveys [98]. Phylogenetic analyses using HIV sequence data
- have been used to infer networks among people who inject drugs and MSM [99-102], and are
- being explored to infer HIV transmission networks of FSW/clients and the wider
- 37 community[100, 103]. Deterministic models assume instantaneous partnerships and with the
- exception of pair models do not explicitly account for duration of partnerships, which may be
- important for casual or long-term partnerships. The type of dynamic mathematical model may
- 40 influence the T-PAF. Early work on model comparison suggests that deterministic models with
- 41 assumptions of instantaneous partnerships may overestimate the role of long-term partnerships in
- 42 transmission compared with network models with explicit partnership duration[104].
- 43
- 44 Characterizing sexual networks includes the different contexts within which sex work takes
- 45 place, such as short-term migration [26], and how networks (or sexual mixing between risk

- 1 groups) change over time. Intersections and overlaps with networks of people who use drugs,
- 2 and casual sex networks, are also an emerging area of study [105, 106]. If we do not account for
- 3 overlaps in transmission networks, we may underestimate the T-PAF of sex work to HIV
- epidemics. Similarly, vertical HIV transmission among FSWs may be high but remains unknown 4
- 5 in SSA. FSWs are less likely to use condoms with non-paying partners – with whom FSWs may
- 6 choose to have children [107].
- 7

8 Program and Biological Data to Characterize Interventions and Engagement in HIV 9 **Prevention and Treatment Programs**

10

Data on program-related protective factors for HIV acquisition and transmission - such as 11

- condom-use, voluntary male circumcision among clients, and HIV viral suppression among 12
- 13 FSW/clients on ART are important to include when estimating the T-PAF, and when designing
- 14 and monitoring HIV programs.
- 15 The only routinely collected indicators of FSW-program reach include awareness of where to
- 16 access HIV testing, and receipt of condoms in the last 12 months [93]. These indicators were
- reported for 20 countries in the 2012 UNAIDS Country Progress Reports. A country-median of 17
- 54.4% (range, 1.5-89.9%) of FSWs surveyed reported knowledge of where to access HIV testing 18
- 19 and receipt of condoms in the last 12 months. The indicators were based on convenience samples
- 20 (18 from surveys), and only one had pre-sampling enumeration; 28 countries did not report or
- 21 have data on FSW coverage with denominators. The extent to which existing HIV prevention
- 22 programs are reaching FSWs and clients and addressing their HIV risk remains highly questionable.
- 23
- 24
- 25 The remainder of the HIV continuum of care for FSWs (or clients) has not been monitored as 26 part of the UNAIDS country reports. Although there are a few studies of the HIV care cascade
- 27 among FSWs [108, 109], the data are limited to FSWs who meet study-specific eligibility criteria
- 28 and agree to participate.. Thus existing HIV care data are likely not representative of the
- 29 underlying FSW populations [108, 109]. Continuum of care data could help estimate the
- 30 additional ART needs of FSW[110, 111]. Monitoring of primary and secondary emergence of
- HIV drug-resistance could be important in populations at highest risk, such as FSWs in 31
- 32 generalized HIV epidemics - as has been done with `sentinel` surveillance of drug-resistant
- 33 gonorrhea in industrialized settings [112]
- 34

35 Conclusions

36

- 37 There is growing empiric and model-based evidence for helping decide whether, how much, and
- 38 how to focus on sex work in generalized HIV epidemics. A small, but growing, body of model-
- 39 based evidence of the transmission PAF and sex work interventions demonstrate the large
- 40 potential for HIV prevention and health benefits to the wider community from sex work
- programs in generalized HIV epidemics. However, gaps remain and limit a comprehensive 41 understanding of the role of sex work. Understanding could be improved by investing in the
- 42 43 collection of specific data, by making the best use of these data, and with appropriate methods of
- 44 estimating the role of sex work in HIV epidemics. To move forward, the HIV scientific
- 45 community must begin by characterizing the epidemiology of generalized HIV epidemics with

- data and more appropriate methods of estimating the contribution of the unmet needs of sex
 workers and their clients.
- 3
- 4
- -
- 5

1 Box 1: Why quantify the role of sex work in HIV epidemics?

Quantifying the role of sex work in generalized HIV epidemics involves:

- Estimating the cumulative fraction of new HIV infections that directly or indirectly originate from unprotected sex in the context of sex work in presence and absence of existing interventions.
- Distinguishing the cumulative fraction of new HIV infections that directly or indirectly originate from unprotected sex in the context of sex work versus other financially-motivated transactional partnerships.

Importance of quantifying the role of sex work in generalized HIV epidemics:

- To better understand local HIV epidemics and identify the main behavioural sources of HIV transmission fuelling the HIV epidemic (i.e. unprotected behaviours that without additional interventions, could undermine HIV epidemic control).
- To help HIV programmes decide when, where, and how to focus on sex work interventions for individuallevel prevention and health benefit to those most-vulnerable to HIV acquisition and transmission.
- To help HIV programmes decide when, where, and how to focus on sex work interventions for populationlevel prevention and health benefits in the wider community.
- To help policy-makers allocate HIV resources effectively and efficiently.
- To reduce inequities in HIV service delivery across risk-groups.

2 3

	Definition	Assumption	Pros	Cons	Implications for designing HIV programmes
Generalized HIV epidemic (Numerical Proxy)	Region where HIV prevalence is currently >1% in the general population (usually measured via ante-natal clinic surveillance) [18]	Sex work is less important than other sexual partnerships to HIV spread	Easy to classify (little data needed)	Does not reflect underlying transmission dynamics and role of key populations in HIV spread	Leads to broad recommendation that HIV prevention is applied to "all segments of society" (no specific focus)
Short-term distribution of newly acquired HIV infections (Modes of Transmission model)	Fraction of new HIV infections acquired across risk-groups (such as FSWs, clients) in one year	No onward transmission chains No overlapping risk- factors	Easy to use with empiric prevalence and size of FSW/client population	Underestimates the transmission PAF in the medium to long-term Cannot disentangle multiple risk- factors (example, sex work and sharing needles) in same subgroup	Could lead us to underestimate the importance of focused HIV programmes for FSWs/clients
Classical PAF	Fraction of prevalent or incident HIV infections that occur in FSWs (or clients) relative to non- FSWs and non-clients	No onward transmission chains	Easy to calculate using empiric HIV prevalence or incidence data and size of FSW/client population	Underestimates the transmission PAF in the medium to long-term Cannot disentangle multiple risk- factors (example, sex work and sharing needles) in same subgroup	Could lead us to underestimate the importance of focused HIV programmes for FSWs/clients
Transmission PAF (T- PAF)	Fraction of cumulative new HIV infections that are due (directly and indirectly) to unprotected sex work	Onward transmission chains We know, or can triangulate or vary, the sexual mixing between risk-groups. Patterns of sexual mixing or size of the sex work population are assumed to remain stable or resemble temporal changes observed in the past only, over the time- frame of the T-PAF estimate.	Accounts for indirect transmission chains; can disentangle multiple risk-factors	Requires dynamic mathematical models to estimate Dependent on the empiric data inputs (including sexual mixing between risk- groups, and sex work definition (thus, population size of FSWs/clients) Can depend on the subgroup-specific data the model is calibrated to [measured HIV prevalence, incidence, HIV sequencing] Will depend on the structure of the model and level of heterogeneity in sexual behaviour	Can be interpreted as the largest potential fraction of new HIV infections that could be averted with ideal interventions that protected all FSWs/clients from HIV.

Table 1: Frameworks for characterizing the role of sex work¹ in HIV epidemics, and the implications for HIV programmes.

"Generalized" HIV epidemic based on underlying transmission dynamics	Region where sex work (or other well-defined high-risk behaviours such as injecting drug use, etc ¹) is neither sufficient nor necessary to enable HIV to establish and spread (for R_0 to exceed 1)	Sex work (or other well- defined high-risk behaviours) are not important to sustain HIV spread	Accounts for indirect transmission chains; can disentangle multiple risk-factors	To date, requires dynamic mathematical models to classify Dependent on same data as with the transmission PAF	Local HIV epidemic could be controlled without sex work interventions
"Mixed" HIV epidemic based on underlying transmission dynamics	Requires either commercial sex or other partnerships (for example, casual sex or multiple partnerships) for HIV to establish and persist, such that both commercial and casual sex acts would need to be protected to achieve long-term elimination (R_0 <1).	Sex work (or other well- defined high-risk behaviours) can sustain HIV spread, but preventing transmission within commercial sex alone would not be enough to control the local HIV epidemic	Accounts for indirect transmission chains; can disentangle multiple risk-factors	To date, requires dynamic mathematical models to classify Dependent on same data as with the transmission PAF Does not specify the contribution of sex work (or other well-defined risk- groups) versus other partnerships to overall HIV spread	Local HIV epidemic control requires interventions focused on sex work and on other risk- behaivors in the general population
"Concentrated" HIV epidemic based on underlying transmission dynamics	Requires that commercial sex exist for HIV to establish and persist in the population, (R_0 is greater than 1 in the presence of commercial sex, and <1 in the absence of commercial sex)	Sex work (or other well- defined high-risk behaviours) can sustain HIV spread	Accounts for indirect transmission chains; can disentangle multiple risk-factors	To date, requires dynamic mathematical models to classify Dependent on same data as with the transmission PAF	Local HIV epidemic could be controlled with sex work interventions

 R_0 (basic reproductive ratio: the average number of new infections due to one infectious case in an otherwise susceptible population) ¹The focus of this paper is on sex work; but behaviours could include those relevant within other key populations (for example, injecting drug use)

System	Approach	Number of generalized HIV epidemics in SSA ² with recent data, of 39 countries (years)	Estimate	Median % (range)	Concerns/Issues	Sources
Routine surveillance	HIV Modes of Transmission Model	18	% of new HIV infections acquired by FSWs and clients, over 1 year	FSWs: 2.0 (0.1,13.7) Clients: 7.0 (0.46,25.6)	Underestimates the transmission PAF in the medium to long- term[29]	UNAIDS Country Reports 2012; Systematic Reviews[40, 43]
Intermittent Surveillance and Research	Based on the relative risk of HIV compared to non-client males	25	Classic PAF of sex work on prevalent HIV infections, males	2.0 (0.0,88.0)	Underestimates the transmission PAF in the medium to long-term	Systematic reviews[44]
	Based on the relative risk of HIV compared to general population females	27	Classic PAF of sex work on prevalent HIV infections, females	6.5 (0.4,71.2)	Underestimates the transmission PAF in the medium to long-term	Systematic Reviews[21, 22]
	Dynamic mathematical models	3	Transmission PAF over 20 years	58.3-88.9 (in the absence of FSW interventions)	Data requirements (see Table 5); Need dynamic mathematical models calibrated to FSW/client HIV prevalence/incidence trends	Systematic reviews[44]

Table 2. Estimates of the contribution	of sex work to generalized HIV	epidemics in SSA.

PAF (population attributable fraction)

CER

Study	HIV prevalence at start of intervention in the model		Sex work intervention (efficacy, coverage, risk-group)	Potential impact in the wider community					
	Overall	FSWs				Outcome ¹		Time-horizon	
				HIV incidence*	HIV prevalence*	# of HIV infections averted	PF	Years	
Botswana									
Nagelkerke [113]	30%	N/A	Condom-use (100%, 75%, FSW)		$27\% \downarrow^2$			30	
Nagelkerke [113]	30%	N/A	Anti-retroviral treatment (100%, 50%, FSW)		13%↓2			30	
Vissers [54]	33% ²	N/A	Oral pre-exposure prophylaxis (90%,75%, FSW)			251 per 100,000 uninfected person- years ²		10	
Vissers [54]	33% ²	N/A	Oral pre-exposure prophylaxis (90%,75%, FSW and clients)			785 per 100,000 uninfected person- years ²		10	
South Africa									
Vickerman [114]	30% ⁴	60%	Vaginal microbicide (40%, 75%, FSW)	1% ² ↓			1.3% ²	4	
Vickerman [115]	27% ³	62%	↑ condom-use (100%,20%) & STI treatment (100%, 20%, FSW)	2% ² ↓		53-65 per 100,000 adults ²		1	
Vickerman [115]	27% ³	62%	↑ condom-use (100%,20%) & STI treatment (100%, 100%, FSW)	14% ² ↓				1	
Vickerman [115]	27% ³	62%	↑ condom-use (100%,20%) & STI treatment (100%, 100%, FSW and clients)	28% ² ↓				1	
Johnson [116]	26% ²	N/A	HIV vaccine (30%, 60%, FSW)			0.4-2.4 per 100 FSWs vaccinated ²		10	
Zimbabwe									
Hallett [53]	22%	N/A	Condom use (100%,80-100, FSW) & STI treatment (100%,10%, FSW)	$10\%^2\downarrow$				5	
Hallett [53]	22% ²	N/A	Condom use (100%,80-100, FSW) & STI treatment (100%,10%, FSW)	35% ² ↓				10	
Kenya									
Vissers [54]	16% ²	N/A	Oral pre-exposure prophylaxis (90%,75%, FSW)			166 per 100,000 uninfected person- vears ²		10	
Vissers [54]	16% ²	N/A	Oral pre-exposure prophylaxis (90%,75%, FSW and clients)			733 per 100,000 uninfected person- years		10	
Decker [117]	6%	33.8%	\downarrow prevalence of sexual violence from baseline 32% to 2.4%		1	53,200 ²	12% ²	5	
Wirtz [118, 119]	6%	33.8%	100% FSW community empowerment from 5% ; leads to \uparrow consistent condom use by 51%			16,661-20,680	6% ²	5	
Steen[24]	24% ²	45%	↑ Condom-use (85%, 100%, FSW)	63% \downarrow^2	46%↓2			20	
Benin									
Boily [9]	1% ²	53%	↑ Condom-use (100%,60%, FSW) & STI treatment (100%,50%, FSW)	19%³↓			58-85%	10	
Vickerman [120]	3% ²	55%	↑ Condom-use (100%, 81%, FSW)	21.5% ² ↓(17.7- 24.9)				4	
Vickerman [120]	3% ²	55%	STI testing & treatment (80%,85%, FSW)				10% (6-12) ²	4	
Vickerman [114]	3.3%4	49%	Vaginal microbicide (40%,75%, FSW)	26% ² ↓	l		24.8%	4	
Williams[13]	3.0% ²	55%	↑ Condom-use (100%, 87.7%, FSW)				33% (20-46)	15	

Table 3. Potential impact of FSW/client interventions on overall HIV transmission in Sub-Saharan Africa [48].

FSW (female sex worker); GP (general population); PF (prevented fraction; the % of HIV infections averted); N/A (not available from the study); *Relative change in HIV incidence or prevalence; ¹Range, uncertainty bounds, or 95% credible intervals from multiple simulations or epidemic realizations are shown in brackets. ²Total population (i.e. including FSWs and clients); ³General population females (i.e. excluding FSWs); ⁴Ante-natal clinic surveillance

Systematic review of mathematical modeling studies (updated January 2014) generated from the peer-reviewed literature [44, 50] Studies were included if they used dynamical models of heterosexual HIV transmission, incorporated behavioural heterogeneity in risk, and provided at least one of the following primary estimates in the wider community (a) the population attributable fraction (PAF) of HIV infections due to sexual partnerships within high-risk groups, or (b) the number per capita or fraction of HIV infections averted, or change in HIV prevalence/incidence due to focused interventions.

MARINE

	System	Approach	Quantify role of sex work in local HIV epidemic	HIV programme-related objectives		
			Transmission PAF and/or re-define HIV epidemic types	Design/adapt HIV programmes	Monitor HIV programme reach & epidemic impact	
Define FSW/clients	Routine Surveillance	Consensus and based on feasibility for programmes; and epidemiological risk (client numbers)	\checkmark	R	N	
		Research on sensitivity and specificity of various definitions (on HIV acquisition)		R		
FSW/client population size	Routine Surveillance	Feasible non-survey-based methods	\checkmark	\checkmark	\checkmark	
		Triangulate multiple size estimation approaches where possible	5			
HIV acquisition risks						
Individual-level	Intermittent Surveillance	Representatively sampled bio-behavioural surveys of FSWs/clients	V	\checkmark		
		Enhanced programmatic routine data collection				
Structural-level	Research	Enhanced programmatic routine data collection		\checkmark		
HIV transmission network	KS					
Sexual partnerships and networks	Intermittent Surveillance	Representatively sampled behavioural surveys of FSWs/clients	\checkmark	\checkmark		
		Sexual network surveys				
		Phylogenetic analyses of HIV sequence data (requires FSW, client, and general population HIV sequencing)				
Other HIV transmission networks (casual sex, MSM and infecting drug use)	Intermittent Surveillance	As above (and including other networks with phylogenetic analyses)	\checkmark	\checkmark		
Reproductive Health Data	Intermittent Surveillance	Representatively sampled behavioural surveys of FSWs	$\sqrt{(to include parent to child transmission in transmission PAF estimates)}$	\checkmark	\checkmark	
		Reproductive Health Programme data				
Baseline HIV intervention	s					
Condom-use	Routine surveillance	Representatively sampled behavioural surveys of FSWs/clients	\checkmark	\checkmark	\checkmark	

Table 4. FSW/client data needs in generalized HIV epidemics.

		FSW programme data			
HIV treatment and care continuum	Routine surveillance	Representatively sampled behavioural surveys of FSWs/clients	\checkmark	\checkmark	\checkmark
		FSW and ART programme data			
Structural (including community-based programmes)	Research	Situational Assessment of Laws	*	V	N
		Gender-Based Violence Programme Data	*		×

The check marks ($\sqrt{}$) reflect the areas (quantify role of sex work; program) in which the data are needed.

*If examining the role of structural and social factors (i.e. distal factors) influencing sex work on overall HIV transmission, then these data should be included.

20

System	Estimate	Approach	Number of generalized HIV epidemics in SSA ² with recent data, of 39 countries (years)	Median values (range)	Concerns/Issues	Sources
HIV burden		·	•	R		
Routine surveillance	HIV prevalence, FSWs	Household Demographic Health Surveys ¹ of adult females	1 (2002-2013)	- 2	Social desirability bias	UNAIDS Country Reports 2012
		FSW bio-behavioural surveys	23 (2002-2013)	23.1% (7.2-70.7)	Sampling frames often not based on pre-sampling enumeration; adjusting estimate based on sampling design	UNAIDS Country Reports 2012; Systematic reviews
	HIV prevalence, clients	Household Demographic Health Surveys ¹ of adult males	23 (2002-2013)	4.7% (0.43-32.0)	Social desirability bias	UNAIDS Country Reports 2012
Intermittent Surveillance and Research	HIV prevalence, FSWs	Programme or clinic-based, intervention trials; FSW bio- behavioural surveys	21 (2002-2013)	22.8% (0.9-69.8)	Sampling frames often not based on pre-sampling enumeration; adjusting estimate based on sampling design; definition of sex work varies	Systematic reviews[22, 46, 83]
	HIV incidence, FSWs	Programme-based cohorts; intervention trials	6 (2002-2013)	2.9 (0.9-7.6) per 100-person years	Selection bias and frailty effect; high attrition (loss to follow-up); missing early period of sex work (25-60% of FSWs already infected with HIV before enrollment in cohorts)	Systematic reviews[46, 121]
	HIV prevalence, clients	Client bio-behavioural surveys	8 (2002-2013)	2.9% (0.42-6.8)	All convenience samples	Systematic reviews[44]
	HIV incidence, clients	None	None			Systematic reviews[44]

Table 5. Current data and methods to characterize the role of sex work in HIV epidemics

Intermittent Surveillance and Research	FSW population size; % of adult females engaged in sex work	Several enumeration methods	23 (2002-2013)	1.8% (range, 0.25- 11.5%)	Each enumeration approach has pros & cons[72]; estimates from general population surveys subject to social desirability bias (especially those conducted via face-to-face interviews); definition of sex work varies	UNAIDS Guidelines on Enumerating Key Populations; Systematic Reviews[44, 122]
	Client population size; % of adult males engaged in sex work	Household Demographic Health Surveys ¹ or general population surveys of adult males	32 (2002-2013)	3.0% (range, 0.025- 19.8%)	Estimates from general population surveys subject to social desirability bias	Systematic reviews[44, 123]
	Client population size; % of adult males engaged in sex work	Indirect method by triangulating FSW population size, and FSW/client behavioural survey data	2 (2002-2013)	7.2-30.0%	Requires FSW data and behavioural data on clients	Systematic reviews[44]
Examples of H	HIV risk factors & cha	aracteristics of sex work		,		
Intermittent Surveillance and Research	Duration engaged in sex work	Behavioural surveys & Programme-based cohorts	5 (1987-2011)	FSWs: 5.5 years (range, 0.6,6.0) Clients: 4.6-5.2 years	Cross-sectional and censured data; no incidence of sex work cessation rate data; no re-entry into sex work	Systematic Reviews[124, 125]
	Sexual partnership types and periodicity of sexual acts by partner	Behavioural surveys & Programme-based cohorts	R		Often doesn't differentiate between regular clients, new clients, and non-paying partners	
	% of FSWs reporting condom- use with last client	Behavioural surveys in major cities	10 (2012)	91% (32-98)	Not part of routine surveillance	UNAIDS Epidemic Update 2013
	Active syphilis prevalence	Bio-behavioral surveys in major cities	10 (2010)	2.4% (0,19.6)	Not part of routine surveillance	UNAIDS Epidemic Update 2011
	Unprotected anal	Behavioural surveys &	7 (1985-2011)	0.0-80.0%	Very little data on frequency of unprotected anal sex	Systematic Review[126]

Routine surveillance	% of FSWs who know where to access HIV testing AND received condoms in last 12 months	Behavioural surveys in major cities	17 (2010-2012)	56.3% (1.5,89.9)	Not indicative of the extent to which FSWs' HIV risk is addressed and reduced; misleading 'coverage' without representative sampling & enumeration	UNAIDS Country Reports 2012
	HIV programmes available to FSWs	Survey of country-offices for HIV control	36 (2010)	-	Not part of routine reporting; no data on uptake of services or FSW coverage	UNAIDS Epidemic Update 2011
Intermittent Surveillance and Research	Community- mobilization	Behavioural Surveys	1 (2014)	aOR 2.39 (1.36- 4.02) for increased condom use	Complex study designs needed since benefits are mediated by increased condom use during commercial sex	Systematic Reviews[89]
	Structural interventions	Programme-based cohorts, Mathematical Models	1 (2014)	Avert 17% (1,31) of incident infections in Kenya over 10 years	Effects are mediated over long	Mathematical Model[97]
	HIV testing (tested for HIV in last 1 year and received results), FSWs	Behavioural surveys in major cities; Programme-based registry data	26 (2010-2012)	64.1% (6.5,93.7)	May decline over time as known HIV-infected FSWs no longer in the denominator; selection bias and non-representative sampling	UNAIDS Country Reports 2012[30]
	Duration in sex work when registered in FSW programmes	Behavioural surveys & Programme-based cohorts	11 (1987-2013)	2.6 years (0.7,5.1)	Reflects time to reach FSWs after entering sex work; selection bias and non-representative sampling	Systematic Reviews[127, 128]
	Age when registered in FSW programmes	Behavioural surveys & Programme-based cohorts	8 (1987-2013)	26.8 years (24,31.5)	Reflects time to reach FSWs after entering sex work; selection bias	Systematic Reviews[127, 128]
	ART coverage & HIV care continuum among HIV-infected FSW	Research cohorts & cross- sectional surveys	2 (2002-2013)	ART coverage (among HIV- infected FSWs): 0.4%-47.5% Retention on ART: 90-97%	Restricted to research settings and may not be representative of HIV care continuum among FSW	Systematic Review[108]

Research	Condom-based education	Community-randomized control trial	1 (2000-2003)	No significant reduction in HIV incidence in the wider community	HIV incidence in the FSW/client population not measured; unclear scope and coverage of FSW interventions	[129]
	Various interventions	Dynamic mathematical modelling studies	5 (2000-2013)	Range of impact (see Table 3) based on time-horizon and outcome measure	Not all models calibrated to FSW HIV data; no systematic evaluation of the same FSW intervention across settings	Updated systematic review[13, 24, 48]
¹ Country-wide, h ² Sub-Saharan Afr	ousehold-based, face-to-fa rica (SSA).	ce interviews.		S		
			A			
		COY				

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