Annals of Epidemiology 26 (2016) 557–569

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Review article

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

Sharmistha Mishra MD, PhD [a,b], Marie-Claude Boily PhD [b,1], Sheree Schwartz PhD, MPH [c,1], Chris Beyrer MD, MPH [c], James F. Blanchard MD, PhD [d,1], Stephen Moses MD, MPH [d,1], Delivette Castor PhD [e], Nancy Phaswana-Mafuya PhD [f], Peter Vickerman PhD [g], Fatou Drame PhD [h], Michel Alary MD, PhD [i], Stefan D. Baral MD, MPH [c,*]

[a] Division of Infectious Diseases, Department of Medicine, St. Michael's Hospital, Li Ka Shing Knowledge Institute, University of Toronto, Toronto, Ontario, Canada
[b] Department of Infectious Disease Epidemiology, Imperial College, London, UK
[c] Center for Public Health and Human Rights, Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD
[d] Centre for Global Public Health, Department of Community Health Sciences, University of Manitoba, Winnipeg, Canada
[e] Office of HIV/AIDS, United States Agency for International Development, Washington, DC
[f] HIV/AIDS, STI, and Tuberculosis Department, Human Sciences Research Council, Port Elizabeth, South Africa
[g] School of Social and Community Medicine, Bristol University, Bristol, UK
[h] Department of Geography, Université Gaston-Berger, St. Louis, Senegal
[i] Département de médecine sociale et préventive, Centre de recherche du CHU de Québec—Université Laval, Québec, Canada

ARTICLE INFO

Article history:
Received 16 November 2015
Accepted 3 June 2016
Available online 15 June 2016

Keywords:
HIV
Generalized HIV epidemics
Sex work
Sub-Saharan Africa
Mathematical models
Population attributable fraction

ABSTRACT

In the context of generalized human immunodeficiency virus (HIV) epidemics, there has been limited recent investment in HIV surveillance and prevention programming for key populations including female sex workers. 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 female sex workers and clients. Emerging empiric and model-based evidence is challenging these assumptions. This article 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.
© 2016 Elsevier Inc. All rights reserved.

Characterizing the role of sex work in generalized HIV epidemics

Early in the human immunodeficiency virus (HIV) pandemic, HIV surveillance and prevention focused on high risk, and high burden populations including female sex workers (FSWs), men who have sex with men, 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]. National expenditure data on HIV suggest that in 17 SSA countries reporting HIV expenditure data after 2007, a median of 0.35% (range, 0.0%–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% and 3.1% of HIV funding including HIV care expenditure benefits FSWs and clients [5]. There are also few biological and behavioral data on key populations (KPs) in generalized HIV epidemics due to challenges in their representative sampling via

* Corresponding author. Stefan D. Baral, Key Populations Programs, Center for Public Health and Human Rights, Department of Epidemiology, Johns Hopkins School of Public Health, E7146, 615 N. Wolfe Street, Baltimore, MD, 21205.
E-mail address: sbaral@jhu.edu (S.D. Baral).
[1] Authors contributed equally.

http://dx.doi.org/10.1016/j.annepidem.2016.06.004
1047-2797/© 2016 Elsevier Inc. All rights reserved.

traditional surveillance systems [6]. This has limited our understanding of KPs, and of their vulnerabilities to HIV, in most generalized HIV epidemics—and limits comprehensive HIV prevention, treatment, and care responses [7,8]. Although we focus here on female sex work, these issues have relevance for other KP in generalized HIV epidemics.

The role of sex work in HIV epidemics refers to the extent to which unprotected sex (condomless and in the absence of antiretroviral-based pre-exposure prophylaxis and treatment) in the context of sex work leads to new HIV infections in a given region. Region-specific knowledge on the role of sex work can inform the design of HIV prevention programs to ensure that they meet the 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 in HIV incidence and prevalence among FSWs [10], with important impacts on the wider population [11–13].

Optimizing the preventive potential of different combinations of behavioral, 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 to what extent, focused HIV programs are needed for FSWs and clients. Yet often implicit 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 of society" will reach FSWs and clients [15]. Emerging empiric and model-based evidence is challenging these assumptions. This article draws on systematic reviews and highlights the current frameworks and estimates of the role of sex work in HIV epidemics; and the relevant empiric data landscape and its strengths and limitations.

> **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 behavioral sources of HIV transmission fueling the HIV epidemic (i.e., unprotected behaviors that without additional interventions, could undermine HIV epidemic control).
> - To help HIV programs decide when, where, and how to focus on sex work interventions for individual-level prevention and health benefit to those most vulnerable to HIV acquisition and transmission.
> - To help HIV programs decide when, where, and how to focus on sex work interventions for population-level 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.

Frameworks for characterizing the role of sex work in HIV epidemics

Five frameworks have been used to estimate the contribution of sex work to overall HIV transmission (Table 1). Traditional approaches include the numerical proxy [15], the UNAIDS HIV modes of transmission (MOT) models [16], and the classic population attributable fraction (PAF). [2,17–21]. Emerging approaches include the "transmission" PAF (T-PAF) [13,22–25] and a redefinition of epidemic types on the basis of their behavioral epidemic drivers [20,26–28]. The term behavioral epidemic driver refers to risk factors (such as unprotected sex in the context of sex work)—such that a failure to address the risk factor would undermine all other efforts at HIV epidemic control and thus, the risk factor can sustain HIV epidemics estimates of the contribution of sex work to overall transmission vary greatly by methods and the time horizon of measurement. The advantages and disadvantages of each of these frameworks are outlined in Table 1. Estimates are summarized in Table 2.

The numerical proxy approach to defining HIV epidemics and inferring role of sex work

By the late 1990s, tailored HIV surveillance and prevention policies were grounded in the user-friendly numerical proxy approach—defining HIV epidemics as concentrated or generalized 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 [32–38]. It 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 [33]. Epidemics were "concentrated" in the early phase, became "generalized," and were sustained by maintenance networks [33]. The numerical proxy emerged when the epidemic phase constructs of "concentrated" and "generalized" HIV epidemics were assigned HIV prevalence thresholds [15]. Epidemics were classified based on whether HIV prevalence exceeded 1% in the general population [15,39,40]. If overall HIV prevalence remained below 1% while HIV burden exceeded 5% in a KP, the epidemic was deemed concentrated and focused HIV strategies recommended [15,39,40]. If HIV prevalence surpassed 1% in the general population, the epidemic was generalized and HIV efforts were to reach all segments of society [15,39,40]. The numerical proxy approach was originally developed to guide HIV surveillance [15], however, in practice often guided resource allocation and programmatic design [39,40].

Overall HIV prevalence in 39 SSA countries exceeds 1%, with considerable variability as defined by the numerical proxy within countries [41]. A limitation of the approach is that 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 mathematical modeling studies of SSA regions with >1% HIV prevalence such as in Cotonou, Benin and across Kenya, suggest that unprotected sex work can be an important risk for onward HIV transmission [9,13,23,28] and challenge the assumption that sex work is not important in these epidemics.

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

Allocation of resources is also informed by estimates of the relative burden of new annual HIV infections acquired in different

Table 1
Frameworks for characterizing the role of sex work* in HIV epidemics, and the implications for HIV programs

Framework	Definition	Assumption	Pros	Cons	Implications for designing HIV programs
Generalized HIV epidemic (numerical proxy)	Region where HIV prevalence is currently >1% in the general population (usually measured via antenatal clinic surveillance) [15]	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 1 y	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 (e.g., sex work and sharing needles) in same subgroup	Could lead us to underestimate the importance of focused HIV programs for FSWs/clients
Classical PAF	Fraction of prevalent or incident HIV infections that occur in FSWs (or clients) relative to non-FSWs and nonclients	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 (e.g., sex work and sharing needles) in same subgroup	Could lead us to underestimate the importance of focused HIV programs 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 behavior	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.
"Generalized" HIV epidemic based on underlying transmission dynamics	Region where sex work (or other well-defined high-risk behaviors such as injecting drug use, etc.*) 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 behaviors) 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 (e.g., 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 behaviors) 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 behaviors 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 behaviors) 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).
* The focus of this article is on sex work; but behaviors could include those relevant within other key populations (e.g., injecting drug use).

risk such as those obtained from the UNAIDS HIV MOT model [16,29], or the classic PAF on HIV prevalence or incidence [17–19,42]. The current MOT model uses data on HIV prevalence across risk groups, population size estimates of different risk groups including KPs and clients, and sexual behaviors such as number of sexual partners [43]. The classic PAF is estimated using point prevalence or within-population incidence data, as well as estimates of the size of different risk groups.

Half of the 39 SSA countries with generalized epidemics have estimated the fraction of annual new HIV infections acquired by FSWs and/or clients using the MOT [29,30], whereas the classical PAF of sex work on prevalent HIV infections in men and women has

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

System	Approach	Number of generalized HIV epidemics in SSA with recent data, of 39 countries (y)	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 y	FSWs: 2.0 (0.1, 13.7) Clients: 7.0 (0.46, 25.6)	Underestimates the transmission PAF in the medium to long term [28]	UNAIDS Country Reports 2012; Systematic Reviews [29,30]
Intermittent surveillance and research	Based on the relative risk of HIV compared to nonclient men	25	Classic PAF of sex work on prevalent HIV infections, men	2.0 (0.0, 88.0)	Underestimates the transmission PAF in the medium to long term	Systematic reviews [31]
	Based on the relative risk of HIV compared to general population women	27	Classic PAF of sex work on prevalent HIV infections, women	6.5 (0.4, 71.2)	Underestimates the transmission PAF in the medium to long term	Systematic Reviews [2,21]
	Dynamic mathematical models	3	Transmission PAF over 20 y	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 [31]

been estimated in 25 and 27 countries, respectively [2,31]. These measures often suggest a small role for sex work in current generalized HIV epidemics (Table 2) but have been shown to underestimate the medium- to long-term contribution of sex work [28,31]. Both approaches ignore a central feature of HIV spread: the propagation of HIV infections via onward HIV transmission (Table 1). Onward transmission refers to the chain of transmission from a single (direct) transmission during 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 the chain of transmission.

Emerging approaches: the "transmission" PAF and redefining HIV epidemic typology by behavioral epidemic drivers

The implications of underestimating the contribution of sex work to HIV spread are important because they can lead to misallocation of resources. From a program perspective, we may erroneously assume that because few infections arise among FSWs and/or clients, there is little to gain from targeted efforts. Two emerging frameworks may address the limitations of the traditional approaches by accounting for behaviors which potentiate HIV epidemics.

The T-PAF of sex work accounts for transmission chains over time—the extent to which the cumulative number of new HIV infections are due—directly or indirectly—to unprotected sex work [9,22,24,25,28,31]. 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 interventions and protect all FSWs and clients from HIV during sex work. It provides information on the potential impact on the total or wider population of a "perfect" intervention for FSWs and clients, without changes in the sexual network or displacement of sex acts As a 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. Dynamic models are used to predict cumulative infections with and without transmission within commercial sex [9,24,25,28]. Like the numerical proxy, MOT, and classic PAF, the T-PAF depends on inputs from the best available empiric data. Other counterfactuals to describe the influence of sex work itself may include displacement of sex acts or changes in the sexual network but are distinguished from the T-PAF.

To date, the T-PAF over different time periods has been estimated for three SSA countries; Benin, Burkina Faso, and Kenya [13,23,28,44]. Estimates of the long-term T-PAF in each suggest that even in the presence of sustained existing FSW interventions and medium to high levels of condom use, 13.5%–37.6% of all new HIV infections over the next 20 years could be due directly and indirectly to sex work [13,31,44]. Without FSW interventions, this figure of new infections attributable to sex work is estimated to be 58.3%–88.9% over the same time period [13,31,44]. Direct comparisons of the MOT estimates and classic PAF with the T-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 T-PAF of sex work in the short term (1 year) but the former are much smaller in the medium to long term [28,31]. This discrepancy occurs because the T-PAF captures onward transmission. Onward transmission is particularly important with behavioral epidemic drivers such as unprotected sex work associated with high frequency of sexual partnerships and mixing between risk groups [32]. A systematic review of dynamic mathematical modeling studies summarized the potential impact of sex work interventions on onward transmission within the wider community in SSA (Table 3) [13,23,45,56]—that is, HIV in the overall population and beyond FSWs and their clients. Most models were calibrated to observed HIV prevalence in FSWs [13,23,28,56]. They suggest that across a range of interventions, focused FSW programming could avert up to 85% of new HIV infections in the total population over 15 years [9] and reduce HIV incidence by up to 35% over 10 years in the general population [51]. Reaching clients could also provide large incremental benefits [47].

Finally, there has been growing momentum to redefine HIV epidemics on the basis of their underlying transmission dynamics—and the role of FSW and/or clients in the emergence and persistence of HIV spread [19,20,26–28]. In this new classification system, HIV epidemics are classified as "generalized" if they are entirely driven by non-KP sexual networks and "mixed" if epidemic control requires preventing transmission within KP and non-KP networks

Table 3
Potential impact of FSW/client interventions on overall HIV transmission in Sub-Saharan Africa [45]

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*				Time horizon
				HIV incidence†	HIV prevalence†	No. of HIV infections averted	PF	Years
Botswana								
Nagelkerke [46]	30%	N/A	Condom use (100%, 75%, FSW)		27%↓‡			30
Nagelkerke [46]	30%	N/A	Antiretroviral treatment (100%, 50%, FSW)		13%↓‡			30
Vissers [47]	33%‡	N/A	Oral pre-exposure prophylaxis (90%, 75%, FSW)			251 per 100,000 uninfected person-years‡		10
Vissers [47]	33%‡	N/A	Oral pre-exposure prophylaxis (90%, 75%, FSW and clients)			785 per 100,000 uninfected person-years‡		10
South Africa								
Vickerman [48]	30%§	60%	Vaginal microbicide (40%, 75%, FSW)	1%↓‡			1.3%‡	4
Vickerman [49]	27%‖	62%	↑ Condom use (100%,20%) & STI treatment (100%, 20%, FSW)	2%↓‡		53–65 per 100,000 adults‡		1
Vickerman [49]	27%‖	62%	↑ Condom use (100%, 20%) and STI treatment (100%, 100%, FSW)	14%↓‡				1
Vickerman [49]	27%‖	62%	↑ Condom use (100%, 20%) and STI treatment (100%, 100%, FSW and clients)	28%↓‡				1
Johnson [50]	26%‡	N/A	HIV vaccine (30%, 60%, FSW)			0.4–2.4 per 100 FSWs vaccinated‡		10
Zimbabwe								
Hallett [51]	22%	N/A	Condom use (100%, 80–100, FSW) & STI treatment (100%,10%, FSW)	10%↓‡				5
Hallett [51]	22%‡	N/A	Condom use (100%, 80–100, FSW) and STI treatment (100%, 10%, FSW)	35%↓‡				10
Kenya								
Vissers [47]	16%‡	N/A	Oral pre-exposure prophylaxis (90%, 75%, FSW)			166 per 100,000 uninfected person-years‡		10
Vissers [47]	16%‡	N/A	Oral pre-exposure prophylaxis (90%, 75%, FSW and clients)			733 per 100,000 uninfected person-years		10
Decker [52]	6%	33.8%	↓ Prevalence of sexual violence from baseline 32% to 2.4%			53,200‡	12%‡	5
Wirtz [53,54]	6%	33.8%	100% FSW community empowerment from 5%; leads to ↑ consistent condom use by 51%			16,661–20,680	6%‡	5
Steen [23]	24%‡	45%	↑ Condom use (85%, 100%, FSW)	63%↓‡	46%↓‡			20
Benin								
Boily [9]	1%‡	53%	↑ Condom use (100%,60%, FSW) and STI treatment (100%, 50%, FSW)	19%↓‖			58%–85%	10
Vickerman [55]	3%‡	55%	↑ Condom use (100%, 81%, FSW)	21.5%↓ (17.7–24.9)‡				4
Vickerman [55]	3%‡	55%	STI testing and treatment (80%, 85%, FSW)				10% (6–12)‡	4
Vickerman [48]	3.3%§	49%	Vaginal microbicide (40%,75%, FSW)	26%↓‡			24.8%	4
Williams [13]	3.0%‡	55%	↑ Condom use (100%, 87.7%, FSW)				33% (20–46)	15

GP = general population; N/A = not available from the study; PF = prevented fraction, the % of HIV infections averted.
Systematic review of mathematical modeling studies (updated January 2014) generated from the peer-reviewed literature [31,45]. Studies were included if they used dynamical models of heterosexual HIV transmission, incorporated behavioral heterogeneity in risk, and provided at least one of the following primary estimates in the wider community: (1) the population attributable fraction (PAF) of HIV infections due to sexual partnerships within high-risk groups or (2) the number per capita or fraction of HIV infections averted, or change in HIV prevalence and/or incidence due to focused interventions.
* Range, uncertainty bounds, or 95% credible intervals from multiple simulations or epidemic realizations are shown in brackets.
† Relative change in HIV incidence or prevalence.
‡ Total population (i.e., including FSWs and clients).
§ Antenatal clinic surveillance.
‖ General population females (i.e., excluding FSWs).

Table 4
FSW/client data needs in generalized HIV epidemics

Data needs	System	Approach	Quantify role of sex work in local HIV epidemic	HIV program-related objectives	
			Transmission PAF and/or redefine HIV epidemic types	Design/adapt HIV programs	Monitor HIV program reach and epidemic impact
Define FSW/clients	Routine surveillance	Consensus and based on feasibility for programs; and epidemiological risk (client numbers) Research on sensitivity and specificity of various definitions (on HIV acquisition)	√		√
FSW/client population size	Routine surveillance	Feasible non–survey-based methods Triangulate multiple size estimation approaches where possible	√	√	√
HIV acquisition risks					
Individual level	Intermittent surveillance	Representatively sampled biobehavioral surveys of FSWs/clients Enhanced programmatic routine data collection	√	√	
Structural level	Research	Enhanced programmatic routine data collection		√	
HIV transmission networks					
Sexual partnerships and networks	Intermittent surveillance	Representatively sampled behavioral surveys of FSWs/clients Sexual network surveys Phylogenetic analyses of HIV sequence data (requires FSW, client, and general population HIV sequencing)	√	√	
Other HIV transmission networks (casual sex, men who have sex with men, and infecting drug use)	Intermittent surveillance	As mentioned previously (and including other networks with phylogenetic analyses)	√	√	
Reproductive health data	Intermittent surveillance	Representatively sampled behavioral surveys of FSWs	√ (to include parent to child transmission in transmission PAF estimates)	√	√
		Reproductive health Program data			
Baseline HIV interventions					
Condom use	Routine surveillance	Representatively sampled behavioral surveys of FSWs/clients FSW program data	√	√	√
HIV treatment and care continuum	Routine surveillance	Representatively sampled behavioral surveys of FSWs/clients FSW and antiretroviral treatment program data	√	√	√
Structural (including community-based programs)	Research	Situational assessment of laws	*	√	√
		Gender-based violence program data	*		

The check marks (√) 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.

(preventing infections among KP are insufficient to control the epidemic, and likewise if only preventing infections among non-KP networks). A growing number of countries are adopting this new nomenclature—particularly the use of the term “mixed” epidemic [19,57]. In practice, this redefinition of epidemic types remains dependent on testing via dynamic mathematical models [28].

Existing data available for the transmission PAF, redefining HIV epidemics, and informing the design of sex work programs across SSA

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 need overlap with the programmatic needs to inform the content and scale of sex work programs (Table 4). Recent reviews shed light on the current FSW and/or client data landscape, how data are being collected, where, and limitations of the data (Table 5). Stigma and criminalization can pose barriers to data collection; working with FSW communities in the design and implementation of surveillance and research tools can help ensure data collection is

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

System	Estimate	Approach	Number of generalized HIV epidemics in SSA with recent data, of 39 countries (years)	Median values (range)	Concerns/Issues	Sources
HIV burden						
Routine surveillance	HIV prevalence, FSWs	Household demographic health surveys* of adult women	1 (2002–2013)	—	Social desirability bias	UNAIDS Country Reports 2012
		FSW biobehavioral surveys	23 (2002–2013)	23.1% (7.2–70.7)	Sampling frames often not based on presampling enumeration; adjusting estimate based on sampling design	UNAIDS Country Reports 2012; Systematic reviews
	HIV prevalence, clients	Household demographic health surveys* of adult men	23 (2002–2013)	4.7% (0.43–32.0)	Social desirability bias	UNAIDS Country Reports 2012
Intermittent surveillance and research	HIV prevalence, FSWs	Program or clinic-based, intervention trials; FSW biobehavioral surveys	21 (2002–2013)	22.8% (0.9–69.8)	Sampling frames often not based on presampling enumeration; adjusting estimate based on sampling design; definition of sex work varies	Systematic reviews [2,31,58]
	HIV incidence, FSWs	Program-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 [31,59]
	HIV prevalence, clients	Client biobehavioral surveys	8 (2002–2013)	2.9% (0.42–6.8)	All convenience samples	Systematic reviews [31]
	HIV incidence, clients	None	None	—	—	Systematic reviews [31]
Population at risk (FSW, client population size)						
Intermittent surveillance and research	FSW population size; % of adult women engaged in sex work	Several enumeration methods	23 (2002–2013)	1.8% (range, 0.25%–11.5%)	Each enumeration approach has pros and cons [60]; 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 [31,61]
	Client population size; % of adult men engaged in sex work	Household demographic health surveys* or general population surveys of adult men	32 (2002–2013)	3.0% (range, 0.025%–19.8%)	Estimates from general population surveys subject to social desirability bias	Systematic reviews [31,62]
	Client population size; % of adult men engaged in sex work	Indirect method by triangulating FSW population size, and FSW/client behavioral survey data	2 (2002–2013)	7.2%–30.0%	Requires FSW data and behavioral data on clients	Systematic reviews [31]
Examples of HIV risk factors and characteristics of sex work						
Intermittent surveillance and research	Duration engaged in sex work	Behavioral surveys and program-based cohorts	5 (1987–2011)	FSWs: 5.5 y (range, 0.6–6.0) Clients: 4.6–5.2 y	Cross-sectional and censured data; no incidence of sex work cessation rate data; no re-entry into sex work	Systematic Reviews [63,64]
	Sexual partnership types and periodicity of sexual acts by partner	Behavioral surveys and program-based cohorts			Often does not differentiate between regular clients, new clients, and nonpaying partners	
	% of FSWs reporting condom use with last client	Behavioral surveys in major cities	10 (2012)	91% (32–98)	Not part of routine surveillance	UNAIDS Epidemic Update 2013
	Active syphilis prevalence	Biobehavioral surveys in major cities	10 (2010)	2.4% (0–19.6)	Not part of routine surveillance	UNAIDS Epidemic Update 2011

(*continued on next page*)

Table 5 (*continued*)

System	Estimate	Approach	Number of generalized HIV epidemics in SSA with recent data, of 39 countries (years)	Median values (range)	Concerns/Issues	Sources
	Unprotected anal sex (ever)	Behavioral surveys and program-based cohorts	7 (1985–2011)	0.0%–80.0%	Very little data on frequency of unprotected anal sex	Systematic Review [65]
HIV engagement, prevention, and care continuum						
Routine surveillance	% of FSWs who know where to access HIV testing AND received condoms in last 12 mo	Behavioral 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 and enumeration	UNAIDS Country Reports 2012
	HIV programs 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	Behavioral surveys	1 (2014)	aOR 2.39 (1.36–4.02) for increased condom use	Complex study designs needed because benefits are mediated by increased condom use during commercial sex	Systematic Reviews [66]
	Structural interventions	Program-based cohorts, mathematical models	1 (2014)	Avert 17% (1–31) of incident infections in Kenya over 10 y	Effects are mediated over long	Mathematical Model [67]
	HIV testing (tested for HIV in last 1 y and received results), FSWs	Behavioral surveys in major cities; program-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 nonrepresentative sampling	UNAIDS Country Reports 2012 [32]
	Duration in sex work when registered in FSW programs	Behavioral surveys and program-based cohorts	11 (1987–2013)	2.6 y (0.7–5.1)	Reflects time to reach FSWs after entering sex work; selection bias and nonrepresentative sampling	Systematic Reviews [7,68]
	Age when registered in FSW programs	Behavioral surveys and program-based cohorts	8 (1987–2013)	26.8 y (24–31.5)	Reflects time to reach FSWs after entering sex work; selection bias	Systematic Reviews [7,68]
	ART coverage and HIV care continuum among HIV-infected FSW	Research cohorts and 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 [69]
Impact of FSW/client intervention on wider community						
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	[70]
	Various interventions	Dynamic mathematical modeling 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 [13,23,45]

ART = antiretroviral treatment.

* Country-wide, household-based, face-to-face interviews.

rights based, appropriate, and reflects the diversity of the population.

Epidemiologically and programmatically meaningful definitions of sex work

Clear definitions of sex work are needed to (1) ensure FSW and/or client interventions are reaching them and (2) design intervention packages that meet their needs [8,71–74]. There is no current consensus on the surveillance definition of sex work. Some define sex work as any exchange of sex for money, favors, or goods [75]. Others limit definitions to only the exchange of money, large client volumes, self-identification, or reference to sexual partners as FSW and/or client, when money was negotiated [71,76–78]. Terms such as informal, part-time, clandestine, or transactional sex permeate the discourse yet their distinction from formal, high-volume sex work, remains unclear [73,76,77,79]. It is important to distinguish sex work within this spectrum even if individuals engage in more than one type or transition between types [80].

Formal sex work with large client volumes in highly connected and high-risk sexual networks has different implications for HIV spread than casual, or long-term, concurrent partnerships that may be financially motivated [81]. Without clear definitions of sex work, T-PAF analyses to estimate the contribution of sex work to HIV epidemics may use conflated FSW and/or client size estimations, risk behaviors, and HIV burdens, thereby underestimating or overestimating the role of sex work—and limit all approaches, including dynamic modeling. Client volume and percent income from sex work has been associated with HIV in a number of generalized HIV epidemics ranging from Nigeria to Swaziland [82,83]. Thus, we suggest a strategy that defines sex work based on client numbers and on a pragmatic basis for focused HIV prevention efforts.

Population size estimation of FSWs and their clients

Size estimates and the duration of sex work are central to understanding the contribution of sex work to HIV epidemics. Every framework (Table 1) needs this information—as direct inputs into mathematical models or as the bases for representative sampling for biobehavioral surveys. Size 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 [84,85].

FSW and/or client population size estimation are not routinely collected as part of traditional HIV surveillance. However, guidelines on different approaches exist, and several countries have started to enumerate FSWs [60,85]. Size estimation methods include network-size analyses of respondent-driven sampling surveys and multistaged key informant and geographic mapping and enumeration of KP hotspots [84–86]. Geographic mapping with enumeration has the added benefit of providing program "catchment areas" for better intervention delivery [87,88]. 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 [31], whereas estimates of client population size range widely from a median of 3% using direct surveys methods to 7%–30% using indirect methods [31]. The indirect method of client population size estimation was first described by 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 clients [18]. These indirect SSA size estimates are similar to those reported in concentrated HIV epidemics characteristic of India [20]. The indirect method requires FSW-specific and client-specific behavioral surveys and FSW size estimations; absence of client surveys has been the limiting factor for estimating client population size. Although the value of size estimation cannot be overstated, it is important to note that a number of biases limit each size estimation method for KPs [60,84], and the indirect method for client size estimation depends on several data from FSW and client-specific surveys. Where possible, triangulating estimates from different methods may be helpful [84].

Size estimations are often conducted once and rarely repeated using the same approach. Thus, the stability or temporal dynamics of FSW and/or client size (relative to the general population) remains unknown. Rates of entry and exit from engaging in sex work ("turn over") and thus, duration in sex work, may be important when estimating downstream HIV transmission from unprotected sex work [63] during the career-span of FSW or after retiring from sex work [89]. Sex work population dynamics and how it may influence the T-PAF remain unexplored.

Representative estimates of relative HIV burden

Representative estimates of HIV prevalence, incidence, and, potentially, superinfection data among FSW and clients can be used to estimate the role of sex work in HIV epidemics (Table 1) [90]. Obtaining unbiased empirical estimates of HIV incidence is challenging, so most dynamic mathematical models will use HIV prevalence data to support model calibration. Optimal estimates can help allocate for HIV care, further risk-stratify FSW and clients, and monitor program impacts.

FSWs and/or client HIV prevalence data in generalized HIV epidemics come from household surveys such as the Demographic Health Surveys, and from FSW and/or client-biobehavioral surveys. General population surveys are limited by willingness to report sex work [91]. Household surveys also tend to undersample mobile or migrant populations, including truckers, miners, fisher-folk, and refugees, who may be more likely to be clients or SWs [92,93]. Although some of these biases are addressed with direct surveys of FSWs and clients, participants in these studies may not be representative of the underlying FSW and/or client population. For example, two-thirds of FSW HIV data in generalized epidemics of SSA come from convenience sampling of sexually transmitted infection clinics or FSW venues [31]. Despite these limitations, the available data suggest 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. Three recent systematic reviews of HIV among FSW in the generalized epidemics of SSA suggest a 9- to 14-fold greater HIV burden compared to all women of reproductive age [2,31,58]. Meanwhile, client-specific studies across six SSA countries suggest a four-fold greater odds of HIV prevalence among self-reported male clients compared to nonclient males [17,19,31,94,95].

Thus, the next phase in HIV surveillance in generalized HIV epidemics should include FSW and client HIV prevalence estimates. Where possible, HIV prevalence estimates should be obtained via representative sampling [96] using presampling size estimations or venue assessments to inform sampling frames [60]. Where size estimations are not possible, using respondent-driven sampling as a chain-referral strategy may support the calculation of less biased estimates of HIV burdens [97].

HIV acquisition and transmission risks and protective behaviors among FSW/clients

Dynamic models of HIV epidemics that include sex work need to parameterize the heterogeneity in HIV acquisition and transmission risk associated with sex work to capture the "mechanistic" processes that underpin transmission events. There is an extensive body of literature that outlines the proximal and distal determinants of HIV acquisition among FSWs and clients [66,72,98]. Proximal determinants include differential patterns of condom use by partner type (regular, new, and nonpaying), numbers of partners, frequency of sexual acts by partners and type of sex (vaginal vs. anal), concomitant sexually transmitted infections, anal and vaginal douching, and use of drying agents and spermicides [99–101]. Proximal determinants are important for estimating the T-PAF and redefining HIV epidemics on the basis of behavioral drivers, whereas proximal and distal factors such as laws, policies, or health-system factors are each critical to the design of HIV programs.

Currently, the only FSW risk-factor data routinely requested and reported in the UNAIDS country reports is condom use at last sex [102]. Most studies on HIV factors among FSWs have focused on assessing individual, proximal risks. Yet distal factors are increasingly recognized as predictors of HIV acquisition and for the coverage of services for FSWs [98,103,104]. In Swaziland, there were significant relationships between increased measures of social capital and condom use and uptake of HIV testing in FSWs [105]. Recent modeling 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 practices [67].

Taken together, these findings suggest the utility of comprehensive risk assessments—and causal pathways of HIV risk and/or protective behaviors—when characterizing HIV risks among FSW and/or clients. An understanding of proximal determinants is needed to reproduce HIV epidemics with dynamic models, and thus, estimate the T-PAF. Estimating the T-PAF of distal determinants requires a strong empirical basis for the full causal pathway. However, developing indicators to measure the full scope of structural and social factors and relating each to individual-level proximal determinants is a challenging and emerging area of research in dynamic modeling. Nonetheless, HIV programs are implemented within structural determinants such as human rights violations, criminalization, sexual and physical violence, condom accessibility, and perceived and experienced stigma and discrimination [98]. Programs need to address determinants along the full casual pathway to HIV acquisition and transmission during sex work.

Characterizing HIV transmission networks of FSWs, clients, and the wider community

Key to the T-PAF is data on how partnerships are formed within sex work and between FSW and/or clients and individuals not directly engaged in sex work, including those involved in other financially motivated partnerships, concurrent or serial multiple partnerships, and the "lower-risk" general population. To date, these have only included sexual partnerships—but can (and should) be extended to include other risks.

For the T-PAF, we usually infer "who has sex with whom" from available data by fitting these data to observed data on HIV prevalence and/or 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, and so forth, of sexual partners by the type of partnership or sexual network surveys [106]. Phylogenetic analyses using HIV sequence data have been used to infer networks among people who inject drugs and men who have sex with men [107–110] and are being explored to infer HIV transmission networks of FSW and/or clients and the wider community [108,111]. 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 influence the T-PAF. Early work on model comparison suggests that deterministic models with assumptions of instantaneous partnerships may overestimate the role of long-term partnerships in transmission compared with network models with explicit partnership duration [112].

Characterizing sexual networks includes the different contexts within which sex work takes place, such as short-term migration [25], and how networks (or sexual mixing between risk groups) change over time. Intersections and overlaps with networks of people who use drugs, and casual sex networks, are also an emerging area of study [113,114]. If we do not account for 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 in SSA. FSWs are less likely to use condoms with nonpaying partners—with whom FSWs may choose to have children [115].

Program and biological data to characterize interventions and engagement in HIV prevention and treatment programs

Data on program-related protective factors for HIV acquisition and transmission—such as condom use, voluntary male circumcision among clients, and HIV viral suppression among FSW and/or clients on antiretroviral treatment are important to include when estimating the T-PAF, and when designing and monitoring HIV programs.

The only routinely collected indicators of FSW program reach include awareness of where to access HIV testing and receipt of condoms in the last 12 months [102]. These indicators were reported for 20 countries in the 2012 UNAIDS Country Progress Reports. A country median of 54.4% (range, 1.5%–89.9%) of FSWs surveyed reported knowledge of where to access HIV testing and receipt of condoms in the last 12 months. The indicators were based on convenience samples (18 from surveys), and only one had presampling enumeration; 28 countries did not report or have data on FSW coverage with denominators. The extent to which existing HIV prevention programs are reaching FSWs and clients and addressing their HIV risk remains highly questionable.

The remainder of the HIV continuum of care for FSWs (or clients) has not been monitored as part of the UNAIDS country reports. Although there are a few studies of the HIV care cascade among FSWs [69,116], the data are limited to FSWs who meet study-specific eligibility criteria and agree to participate. Thus, existing HIV care data are likely not representative of the underlying FSW populations [69,116]. Continuum of care data could help estimate the additional antiretroviral treatment needs of FSW [117,118]. Monitoring of primary and secondary emergence of HIV drug resistance could be important in populations at highest risk, such as FSWs in generalized HIV epidemics—as has been done with "sentinel" surveillance of drug-resistant gonorrhea in industrialized settings [119].

Conclusions

There is growing empiric and model-based evidence for helping decide whether, how much, and how to focus on sex work in generalized HIV epidemics. A small, but growing, body of model-based evidence of the T-PAF and sex work interventions demonstrate the large 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 understanding of the role of sex work. Understanding could be improved by investing in the collection of specific data, by making the best use of these data, and with appropriate methods of estimating the role of sex work in HIV epidemics. To move forward, the HIV scientific 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.

Acknowledgments

The authors thank Branwen Owen (Imperial College London) for providing data. The authors thank members of the KEYPOP partnership hosted at Imperial College for informing the development of this article. S.Mi. is supported by a Canadian Institutes of Health Research and Ontario HIV Treatment Network New Investigator Award, and the research is supported by a Canadian Institutes of Health Research (FDN 143266). C.B. and S.D.B. receive support from the Johns Hopkins University Center for AIDS Research, an NIH funded program (P30AI094189), which is supported by the following NIH cofunding and participating institutes and centers: NIAID, NCI, NICHD, NHLBI, NIDA, NIMH, NIA, FIC, NIGMS, NIDDK, and OAR. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

S.D.B. conceived of the article and provided leadership throughout the review and writing. S.Mi. and S.D.B wrote the article. S.Mi. conducted the data syntheses. S.D.B., S.Mi., M.C.B., S.S., J.F.B., and S.M. developed and designed the article and provided critical intellectual input, ideas, edits, data synthesis, and writing. All authors contributed significantly to the ideas expressed in the article and edited the article.

References

[1] Beyrer C, Baral SD, van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL, et al. Global epidemiology of HIV infection in men who have sex with men. Lancet 2012;380:367–77.
[2] Baral S, Beyrer C, Muessig K, Poteat T, Wirtz AL, Decker MR, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infect Dis 2012;12:538–49.
[3] Strathdee S, Hallett TB, Bobrova N, Rhodes T, Booth R, Abdool R, et al. HIV and the risk environment among people who inject drugs: past, present, and projections for the future. Lancet 2010;376:268–84.
[4] UNAIDS. WHO, guidelines for second generation HIV surveillance. Geneva: WHO; 2000.
[5] National AIDS Spending Assessment (NASA) reports. 2013. Available at: http://www.unaids.org/en/dataanalysis/knowyourresponse/nasacountryreports.
[6] Baral SD, Grosso A, Holland C, Papworth E. The epidemiology of HIV among men who have sex with men in countries with generalized HIV epidemics. Curr Opin HIV AIDS 2014;9:156–67.
[7] Chersich MF, Luchters S, Ntaganira I, Gerbase A, Lo YR, Scorgie F, et al. Priority interventions to reduce HIV transmission in sex work settings in sub-Saharan Africa and delivery of these services. J Int AIDS Soc 2013;16:17980.
[8] Baral S, Mafuya NP. Rewriting the narrative of the epidemiology of HIV in Sub-Saharan Africa. SAHARA J 2012;9:127–30.
[9] Boily MC, Lowndes C, Alary M. The impact of HIV epidemic phases on the effectiveness of core group interventions: insights from mathematical models. Sex Transm Infect 2002;78:I78–90.
[10] Behanzin L, Diabate S, Minani I, Boily MC, Labbe AC, Ahoussinou C, et al. Decline in the prevalence of HIV and sexually transmitted infections among female sex workers in Benin over 15 years of targeted interventions. J Acquir Immune Defic Syndr 2013;63:126–34.
[11] Behanzin L, Buve A, Lowndes CM, Zannou DM, Minani I, Anagonou S, et al. Decline in HIV prevalence among young people in the general population of Cotonou, Benin, 1998-2008. Sex Transm Infect 2011;87:A46.
[12] Behanzin L, Diabate S, Minani I, Lowndes CM, Boily MC, Labbe AC, et al. Decline in HIV prevalence among young men in the general population of Cotonou, Benin, 1998-2008. PLoS One 2012;7:e43818.
[13] Williams J, Alary M, Lowndes C, Buve A, Béhanzin L, Labbé AC, et al. Positive impact of increases in condom use among female sex workers and clients in a medium HIV prevalence epidemic: modelling results from project SIDA-1/2/3 in Cotonou, Benin. PLoS One 2014;9:e102643.
[14] Aral SO, Cates W. Coverage, context and targeted prevention: optimising our impact. Sex Transm Infect 2013;89:336–8.
[15] UNAIDS/WHO Working Group On Global HIV/AIDS and STI Surveillance. Guidelines for second generation HIV surveillance. Geneva: World Health Organization and Joint United Nations Programme on HIV/AIDS; 2000.
[16] Gouws E, White PJ, Stover J, Brown T. Short term estimates of adult HIV incidence by mode of transmission: Kenya and Thailand as examples. Sex Transm Infect 2006;82:iii51–5.
[17] Sobéla F, Pépin J, Gbéléou S, Banla AK, Pitche VP, Adom W, et al. A tale of two countries: HIV among core groups in Togo. J Acquir Immune Defic Syndr 2009;51:216–23.
[18] Cote AM, Sobela F, Dzokoto A, Nzambi K, Asamoah-Adu C, Labbe AC, et al. Transactional sex is the driving force in the dynamics of HIV in Accra, Ghana. AIDS 2004;18:917–25.
[19] Lowndes C, Alary M, Belleau M, Bosu K, Kintin D, Nnorom J, et al. West Africa HIV/AIDS epidemiology and response synthesis: implications for prevention. Global AIDS Monitoring and Evaluation Team (GAMET); 2008. The World Bank. Available at: http://gametlibrary.worldbank.org/.
[20] Mishra S, Sgaier SK, Thompson LH, Moses S, Ramesh BM, Alary M, et al. HIV epidemic appraisals for assisting in the design of effective prevention programmes: shifting the paradigm back to basics. PLoS One 2012;7:e32324.
[21] Prüss-Ustün A, Wolf J, Driscoll T, Degenhardt L, Neira M, Calleja JMG. HIV due to female sex work: regional and global estimates. PLoS ONE 2013;8:e63476.
[22] Vickerman P, Foss AM, Pickles M, Deering K, Verma S, Eric D, et al. To what extent is the HIV epidemic in southern India driven by commercial sex? A modelling analysis. AIDS 2010;24:2563–72.
[23] Steen R, Hontelez JA, Veraart A, White RG, de Vlas SJ. Looking upstream to prevent HIV transmission: can interventions with sex workers alter the course of HIV epidemics in Africa as they did in Asia? AIDS 2014;28:891–9.
[24] Mishra S, Pickles M, Blanchard J, Moses S, Boily M. Distinguishing the source of HIV transmission from the distribution of newly acquired HIV infections: why is it important for HIV prevention programming? Sex Transm Infect 2014;90:19–25.
[25] Deering KN, Vickerman P, Moses S, Ramesh BA, Blanchard JF, Boily MC. The impact of out-migrants and out-migration on the HIV/AIDS epidemic: a case study from south-west India. AIDS 2008;22 Suppl 5:S165–81.
[26] Wilson D, Halperin DT. “Know your epidemic, know your response”: a useful approach, if we get it right. Lancet 2008;372:423–6.
[27] Moses S, Blanchard JF, Kang H, Emmanuel F, Reza Paul S, Becker ML, et al. AIDS in South Asia: understanding and responding to a heterogenous epidemic. Washington: The World Bank; 2006.
[28] Mishra S, Pickles M, Blanchard J, Moses S, Shubber Z, Boily M. Validation of the modes of transmission model as a tool to guide HIV prevention: a comparative modeling study. PLoS One 2014;9:e101690.
[29] Gouws E, Cuchi P. Focusing the HIV response through estimating the major modes of HIV transmission: a multi-country analysis. Sex Transm Infect 2012;88:i76–85.
[30] Shubber Z, Mishra S, Vesga J, Boily MC. The HIV modes of transmission model: a systematic review of its findings and adherence to guidelines. J Int AIDS Soc 2014;17:18928.
[31] Mishra S. Using mathematical models to characterise HIV epidemics for the design of HIV prevention strategies. London, England: School of Public Health, Imperial College; 2014. Available at: https://spiral.imperial.ac.uk/handle/10044/1/24913.
[32] Yorke JA, Hethcote HW, Nold A. Dynamics and control of transmission of gonorrhea. Sex Transm Dis 1978;5:51–6.
[33] Wasserheit JN, Aral SO. The dynamic topology of sexually transmitted disease epidemics: implications for prevention strategies. J Infect Dis 1996;174:S201–13.
[34] Anderson RM, May RM, Boily MC, Garnett GP, Rowley JT. The spread of HIV-1 in Africa: sexual contact patterns and the predicted demographic impact of AIDS. Nature 1991;352:581–9.
[35] Thomas JC, Tucker MJ. The development and use of the concept of a sexually transmitted disease core. J Infect Dis 1996;174:S134–43.
[36] Brunham RC. Core group theory: a central concept in STD epidemiology. Venereology 1997;10:34–5.
[37] Blanchard JF. Populations, pathogens, and epidemic phases: closing the gap between theory and practice in the prevention of sexually transmitted diseases. Sex Transm Infect 2002;78:I183–8.
[38] Anderson R, May R. Infectious diseases of humans: dynamics and control. Oxford, UK: Oxford University Press; 1991.
[39] UNAIDS. HIV Prevention Toolkit. 2008. Available at: http://hivpreventiontoolkit.unaids.org/.
[40] Wilson D, Challa S. HIV epidemiology: recent trends and lessons. In: Lule E, Seifman R, David A, editors. The changing HIV/AIDS landscape: selected papers for the World Bank's agenda for action in Africa, 2007-2011. Washington, DC: World Bank; 2002.
[41] UNAIDS. Report on the global AIDS epidemic. Geneva. 2013. Available at: http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport.
[42] Alary M, Lowndes CM. The central role of clients of female sex workers in the dynamics of heterosexual HIV transmission in sub-Saharan Africa. AIDS 2004;18:945–7.
[43] UNAIDS. Modelling the expected short-term distribution of incidence of HIV infections by exposure group. The Joint United Nations Programme on HIV/AIDS. Geneva. 2012.
[44] Low A, Nagot N, Canci F, Konate I, Weiss H, Meda N, et al. Potential impact of existing interventions and of antiretroviral use in female sex workers on transmission of HIV in Burkina Faso: a modeling study. J Acquir Immune Defic Syndr 2015;68(Suppl 2):S180–8.

[45] Mishra S, Steen R, Gerbase A, Lo YR, Boily MC. Impact of high-risk sex and focused interventions in heterosexual HIV epidemics: a systematic review of mathematical models. PLoS One 2012;7:e50691.
[46] Nagelkerke N, Jha P, De Vlas S, Korenromp E, Moses S, Blanchard J, et al. Modelling HIV/AIDS epidemics in Botswana and India: Impact of interventions to prevent transmission. Bull World Health Organ 2002;80:89–96.
[47] Vissers DC, Voeten HA, Nagelkerke NJ, Habbema JD, de Vlas SJ. The impact of pre-exposure prophylaxis (PrEP) on HIV epidemics in Africa and India: a simulation study. PLoS One 2008;3:e2077.
[48] Vickerman P, Watts C, Delany S, Alary M, Rees H, Heise L. The importance of context: model projections on how microbicide impact could be affected by the underlying epidemiologic and behavioral situation in 2 African settings. Sex Transm Dis 2006;33:397–405.
[49] Vickerman P, Terris-Prestholt F, Delany S, Kumaranayake L, Rees H, Watts C. Are targeted HIV prevention activities cost-effective in high prevalence settings? Results from a sexually transmitted infection treatment project for sex workers in Johannesburg, South Africa. Sex Transm Dis 2006;33:S122–32.
[50] Johnson LF, Bekker LG, Dorrington RE. HIV/AIDS vaccination in adolescents would be efficient and practical when vaccine supplies are limited. Vaccine 2007;25:7502–9.
[51] Hallett TB, Garnett GP, Mupamberiyi Z, Gregson S. Measuring effectiveness in community randomized trials of HIV prevention. Int J Epidemiol 2008;37:77–87.
[52] Decker MR, Wirtz AL, Pretorius C, Sherman SG, Sweat MD, Baral SD, et al. Estimating the impact of reducing violence against female sex workers on HIV epidemics in Kenya and Ukraine: a policy modeling exercise. Am J Reprod Immunol 2013;69 Suppl 1:122–32.
[53] Wirtz AL, Pretorius C, Beyrer C, Baral S, Decker MR, Sherman SG, et al. Epidemic impacts of a community empowerment intervention for HIV prevention among female sex workers in generalized and concentrated epidemics. PLoS One 2014;9(2):e88047.
[54] Kerrigan D, Wirtz A, Baral S, Decker M, Murray L, Poteat T, et al. The global HIV epidemics among sex workers. Washington, D.C: The World Bank; 2013.
[55] Vickerman P, Watts C, Peeling RW, Mabey D, Alary M. Modelling the cost effectiveness of rapid point of care diagnostic tests for the control of HIV and other sexually transmitted infections among female sex workers. Sex Transm Infect 2006;82:403–12.
[56] Anderson SJ, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. Lancet 2014;384:249–56.
[57] National AIDS Control Council. Kenya UNGASS country progress report 2012. The Joint United Nations Programme on HIV/AIDS. Geneva. 2013.
[58] Papworth E, Cessay N, An l, Thiam-Niangoin M, Ky-zerbo O, Holland C, et al. Epidemiology of HIV among female sex workers, their clients, men who have sex with men and people who inject drugs in West and Central Africa. J Int AIDS Soc 2013;16(Suppl 3):18751.
[59] Graham SM, Shah PS, Costa-Von Aesch Z, Beyene J, Bayoumi AM. A systematic review of the quality of trials evaluating biomedical HIV prevention interventions shows that many lack power. HIV Clin Trials 2009;10:413–31.
[60] UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Guidelines on estimating the size of populations most at risk of HIV. Geneva: World Health Organization, Dept of HIV/AIDS, UNAIDS; 2010.
[61] Vandepitte J, Lyerla R, Dallabetta G, Crabbe F, Alary M, Buve A. Estimates of the number of female sex workers in different regions of the world. Sex Transm Infect 2006;82 Suppl 3:18–25.
[62] Carael M, Slaymaker E, Lyerla R, Sarkar S. Clients of sex workers in different regions of the world: hard to count. Sex Transm Infect 2006;82 Suppl:iii26–33.
[63] Watts C, Zimmerman C, Foss AM, Hossain M, Cox A, Vickerman P. Remodelling core group theory: the role of sustaining populations in HIV transmission. Sex Transm Infect 2010;86 Suppl 3:iii85–92.
[64] Fazito E, Cuchi P, Mahy M, Brown T. Analysis of duration of risk behaviour for key populations: a literature review. Sex Transm Infect 2012;88:i24–32.
[65] Owen B, Brock P, Shubber Z, Butler A, Pickles M, Baggaley R, et al. Prevalence and frequency of anal intercourse among female sex workers: a systematic review and meta-analysis, In preparation. Branwen Owen: Personal communication; 2014.
[66] Baral S, Holland CE, Shannon K, Logie C, Semugoma P, Sithole B, et al. Enhancing benefits or increasing harms: community responses for HIV among men who have sex with men, transgender women, female sex workers, and people who inject drugs. J Acquir Immune Defic Syndr 2014;66 Suppl 3:S319–28.
[67] Shannon K, Strathdee SA, Goldenberg SM, Duff P, Mwangi P, Rusakova M, et al. Global epidemiology of HIV among female sex workers: influence of structural determinants. Lancet 2014;385:55–71.
[68] Scorgie F, Chersich MF, Ntaganira I, Gerbase A, Lule F, Lo YR. Socio-demographic characteristics and behavioral risk factors of female sex workers in sub-saharan africa: a systematic review. AIDS Behav 2012;16:920–33.
[69] Mountain E, Mishra S, Vickerman P, Pickles M, Gilks C, Boily MC. Systematic review and meta-analysis of antiretroviral therapy use, attrition, and outcomes among HIV-infected female sex workers. PLoS ONE 2014;9:e105645.
[70] Gregson S, Adamson S, Papaya S, Mundondo J, Nyamukapa CA, Mason PR, et al. Impact and process evaluation of integrated community and clinic-based HIV-1 control: A cluster-randomised trial in eastern Zimbabwe. PLoS Med 2007;4:e102.
[71] Dunkle KL, Jewkes RK, Brown HC, Gray GE, Mcintryre JA, Harlow SD. Transactional sex among women in Soweto, South Africa: prevalence, risk factors and association with HIV infection. Soc Sci Med 2004;59:1581–92.
[72] Baral S, Logie CH, Grosso A, Wirtz AL, Beyrer C. Modified social ecological model: a tool to guide the assessment of the risks and risk contexts of HIV epidemics. BMC Public Health 2013;13:482.
[73] Jewkes R, Morrell R, Sikweyiya Y, Dunkle K, Penn-Kekana L. Transactional relationships and sex with a woman in prostitution: prevalence and patterns in a representative sample of south african men. BMC Public Health 2012;12:325.
[74] Jewkes R, Dunkle K, Nduna M, Shai N. Transactional sex and HIV incidence in a cohort of young women in the stepping stones trial. J AIDS Clinic Res 2012;3:5.
[75] UNAIDS guidance note on HIV and sex work, Geneva 2009. The Joint United Nations Programme on HIV/AIDS,
[76] Robinson J, Yeh Y. Transactional sex as a response to risk in Western Kenya, Policy Research Working Paper 4857. Washington, DC: The World Bank; 2009.
[77] Cooper ML, Barber LL, Zhaoyang R, Talley AE. Motivational pursuits in the context of human sexual relationships. J Pers 2011;79:1333–68.
[78] Dunkle KL, Wingood GM, Camp CM, Diclemente RJ. Economically motivated relationships and transactional sex among unmarried African American and white women: results from a us national telephone survey. Public Health Rep 2010;125:90–100.
[79] Stoebenau K, Nair R, Rambeloson V, Rakotoarison P, Razafintsalama V, Labonté R. Consuming sex: the association between modern goods, lifestyles and sexual behaviour among youth in Madagascar. Global Health 2013;9:1–19.
[80] Zembe YZ, Townsend L, Thorson A, Ekström AM. Predictors of inconsistent condom use among a hard to reach population of young women with multiple sexual partners in peri-urban South Africa. PLoS One 2012;7:e51998.
[81] Prudden H, Watts CH, Vickerman P, Bobrova N, Heise L, Ogungbemi MK, et al. Can the UNAIDS Modes of Transmission Model be improved? A comparison of the original and revised model projections using data from Nigeria. AIDS 2013;27:2623–35.
[82] Baral SD, Grosso A, Mnisi Z, Adams D, Fielding-Miller R, Mabuza X, et al. Examining prevalence of HIV infection and risk factors among female sex workers (FSW) and men who have sex with men (MSM) in Swaziland. In: C.f.C. Program, editor. Project SEARCH, Task Order No.2. Baltimore, MD: USAID; 2013.
[83] Ikpeazu A, Momah-Haruna A, Madu Mari B, Thompson LH, Ogungbemi K, Daniel U, et al. An appraisal of female sex work in Nigeria—implications for designing and scaling up HIV prevention programmes. PLoS One 2014;9:e103619.
[84] Abdul-Quader AS, Baughman AL, H W. Estimating the size of key populations: current status and future possibilities. Curr Opin HIV AIDS 2014;9:107–14.
[85] Emmanuel F, Isac S, Blanchard JF. Using geographical mapping of key vulnerable populations to control the spread of HIV epidemics. Expert Rev Anti Infect Ther 2013;11:451–3.
[86] Sabin KM, Johnston LG. Epidemiological challenges to the assessment of HIV burdens among key populations: respondent-driven sampling, time-location sampling and demographic and health surveys. Curr Opin HIV AIDS 2014;9:101–6.
[87] Odek WO, Githuka G, L. A, Njoroge P, Kasonde L, Gorgens M, et al. Estimating the size of the female sex worker population in Kenya to inform HIV prevention programming. PLoS One 2014;9:e89180.
[88] Centre For Global Public Health (CGPH)University of Manitoba And National AIDS/STI Programme (Nascop), Republic of Kenya. Geographic mapping of most at risk populations for HIV (MARPs) in Kenya Centre for Global Public Health. Winnipeg: University of Manitoba; 2012.
[89] Stigum H, Falck W, Magnus P. The core group revisited: the effect of partner mixing and migration on the spread of gonorrhea, Chlamydia, and HIV. Math Biosci 1994;120:1–23.
[90] Redd AD, Quinn TC, Tobian AA. Frequency and implications of HIV superinfection. Lancet Infect Dis 2013;13:622–8.
[91] Behanzin L, Diabate S, Minani I, Lowndes CM, Boily MC, Labbe AC, et al. Assessment of HIV-related risky behaviour: a comparative study of face-to-face interviews and polling booth surveys in the general population of Cotonou, Benin. Sex Transm Infect 2013;89:595–601.
[92] Aggleton P, Bell SA, Kelly-Hanku A. 'Mobile men with money': HIV prevention and the erasure of difference. Glob Public Health 2014;9:257–70.
[93] Seeley JA, Allison EH. HIV/AIDS in fishing communities: challenges to delivering antiretroviral therapy to vulnerable groups. AIDS Care 2005;17:688–97.
[94] Lowndes CM, Alary M, Labbé AC, Gnintoungbè C, Belleau M, Mukenge L, et al. Interventions among male clients of female sex workers in Benin, West Africa: an essential component of targeted HIV preventive interventions. Sex Transm Infect 2007;83:577–81.

[95] AIDS Control ProgramMinistry of Health, Government of Uganda. The Crane Survey Report 2010. Kampala, Uganda: Makerere University, PEPFAR, Centers for Disease Control and Prevention, Ministry of Health; 2011.
[96] Family Health International. Behavioral surveillance surveys: guidelines for repeated behavioral surveys in populations at risk of HIV. 2000. Available at: https://www.fhi360.org/resource/guide-conducting-behavioral-surveillance-surveys-hivaids.
[97] Handcock MS, Gile KJ, Mar CM. Estimating the size of populations at high risk for HIV using respondent-driven sampling data. Lost Angeles: UCLA; 2014. Available at: http://www.stat.ucla.edu/~handcock/hpmrg/software/handcockgilemarBiometrics2014.pdf.
[98] Shannon K, Goldenberg SM, Deering KN, Strathdee SA. HIV infection among female sex workers in concentrated and high prevalence epidemics: why a structural determinants framework is needed. Curr Opin HIV AIDS 2014;9:174–82.
[99] Van Damme L, Ramjee G, Alary M, Vuylsteke B, Chandeying V, Rees H, et al. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. Lancet 2002;360:971–7.
[100] McClelland RS, Lavreys L, Hassan WM, Mandaliya K, Ndinya-Achola JO, Baeten JM. Vaginal washing and increased risk of HIV-1 acquisition among African women: a 10-year prospective study. Aids 2006;20:269–73.
[101] Civic D, Wilson D. Dry sex in Zimbabwe and implications for condom use. Soc Sci Med 1996;42:91–8.
[102] UNGASS 2012 Country Progress Reports. 2013. Available at: http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries.
[103] Scorgie F, Vasey K, Harper E, Richter M, Nare P, Maseko S, et al. Human rights abuses and collective resilience among sex workers in four African countries: a qualitative study. Global Health 2013;9:33.
[104] Tounkara FK, Diabate S, Guedou FA, Ahoussinou C, Kintin F, Zannou DM, et al. Violence, condom breakage, and HIV infection among female sex workers in Benin, West Africa. Sex Transm Dis 2014;41:312–8.
[105] Fonner VA, Kerrigan D, Mnisi Z, Ketende S, Kennedy CE, Baral S. Social cohesion, social participation, and HIV related risk among female sex workers in Swaziland. PLoS One 2014;9:e87527.
[106] Lorway R, Shaw SY, Hwang SD, Reza-Paul S, Pasha A, Wylie JL, et al. From individuals to complex systems: exploring the sexual networks of men who have sex with men in three cities of Karnataka, India. Sex Transm Infect 2010;86:70–8.
[107] Chow WZ, Ong LY, Razak SH, Lee YM, Ng KT, Yong YK, et al. Molecular diversity of HIV-1 among people who inject drugs in Kuala Lumpur, Malaysia: massive expansion of circulating recombinant form (CRF) 33_01B and emergence of multiple unique recombinant clusters. PLoS One 2013;8:e62560.
[108] Grabowski MK, Redd AD. Molecular tools for studying HIV transmission in sexual networks. Curr Opin HIV AIDS 2014;9:126–33.
[109] Lubelchek RJ, Hoehnen SC, Hotton AL, Kincaid SL, Barker DE, French AL. Transmission clustering among newly diagnosed HIV patients in Chicago, 2008 to 2011: using phylogenetics to expand knowledge of regional HIV transmission patterns. J Acquir Immune Defic Syndr 2015;68:46–54.
[110] Volz EM, Ionides E, Romero-Severson EO, Brandt MG, Mokotoff E, Koopman JS. HIV-1 transmission during early infection in men who have sex with men: a phylodynamic analysis. PLoS Med 2013;10:e1001568.
[111] Volz EM, Kosakovsky Pond SL, Ward MJ, Leigh Brown AJ, Frost SDW. Phylodynamics of infectious disease epidemics. Genetics 2009;183:1421–30.
[112] Johnson LF, Geffen N. A comparison of two mathematical modeling frameworks for evaluating sexually transmitted infection epidemiology. Sex Transm Dis 2016;43:139–46.
[113] Baral S, Todd CS, Aumakhan B, Lloyd J, Delegchoimbol A, Sabin K. HIV among female sex workers in the Central Asian Republics, Afghanistan, and Mongolia: contexts and convergence with drug use. Drug Alcohol Depend 2013;132 Suppl 1:S13–6.
[114] Reza T, Melesse DY, Shafer LA, Salim M, Altaf A, Sonia A, et al. Patterns and trends in Pakistan's heterogeneous HIV epidemic. Sex Transm Infect 2013;89:4–10.
[115] Peitzmeier S, Mason K, Ceesay N, Diouf D, Drame F, Loum J, et al. A cross-sectional evaluation of the prevalence and associations of HIV among female sex workers in the Gambia. Int J STD AIDS 2014;25:244–52.
[116] Mountain E, Pickles M, Mishra S, Vickerman P, Alary M, Boily MC. The HIV care cascade and antiretroviral therapy in female sex workers: implications for HIV prevention. Expert Rev Anti Infect Ther 2014;12:1203–19.
[117] Kato M, Granich R, Duc Bui D, Tran HV, Nadol P, Jacka D, et al. The potential impact of expanding antiretroviral therapy and combination prevention in Vietnam: towards elimination of HIV transmission. J Acquir Immune Defic Syndr 2013;63:e142–9.
[118] Mishra S, Mountain E, Pickles M, Vickerman P, Shastri S, Gilks CF, et al. For the Strategic Epi-Art. In: India Modeling Team, editor. Exploring the population-level impact of antiretroviral treatment: The influence of baseline intervention context., AIDS, Vol. 28; 2014. S61–72.
[119] Kirkcaldy RD, Kidd S, Weinstock HS, Papp JR, Bolan GA. Trends in antimicrobial resistance in Neisseria gonorrhoeae in the USA: the Gonococcal Isolate Surveillance Project (GISP), January 2006-June 2012. Sex Transm Infect 2013;89 Suppl 4:iv5–10.