

Research



Cite this article: Mulberry N, Rutherford AR, Wittenberg RW, Williams BG. 2019 HIV control strategies for sex worker–client contact networks. *J. R. Soc. Interface* **16**: 20190497. <http://dx.doi.org/10.1098/rsif.2019.0497>

Received: 12 July 2019

Accepted: 2 September 2019

Subject Category:

Life Sciences–Mathematics interface

Subject Areas:

biomathematics

Keywords:

bipartite network, dynamic network, epidemic control strategies, survival sex work, HIV, pre-exposure prophylaxis

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Electronic supplementary material is available online at <https://doi.org/10.6084/m9.figshare.c.4663934>.

HIV control strategies for sex worker–client contact networks

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Controlling the spread of HIV among hidden, high-risk populations such as survival sex workers and their clients is becoming increasingly important in the ongoing fight against HIV/AIDS. Several sociological and structural factors render general control strategies ineffective in these settings; instead, focused prevention, testing and treatment strategies which take into account the nature of survival sex work are required. Using a dynamic bipartite network model of sexual contacts, we investigate the optimal distribution of treatment and preventative resources among sex workers and their clients; specifically, we consider control strategies that randomly allocate antiretroviral therapy and pre-exposure prophylaxis within each subpopulation separately. Motivated by historical data from a South African mining community, three main asymmetries between sex workers and clients are considered in our model: relative population sizes, migration rates and partner distributions. We find that preventative interventions targeted at female sex workers are the lowest cost strategies for reducing HIV prevalence, since the sex workers form a smaller population and have, on average, more sexual contacts. However, the high migration rate among survival sex workers limits the extent to which prevalence can be reduced using this strategy. To achieve a further reduction in HIV prevalence, testing and treatment in the client population cannot be ignored.

1. Introduction

The global HIV burden is largely confined to key populations such as the men who have sex with men community, injection drug users and sex workers. Even in the generalized epidemic in sub-Saharan Africa, female sex workers (FSWs) are disproportionately affected [1,2]. In many communities—especially those in which sex work is criminalized—sex workers face widespread human rights violations and high levels of sexual violence, which may lead to an increase in HIV susceptibility [3]. This is coupled with potential barriers to access of treatment and prevention options for HIV [4]. Clients of FSWs act as bridges to the larger community, with many having one or more regular sexual partners outside of commercial sex [5]. This contributes to the wider HIV epidemic.

Much of the sex work in sub-Saharan Africa is ‘informal’, and is often described as transactional or survival sex work [6,7]. These terms encompass a variety of sex-for-goods or -money exchanges, and usually exclude women working as escorts or in brothels. This type of sex work is not unique to sub-Saharan Africa; see [8] for example. Women who engage in survival sex work are at particular risk of exploitation and have limited ability to advocate for their health and welfare [9]. We will consider the sexual contacts described in this work to be of this informal nature.

HIV can be controlled by providing life-long treatment to infected individuals and by a range of preventative options for at-risk individuals. Condoms are an inexpensive prevention measure against HIV and other sexually transmitted

infections. Simulation studies have proposed that condom distribution programmes alone can significantly reduce HIV incidence among FSWs and clients [10]. However, FSWs frequently cite instances of forced unprotected sex, and it has been proposed that pre-exposure prophylaxis (PrEP) may be particularly beneficial in the FSW community [11–14]. Standard PrEP is an oral medication taken daily by HIV-negative individuals which can significantly reduce the likelihood of infection through sexual contact [15–19]. For infected (HIV-positive) individuals, antiretroviral therapy (ART) increases life expectancy and has been shown to be highly effective in reducing transmission events [20]. Therefore, ART also serves to prevent new infections and reduce HIV incidence in the population [21]. Life-long ART is necessary for continued suppression of viral load. Additional control strategies targeting commercial sex workers include creating safer work environments, improving access to care, community empowerment and decriminalization [22].

HIV transmission is associated with complex social interactions, such as sexual relationships or needle sharing. Therefore, knowledge of the underlying social network is important for understanding disease spread and for designing control strategies. We use a random network model to represent heterosexual contact; it is on this network that the model disease process spreads. The use of networks to model epidemics is well established [23], and various authors have investigated immunization strategies on networks [24–28]. In particular, Chen & Lu [28] describe an efficient and feasible immunization strategy for FSWs. All of the cited work focuses on optimized approaches within a single population. By contrast, in the present work, we use a bipartite network model to study the distribution of combination HIV prevention—PrEP and ART—between two *distinct* populations, namely the FSWs and their clients.

Previous HIV models have considered the effect of ART and, more recently, PrEP on HIV prevalence in sub-Saharan Africa and elsewhere. The review by Gomez *et al.* [29] explored the potential impact of a large scale PrEP roll-out alongside existing HIV prevention programmes, such as condoms and ART, and determined that targeting PrEP to key populations would be an effective strategy as measured by cost per infection averted. Pretorius *et al.* [30] conclude that PrEP targeted at 15–35-year-old women could have a positive impact on the South African epidemic, but that the relative effectiveness of PrEP compared to ART decreases with expanded ART coverage. Vissers *et al.* [31] developed a compartmental model which captures links between the high-risk populations of sex workers and their clients, and the low-risk general population. They found that PrEP would have a substantial impact in many African settings when targeting both FSWs and clients, because condom use is frequently low in such settings. Recently, Sarkar *et al.* [32] have presented a systematic review of the cost-effectiveness of current HIV prevention methods in sub-Saharan Africa. They determine that there is strong evidence to support targeting higher-cost interventions (such as PrEP) to high-risk populations; however, there is a lack of economic studies that focus specifically on sex worker populations or on combination intervention strategies.

Although some of the aforementioned modelling studies have examined the potential impact of PrEP in sex worker populations, they do not consider the implications of the nature of survival sex work on the structure of the sexual network. To capture this, we use a dynamic bipartite random

network model with different degree distributions for the sex workers and clients. Using this model—calibrated against historical data from a South African study—we investigate the potential impact of combined PrEP and ART for HIV control and prevention in a population of survival sex workers and their clients. We compare the results from five combination-intervention strategies to determine the lowest-cost strategy to achieve a given HIV prevalence.

2. Data analysis

A major consideration in this work is the characterization of sex worker–client interactions. Previous work has largely focused on FSW communities [5], since clients typically do not form an identifiable group. Therefore, complete social network data between sex workers and their clients appears to be scarce. In this section, we analyse historical data collected on sex worker–client interactions in a South African mining community as part of the Carletonville-Mosuthumpilo Project [33] which took part from 1998 to 2000, and compare statistics of these interactions with those reported in other studies conducted in similar populations. Although complete social network data are unavailable, the Carletonville-Mosuthumpilo Project questionnaire data provides insight into the demographics and behaviour of both clients and FSWs. Table 1 compares some summary metrics from this project with studies of similar communities. The statistics reported in this table indicate strong similarities between the Carletonville-Mosuthumpilo data and other studies of sex work in rural communities [34] and along commercial trucking routes.

Perhaps the most significant feature of FSW–client populations is that the FSWs on average have a greater number of different partners than do clients. The ratio of the number of different partners varies significantly, with FSWs reporting between twice as many to almost 50 times the number of different partners than do the clients. In the Carletonville-Mosuthumpilo data, FSWs report on average approximately 10 times as many different sexual partners over the past year than do clients. The data from Ferguson *et al.* [35] suggest that the majority of clients are likely to be strangers. This is echoed in interviews with FSWs reported in Campbell [39]. The average number of contacts is furthermore linked to the relative population sizes of FSWs and clients. During the time of this study, Carletonville was home to approximately 500 FSWs and 75 000 miners—only a fraction of which would have been clients. Based on the analysis contained in electronic supplementary material, S1 and on the relative numbers of different partners, we estimate a 10:1 ratio of clients to FSWs.

The Carletonville-Mosuthumpilo data indicate that the FSWs are a highly mobile population even by comparison with the client population who are predominantly migrant workers. This is consistent with the Ramjee & Gouws [37] study, which shows similar statistics for both FSWs and clients (in this case, truckers). Although the specific factors contributing to the migration rate of FSWs are uncertain, it is plausible that the challenges faced by such sex workers would motivate their departure once circumstances permit. Meanwhile, the client migration rate is dependent on continued employment; previous work has identified migration as an HIV risk factor among men [40]. We hypothesize that a significantly higher migration rate among FSWs compared with the client

Table 1. Comparison of summary statistics across five studies of FSWs and their clients in sub-Saharan Africa (the range is given where data exist). An x indicates that no data are available.

study	mean age	HIV prevalence	mean number different partners past month/year	mean number encounters past month	mean time working in location
Carletonville [33]					
FSWs	30 (21–51)	70%	x/22 (1–300)	9.7 (0–62)	4 yr
clients (miners)	35 (17–55)	29% ^a	x/1.94 (0–10)	2.7 (0–15)	14 yr
Rural Nyanza [34]					
FSWs	26 (17–37)	75%	2.5 (0–12)/x	6.6 ^{a,b}	x
Trans-Africa Hwy [35,36]					
FSWs	27 (16–46)	50–80%	13.6 (1–79)/129	25 (1–88)	x
clients (truckers)	x	27% ^a	x/2.8	x	x
KwaZulu-Natal [37]					
FSWs	25 (15–48)	56%	x	x	2.5 yr
clients (truckers)	37 (18–71)	56%	x	x	8.4 yr
Uganda [38]					
FSWs	x	33%	19.1/74.5	x	x
clients (truckers)	x	18%	7.4/44.7	x	x

^aThis is the estimated prevalence among sampled miners/truckers, respectively, not just those who are clients.

^bThis statistic is the number of sexual acts reported over the previous 14 days.

subpopulation is a typical characteristic of many survival sex worker–client sexual networks [6].

HIV prevalence data for FSWs and clients is included in table 1. We are especially interested in the difference in disease prevalence between the two populations. We do not have client-only prevalence from Carletonville; 29% HIV prevalence was reported among all miners, and so one expects the client-only prevalence to be higher than 29%. The studies from KwaZulu-Natal [37] and Uganda [38] show a client-only HIV prevalence that is 54–100% of the FSW prevalence.

3. Model description

There are two main components to our model: the contact process (described in §3.1) that governs how HIV spreads throughout the population, and the disease process (described in §3.2) that governs how HIV progresses within a host.

3.1. Sexual contact network

A dynamic bipartite random network is used to model sexual contact between FSWs and their clients. The network comprises of two-node sets, representing FSWs and clients. Edges connect FSWs to clients—representing potential sexual contact—and are rewired at each time step (independently of the disease states of the nodes). Thus we interpret the instantaneous degree of a node as the number of different sexual partners during one-time step (0.1 years). New partnerships are formed randomly, and we assume there is no preference for repeat partners. This assumption is in line with the observations in [39], where FSWs in hotspots indicate in interviews that most of their clients are strangers. The degree sequences for the FSWs and clients are sampled from Poisson and truncated power-law distributions, respectively. Motivated by the Carletonville-

Table 2. Possible node states.

state	interpretation
<i>V</i>	vaccinated, or in an immune state (cannot become infected)
<i>S</i>	susceptible (may become infected)
<i>A</i>	acute (highly infectious, short duration)
<i>L</i>	latent (moderately infectious, long duration)
<i>T</i>	on treatment (cannot become reinfected, non-infectious)

Mosuthumpilo study, we use 5000 client nodes and 500 FSW nodes. The details of the model generation are given in electronic supplementary material, S2.2.

3.2. Population and HIV dynamics

Each node of the bipartite random network is in one of five states, summarized in table 2: protected against HIV, susceptible to HIV infection, acute stage HIV infection, latent stage HIV infection or on treatment with ART. The state diagram is shown in figure 1 and the model parameters are explained and estimated in table 3.

Nodes in the susceptible state may become infected through a contact process on edges which connect to a nearest neighbour in either the (highly infectious) acute state or the (moderately infectious) latent state. The contact process is Markovian, with a fixed probability of disease transmission per unit time on each edge.

Upon initial infection, nodes are in the acute state. Nodes transition from the acute state to the latent state, from which they are randomly placed on treatment, in each case with a

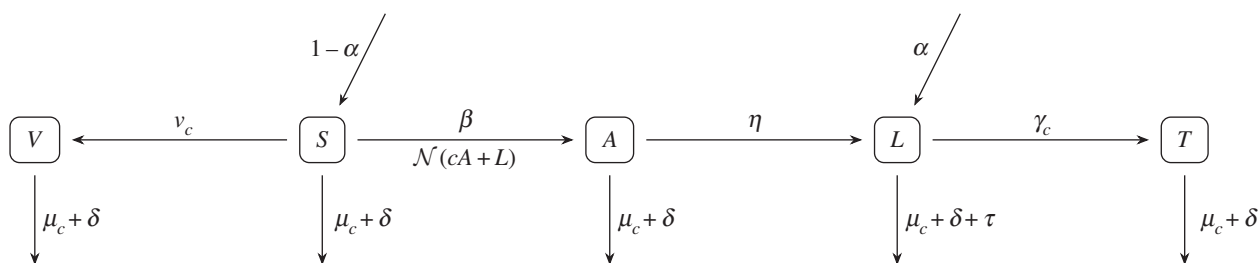


Figure 1. Schematic of model progression in client nodes. The model structure for FSW nodes is identical, but the values of some parameters differ between client and FSW nodes (indicated by subscripts c and f , respectively). The notation $\mathcal{N}(cA + L)$ refers to the total number of infectious nearest neighbours, combining those in the acute state (weighted by parameter c) and in the latent state.

Table 3. Model parameters and estimated values. Rates are given per year.

parameter	interpretation	estimated value
c	relative infectivity of acute to latent individuals	10 [43]
β	infectious contact rate	0.6 (S4)
η^{-1}	expected time spent in acute stage	10.5 weeks [44]
γ_c	client treatment rate	variable, $\gamma_c \in [0, 0.4]$
γ_f	FSW treatment rate	variable, $\gamma_f \in [0, 0.4]$
μ_c	client migration rate	0.077 (table 1)
μ_f	FSW migration rate	0.25 (table 1)
δ	natural death rate	0.016 [45]
τ^{-1}	expected time in latent stage if left untreated	10 years [44]
α	background HIV prevalence	0.2 [33]
v_c	client 'immunization' rate	variable $v_c \in [0, 4.5]$
v_f	FSW 'immunization' rate	variable $v_f \in [0, 4.5]$

fixed probability per unit time. We make the simplifying assumption that nodes in the acute state cannot transition directly to the treated state. This is because the window period for HIV testing, combined with the time to achieve viral suppression after ART initiation, means that a direct transition from the acute state to viral suppression under ART would be rare. The transition to the treated state in the model combines a positive HIV test, engagement in care, initiation of ART and viral suppression; therefore, one could consider the treatment rate in the model to be a combination of the rates for each of these processes. We consider treatment rates γ_c, γ_f ranging from 0 to 0.4 per year. A treatment rate of 0.4 per year corresponds to an expected time to viral suppression of approximately 2.5 years.

Each node may be 'removed' from the population with a probability per unit time that depends on the state of the node. This removal captures migration, natural death and death due to AIDS. The node is then replaced with an equivalent node (all edges remaining intact), which has probability α of being in the latent stage HIV state, and probability $1 - \alpha$

of being in the susceptible state. For simplicity, we assume that nodes are not initialized in the relatively short acute stage HIV state. The value of α is determined by the background HIV prevalence in the general population, which is beyond the scope of our model. Thus, upon entry into the model population, both FSWs and clients have a probability of being infected which is equal to the 20% historical background HIV prevalence in South Africa [33]. We assume the same background HIV rate among incoming FSWs and incoming clients; young women bear a higher burden of disease in South Africa [41], but since transactional sex is a confounding factor in such statistics [42], we conservatively take a single value for α .

We interpret the state V as being an 'on PrEP' state, although from an epidemiological standpoint this is equivalent to a vaccinated state. The primary difference lies in cost, because PrEP requires ongoing treatment to maintain immunity. We assume, for simplicity, that both PrEP and ART are 100% effective in preventing infection and transmission of HIV. Therefore, infection events occur only between nodes in the susceptible state and nodes in the acute and latent HIV states.

4. Calibration and validation

Most of the parameters in table 3 have been estimated using public health sources or the Carletonville-Mosuthumpilo data. The remaining parameter for us to estimate is the infectious contact rate, β . We assume no asymmetry between male-to-female and female-to-male transmission, an assumption that has been shown to be acceptable in sub-Saharan African populations [43]. Since systematic treatment programmes had yet to be introduced in Carletonville at the time of data collection, we calibrate the model in the absence of treatment or PrEP (figure 2). We find that taking $\beta = 0.6$ results in an equilibrium disease prevalence of 69% which closely matches the recorded 70% prevalence among the Carletonville FSWs (table 1). The calibration results correspond to a client prevalence of 48% at equilibrium (a reasonable value given the discussion in §2).

5. Results

The model developed in the previous section is used to investigate possible control strategies by varying both treatment rates (γ_c, γ_f) and the rate at which individuals are placed on PrEP (v_c, v_f). Each simulation is initialized with the calibrated equilibrium prevalences, namely 69% and 48% for the FSW and client populations, respectively. We evaluate our

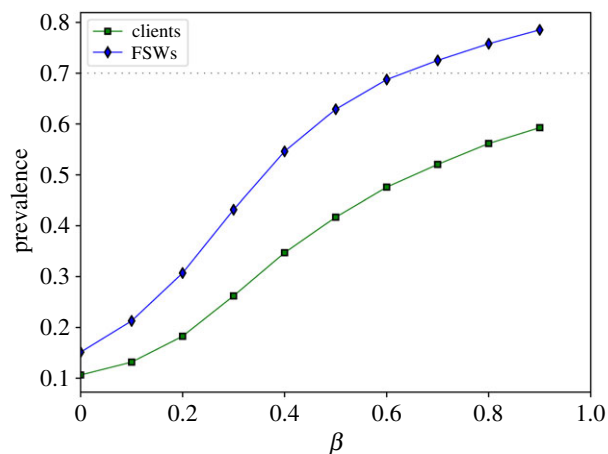


Figure 2. Equilibrium HIV prevalence among each subpopulation without treatment. The dashed line marks the recorded FSW prevalence. Markers represent sample means in this and subsequent figures. (Online version in colour.)

interventions in two ways. First, we consider the total untreated HIV prevalence after 20 years, where total untreated HIV prevalence is defined to be the proportion of the total population (both clients and FSWs) in the acute stage HIV and latent stage HIV states. HIV-positive individuals in the treated state are not included in our computation of HIV prevalence since that would mask the impact of treatment scale-up on the epidemic, and because, in this model, treated individuals do not contribute to the overall incidence.

Additionally, we look at the relative cost for each PrEP and treatment strategy to achieve a given HIV prevalence after 20 years. To compare the cost of PrEP and ART, we conservatively assume that the cost of ART is double that of PrEP [30]. The cost of PrEP is taken to be one unit per individual on PrEP per simulation time step, and so the cost of ART is two cost units per individual on ART per simulation time step. The total cost is normalized to the size of the network.

We consider interventions that combine both PrEP and ART. Susceptible nodes transition to the PrEP state V at rates ν_c for clients and ν_f for FSWs. Nodes in the latent stage HIV state transition to the treated state at treatment rates γ_c for clients and γ_f for FSWs. PrEP coverage is defined to be the proportion of HIV-negative clients or FSWs on PrEP after 20 years. The following combined strategies are evaluated: (A) treat and administer PrEP to FSWs only; (B) treat and administer PrEP to clients only; (C) treat clients and administer PrEP to FSWs; (D) treat FSWs and administer PrEP to clients; and (E) treat both populations while administering PrEP to FSWs only. We do not consider targeted PrEP or ART strategies within each subpopulation. That is, when applying such strategies to FSWs and/or clients, nodes are placed uniformly at random on PrEP or ART, as indicated. For each strategy, we plot the mean prevalence of 10 simulations on each of 40 random networks (lines connecting markers are piecewise-linear interpolants for visualization purposes only). Since both the network size and initial epidemic are large, the sample variance is low (less than 0.1%). In comparison to the uncertainty in model parameters, this variance is negligible.

5.1. Interventions

When both ART and PrEP are targeted at the FSW population (Strategy A), as shown in figure 3, there is a threshold PrEP

coverage of approximately 80%, above which there is not a significant additional decrease in HIV prevalence. Figure 3 shows that focusing only on PrEP is the lowest-cost option for reducing total prevalence to approximately 20%. PrEP should be combined with treatment to reduce prevalence to below 20% in this population.

Figure 4 shows the impact of Strategy B, which targets both treatment and PrEP to the client subpopulation alone. The response of the total prevalence to increasing PrEP coverage in the client subpopulation is more gradual than for the FSW subpopulation so that higher coverage is required to realize the lowest prevalence. When compared with Strategy A, figure 4 shows a larger range over which combining treatment with PrEP is the lowest-cost solution.

The next two interventions considered target both populations. Figure 5 shows the case of treating only clients and providing PrEP to FSWs (Strategy C). For any given total prevalence target, it is cost-beneficial to re-allocate testing and treatment resources from the clients towards increasing PrEP coverage in the FSWs. However, if the targeted total prevalence is below approximately 20%, then a testing and treatment programme for the clients becomes necessary. The results for Strategy D (figure 6) show that if we consider treating only the FSW population, it is never economical to prioritize PrEP to clients.

Strategy E is the final intervention considered, and is arguably the most realistic from a public health policy perspective. In this case, testing and treatment programmes are implemented for both FSWs and clients; however, PrEP is targeted at only FSWs. The results for this scenario are shown in figure 7. As with Strategy D, we find that for a given prevalence target it remains cost-advantageous to prioritize PrEP for FSWs. Figure 7 shows that the cost advantage of prioritizing PrEP is slightly greater when treatment is applied to both subpopulations. However, it remains the case that a treatment programme is required to achieve total HIV prevalence below approximately 20%.

All five strategies are collated in figure 8 for ease of comparison. In particular, this figure shows that strategies B and D—which target PrEP towards clients—are inefficient in that there always exists a lower-cost strategy to achieve the same HIV prevalence. For the remaining strategies, the lowest-cost strategy depends on the desired achievable prevalence after 20 years. As expected, strategies C and E are very similar in both cost and prevalence outcomes, since the proportion of FSWs on treatment is small. However, in an aggressive treatment regime, Strategy E presents the best outcomes. Regardless of treatment allocation, this figure shows that increasing the PrEP coverage among FSWs is always the lowest-cost strategy.

6. Discussion

The sexual network of survival FSW–client populations has several structural features which distinguish it from other sexual networks. We have examined the potential importance of these features in designing control strategies for an HIV epidemic. The sexual network is modelled as a dynamic bipartite network in which the FSW subpopulation is significantly smaller than the client subpopulation. Intuitively, one would expect that the most effective strategy for control of an HIV epidemic on a bipartite network would be to target both treatment and

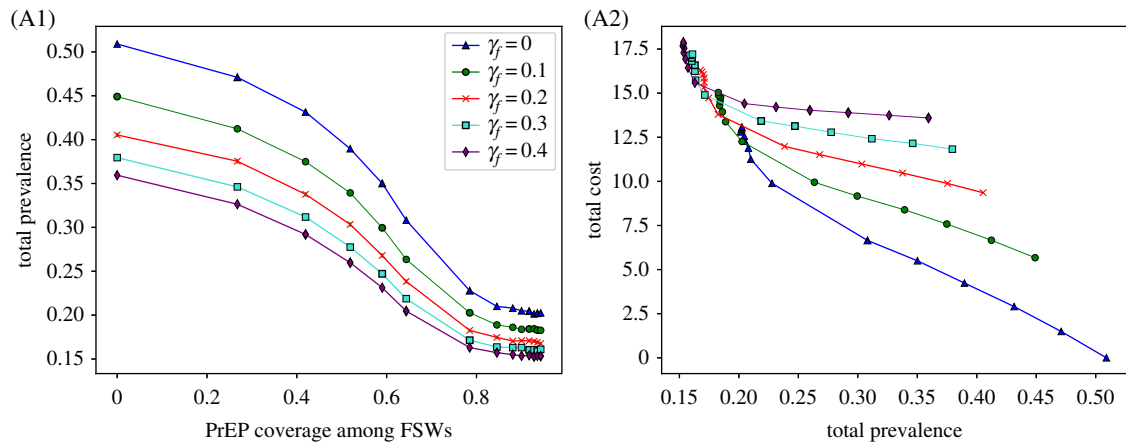


Figure 3. Strategy A: both treatment and PrEP are targeted at FSWs. (A1) Effect of Strategy A on total HIV prevalence after 20 years. (A2) Total cost over 20 years to achieve a given total prevalence. (Online version in colour.)

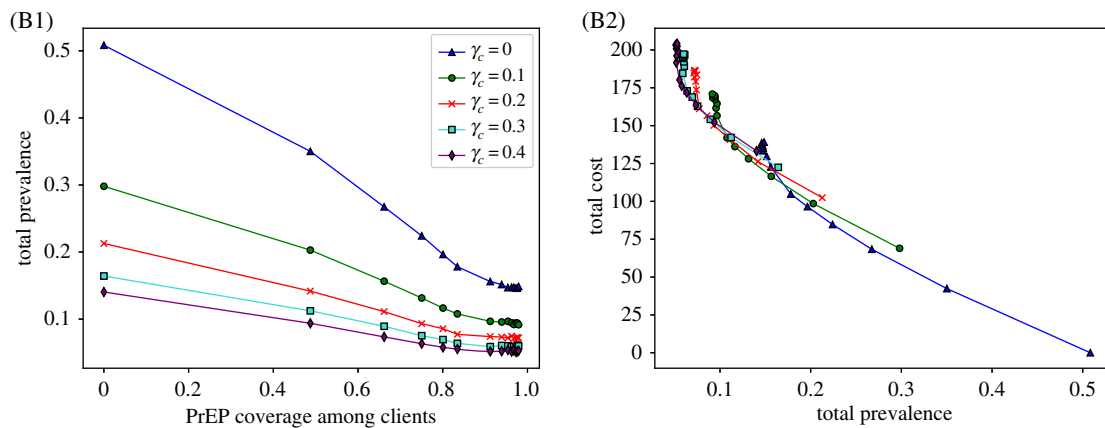


Figure 4. Strategy B: both PrEP and treatment targeted at clients. (B1) Effect on total HIV prevalence after 20 years. (B2) Total cost over 20 years to achieve a given total prevalence. (Online version in colour.)

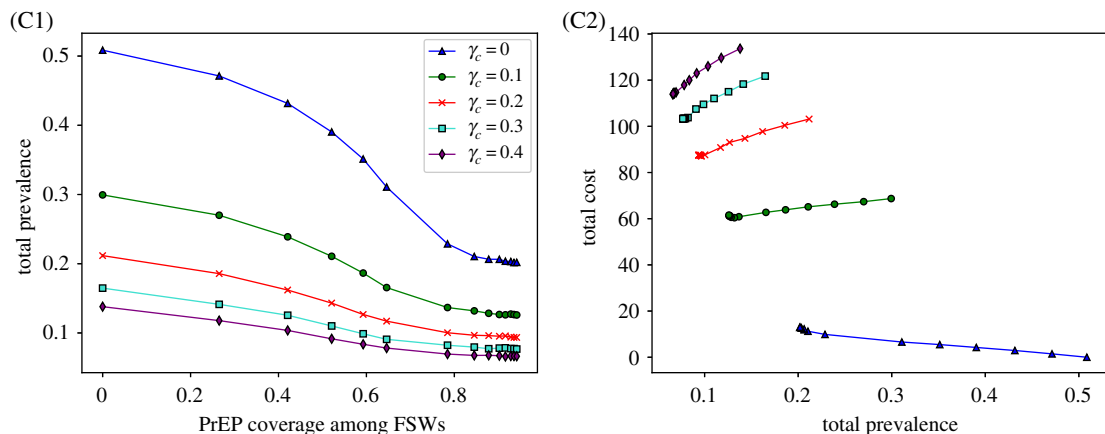


Figure 5. Strategy C: PrEP is targeted at FSWs and treatment is targeted towards clients. (C1) Effect on total HIV prevalence after 20 years. (C2) Total cost over 20 years to achieve a given total prevalence. (Online version in colour.)

prevention strategies to the smaller subpopulation—in this case the FSWs. Our results indeed show that PrEP targeted at FSWs is a highly effective strategy. The caveat is that targeting only the FSW subpopulation cannot reduce the overall HIV prevalence to near-zero levels. This is a consequence of the asymmetry in population sizes and the high migration rate of survival FSWs. Not only does the high migration rate of survival FSWs mean that 100% PrEP coverage is infeasible, but it also introduces new HIV infections from the wider population.

The lowest-cost strategy for further reductions in prevalence is to combine PrEP in the FSW subpopulation with expansion of testing and treatment with ART in both the FSW and client subpopulations.

These results build on previous modelling studies such as those presented in [10,46], who found that PrEP targeted at FSWs could be an impactful addition to existing combination intervention programmes. Our model, however, relies on a number of important assumptions. In particular, we assume

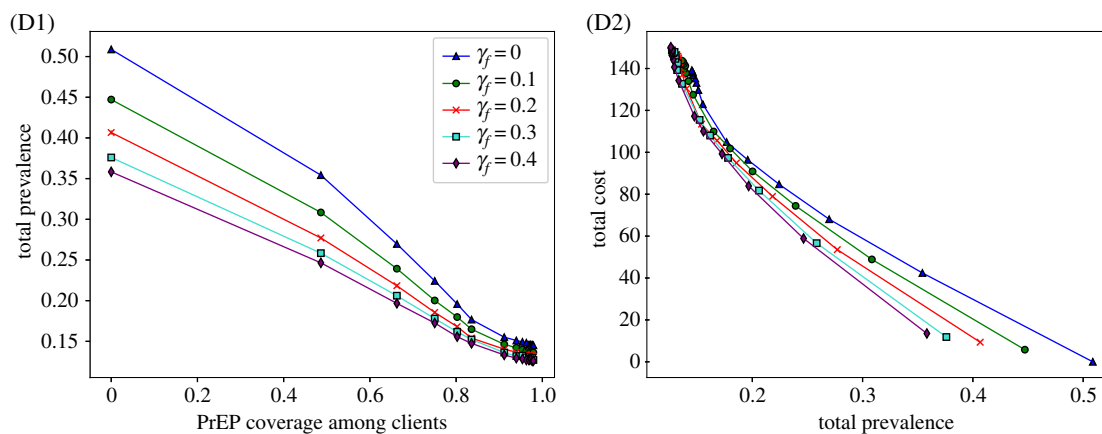


Figure 6. Strategy D: PrEP is targeted at clients and treatment is targeted towards FSWs. (D1) Effect of the combined strategy on total HIV prevalence after 20 years. (D2) Total cost over 20 years to achieve a given total prevalence. (Online version in colour.)

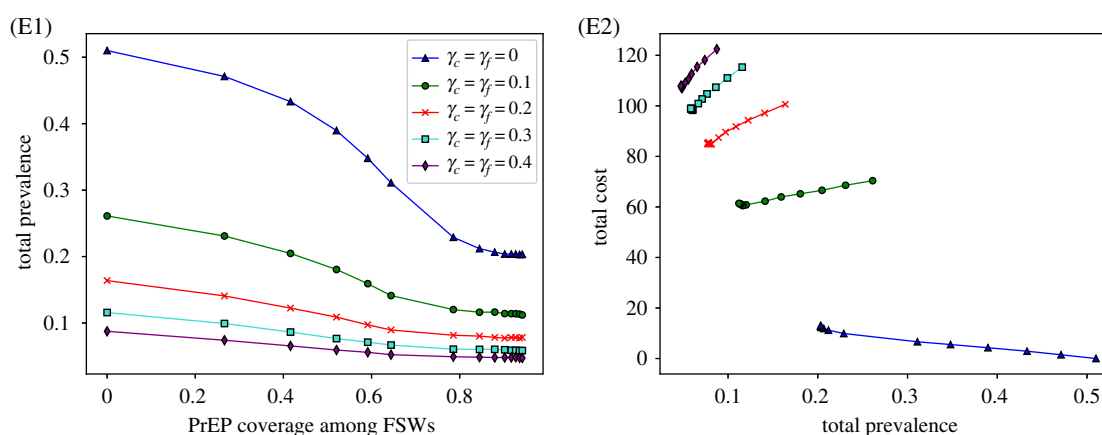


Figure 7. Strategy E: PrEP is targeted at FSWs and treatment is provided equally to both clients and FSWs. (E1) Effect on total HIV prevalence after 20 years. (E2) Total cost over 20 years to achieve a given total prevalence. (Online version in colour.)

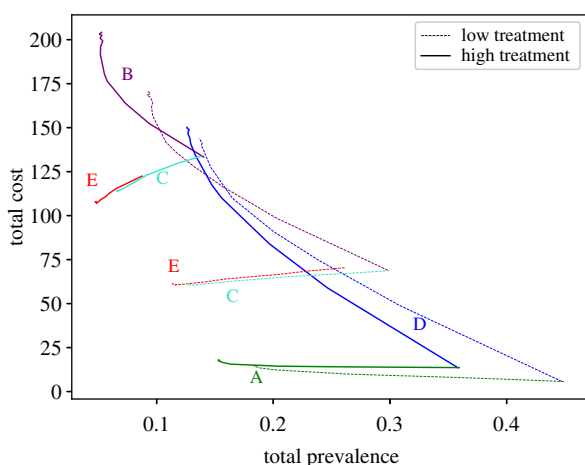


Figure 8. Comparison of strategies A through E under low treatment ($\gamma = 0.1$) and high treatment ($\gamma = 0.4$) regimes. (Online version in colour.)

no loss of adherence to either PrEP or ART (except through migratory events); partnerships are randomly selected at approximately one month intervals; and we ignore other public health interventions such as voluntary male circumcision or condoms (while noting that survival sex workers in particular face substantial difficulties in enforcing safe sex). Although the Carletonville-Mosuthumpilo data gives important insights into an untreated FSW–client population, self-reported questionnaire data are an unreliable indication of sexual contacts [47], and there is a lack of studies that specifically recruit

FSWs for biomedical interventions [14]. Such studies will be essential for future investigation of optimal control strategies in populations where transactional sex is commonplace.

One of our primary assumptions is that PrEP is 100% effective and acts like a perfect vaccine. In reality, behavioural studies have shown that the efficacy of daily oral PrEP depends strongly on adherence [48,49]. While PrEP adherence has been studied among men who have sex with men [17–19], heterosexual couples [15,50] and heterosexual men and women [16,51], we are aware of no studies which have exclusively recruited FSWs. The study of Van Damme *et al.* [51] included a small number (12%) of women who reported recently exchanging money for sex. Unlike in the other cited studies, they found drug adherence—and hence PrEP effectiveness—to be low. There is, however, evidence that risk-perception and adherence seem to be positively correlated [15], and FSWs in South Africa have been shown to be highly receptive to PrEP [11]; these results indicate that adherence may be significantly different among FSWs. Therefore, there is a need for studies that target sex workers specifically. In the absence of such studies, we do not explicitly model adherence. The implementation of long-acting PrEP which is currently in development could further address this issue [52].

Our incorporation of migration somewhat mitigates the assumption that PrEP is 100% effective, by allowing events where a ‘vaccinated’ individual can move directly into the susceptible state or the latent-stage HIV state. However, if PrEP does not completely protect adherent users from infection,

then our model could be underestimating the number of nodes in the acute-stage HIV state. If we instead consider adherence to be the primary factor in PrEP efficacy, and we choose to model individuals as either 'adherers' or 'non-adherers', then we might be interested instead in what happens if 100% PrEP coverage is not attainable. Since the threshold PrEP coverage for FSWs is just over 80%, our optimal strategy accounts for about 20% non-adherence. Even if the number of non-adherers were greater than this threshold amount, the advised strategy would again be to prioritize PrEP to FSWs, although the achievable reduction in prevalence would be lower than predicted.

We use a dynamic network model in which all partnerships are formed between FSWs and clients and are randomly re-assigned at every time step. We neglect any regular partners of either FSWs or clients. One could instead include both casual and regular contacts by constructing a semi-dynamic network model. It has been suggested that condom usage differs significantly between casual and regular partners, and that FSWs may engage in higher-risk behaviour with their regular (or non-paying) partners [53,54]. In addition to dynamic edges which represent casual contact, one could fix certain edges to represent regular contacts. This procedure could form the basis of a study on the impact of regular partnership on the efficacy of a targeted PrEP roll-out. Furthermore, we do not consider the general population outside of the sex worker–client population, nor do we take into account the regular partners of migrant workers (an issue that is explored in [55]). Our focus here is on transmission of HIV within the sex worker–client network, and we assume that the impact of outside partnerships is small in comparison to the within-network interactions.

We have repeated the simulations from §5 using both a static network model (electronic supplementary material, S3) and a compartmental model (electronic supplementary material, S4) in order to ascertain the effects of network structure and dynamics on our conclusions. In our static network model, all partnerships are concurrent and repeat contacts, whereas in our dynamic network, the chances of having concurrent contact is low and the probability of repeat contacts is even lower. While concurrency, in particular, has been shown to affect the nature of an epidemic [56], qualitatively our conclusions remain the same regardless of whether we use the static or dynamic network. Similarly, our conclusion to prioritize PrEP to FSWs is robust to assumptions regarding the degree distributions in our network models, as tested using the compartmental model. That being said, we do observe several important differences among the three models. Both network models (but not the compartmental model) exhibit a threshold PrEP coverage for any given treatment rate. However, these thresholds are markedly lower in the static model than the dynamic model; this effect is particularly apparent when considering PrEP targeted at FSWs in high treatment regimes. While both network models suggest that, under

high treatment of both subpopulations, increasing PrEP to FSWs will lead to cost savings, the compartmental model shows no such behaviour. Nevertheless, all models are consistent with the relative impact of each strategy considered. Therefore, we find that our conclusions regarding resource allocation are robust to our assumptions regarding network structure and dynamics, but that these considerations are key for future economical studies.

7. Conclusion

We have found that the most effective strategy for reducing HIV prevalence in a survival FSW–client population is a PrEP programme targeted at FSWs. As PrEP coverage of the FSWs is scaled up, the projected HIV prevalence after 20 years decreases dramatically until a threshold coverage is reached. Further expansion of PrEP coverage above the threshold level does not lead to significant further reduction in HIV prevalence. In the Carletonville sex worker population studied, we find that this threshold PrEP coverage is approximately 80%. We find that a PrEP programme targeted at the clients is never the lowest-cost strategy for reducing HIV prevalence.

A PrEP programme targeted at FSWs alone cannot effectively eliminate HIV as a public health threat in the sex worker–client population. Although the lowest-cost strategy for achieving a given prevalence is to prioritize PrEP in the FSW population, the impact of the higher migration rate among FSWs and the asymmetric population sizes is to limit the extent to which prevalence can be reduced through this strategy. An aggressive reduction in prevalence requires a combination strategy of PrEP for the FSWs and expanded testing and treatment for both the sex workers and the clients. In general, intervention strategies should be prioritized to the sex workers, but testing and treatment of the client population cannot be neglected.

Data accessibility. Software for performing the simulations is hosted at: <https://github.com/nmulberry/NepidemiX>. Summary data from the Carletonville-Mosuthumpilo project are contained in the electronic supplementary material.

Authors' contributions. N.M. conducted the research and wrote most of the paper. A.R.R. contributed initial ideas behind the work, supervised the research and contributed to writing the paper. R.W.W. supervised the research and provided editorial contributions to the paper. B.G.W. provided data for the research, gave insight into the public health implications of the work, and provided feedback on the paper.

Competing interests. We declare that we have no competing interests.

Funding. R.W.W. is supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

Acknowledgements. This research was enabled in part by support provided by WestGrid (www.westgrid.ca) and Compute Canada (www.computecanada.ca). We thank Lukas Ahrenberg for the development of the NepidemiX software and anonymous reviewers for helpful comments on an earlier draft of this manuscript. We further acknowledge support from SFU Big Data.

Reference

1. Kerrigan D, Wirtz A, Semini I, N'Jie N, Stanciole A, Butler J, Osornoprasop S, Oelrichs R, Beyrer C. 2012 *The global HIV epidemics among sex workers*. Washington, DC: The World Bank.
2. Beyrer C *et al.* 2015 An action agenda for HIV and sex workers. *Lancet* **385**, 287–301. (doi:10.1016/S0140-6736(14)60933-8)
3. Baral S, Beyrer C, Muessig K, Poteat T, Wirtz AL, Decker MR, Sherman SG, Kerrigan D. 2012 Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review

- and meta-analysis. *Lancet Infect. Dis.* **12**, 538–549. (doi:10.1016/S1473-3099(12)70066-X)
4. Decker MR, Crago AL, Chu SK, Sherman SG, Seshu MS, Buthelezi K, Dhaliwal M, Beyrer C. 2015 Human rights violations against sex workers: burden and effect on HIV. *Lancet* **385**, 186–199. (doi:10.1016/S0140-6736(14)60800-X)
 5. Lowndes CM *et al.* 2000 Management of sexually transmitted diseases and HIV prevention in men at high risk: targeting clients and non-paying sexual partners of female sex workers in Benin. *AIDS* **14**, 2523–2534. (doi:10.1097/00002030-200011100-00015)
 6. Scorgie F, Chersich MF, Ntaganira I, Gerbase A, Lule F, Lo YR. 2012 Socio-demographic characteristics and behavioral risk factors of female sex workers in sub-saharan Africa: a systematic review. *AIDS Behav.* **16**, 920–933. (doi:10.1007/s10461-011-9985-z)
 7. Stoebenau K, Heise L, Wamoyi J, Bobrova N. 2016 Revisiting the understanding of ‘transactional sex’ in sub-Saharan Africa: a review and synthesis of the literature. *Soc. Sci. Med.* **168**, 186–197. (doi:10.1016/j.socscimed.2016.09.023)
 8. Shannon K, Kerr T, Allinott S, Chettiar J, Shoveller J, Tyndall MW. 2008 Social and structural violence and power relations in mitigating HIV risk of drug-using women in survival sex work. *Soc. Sci. Med.* **66**, 911–921. (doi:10.1016/j.socscimed.2007.11.008)
 9. Wojcicki JM, Malala J. 2001 Condom use, power and HIV/AIDS risk: sex-workers bargain for survival in Hillbrow/Joubert Park/Berea, Johannesburg. *Soc. Sci. Med.* **53**, 99–121. (doi:10.1016/S0277-9536(00)00315-4)
 10. Bekker LG, Johnson L, Cowan F, Overs C, Besada D, Hillier S, Cates Jr W. 2015 Combination HIV prevention for female sex workers: what is the evidence? *Lancet* **385**, 72–87. (doi:10.1016/S0140-6736(14)60974-0)
 11. Eakle R, Bourne A, Mbogua J, Mutanha N, Rees H. 2018 Exploring acceptability of oral PrEP prior to implementation among female sex workers in South Africa. *J. Int. AIDS Soc.* **21**, e25081. (doi:10.1002/jia2.25081)
 12. Cowan FM, Delany-Moretwe S. 2016 Promise and pitfalls of pre-exposure prophylaxis for female sex workers. *Curr. Opin. HIV AIDS* **11**, 27–34. (doi:10.1097/COH.0000000000000215)
 13. Ye L *et al.* 2014 HIV pre-exposure prophylaxis interest among female sex workers in Guangxi, China. *PLoS ONE* **9**, e86200. (doi:10.1371/journal.pone.0086200)
 14. Syvertsen JL, Bazzi AMR, Scheibe A, Adebajo S, Strathdee SA, Wechsberg WM. 2014 The promise and peril of pre-exposure prophylaxis (PrEP): using social science to inform prep interventions among female sex workers. *Afr. J. Reprod. Health* **18**, 74–83.
 15. Donnell D *et al.* 2014 HIV protective efficacy and correlates of tenofovir blood concentrations in a clinical trial of PrEP for HIV prevention. *J. Acquir. Immune Defic. Syndr.* **66**, 340. (doi:10.1097/QAI.0000000000000172)
 16. Thigpen MC *et al.* 2012 Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *New England J. Med.* **367**, 423–434. (doi:10.1056/NEJMoa1110711)
 17. McCormack S *et al.* 2016 Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* **387**, 53–60. (doi:10.1016/S0140-6736(15)00056-2)
 18. Anderson PL *et al.* 2012 Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci. Trans. Med.* **4**, 151ra125–151ra125. (doi:10.1126/scitranslmed.3004006)
 19. Grulich AE *et al.* 2018 Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. *Lancet HIV* **5**, e629–e637. (doi:10.1016/S2352-3018(18)30215-7)
 20. Attia S, Egger M, Müller M, Zwahlen M, Low N. 2009 Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* **23**, 1397–1404. (doi:10.1097/QAD.0b013e3283282b7dca)
 21. Montaner JS, Hogg R, Wood E, Kerr T, Tyndall M, Levy AR, Harrigan PR. 2006 The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* **368**, 531–536. (doi:10.1016/S0140-6736(06)69162-9)
 22. Beyrer C *et al.* 2015 An action agenda for HIV and sex workers. *Lancet* **385**, 287–301. (doi:10.1016/S0140-6736(14)60933-8)
 23. Pastor-Satorras R, Castellano C, Van Mieghem P, Vespignani A. 2015 Epidemic processes in complex networks. *Rev. Mod. Phys.* **87**, 925–979. (doi:10.1103/RevModPhys.87.925)
 24. Cohen R, Havlin S, ben Avraham D. 2003 Efficient immunization strategies for computer networks and populations. *Phys. Rev. Lett.* **91**, 247901. (doi:10.1103/PhysRevLett.91.247901)
 25. Nian F, Wang X. 2010 Efficient immunization strategies on complex networks. *J. Theor. Biol.* **264**, 77–83. (doi:10.1016/j.jtbi.2010.01.007)
 26. Chen Y, Paul G, Havlin S, Liljeros F, Stanley HE. 2008 Finding a better immunization strategy. *Phys. Rev. Lett.* **101**, 058701. (doi:10.1103/PhysRevLett.101.058701)
 27. Schneider CM, Mihaljev T, Havlin S, Herrmann HJ. 2011 Suppressing epidemics with a limited amount of immunization units. *Phys. Rev. E* **84**, 061911. (doi:10.1103/PhysRevE.84.061911)
 28. Chen S, Lu X. 2017 An immunization strategy for hidden populations. *Sci. Rep.* **7**, 3268. (doi:10.1038/s41598-017-03379-4)
 29. Gomez GB, Borquez A, Case KK, Wheelock A, Vassall A, Hankins C. 2013 The cost and impact of scaling up pre-exposure prophylaxis for HIV prevention: a systematic review of cost-effectiveness modelling studies. *PLoS Med.* **10**, 1–16. (doi:10.1371/journal.pmed.1001401)
 30. Pretorius C, Stover J, Bollinger L, Bacaër N, Williams B. 2010 Evaluating the cost-effectiveness of pre-exposure prophylaxis (PrEP) and its impact on HIV-1 transmission in South Africa. *PLoS ONE* **5**, 1–10. (doi:10.1371/journal.pone.0013646)
 31. Vissers DC, Voeten HA, Nagelkerke NJ, Habbema JDF, de Vlas SJ. 2008 The impact of pre-exposure prophylaxis (PrEP) on HIV epidemics in Africa and India: a simulation study. *PLoS ONE* **3**, 1–7. (doi:10.1371/journal.pone.0002077)
 32. Sarkar S, Corso P, Ebrahim-Zadeh S, Kim P, Charania S, Wall K. 2019 Cost-effectiveness of HIV prevention interventions in sub-Saharan Africa: a systematic review. *EclinicalMedicine* **10**, 10–31. (doi:10.1016/j.eclinm.2019.04.006)
 33. Williams B, MacPhail C, Campbell C, Taljaard D, Gouws E, Moema S, Mzaidume Z, Rasego B. 2000 The Carletonville-Mosuthumpilo project: limiting transmission of HIV through community-based interventions. *S. Afr. J. Sci.* **96**, 351–359. (doi:10.31899/hiv2.1032)
 34. Voeten HACM, Egesah OB, Varkevisser CM, Habbema JDF. 2007 Female sex workers and unsafe sex in urban and rural Nyanza, Kenya: regular partners may contribute more to HIV transmission than clients. *Trop. Med. Int. Health* **12**, 174–182. (doi:10.1111/j.1365-3156.2006.01776.x)
 35. Ferguson AG, Morris CN, Kariuki CW. 2006 Using diaries to measure parameters of transactional sex: an example from the transAfrica highway in Kenya. *Cult. Health Sex.* **8**, 175–185. (doi:10.1080/13691050600665006)
 36. Morris CN, Ferguson AG. 2006 Estimation of the sexual transmission of HIV in Kenya and Uganda on the trans-Africa highway: the continuing role for prevention in high risk groups. *Sex. Transm. Infect.* **82**, 368–371. (doi:10.1136/sti.2006.020933)
 37. Ramjee G, Gouws E. 2002 Prevalence of HIV among truck drivers visiting sex workers in KwaZulu-Natal, South Africa. *Sex. Transm. Dis.* **29**, 44–49. (doi:10.1097/00007435-200201000-00008)
 38. Matovu JKB, Ssebadduka BN. 2012 Sexual risk behaviours, condom use and sexually transmitted infection treatment-seeking behaviours among female sex workers and truck drivers in Uganda. *Int. J. STD. AIDS* **23**, 267–273. (doi:10.1258/ijisa.2011.011313)
 39. Campbell C. 2003 *Letting them die: why HIV/AIDS intervention programmes fail*. Bloomington, IN: Indiana University Press.
 40. Lurie MN, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sturm AW, Sweat MD, Gittelsohn J, Karim SSA. 2003 The impact of migration on HIV-1 transmission in South Africa: a study of migrant and nonmigrant men and their partners. *Sex. Trans. Dis.* **30**, 149–156. (doi:10.1097/00007435-200302000-00011)
 41. Bradshaw D *et al.* 2003 Initial burden of disease estimates for South Africa, 2000. *S. Afr. Med. J.* **93**, 682–688.
 42. Jewkes RK, Dunkle K, Nduna M, Shai N. 2010 Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. *Lancet* **376**, 41–48. (doi:10.1016/S0140-6736(10)60548-X)

43. Wawer MJ *et al.* 2005 Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J. Infect. Dis.* **191**, 1403–1409. (doi:10.1086/jid.2005.191.issue-9)
44. Coffin JM, Hughes SH, Varmus HE. 1997 *Retroviruses*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.
45. Dorrington R, Bourne D, Bradshaw D, Laubscher R, Timæus IM. 2001 *The impact of HIV/AIDS on adult mortality in South Africa*. Cape Town, South Africa: Medical Research Council.
46. Cremin I *et al.* 2017 PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study. *Lancet HIV*. **4**, e214–e222. (doi:10.1016/S2352-3018(17)30021-8)
47. Graham CA, Catania JA, Brand R, Duong T, Canchola JA. 2003 Recalling sexual behavior: a methodological analysis of memory recall bias via interview using the diary as the gold standard. *J. Sex Res.* **40**, 325–332. (doi:10.1080/00224490209552198)
48. Marrazzo JM *et al.* 2015 Tenofovir-based preexposure prophylaxis for HIV infection among African women. *New England J. Med.* **372**, 509–518. (doi:10.1056/NEJMoa1402269)
49. Corneli AL *et al.* 2014 FEM-PrEP: adherence patterns and factors associated with adherence to a daily oral study product for pre-exposure prophylaxis. *J. Acquir. Immune Defic. Syndr.* **66**, 324. (doi:10.1097/QAI.000000000000158)
50. Baeten JM *et al.* 2012 Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *England J. Med.* **367**, 399–410. (doi:10.1056/NEJMoa1108524)
51. Van Damme L *et al.* 2012 Preexposure prophylaxis for HIV infection among African women. *New England J. Med.* **367**, 411–422. (doi:10.1056/NEJMoa1202614)
52. Walensky RP, Jacobsen MM, Bekker LG, Parker RA, Wood R, Resch SC, Horstman NK, Freedberg KA, Paltiel AD. 2015 Potential clinical and economic value of long-acting pre-exposure prophylaxis for South African Women at high-risk for HIV infection. *J. Infect. Dis.* **213**, 1523–1531. (doi:10.1093/infdis/jiv523)
53. Wang C, Hawes SE, Gaye A, Sow PS, Ndoye I, Manhart LE, Wald A, Critchlow CW, Kiviat NB. 2007 HIV prevalence, previous HIV testing, and condom use with clients and regular partners among Senegalese commercial sex workers. *Sex. Trans. Infect.* **83**, 534–540. (doi:10.1136/sti.2007.027151)
54. Peitzmeier S, Mason K, Ceesay N, Diouf D, Drame F, Loum J, Baral S. 2014 A cross-sectional evaluation of the prevalence and associations of HIV among female sex workers in the Gambia. *Int. J. STD AIDS* **25**, 244–252. (doi:10.1177/0956462413498858)
55. Cremin I, Morales F, Jewell BL, O'Reilly KR, Hallett TB. 2015 Seasonal PrEP for partners of migrant miners in southern Mozambique: a highly focused PrEP intervention. *J. Int. AIDS Soc.* **18**, 19946. (doi:10.7448/IAS.18.4.19946)
56. Leung KY, Kretzschmar M. 2015 Concurrency can drive an HIV epidemic by moving R0 across the epidemic threshold. *AIDS* **29**, 1097–1103. (doi:10.1097/QAD.0000000000000676)