CURRENT OPINION

Concentrated HIV subepidemics in generalized epidemic settings

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Purpose of review
A relatively neglected topic to date has been the occurrence of concentrated epidemics within generalized epidemic settings and the potential role of targeted interventions in such settings. We review recent studies in high-risk groups as well as findings relating to geographical heterogeneity and the potential for targeting 'high-transmission zones' in the 10 countries with highest HIV prevalence.

Recent findings
Our review of recent studies confirmed earlier findings that, even in the context of generalized epidemics, MSM have a substantially higher prevalence than the general population. Estimates of prevalence of HIV among people who inject drugs (PWID) in sub-Saharan African countries are rarely available and, when they are, often outdated. We identified recent studies of sex workers in Kenya and Uganda. In all three cases – MSM, PWID, and sex workers – HIV prevalence estimates are mostly based on convenience. Moreover, good estimates of the total size of these populations are not available. Our review of recent studies of high-risk populations defined on the basis of geography showed high levels of both new and existing infections in Kenya (slums), South Africa (peri-urban communities), and Uganda (fishing villages).

Summary
Recent empirical findings combined with evidence from phylogenetic studies and supported by mathematical models provide a clear rationale for testing the feasibility, acceptability, and effectiveness of targeted HIV prevention approaches in hyperendemic populations to supplement measures aimed at the general population.

Keywords
HIV epidemiology, incidence, key populations, spatial analysis, surveillance

INTRODUCTION

Globally, 34.0 million people were estimated to be living with HIV at the end of 2011 [1]. Sub-Saharan Africa remains the most severely affected region, with nearly one in every 20 adults (5%) living with HIV and accounting for nearly 70% of the people living with HIV worldwide. Although some estimates suggest that the rate of new infections is declining in many African settings, HIV incidence remains unacceptably high [1]. Hence, meaningful reductions in HIV incidence in countries worst affected by the epidemic will require more efficient strategies and better use of declining levels of HIV funding. One of the striking features of the HIV epidemic has been the remarkable variation in disease burden not only across population subgroups [2], regions and, countries [1,3,4], but also at a subnational level between provinces [5], districts [6,7], subdistricts and within subdistricts [8–12].

Epidemics are said to be 'concentrated' if transmission occurs largely in clearly defined vulnerable groups such as sex workers, MSM, and people who inject drugs (PWID). Conversely, epidemics are termed 'generalized' if transmission is sustained by sexual behavior in the general population (typically defined on the basis of population prevalence

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KEY POINTS

- Concentrated subepidemics exist within all generalized epidemic contexts.

- Our review of the recent literature combined with empirical evidence from phylogenetic studies and supported by mathematical models suggests that targeted HIV prevention approaches aimed at specific geographic localities as well as key high-risk groups could be effective in generalized epidemic settings as part of an overall combination approach.

- The empirical estimation of population sizes of hidden high-risk groups will be critical. There is currently a knowledge gap on how best to sample and estimate the population sizes of these risk groups in a representative way.

- The feasibility, acceptability, effectiveness, and cost–effectiveness of prevention interventions for most-at-risk groups needs to be established within different cultural and institutional contexts in sub-Saharan Africa. Rigorous impact evaluation of such interventions should accompany the scaling up of targeted interventions for most-at-risk groups.

of >1%) and would likely persist despite effective programs for vulnerable groups. In general, epidemics in Latin America, the Middle East, Europe, and Asia are described as 'concentrated' whereas the epidemics in most of southern and parts of eastern Africa are termed 'generalized' [13]. In generalized epidemics settings, some form of intervention needs to be provided to the general population, whereas in a concentrated epidemic context, the goal is to achieve a high level of coverage of interventions in the most vulnerable groups.

A neglected topic to date has been the occurrence of concentrated epidemics in generalized epidemic settings and the potential role of targeted interventions to supplement measures aimed at the general population in such settings. Even in these so-called hyperendemic communities, targeting efforts at settings in which HIV transmission is most intense is crucial. However, in the context of a severe generalized African epidemic, the value of targeted prevention interventions has seldom been considered. In some countries, notably Kenya and South Africa, substantial numbers of new infections, are estimated to occur among key populations at higher risk of infection, including sex workers and their clients, PWID, MSM, and the prison population in Kenya. These groups are estimated to contribute jointly to about 33% of new infections in Kenya and 26% in South Africa [14]. Despite the stage and severity of the epidemic in many African settings, recent work has revealed the remarkable variation in HIV prevalence and incidence across relatively small areas and within relatively homogenous populations [8–12]. These results have challenged the paradigm of a ubiquitous 'generalized' epidemic in many countries. Given limited resources, clustering of infections in specific localities or population groups can decrease the average effectiveness of population-based prevention approaches. Conversely, targeted interventions are likely to lead to better prevention results for given resources, where HIV incidence clusters geographically or within subgroups [15■■]. Indeed, mathematical models predict that focused interventions have the potential to reduce HIV transmission in the wider community across low- and high-prevalence regions [16■■]. Thus, there is increasing recognition of opportunities for targeting of interventions to increase the effectiveness and cost–effectiveness of HIV prevention interventions supported by both theory and recent empirical findings. At the same time, many critical questions remain. Can the most-at-risk populations be effectively reached? Which interventions will be acceptable and attractive to different subpopulations? What are the costs of targeted interventions requiring potentially expensive approaches to identify and engage with most-at-risk populations?

In this article, we sought to review findings from work published since 2012 on concentrated subepidemics in generalized epidemic settings. We selected the 10 highest prevalence countries in the world where prevalence in the general population was more than 5% [1] (Kenya, Lesotho, Malawi, Mozambique, South Africa, Swaziland, Tanzania, Uganda, Zambia, and Zimbabwe) and focussed our review on recent studies in three high-risk groups (sex worker, MSM, and PWID) as well as findings relating to geographical heterogeneity and the potential for targeting 'hot-spots' or 'high-transmission zones'. We further review recent findings from phylogenetic work to assess our knowledge regarding the extent to which transmission of HIV in the general population in these generalized epidemic settings is driven by contact with members of concentrated subepidemics.

MSM

Attention to MSM within generalized epidemics is relatively recent [17]. Studies published over the past 2 years have confirmed earlier findings that, even in the context of generalized epidemics, MSM have higher prevalence than the general populations [18]. Two South African studies recorded HIV prevalence of 27 and 11% among MSM as

compared with 17 and 5% in men who had sex with women only [19,20]. Incidence of HIV among MSM has been found to be notably higher than that of other high-risk populations and the general population (Table 1). In Kenya, incidence of HIV among MSM was 6/100 person-years (PY) in Kilifi and 10/100 PY in Nairobi [22]. Another study conducted in coastal Kenya found an HIV-1 incidence of 6/100 PY among men who have sex with men and women and 35/100 PY among MSM exclusively [23].

Experience of stigma and discrimination by MSM could also exacerbate an already efficient transmission by contributing to high-risk behaviors [24]. For example, internalized homophobia has been associated with an increased risk of unprotected anal intercourse [25] and higher level of HIV misinformation [26], whereas homophobic abuse was also significantly associated with being HIV infected [21,27]. Further, stigma and discrimination could also increase barriers to testing HIV [28–31] and adherence to antiretroviral therapy (ART) [32].

Few studies have recently evaluated interventions for MSM in sub-Saharan countries, but they mostly focused on their acceptability [33■,34] or on peer-outreach activities [35]. Qualitative interviews conducted in Kenya among MSM highlighted lack of health information, safe lubricants, condoms, and MSM-friendly health services as unmet needs [36]. Interviews with service providers also emphasized the lack of appropriate training to effectively deliver MSM-specific risk reduction counseling [37]. Interventions targeted at MSM in sub-Saharan Africa could face additional challenges that would limit their effectiveness, however, because such behaviors are often criminalized, culturally taboo, or because different high-risk groups often overlap [38,39].

PEOPLE WHO INJECT DRUGS

Estimates of prevalence of HIV among PWID in sub-Saharan countries are rarely available and, when they are, often outdated. This absence of good data is surprising because the total size of this high-risk population is potentially very large, with an estimated 1.7 million heroin users in Africa [40]. National key informants with expertise in PWID and HIV estimated that prevalence of HIV among PWID was 36–43% in Kenya and 42% in Tanzania (Table 2) [41]. In Dar es Salaam (Tanzania), PWID recruited through snowball and targeted sampling were found to have a prevalence of HIV (35%) [42] much higher than that recorded for noninjecting drug users (12%). Further, there is high overlap between female PWID and sex work in Dar es Salaam, with an estimated 31% of female PWID

engaging in commercial sex work as compared with less than 1% for men [43].

Very little advances have been made to scale up needle and syringe programs (NSPs) and opioid substitution therapy (OST) in sub-Saharan Africa despite the proven effectiveness of such interventions in other parts of the world [44■]. Important barriers to implementation include the criminalization of drug dependency and needle possession in some jurisdictions, and explicit policies against OST [42,44■]. Tanzania is currently at the forefront of harm reduction in sub-Saharan Africa with its recent implementation of a first NSP site, medication-assisted treatment, and 'sober houses' [41,45] – mostly in the urban center of Dar es Salaam. Given that PWID have been described as the high-risk group with the largest unmet needs [46], there are important opportunities to reduce HIV burden among PWID through the implementation of evidence-based strategies.

SEX WORKERS

Sex work was an early driver of many epidemics in sub-Saharan Africa [47]. A recent study estimates that 18% of all HIV infections in the general female population (aged 15+) are attributable to female sex work in sub-Saharan Africa [48]. Many African countries with generalized epidemics have documented HIV prevalence levels three to 10 times higher among populations of sex workers, compared with the general population. In 26 countries with medium and high background HIV prevalence, 31% (95% confidence interval, CI: 30–31) of sex workers were HIV-positive and the odds ratio for infection was 12 (95% CI: 9–15) [49■■]. The authors estimate the pooled HIV prevalence among female sex workers in sub-Saharan Africa is 37%.

We identified three recent studies of sex worker populations from Kenya and Uganda (Table 3). HIV prevalence was highest among sex workers in Kisumu at nearly 57%, considerably less than 75% prevalence identified in the same location in 1997. These data suggest an urgent need to scale up access to quality HIV prevention programs. The largest source of data on levels of infection among female sex workers in Africa comes from Kenya where in 2010, the Kenyan National AIDS and STI Control Program (NASCOP) developed a set of National Guidelines for HIV and STI Programs for sex workers [52]. These guidelines were developed in response to the Kenya National HIV Strategic Plan, which identified female sex workers as a population who are most at risk of infection as well as having limited access to health services. Sex workers are a particularly vulnerable population in many African

Table 1. Review of studies published since 2012 that assessed either prevalence or incidence of HIV among MSM in the 10 countries in sub-Saharan Africa with the highest HIV burden

Authors	Country (city or region)	Sample	Design	Sample size	Outcome	Results
Hladik et al. [21]	Uganda (Kampala)	MSM	Respondent-driven sampling	300	HIV prevalence	13.7% (95% CI: 7.9–20.1%)
Dunkle et al. [19]	South Africa (Eastern Cape and KwaZulu-Natal provinces)	Men from eligible households	Cross-sectional	1220	HIV prevalence	27.4% (95% CI: 17.6–40.0%) as compared with 17% (14–20%) among men who reported nonmale-on-male contact
Eaton et al. [20]	South Africa (Cape Town)	Men who have sex with men and women and men who have sex with women	Convenience sample	1203	Self-reported HIV prevalence	10.5% of MSMW versus 4.6% for MSW
Price et al. [22]	Kenya (Kilifi and Nairobi) and South Africa (Cape Town)	Volunteers	Convenience sample of volunteers	327	HIV incidence	6.8 per 100 person-years (95% CI: 4.9–9.2).
Sanders et al. [23]	Coastal region of Kenya	MSM, men who have sex with men and women, and MSM exclusively	Combination of convenience sample and respondent-driven sampling	449 MSM	HIV incidence	MSM overall: 8.6 per 100 person-years (95% CI: 6.7–11.0)
				372 MSMW		MSMW: 5.8 per 100 person-years (95% CI: 4.2–7.9)
				77 MSME		MSM: 35.2 per 100 person-years (95% CI: 23.8–52.1)

CI, confidence interval.

Table 2. Review of studies published since 2012 that assessed either prevalence or incidence of HIV among people who inject drugs in 10 countries of sub-Saharan Africa with the highest HIV burden

Authors	Country (city or region)	Sample	Design	Sample size	Outcome	Results
Petersen *et al.* [41]	Kenya	Person who inject drugs (PWID)	Information collected from key national contacts who were experts in IDU and HIV (supplemented with literature search)	Not applicable	HIV prevalence	Kenya (range): 36.0–43.0%
	Tanzania					Tanzania: 42.0%
Bowring *et al.* [42]	Tanzania	People who inject drugs (PWID) and non-injecting drug users (NIDU)	Targeted sampling and snowball	PWID: 267	HIV prevalence	PWID: 34.8% (95% CI: 29.1–40.9%)
				NIDU: 19		NIDU: 11.7% (7.2–17.6%)

countries and hence careful consideration of the environments in which sex workers operate is needed [49■■]. In many African countries, a large proportion of sex workers are also migrants placing them at even greater risk of infection. For example, in a survey of 1653 female sex workers in Johannesburg Rustenburg and Cape Town (South Africa), 85% of sex workers were migrants and 46% were cross-border migrants [53].

GEOGRAPHICAL 'RISK SPACES'

Our review of recent studies of high-risk populations defined on the basis of geography showed high levels of both new and existing infections in Kenya (slums), South Africa (peri-urban communities), and Uganda (fishing villages; Table 4). For example, a study among residents of informal peri-urban settlements showed an incidence of 15/100 PY (95% CI: 10–20) [56]. One of the main challenges of a strategy incorporating targeting of high-risk individuals

remains the identification of such individuals. The membership of a 'risk group' is highly dynamic with many individuals moving into and out of high risk groups over the course of their sexual lives making targeting problematic [59]. However, notwithstanding this, one of the most stable aspects of such groupings appears to be their geography [60]. Indeed, the notion of a 'core group' in sexually transmitted diseases evolved from studies showing geographic clustering of infections [61]. This concept of 'risk places' holds for HIV in many generalized epidemic settings as well [62]. In fact, far from experiencing 'epidemic burn-out' as the epidemic has progressed, studies have consistently documented examples of 'risk spaces' that are characterized by substantially higher levels of new and existing infections in comparison to the surrounding populations over a duration of 15 years or more – for example, informal settlements near National Roads in KwaZulu-Natal, South Africa [10,63] and fishing villages in rural Uganda [58,64]. In the

Table 3. Review of studies published since 2012 that assessed either prevalence or incidence of HIV among sex workers in the 10 countries in sub-Saharan Africa with the highest HIV burden[a]

Authors	Country (city or region)	Sample	Design	Sample size	Outcome	Results
Vandepitte *et al.* [50]	Uganda (Kampala)	Female sex workers	Cross-sectional	1025	HIV prevalence	36.9% (95% CI: 34–40)
Baral *et al.* [49■■]	Kenya (Nairobi)	Female sex workers	Meta-analysis of nine studies	7544	HIV prevalence	45.1% (95% CI: 44.0–46.2)
Vandenhoudt *et al.* [51■]	Kenya (Kisumu)	Female sex workers	Cross-sectional	481	HIV prevalence	56.5% (95% CI: 52.0–61.6).

CI, confidence interval.
[a]An additional study [22] was not included due to the small numbers of sex workers included for HIV incidence measurement.

Table 4. Review of studies published since 2012 that assessed either prevalence or incidence of HIV among geographically defined 'risk spaces' in 10 countries in sub-Saharan Africa with the highest HIV burden

Authors	Country (city or region)	Sample	Design	Sample size	Outcome	Results
Madise et al. [54]	Kenya (Nairobi)	Slum residents	Cross-sectional data from the Kenya Demographic and Health Survey	3048	HIV prevalence	11.8% (95% CI: 10.7–13.0) comparative estimates for nonslum urban residents was 5.3% and rural residents was 6%
Kimani et al. [55]	Kenya (Nairobi)	Slum residents	Cross-sectional population-based survey nested in an ongoing Demographic Surveillance System in two urban slums	2721	HIV prevalence	11.5% (95% CI: 10.3–12.7)
Nel et al. [56]	South Africa (Ladysmith) South Africa (Edenvale) South Africa (Pinetown)	Peri-urban residents	Sexually active women 18–35 years	2773	HIV prevalence	42.0% (95% CI: 38.5–45.5) in Ladysmith, 46.1% in Edendale (95% CI: 43.1–49.1), and 41.3% (95% CI: 38.0–44.6) in Pinetown
				900	HIV incidence	14.8/100 person-years (PY) (95% CI: 9.7–19.8) in Ladysmith, 6.3/100 PY (95% CI: 3.2–9.4) in Edendale, and 7.2/100 PY (95% CI: 3.7–10.7) in Pinetown
Opio et al. [57]	Uganda (Lake Victoria Basin)	Residents of fishing villages	A cross-sectional survey of 46 fishing communities was conducted in respondents aged 15–59 years	911	HIV prevalence	Men = 25.5% (95% CI: 19.4–31.5) Women = 20.4% (95% CI: 15.6–25.2)
Seeley et al. [58]	Uganda (Lake Victoria Basin)	Residents of fishing villages	Prospective cohort study	1000	HIV incidence	Overall incidence rate of 4.9 (95% CI: 3.8–6.3) per 100 PY.

CI, confidence interval; PY, person-years.

absence of targeted interventions, these differences are likely to persist into the future. The disproportionately large burden of HIV in urban slums/peri-urban informal settlements has received minimal attention to date [65]. Research from South Africa and some other African countries shows that the HIV prevalence in informal settlements or slum populations is double (or more) that in the nonslum population of the same city [66]. In our population-based HIV surveillance site in northern KwaZulu-Natal South Africa, for example, one out of three seroconversions observed over a 7-year period took place in peri-urban communities located along the National Road (where both HIV incidence and population density are high) [11]. These communities occupy less than 6% of the study area. These findings imply that targeting the easy-to-reach peri-urban communities in close proximity to major transport routes – a strategy considered in early stages of the epidemic – could be highly cost-effective in reaching large proportions of people at risk of HIV acquisition in late-stage, 'generalized' epidemics [67]. One advantage of geographic targeting is that it is comparatively easy to execute. Targeting of 'hidden populations' may be implicit in geographic targeting because particular most-at-risk populations may cluster in certain zones. Future research needs to establish the differential effectiveness and cost–effectiveness of geographic HIV intervention targeting compared with other targeting approaches, such as through social networks or particular facilities.

PHYLOGENETIC ANALYSES

Phylogenetic studies can reveal the extent to which the transmission of HIV in the general population is driven by contact with members of concentrated subepidemics and speak to the potential for any intervention directed at such groups to extend beyond the high-risk subpopulations.

The increase of transport connectivity and mobile populations may explain the hyperendemic outbreaks experienced in eastern and southern Africa [68]. In a study in one community in rural coastal Kenya, multiple subtypes and recombinant forms were identified, suggesting that communities with high transport connectivity may have local HIV epidemics supported by a significant proportion of transmissions from outside communities [69].

Recently, molecular epidemiology studies were combined with detailed demographic information in order to identify subpopulations driving HIV subepidemics in Uganda. Transmission clusters combined with participant life histories revealed a high degree of sexual partner mixing in a high-incidence cohort in Ugandan fishing communities as only two of the five transmission clusters were from sexual partners [70]. Another study in Uganda that combined partnership histories and phylogenetic analysis of female sex workers identified partial sexual networks and multiple infections, suggesting mixing in these sex workers and their clients [71]. In the same country, another study suggested that the presence of super transmitters in early HIV infection contributed a disproportionate number of transmissions in a low-risk rural cohort [72]. These kinds of studies are currently being expanded to other large demographic sites in generalized epidemics in Africa, for example, the Mochudi treatment as prevention (TasP) trial in Botswana and TasP trial at the Africa Centre in rural South Africa [73], which has started to produce large molecular epidemiology datasets.

Evidence from Kenya shows that 34% of male sex workers who sell sex to men also had sex with a woman in the previous 30 days [74]. The same pattern was observed in Tanzania and South Africa, where 37 and 50% of MSM reported having had a female sexual partner, respectively [30,75]. Interventions targeting MSM, thus, have the potential to yield benefits for both the MSM and the heterosexual community, depending on the extent with which the two sexual communities are linked. Despite the potential contribution of MSM to HIV transmission in generalized epidemics, few phylogenetic studies have examined to which extent transmission is behaviorally segregated between MSM and the general population. A recent study conducted in coastal Kenya, using convenience sample of 84 MSM, suggested a weak link between MSM and the general population [76].

DISCUSSION

In reality, the HIV epidemic is composed of multiple subepidemics that make up the composite epidemic in any given population. Concentrated subepidemics exist within all generalized epidemic contexts, and addressing the subpopulations within these constituent epidemics will likely be key to substantially reducing population-level incidence. Our article has highlighted recent studies from hyperendemic countries with generalized epidemics, documenting concentrated subepidemics among most-at-risk population subgroups as well as by geographical 'risk spaces' [60]. These studies provide further clear examples of clustering of infections in subpopulations and geographies and imply that targeted prevention strategies could be effective in these hyperendemic settings as a supplement to

measures aimed at the general population. Although it is true that in these populations the HIV epidemic can be sustained by the general-population (apart from the high-risk populations), mathematical models show that maximum reductions in HIV incidence can be achieved by incorporating interventions that specifically target high-risk populations [16■■]. The modeling results are supported by our review of recent phylogenetic analyses, which have shown in countries such as Uganda that infections generated within these concentrated subepidemics help fuel the rate of new infections in the general population. By implication, large reductions in incidence among the general population cannot be achieved without addressing the high levels of intra-transmission and extra-transmission within these risk groups or risk spaces.

Some countries like Kenya have introduced intervention programs that focus on most-at-risk groups, such as sex workers [52,77]. However, few countries in Africa have explicitly adopted a geographically focused approach to HIV prevention targeting high-risk settings such as adopted by India [78]. This is set to change in the very near future. The new funding model of the Global Fund, for example, aims to allocate funding for HIV within countries on the basis of identification of geographic areas of highest transmission [79]. A forthcoming report by UNAIDS emphasizes the potential gains that might be achieved if countries took a more focussed approach at dealing with their HIV epidemic from identifying the geographic location where more new infections are occurring to focusing services toward key populations at increased risk to HIV [80]. The report provides examples from numerous countries around the world and suggests steps that countries should take to generate a more efficient and effective HIV response. The newly devised President's Emergency Fund for AIDS Relief (PEPFAR) strategy for South Africa recognizes the tremendous heterogeneity in the distribution of HIV outcomes at the subnational and local levels [81]. The strategy allocates resources on the basis of a geographic prioritization of districts and focuses on those geographic regions and localities where most transmission is occurring and recognizes that the key populations implicated in these subepidemics are vital to achieving large reductions in population-level incidence.

The allocation of resources to target some high-risk groups could be fraught with difficulties due to the considerable uncertainty in the estimation of the underlying population sizes of sex workers, MSM, and PWID. One reason for the lack of good data on these populations in sub-Saharan African

countries is that stigma and discrimination make it difficult to identify them in population-based samples, such as in national representative household surveys or Health and Demographic Surveillance sites. In this sense, sex workers, MSM, and PWID remain largely 'hidden populations' [82,83]. Accurate estimation of the population size of such high-risk groups should be undertaken to ensure that sufficient resources are allocated to meet the HIV intervention needs in this region [82,84]. Another important knowledge gap is the cost–effectiveness of targeted intervention strategies to these 'hidden populations'. On the one hand, targeting can focus on people who can benefit most from an intervention, potentially increasing the effectiveness per intervention dollar. On the other hand, most-at-risk populations may also be most resistant to interventions and they may be difficult to identify and engage with, potentially reducing the intervention cost–effectiveness.

RESEARCH AGENDA

In this review we have highlighted number of priority research areas. The first is the need to identify localities where disproportionately large numbers of transmissions are taking place and to characterize these risk spaces using methodologies such as the 'place-based' method [62]. At a country level, there is a need to ensure that districts with overall high levels of infection receive a strong intervention response such as been adopted by India [78] (country districts are graded A–D. Grade 'A' districts receive the full intervention response, whereas 'D' districts only receive some elements of the package) and will be used by PEPFAR in South Africa [80]. At a more local scale, there is a clear and urgent need to focus on informal settlements in urban slums and peri-urban populations and to assess what combination of interventions best work in these communities. In comparison to the other risk groups defined on the basis of behavior, not only are these communities at overall high risk of infection, contain large populations and are relatively easy to access, but also contain higher numbers of individuals in other high-risk groups such as sex workers. Hence, a systematic enumeration and characterization of populations within these communities is vital.

Second, the empirical estimation of population sizes of hidden high-risk groups such as MSM and PWID is critical. Specifically, there is a knowledge gap on how best to sample and estimate the population sizes of these risk groups in a representative way. The respective robustness of respondent-driven sampling, snowballing, and capture-recapture

methods should be assessed. Obtaining reliable and representative population size and HIV prevalence estimates will help raise awareness, allocate sufficient resources, and guide prevention efforts.

Third, conducting phylogenetic studies assessing the impact of high-risk groups and risk spaces on overall transmission within generalized epidemics should be an important research focus. Such information would be crucial to inform mathematical models that could be used to estimate the impact of interventions targeted at risk groups on overall HIV epidemic dynamics and the cost–effectiveness of such prevention approaches. A recent review of mathematical models investigating the impact of interventions aimed at female sex workers highlighted the fact that the preventive potential of this type of intervention has been underresearched in high prevalence settings [16▪▪]. Future research should focus on the development of spatially explicit, individual-based models of HIV transmission that allow for the highly uneven distribution of HIV transmissions across risk spaces as well as risk groups.

Fourth, formative research with people belonging to risk groups on the social and cultural acceptability of interventions is crucially important to ensure rapid uptake, effectiveness, and sustainability of interventions. Such studies should be complemented by conducting formative research in different countries on political, cultural, and structural constraints for interventions targeted at these risk groups, which are also commonly stigmatized, discriminated against, and abused.

Finally, the effectiveness and cost–effectiveness of prevention for most-at-risk groups needs to be established within the context of different cultural and institutional settings in sub-Saharan Africa. Rigorous impact evaluation of such interventions should, thus, accompany the scaling up of targeted interventions for high-risk groups. Demonstrating impact could also help improve acceptability of interventions and alleviate the structural constraints faced by some of the potential interventions.

CONCLUSION

The occurrence of concentrated epidemics in generalized epidemic settings and the potential role of targeted interventions to supplement measures aimed at the general population in such settings has been a neglected topic to date. Our review of the recent literature combined with empirical evidence from phylogenetic studies and supported by mathematical models suggests that targeted HIV prevention approaches aimed at specific geographic localities as well as other key high-risk groups could be effective in generalized epidemic settings as part of an overall combination approach.

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