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A Call to Action for Concentrated HIV Epidemics

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INTRODUCTION

As the HIV community attempts to define what is meant by terms like “The End of the AIDS Epidemic,” or the goal of “An AIDS Free Generation,” as articulated by the U.S. Government [1], the relevance of accurate, granular, and precise epidemiologic characterization of HIV prevalence, incidence trends, and other key indicators has only increased. The level or declining resource base for global HIV surveillance, prevention, treatment, and care mandates strategic and much more nuanced use of resources where they will matter most. The current conceptualization of geographic, geospatial, ‘hot spot,’ or high transmission and burden zones of HIV is one approach aimed at focusing resources to where HIV is currently spreading, where high proportions of people living with HIV infection remain untested and untreated, or where sub-epidemics, often among those at risk for both HIV infection and lack of access to services, persist [2]. A sea change in thinking is underway, and is long overdue, in responding to what have long been characterized as concentrated epidemics [3]. As the papers in this issue demonstrate, this understanding is also changing the way we think about the role of concentrated epidemics within generalized ones. We can no longer afford broad and low efficacy or inefficacious campaigns aimed at “youth” or “reproductive aged adults” when relatively small numbers of people, largely excluded from such programs, are those most in need of services, and of services tailored to their actual risks, HIV treatment needs, and lived experiences.

The last several years have seen heartening decreases in HIV incidence in many of the world’s (relatively few) generalized epidemic contexts [4]. With a handful of exceptions,

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these epidemics have been limited to Southern and Eastern Sub-Saharan Africa, and they have been devastating. Few epidemiologists predicted that we would see the impressive gains in HIV control now being reported from many of these hardest hit regions. Fewer still would have predicted that in 2013 we would be seeing so much success in control of these primarily sexually and perinatally driven epidemics, and so little in the concentrated epidemics. The latter involve many fewer people, are much more likely to be focused in urban areas, and have been primary foci of HIV research, programs, and community efforts since the initial identification of HIV/AIDS in the 1980s. Yet this is what the papers in this issue clearly demonstrate. That over 60% of new HIV infections in the U.S. in 2011 (the year for which we have the most current data from the U.S. CDC) [5] should be occurring among the relatively small percentage of the population who are men who have sex with men [6] is just one example among all too many of the persistence of these concentrated epidemics [7], persistence which has continued despite the development and rollout of effective antiretroviral therapy (ART) in much of the world.

CONCENTRATED EPIDEMICS

Outside East and Southern Africa, HIV in most of the world is predominately found in concentrated epidemics—with the highest burdens among persons and groups long associated with high HIV disease burdens: men who have sex with men (MSM), sex workers of all genders, people who inject drugs (PWID), transgender women (TGW), and some specific risk groups such as fishing communities in Uganda and rural blood donors in China, for whom quite specific outbreaks have been identified [7–14]. De Boni, Veloso & Grinsztejn (this issue), reviewed the epidemiology of HIV in Latin American and the Caribbean, and found the region is remains largely one of concentrated epidemics in MSM, TGW, and female sex workers (FSWs) in a few sites. There is striking consistency across these epidemics—and a disturbingly low reported rate of spending (just 4% regionally) of prevention resources on these populations [15].

In West Africa pooled HIV prevalence estimates for FSWs are near 35–40% in several countries [8] and individual studies with MSM show prevalence ranging from 10% in Gambia [16] to 50% in Cote d'Ivoire [17]. Data on PWID are generally lacking, but the use of heroin has increased in West Africa as that area has emerged as a major trafficking route [18]. Djomand and Quaye (this issue) argue that the laws criminalizing sex work and same sex practices affect the uptake of prevention and treatment services and that the engagement of key stakeholders will be essential for countering these concentrated epidemics in West Africa.

Although only 4 of 23 Middle East and North Africa countries have surveillance systems sufficient for tracking the HIV epidemic [19], a growing number of point-prevalence and other studies are helping to fill in the knowledge gaps. With the exception of Djibouti and parts of Somalia, HIV prevalence among general populations of Middle East and North Africa countries remains low [20], but, as discussed by Mumtaz, Riedner, and Abu-Raddad (this issue), concentrated epidemics exist to varying degrees within key populations. HIV prevalence is high among PWID in Iran, Afghanistan, Pakistan, Egypt, Libya, and Morocco [21] with an estimated prevalence of 87% among PWID in Tripoli [22]. Prevalence among

MSM appears to be generally low, but there is some evidence of emerging epidemics among MSM in Egypt, Jordan, Lebanon, Oman, and Syria [23]. In their review, no recent prevalence estimate was available for any risk group in 11 of the 23 Middle East and North Africa countries, and data on TGW was largely absent except for evidence of increasing prevalence among TGW in Pakistan [24].

Injection drug use remains an important driver of HIV transmission. El-Bassel and colleagues (this issue) note that between 2001 and 2011 HIV incidence increased by over 25% in nine countries—in six of those, the major route of HIV transmission was injection drug use [25]. Epidemics reported as being driven by sex between men and women, particularly in Central Asia, may be driven by epidemics among PWID with poor access to sterile injecting equipment and opioid substitution therapy. This pattern is especially evident in countries with more severe stigmatization of injection drug use and limited resources for PWID [26]. In Greece, the alarming increases in HIV incidence among PWID highlight the influence of global and national economic crises and austerity policies [27]. El-Bassel and colleagues (2013) also draw attention to how drug availability and trafficking routes are shaping injection and non-injection drug use with methamphetamine or other stimulant use becoming more prevalent in South America, East and Southeast Asia, and South Africa [28–30]. In Eastern Europe and Central Asia the production and use of synthetic opiates, such as *krokodil*, has increased [31;32].

Female injectors continue to be at increased risk relative to male injectors, with important determinants of their elevated risk including sex with injection drug users, social isolation, male control over injection equipment, and more limited access to prevention services [33]. Female injectors who also trade sex may face additional vulnerabilities in regards to lack of access to prevention services, discrimination, criminalization of sex work, and exploitation by police and others [34]. Stigmatization, criminalization, and exploitation continue to foster HIV transmission among PWID and their sex partners, and changes in laws, policies, and practices will be needed. Research in Kyrgyzstan reveals that police education programs can be effective in changing policing practices towards concordance with harm reduction principles [35].

Very high disease burdens have also been reported among male-to-female TGW, with a recent systematic review and meta-analysis revealing that across 15 countries, nearly one-in-five TGW is HIV infected—a 48-times higher odds of infection than among adult heterosexuals [9]. Poteat, Reisner and Radix (this issue) argue that while unique biologic factors are often an important risk factor for transgender women, structural and psychosocial factors play a dominant role in the alarmingly high HIV prevalence. Although multiple dimensions of discrimination and stigmatization are often faced by populations at high risk for HIV, these may be particularly severe for transgender women and may affect HIV treatment utilization [36;37]. The psychosocial need for gender validation may be counterposed with societal barriers to gender expression—the former may lead to increased sex with men and the latter, including interpersonal gender abuse [38], may lead to riskier sexual behavior. The number of studies with transgendered women continues to increase, but studies are needed to understand important local variations in HIV epidemiology and samples of sufficient size for inferences regarding risk factors.

Sullivan, Jones and Baral reported in this issue on HIV in 33 high-income countries (HIC) which account for some 2.26 million infections, an estimated 6–7% of the global burden. Roughly half of all these HIC HIV infections were among MSM, and the overall median ratio of male to female HIV Infections was 2.5:1, as would be expected in epidemics that so disproportionately burden MSM. Strikingly, they found that among HIC, the U.S. accounts for over 30% of total infections, underscoring the severity of the U.S. epidemic, which is predominately among MSM.

CONCENTRATED EPIDEMICS WITHIN GENERALIZED EPIDEMICS

The ten countries with the highest HIV prevalence worldwide are all located in Southeastern Africa. While the prevalent HIV surveillance systems have generally excluded key populations, the limited available data suggest a disproportionate burden of HIV among these populations (Tanser et al., 2013, this issue). Epidemics among PWID have also been identified in Eastern Africa with HIV prevalence approximating 40% [39]. Tanzania has been among few countries in the region to offer needle and syringe exchange programs and opioid substitution therapy [39].

Among sex workers, the majority of data have focused on female sex workers. An estimated 37% of FSWs are living with HIV across the continent equating to a 14 times odds ratio of living with HIV among FSWs compared to other women [8]. Moreover, while limited data are available among male sex workers, recent studies from Kenya indicate that male sex workers similarly share a high burden of HIV [40]. Separately, sex work among MSM across Sub-Saharan Africa has been consistently associated with seroprevalent HIV infections among MSM [41;42]. No studies have been completed among transgender sex workers in the context of generalized epidemics though transgender sex workers have been previously demonstrated to be among the highest risk populations for HIV infection [43;44]. As explored by Baral et al in this issue, there is similarly a growing evidence base supporting that MSM have higher burdens of HIV than do other men in the context of generalized epidemics. In the review of the 51 countries with generalized epidemics, the burden is consistently higher among MSM where data are available. However, nearly half of these countries (22) had no surveillance data on HIV among MSM and evidence of limited financial investments targeted for MSM. Risk factors for HIV identified in their review of recent studies include social isolation, health-care and social stigma limiting sensitive HIV surveillance and the coverage of comprehensive HIV prevention programs.

A trend appears to have emerged in that the broader the HIV epidemic, the less attention has been given to the needs of key populations with the assumption that HIV risks are evenly distributed in the context of these epidemics. As HIV surveillance systems are reconsidered, we may continue to learn more about the existence of hot spots in the context of generalized epidemics, which will inform us of the best approaches to mitigate the risks of HIV acquisition and transmission within them.

METHODOLOGICAL CHALLENGES AND ADVANCES

The judicious allocation of prevention and treatment resources requires understanding the magnitude of concentrated epidemics and the level of unmet prevention and treatment needs

among high-risk groups such as MSM, PWID, and FSWs. The vast majority of surveillance studies have demonstrated high prevalence or incidence rates among these groups, but data on the size of these groups in different national or regional settings are often lacking, leaving as a matter of gross conjecture the number of individuals infected with HIV or at risk of infection in these groups. We have only indirect ways of estimating the number of men in any given population who have sex with other men, and in contexts where risk behaviors are more stigmatized, the harder these estimates are to make. In their review of methods recently used to estimate sizes of key populations, Abdul-Quader, Baughman and Hladik (this issue) concluded that different methods (e.g., capture-recapture, multiplier method, and network scale-up method) may give very different results, that ideally multiple methods should be employed, and that members of key populations should be included in study planning. Sabin and Johnston (this issue) address advances in respondent-driven sampling, time-based sampling and other methods, and the field will need to make rapid headway on the development and rollout of surveillance tools to better assess population sizes, estimate disease burdens, and protect the rights of marginalized persons and groups at risk.

Grabowski and Redd (this issue) reviewed the emerging use of molecular epidemiology tools to understand HIV viral dynamics at couple, network, and population levels. They identified the limited use of these tools to date in generalized epidemic contexts, but also the power of these methodologic advances to understand HIV transmission dynamics in concentrated HIV epidemics. Citing the groundbreaking work of Lewis, et al, in mapping epidemic spread among gay, and other MSM in London [45], this approach can help explain why clusters, or bursts of HIV transmission, may play critical roles in undermining the efficacy of ART treatment to reduce HIV incidence in these networks. Onward transmission from acute and recent infections may play much larger roles in the clustered outbreaks among networks of MSM, and may be too “upstream” in infection course to be affected by treatment. Molecular epidemiology may be a critical tool to better defining HIV dynamics in concentrated epidemics, and to improving intervention approaches. To do so, we will need faster and more “real time” approaches to surveillance, less biased samples for linkage analysis, and much better links between surveillance and research efforts.

In their review of recent mathematical modeling of HIV in concentrated epidemics, Bioly and Shubber (this issue) noted the increasing use of deterministic and stochastic models for understanding HIV transmission dynamics and for predicting the effects and cost-effectiveness of different combinations of prevention interventions in different settings. Research by Vickerman and colleagues [46] indicates that the hepatitis C coinfection prevalence among HIV positive PWID may be an important marker for understanding the proportion of HIV infections due to injection versus sexual transmission among PWID. Bioly and Shubber note that recent models indicate that PrEP and treatment-as-prevention may be cost-effective but ideally targeted towards higher risk individuals [47–49], and that needle and syringe exchange programs, opioid-substitution therapy, and condom use are highly cost-effective [50–54] and, in some settings, may be sufficient to substantially reduce long-term HIV prevalence [55;56].

Understanding and best responding to the distribution of HIV within and amongst key populations and countries will also be predicated on understanding the distribution of the

causes of HIV acquisition and transmission. For FSWs, Shannon and colleagues (this issue) argue that the HIV risks may be better understood using a structural determinants framework. Macro-structural factors include laws and policies governing sex work, migration and mobility, stigma, education and literacy, gender inequalities, and forced labor and sex trafficking. At the meso-level, the strengthening of community organization through empowerment interventions has impacted HIV-related risk behaviors [57]. Micro-work environment factors include policing practices and various venue supports and features, and micro-social factors include physical and sexual violence and the use of alcohol and other drugs.

CONCLUSIONS

What does a review of the current epidemiology of HIV in concentrated epidemics suggest for the next phases of the HIV response? First, it is now clear that the declining HIV incidence seen in many generalized epidemics are not occurring for concentrated ones. Second, much of the global expansion of HIV in concentrated epidemics is due to spread among sex workers, MSM and PWID. Treatment as prevention, HIV testing and counseling, and other interventions have emerged as integral to the prevention of HIV transmission, and such efforts should be taken to scale for populations disproportionately affected by HIV. Respect for human rights and efforts to combat stigma, discrimination, and social exclusion will be critically important for these interventions to deliver meaningful change for key populations. Doing so effectively will require the local expertise of members of these affected communities and will also require redressing contextual factors that foster and maintain risk environments, including political, legal, rights-related, and social and economic marginalization. Surveillance mechanisms are not only needed to determine the level of need within concentrated epidemics—surveillance will also be needed to evaluate the success of prevention efforts, such as the suppression of viral loads within key populations and where in the continuum of care such efforts may be failing.

In the case of MSM, the ongoing epidemics require much more vigorous efforts to reach younger MSM, expansions of testing and treatment, and the implementation of new prevention tools, like pre-exposure prophylaxis, which may help control these expanding epidemics. These will likely have to be coupled with re-invigorated community efforts around safe sex practices and condom use, which showed such remarkable efficacy among gay men in the first decades of the epidemic [58]. For PWID, we have known what works for control of HIV spread for decades, and these ongoing epidemics are fundamentally policy failures exemplified by the failures across Russia and the Former Soviet Union to implement the basics of HIV prevention for PWID. With the focus on recently emerging prevention strategies, it is essential that we not lose sight of the basics of HIV prevention such as condom and lubricant provision, counseling and testing, opioid substitution therapy, and needle and syringe exchange programs. As highlighted by Bioly and Shubber (this issue), some of these approaches remain the most cost effective and must be considered as essential to combined prevention strategies.

The challenge ahead is really to ask how the 4th and 5th decades of the HIV epidemic will differ from the first thirty years, where HIV among these populations went under-addressed

and effective programs failed to be made available and taken to scale for those in need. In 2013, the answers are clear—we are not doing nearly enough to control these epidemics. This must change if the promise of an “AIDS Free Generation” is not to remain rhetoric.

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