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Characterizing the Role of Intersecting Stigmas and Sustained Inequities in Driving HIV Syndemics Across Low- and Middle-Income Settings

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Abstract

Purpose of review: In 2020, key populations around the world still have disproportionate risks for HIV acquisition and experiencing HIV-related syndemics. This review presents current data around HIV-related syndemics among key populations globally, and on the role of intersecting stigmas in producing these syndemics in low- and middle-income settings.

Recent findings: Sex workers, sexual and gender minorities, prisoners, and people who use drugs experience high burdens of tuberculosis, sexually transmitted infections, viral hepatitis, and violence linked to heightened HIV-related risks or acquisition. Adverse sexual, reproductive and mental health outcomes are also common and similarly amplify HIV acquisition and transmission risks, highlighting the need for psychosocial and reproductive health services for key populations.

Summary: Achieving the promise of biomedical interventions to support HIV care and prevention requires action towards addressing syndemics of HIV, and the stigmas that reproduce them, among those most marginalized globally.

Keywords

stigma; HIV; key populations; sex work; syndemics

Introduction

In both concentrated and generalized HIV epidemics globally, key populations have consistently been demonstrated to have disproportionate risks of HIV acquisition, including cisgender female sex workers (FSW), gay, bisexual, and other men who have sex with men (MSM), incarcerated populations, people who use drugs (PWUD), and transgender women [1–6]. Moreover, risks of HIV transmission are also concentrated among key populations living with HIV - with the Joint United Nations Programme on HIV/AIDS (UNAIDS) now estimating that more than half of new HIV infections are among key populations and their immediate sexual partners, with stigma cited as the fundamental barrier to sustained

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engagement in HIV treatment [7]. In 2020, it is increasingly clear that intersections of biological, social and structural factors result in syndemics of HIV and drug use, violence, incarceration, co-infections with tuberculosis (TB), viral hepatitis, and other sexually transmitted infections (STIs), and suboptimal sexual and reproductive health (SRH) outcomes. Moreover, the data are clear that there is great heterogeneity in HIV acquisition risks, and similar heterogeneity in the likelihood of experiencing HIV-related syndemics across populations. Here, we present the current data characterizing HIV-related syndemics among key populations globally, including burdens of STIs, TB, hepatitis, drug use, experiences of violence, suboptimal reproductive and mental health outcomes, and how varying and intersecting forms of stigmas act as underlying determinants in HIV-related syndemic production.

Intersectional stigmas in syndemic production

Stigma has consistently emerged qualitatively and increasingly quantitatively in studies as a syndemic factor associated with HIV-related risk behaviors, new HIV infection, treatment cascade gaps, substance use, and mental health among key populations [8]. The minority stress model and intersectionality theory have been applied to describe the intersection of stigmas from multiple identities and practices, as well as sources of stigma at social and individual levels [9, 10]. These include stigma attributable to HIV status, gender minority, race/ethnicity, and behaviors such as sex work, drug use, and non-heteronormative sexual preferences and practices viewed through a ‘morality’ lens. Sources of stigmas primarily include enacted stigma (e.g.: discrimination from education, employment, healthcare settings), anticipated stigma (e.g.: expectations of rejection or discrimination by others), internalized stigma, and perceived stigma [11]. Intersectional, enacted stigmas due to sexual orientation, Indigenous and Latinx identity (racism), undocumented status, sex work and drug use among women undertaking sex work have been qualitatively studied as syndemic factors in housing instability, mental health, and barriers to healthcare engagement [12, 13].

While most HIV-related stigma research over the past two decades has focused on gay men and other MSM in North America [8], recent literature has expanded to measure stigmas and syndemic production globally and among multiple populations [14–21]. These present opportunities to consider how criminalization across the globe, as a macrostructural manifestation of stigma through laws targeting sexual and gender minorities (SGM) and sex work, can: 1) reproduce stigmas at the community, interpersonal and individual level, such as through repressive policing, enacted stigma from family, employers, and healthcare providers; and 2) influence downstream determinants of HIV outcomes, such as housing instability, violence, substance use, sexual risk behaviors, and engagement in the HIV prevention and treatment continuums [9, 22]. Furthermore, these syndemics reflect that key population groups are not mutually exclusive. Understanding and tailoring services to the unmet needs of individuals - sex workers of all genders who may use drugs, PWUD that sell sex to buy drugs, current and formerly imprisoned marginalized groups who are criminalized due to their status as sex workers, PWUD, LGBTQ persons – require understanding intersectional stigmas and the pathways in which these affect health outcomes. Throughout this review, we will present available evidence of stigmas as an underlying determinant of

HIV-related syndemics among key populations, with a focus on low-to-middle-income country (LMIC) settings.

STIs, tuberculosis and viral hepatitis co-infections

Recent studies and meta-analyses have highlighted the STI burdens among MSM in trials testing HIV pre-exposure prophylaxis (PrEP) use [23–25]. This includes a composite bacterial STI prevalence (gonorrhea, chlamydia, or syphilis) of 23.9% at baseline among MSM starting PrEP globally, as well as high pooled incidence of any bacterial STI in cohorts of MSM on PrEP, at 72.4/100 person-years (95% CI: 58.8 – 89.1) [23, 24]. In another meta-analyses, PrEP use was significantly associated with an increase in rectal chlamydia and any STI diagnosis in MSM, often attributed to risk compensation through reduced condom use [25]. There is also recognition of high STI prevalence among FSW, though PrEP outcomes differ compared to MSM. An observational study of FSW on PrEP in Benin found decreased STI prevalence at 24 months follow up compared to baseline, suggesting less risk compensation [26]. However, barriers to PrEP retention and STI diagnosis among FSW must be better understood to address the HIV/STI syndemic. While studies are emerging on the efficacy of doxycycline PrEP/PEP for bacterial STIs [27], data are limited, and the current evidence makes a strong case for ensuring PrEP programming is included as part of a service package that also emphasizes STI prevention, monitoring and treatment [28]. While recent studies have examined trends of STI incidence in relationship to HIV in North America [29–31], comprehensive data on HIV-STI co-infections among key populations across LMICs are still emerging [32–36].

Prisoners bear a disproportionate burden of HIV-TB co-infections, with approximately a third of prisoners living with HIV globally co-infected with TB, though there has been a recent downward trend [37]. By region, co-infection prevalence among prisoners living with HIV ranges from 14% in the African region to 37% in the Americas [37]. Correlates of HIV-TB co-infection, where studied, have suggested associations with overcrowding, high turnover of prisoners, long duration of incarceration, and re-incarceration – but few of these correlates have been investigated in regions where co-infection prevalence is highest [37]. Few studies have looked at HIV-related comorbidities among transgender populations [6], and only one study of imprisoned transgender populations captured hepatitis or TB in addition to HIV in recent systematic reviews [38].

Existing reviews on viral hepatitis have found disproportionate burdens of HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV) among key populations in and out of prison, particularly among PWUD [39, 40]. Further, among people who inject drugs (PWID), recent incarceration was associated with an 81% increase in HIV acquisition risk, and a 62% increase in HCV acquisition risk [40*]. Among imprisoned key populations globally, Wirtz et al identified a pooled prevalence ratio (PPR) of HBV in imprisoned MSM twice that of male prisoners who did not report sex with men; the PPR of HBV and HCV in imprisoned PWID was respectively 2 and 8 times that of their counterparts who did not inject drugs [39]. There are few updated global reviews specifically examining HIV-hepatitis co-infections among key populations. While sub-Saharan Africa represents 69% of the total global cases of HIV-HBV co-infection among people living with HIV (PLHIV) [41], studies

of HIV-HBV co-infection among key populations in African settings were scarce in a recent review, identifying one study among PWID and none among MSM; most studies on the African continent took place in general population settings (n=33) and heterosexual and pregnant women (n=56) [41]. Among all population groups, PWID living with HIV had the highest global mid-point prevalence of HBV infection at 11.8%, ranging from 3.6% in North Africa/Middle East, to 27.3% in Latin America (n=1) [41]. Among MSM living with HIV, HBV prevalence ranged from 7.2% in Latin America to 10.6% in South and Southeast Asia, similar to other population groups studied.

Outside of PWID, the limited association between key population status and HIV – hepatitis co-infections should be considered in the context of limited investment in research and consequentially, scarce data. As review authors have noted, current research suggests that blood-borne virus burdens may be linked to patterns of imprisonment that can disrupt prevention and treatment services, healthcare, and livelihoods, which in turn can potentiate risks for HIV and hepatitis [39]. Ultimately, the increased burden of lifetime arrest and re-incarceration rates among people who use drugs, sex workers, and SGM communities, characterizing the actual burden of co-infections among key populations is critical [39].

Co-morbidities in HIV and reproductive health outcomes

Pregnancy and motherhood are common among cisgender FSW globally. The relationship between motherhood and sex work is complicated, however, as the need to provide for children may be a determinant of sex work entry, and unintended pregnancy is a potential occupational risk. Further, factors that increase risks of unintended pregnancy also amplify risks for HIV acquisition. A recent systematic review of longitudinal data found a heterogeneous, but high, incidence of pregnancy among FSW in observational cohorts (27.1/100 woman-years, 95% CI: 24.4–29.8), and called for additional strategies to expand contraception delivery to reduce unintended pregnancy [42]. Non-barrier contraception coverage is inadequate given the elevated number of sexual partners, sex acts and inconsistent condom use reported among FSW, and unmet needs are often higher among FSW living with HIV [43]. Among FSW, abortion has also been linked to HIV status and a history of sexual violence; further, the absence of safe pregnancy termination and post-abortion care services increase morbidity and mortality risks among already marginalized women[44].

However, it should not be assumed that all FSW and women in other key population groups want to prevent pregnancy, as data continue to demonstrate that women, independent of occupation and behavior, wish to have children, leading to decreases in contraceptive use [45, 46]. Given the sexual risks of acquiring and transmitting HIV in the context of condomless sex, there is a need for reproductive rights-affirming screening of fertility intentions and safer conception counseling, along with a critical need to integrate pregnancy screening, counseling, and treatment related to vertical transmission prevention in programs for FSW and women who use drugs [47]. To-date, data on effectiveness of safer conception strategies among key populations are limited, but available data from non-key population safer conception services highlight its potential for improving viral suppression to reduce HIV transmission and promote safer pregnancy [48].

Among transgender persons, there is increasing recognition in high-income settings that culturally competent contraception, fertility preservation and planning, and pregnancy care should be incorporated into counseling and services where appropriate [49]. Given the high HIV burden among transgender women, and the high HIV-related risk of sexual assault and early sexual debut among lesbian, bi-sexual, queer-identified women and transgender men, further attention to optimization of HIV and reproductive care is warranted, particularly in LMICs [50].

Finally, the number of female prisoners has risen, and data from incarcerated women suggest heterogeneity in antenatal and reproductive care provision among pregnant women. A scoping review including countries across sub-Saharan Africa found that HIV testing was forced on pregnant women in some settings, while not offered in others [51]. HIV treatment access, breastfeeding counseling and practices, and considerations around maternal-infant attachment are inconsistent within prisons. Evidence-based policies within this space are warranted, particularly to reduce vertical transmission risks and maximize maternal and infant health [51].

Violence

The disproportionate burdens of violence among sex workers and SGM communities are well-documented, as well its association with HIV among sex workers globally [52]. Primary studies and meta-analyses have further delineated factors that contribute to the syndemics of violence and HIV, including institutional practices resulting from stigmatization and criminalization - of sex work, drug use, and of non-heteronormative sexual practices and identities [53]. Broadly, violence has been measured in these studies by perpetrator (sex work clients, police, intimate partners), types of interpersonal violence (sexual, physical, and emotional violence), as well as institutional violence in the form of police harassment, arrest, and extortion, such as demanding bribes or coerced sex to avoid fines or arrest [52]. Studies have consistently demonstrated high burdens of both lifetime and recent sexual violence among sex workers of all genders [32, 54–56], and has further identified varying burdens of HIV-related risks in relationship to violence among sex workers, MSM and transgender individuals based on perpetrator [55], gender identity [32, 56] and migration status [18]. Platt and colleagues' global systematic review and meta-analyses of the associations between sex work legislation and health outcomes reinforced the role of criminalization in violence and HIV/STI outcomes by way of repressive policing: those who were exposed to any type of repressive police activity, including extortion, had twice the odds of HIV/STIs and more than twice the likelihood of experiencing physical or sexual violence from clients, police, and other individuals, compared to those not exposed [53**]. Furthermore, Lyons et al demonstrate that stigmas and criminalization may synergistically play a role in healthcare engagement and HIV outcomes: in criminalized sex work settings, HIV prevalence is associated with higher odds of physical violence, fear of seeking health services and mistreatment in healthcare settings compared to partially legalized settings [57*].

More data on transgender women disaggregated from samples of cisgender MSM are emerging, finding differing burdens of violence and HIV, particularly among those in sex

work. In Guatemala, MSM and transgender sex workers were over 6 times as likely to experience forced sex than MSM non-sex workers, and transgender sex workers reported discrimination and physical abuse at significantly higher proportions than both MSM who did and did not undertake sex work [56*]. These patterns suggest that intersecting stigmas attributed to gender identity and sex work may heighten the risk of both violence and HIV. In Haiti, HIV infection was associated with forced sex among transgender women and past-year intimate partner violence (IPV) among MSM [32].

Beyond HIV and physical violence, preliminary results of young FSW living with HIV in South Africa suggest extraordinarily high levels of mortality emanating from intersecting experiences of homelessness, drug use, and homicide [58]. Here and in other country settings, including North America, sex work criminalization is a root cause of these experiences yet limits their visibility [13, 59–61], inhibiting research. These results highlight the critical need for data assessing - and policies addressing - protective factors and structural syndemic risk factors that multiply vulnerabilities such as housing instability [13, 59] in relationship to violence, trauma, attempted suicide [62], and attempted murder [62].

Mental Health and Substance Use

Recent studies have examined the associations of mental health, violence and substance use, with sex workers and SGM reporting substantive burdens of depressive symptoms [15, 54, 63–66], suicidal ideation [14, 19], and post-traumatic stress disorder (PTSD) [63]. Among SGM, significant correlates of depressive symptoms include experiencing lifetime sexual assault [63], experiencing and perpetrating IPV [64], physical assault [65], higher experienced (enacted) stigma [14, 15, 65], and internalized homonegativity [64]. Among gay, bisexual and other MSM in Baltimore, physical assault and verbal harassment were each measured as a dimension of enacted stigma, and each were significantly associated with depressive symptoms [65]. Path analyses among black MSM in the US found direct and indirect effects from exposure to community violence on substance use, mediated by community justice involvement and psychological distress [67*]. These results were remarkably similar to a study among women who injected drugs in Indonesia who reported both depressive symptoms and IPV and had over twice the odds of STI symptoms compared to those who reported neither [68].

Recent literature has also provided more evidence from latent class analyses studying associations of latent constructs of violence and of stigma with mental health and HIV-related risk factors, aiming to capture the synergies of various, related measures [15, 54]. Among FSW in Kenya, the ‘severe’ class of gender-based violence (GBV) - composed of observed severe physical and emotional violence and any level of sexual violence - was linked with increased sexual risk behaviors, symptoms of depression and PTSD, compared to women in the ‘low’ GBV class, though no significant association with HIV incidence was observed [54]. Latent constructs of sexual stigma combining enacted, perceived and internalized stigma indicators had significant direct and indirect effects on recent depressive symptoms among SGM, with a suggested combined effect on depressive symptoms greater than that of observed enacted stigma [15*].

While the syndemics of substance use and HIV have been widely studied among MSM, studies are increasingly measuring the overlap of injecting and non-injecting forms of drug use with sex work, SGM status, and their correlates. MSM sex workers in Guatemala were twice as likely to report drug use as MSM who were not sex workers [56], and higher proportions of transgender women living with HIV in Brazil reported problematic cocaine use, and sex work, than did those not living with HIV [66]. Platt and colleagues' sub-group analyses found that sex workers using drugs who had their needles, syringes, or condoms confiscated had higher odds of HIV/STIs and of any kind of violence [53]. Injecting drug use among sex workers in Asia, Europe and North America has been documented as a co-occurring risk for HIV, though less prevalent among sex workers across sub-Saharan Africa [5, 69]. A systematic review of substance use among sex workers and other occupational high-risk groups across sub-Saharan Africa highlighted gaps in the broader examinations of illicit drug use correlates and associations with HIV outcomes in the region, finding large heterogeneity in measurement of drug use, including drug types and timeframes, and limited studies of their correlates [69]. The role of non-injecting forms of drug use among sex workers in impairing decision-making around sexual risk behaviors are increasingly visible in the qualitative literature. However, non-injecting drug use among sex workers is understudied globally in its relationship to HIV outcomes, and its potential mechanisms as coping with psychological distress, lifetime exposure to violence, and poverty.

Conclusion

In 2020, there were three times as many HIV infections compared to the goal of 500,000 new infections. In 2030, the goal is zero new infections [70]. Hypothetically, it is achievable to end new HIV infections as we do have the tools to stop HIV acquisition and transmission. However, the syndemics underlying sustained HIV risks including co-infections, suboptimal reproductive health and mental health outcomes, violence exposure and substance use have not declined in recent years. In part, the lack of decline in syndemics is because of limited investment into their characterization, measurement, and intervention. But opportunities to intervene exist and range from mitigating the effects of stigma on individuals and addressing stigma in health care settings, to decreasing structural stigmas through decriminalization or, at least, decreased enforcement of laws focused on same-sex practices, gender identities, sex work, and substance use [71] [72] [73]. Ultimately, to achieve the promise of biomedical interventions in supporting those living with HIV to live well and prevent new HIV infections, necessitates moving from rhetoric to action in addressing syndemics of HIV among those most marginalized in societies across low- and middle-income settings.

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Key points:

- Intersectional stigmas among key populations are emerging in studies as determinants of HIV-related syndemics, particularly with links to violence, reproductive health and mental health outcomes.
- Prisoners and people who use drugs in particular are facing higher risks of both hepatitis and HIV acquisition and co-infections of HIV-TB, with MSM and sex workers experiencing HIV/STI burdens that must be addressed through services packages that emphasize STI monitoring and treatment alongside PrEP.
- Burdens of violence and HIV differ by sex work status and gender identity among sexual and gender minorities, and are being observed in association to drug use and adverse mental health outcomes.
- Criminalization of sex work, drug use, sexual and gender minority status globally in relationship to structural syndemic risks are understudied but critical to informing effective strategies to improve health outcomes among marginalized communities who bear the highest syndemic burdens.