Maximizing the benefits of antiretroviral therapy for key affected populations

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Abstract
Introduction: Scientific research has demonstrated the clinical benefits of earlier initiation of antiretroviral treatment (ART), and that ART can markedly reduce HIV transmission to sexual partners. Ensuring universal access to ART for those who need it has long been a core principle of the HIV response, and extending the benefits of ART to key populations is critical to increasing the impact of ART and the overall effectiveness of the HIV response. However, this can only be achieved through coordinated efforts to address political, social, legal and economic barriers that key populations face in accessing HIV services.

Discussion: Recent analyses show that HIV prevalence levels among key populations are far higher than among the general population, and they experience a range of biological and behavioural factors, and social, legal and economic barriers that increase their vulnerability to HIV and have resulted in alarmingly low ART coverage. World Health Organization 2014 consolidated guidance on HIV among key populations offers the potential for increased access to ART by key populations, following the same principles as for the general adult population. However, it should not be assumed that key populations will achieve greater access to ART unless stigma, discrimination and punitive laws, policies and practices that limit access to ART and other HIV interventions in many countries are addressed.

Conclusions: Rights-based approaches and investments in critical enablers, such as supportive legal and policy environments, are essential to enable wider access to ART and other HIV interventions for key populations. The primary objective of ART should always be to treat the person living with HIV; prevention is an important, additional benefit. ART should be provided only with informed consent. The preventive benefits of treatment must not be used as a pretext for failure to provide other necessary HIV programming for key populations, including comprehensive harm reduction and other prevention interventions tailored to meet the needs of key populations. An end to AIDS is only possible if we overcome the barriers of criminalization, stigma and discrimination that remain key drivers of the HIV epidemics among key populations.

Keywords: treatment; HIV/AIDS; human rights.

Introduction

During the past 20 years, antiretroviral treatment (ART) has achieved remarkable success in delaying HIV-related disease progression and reducing AIDS-related mortality. In addition to the individual clinical benefits [1], early initiation of ART also has been shown to reduce transmission [2] and decrease HIV acquisition risk at the population level [3]. These results are mobilizing the global HIV/AIDS community to seek accelerated scale-up of earlier ART as both a treatment and a prevention strategy. The effort is accompanied by new, comprehensive guidelines on treatment from the World Health Organization (WHO) [4] indicating earlier initiation of treatment. The new guidelines markedly increase the number of people potentially eligible for this life-saving therapy. While resources and operational issues remain an enormous challenge to maximizing the benefits of ART, the fundamental concept that universal access to ART is a key next step in the global response to HIV/AIDS is now widely accepted. Universal access is an essential goal both on human rights and on scientific grounds.

Achieving universal access in the coming years necessarily involves addressing the needs of key affected populations (KP). KP are defined by the International AIDS Society (IAS) as having disproportionate burdens of HIV infection, as well as low levels of access to essential HIV services. This includes gay, bisexual and other men who have sex with men (MSM), sex workers of all genders, people who inject drugs (PWID) and transgender people. In some settings, prisoners and migrants may also be particularly vulnerable to HIV and to exclusion from HIV services. While extending the benefits of ART to these highly marginalized populations will ultimately increase the impact of ART and the effectiveness of the HIV response, it also involves addressing with urgency a wide range of social, political, legal and economic barriers that continue to limit their access to healthcare, including HIV prevention and
treatment. A further challenge to HIV responses for KP is the lack of disaggregated data, and this is particularly true for adolescents who may be within these groups.

Despite gaps in current knowledge, it is clear that social and cultural attitudes, including stigma, discrimination and punitive laws, policies and practices, present barriers to access. To benefit from ART, people living with HIV/AIDS (PLHA) must first know their status, and this requires voluntary HIV testing and linkage to care in contexts of safety, dignity, and confidentiality. However, in too many countries and contexts, KP are discriminated against, stigmatized in communities and in healthcare settings, criminalized, and excluded – or exclude themselves – from essential HIV services.

In 2014, KP are arguably facing rising threats to accessing care. The recent wave of anti-homosexual court decisions and legislation in Russia, India, Nigeria and Uganda underscores the threats to universal access faced by these populations and is illustrative of the fundamental challenges involved in extending the benefits of ART access to those who need it. It cannot be assumed that because the scientific community has now reached consensus on the benefits of earlier treatment initiation that this will become genuinely available to KP without extraordinary effort. This article, a joint undertaking of the KP Working Group and the Treatment as Prevention Working Groups of the IAS, aims to describe and analyse the challenges and barriers that KP face in accessing and using ART for both treatment and prevention, and it provides context to the new “Consolidated Guidelines” on HIV among key populations, which were released by WHO in July 2014.

Disproportionate Burdens
KP experience disproportionately high disease burden and multiple risk factors in nearly all countries. It has long been assumed that KP represent a modest share of the epidemic globally, and that the HIV prevalence among them is largely confined to countries with low-level and concentrated epidemics. It is now increasingly recognized that KP and their sex partners not only represent most of the PLHA outside sub-Saharan Africa, but also a significant proportion of new infections in sub-Saharan Africa [5–8]. As HIV begins to spread to other populations, the distinction between concentrated and generalized epidemic settings is becoming less relevant.

In many countries, however, coverage of HIV prevention interventions for KP is grossly inadequate, and access to health services, including HIV testing and ART, is limited by discrimination, stigma, punitive laws and policies and lack of community empowerment.

HIV burden and risk factors
The burden of HIV among KP in generalized epidemics has been poorly understood due to their limited representation in national surveillance data and the fact that they are criminalized and stigmatized in many settings. Table 1 highlights the HIV burden for MSM, sex workers, PWID and transgender people, where data are available, and lists some known risk factors and current intervention recommendations. This is not a comprehensive review of the evidence; rather, it gives a sense of the epidemic’s magnitude among KP. Common to all the populations, and not reflected in the table, are the structural risk factors they face, such as criminalization, discriminatory and punitive laws and policies, and pervasive stigmatization, all of which limit their abilities to protect themselves from HIV acquisition and transmission. These structural risk factors and barriers are too numerous to list here; specific examples include condoms being used as evidence for prostitution, the lack of condoms in prisons due to sodomy laws, and the lack of methadone due to laws against its use in the Russian Federation [9–12].

Globally, epidemics of HIV are expanding among MSM with consistently high incidence rates [26]. Data from multiple continents show consistently high incidence rates, particularly among the youngest age groups, and in many high-income settings, overall epidemic trends are in decline except among MSM [6]. MSM now account for more than one-third of new infections in China [27], and may constitute half or more of all new infections in Asia by 2020 [28]. HIV prevention efforts among MSM have yielded many successes but have been insufficient, and in sub-Saharan Africa, they are extremely rare [29]. Biomedical and behavioural combination interventions are increasingly emphasized [30].

Sex workers have been reported to be at high risk of HIV infection in many settings. Especially high prevalence among FSW has been reported in sub-Saharan Africa, from 24% (Rwanda) to 71% (Malawi), and FSW are estimated to account for large proportions of new infections [18]. Structural and behavioural interventions have successfully decreased HIV transmission among FSW, and in most settings, consistent condom use and HIV testing are higher among FSW than other women [31]. Still, on-going HIV prevention programmes cover fewer than half of sex workers worldwide [32]. Relatively little research has been undertaken among male and transgender sex workers, but they are likely at increased risk [33].

There are an estimated 16 million PWID worldwide, of whom three million are living with HIV. They account for roughly one-third of all HIV infections outside sub-Saharan Africa, and HIV epidemics among PWID are increasing across Eastern Europe and Central Asia [22]. PWID are also at high risk for incarceration and tuberculosis (TB). Additionally, PWID need services for drug dependence treatment, which can have easily manageable interactions with HIV, TB or hepatitis C virus (HCV) medications [34].

Transgender women are people who are assigned male gender at birth but identify as women. They have long been known to be at high risk of HIV infection, but national surveillance systems have not captured HIV data among them, and many transgender women are unaware of their status. The severity of transgender people’s disease burden is consistent across all regions, notwithstanding the widely varying cultural, social, political and legal contexts in which they live. Data on HIV burden among transgender men are limited, but recent studies challenge the assumption that their risks are low [35, 36].

HIV prevalence among prisoners ranges from 0% (Middle East) to 41.4% (South Africa) [37, 38], and levels are usually several times higher than in outside communities [37]. This is partly due to high rates of incarceration among PWID [39]. An estimated one in seven PLHA enters a correctional facility each year in the United States [40], and injection drug use in
African prisons has reportedly been increasing [41]. In Asia, PWID and other KP are arbitrarily detained for lengthy periods, and are subject to forced labour and other abuses, including lack of access to healthcare [42]. Risk factors include reusing injection equipment, untreated mental illness, lower socioeconomic status, belonging to an ethnic minority [37,38], tattooing and piercing, violence and rape [43]. High rates of other sexually transmitted infections (STI), HCV and TB are also widely reported [32,43]. Available interventions and technologies are sufficient to control the HIV epidemic among prisoners, but harmful policies, laws and policing practices, as well as low access to services, are the principle barriers to achieving effective impact.

Given the diverse contexts in which migrants live, it is difficult to summarize their HIV burden, even where data exist. Migrants from high-prevalence countries may have higher likelihoods of HIV infection than host country nationals in some settings, while elsewhere they may be moving from lower to higher prevalence contexts. HIV risk can be exacerbated by low access to services, legal status, language barriers and illiteracy, unemployment, laws and practices that expel PLHA, mobility, and post-conflict mental health issues, and internal migrants can also face many of these same issues [47–50]. Frequently, migrants are blamed for and unjustly stigmatized as spreading HIV [47], and they may also be more frequently prosecuted for transmission and exposure than other populations [51]. Migrants need standard protection under the law regardless of citizenship, voluntary rather than compulsory HIV testing and an end to punitive laws against migrants and PLHA [51].

### Table 1. HIV burden and risk factors among key affected populations

| Population      | Prevalence | Incidence | OR      | Major risk factors                                                                                                                                                                                                 | Existing interventions                                                                 |
|-----------------|------------|-----------|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| MSM             | 15% (N. America, S. and SE Asia) | 6.8/100 py (Kenya and South Africa) [13] | 19.3a   | Unprotected receptive anal intercourse; high number of male partner frequency; high number of lifetime male partners; injection drug use; high viral load in index partner; non-injection drug use (stimulants); network-level effects [5] | Behavioural: reduce alcohol and drug use; reduce number of partners; increase condom use and adherence to ART; Biomedical: ART; oral PrEP; Structural: decriminalization of homosexuality and “sodomy”; accessible and acceptable health services [9] |
|                 | 18% (sub-Saharan Africa) | 7.7% (Thailand) [15] |         |                                                                                                                                                                                                                       |                                                                                        |
|                 | 25% (Caribbean) | 10% (China) [16] |         |                                                                                                                                                                                                                       |                                                                                        |
| SW              | 11.8% (50 countries) | 3.6/100 py (Cambodia) [17] | 13.5b   | High-risk sexual exposures; high prevalence of STI; poverty; gender inequity; sexual violence [10]                                                                                                                  | Behavioural: condom use; HIV testing; Biomedical: STI diagnosis and treatment; ART; HBV immunization; Structural: decriminalization of sex work; anti-discrimination laws; accessible and acceptable health services; addressing violence; empowerment and community mobilization [10] |
|                 | 36.9% (sub-Saharan Africa) | 13.9/100 py (Tanzania) [19] |         |                                                                                                                                                                                                                       |                                                                                        |
| PWID            | 18.8% worldwide (9–22% in 6 highest burden countries) | 4.5/100 py (Russia) [20] | No data | Reusing injecting equipment; detention and incarceration [21]                                                                                                                                                          | Behavioural: HIV testing; condom promotion for PWID and their partners; tailored education and communication; Biomedical: opioid substitution therapy; ART; STI treatment; prevention and treatment of TB; prevention, vaccination, and treatment of viral hepatitis; Structural: needle and syringe programmes [11] |
|                 |             | 8.01/100 py (India) [23] |         |                                                                                                                                                                                                                       |                                                                                        |
| Transgender women | 27.7% (US) [24] | No data | 4c      | Unprotected receptive anal sex; network-level effects (sexual networks overlap with MSM populations) [12]                                                                                                              | Behavioural: increase condom and lubricant use; HIV testing; Biomedical: PrEP; early ART; microbicides; Structural: decriminalization of “cross-dressing” and “sodomy”; anti-discrimination laws; legal recognition of gender identity; gender-affirming health services; community engagement and empowerment; peer outreach [26] |
|                 | 27.3% (TG sex workers, 13 countries) |         |         |                                                                                                                                                                                                                       |                                                                                        |
|                 | 14.7% (13 countries) |         |         |                                                                                                                                                                                                                       |                                                                                        |
|                 | 19.1% (15 countries) |         |         |                                                                                                                                                                                                                       |                                                                                        |

*OR compared to general male population, low- and middle-income countries; bOR compared to general female population, low- and middle-income countries; ctransgender sex workers versus female sex workers.*

African prisons has reportedly been increasing [41]. In Asia, PWID and other KP are arbitrarily detained for lengthy periods, and are subject to forced labour and other abuses, including lack of access to healthcare [42]. Risk factors include reusing injection equipment, untreated mental illness, lower socioeconomic status, belonging to an ethnic minority [37,38], tattooing and piercing, violence and rape [43]. Available interventions and technologies are sufficient to control the HIV epidemic among prisoners, but harmful policies, laws and policing practices, as well as low access to services, are the principle barriers to achieving effective impact.

Given the diverse contexts in which migrants live, it is difficult to summarize their HIV burden, even where data exist. Migrants from high-prevalence countries may have higher likelihoods of HIV infection than host country nationals in some settings, while elsewhere they may be moving from lower to higher prevalence contexts. HIV risk can be exacerbated by low access to services, legal status, language barriers and illiteracy, unemployment, laws and practices that expel PLHA, mobility, and post-conflict mental health issues, and internal migrants can also face many of these same issues [47–50]. Frequently, migrants are blamed for and unjustly stigmatized as spreading HIV [47], and they may also be more frequently prosecuted for transmission and exposure than other populations [51]. Migrants need standard protection under the law regardless of citizenship, voluntary rather than compulsory HIV testing and an end to punitive laws against migrants and PLHA [51].
ART coverage for KP

While the benefits of ART are established, and treatment adherence for KP is comparable to that of other adults in similar treatment contexts, given appropriate structural support [34,52,53], there are major gaps in the knowledge about ART coverage among KP. This is partly because national data systems rarely disaggregate data and because of concerns that classifying people may lead to human rights violations. Nevertheless, the available data reveal significant inequities in coverage for all KP.

For MSM, ART coverage reportedly ranges from 14% (low-income countries) to 51% (high-income countries) [54]. The percentage of MSM who know their HIV status is low, indicating that ART coverage is also low [55]. Studies on ART and transmission dynamics among MSM suggest a complex and challenging picture [26,56], but preliminary data suggest that treatment may be as effective for MSM couples as for heterosexual ones [57]. Efforts to increase coverage should also address such issues and other barriers to maximize benefit. A modelling exercise estimated that significantly increased investments and coverage of ART for MSM could avert 75,000 infections in one year alone [58].

Among sex workers, knowledge of HIV status can be low, ranging from 16% (Asia) to 40% (sub-Saharan Africa), which suggests that ART coverage is also low [49]. The data that do exist indicate that FSW are less likely than other women to receive timely and adequate HIV treatment and care [59–61]. Significant barriers remain, even in contexts of extensive efforts to scale up ART among them [62]. Modelling suggests some prevention benefit of earlier treatment initiation for FSW [63], and for those in serodiscordant relationships with primary partners, treatment as prevention has high biological and clinical plausibility. Despite low levels of ART access, FSW accessing ART in Kenya were reported to have good treatment outcomes and no evidence of increased sexual risk behaviours [64]. One study has estimated that expanding access to ART for FSW in Kenya could reduce the number of FSW acquiring HIV by 25% [65].

For PWID, early treatment initiation, in combination with an evidence-based package of other preventive interventions, can be highly effective in reducing mortality and morbidity and controlling HIV transmission [21,66]. Despite this, an estimated 4% of PLHA who inject drugs worldwide were receiving ART, compared to 18% among all PLHA [67]. In the five countries with the largest HIV epidemics among PWID, PWID were 67% of HIV cases, but only 25% of those receiving ART [39]. Slightly increased levels of ART access for PWID were reported in three high-burden countries in 2010–2012 [22]. Many countries know that they have a high prevalence of HIV-positive PWID, but they do not attempt to measure ART coverage; estimates were available for only 10 out of 21 countries studied and ranged from 0.06% (Afghanistan) to 22% (Bangladesh) [68]. Furthermore, PWID may be less likely to be given ART in healthcare settings. More than a quarter of healthcare providers in Canada and the United States reported that they would defer ART for eligible people if they injected drugs [69], and a prospective cohort study in Ukraine found that pregnant PWID were less likely to receive ART than their counterparts who did not inject drugs [70].

As gender disaggregation does not take account of transgender status, there are virtually no ART coverage data for transgender people. A US study found that transgender women were less likely to have received ART compared to non-trans participants (59% vs. 82%) and that transgender women have higher HIV-related mortality and higher community viral load compared to non-trans people [71]. Another study of transgender women on ART in the United States found that the women were less likely to report good adherence, and they reported less confidence in their abilities to integrate treatment regimens into their daily lives and significantly fewer positive interactions with healthcare providers than other people [72]. A study in India found that widespread HIV stigma and prejudice based on gender identity and expression, sexual orientation and sex work motivated many transgender women to keep their HIV status secret, and they were powerful disincentives to access ART [73].

Data on ART coverage among prisoners are rare, though coverage is likely very low, as evidenced by poor coverage for other high-prevalence infections such as HCV and TB, as well as widespread human rights abuses in prisons worldwide. Prison health is frequently disregarded because Ministries of Interior or Justice, rather than Ministries of Health, are responsible for prison health services. In Uganda, for example, HIV prevalence in prisoners is double that in the general population, but ART is provided in only one out of 223 prisons [74]. Few countries implement comprehensive HIV and HCV prevention, treatment and care programmes in prisons, often because of ideological objections or denial about sex and drug use among prisoners, and many fail to adequately link health services in prisons to national programmes [75]. Abuses are starkly evident in the notorious detention centres in several Asia countries in which KP and others are arbitrarily detained for lengthy periods for “rehabilitation,” and are subject to forced labour and other abuses, including lack of access to adequate healthcare [42]. The high prevalence of infections in prison settings cannot be separated from broader public health concerns, and the fulfilment of the right to health of people in prisons needs to be seen as a part of state obligations to fulfil the right to health of the population as a whole.

Rates of ART coverage among migrants and refugees are unknown. The Global Commission on HIV and the Law estimated some 214 million international migrants worldwide, and 740 million internal migrants, in 2012 [76]. The Commission was clear in its findings for migrant populations: “In matters relating to HIV and the law, countries should offer the same standard of protection to migrants, visitors and residents who are not citizens as they do to their own citizens.” The reality is that migrants in most countries do not have equal access to healthcare or adequate standards of legal protection. Despite internationally recognized legal status [77], refugees often do not receive access to medical care on par with that received by citizens. Governments may cite migrants’ mobility or instability and the prioritization of care of its own citizens as reasons to deny ART to migrants [78]. People who have left their countries of origin do not lose the human right to healthcare, and migrants cannot be
excluded from accessing services if the global HIV pandemic is to be controlled.

**Global guidance on antiretroviral therapies for treatment and prevention among KP**

The WHO 2013 “Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection” [4] and new 2014 consolidated guidance on HIV among KP offer the potential for KP’s increased access to HIV testing and counselling (HTC) and ART for both treatment and prevention.

**ART**

New clinical recommendations in the consolidated guidelines raised the threshold for treatment initiation to $< 500$ CD4 cells/mm$^3$, giving priority to individuals with severe or advanced HIV disease and those at $< 350$ CD4 cells/mm$^3$ [4]. Consistent with earlier WHO guidance [9,10], the 2013 guidelines recommend that ART initiation in KP should follow the same principles as for the general population (i.e. in general, initiated at a CD4 count of $< 500$ cells/mm$^3$). However, recommendations that ART should be initiated regardless of CD4 count for people in particular circumstances may apply to certain KP, including people who have HIV and active TB and people with an HIV-hepatitis B co-infection and severe chronic liver disease (this would include PWID, prisoners and migrants, among others), pregnant women (pregnant FSW living with HIV, women with HIV who inject drugs, prisoners and migrants, among others) and people in serodiscordant relationships (male same-sex couples, sex workers and their primary partners, and PWID and their primary partners, among others).

Additionally, WHO guidelines recommend fixed dose combinations including tenofovir as first-line regimens. While it has been extensively demonstrated that age, race, sex, educational level, socioeconomic status and a past history of alcoholism or drug use do not reliably predict suboptimal adherence, the indication of simpler combinations may reduce the risk of non-adherence, which can lead to resistance. Despite the WHO recommendations, the best nontoxic and easy-to-use ART may not be routinely available in resource-limited settings. Furthermore, specific populations like KP, due to structural factors, generally have difficult or very limited access to quality care and treatment options. Converging efforts, from the public and the private sector, must be made to ensure that the best drugs and the new drug classes, including the new HIV integrase inhibitors, become readily available worldwide and specifically for KP, to reach the levels of full and sustained HIV suppression which not only have a clinical and HIV transmission benefit, but also minimize the risk of a progressive spread of drug resistance.

WHO estimates that an additional 11 million PLHA globally will become eligible for ART under the 2013 guidelines. While it is unknown how many KP are newly eligible, it is plausible that the new guidelines could help to expand access to ART for both treatment and prevention for them. However, in many countries, the recommendations are unlikely to result in expanded access for KP unless special attention is paid to issues of equity, human rights and barriers that they face in accessing HIV and other health services.

**HIV testing and counselling**

The guidelines affirm earlier WHO guidance that in generalized epidemics, HTC should be routinely recommended for KP in all health facilities, and that in low and concentrated epidemics it should be considered in health facilities offering services for STI, hepatitis, TB and antenatal care, as well as in health services specifically for KP. Recognizing that many people from KP may not attend health facilities, the guidelines also recommend that community-based HTC should be available to KP in all epidemic settings, with appropriate confidentiality and informed consent.

**Pre-exposure prophylaxis**

The 2013 ART guidelines affirmed existing WHO guidance [55,79,80] that daily oral pre-exposure prophylaxis (PrEP) may be considered as a possible intervention for uninfected partners in serodiscordant couples on a limited basis through “demonstration projects.” New WHO KP guidance in 2014 recommends that PrEP be available as an option for serodiscordant couples and for men or transgender women who have sex with men, but there is no specific recommendation for other KP.

**Post-exposure prophylaxis**

Post-exposure prophylaxis (PEP) is the use of ART to prevent HIV infection after a single high-risk HIV exposure, and it has been used in some countries for MSM and sex workers. Since PEP must be started as soon as possible and must be taken for 28 days, it has had limited use as a prevention tool, but there is considerable evidence for its effectiveness. While PEP is an important prevention tool, it cannot substitute for other proven HIV prevention methods, such as consistent condom use or use of sterile injecting equipment [81], and PEP services may be an effective entry point for accessing these methods and other prevention services.

**Protecting rights and addressing barriers**

Stigma, discrimination and punitive laws, policies and practices significantly limit access to ART and other HIV interventions [58,82,83]. Eighty countries outlaw same-sex activity [84]; more than 100 countries criminalize some aspect of sex work; many countries require registration of drug users or employ predominantly criminal justice – rather than public health – approaches to drug use; and effective drug dependence treatment is not legally available in many countries [85]. Criminalization of HIV transmission and failure to legally recognize transgender status also present barriers to ART access in many countries [71].

Data on KP remain very limited, including population size estimates and data relating to access and barriers to services. Data collection systems in countries need to more adequately address issues for KP, while always protecting individuals’ confidentiality and security. The international community must also more effectively address trade and intellectual property barriers to ART access, including TRIPS and “TRIPS-plus” provisions [51].
Rights-based approaches and investments in evidence-based critical enablers, such as supportive legal and policy environments, are essential to increase access to ART and other HIV interventions for KP. Evidence-based approaches can include strategic litigation [85]. Particular attention is needed to ensure that available services for KP are equipped to meet the needs of adolescents and young adults. Approaches must include measures to combat stigma and discrimination, mobilize and empower communities and increase the availability of non-judgmental, community-based services.

Conclusions
Universal access to ART for those who need and want it has long been a core human rights principle of the HIV response, and it now has an expanded clinical and public health rationale. This article provides clear evidence that KP account for a significant proportion of the global burden of HIV, and that epidemics among KP are characterized by extraordinarily high prevalence levels and remarkably low levels of access to HIV treatment and prevention worldwide. Extending the benefits of ART to KP is critical to increasing the impact of ART and the overall effectiveness of the HIV response, but this can only be achieved through an extraordinary effort to address the barriers that KP face, including stigmatization, discrimination and punitive laws, policies and practices.

Communities at risk are justifiably sceptical that ART will be made available with the necessary equity, respect for human rights and non-discrimination that are required to ensure success. ART should always be offered in the context of comprehensive HIV care and prevention services, and only with informed consent. The primary objective of ART should always be to treat the person living with HIV; prevention is an important, secondary benefit. Additionally, governments must not use the preventive benefits of treatment as a pretext for failing to provide critical and comprehensive prevention interventions for KP, including condom promotion, behaviour change, comprehensive harm reduction for PWID, and community empowerment and other rights-based approaches. An end to AIDS is possible only if we overcome the barriers of criminalization, stigma and discrimination that remain key drivers of the epidemic.

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References
1. Nolan S, Wood E. End of the debate about antiretroviral treatment initiation. Lancet Infect Dis. 2014;14(4):258–9.
2. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365(6):493–505.
3. Tanser F, Barnighauser T, Grapa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural Kwazulu-Natal, South Africa. Science. 2013;339(6122):966–71.
4. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating adults and children. Geneva: World Health Organization; 2013.
5. Baral SD, Grosso A, Holland C, Papworth E. The epidemiology of HIV among men who have sex with men in countries with generalized epidemics. Curr Opin HIV AIDS. 2014;9(2):156–7.
6. Beyrer C, Baral SD, Weir BW, Curran IW, Chaisson RE, Sullivan PS. A call to action for concentrated HIV epidemics. Curr Opin HIV AIDS. 2014;9(2):95–100.
7. UNAIDS, World Bank. New HIV infections by modes of transmission in West Africa: a multi-country analysis. Geneva: UNAIDS Regional Support Team for West & Central Africa; 2010.
8. Gelmon L, Kenya P, Oguya F, Cheluget B, Haile G. Kenya HIV prevention response and modes of transmission analysis. Nairobi: Kenya National AIDS Control Council, World Bank, UNAIDS; 2008.
9. World Health Organization. Prevention and treatment of HIV and other sexually transmitted infections among men who have sex with men and transgender people: recommendations for a public health approach, 2011. Geneva: World Health Organization; 2011.
10. World Health Organization. Prevention and treatment of HIV and other sexually transmitted infections among men who have sex with men and transgender people: recommendations for a public health approach. Geneva: World Health Organization; 2012.
11. World Health Organization, UNODC, UNAIDS. Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users, 2012 revision. Geneva: WHO; 2012.
12. Baral SD, Poteat T, Strimbaldi S, Wirtz A, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. Lancet Infect Dis. 2013;13:214–22.
13. Price MA, Rida W, Mwamgome M, Mutua G, Middlekoop K, Roux S, et al. Identifying at-risk populations in Kenya and South Africa: HIV incidence in cohorts of men who report sex with men, sex workers, and youth. J Acquir Immune Defic Syndr. 2012;59(2):185–93.
14. Baral S, Sifakis F, Cleghorn F, Beyrer C. Elevated risk for HIV infection among men who have sex with men in low- and middle-income countries: recommendations for a public health approach. Geneva: World Health Organization; 2011.
15. Van Griensven F, Varangrat A, Wimonsate W, Tanpradech S, Kladswad K, Chennasiri T, et al. Trends in HIV prevalence, estimated HIV incidence, and risk behavior among men who have sex with men in Bangkok, Thailand, 2003–2007. J Acquir Immune Defic Syndr. 2010;53(2):234–9.
16. Zhang M, Chu Z, Wang H, Xu J, Lu C, Shang H. A rapidly increasing incidence of HIV and syphilis among men who have sex with men in China. J Acquir Immune Defic Syndr. 2007;47(2):e339.
17. Couture MC, Sansothy N, Sapphon V, Phal S, Sichan K, Stein E, et al. Young women engaged in sex work in Phnom Penh, Cambodia, have high incidence of HIV and sexually transmitted infections, and amphetamine-type stimulant use: new challenges to HIV prevention and risk. Sex Transm Dis. 2011;38(1):33–9.
18. Baral S, Beyrer C, Muesing K, Poteat T, Wirtz AL, Becker MR, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12(7):538–49.
19. Riedner G, Hoffmann O, Ruszoa M, Mmbando B, Nabakka L, Grosskurth H, et al. Decline in sexually transmitted infection prevalence and HIV incidence in female barworkers attending prevention and care services in Mbeze Region, Tanzania. AIDS. 2006;20(4):609–15.

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There are no conflicts of interest to declare.

Authors' contributions
The IAS Treatment for Key Affected Populations Working Group conceptualized the idea for the longer, white paper version of this article. CB directed the writing and conceptualization of this version of the paper. IG was the lead writer, with writing and editing also done by SB and CB. The other authors contributed to the overall manuscript edits and ideas.
20. Kozlov AP, Shaboltas AV, Yousovo SV, Verevokhin SV, Masse R, Perdue T, et al. HIV incidence and risk factors associated with HIV acquisition among injection drug users in St. Petersburg, Russia. AIDS. 2006;20(6):901–6.

21. Strathean SA, Hallett TB, Bobrova N, Rhodes T, Booth R, Abdool R, et al. HIV and risk environment for injecting drug users: the past, present, and future. Lancet. 2010;376(9737):268–84.

22. Degenhardt L, Mathers BM, Wirtz A, Wolfe D, Kamarulzaman A, Carrié MP, et al. What has been achieved in HIV prevention, treatment and care for people who inject drugs, 2010–2012? A review of the six highest burden countries. Int J Drug Policy. 2013;25(1):54–60.

23. Sarna A, Sarawati LR, Sebastian M, Sharma V, Madan J, Lewis D, et al. High HIV incidence in a cohort of male injection drug users in Delhi, India. Drug Alcohol Depend. 2014;139:106–14.

24. Herbst JH, Jacobs ED, Finlayson TJ, McIelry VS, Neumann MS, Cepa N, et al. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. AIDS Behav. 2008;12(1):1–17.

25. Operario D, Soma T, Underhill K. Sex work and HIV status among transgender women: systematic review and meta-analysis. J Acquir Immune Defic Syndr. 2008;48(1):97–103.

26. Beyer C, Baral SD, van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz A, et al. A global epidemiology of HIV infection in men who have sex with men. Lancet. 2012;380(9839):367–77.

27. UNAIDS. Country snapshot: China — men who have sex with men. HIV/ AIDS Asia Pacific Research Statistical Data Information AIDS Data Hub; 2012 [cited 2014 Jun 13]. Available from: www.aidsdatahub.org

28. AmfAR, Treat Asia. HIV/AIDS in Asia overview. 2010 [cited 2014 Jun 13]. Available from: http://www.amfar.org/around-the-world/treat-asia/aids-in-asia/hiv-aids-in-asia

29. Smith AD, Tapsoba P, Ndes N, Sanders EJ, Sanders E, Jaffe HW. Men who have sex with men and HIV/AIDS in sub-Saharan Africa. Lancet. 2009;374(9687):846–22.

30. Sullivan PS, Carballo-Điéguez A, Coates T, Goodreau SM, McGowan L, Sanders EJ, et al. Successes and challenges of HIV prevention in men who have sex with men. Lancet. 2012;380(9839):388–99.

31. Yang C, Latkin C, Luan R, Nelson K. Condom use with female sex workers among male clients in Sichuan Province, China: the role of interpersonal and venue-level factors. J Urban Health. 2010;87(2):292–303.

32. UNAIDS. Global report: UNAIDS report on the global AIDS epidemic 2010. Geneva: UNAIDS; 2010.

33. Aggleton P. Men who sell sex: international perspectives on male prostitution and HIV/AIDS. Philadelphia: Temple University Press; 1999.

34. Atice FL, Kamarulzaman A, Soriano VV, Schechter M, Friedland GH. Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. Lancet. 2010;376(9738):367–87.

35. New York City Department of Health and Mental Hygiene. New York City HIV/AIDS surveillance slidesets, 2010. New York: New York City Department of Health and Mental Hygiene; 2012.

36. Stephens SC, Bernstein KT, Philip SS. Male to female and female to male transgender persons have different sexual risk behaviors yet similar rates of STDs and HIV. AIDS Behav. 2011;15(3):683–6.

37. Jürgens R, Nowak M, Day M. HIV and incarceration: prisons and detention. Int J AIDS Soc. 2011;14:26.

38. Stein MS, Spaulding AC, Cunningham M, Messina LC, Kim BI, Chung KW, et al. HIV-positive and in jail: race, risk factors, and prior access to care. AIDS Behav. 2013;17(Suppl 2):S108–17.

39. Wolfe D, Carrié MP, Shepard D. Treatment and care for injecting drug users with HIV infection: a review of barriers and ways forward. Lancet. 2010;376(9738):555–66.

40. Centers for Disease Control. HIV in correctional settings. Centers for Disease Control. [cited 2014 Jun 13]. Available from: http://www.cdc.gov/hiv/risk/other/correctional.html

41. World Bank AIDS Campaign Team for Africa, Joint United Nations Programme on HIV/AIDS, and United Nations Office on Drugs and Crime. HIV and prisons in sub-Saharan Africa: opportunities for action. Vienna: United Nations Office on Drugs and Crime; 2007.

42. Amon J, Pearshouse R, Cohen J, Schleifer R. Compulsory drug detention centers in China, Cambodia, Vietnam, and Laos: health and human rights abuses. Health Hum Rights. 2013;15(2):114–37.

43. World Health Organization. Evidence for action technical papers: effectiveness of interventions to address HIV in prisons. Geneva: World Health Organization; 2007.

44. World Health Organization. TB in prisons. WHO. [cited 2014 Jun 16]. Available from: http://www.who.int/tb/challenges/prisons/tb_in_prisons_lit_review_10feb08.pdf?ua=1

45. World Health Organization. Literature review on TB in prisons. WHO. [cited 2014 Jun 16]. Available from: http://www.who.int/tb/challenges/prisons/prisons_story_1/en/

46. Stuckler D, Basu S, McKee M, King L. Mass incarceration can explain population increases in TB and multi-drug resistant TB in European and Central Asian countries. Proc Natl Acad Sci USA. 2008;105(36):13280–5.

47. International Federation of Red Cross and Red Crescent Societies. HIV and population mobility. In: Knight L, editor. World disasters report 2008: focus on HIV and AIDS. Geneva: International Red Cross; 2008. p. 96–117.

48. Southern African HIV Clinicians Society, UNHCR. Clinical guidelines for antiretroviral therapy management for displaced populations. Meadowdale, South Africa: Southern African HIV Clinicians Society; 2007.

49. Trippayya V. Botswana: refugees not entitled to same services as citizens. HIV AIDS Policy Law Rev. 2005;10(3):27–8.

50. Beyer C, Baral S, Zenilman J. STDs, HIV/AIDS and migrant populations. In: Holmes K, Sparling PF, Stamm WE, Plotz P, Wasserheit J, Corey L, et al., editors. Sexually transmitted diseases. Seattle: McGraw-Hill Professional; 2007. p. 257–68.

51. UNDP HIV/AIDS Group. Global commission on HIV and the law: risks, rights and health. New York: UNDP HIV/AIDS Group; 2012.

52. Mayer KH, Bekker LG, Stal R, Grulich AE, Colfax G, Lama JR. Comprehensive clinical care for men who have sex with men: an integrated approach. Lancet. 2010;376(9839):378–87.

53. Bekker L, Johnson L, Overy S. Combination HIV prevention for female sex workers: what is the evidence? Lancet. 2014. doi: http://dx.doi.org/10.1016/S0140-6736(14)60740-0

54. Arreola S, Hebert M, Makone K, Beck J, Ayala G. Access to HIV prevention and treatment for men who have sex with men: finding from the 2012 global mens health and rights survey (GMHR). Oakland, CA: The Global Forum on MSM & HIV (MSMGF); 2012.

55. World Health Organization, UNICEF. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: progress report 2009. Geneva: World Health Organization; 2009.

56. Beyer C, Sullivan P, Sanchez J, Baral SD, Collins C, Wirtz AL, et al. The increase in global HIV epidemics in MSM. AIDS. 2013;27(17):2665–78.

57. Rodger A, Bruun T, Cambiano V, Vernazza P, Estrada V, Van Lunzen J. HIV transmission risk through condomless sex if HIV + partner on suppressive ART: PARTNER study. Proceedings of the Conference on Retroviruses and Opportunistic Infections. Boston, MA: Pittsburg, PA: CRDI Foundation; 2014.

58. Beyer C, Sullivan PS, Sanchez J, Dowdy D, Altman D, Trapence G, et al. A call to action for comprehensive HIV services for men who have sex with men. Lancet. 2012;380(9839):424–38.

59. World Health Organization, UNICEF, UNAIDS. Global update on HIV treatment 2013: results, impact and opportunities. Geneva: World Health Organization; 2013.

60. Becker ML, Mishra S, Satyanarayana, Gurur K, Doshi M, Buujand G, et al. Rates and determinants of HIV-attributable mortality among rural female sex workers in northern Karnataka, India. Int J STD AIDS. 2012;23(1):36–40.

61. Chakrapani V, Newman PA, Shunugapag M, Kuriak AN, Dubrov R. Barriers to free antiretroviral treatment access for female sex workers in Chennai, India. AIDS Patient Care STDs. 2009;23(11):973–80.

62. Goldberg S, Duff P, Gulliemi S, Dobrer S, Montaner J, Shannon K. Migration and mobility, incarceration, and younger age predict HAART discontinuation among female sex workers: a longitudinal study in Vancouver, Canada. Proceedings of the International AIDS Society Conference. Melbourne, Australia. Geneva: International AIDS Society; 2014.

63. Shannon K, Strathdee SA, Goldenberg SM. The global epidemiology of HIV among female sex workers: the influence of structural determinants. Lancet. 2014. doi: http://dx.doi.org/10.1016/S0140-6736(14)60931-4

64. McClelland RS, Graham SM, Richardson BA, Peshu N, Masese LN, Wanje GH, et al. Treatment with antiretroviral therapy management for displaced populations. Meadowdale, South Africa: Southern African HIV Clinicians Society; 2007.

65. World Health Organization. HIV and prisons in sub-Saharan Africa: opportunities for action. Vancouver, Canada. Proceedings of the International AIDS Society Conference. Melbourne, Australia. Geneva: International AIDS Society; 2014.
HIV/AIDS morbidity, mortality and HIV transmission: the HIV treatment as prevention experience in a Canadian setting. PLoS One. 2014;9(2):e87872.

67. Mathers BM, Degenhardt L, Ali H, Wiessing L, Hickman M, Mattick RP, et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet. 2010;375(9719):1014–28.

68. Petersen Z, Myers B, van Hout MC, Plüddemann A, Parry C. Availability of HIV prevention and treatment services for people who inject drugs: findings from 21 countries. Harm Reduct J. 2013;10:13.

69. Westergaard RP, Ambrose BK, Mehta SH, Kirk GD. Provider and clinic-level correlates of deferring antiretroviral therapy for people who inject drugs: a survey of North American HIV providers. J Int AIDS Soc. 2012;15(1):10.

70. Thorne C, Semenenko I, Malyuta R, Ukraine European Collaborative Study Group in EuroCoord. Prevention of mother-to-child transmission of human immunodeficiency virus among pregnant women using injecting drugs in Ukraine, 2000–10. Addiction. 2012;107(1):118–28.

71. Poteat T, Reisner SL, Radix A. HIV epidemics among transgender women. Curr Opin HIV AIDS. 2013;9:168–73.

72. Sevelius JM, Carrico A, Johnson MO. Antiretroviral therapy adherence among transgender women living with HIV. J Assoc Nurses AIDS Care. 2010;21(3):256–64.

73. Chakrapani V, Newman PA, Shumugam M, Dubrow R. Barriers to free antiretroviral treatment access among kothi-identified men who have sex with men and aravanis (transgender women) in Chennai, India. AIDS Care. 2011;23(12):1687–94.

74. Wiltenburg Todrys K, Kwon S-R. Even dead bodies must work: health, hard labor, and abuse in Ugandan prisons. New York: Human Rights Watch (HRW); 2011.

75. UNODC, ILO, UNDP, WHO, UNAIDS. Policy brief on HIV prevention, treatment and care in prisons and other closed settings. Vienna: UNODC; 2013.

76. Global Commission on HIV and the Law. Regional issues brief: laws and practices related to criminalization of people living with HIV and populations vulnerable to HIV. New York: Global Commission on HIV and the Law; 2011.

77. United Nations. Convention relating to the status of refugees. New York: United Nations; 1951.

78. Mendelsohn JB, Schliproo M, Spiegel P, Balasundaram S, Radhakrishnan A, Lee CK, et al. Is forced migration a barrier to treatment success? Similar HIV treatment outcomes among refugees and a surrounding host community in Kuala Lumpur, Malaysia. AIDS Behav. 2014;18(2):323–34.

79. World Health Organization. Guidance on couples HIV testing and counseling including antiretroviral therapy for treatment and prevention in serodiscordant couples: recommendations for a public health approach. Geneva: World Health Organization; 2012.

80. World Health Organization. Guidance on pre-exposure oral prophylaxis (prep) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV: recommendations for use in the context of demonstration projects. Geneva: World Health Organization; 2012.

81. Smith DK, Grohskopf LA, Black RJ, Auerbach JD, Veronesi F, Struble KA, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep. 2005;54(RR-2):1–20.

82. UNAIDS. Key programmes to reduce stigma and discrimination and increase access to justice in national HIV responses. Geneva: UNAIDS; 2012.

83. Heywood M, Altman D. Confronting AIDS: human rights, law and social transformation. Health Hum Rights. 2000;5(1):149–79.

84. Kyomya M, Todrys KW, Amon JJ. Laws against sodomy and the HIV epidemic in African prisons. Lancet. 2012;380(9839):310–2.

85. Jurgens R, Cuesta J, Amon JJ, Baral S, Beyer C. People who use drugs, HIV, and human rights. Lancet. 2010;376(9739):475–85.