HHS Public Access

Author manuscript

Sex Transm Dis. Author manuscript; available in PMC 2022 July 01.

Published in final edited form as:

Sex Transm Dis. 2021 July 01; 48(7): 466–473. doi:10.1097/OLQ.0000000000001341.

Collateral Damage: A Narrative Review on Epidemics of Substance Use Disorders and their Relationships to Sexually Transmitted Infections in the United States

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Abstract

Associations between substance use disorders (SUDs) and outbreaks of HIV and acute viral hepatitis have received considerable attention, but less research has focused on links between SUDs and sexually transmitted infections (STIs), apart from alcohol misuse. This narrative review describes the history of this public health crisis in the US and direct and indirect effects opioids and specific stimulants have on high risk sexual behaviors. We also review the epidemiology of STIs associated with opioids and stimulants in the U.S. and discuss opportunities for integrated interventions.

Short Summary:

This narrative review describes the relationship between the U.S. opioid epidemic, its relationship with the epidemiology of sexually transmitted infections, and opportunities for integrated interventions.

Introduction

Although the U.S. has been a major consumer of opiates for centuries, daily consumption of opioids per capita skyrocketed in the early 21st Century, with major impacts on the incidence of overdose, blood-borne infections and life expectancy.[1] Associations between substance use disorders (SUD) and outbreaks of HIV and acute viral hepatitis have received considerable attention, but less research has focused on the link between SUD and sexually transmitted infections (STIs), apart from alcohol misuse.[2] An otherwise excellent 2020 report from the National Academies of Science, Engineering and Medicine on opportunities to improve services for opioid use disorder (OUD) and infectious disease did not mention any STIs.[3] This narrative review describes the history of this public health crisis and direct

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Conflict of Interest Statement: None

and indirect effects opioids and specific stimulants have on high risk sexual behaviors. We also review the epidemiology of STIs associated with opioids and stimulants in the U.S. and discuss opportunities for integrated interventions.

In the 1990's, the U.S. Food and Drug Administration (FDA) granted approvals for prescription opioids such as oxycodone and fentanyl to treat chronic pain,[4] following assurances from their manufacturers that they were non-addictive. This was followed by increasing reports of deaths associated with prescription opioid misuse, especially oxycodone, marketed as Oxycontin,® which by 2003 was already being used by 2.8 million Americans. After an extended-release (ER) oxymorphone, OpanaER,® was approved by the FDA in 2006, contentions about the non-addictive properties of prescription opiates were disproven,[5] but not before millions more Americans developed an OUD. In 2012, Opana's® manufacturer switched to a more tamper-resistant formulation and policy reform reduced the number of physicians who were prescribing opioids for chronic pain. This did not reduce the number of people with OUD, however, since the number of physicians prescribing medications to treat opioid disorder (MOUD) across the U.S. was limited, primarily due to a number of structural barriers.[3] Instead, some people with OUD began injecting Opana,®[6] while others transitioned to injecting black-tar heroin, which had become widely available and less expensive.[7]

In the first decade of the 21st Century, the U.S. opioid use epidemic was linked to increases in other health problems, especially in the country's most socially disadvantaged regions, like Appalachia.[8] In Tennessee, Kentucky, Virginia and West Virginia, incidence of acute hepatitis C virus (HCV) infection increased 364% between 2006 and 2012 among people who inject drugs (PWID) under thirty years of age.[9] In 2015, an HIV outbreak occurred among PWID in a rural county in southern Indiana, which quickly spread to their sexual partners, leading to a community-level HIV prevalence of 5%.[10] Subsequent HIV outbreaks among PWID occurred in other rural and suburban counties, such as those in West Virginia, Massachusetts and Washington.[11, 12] Nationally, the number of overdose deaths associated with prescription opioids, heroin and fentanyl soared, with annual U.S. overdose deaths from 2017 to 2019 surpassing that for HIV/AIDS at its peak. In 2018, an estimated 10.3 million Americans aged 12 or older misused opioids in the past year (9.9 million of whom misused prescription pain relievers and 808,000 people used heroin).[13] These trends were compounded by a concomitant rise in stimulant use; from 2015 to 2018, 1.6 million Americans reported using methamphetamine in the past year,[14] of whom nearly half met criteria for a methamphetamine use disorder.

Direct and Indirect Influences of Substance Use on Sexual Behaviors

Substance use and misuse can have a direct and/or an indirect effect on sexual behaviors[15, 16] that can predispose to STIs. Some substances have a direct effect on sexual behaviors due to mood-altering effects on the brain.[17] Alcohol is the most frequently used substance to facilitate sex, as it can relax inhibitions[18] and increase motivations to engage in sex. In one study of STI clinic clients, men reported drinking more alcohol and having more sexual partners than women, but among women, alcohol use associated with a higher number of sexual partners.[19] After alcohol, marijuana is the most commonly used

psychotropic drug in the U.S.[20] However, there are no consistent links between marijuana use and HIV/STI transmission risks,[21] with a few exceptions.[22] In a review of sexual health services in primary care, marijuana use was significantly associated with multiple sexual partnerships[23] among women of child-bearing age but not with HIV/STI outcomes. In a study of youth living with HIV, marijuana use was associated with STIs.[24]

Compared to alcohol, fewer people use stimulant drugs such as cocaine/crack, methamphetamine and ecstasy, but their impact on sexual behaviors is profound. Stimulants are associated with increased sexual behavior among both sexes,[25] although motivations for their use can differ between men and women[26] and heterosexuals versus sexual minorities, especially men having sex with men (MSM).[27] Methamphetamine use has been associated with enhanced sexual function[28, 29] and libido, sexual compulsivity[30] and reduced sensation of pain.[31] Compared to non-users, MSM reporting methamphetamine use report greater numbers of anal sex partners in a short period of time, longer duration of sexual activity (e.g., “sex marathons”), and physically traumatic sexual activity such as “fisting” that can rupture rectal tissue predisposing to an increased risk of STI acquisition.[32-36] Among men, prolonged, heavy use of methamphetamine can cause an inability to achieve and maintain an erection.[37, 38] When erectile dysfunction medications became available, some users also began using them with stimulants.[16]

Both heterosexual and MSM methamphetamine users also report frequently engaging in anal sex and trading sex for methamphetamine.[30, 39] Some female sex workers (FSW) report using methamphetamine to stay awake, or to cope with the occupational hazards of sex work.[40] For example, in studies of FSW in Mexico, engaging in substance use prior to or during sexual transactions was independently associated with incidence of gonorrhea, Chlamydia[41] and syphilis titers consistent with active infection.[42]

Recent data suggests that methamphetamine use releases pro-inflammatory cytokines in the gut[43, 44] (a key site for establishing HIV, Chlamydia and rectal gonorrheal infections).[45, 46] Significant variation in microbiota species in the gut has been observed for MSM living with HIV who report receptive anal intercourse and recent use of methamphetamine or marijuana.[47] Considering that some STIs can contribute to inflammation from HIV to enhance inflammation within the gut,[48] this direction offers a new area of research that may uncover mechanistic insights into HIV and STI transmission.

In contrast to stimulants, opioids tend to dampen interest and desire for sex[49] and their influence on STI risk appears indirect, as a consequence of addiction. The physically painful withdrawal symptoms that accompany OUD can motivate high-risk sexual behaviors, such as trading sex for money or drugs, with greater dependence driving more frequent sexual transactions as well as drug use.[50] Sex workers experiencing OUD withdrawal may be more likely to acquiesce to their client’s demands for condomless sex for more money, or in exchange for drugs.[51] Opiate users may also engage in polypharmacy, for example combining stimulants with opioids to provide libido or energy needed to engage in sex.

A form of sexualized drug use mostly engaged in by MSM involves “chemsex,” which is the use of any one or combination of alcohol, stimulants (e.g., methamphetamine, cocaine,

ecstasy), GHB, and erectile dysfunction drugs to intensify or to prolong sexual encounters. Sexualized drug use has been documented in communities of MSM for over 25 years,[52] and exists on every continent.[53-57] In a systematic review of 38 studies, chemsex was reported more consistently by HIV-positive than HIV-negative MSM, primarily to enhance condomless anal intercourse.[55] Unique linkages between substances, sex and other factors are found among military personnel, where drug use was strongly associated with STIs for men who only have sex with women (MSW).[58] A separate study showed similar associations between substances used, numbers of partners and STIs in both sexes.[59]

Sex differences have been observed in the subjective effects and pharmaco-toxicological responses to various drugs.[60, 61] In general, men are more likely than women to use almost all types of illicit drugs and to present at emergency departments (ED) for overdose.[61] However, relative to men, women are just as likely to develop SUDs, and may be more disposed to craving and relapse.[61]

Epidemiology of STIs linked to Substance Use

In the U.S., STI incidence rates are the highest in over 25 years.[62] After years of decline, incidence of syphilis, gonorrhea and chlamydia have been on the rise, with a combined total of nearly 2.5 million cases reported to the U.S. Centers for Disease Control and Prevention (CDC) in 2018. The US incidence of chlamydia is the highest of any bacterial STI at 692.7 cases per 100,000 for women and 380.6 cases per 100,000 among men.[62] Rates of both gonorrhea and syphilis are highest among men, particularly among MSM, but have also been increasing among women.[63] High rates of gonorrhea are particularly concerning given the growing threat of *Neisseria gonorrhoeae*, the bacteria that cause gonorrhea, that are resistant to multiple antibiotics.[64]

Increasing rates of primary and secondary syphilis among adults have coincided with increasing cases of congenital syphilis,[62] which can result in newborn death, miscarriage or severe lifelong physical and neurological problems.[65] *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections can result in lifelong consequences including pelvic inflammatory disease, infertility, and ectopic pregnancy. STIs can also increase the risk of HIV acquisition and among those who are living with HIV, can increase the risk of onward HIV transmission.[66-69] CDC surveillance data does not stratify rates of STIs among transgender people; however, a recent systematic review found that prevalence of syphilis, gonorrhea, and chlamydia ranged from 1.4% to 50.4%, 2.1% to 19.1%, and 2.7% to 24.7% in transgender women, respectively, and from 0% to 4.2%, 0% to 10.5%, and 1.2% to 11.1% in transgender men, respectively.[70]

Use of recreational drugs may increase risk of both bloodborne and non-bloodborne STIs. In systematic reviews, prevalence of HSV-2 was high among people who use drugs.[71] Crack cocaine use has been consistently associated with higher STI incidence.[72] A recent nationally representative survey of 18-25 year olds in the U.S. showed that odds of contracting STIs in the preceding year was over three times higher among those who reported use of illicit drugs in the last year compared to those who did not report illicit drug use.[73] During 2014-2018, the rate of primary and secondary syphilis increased 171.4%, the

proportion of women with primary and secondary syphilis reporting injection drug use in the past 12 months increased from 6.1% to 11.4%,[74] and the rate of congenital syphilis increased 185.3%.[62, 75] There was also an increase in the proportion of primary and secondary syphilis cases among MSW who reported injection drug use, from 3.7% to 7.4%, [74] but this trend was not observed among MSM. Additionally, during 2014-2018, there were substantial increases, more than doubling in some cases, for the proportions of women and MSW with primary and secondary syphilis who reported methamphetamine use (6.8% to 18.9% for women; 7.4% to 14.8% for MSW), heroin use (3.1% to 7.3% for women; 1.8% to 4.3% for MSW), or sex with a PWID (8.3% to 12.6% for women; 5.8% to 9.8% for MSW). [74] Women may experience unique challenges to STI prevention. Over a third (34.7%) of women with primary and secondary syphilis report sex while intoxicated or on drugs and 9.5% have exchanged sex for drugs or money.[76] FSW may be less likely to receive and access STI prevention services[77] than other at-risk populations and drug use among FSWs may be associated with an even higher risk of STIs compared to FSW that do not use drugs. [78] Epidemics of substance use and syphilis among U.S. heterosexual men and women can be considered syndemics, which are overlapping epidemics that share common root causes, including poverty, unemployment, intimate partner violence and homelessness.[79-83]

Persons seeking treatment for STIs often have SUD. In a study of Baltimore STD clinics, 57% of clients had SUD (35% alcohol, 31% cannabis, 11% opioids, and 8% stimulants),[84] which is higher than expected for the general U.S population. Additional variations in prevalence of substance use, misuse and SUD are observed by sexual orientation with sexual minorities having higher prevalence compared to their heterosexual peers (through age 25), [85-87] with less consistent findings in later age groups. In a prospective study of attendees at STI treatment clinics,[88] latent class analysis identified four classes of subjects - low substance use and mostly marijuana use; two classes of subjects with severe club drug use (powder cocaine, GHB, ecstasy) and a class with severe street drug use (injection drug use, heroin, cocaine). STI prevalences were highest for the classes with severe club drug and severe street drug use, compared to STI prevalences in the other two classes across all sexual orientations. Notable exceptions involved the mostly marijuana use class which showed higher STI rates than the other three classes for MSM and women who have sex with women. This suggests that specific subgroups of substance users who have higher STI prevalence could be targeted for interventions.

Racial/Ethnic and Geographic Disparities in STIs associated with Substance Use

There are significant racial/ethnic and geographic disparities in the prevalence of both STIs and substance use.[89-93] National U.S. surveillance reports consistently indicate that gonorrhea, chlamydia and syphilis incidence are substantially higher among racial/ethnic minorities relative to Whites.[62] In 2018, African Americans had the highest rates of gonorrhea (548.9 cases per 100,000) and chlamydia (1,192.5 cases per 100,000). American Indians/Alaska Natives (AI/AN) had the second highest rates of gonorrhea (329.5 cases per 100,000) and chlamydia (784.8 cases per 100,000) in the U.S. Combined, these rates were approximately 4-8 times the rate among Whites in 2018. Moreover, primary and secondary

syphilis cases have increased for all racial/ethnic groups from 2014-2018, more than doubling for AI/AN (7.2 to 15.5 cases per 100,000) and multiracial individuals (4.6 to 9.4 cases per 100,000). In 2018, African Americans and Hispanics accounted for just over half of all reported primary and secondary syphilis with known racial/ethnic information.[62] Geographical variations have also been well documented with Southern states having clusters of high STI prevalence.[94-96]

Differing rates of illicit substance use have also been observed by race/ethnicity. According to the 2019 National Survey on Drug Use and Health (NSDUH), 13.1% multiracial, 11.3% AI/AN, and 9.1% White individuals age 12 and older used illicit drugs in the past year, exceeding the national average of 8.6%; whereas the proportion of African Americans, Hispanics, and Asians with past year illicit drug use was below the national average.[20]

Although illicit drug use can lead to unsafe sexual practices including condomless sex and multiple sexual partners, national population-based studies suggest that racial/ethnic disparities in STIs are not fully explained by differences in individual sexual and drug use patterns.[89, 97] Rather, social and environmental conditions including social and sexual networks, shortage of healthcare providers, differential access to health services, and economic inequalities contribute to persistent disparities.[98] For racial/ethnic groups residing in rural/remote regions of the U.S. including American Indian tribal reservations and Southern states, geographic isolation, privacy and confidential concerns also contribute to differential STI prevalence.[99-101] For example, studies have shown rurality and proximity to healthcare services influence STI screening and treatment.[102-104] Additionally, one study found STD clinic patients were more likely to seek sexual partners in close geographic proximity.[105] Where people live, work and interact can create and sustain geographic disparities in STIs.[106]

The national prevalence of past month illicit drug use, including misuse of prescription psychotherapeutics, cocaine, heroin, hallucinogens, inhalants, or methamphetamine was 3.2% among people aged 12 or older. [20, 74] Similar to racial/ethnic disparities with STIs, there is a geographical component to drug use patterns in the US. In 2018, although prevalence of past month illicit drug use was similar in Western states (3.5%) versus Southern states (3.1%),[20, 74] Western states reported the highest prevalence of substance use behaviors among women and MSW with syphilis in 2018. In particular, 13.7% of MSW and 17.8% of women in the West with syphilis reported injection drug use in the past 12 months, and 25.6% of MSW and 32.1% of women with syphilis in the West reported meth use in the past 12 months.[74] The 2017-2018 NSDUH found several substate regions (e.g., counties or groups of counties) in Mississippi, Alabama, Florida and South Carolina had past month illicit drug use prevalence estimates that were higher than the national average.[107] These regions also overlapped with Southern U.S. counties reporting some of the highest prevalence of chlamydia and gonorrhea.[62]

More recently, there has been a spike in synthetic opioid deaths throughout the U.S., primarily driven by fentanyl.[108] Northeastern states had the highest rate of synthetic opioid involved deaths, a region of the U.S. also experiencing an increase in illicit fentanyl,[109] though evidence of parallel increases in the West are now evident.[110] A rise in heterosexual

syphilis transmission has been reported in these regions as well. Over a 5-year period, Western states had the highest proportion of heterosexual men and women with primary and secondary syphilis who also reported in the past year, having sex with PWID. During the same 5-year period, Northeastern states experienced a slow increase in heterosexual syphilis transmission among individuals with sexual partners who were PWID.[63]

Overall, prior research indicates geographic heterogeneity in drug related morbidity and mortality is driven by structural factors at the population level including economic insecurity, high unemployment, low educational attainment, and poverty.[111, 112] Within these regions of concentrated disadvantage, social conditions further contribute to disparate STI prevalence by race/ethnicity.[113, 114] A recent study found that mortgage discrimination and racial/ethnic concentration were independently associated with same race/ethnicity sexual partnerships among PWID in 19 U.S. cities, suggesting that structural interventions to eliminate racism and discrimination could have downstream influences on STI risks.[115]

Venue-based Interventions

Given that many persons with SUD are at increased risk of acquiring and transmitting STIs, identifying opportunities where these individuals can obtain STI screening and treatment is in the broad interest of public health. Examples of such venues include detoxification and substance abuse treatment programs, criminal justice settings, EDs and harm reduction programs. However, since both the epidemiology of STIs and SUDs varies significantly by geographic region and key sociodemographic factors (e.g., sex, race/ethnicity, age, sexual minority subgroup, socioeconomic status), implementing universal screening and treatment across all these programs is unlikely to be cost-effective. This is especially true for non-residential programs using STI testing platforms that require considerable turnaround time, since the opportunity to diagnose and treat clients may be lost. The development of an increasing number of rapid, point-of-care tests for multiple pathogens offers hope that on-site screening and treatment can be offered for STIs of greatest public health importance.

Studies examining the utility of STI screening in SUD treatment programs have generated mixed results. In a study of an inpatient drug treatment program in Birmingham, AL in 1999, Bachmann et al found that high risk sexual behaviors were common and prevalence of *Chlamydia trachomatis, Neisseria gonorrhoeae*, trichomoniasis and syphilis, was 2.3%, 1.6%, 43% and 6%, respectively. These authors concluded that screening at SUD treatment clinics was warranted.[116] In contrast, in a large study of people attending detoxification and methadone programs in Boston, MA in 2001, Liebshutz and colleagues[117] found 0.9% prevalence of *Chlamydia trachomatis* infection and 0% prevalence of gonorrhea. All *Chlamydia* cases were identified in detox programs. These authors recommended that universal screening in this setting was not warranted but that routine screening among younger clients and in settings with high STI prevalence should be considered. Importantly, since both of these studies preceded the worsening of the opioid epidemic, their findings may no longer be generalizable. In particular, Boston recently documented a cluster of HIV cases among PWID,[118] serving as a reminder that surveillance of drug use trends could serve as an indicator about when and where screening for STIs and PrEP for HIV infection should be stepped up.

Even in settings where STI prevalence is relatively low, drug treatment programs can serve as venues where use of condoms and other contraceptives are offered in the context of improving sexual and reproductive health. Furthermore, since methadone and buprenorphine are known to be cost-effective treatment modalities for reducing OUD,[3] efforts to increase their initiation and adherence among people with OUD are likely to indirectly reduce the number of STIs attributable to high risk sexual behaviors in this population. In particular, residential programs that offer childcare, on-site reproductive health services and a trauma-informed approach to addiction treatment may encourage greater numbers of pregnant women and those with dependent children to seek sexual and reproductive health care, which could reduce the number of congenital syphilis cases. A recent study found that mirtazapine, a drug used to treat depression, significantly reduced methamphetamine use and associated high risk sexual behaviors among MSM, which offers hope that this treatment could also indirectly reduce STI incidence.[119]

Studies of STI screening in U.S. correctional settings have more consistently indicated that such settings could be sustainable for routine screening. In a recent systematic review of screening for chlamydia, gonorrhea, and syphilis in a variety of U.S. non-clinical sites (i.e., correctional settings, bathhouses and sex venues, self-collected at-home testing), Bernstein and colleagues[120] found that criminal justice settings such as prisons and jails tended to identify a significant proportion of asymptomatic STI cases, supporting earlier research.[121] However, the value and sustainability of STI screening in the other non-clinical venues examined was not clear, in part because key metrics such as proportion of new positives treated and programmatic costs were often lacking. A modeling study found that condom provision in male prisons could significantly reduce transmission of syphilis, gonorrhea, HBV and HIV, but had a modest impact on controlling chlamydia.[122] In a recent study of opt-out STI screening in two U.S. immigration detention centers,[123] 8.5% tested positive for at least one STI and cost to detect any STI ranged from $500 to $961. However, half of inmates declined to be tested, which underscores the need for culturally sensitive and non-coercive approaches to STI testing and treatment.

ED and urgent care clinics offer another opportunity for identifying asymptomatic STIs, while simultaneously identifying persons with SUDs who may be in need of treatment. In a systematic review of literature from 1995 to 2010, positivity of gonorrhea and chlamydia was comparable with other high-risk populations, and deemed sufficient for selected screening to be cost-effective, especially if point-of-care testing is available.[124] However, a recent study of urgent care clinics found that while most could treat on-site for chlamydia and gonorrhea, they continued to rely on referrals and prescriptions for treating syphilis.[125] Further, in a national survey of 135 pediatric ED directors, only 16% reported having a universal STI-screening program, 59% said they “always” asked parents to leave the room before asking sensitive questions, and only 18% always notified patients who tested positive for an STI.[126] Additional efforts are needed to help ED providers overcome structural barriers such as knowledge of CDC guidelines, laboratory testing and reporting requirements, and creating adequate and appropriate time for obtaining sexual history and offering risk reduction counseling.[124, 125]

Apart from the correctional system, reaching substance users that are at the highest risk of having asymptomatic STIs means extending screening outside the traditional health care system. There are now over two hundred syringe service programs (SSPs) in the U.S. that provide PWID sterile syringes in exchange for used ones, many which offer ancillary services. STI prevalence can be high among SSP users, especially among women.[127, 128] In a study of 1445 SSP users in California conducted in 2000, 11% of women reported having had an STI in the prior five years, compared to 5% among men.[128] A study of SSP users in New Jersey found a prevalence of 17.5% for chlamydia or gonorrhea, with women being three times more likely to test positive. This study also concluded that it was feasible to co-locate STI testing and treatment within mobile and stationary SSPs with treatment completion levels that rivalled that of traditional STD control programs.[127] More recently, a study of female SSP users in Philadelphia who were offered pre-exposure prophylaxis (PrEP) for HIV infection found that 66% initiated treatment, and adherence was higher among more frequent SSP users.[129] These studies underscore the need for comprehensive sexual and reproductive health care assessments among high risk substance users, such as those attending SSPs.

Unfortunately, historical opposition against these programs in the U.S. has forced many to operate illegally, despite that the overturning of a Congressional ban preventing the use of federal funds to support SSPs in 2015. In 2013, a nation-wide survey of SSPs[130] found that while the majority offered on-site HIV testing and counseling, the proportion offering STI screening was much lower and varied by urbanicity (50% urban, 40% rural, 27% suburban). In 2020, of 173 SSPs surveyed, 43% reported diminished services such as STI testing due to the COVID-19 epidemic, and 25% had closed down.[131] In countries such as Canada, Australia and in some Western European countries, supervised injection facilities represent yet another ‘touch point’ where PWID can potentially be reached for STI screening and on-site treatment. To date, moral opposition has also hampered the legal implementation of these programs in the U.S. to the detriment of prevention programs for overdose, HIV and STIs.

Conclusions:

The U.S. epidemics of opioid and methamphetamine use have led to dramatic increases in overdose deaths, as well as rising incidence of blood-borne and STIs. The intersection between drug use and STI epidemics is not new. The U.S. crack epidemic in the mid-1980’s was followed by similar increases in primary, secondary and congenital syphilis associated with high-risk sexual behaviors such as trading of sex for money or drugs.[132] Efforts to improve STI surveillance among substance users are needed, for example through programs such as the National HIV Behavioral Surveillance Study. National and state-level monitoring of substance use trends, such as recent increases in methamphetamine[14] and fentanyl[110] may also help policymakers and program planners decide how STI screening and treatment approaches can be tailored to local needs. However, current CDC testing and treatment guidelines do not consider people who use drugs, including PWID, to be a "special" population worthy of attention, unlike key populations such as adolescents, MSM, incarcerated populations and pregnant women. As a result, there is no funding earmarked for sentinel surveillance and outreach programs to increase STI case finding for substance users.

When the HIV epidemic began in the early 1980's, STI prevention and treatment became a lower public health priority and state policymakers and health departments have struggled to obtain adequate resources for STI screening and contact tracing. More recently, significant funding for prevention and treatment of HIV, TB and malaria has been re-directed towards the COVID-19 pandemic,[133] which may further tighten resources for STI prevention and treatment. In addition to these competing health priorities, there are renewed concerns that Roe vs. Wade may be rescinded, making it more difficult for uninsured people to obtain STI testing and treatment, and harder for women to seek abortions. As a consequence, rates of STIs and congenital syphilis may continue to increase, especially among economically disadvantaged people, which includes substance users.

In light of these ongoing challenges, efforts are needed to determine how to best integrate health services for populations that are at risk of substance use and syndemic infections, such as HIV, STIs and HCV and COVID-19, which has disproportionately affected under-represented minorities.[134] Zang et al. recently used dynamic modeling to show that if an opt-out approach to HIV testing was linked with SARS-CoV-2 testing campaigns, it could substantially reduce HIV incidence and direct and indirect health care costs attributable to HIV in six U.S. cities.[135] Similar modeling exercises could be used to determine how to optimize STI screening, as well as PrEP, at venues frequented by high risk substance users. Removing structural barriers to promote MAT uptake would reduce the public health burden of opioid addiction, but could also have a significant downstream impact on STI incidence. Cooperation is needed across agencies and sectors to address structural drivers that influence high risk sexual networks and impede access to STI testing and treatment, and to provide integrated care delivery models for STIs and related syndemics, including HIV, HCV and substance use.

Acknowledgements:

Components of this paper were presented at a plenary presentation at the 2020 Conference on Sexually Transmitted Diseases. The authors thank Kyle Bernstein, Casey Copen, Kendra Cuffe, Jonathan Mermin, Sarah Kidd, Michelle van Handel and Thomas L. Patterson for helpful discussions, as well as the anonymous reviewers who improved the manuscript. We also thank Sharon Park for assistance with manuscript preparation.

Financial Support Statement: CCB acknowledges funding from National Institute of Allergy and Infectious Diseases (K01AI136725). SAS acknowledges funding from the National Institute of Drug Abuse (NIDA; R01DA049644). TG acknowledges funding from NIDA (R21DA045293). SAS and SS are members of HIV Prevention Trial Network (HPTN), a NIAID-funded program (UM1 AI068619).

References

1. Volkow ND, Blanco C. The changing opioid crisis: development, challenges and opportunities. Mol Psychiatry. 2020. *In Press*.
2. Allen MS, Walter EE. Health-Related Lifestyle Factors and Sexual Dysfunction: A Meta-Analysis of Population-Based Research. J Sex Med. 2018;15(4):458–75. [PubMed: 29523476]
3. National Academies of Sciences Engineering and Medicine. Opportunities to Improve Opioid Use Disorder and Infectious Disease Services: Integrating Responses to a Dual Epidemic. Available at: http://nationalacademies.org/hmd/Activities/PublicHealth/ExaminationoftheIntegrationofOpioidandInfectiousDiseasePreventionEffortsinSelectPrograms.aspx.
4. U.S. Food & Drug Administration. Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse. Available at: https://www.fda.gov/drugs/information-drug-

class/timeline-selected-fda-activities-and-significant-events-addressing-opioid-misuse-and-abuse. Accessed October 13, 2020.

5. Van Zee A The promotion and marketing of oxycontin: commercial triumph, public health tragedy. Am J Public Health. 2009;99(2):221–7. [PubMed: 18799767]
6. Broz D, Zibbell J, Foote C, et al. Multiple injections per injection episode: High-risk injection practice among people who injected pills during the 2015 HIV outbreak in Indiana. Int J Drug Policy. 2018;52:97–101. [PubMed: 29278838]
7. Cicero TJ, Ellis MS, Surratt HL, et al. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry. 2014;71(7):821–6. [PubMed: 24871348]
8. Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis. 2014;59(10):1411–9. [PubMed: 25114031]
9. Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged </=30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Morb Mortal Wkly Rep. 2015;64(17):453–8. [PubMed: 25950251]
10. Peters PJ, Pontones P, Hoover KW, et al. HIV Infection Linked to Injection Use of Oxymorphone in Indiana, 2014-2015. N Engl J Med. 2016;375(3):229–39. [PubMed: 27468059]
11. Strathdee SA, Kuo I, El-Bassel N, et al. Preventing HIV outbreaks among people who inject drugs in the United States: plus ca change, plus ca meme chose. AIDS. 2020;34(14):1997–2005. [PubMed: 32826391]
12. Lyss SB, Buchacz K, McClung RP, et al. Responding to Outbreaks of Human Immunodeficiency Virus Among Persons Who Inject Drugs-United States, 2016-2019: Perspectives on Recent Experience and Lessons Learned. J Infect Dis. 2020;222(Supplement_5):S239–S49. [PubMed: 32877545]
13. Substance Abuse and Mental Health Services Administration. 2017-2018 National Survey on Drug Use and Health State Prevalence Estimates (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2018. Available at: https://www.samhsa.gov/data/nsduh/state-reports-NSDUH-2018
14. Jones CM, Compton WM, Mustaquim D. Patterns and Characteristics of Methamphetamine Use Among Adults - United States, 2015-2018. MMWR Morb Mortal Wkly Rep. 2020;69(12):317–23. [PubMed: 32214077]
15. Frohmader KS, Pitchers KK, Balfour ME, et al. Mixing pleasures: review of the effects of drugs on sex behavior in humans and animal models. Horm Behav. 2010;58(1):149–62. [PubMed: 20004662]
16. Drumright LN, Patterson TL, Strathdee SA. Club drugs as causal risk factors for HIV acquisition among men who have sex with men: a review. Subst Use Misuse. 2006;41(10-12):1551–601. [PubMed: 17002993]
17. Kroll DS, Feldman DE, Wang SA, et al. The associations of comorbid substance use disorders and psychiatric conditions with adolescent brain structure and function: A review. J Neurol Sci. 2020;418:117099. [PubMed: 32866814]
18. Kallmen H, Gustafson R. Alcohol and disinhibition. Eur Addict Res. 1998;4(4):150–62. [PubMed: 9852367]
19. Carey KB, Senn TE, Walsh JL, et al. Alcohol Use Predicts Number of Sexual Partners for Female but not Male STI Clinic Patients. AIDS Behav. 2016;20 Suppl 1:S52–9. [PubMed: 26310596]
20. Substance Abuse and Mental Health Services Administration. 2018 National Survey on Drug Use and Health Detailed Tables. 2019. Available at: https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables. Accessed November 24, 2020.
21. Latini A, Dona MG, Alei L, et al. Recreational drugs and STI diagnoses among patients attending an STI/HIV reference clinic in Rome, Italy. Sex Transm Infect. 2019;95(8):588–93. [PubMed: 31101722]
22. Smith AM, Ferris JA, Simpson JM, et al. Cannabis use and sexual health. J Sex Med. 2010;7(2 Pt 1):787–93. [PubMed: 19694929]

23. Edelman NL, de Visser RO, Mercer CH, et al. Targeting sexual health services in primary care: A systematic review of the psychosocial correlates of adverse sexual health outcomes reported in probability surveys of women of reproductive age. Prev Med. 2015;81:345–56. [PubMed: 26441301]
24. Gamarel KE, Nichols S, Kahler CW, et al. A cross-sectional study examining associations between substance use frequency, problematic use and STIs among youth living with HIV. Sex Transm Infect. 2018;94(4):304–8. [PubMed: 29180537]
25. Grant JE, Redden SA, Lust K, et al. Nonmedical Use of Stimulants Is Associated With Riskier Sexual Practices and Other Forms of Impulsivity. J Addict Med. 2018;12(6):474–80. [PubMed: 30095567]
26. Cheng WS, Garfein RS, Semple SJ, et al. Differences in sexual risk behaviors among male and female HIV-seronegative heterosexual methamphetamine users. Am J Drug Alcohol Abuse. 2009;35(5):295–300. [PubMed: 19591066]
27. Semple SJ, Strathdee SA, Zians J, et al. Sexual risk behavior associated with co-administration of methamphetamine and other drugs in a sample of HIV-positive men who have sex with men. Am J Addict. 2009;18(1):65–72. [PubMed: 19219667]
28. Buffum J Pharmacosexology: the effects of drugs on sexual function a review. J Psychoactive Drugs. 1982;14(1-2):5–44. [PubMed: 6126532]
29. Kurtz SP. Post-circuit blues: motivations and consequences of crystal meth use among gay men in Miami. AIDS Behav. 2005;9(1):63–72. [PubMed: 15812614]
30. Semple SJ, Strathdee SA, Zians J, et al. Correlates of trading sex for methamphetamine in a sample of HIV-negative heterosexual methamphetamine users. J Psychoactive Drugs. 2011;43(2):79–88. [PubMed: 21858954]
31. Green AI. "chem friendly": the institutional basis of" club-drug" use in a sample of urban gay men. Deviant Behavior. 2003;24(5):427–47.
32. Giorgetti R, Tagliabracci A, Schifano F, et al. When "Chems" Meet Sex: A Rising Phenomenon Called "ChemSex". Curr Neuropharmacol. 2017;15(5):762–70. [PubMed: 27855594]
33. Ostrow DG, Plankey MW, Cox C, et al. Specific sex drug combinations contribute to the majority of recent HIV seroconversions among MSM in the MACS. J Acquir Immune Defic Syndr. 2009;51(3):349–55. [PubMed: 19387357]
34. Semple SJ, Zians J, Strathdee SA, et al. Sexual marathons and methamphetamine use among HIV-positive men who have sex with men. Arch Sex Behav. 2009;38(4):583–90. [PubMed: 18185990]
35. Chmiel JS, Detels R, Kaslow RA, et al. Factors associated with prevalent human immunodeficiency virus (HIV) infection in the Multicenter AIDS Cohort Study. Am J Epidemiol. 1987;126(4):568–77. [PubMed: 3651095]
36. Figueroa JP, Brathwaite A, Morris J, et al. Rising HIV-1 prevalence among sexually transmitted disease clinic attenders in Jamaica: traumatic sex and genital ulcers as risk factors. J Acquir Immune Defic Syndr (1988). 1994;7(3):310–6. [PubMed: 8106971]
37. Bell D, Trethowan WH. Amphetamine addiction and disturbed sexuality. Archives of General Psychiatry. 1961;4(1):74–8.
38. Frosch D, Shoptaw S, Huber A, et al. Sexual HIV risk among gay and bisexual male methamphetamine abusers. J Subst Abuse Treat. 1996;13(6):483–6. [PubMed: 9219145]
39. Semple SJ, Strathdee SA, Zians J, et al. Social and behavioral characteristics of HIV-positive MSM who trade sex for methamphetamine. Am J Drug Alcohol Abuse. 2010;36(6):325–31. [PubMed: 20955106]
40. Bucardo J, Semple SJ, Fraga-Vallejo M, et al. A qualitative exploration of female sex work in Tijuana, Mexico. Arch Sex Behav. 2004;33(4):343–51. [PubMed: 15162080]
41. Loza O, Strathdee SA, Martinez GA, et al. Risk factors associated with chlamydia and gonorrhoea infection among female sex workers in two Mexico-USA border cities. Int J STD AIDS. 2010;21(7):460–5. [PubMed: 20852194]
42. Loza O, Patterson TL, Rusch M, et al. Drug-related behaviors independently associated with syphilis infection among female sex workers in two Mexico-US border cities. Addiction. 2010;105(8):1448–56. [PubMed: 20456292]

43. Fulcher JA, Shoptaw S, Makgoeng SB, et al. Brief Report: Recent Methamphetamine Use Is Associated With Increased Rectal Mucosal Inflammatory Cytokines, Regardless of HIV-1 Serostatus. J Acquir Immune Defic Syndr. 2018;78(1):119–23. [PubMed: 29419567]
44. Miller M, Lee JY, Fulcher JA, et al. Getting to the point: Methamphetamine injection is associated with biomarkers relevant to HIV pathogenesis. Drug Alcohol Depend. 2020;213:108133. [PubMed: 32580112]
45. Dillon SM, Frank DN, Wilson CC. The gut microbiome and HIV-1 pathogenesis: a two-way street. AIDS. 2016;30(18):2737–51. [PubMed: 27755100]
46. Rank RG, Yeruva L. Hidden in plain sight: chlamydial gastrointestinal infection and its relevance to persistence in human genital infection. Infect Immun. 2014;82(4):1362–71. [PubMed: 24421044]
47. Fulcher JA, Hussain SK, Cook R, et al. Effects of Substance Use and Sex Practices on the Intestinal Microbiome During HIV-1 Infection. J Infect Dis. 2018;218(10):1560–70. [PubMed: 29982500]
48. Heiligenberg M, Lutter R, Pajkrt D, et al. Effect of HIV and chlamydia infection on rectal inflammation and cytokine concentrations in men who have sex with men. Clin Vaccine Immunol. 2013;20(10):1517–23. [PubMed: 23904458]
49. Briand Madrid L, Morel S, Ndiaye K, et al. Factors associated with perceived loss of libido in people who inject opioids: Results from a community-based survey in France. Drug Alcohol Depend. 2018;190:121–7. [PubMed: 30014887]
50. Bluthenthal RN, Simpson K, Ceasar RC, et al. Opioid withdrawal symptoms, frequency, and pain characteristics as correlates of health risk among people who inject drugs. Drug Alcohol Depend. 2020;211:107932. [PubMed: 32199668]
51. Strathdee SA, West BS, Reed E, et al. Substance Use and HIV Among Female Sex Workers and Female Prisoners: Risk Environments and Implications for Prevention, Treatment, and Policies. J Acquir Immune Defic Syndr. 2015;69 Suppl 2:S110–7. [PubMed: 25978477]
52. Reback CJ. The social construction of a gay drug: Methamphetamine use among gay and bisexual males in Los Angeles. Available at: https://static1.squarespace.com/static/5a1dda626957daf4c4f9a3bb/t/5acfa4f72b6a28b299792da0/1523557626159/SocialConstruction_Reback.pdf. Accessed October 13, 2020.
53. Liu Y, Ruan Y, Strauss SM, et al. Alcohol misuse, risky sexual behaviors, and HIV or syphilis infections among Chinese men who have sex with men. Drug Alcohol Depend. 2016;168:239–46. [PubMed: 27723554]
54. Delgado JR, Segura ER, Lake JE, et al. Event-level analysis of alcohol consumption and condom use in partnership contexts among men who have sex with men and transgender women in Lima, Peru. Drug Alcohol Depend. 2017;170:17–24. [PubMed: 27865150]
55. Maxwell S, Shahmanesh M, Gafos M. Chemsex behaviours among men who have sex with men: A systematic review of the literature. Int J Drug Policy. 2019;63:74–89. [PubMed: 30513473]
56. Guerras JM, Hoyos Miller J, Agusti C, et al. Association of Sexualized Drug Use Patterns with HIV/STI Transmission Risk in an Internet Sample of Men Who Have Sex with Men from Seven European Countries. Arch Sex Behav. 2020. *In Press*.
57. Melendez-Torres GJ, Noori T, Pharris A, et al. Country level homophobia and protective sexual health behaviours among HIV negative or untested men who have sex with men in 45 countries. AIDS Care. 2020;32(12):1589–93. [PubMed: 32423315]
58. Harbertson J, Scott PT, Lemus H, et al. Cross-Sectional Study of Sexual Behavior, Alcohol Use, and Mental Health Conditions Associated With Sexually Transmitted Infections Among Deploying Shipboard US Military Personnel. Mil Med. 2019;184(11-12):e693–e700. [PubMed: 31004170]
59. Stahlman S, Javanbakht M, Cochran S, et al. Self-reported sexually transmitted infections and sexual risk behaviors in the U.S. Military: how sex influences risk. Sex Transm Dis. 2014;41(6):359–64. [PubMed: 24825331]
60. Farkouh A, Riedl T, Gottardi R, et al. Sex-Related Differences in Pharmacokinetics and Pharmacodynamics of Frequently Prescribed Drugs: A Review of the Literature. Adv Ther. 2020;37(2):644–55. [PubMed: 31873866]

61. Fattore L, Marti M, Mostallino R, et al. Sex and Gender Differences in the Effects of Novel Psychoactive Substances. Brain Sci. 2020;10(9).
62. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2018. Atlanta: U.S. Department of Health and Human Services; 2019. Available at: https://www.cdc.gov/std/stats18/default.htm
63. Kidd SE, Grey JA, Torrone EA, et al. Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis - United States, 2013-2017. MMWR Morb Mortal Wkly Rep. 2019;68(6):144–8. [PubMed: 30763294]
64. Rubin DHF, Ross JDC, Grad YH. The frontiers of addressing antibiotic resistance in Neisseria gonorrhoeae. Transl Res. 2020;220:122–37. [PubMed: 32119845]
65. Korenromp EL, Rowley J, Alonso M, et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes-Estimates for 2016 and progress since 2012. PLoS One. 2019;14(2):e0211720. [PubMed: 30811406]
66. Jones J, Weiss K, Mermin J, et al. Proportion of Incident Human Immunodeficiency Virus Cases Among Men Who Have Sex With Men Attributable to Gonorrhea and Chlamydia: A Modeling Analysis. Sex Transm Dis. 2019;46(6):357–63. [PubMed: 31095100]
67. Sellati TJ, Wilkinson DA, Sheffield JS, et al. Virulent Treponema pallidum, lipoprotein, and synthetic lipopeptides induce CCR5 on human monocytes and enhance their susceptibility to infection by human immunodeficiency virus type 1. J Infect Dis. 2000;181(1):283–93. [PubMed: 10608777]
68. Kofoed K, Gerstoft J, Mathiesen LR, et al. Syphilis and human immunodeficiency virus (HIV)-1 coinfection: influence on CD4 T-cell count, HIV-1 viral load, and treatment response. Sex Transm Dis. 2006;33(3):143–8. [PubMed: 16505739]
69. Sadiq ST, Taylor S, Copas AJ, et al. The effects of urethritis on seminal plasma HIV-1 RNA loads in homosexual men not receiving antiretroviral therapy. Sex Transm Infect. 2005;81(2):120–3. [PubMed: 15800087]
70. Van Gerwen OT, Jani A, Long DM, et al. Prevalence of Sexually Transmitted Infections and Human Immunodeficiency Virus in Transgender Persons: A Systematic Review. Transgend Health. 2020;5(2):90–103. [PubMed: 32656353]
71. Semaan S, Leinhos M, Neumann MS. Public health strategies for prevention and control of HSV-2 in persons who use drugs in the United States. Drug Alcohol Depend. 2013;131(3):182–97. [PubMed: 23647730]
72. Butler AJ, Rehm J, Fischer B. Health outcomes associated with crack-cocaine use: Systematic review and meta-analyses. Drug Alcohol Depend. 2017;180:401–16. [PubMed: 28982092]
73. Haider MR, Kingori C, Brown MJ, et al. Illicit drug use and sexually transmitted infections among young adults in the US: evidence from a nationally representative survey. Int J STD AIDS. 2020;31(13):1238–46. [PubMed: 32996867]
74. Centers for Disease Control and Prevention. Syphilis Surveillance Supplemental Slides, 2014-2018. Available at: https://www.cdc.gov/std/stats18/syphilis2018/. Accessed October 13, 2020.
75. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2014. Atlanta: U.S. Department of Health and Human Services; 2015. Available at: https://www.cdc.gov/std/stats/archive/surv-2014-print.PDF
76. Bowen V Increases in Congenital Syphilis: perspectives from around the nation. Presented at: CDC STD Prevention Conference; 2020. Virtual.
77. Harawa NT, Bingham TA. Exploring HIV prevention utilization among female sex workers and male-to-female transgenders. AIDS Educ Prev. 2009;21(4):356–71. [PubMed: 19670970]
78. Ulibarri MD, Strathdee SA, Patterson TL. Sexual and drug use behaviors associated with HIV and other sexually transmitted infections among female sex workers in the Mexico-US border region. Curr Opin Psychiatry. 2010;23(3):215–20. [PubMed: 20308903]
79. Singer M Introduction to syndemics: A critical systems approach to public and community health. San Francisco, CA: John Wiley & Sons; 2009.

80. Dickson-Gomez J, McAuliffe T, Quinn K. The Effects of Housing Status, Stability and the Social Contexts of Housing on Drug and Sexual Risk Behaviors. AIDS Behav. 2017;21(7):2079–92. [PubMed: 28243936]
81. Nydegger LA, Claborn KR. Exploring patterns of substance use among highly vulnerable Black women at-risk for HIV through a syndemics framework: A qualitative study. PLoS One. 2020;15(7):e0236247. [PubMed: 32722724]
82. El-Bassel N, Gilbert L, Witte S, et al. Intimate partner violence and HIV among drug-involved women: contexts linking these two epidemics--challenges and implications for prevention and treatment. Subst Use Misuse. 2011;46(2-3):295–306. [PubMed: 21303249]
83. Cross D, Crow T, Powers A, et al. Childhood trauma, PTSD, and problematic alcohol and substance use in low-income, African-American men and women. Child Abuse Negl. 2015;44:26–35. [PubMed: 25680654]
84. Gryczynski J, Nordeck CD, Mitchell SG, et al. Pilot Studies Examining Feasibility of Substance Use Disorder Screening and Treatment Linkage at Urban Sexually Transmitted Disease Clinics. J Addict Med. 2017;11(5):350–6. [PubMed: 28590392]
85. Peralta RL, Victory E, Thompson CL. Alcohol use disorder in sexual minority adults: Age- and sex- specific prevalence estimates from a national survey, 2015-2017. Drug Alcohol Depend. 2019;205:107673. [PubMed: 31707274]
86. Schuler MS, Dick AW, Stein BD. Sexual minority disparities in opioid misuse, perceived heroin risk and heroin access among a national sample of US adults. Drug Alcohol Depend. 2019;201:78–84. [PubMed: 31200278]
87. Schuler MS, Rice CE, Evans-Polce RJ, et al. Disparities in substance use behaviors and disorders among adult sexual minorities by age, gender, and sexual identity. Drug Alcohol Depend. 2018;189:139–46. [PubMed: 29944989]
88. Feaster DJ, Parish CL, Gooden L, et al. Substance use and STI acquisition: Secondary analysis from the AWARE study. Drug Alcohol Depend. 2016;169:171–9. [PubMed: 27837708]
89. Hallfors DD, Iritani BJ, Miller WC, et al. Sexual and drug behavior patterns and HIV and STD racial disparities: the need for new directions. Am J Public Health. 2007;97(1):125–32. [PubMed: 17138921]
90. Adimora AA, Schoenbach VJ. Contextual factors and the black-white disparity in heterosexual HIV transmission. Epidemiology. 2002;13(6):707–12. [PubMed: 12410013]
91. Kerr JC, Valois RF, Siddiqi A, et al. Neighborhood Condition and Geographic Locale in Assessing HIV/STI Risk Among African American Adolescents. AIDS Behav. 2015;19(6):1005–13. [PubMed: 25108404]
92. Noah AJ, Yang TC, Wang WL. The Black-White Disparity in Sexually Transmitted Diseases During Pregnancy: How Do Racial Segregation and Income Inequality Matter? Sex Transm Dis. 2018;45(5):301–6. [PubMed: 29485542]
93. Marotta P Assessing Spatial Relationships between Race, Inequality, Crime, and Gonorrhea and Chlamydia in the United States. J Urban Health. 2017;94(5):683–98. [PubMed: 28831708]
94. Aral SO, O'Leary A, Baker C. Sexually transmitted infections and HIV in the southern United States: an overview. Sex Transm Dis. 2006;33(7 Suppl):S1–5. [PubMed: 16794550]
95. Farley TA. Sexually transmitted diseases in the Southeastern United States: location, race, and social context. Sex Transm Dis. 2006;33(7 Suppl):S58–64. [PubMed: 16432486]
96. Reif SS, Whetten K, Wilson ER, et al. HIV/AIDS in the Southern USA: a disproportionate epidemic. AIDS Care. 2014;26(3):351–9. [PubMed: 23944833]
97. Eitle D, Greene K, Eitle TM. American Indians, substance use, and sexual behavior: do predictors of sexually transmitted infections explain the race gap among young adults? Sex Transm Dis. 2015;42(2):64–7. [PubMed: 25585062]
98. Haley DF, Edmonds A, Belenky N, et al. Neighborhood Health Care Access and Sexually Transmitted Infections Among Women in the Southern United States: A Cross-Sectional Multilevel Analysis. Sex Transm Dis. 2018;45(1):19–24. [PubMed: 28876296]
99. Smartlowit-Briggs L, Pearson C, Whitefoot P, et al. Community-Based Assessment to Inform a Chlamydia Screening Program for Women in a Rural American Indian Community. Sex Transm Dis. 2016;43(6):390–5. [PubMed: 27196261]

100. Tingey L, Strom R, Hastings R, et al. Self-administered sample collection for screening of sexually transmitted infection among reservation-based American Indian youth. Int J STD AIDS. 2015;26(9):661–6. [PubMed: 25228666]
101. Lichtenstein B Stigma as a barrier to treatment of sexually transmitted infection in the American deep south: issues of race, gender and poverty. Soc Sci Med. 2003;57(12):2435–45. [PubMed: 14572849]
102. Parekh N, Donohue JM, Corbelli J, et al. Screening for Sexually Transmitted Infections After Cervical Cancer Screening Guideline and Medicaid Policy Changes: A Population-based Analysis. Med Care. 2018;56(7):561–8. [PubMed: 29781922]
103. Amiri S, Pham CD, Amram O, et al. Proximity to Screening Site, Rurality, and Neighborhood Disadvantage: Treatment Status among Individuals with Sexually Transmitted Infections in Yakima County, Washington. Int J Environ Res Public Health. 2020;17(8).
104. Institute of Medicine. State of the USA Health Indicators: Letter Report. Washington, DC: 2009.
105. Zenilman JM, Ellish N, Fresia A, et al. The geography of sexual partnerships in Baltimore: applications of core theory dynamics using a geographic information system. Sex Transm Dis. 1999;26(2):75–81. [PubMed: 10029979]
106. Chesson HW, Kent CK, Owusu-Edusei K Jr., et al. Disparities in sexually transmitted disease rates across the "eight Americas". Sex Transm Dis. 2012;39(6):458–64. [PubMed: 22592832]
107. Substance Abuse and Mental Health Services Administration. 2016-2018 Substate Estimates Of Substance Use And Mental Illness. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2018. Available at: https://www.samhsa.gov/data/report/2016-2018-substate-estimates-substance-use-and-mental-illness
108. Wilson N, Kariisa M, Seth P, et al. Drug and Opioid-Involved Overdose Deaths - United States, 2017-2018. MMWR Morb Mortal Wkly Rep. 2020;69(11):290–7. [PubMed: 32191688]
109. Gladden RM, Martinez P, Seth P. Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths - 27 States, 2013-2014. MMWR Morb Mortal Wkly Rep. 2016;65(33):837–43. [PubMed: 27560775]
110. Shover CL, Falasinnu TO, Dwyer CL, et al. Steep increases in fentanyl-related mortality west of the Mississippi River: Recent evidence from county and state surveillance. Drug Alcohol Depend. 2020;216:108314. [PubMed: 33038637]
111. Case A, Deaton A. Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. Proc Natl Acad Sci U S A. 2015;112(49):15078–83. [PubMed: 26575631]
112. Meara E, Skinner J. Losing ground at midlife in America. Proc Natl Acad Sci U S A. 2015;112(49):15006–7. [PubMed: 26556887]
113. Brawner BM, Guthrie B, Stevens R, et al. Place Still Matters: Racial/Ethnic and Geographic Disparities in HIV Transmission and Disease Burden. J Urban Health. 2017;94(5):716–29. [PubMed: 28879489]
114. Jennings JM, Polk S, Fichtenberg C, et al. Social place as a location of potential core transmitters-implications for the targeted control of sexually transmitted disease transmission in urban areas. Ann Epidemiol. 2015;25(11):861–7. [PubMed: 26371418]
115. Linton SL, Cooper HLF, Chen YT, et al. Mortgage Discrimination and Racial/Ethnic Concentration Are Associated with Same-Race/Ethnicity Partnering among People Who Inject Drugs in 19 US Cities. J Urban Health. 2020;97(1):88–104. [PubMed: 31933055]
116. Bachmann LH, Lewis I, Allen R, et al. Risk and prevalence of treatable sexually transmitted diseases at a Birmingham substance abuse treatment facility. Am J Public Health. 2000;90(10):1615–8. [PubMed: 11029998]
117. Liebschutz JM, Finley EP, Braslins PG, et al. Screening for sexually transmitted infections in substance abuse treatment programs. Drug Alcohol Depend. 2003;70(1):93–9. [PubMed: 12681529]
118. Brown CM, Jaeger JL. Increase in newly diagnosed HIV infections among persons who inject drugs in Boston. Available at: https://www.bphc.org/whatwedo/infectious-diseases/Documents/Joint_HIV_in_PWID_advisory_012519%20(1).pdf. Accessed October 22, 2020.

119. Coffin PO, Santos GM, Hern J, et al. Effects of Mirtazapine for Methamphetamine Use Disorder Among Cisgender Men and Transgender Women Who Have Sex With Men: A Placebo-Controlled Randomized Clinical Trial. JAMA Psychiatry. 2020;77(3):246–55. [PubMed: 31825466]
120. Bernstein KT, Chow JM, Pathela P, et al. Bacterial Sexually Transmitted Disease Screening Outside the Clinic--Implications for the Modern Sexually Transmitted Disease Program. Sex Transm Dis. 2016;43(2 Suppl 1):S42–52. [PubMed: 26779687]
121. Spaulding AC, Miller J, Trigg BG, et al. Screening for sexually transmitted diseases in short-term correctional institutions: summary of evidence reviewed for the 2010 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. Sex Transm Dis. 2013;40(9):679–84. [PubMed: 23945422]
122. Scott N, McBryde E, Kirwan A, et al. Modelling the Impact of Condom Distribution on the Incidence and Prevalence of Sexually Transmitted Infections in an Adult Male Prison System. PLoS One. 2015;10(12):e0144869. [PubMed: 26658518]
123. Lederman E, Blackwell A, Tomkus G, et al. Opt-out Testing Pilot for Sexually Transmitted Infections Among Immigrant Detainees at 2 Immigration and Customs Enforcement Health Service Corps-Staffed Detention Facilities, 2018. Public Health Rep. 2020;135(1_suppl):82S–9S. [PubMed: 32735186]
124. Jenkins WD, Zahnd W, Kovach R, et al. Chlamydia and gonorrhea screening in United States emergency departments. J Emerg Med. 2013;44(2):558–67. [PubMed: 23102593]
125. Williams SP, Kinsey J, Carry MG, et al. Get In, Get Tested, Get Care: STD Services in Urban Urgent Care Centers. Sex Transm Dis. 2019;46(10):648–53. [PubMed: 31268957]
126. Ahmad FA, Jeffe DB, Carpenter CR, et al. Emergency Department Directors Are Willing to Expand Reproductive Health Services for Adolescents. J Pediatr Adolesc Gynecol. 2019;32(2):170–4. [PubMed: 30339833]
127. Roth AM, Goldshear JL, Martinez-Donate AP, et al. Reducing Missed Opportunities: Pairing Sexually Transmitted Infection Screening With Syringe Exchange Services. Sex Transm Dis. 2016;43(11):706–8. [PubMed: 27893601]
128. Bogart LM, Kral AH, Scott A, et al. Sexual risk among injection drug users recruited from syringe exchange programs in California. Sex Transm Dis. 2005;32(1):27–34. [PubMed: 15614118]
129. Roth AM, Tran NK, Felsher MA, et al. Integrating HIV pre-exposure prophylaxis with community-based syringe services for women who inject drugs: Results from the Project SHE demonstration study. J Acquir Immune Defic Syndr. 2020.
130. Des Jarlais DC, Nugent A, Solberg A, et al. Syringe Service Programs for Persons Who Inject Drugs in Urban, Suburban, and Rural Areas - United States, 2013. MMWR Morb Mortal Wkly Rep. 2015;64(48):1337–41. [PubMed: 26655918]
131. Glick SN, Prohaska SM, LaKosky PA, et al. The Impact of COVID-19 on Syringe Services Programs in the United States. AIDS Behav. 2020;24(9):2466–8. [PubMed: 32333209]
132. Wilson T, DeHovitz JA. STDs, HIV, and crack cocaine: a review. AIDS Patient Care STDS. 1997;11(2):62–6. [PubMed: 11361764]
133. The Global Fund. Mitigating the Impact of COVID-19 on Countries Affected by HIV, Tuberculosis, and Malaria. Available at: https://www.theglobalfund.org/media/9819/covid19_mitigatingimpact_report_en.pdf. Accessed November 24, 2020.
134. Webb Hooper M, Napoles AM, Perez-Stable EJ. COVID-19 and Racial/Ethnic Disparities. JAMA. 2020;323(24):2466–7. [PubMed: 32391864]
135. Zang X, Krebs E, Chen S, et al. The potential epidemiological impact of COVID-19 on the HIV/AIDS epidemic and the cost-effectiveness of linked, opt-out HIV testing: A modeling study in six US cities. Clin Infect Dis. 2020. *In Press*.