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Risk Reduction Regarding Stigmatized and Marginalized Communities

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Abstract

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While there are several perspectives on marginalization, there are multiple marginalized individuals, social groups, and communities globally. This process of marginalization produces individuals, groups and communities which are refused complete privileges, rights, and power within the broader political and social framework. Social, cultural, biological, and economic factors can thus be used as yardsticks to marginalize individuals and communities. Marginalization can be based on gender, race and ethnicity, social class, and sexuality, among others.

Clearly, marginalized communities face poorer health outcomes and these outcomes are sometimes linked to risky behaviors more prevalent in such demographics. Marginalization is associated with reduced health outcomes and can limit the agency of marginalized communities. However, even within sites of marginalization, affected communities make significant attempts to mitigate health risks and retain agency. For example, marginalized men who have sex with men in China face severe discrimination which affects their health outcomes. Even within such contexts, these men still encourage peers to receive sexually transmitted infection testing. I explore how marginalized communities reduce health risks likely produced by marginalization and retain agency through doing so. I explore sexually transmitted infection testing and related issues in Chinese men who have sex with men, the United States legal cannabis industry, and medication for those with opioid use disorder. In

doing so, I will provide understanding on risk reduction of health behaviors in marginalized communities, building a knowledge base to aid overall health outcomes.

In the first chapter, I detailed a range of cannabis-centric studies. First, I detailed cannabis usage preferences among United States cannabis users. I put forth that frequent cannabis use may increase risk of health harms and highlighted the need to minimize problematic use. I also explored sociodemographic indicators and their association with likelihood for cannabis-related emergency department admissions in New York City. Results suggested that cannabis use may further burden marginalized groups. I investigated large cannabis firms' motivations for participating in the cannabis space. I put forth that policymakers be aware that non-profits and for-profits both seek to expand cannabis access and consider the groups as a unified whole.

In the second chapter I explored concerns regarding sexually transmitted infection testing in the Chinese men who have sex with men environment. I first detailed factors associated with sexually transmitted infection testing. Results detailed the role of altruism in a sexually transmitted infection testing intervention. Expressions of altruism may promote contributions toward public health initiatives in marginalized communities. In the same vein, I detailed the association between men who have sex with men community-centric behaviors and contributions toward others' sexually transmitted infection testing. I proposed that community-oriented behaviors may be related with a reduction in testing service costs. Then, I evaluated whether men who have sex with men selected a sexually transmitted infection test appropriate for their sexual behavior. I suggested that disclosing sexual identity to treatment providers can improve men who have sex with men sexually transmitted infection prevalence estimates. I also detailed the correlates of antisocial behavior on the world's largest gay dating

app among Chinese men who have sex with men. I suggested that age, condom use, and number of social ties may be associated with antisocial behavior, with implications for the design of online sexual health interventions. Finally, I assessed if same-sex sexual behavior disclosure of Chinese men who have sex with men was related to number of HIV self-testing kits requested, and number of test results successfully uploaded by alters in a network-based HIV self-testing intervention. Findings had implications for the development of network-based interventions for key populations.

In the final chapter I detailed that various forms of social support may influence medication for opioid use disorder treatment outcomes. Failure to implement successful social support programs within medication for opioid use disorder treatment settings may represent an important missed opportunity to engage patients at risk of treatment failure.

While the topics here are broad, they all share similar thematic arcs. Low sexually transmitted infection testing uptake, opioid use disorder and cannabis use are issues often disproportionately faced by marginalized communities. Establishing marginalization as the causal factor behind these concerns is often complex, but there is significant work indicating that problematic patterns of drug use and poor sexual health outcomes are engendered by marginalization. Marginalization is associated with conditions inimical to health and well-being, creating a host of health risks. Such marginalization limits the agency of affected communities. However, even within these sites of marginalization, men who have sex with men seek testing and opioid use disorder patients seek medication, mitigating health risks borne from marginalization. I advance that marginalized communities are not completely helpless considering reduced health outcomes, indicating how agency is reclaimed. Finally, I

indicated other cases where fostering agency in marginalized communities needs to be carefully considered.

Risk Reduction Regarding Stigmatized and Marginalized Communities

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Contents

Introduction

While there are several perspectives on marginalization,[1,2] it is clear that there are multiple marginalized individuals, social groups and communities globally. I define marginalization as the complex process through which certain people and ideas are privileged over others at a specific time, and the process by which given groups can be ignored, and made inconsequential.[3] This process of marginalization produces individuals, groups and communities which are refused privileges, rights and power within the broader political and social framework.[2] Social, cultural, and economic factors are thus used as yardsticks to marginalize individuals and communities.[4] Marginalized communities can face a lack of support and resources for pursuing higher education[5] and are often less likely to complete high school.[6] In the job market, marginalized communities often experience discrimination and obstacles to workplace success.[7] Marginalization can be based on gender,[8] race and ethnicity,[9] social class,[10] and sexuality,[11] among other factors. While these factors marginalize people in different ways, everyone can be affected in some form, where an unfortunate circumstance can cause someone to be marginalized.[2]

The unequal distribution of wealth, health and life outcomes is associated with the interaction of biological, social, cultural, economic and political factors.[11] One's social, cultural, and economic context affects one's daily experiences and their relationship to the broader social system influencing health outcomes. Broadly, social, cultural, and economic context of marginalized individuals and communities can, but not always, create conditions inimical to good health. I note that marginalization may not always lead to reduced health outcomes.

Within various marginalized communities, behaviors associated with poor health outcomes are commonplace. Marginalization can cause and magnify such behaviors. Examples of these

types of behaviors are smoking, drinking alcohol, drug use, unprotected sexual intercourse, diet and gun violence.[12]

Marginalized communities can thus sometimes face poorer health outcomes and these outcomes are sometimes linked to health-related behaviors more prevalent in such demographics. For example, men who have sex with men suffer from stigma and discrimination globally.[13] Men who have sex with men are male-identified persons who engage in sexual activity with members of the same sex, regardless of how they identify themselves.[14] They may identify as gay, homosexual, bisexual, pansexual, or heterosexual; or dispense with sexual identification altogether. Men who are have sex with men are considered part of the broader lesbian, gay, bisexual, and transgender community. In China, majority of people believe that homosexual behaviors were a psychological disorder.[15,16] In such contexts, men who have sex with men may be more likely to get married to women, and hide their sexual orientation and put their wives and children at risk of sexually transmitted infections and HIV/AIDS.[17]

Similarly, substance users are often marginalized, facing stigma from health providers who see a patient's drug or alcohol use as their own fault. Such views may lead to substandard care or even the rejection of individuals from seeking treatment.[18] Those who show signs of acute intoxication or withdrawal symptoms are sometimes expelled from emergency rooms by staff fearful of such behavior.[19] Some health professionals may not see substance use as a medical condition and refuse to provide treatment.[18] People who use drugs may internalize this stigma, incurring further marginalization, and perhaps refuse to seek treatment. For example, substance users with other medical issues may refuse to seek treatment, fearing dismissal as a

drug addict.[18] Marginalization and stigma may also worsen isolation and encourage further drug use, worsening the condition.[18]

However, even within sites of marginalization, affected communities make significant attempts to mitigate health risks and retain agency. While some communities face great marginalization, it is not uncommon to see these same communities marshal the sense of shared identity formed around marginalization, to improve overall community well-being. This concept of marginalized communities reclaiming agency is central to this thesis. For example, men who have sex with men in China, a marginalized group, often face severe discrimination which affects their health outcomes. Despite facing discrimination, these men still encourage peers to receive sexually transmitted infection testing.[20] I explore how marginalized communities reduce health risks likely produced by marginalization and retain agency through doing so. I explore sexually transmitted infection testing and related issues in Chinese men who have sex with men, the United States legal cannabis industry, and medication for those with opioid use disorder. In doing so, I will provide understanding on risk reduction of health behaviors in marginalized communities, building a knowledge base to aid overall health outcomes.

Underlying the themes here, is the idea that agency and solidarity within marginalized communities needs to be fostered and encouraged. I suggest that when marginalized individuals support each other, reduced health outcomes from marginalization can be mitigated. However, the cases selected here do not indicate that solidarity and agency within marginalized communities should always be promoted. I then extend the argument central to this thesis around fostering agency in marginalized communities and explore other cases where increased agency and solidarity may not always augur positive outcomes.

Dissertation Structure

I first detail research around marginalization and health outcomes within the men who have sex with men population, with a focus on men who have sex with men in China, and marginalization and problematic drug use, centering on cannabis use and medication for opioid use disorder. Finally, I detail empirical chapters as follows: Sexually transmitted infection testing and related issues in Chinese men who have sex with men; the United States legal cannabis industry; medication for opioid use disorder.

Marginalization versus stigma

Building on the earlier provided definition, I note that marginalization can refer to a personal or paradigmatic perspective, a personal or group experience, a condition, a socio-politically influenced process, and the outcomes of such a process.[21] Marginalization is further defined as a process by which persons or groups are socio-politically peripheralized from dominant, central experiences, they are deprived of mobility, control over self-will or critical resources; indignified and humiliated, exposed to toxic environments, or exploited physically or mentally, such that they face increased safety, health, social, and political risk.[21] The outcomes of marginalization include distress and health disparities, but also survival and empowerment. The pattern of disparate risks parallel to modes of social categorization make marginalization a major health concern.[21] Marginalizing ideologies such as vilifying religious beliefs, colonialism, heteronormativity, racism, classism, sexism, commodification of personhood, globalization, and white supremacy[22,23] support marginalizing dynamics. Marginalizing dynamics include scapegoating, stigmatization, bullying, exclusion, incarceration, deprivation of basic resources, control, symbolic violence, intersectionality of several sources of oppression, microaggressions, implicit biases, and toxic environmental exposure.[24–28]

Stigma is here defined as the co-occurrence of labeling, stereotyping, separation, status loss, and discrimination in a context in which power is exercised.[29] Stigma has a negative effect in the health and well-being of individuals and can contribute to psychosocial stress, coercion, violence, job loss, and social exclusion.[30] The communities in this dissertation, such as men who have sex with men, and people who use drugs, are at the intersection of stigma and prejudice against their identities, occupations or behaviors, often worsening their experiences of stigma and discrimination.[31]

Marginalization and stigma are related and often intersect. Stigma is often associated with or attached to marginalized individuals (e.g. Men who have sex with men or people who use drugs).[21] Stigma in such scenarios can often affect marginalized communities' relationship with the broader community.[32] Stigma may also result in feelings of helplessness or homelessness, which may cause distress for marginalized individuals or communities.[33]

Marginalization and Health Outcomes in the men who have sex with men Population

Men who have sex with men are more vulnerable to conditions of poverty as compared to the heterosexual population.[34] Men who have sex with men are more likely to receive cash assistance and food stamps compared to their heterosexual counterparts, among other indicators.[35] Men who have sex with men's socio-economic position may relate to experiences of discrimination. Higher earning men who have sex with men were less likely to report discrimination compared to those of a lower socioeconomic status, with discrimination linked to higher depressive symptoms and anxiety.[36] This effect is further compounded as workplace discrimination against men who have sex with men can exacerbate socioeconomic differences.[37] Young men who have sex with men also face various deleterious outcomes due

to marginalization. Young men who have sex with men experience homelessness at a disproportionate rate, and also experience mental health issues at a far higher rate compared to the heterosexual population.[38] Homelessness in this demographic tends to arise from parents not accepting the child's sexual identity or possible violence towards men who have sex with men in foster care.[38] Men who have sex with men experience various health issues, such as depression and suicidality, at greater rates than the heterosexual population.[39,40] Men who have sex with men also are one of the populations most affected by HIV infection.[41]

HIV/AIDS, stigma, and marginalization

The first AIDS cases were identified in the United States in 1981 and almost immediately people with AIDS were faced with marginalization and stigma.[42] People with AIDS were evicted from their homes, fired from jobs and shunned by family and friends. Public opinion surveys at the time indicated widespread fears around HIV/AIDS, lack of accurate information and willingness to support policies that would restrict civil liberties to combat AIDS.[43,44] HIV/AIDS stigma globally is represented through social ostracism and rejection of people with HIV.[45]

AIDS manifests several characteristics that relate to stigma and marginalization.[46,47] Firstly, stigma is more often related to a condition whose cause is perceived to be the bearer's responsibility.[42] If a medical condition is perceived as having been contracted through voluntary and avoidable behaviors, especially if such behaviors evoke social disapproval, it is likely to be stigmatized and associated with anger and marginalization.[48] As the primary transmission routes for HIV are often regarded as voluntary and immoral, those with HIV are often viewed as responsible for their condition and stigmatized.[49] Secondly, more stigma is related with conditions that are incurable or degenerative. In the earliest days of the epidemic,

HIV/AIDS was regarded as fatal.[50] Diagnosis with such a condition is often equivalent to dying, as those with the condition may be a reminder or personification of death.[51] Thirdly, greater stigma is associated with conditions believed to be contagious or harm others. Perceptions of danger and fears of contagion have enveloped AIDS since the epidemic began.[52] Fourth, a condition is more stigmatized when it is readily apparent to others, when it disrupts a social interaction or viewed as off-putting or upsetting.[42] The advanced stages of untreated AIDS often affect one's physical appearance and stamina, evoking distress, stigma and marginalization.[53] AIDS stigma may result from the communicability and possible lethality of HIV. HIV/AIDS reflects the fear and apprehension likely associated with any transmissible and deadly illness. HIV/AIDS stigma is best indicated by the experiences of people who acquired HIV through blood transfusion. Compared to men who have sex with men and people who use drugs, such individuals did not previously face societal stigma. After HIV/AIDS, such individuals faced rejection and isolation due to fears about the spread of HIV.[54] Symbolic stigma around HIV/AIDS is related to the social meanings attached to AIDS. This stigma represents the use of the condition as a mode for expressing a range of attitudes. Historically, AIDS stigma has centered on men who have sex with men communities and AIDS is often related to men who have sex with men.[42,52]

The Lesbian, Gay, Bisexual, And Transgender Community in China

China has the world's largest lesbian, gay, bisexual, and transgender population. There are about 30 million LGBT individuals in China.[55] Until 10 years ago, lesbian, gay, bisexual, and transgender individuals were an invisible and hidden community in China.[56] While legal persecution against lesbian, gay, bisexual, and transgender communities was repealed in 1997, discrimination is still rampant.[57] Chinese culture prizes filial piety for raising children and continuing the family line. Not doing so is often considered a social transgression. While

rescinded in 2015, China's one-child policy created great pressure on lesbian, gay, bisexual, and transgender individuals to continue the family line. Marriage pressures resulted in *Tonggi* (wives of gay men) and *Tongfu* (husbands of lesbians). While the Chinese government does not directly prohibit lesbian, gay, bisexual, and transgender content, most lesbian, gay, bisexual, and transgender-centric media is censored as unsuitable for the general population. Discrimination against the lesbian, gay, bisexual, and transgender community has broader implications for Chinese society. Social stigmatization of lesbian, gay, bisexual, and transgender communities can manifest as barriers to sexually transmitted infection prevention.[58]

In 2000, the Chinese Classification of Mental Disorders 3 removed homosexuality and bisexuality from the mental disorders categories.[59] However, a significant number of Chinese mental health professionals still consider homosexuality a disorder treatable by sexual orientation conversion efforts. Sexual orientation conversion efforts is provided by several hospitals across China and several leading medical centers in major Chinese cities.[60] In Chinese Classification of Mental Disorders 3, transgender presentations are still categorized as mental disorders.[59] While the recent International Classification of Diseases has removed gender incongruence from its mental disorders section,[61] it is not clear whether Chinese Classification of Mental Disorders 3 will follow similarly. Such reclassification may be key in reducing stigma.[62] It is difficult for transgender individuals to access hormone treatment or gender affirming surgery and there is limited availability of transgender healthcare.[63] Moreover, despite changes in international standards, transgender individuals in China require at least a year of psychotherapy before gaining approval for gender-affirming surgery.[64]

A recent survey by the United Nations Development Program and Beijing lesbian, gay, bisexual, and transgender Center indicates that 11.1% of heterosexual participants reported being unable to accept lesbian, gay, bisexual, and transgender family members.[56] The rejection rare was far greater when heterosexual participants were asked about the acceptance of their own children being bisexual (25.1%), homosexual (17.5%), or transgender (66.8%). In addition, more than 10% of heterosexual participants rejected the idea of being close, relationship-wise, to lesbian, gay, bisexual, and transgender individuals. They did not believe that bisexual (6.0%), homosexual (8.2%), or transgender (21.9%) people should be allowed to raise children.[56]

Marginalization and Problematic Drug Use

Recent research has indicated that social exclusion and marginalization foreshadow may be related to problematic illicit drug use.[65,66] In general, those experiencing problematic drug use tend to be those in the most deprived and socially excluded communities.[67] While it may appear that deprivation is an inevitable outcome for drug users, for a significant proportion of users, exclusion and disadvantage are major issues prior to drug use.[68] Various studies have indicated that, compared to the wider population, those with problematic drug usage patterns are much more likely to have suffered difficult childhoods, encountered issues in formal education, been unemployed more frequently, and committed crime.[69–71] Clearly, many of those who engage in problematic drug use have encountered marginalization prior to drug use. For this group, drug use may lead to further marginalization when users become stigmatized e.g. they are refused medical treatment. Often, this stigmatizing of drug users is reinforced by governments trying to protect the public from the supposed dangers posed by drug users.[72] Thus, the war against drugs can easily evolve in to a war against drug users, worsening marginalization.[70] The increased exclusion faced by drug users can worsen their familial relationships and broader

connections to their community, possibly resulting in increased stigma and lack of treatment for problematic drug use.[73]

Within marginalized communities in the United States, problematic drug use in low-income Black and Hispanic communities can sometimes result in far worse outcomes when compared to drug use in white middle class youth.[74] For example, white middle class adolescents may have economic and social resources not available to Black and Hispanic low income youth, such as insurance to cover drug treatment, and money for legal counsel.[75] While low-income Black and Hispanic youths experience many of the developmental transitions as their white middle class counterparts, they also experience inadequate education, family stressors and poor job opportunities.[76] While marginalization can worsen outcomes for drug users, it can be particularly damaging for health, with the health of drug users bound to their social environment.[77] As indicated, possibly problematic drug use behaviors can be affected by social processes, and the health of drug users is a product of both drug use behaviors and social determinants. For example, homeless drug users are more likely to engage in high-risk sexual activity.[78] Social factors can establish the living condition and resources that indirectly worsen the consequences of drug use. Inadequate housing can increase the likelihood of infectious disease transmission and conversely, social relationships can offer protective financial and emotional resources.[77] As with broader outcomes, the role of marginalization is highly relevant to the health of minority drug users. While minorities report levels of drug use similar to or lower than nonminorities, minorities, especially marginalized minority drug users experience a disproportionate number of health consequences from drug use.[79,80] Fatal drug overdoses are more common in minorities, and high rates of homicide for Black and Hispanic Americans are associated with drug use and sale.[81,82] Thus, marginalization can contribute to and worsen possibly problematic illicit drug use.

Cannabis and drug policy

Around 1853, recreational cannabis use was considered fashionable in the United States.[83] Cannabis was used in home remedies and patented medicines, and hemp as a commercial product. Despite the ubiquity of cannabis, its use began to be equated with Mexican immigrants and their recreational cannabis use. Anti-drug campaigners in the early 20th century warned against the encroaching *Marijuana Menace* and a range of crimes were attributed to cannabis and the Mexican and Black individuals who were perceived as using it.[84] Cannabis restrictions in the United States began when it was labelled as a poison in 1906 at the state-level, with outright prohibition in the 1920s.[85] By the mid-1930s, cannabis was regulated as a drug in every United States state, along with 35 states that adopted the Uniform State Narcotic Drug Act.[83] A federal excise tax on hemp sales made possession or transfer of cannabis illegal throughout the United States.[86] In the early 20th century, cannabis became criminalized in several countries,[87] with multiple nations having international agreements to control drugs.[88] The United States became a signatory to international drug treaties that restricted the trade, production and supply of cannabis.[89,90]

As cannabis use grew beyond marginalized ethnic enclaves and was taken up by white college students, United States drug policy became increasingly conservative.[83] Beginning in late 1969 and continuing to date, the United States has made a concentrated effort to stem the tide of illegal drugs, including cannabis.[91] Several statutes such as the Racketeer-Influenced and Corrupt Organizations and Continuing Criminal Enterprise (CCE) laws of 1970 served as harsh anti-drug platform to allow for forfeiture of property and assets associated with criminal operations.[91] Air and sea blockades of illicit drug producing nations' have served as reminders of United States drug policy. Operation Intercept in 1969 and a series of similar efforts further buttressed drug policy efforts.[92] President Richard Nixon formed the Drug Enforcement

Administration as a single federal agency to enforce federal drug laws.[93] During Reagan's Presidency, mandatory sentencing guidelines were established and mandatory prison sentences were re-established for large-scale cannabis distribution.[94]

However, in the late 1970s, the Carter Administration considered decriminalizing cannabis and indicated it was not interested in prosecuting individuals possessing small amounts of cannabis.[95] Despite the Administration's stance and efforts by various non-profits, decriminalization was unsuccessful, possibly due to a lack of public opinion consensus and concern to precipitate legislative action. In the 1980s and more recently, harsh drug policies have continued with cannabis as a key theme. Under the Reagan and Bush administrations, interdiction became a priority.[96,97] The Posse Comitatus Act was amended in 1982, allowing the United States military to engage in drug supply reduction activities like intelligence gathering and detection.[98] These interdiction efforts were somewhat successful in reducing the amounts of cannabis smuggled into the United States. The reduction in supply created a shortage of cannabis but was swiftly filled by increased domestic cultivation. Cannabis policy parallels were also observed in the military. The United States military had previously emphasized drug use prevention and treatment,[99] but in the 1980s adopted a zero tolerance policy.[100] Urine screening regimens were introduced in the military to locate and discharge drug users, with this policy spreading to the workplace. In 1995, the Senate introduced the Violent Crime Control and Law Enforcement Act of 1995 (S-3).[101] This act specifically targeted, with mandatory minimum sentences, drugs sales to minors and near schools, among other activities. Although cannabis was not specifically mentioned, the act was used to criminalize cannabis and its users.[91]

In the United States, Federal, State, and local law enforcement agencies share responsibility for enforcing drug laws, although most arrests are made by State and local authorities. The Drug Enforcement Administration and the Federal Bureau of Investigation make arrests at the Federal level. There were less than 30000 arrests for drug offenses in 1960.[102] In the same year, 169 federal cannabis violations were recorded.[103] In 1965, there were about 20000 arrests for all cannabis offences in the United States. By 1970, this figure had risen significantly to 190000 and then at an even greater rate to 421000 in 1973. Overall, drug arrests began their rapid escalation after 1983.[104] The increase in arrests since 1983 is likely attributable to the increase in arrests for opium and cocaine, not cannabis. Between 1945 and 1968, the numbers of federal defendants charged in United States District Courts was relatively stable. The number of drug offenders gradually increased from 1968, stabilized and may be decreasing. About three-quarters of defendants charged in United States District Court in 1985 with a cannabis violation were convicted. The percentage convicted has been growing steadily.[104,105] Of those convicted in 1985, 67% received prison time, with this number rising steadily.[104,105] However, the average length of prison sentence among those convicted for cannabis violation in United States District Courts has remained relatively unchanged till recently.

When considering all drug offenses, the number of Americans incarcerated has risen from 40900 in 1980 to 452900 in 2017.[106] In 1986, people were released after serving an average of 22 months in prison. By 2004 however, people convicted on federal drug offenses were expected to serve 62 months in prison.[107] At the federal level, people incarcerated for drug offenses are about half the prison population. At the state level, those in prison for drug offenses has been increasing since 1980 but is currently on the decline. Most of those incarcerated are low in the drug sale hierarchy and have no prior criminal record for a violent offense.[106]

There are significant ethnic disparities in drug-related sentencing. Black individuals in the United States are four times more likely to be arrested for cannabis charges compared to their white peers.[108] Black individuals in the United States are about 30 percent of all drug-related arrests, despite only being 12.5 percent of substance users.[109] Almost 80 percent of people in prison for a federal drug offense are Black or Latinx individuals.[110] In the federal system, the average Black defendant convicted of a drug offense will serve about the same amount of time (58.7 months) as a white defendant would for a violent crime (61.7 months). People of color account for 70% of all defendants convicted of charges with a mandatory minimum sentence. Prosecutors are twice as likely to pursue a mandatory minimum for a Black defendant than a white defendant charged with the same offense.[110] However, despite the sometimes exaggerated public health messages around cannabis, many have stopped believing in and mock anti-cannabis programming.[111] Such messages often contradict the lived experiences of many people who use cannabis.[100]

The earliest survey data on cannabis use in the United States was obtained in 1967.[112] The nationally-based telephone poll of college students indicated a 5% lifetime prevalence of cannabis use. Two years after, this proportion had increased to 22%, with similar trends in the years after.[113] It is possible cannabis use first rose among college students and then spread to those of younger ages. Data from these surveys and other similar data indicate that there was almost no cannabis use in the United States prior to the 1960s.[114]

According to the National Survey on Drug Use and Health in 2014, past year use of cannabis in the United States was 13.3%.[115] Many prominent individuals, celebrities and politicians admitted to cannabis use, without any significant impact on their careers.[116] However, not everyone who uses cannabis is treated the same. In the United States, about 663367 people

were arrested in 2018 for cannabis-related offenses.[117] Of those, about 608775 were arrested for possession only.[118] The penalties for an ordinary person with a cannabis felony can continue for the rest of the individual's life. They become legally distanced from their civil rights,[119] cannot vote, serve on a jury, hold office, own a firearm or possess an occupational licence.[120,121]

In line with the move toward stringent penalties for cannabis use, several organizations have worked for reducing penalties, easing access to, and decriminalizing cannabis.[122] Due to the efforts of these organizations and other factors, sanctions against cannabis use have eased in several jurisdictions.[123] Persons with certain medical conditions were allowed to obtain cannabis from the Federal Government since 1978.[124] In 1996, California became the first state to legalize medical cannabis[125] and several other jurisdictions continue to do so.

Medication for opioid use disorder

In the 19th century, substance use was not generally associated with crime. However, opium smoking was an exception.[126] Opium eating was common among the upper classes but not among criminals.[127] Opioid use disorder was generally not as maligned as alcoholism and opioids were a treatment for treatment-resistant alcoholism.[126] The Harrison Act in 1914 marked a change in the American drug landscape. It seemed to be an effort to increase revenue, but it did not seek to punish drug users. The Act did not seek to penalize medical practitioners either.[127] However, by 1938, about 25000 physicians were arraigned on narcotics charges.[126] In light of the decreased role of physicians in the treatment of opioid use disorder, more than 40 clinics were started. Many of these sites were under governmental oversight but were eventually closed.[128] After these clinics were closed, many individuals were incarcerated.[129] Thus, the government set up several prison-hospital complexes to treat substance abuse

disorder. In 1922, it became a crime for a physician to prescribe narcotics to an individual a substance use disorder.[127] By World War II, opioid use disorder rates had dropped, not because of governmental or medical efforts, but more to do with reduced opioid supplies from Asia.

Methadone was mistakenly believed to be developed during World War II but was developed during research on spasmolytic compounds. Methadone was synthesized in Germany by Bayer and then brought to the United States, primarily researched at Harvard for use in pain management.[130] Methadone had little resemblance to any known compounds so its analgesic properties were surprising.[126] Despite the morphine shortage, methadone was not used as an analgesic till the postwar period.[131] Oral methadone was established as treatment for opioid use disorder in the United States Public Health Service hospitals in 1950.[126]

A heroin epidemic hit New York City in the 1950s and early 1960s, with a rise in heroin-related deaths. Several groups such as the American Medical Association and the New York Academy of Medicine called for reestablishment of methadone clinics.[132] In 1963, Vincent Dole received a research grant and the next year methadone maintenance treatment was discovered. The first methadone maintenance treatment program had two patients and by 1968 there were 1139 individuals in the program. A report on the first 17500 patients in treatment indicated that those in treatment experienced a 35% increase in productive behavior and a decrease in arrests.[132]

The early rapid expansion of methadone maintenance treatment was tolerated by the public because of its possible link with reduction in crime.[126] Public and governmental concerns shifted toward the economy in the 1970s and publicly funded programs faced reduced budgets. Private enterprise entered the methadone maintenance treatment environment in response to government cutbacks. Methadone experienced a slight resurgence in public acceptability when

methadone maintenance was linked to the reduced spread of AIDS.[133] Over the next few decades, multiple studies documented the safety, efficacy and effectiveness of methadone.[130]

While there are over a millions individuals in the United States with opioid use disorder, only a minority are enrolled in some form of medication for opioid use disorder treatment.[134] While data indicates that methadone doses above 80mg significantly improve treatment outcomes, doses provided are generally below this threshold.[135] Several factors explain this trend. Firstly, there are philosophical objections to the treatment of addiction through a medication. Secondly, there are numerous social and societal objections to medication for opioid use disorder. Thirdly, polysubstance use can affect treatment outcomes. Finally, there are several restrictions around clinical practice and medication for opioid use disorder regulations.

Philosophical objections are related to a misunderstanding of methadone. The therapeutic community movement, 12-Step Fellowship groups and a range of *drug-free* treatment providers have opposed medication for opioid use disorder. These groups believe that medication for opioid use disorder is essentially substituting one drug for another. As a result, medication for opioid use disorder patients are often stigmatized. Societal and social objections to medication for opioid use disorder generally take two forms. Firstly, family and friends pressure patients to end their medication for opioid use disorder treatment. Some patients may thus discontinue treatment prematurely. Secondly, some communities do not allow medication for opioid use disorder treatment centers to be built in a particular jurisdiction.[136,137] Similarly, mass media outlets in such environments often portray medication for opioid use disorder in a poor light. Societal objections to medication for opioid use disorder can operate even within medication for opioid use disorder treatment programs. Lower doses of methadone are often administered in clinics which prefer an abstinence model of treatment.[138] Clinics that treat primarily more

Black patients also tend to prescribe lower doses, possibly due to decreased funding and less well-trained staff.[138] It is unclear to what extent negative attitudes toward methadone have extended to buprenorphine treatment.[139] Urine test results are called *clean* or *dirty* instead of *positive*, *negative*, *expected* or *unexpected*. Medically indicated situation in which patients receive medication for opioid use disorder are reducing their doses are often described as detoxification, as if medications are toxins harmful to the body.[136]

In the early days of medication for opioid use disorder, polysubstance use was common with patients. However, usage patterns evolved such that heroin became the main drug of choice for most patients.[132] More recently, patients present with comorbid dependence on alcohol, cocaine and benzodiazepines.[140] The final issue facing medication for opioid use disorder is the nature of the clinics and their regulations. The economic dependency and poly-drug use of medication for opioid use disorder patients is often ascribed to treatment rather than broader systemic factors, often leading to further restrictions in funding. Patients often must pick up medication during limited clinic hours which can impact patient ability to attend school or work. Treatment providers are often low paid and have large caseloads, thus unable to meet therapeutic goals.[134]

Three strategies have been highlighted to address stigma associated with opioid use disorder and medication for opioid use disorder: 1) personal or mass protest; 2) public and professional education; and 3) strategies that enhance contact between stigmatized and non-stigmatized groups.[141] The recovery status of medication for opioid use disorder patients is unlikely to be fully embraced by policymakers, the public, addiction professionals and recovery communities till a vanguard of current and former patients and their communities declare their positive treatment outcomes.[142] Changes in attitudes and treatment outcomes around medication for

opioid use disorder are most likely to occur not from acceptance of addiction as a medical condition, but through identification with an admired figures in one's medication for opioid use disorder social support network.[143,144]

Chapter 1: The United States Legal Cannabis Industry

This chapter details concerns in the United States legal cannabis industry. I first look at cannabis use patterns at the dawn of United States cannabis reform. I then explore correlates of cannabis-related emergency department visits and present a qualitative study that explores motivations for large United States cannabis firms' participation in the space. Through these, I hope to provide more insight on the rapidly developing United States cannabis space, charting trajectories of cannabis usage and the consequent policy outcomes. On a broader arc, I will demonstrate risk reduction around cannabis use and the intersections with individual agency within a marginalized community.

Cannabis Use Patterns at the Dawn of United States Cannabis Reform

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In the United States, three in 10 cannabis users develop cannabis use disorder under Diagnostic and Statistical Manual of Mental Disorders-IV guidelines.[145] When using Diagnostic and Statistical Manual of Mental Disorders-5 guidelines, 19.5% of lifetime cannabis users met the criteria for cannabis use disorder.[146] I define cannabis use disorder as a problematic pattern of cannabis use leading to clinically significant impairment or distress as manifested by at least two of the markers of cannabis use disorder, as defined by the Diagnostic and Statistical Manual of Mental Disorders 5.[147] Usage patterns in line with cannabis use disorder may be associated with socio-economic disadvantage, including unemployment or decreased financial stability.[148] Research on cannabis use disorder is paramount, to guide policy and interventions, especially with the rapid growth of United States

legal cannabis markets, given that states with legalized cannabis have greater rates of cannabis use and cannabis use disorder.[149] Cannabis may also provide some therapeutic benefits, for conditions such as multiple sclerosis and nausea.[150,151] There are also recommendations for lower risk use, such as avoiding early initiation of use, and using low-potency products.[152] In this vein, some of the risk from cannabis use may be mitigated through informed behavioral choices by users.[152]

Thus, to provide understanding around cannabis use disorder, it is necessary to detail cannabis usage preferences. However, there is a paucity of research exploring preferences around United States cannabis use. Past work has explored demographic characteristics and cannabis use preferences, but these generally use data prior to rapid legalization in recent years.[123,153–155] More recent data is key as additional jurisdictions rapidly legalize medical and recreational cannabis use, and the possibly associated changes in cannabis use disorder. Moreover, while these studies report cannabis prevalence, primarily utilizing the National Survey on Drug Use and Health, National Epidemiologic Survey on Alcohol and Related Conditions, and Monitoring the Future, they do not indicate nuanced data on usage preferences, such as time of use and preferred cannabis variants (edibles, resin etc.). For example, given the sheer range of cannabis products,[156] charting prevalence of cannabis is not sufficient if users have preferences for different products and some are more likely to contribute to cannabis use disorder compared to others.[157] With the shifting United States cannabis landscape, granular data on cannabis usage practices are key to pioneering policy and crafting future research. Using a United States-subset of a large cross-sectional online global survey, this paper describes a range of cannabis usage preferences, including time of first and last joint, quantities of use, and preferred forms of cannabis preparations. The survey questions I highlight are not

in themselves the strongest markers of cannabis use disorder but understanding prevalence of cannabis use from a large sample may shed light on patterns of cannabis use disorder.

Methods

The Global Drug Survey annually conducts anonymous, online surveys to investigate international trends in drug use, both legal and illicit. Data from Global Drug Survey 2017, collected from November 15, 2016 to January 18, 2017, is utilized in this paper. The age and sex distributions of cannabis users who completed the Global Drug Survey in Australia, the United States, and Switzerland were similar to their respective countries' demographic distributions in a household survey across the three countries.[158] When the Global Drug Survey (2014) is compared to the similar National Survey on Drug Use and Health (2013) data, there are several key similarities. For example, regardless of age, men were more likely to report cannabis use compared to women. Both men and women typically demonstrate similar trends of a decreasing probability of lifetime and previous-year cannabis use with age. While the probability of ever using cannabis is greater in the Global Drug Survey (2014) sample, the probability of using cannabis in the past year among lifetime users, and using within the past month among past-year users is comparable across Global Drug Survey (2014) and National Survey on Drug Use and Health (2013) data. While non-response bias and volunteer bias may influence Global Drug Survey samples, unmeasured confounders may affect data in household surveys.[159] Household surveys may underestimate the prevalence of illicit drug use due to stigma and other factors.[160,161] In addition, Global Drug Survey is far cheaper given its higher response rate, compared to household surveys.[158] For example, in Global Drug Survey (2014), 6419 users were surveyed to recruit 3879 past-month cannabis users. In comparison, the National Survey on Drug Use and Health (2013) surveyed 43465 to recruit 5664. Thus, the Global Drug Survey is an effective way of gaining a nuanced understanding of stigmatized

behaviors, if it is not used to estimate drug prevalence of the general population.[158] Sample representativeness may only be necessary when exploring research questions about population prevalence estimates,[158] and the Global Drug Survey is thus appropriate to provide insight about United States cannabis usage preferences within specific samples such as young males.

The survey was actively promoted on social media platforms, such as Twitter, Facebook, and through media partners, such as, Mixmag and The Guardian (United States). All respondents confirmed they were 16+ years and provided informed consent. The study received institutional review board approval from The Psychiatry, Nursing and Midwives Ethics subcommittee at Kings College, London (141/02), The University of Queensland (No: 2017001452) and The University of New South Wales (HREC HC17769). Analyses were first restricted to United States-based respondents. Responses were included only if individuals indicated use of cannabis in the last 12 months, through all forms of administration, such as smoking, eating or vaporizing. The measures described in this paper (see Appendix) included demographic characteristics, whether cannabis was mixed with tobacco in the last year, time of first joint, amount of cannabis used per session, number of hours of day spent stoned in a session, time of last joint, number of days cannabis was used in the last year, preferred form of cannabis in the last year, and most common method of administration.

Results

TABLE 1. Descriptive Variables (Number of Participants Reporting Cannabis Use in Last Year=8345)

Age (N=8345)	-16-20	28.4%
	-21-30	41.7%
	-31-40	14.9%
	-41-79	15.0%
Sex (N=8345)	-Male	75.5%
	-Female	23.6%
	-Transgender	0.9%
Time of First Joint (N=7033)	>60mins	78.0%

	<60mins	22.0%
Time of Last Joint (N=7034)	-Last Thing before Bed	31.3%
	-1-2 hours before bed	49.1%
	-3-4 hours before bed	15.4%
	-More than 4 hours before bed	4.2%
Mixing Tobacco with Cannabis (N=8345)	No	78.0%
	Yes	22.0%
Cannabis Used Per Session (Grams) (N=7667)	Median	0.5
	Interquartile Range	0.125-1.000
Number of Hours Stoned in a Session (N=6970)	Median	4
	Interquartile Range	3.0-6.0
Number of Days Cannabis was Used in the Last Year (N=7389)	Median	250
	Interquartile Range	50-360
Preferred Form of Cannabis (N=7565)	-High potency herbal cannabis	62.1%
	-Resin/hash	11.2%
	-Normal weed/bush/pressed	1.7%
	-Edibles	1.3%
	-Kief	8.3%
	-Oil	8.0%
	-Butane Hash Oil	7.6%
Most Common Mode of Cannabis Consumption (N=7913)	-Smoked in a joint with tobacco	3.8%
	-Smoked in a joint without tobacco	11.3%
	-Smoked in a blunt with tobacco	0.7%
	-Smoked in a blunt without tobacco	7.5%
	-Smoked in a pipe with tobacco	0.5%
	-Smoked in a pipe without tobacco	33.3%
	-Smoked in a bong/water pipe with tobacco	2.6%
	-Smoked in a bong/water pipe without tobacco	23.0%
	-Bucket bong	1.5%
	-Hot knife	0.2%
	-Vaporizer	12.7%
	-Eaten in food	2.4%
	-Tincture/drank as tea	0.4%
	-Medical spray	0.1%

Sample

A total of 10,183 respondents from the United States completed the survey between November 2016 and January 2017. Of these respondents, 8345 (82%) participants reported cannabis use in the past year. There was missing data on some variables, and I have indicated the total number of cases for each variable (see Table 1). Males accounted for 75.48% of the sample, with a median age of 23 (interquartile range (Interquartile range): 19-32, Range: 16-79, see Table 1).

Characteristics of Cannabis Use

Of those who reported cannabis use in the past year, most (78%) reported consuming their first joint more than an hour after waking, and about half the sample had their last joint 1-2 hours before bed (49%) (see Table 1). The majority (78%) tended not to mix tobacco with cannabis. Respondents reported using cannabis for a median of 250 days in the last year (almost daily), with 0.500 grams the median per session. Respondents spent a median of four hours a day stoned when cannabis was used. Most (62%) of respondents reported high potency herbal cannabis as their preferred cannabis preparation in the last year, followed by resin/hash (11%). About a third (33%) of participants smoked cannabis in a pipe without tobacco, followed by (23%) smoking it in a bong/water pipe without tobacco.

Discussion

I sought to provide a descriptive report on cannabis use among a large sample of United States-based survey respondents, largely young men, including time of first and last joint, mixing cannabis with tobacco, and other patterns of use. A low proportion of respondents used cannabis within the first hour of waking, suggesting limited preference for *waking and baking*[162] within young males. By avoiding waking and baking, young male cannabis users may

possibly mitigate reductions in poor judgement later in the day, a common outcome when drugs are consumed earlier in the day.[162] Factors that affect altered judgment are key for a demographic prone to risky behaviors.[163,164] The high proportion of respondents stating time of last joint just before bed may indicate cannabis being used as a sleep aid. Thus, interventions to reduce problematic cannabis use may target young male users who indicate sleep issues as a symptom when purchasing legal cannabis. Most participants do not mix cannabis with tobacco, perhaps indicating an awareness of tobacco's harmful properties[165] within young men. Recent research has indicated the increasing use of electronic nicotine delivery systems,[166,167] and perhaps such developments are associated with low levels of mixing cannabis with tobacco by young men. Most participants smoked cannabis in a pipe without tobacco. There is some evidence that this may not be the safest way to consume cannabis.[168] Nevertheless, consuming cannabis without tobacco may be safer than the less popular option of combining the product with tobacco,[169] adding to research around lower risk use. Near daily cannabis use was reported by the majority of respondents, a possible health concern not in line with lower risk cannabis use[152] and such patterns of use may be related to growing United States cannabis markets. High potency herbal cannabis was the preferred variant, which may be less harmful compared to more potent, but less popular concentrates.[170,171] High potency herbal cannabis can contain up to 15% tetrahydrocannabinol,[172] but concentrates can have up to 40% tetrahydrocannabinol content.[173] The factors underpinning such a product preference may aid understandings around the long-term trajectory of United States cannabis use, especially within young men. Several studies, primarily utilizing the National Survey on Drug Use and Health, National Epidemiologic Survey on Alcohol and Related Conditions and Monitoring The Future report the prevalence of United States cannabis use, cannabis use disorder and frequency of use, along with demographic associations.[74,149,162] I extend their work by providing

granular data around usage practices, such as cannabis product preferences and time of use, primarily in the young male demographic. Such nuanced data on usage preferences is key given the large range of cannabis products and modes of use. In addition, previous studies were conducted prior to the recent legalization of recreational cannabis in several states, and thus I extend past authors' work by providing recent data possibly more reflective of current practices.

Limitations

To the best of my knowledge, this study is the largest United States-based study detailing cannabis use patterns. This research design has advantages and disadvantages, such as reliability and validity at a population-based level.[158,174,175] Online surveys are considered valid and useful when data are scarce, as with the current study. As hidden samples cannot be efficiently analyzed in generalized population-based surveys, comparable probability samples and ethnographic fieldwork may also be necessary to increase the external validity of the sample.[176] Also, as I used an online survey of drug users, the sample was skewed toward younger male participants, and may draw more regular cannabis users.

Conclusion

I provided data on United States cannabis use patterns with largely young male participants, in the wake of rapid growing United States legal cannabis markets. Overall, respondents engaged in less problematic modes of cannabis consumption, such as in a pipe without tobacco or in a bong without tobacco. However, the sample were stoned almost daily. High potency herbal cannabis was the preferred variant, which may be less harmful compared to more potent, but less popular concentrates. Frequent drug use may not be an issue, but

repeated use of any drug may increase risk of health harms, and thus I suggest that future research explore patterns of cannabis use in the changing United States market.

Correlates of Cannabis-related emergency department Visits in New York City

The analysis for this paper was conducted while I was employed at the New York City Department of Health and Mental Hygiene. Due to data restrictions, I was not allowed to use the tables in my thesis till approval had been obtained from my supervisors. Currently, most of the Department has been repositioned toward pandemic-related efforts. Thus, I have not been able to contact my past supervisors at the Department for data access, either to provide tables below or for further analysis.

In 2017, in the United States, there are approximately 40.9 million people (15.0%) aged 12 or older who used cannabis in the last year.[177] In 2017, 49.4% of men and 41.2% of women aged ≥12 years reported cannabis use in their lifetime.[177] In the same period, the prevalence for white, Black and Hispanic persons was 50.8%, 42.4% and 33.4% respectively.[177] For those aged 12-17, 18-25 and ≥26, the prevalence was 15.3%, 52.7% and 47.5% respectively. Cannabis is available through the New York State Department of Health Medical Marijuana Program to treat a select number of medical conditions, but is not legal for use in the state otherwise.[178] From 2015-2016, 16% of New York City residents reported cannabis use at least once in the past year.[178] Use prevalence has been stable since 2009-2010.[178] In New York City, 19% of men and 13% of women indicated cannabis use in the past year.[178] Sixteen percent of New York City youth in 2017 reported cannabis use in the last month.[178] The prevalence was greater in white residents (24%) compared to Black (14%) and Latinx residents (12%).[178]

In the United States, about one in 11 cannabis users aged 15 or older develops dependent patterns of use, with about 4.2 million people meeting diagnostic criteria for frequent or

problematic use.[179] Such patterns of cannabis use are associated with psychotic symptoms, suicidal ideation, and major depressive disorder.[180–182] These findings are not causal and it is not clear if cannabis is used as self-medication for mental health conditions. Multiple studies have detailed cannabis use prevalence[146,183,184] but the possible impact of cannabis use on emergency department visits has not been sufficiently explored.[183,185,186]

In the United States, in 2011, there were 456000 emergency department visits associated with cannabis use, a 21% increase from 2009.[187] About 1.7% of lifetime adult cannabis users reported an emergency department visit[188] and 12.1% of adults nationally who sought medical care in emergency department used cannabis in the past year compared with 9.7% of adults receiving emergency department care.[189] Post-cannabis legalization in Colorado, there were increases in cannabis abuse-related hospitalizations and overdose injuries.[190] In California, cannabis use disorder patients were more likely to have an emergency department admission compared to those without.[191] Thus, cannabis may related to increased emergency department admissions. Although there are concerns about the negative effects of cannabis use on health and healthcare utilization,[192] there is minimal data on cannabis-centric emergency department admission.[186]

A Colorado study detailing 2005-2015 cannabis-related emergency department visits indicated that most (71%) had a comorbid psychiatric diagnosis.[193] Similarly, the prevalence of mental health conditions in emergency department visits with cannabis-related International Classification of Diseases codes is higher than those without cannabis.[194,195] cannabis use disorder patients in California with co-occurring psychiatric conditions had higher odds of emergency department admission compared to those without.[191] Anxiety,

mood and bipolar disorders were also most common among daily cannabis users. [196,197] However, other studies indicate no association between cannabis use and anxiety [197,198] or mood disorders.[199]

Cannabis in combination with alcohol is associated with violence-related injuries and motor vehicle accidents,[200,201] perhaps due to reduced risk perception.[202] Along with cannabinoids, there is a higher prevalence of alcohol in blood samples from drivers involved in traffic accidents, compared to controls.[201,203] Cannabis may also function as a medication for opioid use disorder,[204] especially since the New York State Department has added opioid replacement therapies as a qualifying condition for medical cannabis.[205] Of those who had been prescribed opioids to relieve chronic non-cancer pain, users reported more pain relief in combination with cannabis compared to when only opioids were used.[206]

Males are generally more likely than females to have cannabis use disorder.[207] About 13% of adolescents nationally used cannabis in the past year and adolescent users were more likely to meet cannabis use disorder criteria in the past year compared to adults.[207] From 2004-2011, there was a 61% increase in cannabis-related emergency visits for adolescents nationally[208] with similar increases for those >12 years of ages, with the greatest prevalence for non-Hispanic Black persons.[186] Black adolescents were more likely than white adolescents to have used cannabis and to have cannabis use disorder in the past year.[209] When detailing frequent cannabis use, adolescents of a lower socioeconomic status tend to have a greater odds ratio of use compared to those of a higher socioeconomic status.[210]

These studies indicate that there is a need to detail the associations between cannabis-related emergency department visits and sex, age, socioeconomic status, co-morbid psychiatric conditions, and other drug use.[186] I am interested in the relationship between the above characteristics and cannabis-related emergency department diagnoses. I used the Statewide Planning and Research Cooperative System for New York City to identify groups with higher odds of discharge from emergency department with cannabis-related diagnoses. These findings will inform cannabis-related emergency department utilization and identify demographic groups disproportionally affected by cannabis-related emergency department utilization.

To my knowledge, this study is one of the first to detail the sociodemographic factors associated with cannabis-related emergency department visits in New York City. Findings will have timely clinical implications for informing demographic groups impacted by cannabis-related emergency department visits, especially as New York state moves closer to legalization of recreational cannabis.[211–213]

Methods

Data source

Data was obtained from the 2016 Statewide Planning and Research Cooperative System, which is a comprehensive, all payer data reporting system. Statewide Planning and Research Cooperative System collects patient level detail on patient characteristics, diagnosis and treatments, services and charges for each hospital inpatient and outpatient visit in New York state.[214] This study focused on a subsample of unintentional emergency department visits for admitted patients aged ≥13 years in New York City. The use of

Statewide Planning and Research Cooperative System dataset was determined to be exempt from review by the Institutional Review Board of the New York City Department of Health and Mental Hygiene.

Statistical analysis

I first indicated the number of unintentional emergency department visits, stratified by cannabis and non-cannabis related (see Appendix for more info on study variables). I performed binomial logistic regression analysis to determine associations between demographic characteristics, co-occurring diagnoses and cannabis-related emergency department visit. I also provide age-adjusted rates in the demographic breakdown of emergency department visits. Comparing crude age-specific rates over time and between populations may not be accurate if the underlying age compositions differ in the populations of interest.[215] age-adjusted rates may allow for more accurate comparison of different groups.[216] Analysis was conducted using R.[217]

Results

FIGURES AND TABLES CURRENTLY UNDER EMBARGO

Characteristics of cannabis-related emergency department visits

In 2016, there were 2397417 emergency department visits in New York City, with 15016 cannabis-related visits. The largest age group, 25-34, represented 30.8% of cannabis-related visits (see Table 1). The next largest age group, 18-24, represented 24.7% of visits. Compared to those aged 65-84, all age groups were more likely to receive a cannabis-related diagnosis (see Table 2). The age groups of 13-17 (adjusted odds ratios 12.26; CI 12.1-12.4) and 18-24 (adjusted odds ratios 15.07; CI 14.9-15.2) had the greatest adjusted odds ratios.

Males (70.8%) and Black non-Hispanic persons (43.4%) were the greatest proportions for gender and ethnicity, respectively. Compared to women, men were more likely to receive a cannabis-related emergency department diagnosis (adjusted odds ratios 2.67; CI 2.6-2.7). Compared to white residents, Black (adjusted odds ratios 2.11; CI 2.1-2.2) and Hispanic residents (adjusted odds ratios 1.16; CI 1.1-1.2) were more likely to get a cannabis diagnosis. Neighborhoods with 20 to <30% poverty represented the largest (34.3%) group of cannabis-related visits. Compared to those in neighborhoods with <5% poverty, those living in neighborhoods with 5% to <10% (adjusted odds ratios 0.87; CI 0.6-1.1), 10% to <20% (adjusted odds ratios 0.78; CI 0.5-1.0) and 30% to <40% (adjusted odds ratios 0.82; CI 0.6-1.1) poverty were less likely to receive a cannabis-related emergency department diagnosis. However, those in 20% to <30% (adjusted odds ratios 1.04; CI 0.8-1.2) and ≥40% (adjusted odds ratios 1.20; CI 0.9-1.4) poverty neighborhoods were more likely to receive a cannabis-related diagnosis. Most people reporting for cannabis-related emergency department visits did not receive a comorbid diagnosis for other drug use (alcohol, opioids, cocaine) or mental health conditions (anxiety disorder, mood disorder and schizophrenia and other psychotic disorders). Those who received an alcohol (adjusted odds ratios 3.96; CI 3.9-4.0), opioid (adjusted odds ratios 2.60; CI 2.5-2.7) or cocaine (adjusted odds ratios 10.63; CI 10.6-10.7) diagnosis were more likely to receive a cannabis-related diagnosis. Similarly, those who received a diagnosis for anxiety disorder (adjusted odds ratios 2.35; CI 2.3-2.4), mood disorder (adjusted odds ratios 4.34; CI 4.3-4.4) or schizophrenia and other psychotic disorders (adjusted odds ratios 6.37; CI 6.3-6.4) were more likely to receive a cannabis-related emergency department diagnosis.

Discussion

This study utilized a New York City-based sample of emergency department visits to inform demographic predictors of cannabis-related emergency department visits. The results indicate that younger people, men, nonwhite residents, those in neighborhoods with the greatest poverty levels, those with alcohol, opioid, cocaine, anxiety disorder, mood disorder or schizophrenia and other psychotic disorders were more likely to receive a cannabis-related emergency department diagnosis. These findings may indicate that cannabis use may add burden to the healthcare system for those already disproportionately affected.

The results extend research around cannabis use and cannabis-related health conditions, such as cannabis use disorder and respiratory illnesses. The health effects of cannabis use are not just dependent on cannabis prevalence, but also potency, dose, type of cannabis product and interactions with other drugs[184,218] Cannabis potency in seized samples seems to be steadily increasing[219] and high potency products may be linked to heavier use.[157,220] The results are in line with reports indicating greater likelihood of cannabis-related emergency department visits among adolescents and Black persons,[186] and increasing proportions of cannabis-related admissions to addiction-related treatment facilities among those aged ≥12 years.[221] As more states legalize recreational cannabis, the results reinforce the need for research on identifying demographics at increased risk for cannabis use disorder and healthcare utilization. This should be understood keeping in mind the data does not include larger structural factors like stigma and discrimination.

Emergency department visits and gender

I indicated that men were more likely than women to receive a cannabis-related emergency department diagnosis. This could mean that men are at greater risk for problematic cannabis use, although it must be noted that men are more likely to visit emergency departments.[222,223] From 2002-2014, men used more cannabis than women, with an increasing gender gap.[224] Men also reported more frequent and larger amounts of cannabis use, along with higher potency products compared to women.[225] In general, men are more likely to engage in substance use and other risky behaviors compared to women,[226] which may explain increased emergency department visitations for cannabis use.

Emergency department visits and age

I found that all age groups within 13-64 were more likely than those 64-84 to receive a cannabis-related emergency department diagnosis. The age groups of 13-17 and 18-24 had the greatest adjusted odds ratios. This finding may indicate that adolescents are at greater risk for problematic cannabis use. However, Statewide Planning and Research Cooperative System data represents treatment admissions and the results may be influenced by a subset of adolescents who had frequent cannabis-related admissions.[186]

Emergency department visits and ethnicity

I found that Black and Hispanic residents were more likely than white residents to receive a cannabis-related diagnosis. The ethnicity-based results may indicate a combination of the effects of family socioeconomic status and neighborhood socioeconomic status on the likelihood of a cannabis-related visit.[227] In line with other studies, I suggest the need to monitor cannabis-related health events and develop interventions for Black and Hispanic

cannabis users. Past studies reaffirm the results, where past year-cannabis use and cannabis use disorder among Black adults increased between 2001-2002 and 2012-2013.[183]

Emergency department visits and poverty level

Our findings indicate that those of medium poverty level were less likely to receive a cannabis emergency department diagnosis compared to those with low poverty. However, those with high and very high poverty were more likely to receive a cannabis diagnosis compared to those with low poverty. I put forward the need to develop interventions targeted specifically at cannabis users of a lower socioeconomic status. Previous work indicates that cannabis use, especially heavier use,[210,228] is common among those facing socioeconomic disadvantage.[229]

Emergency department visits and alcohol use

The results demonstrate that those with an alcohol diagnosis were more likely to receive a cannabis-related diagnosis. These results may indicate that those with possibly problematic alcohol use may be at increased risk for risky cannabis use. While there is an association between alcohol and cannabis for young adults, users tend to use one substance predominantly at a particular time.[230] More research is thus required to determine how cannabis and alcohol use are related, resulting in possible emergency department visits.

Emergency department visits and opioid use

Findings indicate that those with an opioid diagnosis had a greater likelihood to receive a cannabis diagnosis. These findings may suggest that those with possibly problematic patterns of opioid use may be at greater risk for increased risky cannabis use. Past studies reinforce the results. Usage of cannabis was common for those with chronic non-cancer

pain and had an opioid prescription, despite no evidence of cannabis improving patient outcomes.[231,232] Problematic opioid use is more prevalent than problematic cannabis use for those with a medical cannabis recommendation.[233]

Emergency department visits and cocaine use

Our findings indicate that people with a cocaine diagnosis were more likely to receive a cannabis-related diagnosis. These results may represent the need for cannabis use related interventions for cocaine users. Cannabis onset may trigger cocaine use[234] and for a subset of at-risk users, cannabis use may be related to later cannabis use.[235] Participants in the study may demonstrate problematic substance use behavior and thus may exhibit concurrent problematic cocaine and cannabis use.

Emergency department visits and psychiatric conditions

The results indicate that those with anxiety disorders, mood disorders or schizophrenia and other psychotic disorders were more likely to receive a cannabis-related diagnosis. These findings may put forward the need to target interventions around problematic cannabis for those with psychiatric conditions such as anxiety, mood disorder and schizophrenia and other psychotic disorders. Past research reaffirms the results, around the increased prevalence of mental health conditions for cannabis-related emergency department visits.[194,195] Similarly, heavy cannabis use (at least daily) is associated with anxiety and mood disorders.[196,197] Further research is thus key in determining the relationship between problematic cannabis use and various psychiatric conditions.

Limitations

These results should be interpreted in line with several limitations. While cannabis use may be considered a direct cause for an emergency department visit, causality between cannabis use and emergency department visits cannot be assumed. The data also does not include information about cannabis use frequency and dose, nor larger sociocultural and contextual variables that may confound or serve as mediators in the relationships described.

Conclusion

Younger age, nonwhite ethnicity, increased neighborhood poverty, other drug use and mental health conditions were associated with greater likelihood for cannabis-related emergency department visits. Infrequent screening for problematic drug use and lack of treatment for drug use disorders within healthcare setting may relate to emergency department admissions.[236] Adolescents, parents and healthcare providers may overlook cannabis-related health concerns,[237] and toxicology screening may improve identification of problematic cannabis use, especially for adolescents.[238] The data also indicates the importance of age, ethnicity and psychiatric conditions in conducting screening for cannabis use and related interventions to reduce cannabis use.[239,240] There is a need to develop risk-stratified screening and targeted interventions for high risk groups, especially in emergency department settings where drug-related events are more common.

Understanding Motivations for Large United States Cannabis Firms' Participation in the Cannabis Space: Qualitative Study Exploring Views of Key Decision-Makers

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In the 1990s, United States activists such as the civil rights movement, drug reformers and libertarians, campaigned to legalize medical cannabis. In 1996, California became the first state to approve a citizen-initiated referendum that legalized medical cannabis.[241] By 2010, 23 states and the District of Columbia allowed medical cannabis use in some form.[242] In November 2012, Colorado and Washington voters endorsed a legal cannabis market for non-medical use.[242] In the years that followed, other states have allowed for recreational markets, while other states are preparing to push for legalisation.[243] Although several states have legalised recreational or medical cannabis, the United States federal government prohibits cannabis sale, resulting in conflict between United States federal and state cannabis legislation.[244] However, as of September 2018, there have been no injunctions or lawsuits filed by the Department of Justice regarding these conflicts.[245]

In the United States, legal cannabis is sold and cultivated by a range of firms, ranging from moderately-sized owner-operated dispensaries to large firms which own multiple dispensary licenses and plantations.[246] I define firms as business organizations, such as corporations, that sell goods or services primarily for profit. The United States cannabis

space, market or industry represents firms involved in the sale of cannabis, including those involved with the plant (e.g. Growers, dispensary owners, concentrate manufacturers) or related equipment (e.g., hydroponic equipment manufacturers, pipe manufacturers), firms that invest in or acquire firms involved in cannabis sale, information providers and service providers to cannabis firms.[247]

The United States legal cannabis market has been growing rapidly in recent years, from $2.7 billion in 2014[248] to $10.4 billion in 2018[249] and this continued growth seems to have attracted big-name investors to the space.[250] Given burgeoning United States cannabis markets, heavy frequent use and cannabis use disorder are a concern.[198] In the United States, about one in 11 cannabis users aged 15 or older develops dependent patterns of use, with about 4.2 million people meeting diagnostic criteria for frequent or problematic use.[179] Such patterns of cannabis use are often associated with psychotic symptoms, suicidal ideation, and major depressive disorder.[180] Research conducted in states with medical cannabis laws found that residents had higher odds of cannabis use and cannabis use disorder compared to residents in states without such laws.[149] Thus, changing patterns of cannabis usage may be affected by profit-centric legal cannabis markets.[251]

A major driver of legal cannabis markets are large cannabis firms.[252] Such firms may be engaging in actions that could contribute to changes in cannabis usage patterns.[253] For example, cannabis advertising and availability has been associated with greater likelihood of use.[254] The use of cannabis concentrates, developed by large firms following pressure from retailers to make high-potency products[255] has also been linked to heavier use.[220]

Lobbying by large cannabis firms is also a concern, with well-organized industry interests influencing legislation.[252]

However, this is not to suggest that growth in the legal cannabis markets or efforts by large cannabis firms which may contribute to nationwide legalization, may solely result in negative effects. Cannabis legalization also heralds benefits, such as greater ease in monitoring the amount of cannabis sold and increased research on therapeutic benefits of the plant.[256] A leading drug advocacy group cites harm reduction, job creation and reduced government spending on law enforcement and incarceration as further benefits of legalisation.[257] Other gains include improved environmental conditions in cannabis growing areas, and state revenue increases.[258]

Some large cannabis firms are claiming their product and its marketing are socially responsible[259] and leverage the medical potential of cannabis[260] to possibly increase sales. A few firms provide free cannabis to cancer patients, and mentor newcomers to the space,[261] portraying cannabis companies as benevolent actors, in line with the potential role of firms in indirectly reducing arrests and incarcerations[262] and improving medical outcomes.[263] Such actions create the impression that firms are concerned about improved social outcomes. However, firms may also have a role in greater availability of legal cannabis and similar rises in frequency of use.[264] Firm actions thus appear to have counterintuitive motivations: Augmenting social outcomes and contributing to possibly problematic cannabis usage practices. Firms' motivations can inform their decisions in the market,[265] and thus better understanding of motivations can provide insight on how the cannabis market will develop. By gaining insight on the cannabis market, I can understand

possible shifts in usage practices.[266] Thus, by providing information around firms' motivations for engaging in the space I can better comprehend cannabis usage patterns.

There has been little study of cannabis firms' motivations for participating in the market. Despite firms attempting to improve social outcomes, past research generally has focused on firms having a possibly singular motivation of increasing the size of the market to generate profit.[252,267] In addition, previous work[252] does not provide data from key decision-makers in the cannabis space. I define key decision makers as upper-level management such as the Chief Executive Officer, Chief Operating Officer, and vice-president etc. Given their position, key decision makers may have information unavailable to lower ranking staff and may influence firm decision making[268] consequently affecting shifts in usage practices. Key decision makers may thus be able to provide deeper insight on the cannabis space, expanding on firms' motivations explored in previous research. To provide some understanding on this gap in the literature, I used ethnographic data collected at a cannabis firm and interviews with key decision makers from large for-profit cannabis firms, and major non-profit organizations in the cannabis space, to address the following question: What are the views of key decision makers on motivations for large United States cannabis firms' participation in the space?

The cannabis investment landscape

This section provides information about the legal cannabis investment space, using data drawn from an online platform which provides information about investment activity in the cannabis space from 2009-2016. The online platform drew from publicly available

records released by the United States Securities and Exchange Commission. Investment activity was used to construct social network diagrams.

Figure 1 indicates investments in the cannabis space, from 2009 – 2016, against a map of the contiguous United States. Edges in the network represent mergers and acquisitions or investments between two firms. Each node represents a cannabis firm, with subsidiaries and holding companies represented as a single node. Firms were coded based on the state they were headquartered in. Investment activity between companies in the same state is displayed with a single point. From 2009 – 2011, activity was sparse. In 2012, there was investment between California and Colorado, and Arizona and Wyoming. While California, Colorado and Arizona already allowed medical cannabis by 2012, cannabis was still illegal in Wyoming. In 2014 and 2015 investment in the space became more fevered, with ties from coast to coast. In 2016, investment continued to occur across the map, not confined to specific regions, with firms in states not traditionally associated with cannabis, such as Utah and Ohio.

Methods

An exploratory qualitative study design was used. Data were collected through a 320-hour ethnographic field study at Green For-profit, a cannabis firm, and 37 semi-structured interviews with key decision makers in the cannabis space, representing both major for-profit and non-profit organizations. As key decision makers in large cannabis firms may distort the data by providing an overly positive impression of the space,[269] the study design attempted to mitigate this risk by including key decision makers in the non-profit space, who could confirm or oppose themes brought up by for-profit counterparts. For

anonymity, organization names were replaced with colors, and one of two suffixes allotted to indicate that the participant represented either a major for-profit organization (e.g. Yellow For-profit) or non-profit firm (e.g. Blue Non-profit). Pseudonyms were assigned to all participants. The study received university institutional review board approval from the Yale Human Subjects Committee #2000020385.

Green For-profit is a New York City based financial services firm specializing in the cannabis space. Services Green For-profit provided include advising cannabis companies on mergers and acquisitions, and capital raising. Green For-profit also aids in professionalizing companies prior to a capital raise, by forming a board of directors, developing financial controls, and creating forecasts and budgets. Green For-profit has three in-house office staff; the Chief Executive Officer, and two analysts, as well as several others who work remotely. Pseudonyms were assigned for all Green For-profit staff. The Chief Executive Officer, James, is in his 50s and was previously an investment banker in another industry. Both analysts were in their 20s. One analyst, Thomas, acts as a personal assistant for James. The other analyst, Nick, looks for potential investment opportunities. I spent an average of 40 hours each week for eight weeks observing, assisting and interacting with staff at Green For-profit. Observations and informal interviews were conducted at Green For-profit. At Green For-profit, I served as an intern, specializing in data analysis, where I drafted reports about the state of the cannabis space for use by Green For-profit's clients. My status as a researcher and a staff member was consistently revealed to all employees at Green For-profit.[270] Consent to collect data during the internship and publish findings was obtained from Green For-profit's Chief Executive Officer prior to

the start of the position. Field notes were typed directly into a laptop in real time to ensure high fidelity capture of the conversations and observations.[271]

Green For-profit's staff wore standard business attire and nothing about the firm logo or any items in the office suggested a link to the cannabis space. At first glance, Green For-profit is indistinguishable from any other boutique investment bank.[272] All introductory calls are taken by James, who starts the call by narrating the history of the firm. Prior to entering the cannabis space, the firm specialized in investment banking for companies in the physical and cyber security industry. Seeing the lack of professionalism and possible profit in the space, the Chief Executive Officer decided to reorient his business toward cannabis. When asked why Green For-profit felt a need to provide such a spiel, Thomas said that clients *want to hear these things*.

Coupled with the small staff size and open office environment, this meant I could engage in unstructured interviews with staff members during the internship. My interpretations of the cannabis space and Green For-profit's role in the industry clearly affected the data from the informants. The key to rigor when studying an organization one is part of, is to be reflexive and transparent about one's own impact and to triangulate insights with a multiplicity of data sources, along with considering one's own role when theorizing about organizational processes observed .[273,274] I endeavored to follow these prescriptions throughout the work and specifically when crafting the theoretical insights.

The two months of in-office observation included many opportunities for spontaneous participant observation, in contexts where it was easy to observe and record processes through which Green For-profit engaged with the cannabis space. In informal

conversations and interviews, participants were highly frank throughout the two months of observation, sharing their views on the cannabis space, the broader business environment and their firm's relationship with various stakeholders. I believe that this access and openness were facilitated by two factors. Firstly, I was viewed as a valuable member of the team due to his data analysis skills, in line with Green Capital's tagline of being a data-driven financial advisory firm. Secondly, investment bankers are rather candid about their experiences and thoughts with team members,[275] possibly due to the team-oriented nature of the job.

I also attended a half-day cannabis conference organized by Green For-profit, about gender and ethnic diversity in the cannabis space, where I collected observational data. Several organizations, mostly non-profits, had rented booths at the conference. About 200 people attended the conference, with founders of cannabis startups, activists, representatives from institutional funds, and college students present. I took note of promotional materials given out by Green For-profit at the conference and wrote field notes at the end of the day.

For the semi-structured interviews, I identified potential participants using a range of sources, including attendee lists for major U.S. Cannabis conferences, a list from major U.S. Universities of those employed in the cannabis space (assembled through publicly available LinkedIn data), and referrals. Attendee lists for the indicated cannabis conferences were publicly available, and thus, I did not have to obtain email consent. Referrals were obtained from participants emailed in the initial contact phase.

I ensured that participants were distributed across the United States, to account for differences in U.S. Cannabis legislation. I then contacted academic experts and key decision makers in the for-profit and nonprofit cannabis spaces to ensure that the list of potential interviewees represented a variety of for-profit firms within the cannabis space, as well as firms that were likely to have key decision makers who may make decisions which possibly affect health outcomes. For each firm in the final list, I sent two personalized emails to an organization contact: An initial email requesting a phone interview and a reminder a week later. The introductory email introduced me as a PhD student researching the legal cannabis space, briefly introduced the project, and asked the potential participant to nominate a convenient time for a phone interview.

To identify upper level management, I used the list of employee titles provided in past research.[276] Within an organization, I emailed all staff in upper level management. I successfully sent email requests to 350 contacts and received email responses from 37 people from 32 organizations, for a total response rate of 11%. In some organizations, multiple key decision makers responded, but in most firms, only one key decision maker responded. It was not clear why some firms were more willing to participate compared with others. All participants who replied to the email offered to participate; thus, I was not aware of reasons for declining to participate.

To develop the interview schedule, I first collected relevant literature using the following databases: PubMed, MEDLINE, Embase, PsycINFO, and Sociological Abstracts. I used keywords derived from themes such as major cannabis and tobacco firms, their public health impact, cannabis legalization, and cannabis usage preferences. I used the resultant

literature in combination with the research questions to develop a set of 20 interview questions. I then refined these interview questions with academic, industry, and nonprofit experts, resulting in 15 interview questions.

Academic research in cannabis spans several areas. Thus, I selected three academic experts, one each from public health, sociology, and criminology. I identified key scholars in each of these subject areas through the number of articles published on the cannabis space. I then contacted the identified researchers and asked them to assist. I emailed 30 researchers (10 per subject area) and five agreed to assist. Of those who replied, I selected one researcher per subject area based on the number of articles they had published on cannabis in 2015–2018.

To select industry and nonprofit experts, I identified the largest for-profit and nonprofit cannabis organizations by revenue and overall budget, respectively. I emailed 10 key decision makers each from the for-profit and nonprofit spaces to assist with the study; five for-profit and six nonprofit key decision makers agreed to assist. I then selected two key decision makers, one each from the nonprofit and for-profit spaces, based on greatest revenue and overall budget, respectively. All key decision makers who successfully contacted for the drafting of the interview schedule were also interviewed for the study. The feedback from these experts allowed us to align the questions with the academic literature and to be jargon-free and succinct. Examples of removed questions include the following:

How is cannabis analogous to other stigmatized substances?

Do you think the cannabis space is in line with hegemonic business norms?

Examples of final interview questions are as follows:

What do you characterize cannabis as?

What are large firms' motivations for being in the space?

What is the dynamic between nonprofits and firms?

The open-ended semi-structured interview questions primarily focused on exploring participants' opinions about why firms would participate in the cannabis space. The interview schedule, or set of interview questions, facilitated the development of new themes that could occur during the interview.[277] Examples of new themes were participants' personal motivations for entry into the space and their interest in the legalization of other illicit substances. The interview schedule contained cues and prompts to encourage further discussion, especially when the interviewee provided an unclear or brief answer.[278] Examples of such cues included making encouraging noises, reflecting on remarks made by participants, and probing the last remark made by the participant.[279]

Following verbal informed consent procedures, I conducted telephone interviews with each participant, averaging 25 min in length. Interviews were recorded, using publicly available mobile phone call recording software, with participant consent. I hired a professional transcriber through a freelance jobs website to transcribe the interviews.

Theoretical saturation on the study's key topics of interest—that is, the point when no new themes are identified and no further issues come up regarding a new data category[280]—was reached by the 34th participant, and thus, further participant recruitment was not conducted.

I removed from the transcripts identifiable quotes and accounts that potentially could affect individuals' and firms' reputations. Cannabis firms often list their motivations for entering the space on their respective websites. Quotes that were exceedingly like their employers' publicly available narratives were removed from the transcripts to ensure anonymity. It is possible that this process of omission affected the veracity of the findings. However, I believe this process likely allowed for data variant from firms' official narrative to arise, expanding the diversity of emergent themes.

I exported all field notes and interviews into NVivo 11,[281] a qualitative data analysis software. I used thematic analysis to analyze the data. Thematic analysis is apt for detailing the views of a multitude of research participants[282] and reducing large data sets into easily identifiable categories.[283] Given the nature of the study and familiarity with the topic, there were likely to be several possible preconceptions about the motivations for cannabis firms' participation in the space. Thus, I applied a deductive approach to craft themes,[282] and used a reflexive approach throughout analyses to account for researcher biases and fluency with the literature that may possibly predispose the identification of emergent themes.[282,284] Deductive techniques are those which test theory beginning with an established theory and then seeing if that theory applies to specific instances.[285] A self-reflexive approach is one that harnesses an awareness of the relationship between the investigator and the research environment.[286] I used the six-phase protocol indicated by Virginia Braun and Victoria Clarke (2006) to identify themes which emerged in the qualitative dataset and that also were relevant to the views of key decision makers on why cannabis firms participate in the space. After repeated familiarization with the data, I identified initial recurring patterns of

responses and meaning in the data. Examples of recurring themes were participant motivations for entering the market, profit, and mitigating inequity. After this procedure, I re-read the data several times, critically analyzed the emergent patterns, and coded and collated them into broader themes. Once themes had been developed, I reread the transcripts to see if the themes provided insight into participant narratives. These themes were then stratified by groups (for-profit vs. Nonprofit organizations). I then discussed the codes and themes extensively with my co-authors to resolve minor coding discrepancies and to maintain consistency. I discussed the interpretive scheme with the key decision makers selected to review the interview schedule. The indicated key decision makers confirmed that the interpretive scheme was sensible to and affirmed by those in the phenomena of interest.[287] I emailed the previously indicated team of experts about the interpretive scheme and asked them to provide feedback. Specifically, I asked whether terms used in the interview schedule would be easily comprehensible in the cannabis space, whether interview questions were neutral—neither favoring nor maligning the cannabis space—and whether the schedule was representative of recent developments in the cannabis space.

Results

FIGURE 1
Nationwide Investments in the Cannabis Space: 2009–2016

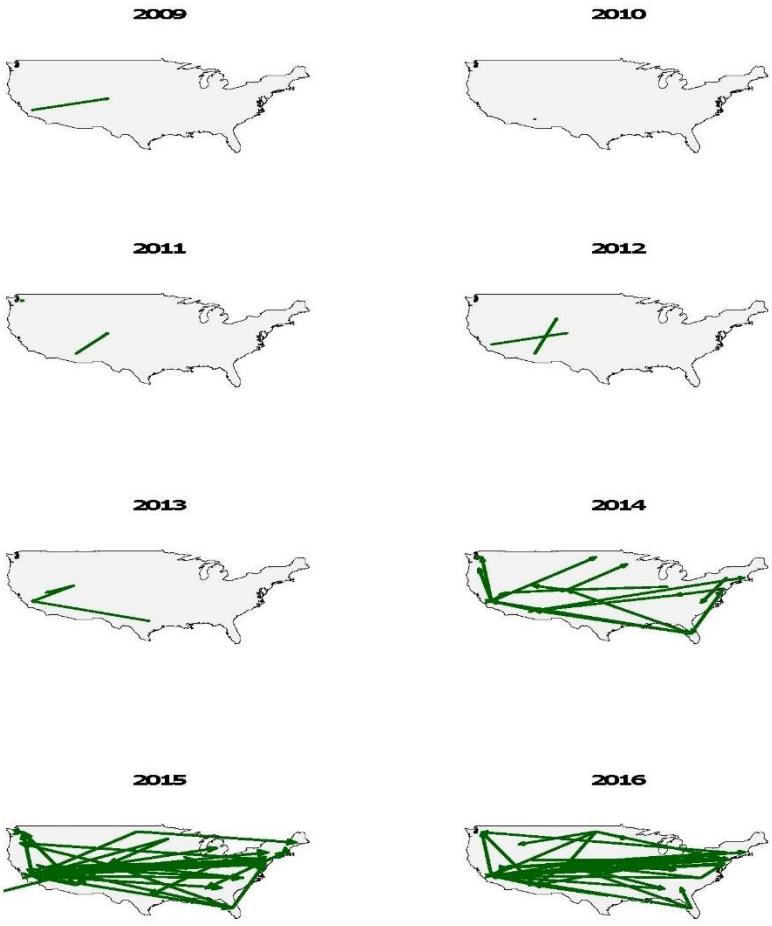

Table 1. Informant Characteristics

Pseudonym	Gender	Organization	Role	Description	Reach
Elizabeth	F	Blue For-profit	Vice-president	Cultivator	State
Clarence	M	Beige For-profit	Chief Executive Officer	Retailer	National
George	M	Purple For-profit	Chief Financial Officer	Agriculture Technology	National
Louis	M	Lavender For-profit	Senior vice-president	Market Research	National
Ruth	F	Teal Nonprofit	Director	Research	National
Raymond	M	Orange For-profit	Senior Vice President	Private Equity	National
Anthony	M	Teal For-profit	President	Private Equity	National
Catherine	F	Green Nonprofit	Director	Legalization Advocacy	National
Fred	M	Olive For-profit	Director	Social Media	National
Jack	M	Maroon For-profit	Chief Executive Officer	Private Equity	National
Randy	M	Teal Nonprofit	Founder	Research	National
Patrick	M	Blue Nonprofit	Founder	Legalization Advocacy	National
Samuel	M	Pink Nonprofit	Manager	Legalization Advocacy	National
Ryan	M	Brown For-profit	Founder	Consulting	National
Ronald	M	Black For-profit	Founder	Consulting	National
Kelly	F	Blue For-profit	Founder	Accessories	National
Paula	F	Blue Nonprofit	Director	Legalization Advocacy	National
Jesse	M	Coral For-profit	Chief Executive Officer	Private Equity	National
Ann	F	Cyan For-profit	Founder	Private Equity	National
Earl	M	Grey For-profit	Chief Executive Officer	Consulting	National
Heather	F	Lime For-profit	Founder	Private Equity	National
Lilian	F	Lime Nonprofit	Founder	Legalization Advocacy	State
Phillip	M	Magenta For-profit	Chief Executive Officer	Private Equity	National
Emma	F	Mahogany Nonprofit	Chief Executive Officer	Dispensary	National

Roger	M	Mint For-profit	Chief Executive Officer	Retailer	National
Ernest	M	Navy For-profit	Manager	Consulting	National
Noah	M	Ochre Nonprofit	Chief Executive Officer	Consulting	National
Barbara	F	Orange Nonprofit	Director	Gender Representation Advocacy	National
Helen	F	Orange Nonprofit	State Director	Gender Representation Advocacy	National
Deborah	F	Purple Nonprofit	Founder	Education	State
Matthew	M	Red Nonprofit	Director	Trade Organization	National
Douglas	M	Pink For-profit	Partner	Private Equity	National
Ashley	F	Vermillion Nonprofit	Chief Executive Officer	Ethnic Representation Advocacy	National
James	M	Green For-profit	Chief Executive Officer	Private Equity	National
Thomas	M	Green For-profit	vice-president	Private Equity	National
Nick	M	Green For-profit	vice-president	Private Equity	National
Tina	F	Yellow Nonprofit	Director	Government	State

Table 1 summarizes interviewees' characteristics, including respondent pseudonym, organization pseudonym, role, organization description, and reach (state/national). Thirty-seven participants, representing 32 organizations, took part in this study. Twenty-three (62.2%) of the respondents were men and 14 (37.8%) were women. Twenty-six (70.3%) participants were from for-profits, and 11 (29.7%) were from non-profits. Within for-profits, 11 participants were from cannabis financial services firms, followed by consulting firms (5), growers/retailers (4) and others (6), such as market research and social media firms. Within non-profits, five participants were from legalization advocacy organizations, followed by gender representation advocacy organizations (2), research organizations (2),

education organizations (1) and ethnic representation advocacy entities (1). Legalization advocacy organizations generally push for greater access to medical or recreational cannabis. Gender and ethnic representation advocacy organizations support increased representation of women and ethnic minorities in the cannabis market, respectively. Education organizations support increased education around the responsible use of medical and recreational cannabis. I present the results according to the themes of the analysis. The terms *for-profit* and *firm* are used to connote large for-profit cannabis companies.

Motivations for large cannabis firms' participation in the space

To seek profit

This section summarizes participants' views on major cannabis firms participating in the space largely for profit. Profit-centric motivations were the most identified theme.

Green For-profit sought greater representation of profit-oriented versus socially conscious firms in the cannabis space. This may indicate that profit was a primary driver for some, but not all, members of large cannabis firms. Green For-profit did not connect non-profits with other organizations. When Green For-profit put for-profits in touch with each other for potential business opportunities, it only referred firms with two variants of board leadership composition: (1) a mix of directors from within the cannabis space and industries outside the space, or (2) all directors hailing from outside the cannabis space. Firms that drew most or all their leadership from the cannabis space, especially activist-led firms, were not recommended. Activist-led companies were apparently not profit-oriented, and thus unsuitable to be recommended:

> *You (activists) fight so hard, but don't want to profit.* (Thomas, Green For-profit)

Similarly, Green For-profit indicated the clear superiority of firms led by people not from the cannabis space:

> *A real firm and not a bunch of potheads trying to raise money.* (Thomas, Green For-profit)

A non-profit representative noted that more business-oriented, and perhaps largely profit-motivated people were now involved in the cannabis space.

> *Now we are seeing more and more business types who are less inclined to help others.* (Catherine, Green Non-profit)

Similarly, a firm employee indicated a shift toward a more profit-minded approach in the cannabis space:

> *There's a…capitalistic approach that has gained momentum as the industry has grown. There has been a transition as the industry is growing, where you are getting a lot more…Wall Street type people who are very effective at running businesses but really don't come in with that social element to it. They don't bring that same commitment or orientation towards some of the advocacy and some of the community aspects that are central to this industry today.* (Louis, Lavender For-profit)

Within the theme of cannabis firms participating in the space for profit, some key decision makers touched on the synergistic relationship between for-profits and non-profits. Many large cannabis firms donated money to non-profits, but for most, their motivations behind funding non-profits were not entirely altruistic. A respondent from a large cannabis firm

was clear that contributing funds to a non-profit had to result in some benefit for the firm itself:

> *So, when I'm making a decision here, I mean, a lot of it is, how much they're asking for?…I'm looking for how much they're asking for, what it is they going to support, and then also what is Yellow For-profit getting out of the deal.* (Elizabeth, Yellow For-profit)

Several large cannabis firms donated to non-profits, in the hope that non-profits would change laws around cannabis, thus increasing the size of the United States cannabis market:

> *We're a publicly traded for-profit corporation…most of our money right now is going to policy-based organizations. People are lobbying at same federal level to change laws because obviously if there are more states that have legal cannabis, that's a bigger market for us to sell our…products.* (Fred, Olive For-profit)

> *Non-profits are actively working to change the laws, and the more laws they can change, the larger the market will be for the businesses.* (Jack, Maroon For-profit)

> *…for-profits, some of them then donate back to the NGOs to try to help expand the states that will have the medical marijuana laws.* (Randy, Purple Non-profit)

Some non-profits were aware that large cannabis firms saw them as vehicles to increase the size of the United States cannabis market. A few non-profits accepted funding from large cannabis firms and in return, allowed firms to add provisions into non-profit initiatives:

> *Let's say he's (Chief Executive Officer of major non-profit) drafting a legalization initiative in [redacted], if he could get the distributors to contribute money to the initiative in return for putting*

> *a provision that helps them, then he would do that…There was one significant industry player I met, he…offered to put up a couple of million dollars and be part of the partnership…I think he was able to get a few provisions that he wanted into the initiative.* (Patrick, Blue Non-profit)

To mitigate social inequality

This section details participants' views on cannabis firms participating in the space to mitigate social inequality. Green For-profit organized conferences about twice a year. Conference promotional materials indicated how the cannabis industry could mitigate stigma and inequity:

> *Successful women who used their skill sets that helped them lead businesses or climb corporate ladders are quickly rising to the top in the cannabis industry. Our [redacted] panel will highlight the successes of some of the women in the cannabis industry as our panelists share their stories of transitioning, fighting stigmas, and leading organizations and businesses* (Conference panel description)

While the majority of large firms indicated profit-oriented motivations for participating in the space, a few appeared to be driven by socially conscious motives:

> *Everybody that's involved in the business believes that businesses are part of the community and are not independent from the community they exist in and have a responsibility to that community…I should dedicate some portion of our efforts, it might be just one percent, to the community.* (George, Purple For-profit)

When firms referred to socially conscious motives or responsibility to the community, they generally indicated activities such as funding criminal record expungement initiatives or training minority entrepreneurs:

> *I funded the largest expungement clinic in [redacted] to date. We've helped some 800 people and not just with expungements but also with services like housing and job training, healthcare.* (Raymond, Orange For-profit)

Another firm created a manual to train minority entrepreneurs in the cannabis market:

> *We're going to create a syllabus to train potential entrepreneurs from minority backgrounds…so that if somebody wants to get in this business, we'll provide them with access to a curriculum and our management teams, so that they can learn from our experience and prepare them for getting into this industry.* (Clarence, Beige For-profit)

> *To provide cannabis as medicine*

This section indicates key decision makers' views on cannabis firms participating in the space as providers of medicine. Several large cannabis firms have characterized cannabis as medicine [288,289], and in this vein, a firm representative described cannabis as a medicine:

> *Now for cannabis, it's a weird situation because it is a medicine like pharmaceutical drugs but safer than pharmaceutical drugs.* (Elizabeth, Yellow For-profit)

In the cannabis-as-medicine vein, some firms set aside funds to purchase cannabis for marginalized medical cannabis patients.

> *All of the employees from our firm contribute a portion of their salary into a fund… that provides access to patients who don't have the financial means to purchase medical cannabis without the assistance of insurance.* (Clarence, Beige For-profit)

In line with views that firms were motivated to participate in the space as providers of medicine, several firms gave free cannabis to medical cannabis patients who typically could not afford it, perhaps to reinforce the idea of cannabis as medicine or to provide what firms perceived as free medical assistance. This point seems to have some overlap with the previous theme, given that firms wish to help the less fortunate.

> *There's a dispensary in…that offers a couple of programs for…low income medical patients in the community…they give away very cheap or inexpensive clones for the patient who're consuming very high quantities of cannabis... In that way, they are not spending as much money on the product.* (Louis, Lavender For-profit)

> *Some dispensaries have huge programs for people who can't afford medicine.* (Ruth, Teal Non-profit)

Discussion and Conclusion

Given concerns around changing usage patterns and potency in line with growing United States cannabis markets,[149,255] this study provides improved understanding around the cannabis space specifically regarding views on motivations for large United States cannabis firms' participation in the space. Key decision makers' views are important as they may possess information not available to lower ranked employees, may influence firm decisions[268] and consequently impact United States cannabis usage patterns. Participants

reported that large cannabis firms participated in the space because of three, non-exclusive reasons: To seek profit, to mitigate social inequity, to provide cannabis as medicine.

Firstly, participants indicated that cannabis firms may participate in the space largely to seek profit. Participants detailed that there seemed to be more business-centric persons becoming involved in the space, given the perceived lucrative nature of cannabis. A greater business-oriented focus in the cannabis market could mean an increased likelihood of the product being marketed to a broader range of demographics, shifting usage practices, and causing a reduced public health agenda. Firm engagement with socially conscious causes was generally motivated by larger cannabis markets. If firms' engagement in socially conscious causes are driven primarily by profit motivations, only causes that generate the greatest perceived increase in the bottom line may be selected and thus some marginalized groups may not benefit from cannabis firms' socially conscious activities. In addition, while the profit-centric nature of firms may lead to possibly deleterious public health outcomes, firms' desire to increase the size of the cannabis market may reduce stigma around cannabis and make it easier to conduct research around the plant.

Within the theme of firms participating in the space for profit, participants indicated the synergistic dynamic between for-profit and non-profits in the cannabis arena. Some non-profits were aware that large cannabis firms saw non-profits as means to increase the size of the legal market, and engaged with firms, in exchange for funding. Participants seemed to indicate that the cannabis space is a business, but also one with social benefits and stigma, and limited growth potential that working with a non-profit might help to ease, through facilitating larger markets and more business-friendly legislation. Thus, for-profit

and non-profit organizations in the space may be symbiotic and possibly cognizant of the other's goals and their relationship could possibly be described as synergistic rather than parasitic.

Although agendas of nonprofits and for-profits are ostensibly somewhat different, this is a complicated arena where no group is wholly oriented toward the social good and against profiteering, but the bottom line for both groups is to expand access. So policy-makers should be aware of that fact, consider the two groups as a unified whole and set policies with a watchful eye to the evidence of potential benefit or detriment to public health. Policymakers should thus avoid characterization of non-profits as countervailing powers to for-profits. If non-profits are conceptualized as checks on for-profits, I may underestimate the growth of the cannabis market. As both groups appear to be working together cohesively, growth of the cannabis space and the resultant changes in usage practices may be more rapid than previously predicted.

Secondly, while participants mostly indicated that firms participated in the space with largely profit-oriented notions, some firms seemed to participate in the space perhaps to mitigate social inequality[290] through community-oriented programs such as criminal record expungement initiatives likely funded by cannabis profits. Such firms appeared at least partially driven by socially conscious motives, perhaps encouraged by the perceived ability of the plant to mitigate social concerns such as increasing incarceration rates and associated costs.[257] These firms may herald a cannabis space that is not wholly profit-motivated and can serve as models for other cannabis corporations. Finally, participants reported that some firms entered the space as providers of medicine.[288] Past research indicates that

cannabinoids, the active ingredients in cannabis may be useful in treating cancer chemotherapy-induced nausea, anorexia relating to AIDS wasting syndrome and cancer-related pain.[291] In the United States, some have utilized cannabis for anxiety, chronic pain and poor appetite.[292] However, as of January 2019, the United States Food and Drug Administration has not approved cannabis as a safe and effective drug.[293] It is not clear whether firms espoused cannabis-as-medicine views to increase sales, because they genuinely believed in cannabis' therapeutic properties or both. Such rhetoric may mitigate stigma around cannabis and aid research efforts into its medical use, while also increasing sales and affecting usage practices.

I provide support to Subritzky et al.'s (2016) study by providing evidence on the role of non-profits in facilitating more favorable legislation. More importantly, I extend their work by providing information on the dynamic between non-profits and firms, and specific instances of non-profit activities that grow the cannabis market. In addition, I support Barry and Glantz's (2016) position that large firms are motivated to participate in the cannabis space to increase cannabis use. I extend their argument by providing evidence on techniques used by such firms to grow the market. However, I differ from Barry and Glantz's (2016) argument by suggesting that some firms enter the market not solely for increasing cannabis use, but also to mitigate social inequity and to provide cannabis as a medicine. In addition, while the authors center on the role of firms in expanding the market, they neglect how non-profits are helping to grow the space. I support the role of key decision makers in research studies as they can provide valuable insights not known to lower level staff, and I believe that the extensions to past work are underpinned by

harnessing key decision makers' insights. Broadly, I support past research around cannabis firms trying to grow the market and increase use. I extend and develop previous arguments by suggesting that firms may have reasons to enter the space that are not necessarily centered on simply increasing use, and also highlight the role of non-profits in expanding the cannabis market.

The results and analysis presented here used qualitative research techniques, which may be limited in generalizability. Nevertheless, given the sampling strategy, number of interviewees, feedback received from academic, industry and non-profit experts in the space, and the theoretical saturation achieved, I believe that the data provided a broad range of participants' viewpoints within the United States cannabis space. In addition, given the exploratory nature of this study, underpinned by a desire to understand motivations for large cannabis firms' participation in the cannabis market, qualitative methods are appropriate.[294] Conducting ethnographic observations at a financial services firm may have biased the data, compared to research at a production or sales firm. However, Green For-profit performed key financial services in the space, such as investment advice, and had numerous visitors from major firms each day, and thus is a suitable site for understanding motivations of large firms in the cannabis space. As the conference the first author collected ethnographic data at was organized by a financial services firm, there may have been some bias in terms of conference content. However, the range of content at the conference was broad, comprising gender and ethnic diversity in the space, as well as various investment opportunities. Another limitation is that I conducted a cross-sectional study, where findings represented a snapshot in time. Future

research can utilize longitudinal research techniques to study changes in legislation over time. In addition, non-profit participants in the study tended to see medical and recreational cannabis as part of the larger cannabis legalization process and did not view these as distinct policy goals. Some smaller non-profits may view medical and recreational cannabis as orthogonal concepts, but such viewpoints were not represented due to the sampling strategy. Future research could incorporate a larger range of non-profit viewpoints.

Conclusion: Chapter One

I first described cannabis usage preferences among United States Global Drug Survey respondents, primarily young men. I suggested that frequent use of cannabis may increase risk of health harms and highlighted the need to mitigate problematic use. With the rapidly developing United States cannabis market, possibly problematic usage patterns may indicate potential for cannabis use disorder especially within young men. I then explored if sociodemographic indicators were associated with increased likelihood for cannabis-related emergency department admissions in New York City. Findings may indicate that cannabis use adds burden to the healthcare system for those already disproportionately affected. As more states legalize recreational cannabis, results reinforce the need for research on identifying demographics at increased risk for cannabis use disorder and emergency department visits. I finally presented the findings of a qualitative study investigating the views of key decision-makers in the cannabis market, on large cannabis firms' motivations for participation in the space. I suggested that firms may have reasons to enter the space not necessarily centered on increasing use. Although non-profits and for-profits have different agendas, the bottom line for both groups is to expand access. Policymakers should be aware of that fact and set policies which consider the two groups as a unified whole.

I suggest that increasing proliferation of legal cannabis may disproportionately affect marginalized communities. While cannabis use is not necessarily harmful, the possible harms of psychoactive substances often fall on marginalized communities. I propose that policymakers ensure that cannabis firms do not engage in predatory targeting of

marginalized communities. Harm reduction may also be a salient theme. By promoting harm reduction practices within cannabis use, communities may be able to engage in moderate recreational use while also minimizing possible harms. It is not clear if cannabis use causes psychosis and other similar conditions.[295] Thus, any attempts by policymakers to educate possibly at-risk demographics about risks of cannabis use should be done with caution and avoid stigmatizing people who use cannabis.

Firms involved in the cannabis space may not be solely motivated by profit. The diversity of viewpoints in the cannabis space may be a platform for a cannabis space that attempts to profit from a substance that may have risks but is cognizant of the possible health harms relating to marginalized communities. Cannabis firms that engage in socially responsible behaviors may be a platform for other industries that market potentially addictive substances. With the recent rise in use of e-cigarettes by adolescents,[296] firms that sell such products may benefit from a socially responsible framework pioneered by the cannabis space.

The proliferation of legal cannabis in the United States may lead to a greater burden of health harms in marginalized communities. However, within this paradigm of reduced agency, people who use cannabis engage in harm reduction and cannabis firms seek to mitigate forms of marginalization. Thus, I suggest that while marginalization may relate to health harms and diminish agency, actors in these spaces still seek to mitigate risk and retain agency.

Chapter 2: Sexually Transmitted Infection Testing in The Chinese Men Who Have Sex with Men Environment

This chapter will explore concerns within sexually transmitted infection testing in the Chinese men who have sex with men environment. The first section details a behavioral strategy to increase sexually transmitted infection testing rates, and the second section details the association between men who have sex with men community-centric behaviors and contribution towards another's sexually transmitted infection testing cost. The third portion explores sexual role and choice of test. The fourth section characterizes determinants of antisocial online behavior among Chinese men who have sex with men. The final section examines the relationship between sexual behavior disclosure and the number of HIV self-test kits distributed and completed. Through these studies, I hope to provide insight on a key marginalized population, mitigating stigma and informing policy.

Determinants of altruism in interventions for men who have sex with men in China

This section is currently under review at BMJ Global Health, with Marcus Alexander and Laura Forastiere et. al as co-authors.

While experiments show that humans express social preferences in decision-making,[297,298] benefiting others even at a cost to themselves, little is known about what explains heterogeneity in altruism across the human population.[299] To provide insight, I detailed a novel intervention (pay-it-forward) designed to mobilize social preferences to increase rates of sexually transmitted infection testing among men who have sex with men in China, currently experiencing a sexually transmitted infection epidemic.[300,301] Pay-it-forward is a

variant of cooperative behavior where people who have benefited from others return the favor anonymously to persons other than their original benefactor. While there are many types of social preferences, my focus is on altruism as measured by the amount contributed to a pay-it-forward experiment. Pay-it-forward chains can arise spontaneously in everyday settings, such as among coffee shop customers.[302] In medicine, features of pay-it-forward can be seen in kidney transplant matching mechanisms, where undirected living donor kidney transplant programs serve to increase availability of donors and shorten waiting times for renal failure patients.[303]

The public health setting allows us to examine how specific sexual behaviors (anal sex role and disclosure of sexuality) may be related to different variants of altruism in the pay-it-forward context. Previous work on sexuality and cooperation has been limited to studies on the role of biological sex and sex-related hormones in the expression of cooperation, including testosterone,[304] and oxytocin.[305] Limited research has explored human sexual behavior and altruism. This study explores how sexual behaviors are related to participation and contribution levels in two pay-it-forward experiments. The study may provide insight around the relationship between altruism and sexual behaviors, which may have implications for promoting contributions toward public health initiatives especially in stigmatized settings.

Methods

Study design

The first study was conducted from December 2017 to February 2018 in Guangzhou, China, in partnership with a sexually transmitted infections clinic in a hospital and local

community-based organizations. This was a quasi-experimental study with two arms: Pay-it-Forward, and Standard of Care. In the pay-it-forward arm, men who have sex with men waiting for free HIV or syphilis testing received information about a gonorrhea and chlamydia test (cost ¥150/$23.87) and were told that that the previous respondent had donated money to cover the cost. Subjects decided whether to test and after testing were given an option to contribute to the next person. Donations were optional and could be any amount. Test costs were covered by participant donation and an initial sum from the sexually transmitted infection clinic. Participants were told all data would be confidential and test results sent after a week. After the test, participants decided whether to make their contributions in cash or via WeChat, a messaging and mobile payment smartphone app. Regardless of their decision to participate, individuals also reported their sociodemographics, and their attitudes towards the pay-it-forward experiment if they decided to participate. Test results were disseminated through WeChat. In the standard of care arm, participants were offered a test and had to pay the full cost if they wanted to get tested.

The second study was conducted from December 2019 to January 2019 in Guangzhou and Beijing, China, at three sites with community-based organizations. This was a randomized controlled trial with three arms: Pay-it-Forward, Pay-as-you-Want, and Standard of Care (NCT03741725). The second study was like the first, with the addition of randomization and new pay-as-you-what condition. In pay-as-you-what, instead of being asked to pay-it-forward, subjects were asked to pay as they wished for their own test.

Participants and study sites in both studies were not provided incentives. Free gonorrhea and chlamydia testing were not normally provided at study sites.

Ethical review

Participant anonymity was maintained during the entire project and participant consent was obtained prior to study participation. No identifying information was collected. Institutional Review Board approval was obtained from the Dermatology Hospital of Southern Medical University (GDDHLS-20180503) and the University of North Carolina at Chapel Hill (18-1358).

Statistical Analysis

Prior to analysis, I coded responses to the question 'What do you believe are the main benefits to participating in the pay-it-forward program?' to reflect overall, directed, and generalized altruism. The option 'More men who have sex with men can get tested' was denoted as directed altruism, and 'Someone has helped me, and I can help someone else' was coded as generalized altruism. These two options were combined to denote overall altruism. The option 'Discounted sexually transmitted infection test' was denoted as self-interest.

I calculated descriptive statistics for all men who have sex with men surveyed. I conducted the following analyses for the first study: 1) assessed factors associated with participation in the pay-it-forward arm; 2) explored factors associated with pay-it-forward contribution levels. For the second study, I: 1) estimated contribution levels across the pay-it-forward and pay-as-you-what arms; 2) divided the sample by sexual behavior (sex role, disclosure of sexuality) and then assessed if the relationship between altruism and contribution level

differed by sexual behavior. Covariates used in the analysis were: Sexual behavior [male partners (number of male partners in the past three months), unprotected anal sex (anal sex without condom use in the past three months), previous HIV test (whether men who have sex with men had received HIV testing prior), HIV test frequency (frequency of HIV testing), symptoms (whether men who have sex with men had noticed any sexually transmitted infection-related symptoms), sexual role (role during anal sex with men), outness (disclosure of men who have sex with men sexual behavior to wife, family, friends healthcare provider or no one)], altruism (overall, directed, generalized altruism, self-interest), sociodemographic categories (income, age, marital status), pay-it-forward arm assignment (assignment to pay-it-forward or pay-what-you-want arm).

To estimate the factors associated with contribution levels, I used the Heckman selection model. The first stage of the model was the selection equation, which modelled whether a subject decided to take the test. The model included sociodemographic and sexual history variables. In this model, I included all variables from the outcome equation except medical and personal history items which may explain the decision to test for chlamydia and gonorrhea, to achieve formal identification. The outcome stage of the equation modelled contribution levels. Site fixed effects were included in the selection equation since they were correlated with the probability of testing. Finally, given the small sample of subjects who were out to their health provider, I was limited in the number of controls I could include, leaving out those co-linear with other key variables (e.g. Marital status, unprotected sex or previous HIV test). I reported coefficient estimates and standard errors for all

models. I also reported unconditional marginal effects computed using both selection and outcome equations coefficients, and the inverse mills ratio from the first stage probit.

Results

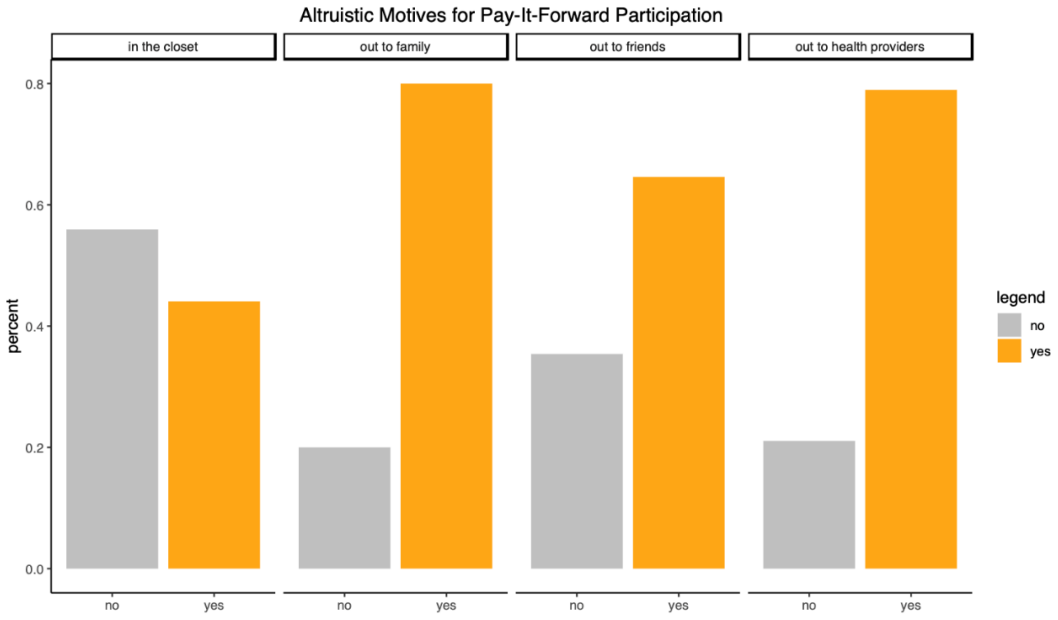

Figure 1. Differences in motivations for participating in pay-it-forward, by variants of sexual behavior disclosure (in the closet, out to family, out to friends, and out to health providers), for Chinese men who have sex with men, collected from a quasi-experimental study in Guangzhou, China.

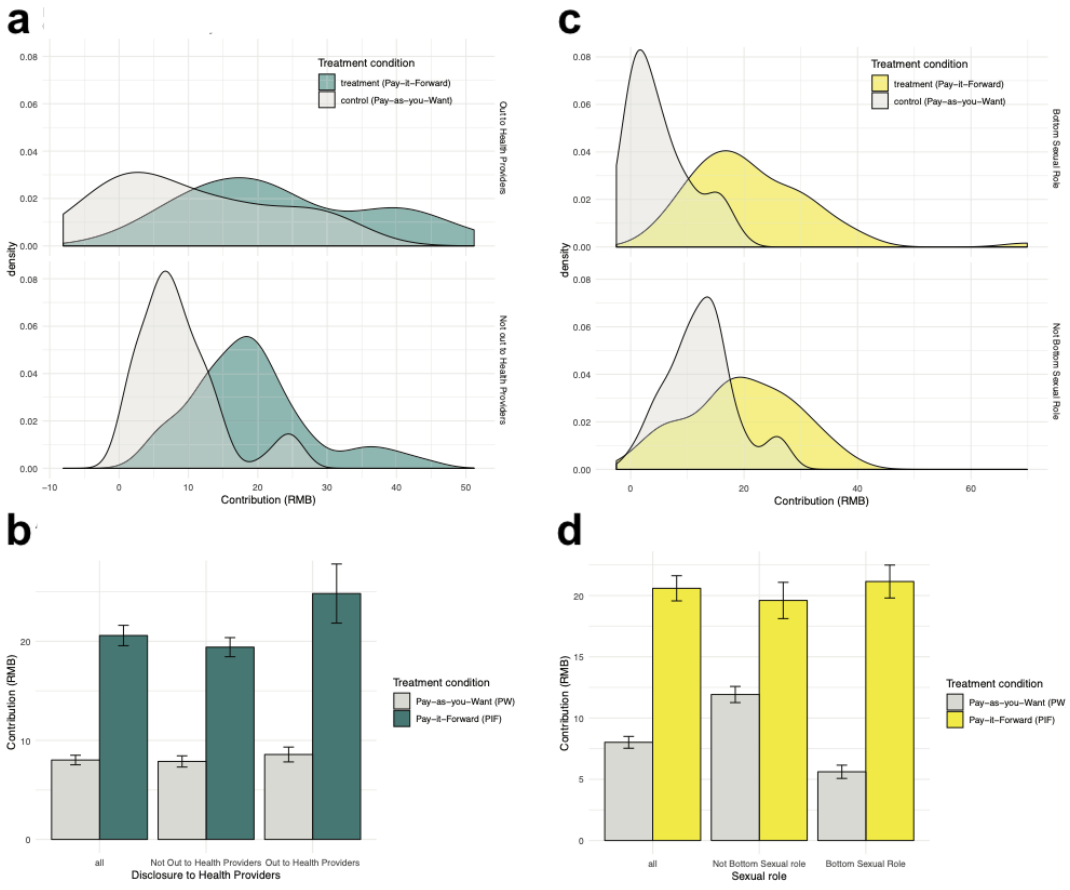

Figure 2. A) Distribution of contribution level by treatment arm, conditioning on sexual behavior disclosure to healthcare provider, for Chinese men who have sex with men, collected from a randomized controlled trial in Beijing and Guangzhou, China. (b) Differences in contribution level, divided by sexual behavior disclosure to healthcare provider and treatment arm, for Chinese men who have sex with men, collected from a randomized controlled trial in Beijing and Guangzhou, China. (c) Distribution of contribution level by treatment arm, conditioning on anal sex role, for Chinese men who have sex with men, collected from a randomized controlled trial in Beijing and Guangzhou, China. Pay-it-forward has stronger effect on contributions among those who preferred receptive anal sex (bottom). (d) Differences in contribution level, divided by anal sex role and treatment arm, for Chinese men who have sex with men, collected from a randomized controlled trial in Beijing and Guangzhou, China. Pay-it-forward has a stronger effect on

contributions for all participants but appeared to have the greatest effect for those who preferred receptive anal sex. All values were mean predictions and standard errors estimated using the Heckman selection model controlling for confounders. Each column estimated two models, where the sample is divided by a different sexual behavior.

Table 1: Participant characteristics for Chinese men who have sex with men from two studies in Guangzhou and Beijing, China

	First Study	Second study (RCT)	
	Pay-it-Forward	Pay-it-Forward	Pay-as-you-Want
Variable	%	%	%
Age			
18 - 20	6.9	7.4	7.6
21 - 25	37.4	31.6	46.7
26 - 30	30.5	29.5	26.1
21 - 40	21.2	24.2	16.3
41+	3.9	7.4	3.3
	(n =203)	(n=95)	(n=92)
Marital status			
Never married	87.6	90.3	88.9
Married, Engaged	9.9	7.5	10.2
Widowed, Separated, Divorced	2.5	2.2	1.0
	(n =202)	(n=93)	(n=98)
Income			
≤ ¥1,000	11.9		
	31.8		
¥5,000 - ¥10,000	38.3		
> ¥10,000	17.9		
	(n =201)		
≤ ¥1,500		11.2	14.0
¥1,500 - ¥3,000		7.1	9.7
¥3,001 - ¥5,000		17.3	16.1
¥5,001 - ¥8,000		23.5	24.7
> ¥8,000		40.8	35.5
		(n=98)	(n=91)
Male partners			
0 - 1	55.0	0	0
2 - 4	40.0	49.0	51.6
5 +	5.0	51.0	48.4
	(n=200)	(n=96)	(n=91)
Unprotected sex			
Yes	35.6	32.7	40.9
No	64.4	67.3	59.1
	(n=202)	(n-98)	(n=93)
Sexual role			
Bottom (mostly receptive)	30.6	30.9	33.0
Versatile	34.7	33.0	24.2
Top (mostly insertive)	34.7	36.1	42.9
	(n=196)	(n=97)	(n=91)

Table 2: Multivariate analysis of sexual behaviors and participant contribution levels, for Chinese men who have sex with men, collected from the pay-it-forward arm of a quasi-experimental study in Guangzhou, China.

Variables	(I) Baseline model	(II) Private sexual Behavior	(III) Outness To health provider	(IV) Altruism vs. self-interest	(V) Altruism generalized vs. directed
Outcome Stage: Estimating Contribution Levels					
Number of male partners	−1.62	−1.39	−1.99	−2.23	−2.19
	(2.38)	(2.33)	(2.34)	(2.29)	(2.35)
Unprotected anal sex	−21.22	−21.89*	−19.24	−21.79*	−23.77*
	(10.97)	(10.67)	(10.68)	(10.48)	(10.74)
Age	−1.62	−1.56	−1.58	−1.21	−1.31
	(0.85)	(0.83)	(0.83)	(0.83)	(0.84)
Marital status	9.11	7.64	13.51	14.32	12.37
	(18.37)	(17.80)	(18.10)	(17.57)	(17.90)
Income	19.79**	22.50***	20.05***	19.34***	18.86**
	(6.04)	(5.99)	(5.86)	(5.78)	(5.87)
Clinic fixed-effect	1.07	−0.26	−4.59	−1.30	−4.51
	(10.92)	(10.72)	(10.93)	(10.46)	(10.77)
Bottom sexual role		23.13*			
		(11.34)			
Out to health provider			26.65*		
			(13.29)		
Stated benefits of PIF					
Overall altruism				39.38**	
				(12.18)	
Directed altruism to MSM					21.41*
					(10.90)
Generalized altruism					10.97
					(10.57)
Self-interest					−12.83
					(31.16)
Selection Stage: Estimating the Probability of Testing					
Previous HIV test	0.39	0.41	0.38	0.42	0.41
	(0.25)	(0.26)	(0.25)	(0.25)	(0.25)
Symptoms	1.11***	1.18***	1.07**	1.11***	1.10***
	(0.32)	(0.34)	(0.32)	(0.32)	(0.32)
Number of male partners	0.17**	0.19**	0.17**	0.17**	0.17**
	(0.06)	(0.07)	(0.06)	(0.06)	(0.06)
Unprotected anal sex	0.03	0.03	0.04	0.04	0.03
	(0.20)	(0.20)	(0.20)	(0.20)	(0.20)
Age	0.02	0.02	0.02	0.02	0.02
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Marital status	0.70	0.63	0.71	0.71	0.71
	(0.44)	(0.45)	(0.45)	(0.45)	(0.45)
Income	0.03	0.07	0.03	0.04	0.03
	(0.12)	(0.12)	(0.12)	(0.12)	(0.12)
Clinic fixed effect	−0.10	−0.03	−0.12	−0.11	−0.11
	(0.20)	(0.20)	(0.20)	(0.20)	(0.20)
Bottom sexual role		0.25			
		(0.21)			
Out to health provider			0.11		
			(0.25)		
Num. obs.	196	190	196	196	196

Notes: ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$, Above table indicates: Estimate (standard error)

Table 3: Multivariate analysis of altruism, sexual role, and participant contribution levels, for Chinese men who have sex with men, collected from a randomized controlled trial in Beijing and Guangzhou, China.

Variables	Outcome Stage: Estimating contribution level	
	Bottom Sexual Role	Non-bottom Sexual Role
Pay-it-Forward arm assignment	22.94**	11.20
	(6.90)	(9.30)
Out to health provider	5.73	−4.29
	(7.61)	(13.07)
Age	0.80	−0.44
	(0.89)	(0.58)
Income	0.56	4.81*
	(2.06)	(2.12)
Marital status	−0.64	−2.19
	(14.54)	(10.95)
Unprotected anal sex	0.36	6.84
	(17.13)	(8.92)
Male partners	−2.16	−0.89
	(1.24)	(0.98)
	Selection Stage: Estimating probability of participation	
	Bottom Sexual Role	Non-bottom Sexual Role
Pay-it-Forward arm assignment	0.47	0.06
	(0.31)	(0.25)
Symptoms	0.98**	0.58
	(0.35)	(0.77)
Previous HIV test	0.35	0.42
	(0.37)	(0.90)
HIV test frequency	0.07	−0.18
	(0.14)	(0.23)
Out to health provider	0.30	−0.21
	(0.40)	(0.03)
Age	0.02	−0.01
	(0.03)	(0.03)
Income	−0.19	−0.09
	(0.11)	(0.12)
Marital status	0.47	0.36
	(0.70)	(0.74)
Unprotected anal sex	0.75	−0.10
	(0.51)	(0.56)
Male partners	−0.01	−0.05
	(0.05)	(0.07)
Clinic 1 fixed effect	−1.49*	−1.08*
	(0.61)	(0.54)
Clinic 2 fixed effect	−0.95	−0.34
	(0.58)	(0.31)
Num. obs.	95	70

Notes: ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$, Above table indicates: Estimate (standard error)

In the pay-it-forward arm, participants paid forward ¥61.96/$9.87 on average (SD=¥56/$8.92), and the median contribution was ¥50.00/$7.96 (see Table 2). I found that receptive partners contributed ¥26.98/$4.30 more than insertive partners (p=0.04). Subjects practicing anal sex with a condom gave ¥21.47/$3.42 more (p=0.04). Higher-income participants gave more, with a single income category translating into ¥20.44/$3.25 higher contributions (p<0.011). Subjects in the pay-it-forward arm perceiving altruistic benefits in the program contributed ¥12.17/$1.94 more (p<0.001) compared to than those who did not see such benefits.

Finally, I found that outness was positively associated with directed altruism (p<0.05). Those who did not disclose their sexual identity were more likely to perceive only self-interested benefits of the program. In contrast, those out to their family, friends, and/or health providers (outside the men who have sex with men sexually transmitted infection clinic) were more likely to report altruistic motivations (Figure 1). Similarly, those who had disclosed their sexual behavior to a healthcare provider tended to have higher contribution levels (see Figure 2a, 2b).

In the second, randomized controlled trial study, out of the 103 subjects who participated in testing (pay-it-forward arm: 57/101; pay-as-you-what arm: 46/100), 96 contributed (pay-it-forward arm: 54/57; pay-as-you-what arm 42/46). The sociodemographic profile of participants was like the first study. In the combined analysis of both arms, like the first study, I found that men who have sex with men who preferred a receptive sexual role contributed ¥16.94/$2.70 more (p<0.05, Table 3). I also found that of 15 individuals who paid the full cost of the test or more, 14 preferred the receptive sexual role. I then explored

the role of the sexual role on contributions. For those who preferred a receptive role in anal sex, I found that the pay-it-forward intervention was associated with ¥15.90/$2.53 higher contributions compared to the Pay-as-you-Want condition ($p<0.001$, see Figure 2c, 2d, Table 3).

Discussion

The main finding was that sexual behavior disclosure (outness) was associated with altruism as a motivation for pay-it-forward participation, which was itself positively related to higher contribution levels. Results were consistent with previous research which suggested that sexual behavior disclosure was associated with increased HIV testing rates and linkage to care.[306,307] Past work in the Chinese context indicated that larger disclosure networks were associated with greater propensity of HIV testing.[308,309] The strength of this study is that I measured the relationship between sexual behavior disclosure and its relationship to intervention outcomes. Such outcome measurement is key to demonstrating the importance of sexual behavior disclosure, both for mitigating stigma and optimizing sexually transmitted infection testing interventions for sexual minorities.

Men who preferred receptive anal sex tended to contribute more funds to the intervention. While there is research on reducing levels of unprotected receptive anal sex among men who have sex with men,[310] studies on how preference for receptive anal sex may influence intervention outcomes is limited. As men who have sex with men preferring receptive anal sex may have a greater sexually transmitted infection risk,[311] they may contribute more to interventions to reduce their own overall exposure by ensuring others get tested.

Alternatively, men who have sex with men preferring receptive sex may be more engaged in the men who have sex with men community and thus contribute more.

Future research can explore how the utility of a person's ties in a social network and concern for collective group well-being, are positively associated with altruism. The study has policy implications for improving health outcomes. Men who have sex with men in many settings face discrimination, limiting access to health services.[312] There is potential for targeted interventions to harness collective altruism in settings of marginalization, helping improve cost-effectiveness and reach of public health programs by drawing on the positive role of different identities.

Limitations

Results should be read in line with some limitations. While the Heckman model is a standard approach to dealing with selection bias, its power depends on the exclusion criterion: Previous testing and symptoms must correlate with participation but not with the contribution decision. I found strong correlation of symptoms with the decision to participate, and no such correlation with the level of contributions. But ultimately exclusion cannot be empirically proved and remains an assumption of the model. Additional limitations to the study were those inherent in observational research relying on subject-reported data. While the outcome variable was measured objectively (contributions made), subject baseline data is subject to recall error and subjective biases. There may be social desirability bias that can be accounted for in future studies. For example, some men may feel pressure to participate in the intervention as recruitment was conducted with other men who have sex with men present. The results may not be

generalizable to other contexts as there may be substantial cultural differences between men who have sex with men in China compared to other nations.

Community-centric Behaviors and Chinese Men who have Sex with Men

Introduction

A range of evidence-based preventive services are not affordable for those in the Global South.[313,314] Individuals in such settings routinely pay out-of-pocket fees for vaccines, drugs and diagnostic services.[315] Compulsory fee payment decreases the uptake of health services and disproportionately affects marginalized communities.[316,317] Government run preventive services have come under increasing strain,[318] with the cost of such services often determined by for-profit entities.[319] Programs that decrease fees associated with preventive services have not been scaled up[315,320] and thus, innovative techniques are necessary to stimulate access to preventive services.

An example of a novel technique for promoting service uptake in healthcare is pay-it-forward.[321] Pay-it-forward has one person receive a gift and then asks whether they would like to provide another person with a similar gift.[322] A previous study used pay-it-forward where men who have sex with men received a free gonorrhea/chlamydia test and then decide whether to donate toward the next person's test, where pay-it-forward increased gonorrhea/chlamydia test uptake among men who have sex with men.[321] pay-it-forward changes the transactional exchange between buyer and seller to a social exchange between a gift-giver and receiver.[323] This technique may augment trust and community engagement in health service uptake which are commonly associated with sexually transmitted infection test uptake and wellbeing.[324]

This study draws data from a multi-site, three-arm, cluster randomized controlled trial that evaluated the effectiveness of a pay-it-forward model in promoting gonorrhea/chlamydia

test uptake compared to a standard fee-based system. The primary outcome of the randomized controlled trial was gonorrhea/chlamydia test uptake. Gonorrhea/chlamydia test is available in most Chinese hospitals for about USD22.[325] gonorrhea/chlamydia test rates among Chinese men who have sex with men are low despite a gonorrhea and chlamydia epidemic.[326] Gonorrhea and chlamydia are often asymptomatic and associated with increased risk of HIV transmission and acquisition.[327,328]

Within men who have sex with men communities, engaging in community-centric behaviors can improve HIV/sexually transmitted infection testing outcomes and augment overall wellbeing.[329] Community engagement is associated with community-centric behaviors such as donating money and providing feedback.[330] Thus, men who have sex with men who engage in community-centric behaviors may contribute more toward others' testing within a pay-it-forward program. I operationalize community-centric behaviors into being part of a community and being an advocate for the community, leading to the following hypotheses: H1: Men who have sex with men who feel they are part of the men who have sex with men community are more likely to make a greater pay-it-forward contribution; H2: Men who have sex with men who believe that it is important to be an advocate for the men who have sex with men community are more likely to make a greater pay-it-forward contribution. I test these hypotheses using data from the indicated randomized controlled trial. Deeper understanding of the relationship between the extent of participation in community-centric behaviors and pay-it-forward contributions may aid in improving the efficacy of programs designed to reduce costs of paid testing services.

Methods

Study Design and Participants

I draw data from a randomized controlled trial to study sexually transmitted infection test uptake in men who have sex with men from December 2018 – January 2019. The randomized controlled trial was conducted in Guangzhou, China (two sites in hospital sexually transmitted infection clinics) and Beijing, China (community-based organization). All sites provided free HIV testing and were selected based on men who have sex with men input and ability to deliver testing. Sites were staffed with a mix of men who have sex with men volunteers, nurses, and public health staff. No physicians were present. Blood draws, testing, results reporting, and test follow-up was conducted by site staff. Sites had identical study procedures. The inclusion criteria was as follows: Born biologically male; ≥ 16 years of age; reported anal intercourse with other men; did not have a gonorrhea/chlamydia test in the past year; did not previously participate in the study; were willing to provide a mobile number or WeChat ID (popular Chinese mobile application) for sexually transmitted infection results notification. Institutional Review Board approval for the study was received from the University of North Carolina at Chapel Hill (IRB 18-2142), Southern Medical University Dermatology Hospital (China) and Yale University. The parent randomized controlled trial was registered on ClinicalTrials.gov (NCT03741725).[20] Written informed consent was obtained from all men.

Randomization

Clusters of ten participants were randomly assigned to pay-it-forward and two other arms (pay-what-you-want, standard of care) at each study site. A cluster was ten eligible men

who have sex with men who arrived in order and agreed to participate. A cluster size of ten was selected based on sample size calculation. All in the same cluster were assigned to the same study arm. Those who came with partners were assigned to the same cluster. STATA 15[331] was used to generate the randomization sequence. Study organizers and participants were not masked to arm assignment.

Procedures

The pay-it-forward program was developed through community feedback and crowdsourcing.[321] Program procedures were designed through an iterative process of consultation with community partners and pilot trials at each site. Through results from the pilot trial, the pay-it-forward procedure was modified accordingly.[20] The program's Chinese name was developed through crowdsourcing.[332] Handwritten notes were also presented to participants in the pay-it-forward arm. Figure 1 demonstrates the key concepts of pay-it-forward and the other two study arms. Those assigned to the pay-it-forward program were introduced to gonorrhea/chlamydia test, followed by an overview of pay-it-forward. Participants were told the standard price of gonorrhea/chlamydia test (USD22/RMB150) and that previous participants donated toward test fees to cover the cost. Men could thus receive a free test and contribute towards others' testing. Participants were also shown postcards with messages from previous participants and told that they could write a message for the next person. Testing and donation were voluntary and men who have sex with men could donate any amount after receiving the test.

Men who decided to test were asked about their sexual practices and advised to consider urethral, rectal, or both urethral and rectal gonorrhea/chlamydia test. Irrespective of the

testing decision, men were asked to complete a survey about their sexual history, testing history, attitudes toward the testing program and the men who have sex with men community (see Appendix). Samples collected were stored at room temperature overnight and transported to laboratories for testing. Men who received a positive test result were counseled and directed to the website of the designated partner hospital in each city, where they could make an appointment.

Outcome

The primary outcome was the contribution for pay-it-forward. Data from the other two arms was not considered.

Statistical analysis

I used the following survey items to represent being part of the men who have sex with men community and being proud of the men who have sex with men community, respectively: You feel that you are a part of the men who have sex with men community; It is important for you to be an advocate for the men who have sex with men community. These questions had the following options: Strongly Agree; Agree; Disagree; Strongly Disagree. These questions were not formally validated, but have been used in multiple studies in the China research environment.[321,333,334] Selection bias was a concern in the analysis. Those who did not want a gonorrhea/chlamydia test may be different from those who received a gonorrhea/chlamydia test. Such issues are common in most testing environments. Gonorrhea/chlamydia test selection may lead to inaccurate results of the factors responsible for the decision around test taking are related to the main variables of interest. I used the Heckman selection model to estimate whether the indicated items were

associated with the level of pay-it-forward contributions. I simultaneously modeled the decision to take the test and the subsequent test choice.

Test uptake (selection stage) was operationalized as a dichotomous variable indicating whether men had selected the gonorrhea/chlamydia test. Level of pay-it-forward contribution was the variable of interest for the outcome stage. Statistical analysis was conducted with R.[335] P<.05 was considered statistically significant. The first-stage model applied a probit model to represent the propensity to choose a gonorrhea/chlamydia test based on certain variables (see Table 2). The first model's assessment of the probability of gonorrhea/chlamydia test choice was then used in the second stage to adjust the estimates produced from a probity model that accounted for selection bias. To use the Heckman model, I had to understand the factors that influenced pay-it-forward contribution amounts and the decision to receive a gonorrhea/chlamydia test. The following variables likely influenced test uptake: Number of male partners last three months; Frequency of condomless anal intercourse last three months; Number of partners last three months; Frequency of HIV test; Possible sexually transmitted infection Symptoms; Out to health provider; Site. The following are likely to have influenced level of pay-it-forward contribution: Top; Bottom; Age; Income; Part of the men who have sex with men community; Advocate for the men who have sex with men community.

Results

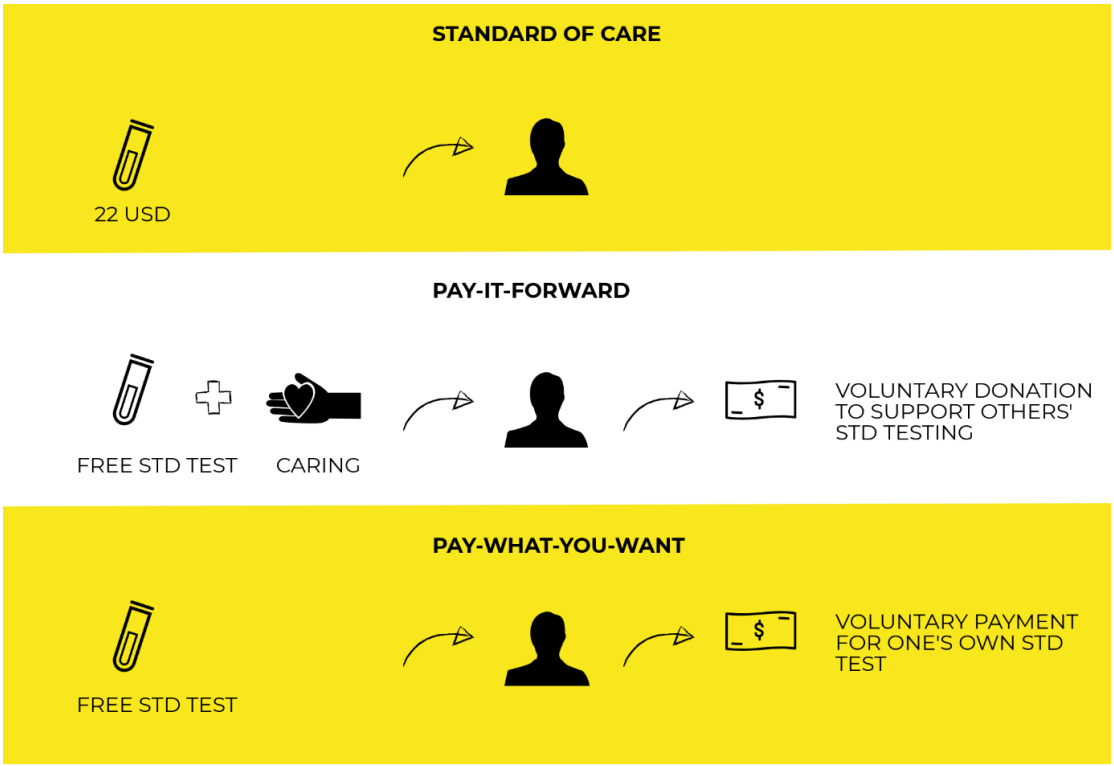

Figure 1. Concepts of standard of care, pay-it-forward, and pay-what-you-want gonorrhea/chlamydia testing. This schematic illustrates respective trial arms from the perspective of a participant. In standard of care, participant was offered a test at standard price (USD22). In pay-it-forward, the participant was offered a gift of a free test ("test kit") and told that previous men donated to make this test possible as well as shown postcards written by previous men ("caring"). Then, the participant was asked whether they would donate toward testing for future men ("voluntary donation"). In pay-what-you-want, the participant was offered a free test ("test kit"). Then, the participant was told they could pay any desired amount for their own test ("voluntary payment").

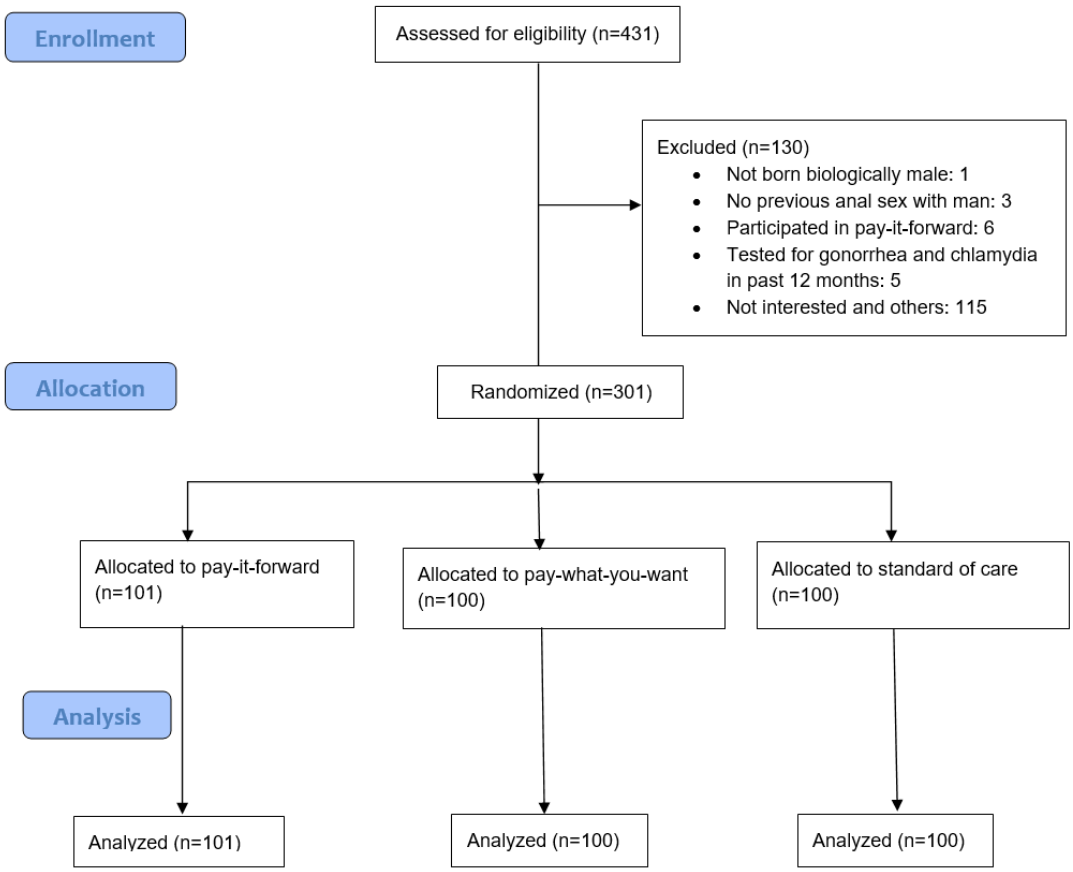

Figure 2. Study flow chart, 2018-2019.

* There is no loss-to-follow-up in this study. Participants made decisions on whether to test immediately after the interventions.

TABLE 1-Characteristics of Participants

Variable	Mean (SD)
Age	28.10 (7.10)
Number of male partners last three months	2.30 (2.98)
	%
Gonorrhea test site	
Rectal	43.9
Urethal	56.1
	n=114
Anal Sex Role	
Bottom	31.8
Top	37.8
Versatile	30.4
	n=283
Yearly income, $	
<2690.88	11.5
2690.88 - 5381.64	9.0
5381.64 - 8,969.40	14.9
8969.40 – 14351.04	26.4
>14351.04	38.2
	n=288
Experienced sexually transmitted infection symptoms	
No	11.2
Yes	88.8
	n=285
HIV test frequency	
<Once every two years	16.9
Once a year	23.0
Once every six months	28.1
Once every three months	26.3
Monthly	5.8
	n=278
Previous HIV test	
No	9.0
Yes	91.0
	n=288

Frequency of condomless anal intercourse last three months	
0% condom use	6.0
<50% condom use	10.3
>50% condom use	29.5
100% condom use	54.3
	n=234
Out to anyone	
No	35.1
Yes	64.9
	n=288
Out to health provider	
No	79.5
Yes	20.5
	n=288
Gonorrhea test result	
Negative	98.3
Positive	1.7
	n=114
Chlamydia test result	
Negative	93.7
Positive	6.3
	n=114
You feel that you are a part of the men who have sex with men community	
Strongly Disagree	3.2
Disagree	8.5
Agree	57.6
Strongly Agree	30.7
	n=283
It is important for you to be an advocate for the men who have sex with men community	
Strongly Disagree	1.1
Disagree	10.6
Agree	56.4
Strongly Agree	31.9
	n=282

TABLE 2: Pay-it-forward Contribution Amounts and Gonorrhea and Chlamydia Test Choice Among Chinese men who have sex with men

Variable	Coefficients (SE)	*P*	Coefficients (SE)	*P*
	H1		**H2**	
Outcome stage. Dependent variable: Rectal test				
Top	-63.088 (18.497)	.001	-56.971 (18.403)	.002
Bottom	-50.428 (17.694)	.005	-41.476 (17.366)	.019
Age	2.605 (1.055)	.016	3.001 (1.090)	.007
Income	11.036 (5.544)	.050	9.748 (5.626)	.087
Part of the men who have sex with men community	26.262 (10.041)	.011	-	-
Advocate for the men who have sex with men community	-	-	25.941 (9.786)	.010
Selection stage. Dependent variable: Test uptake				
Number of male partners last three months	0.072 (0.080)	.373	0.072 (0.080)	.373
Frequency of condomless anal intercourse last three months	0.010 (0.179)	.953	0.010 (0.179)	.953
Number of partners last three months	0.072 (0.080)	.373	0.072 (0.080)	.373
Frequency of HIV test	-0.088 (0.120)	.463	-0.088 (0.120)	.463
Possible sexually transmitted infection Symptoms	5.709 (361.380)	.987	5.709 (361.380)	.987
Out to health provider	0.060 (0.388)	.877	0.060 (0.388)	.877
Site				
Site 2	-0.468 (0.595)	.434	-0.468 (0.595)	.434
Site 3	0.190 (0.517)	.714	0.190 (0.517)	.714
N	82		82	

Note: Coefficients of probit with sample selection.

Between December 2018 and January 2019, four hundred and thirty-one men intending to test for HIV were approached. Fifteen were deemed ineligible for having participated in pay-it-forward before (n=6), having received a gonorrhea/chlamydia test in the last year

(n=5), having never had anal intercourse with men (n=3), and not born biologically male (n=1). In addition, 115 eligible men declined to participate due to lack of interest or time conflict. There was a final sample of 301 men who were enrolled and assigned to clusters within the three arms (see Figure 2). After accounting for missing data, 283 records remained. Descriptive statistics are presented in Table 1. Most men who have sex with men (88.3%) felt that they were a part of the men who have sex with men community. Similarly, a large proportion (62.7%) indicated that they were proud of the community. The majority (88.3%) believed that it was important to be an advocate for the men who have sex with men community.

Proportions of receiving gonorrhea/chlamydia test in the pay-it-forward, pay-what-you-want, and standard of care arms were 56%, 46% and 18% respectively. Of the 121 who tested for gonorrhea and chlamydia, five (4.1%) had gonorrhea and 19 (15.7%) had chlamydia. Of the 57 who received testing through pay-it-forward, 54 (94.6%) donated to future participants. The total amount donated in the pay-it-forward arm was $472.78 (mean=$8.29, SD=$7.35).

With two separate models, I detailed results regarding the hypotheses, exploring if men who have sex with men community-centric behaviors are related to pay-it-forward contribution (see Table 2). The model for H1 indicates that increased belonging to the men who have sex with men community was associated with greater pay-it-forward contribution. The model for H2 details that increased importance assigned to being an advocate for the men who have sex with men community was associated with greater pay-it-forward contribution.

Discussion

The aim of this study was to determine the association between men who have sex with men community-centric behaviors and contribution towards another's sexually transmitted infection testing cost. I found that increased support for community-centric behaviors was associated with greater pay-it-forward contribution in the sexually transmitted infection testing environment. This extends the literature by drawing data from a randomized controlled trial and suggests that community-centric behaviors may be associated with a reduction in testing service cost that would otherwise be associated with fees.

The possible cost-saving effect of men who have sex with men community-centric behaviors is consistent with research indicating that gay community participation can help to create safe environments for testing and care.[329] Similarly, identification with the gay community protected against HIV risk and younger men who have sex with men who identified with the gay community reported reduced sexual risk.[336] Results may add to a more complex view of men who have sex with men community-centric behaviors. Compared to non-MDMA users, MDMA users were more likely to participate in and indicate affiliation to men who have sex with men community.[337] In the same vein, gay social engagement was associated with a HIV positive serostatus, unprotected anal intercourse with regular partners and high frequency of HIV/sexually transmitted infection testing.[338] Perhaps increased community-centric behaviors may be related to improved frequency and prosocial behavior around HIV/sexually transmitted infection testing, but possibly more risky sexual behavior.

While previous research demonstrates associations between community-centric behaviors and aspects of sexual health, results provide evidence that community-centric behaviors can reduce testing costs. Such findings are relevant to China and other Global South environments where limited resources have been allocated to sexually transmitted infection prevention and treatment.[326,339] Harnessing community-centric behaviors in the Chinese men who have sex with men environment could allow more to receive free or subsidized sexually transmitted infection testing services. On a broader arc, community-centric behaviors may also be relevant in settings where groups of individuals pay mandatory fees for preventive services.

Results should be interpreted in line with a few limitations. The study was conducted in two metropolitan cities in China and generalizability may be limited. Even so, there are several settings in the Global South where well-defined communities pay fees for preventive health services. The study was conducted in a controlled research setting and it is not clear if community-centric behaviors can be similarly utilized in non-research contexts.

Findings have several implications for research and policy. From a research standpoint, this study expands on the limited data detailing how community-centric behaviors are related to the efficacy of behavioral interventions. Further research is key to better understand the role of community-centric behaviors in testing provision. From a policy perspective, the intervention does not seek to replace public provision of sexually transmitted infection testing. Instead, results may lead to exploration on how community-centric behaviors can be drawn upon when needed to reduce costs and allow for a more

financially sustainable model of sexually transmitted infection testing, before large scale public programs are rolled out. In conclusion, community-centric behaviors may improve pay-it-forward contributions in the Chinese men who have sex with men environment.

Lack of Sexual Behavior Disclosure May Distort sexually transmitted infection Testing Outcomes

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Men who have sex with men globally have a high burden of curable sexually transmitted infections.[340] The World Health Organization estimates that there are annually 131 million and 78 million new cases of Chlamydia trachomatis and Neisseria gonorrhoeae, respectively.[341] Among men who have sex with men worldwide, gonorrhea and chlamydia are the two most common bacterial sexually transmitted infections.[342] The World Health Organization recommends men who have sex with men receive regular gonorrhea and chlamydia testing.[343]

The risk of contracting sexually transmitted infections can vary with sexual behaviors.[344] There are a variety of ways men who have sex with men engage in intercourse, some related to preference and some not. Sometimes the reason for sexual positioning is strategic e.g. Seropostioning.[345] Some men who have sex with men prefer to engage in receptive anal intercourse (top), others prefer insertive anal intercourse (bottom) and some enjoy all types of intercourse (versatile).[346] A preference for receptive anal intercourse is associated with increased likelihood of a gonorrhea and chlamydia infection.[344] Men who have sex with men do not frequently receive rectal sexually transmitted infection testing because of several barriers, including: Stigma, shame, fear of invasive sampling, confidentiality concerns and clinician's time pressures.[347] Thus, both clinician and patient factors are key

to rectal sexually transmitted infection testing. While clinician factors are important, I center on patient factors because: 1) Self-testing and self-collection now allow rectal testing at home, prior to seeing a clinician.[348] Self-testing also happens in clinical settings.[348] Moreover, home-based self-testing has had several innovations, such as internet-based testing which obviates the need to see a clinician[349] and social entrepreneurship models that promote self-testing;[350] 2) Substantial heterogeneity in men who have sex with men preferences may drive rectal test uptake[339] along with a range of unaccounted factors such as disclosure of sexual behavior (outness); 3) The broader randomized controlled trial, from which I drew data to conduct secondary analysis of a cross-sectional survey, provided a unique context where all providers were offered rectal testing, allowing us to observe differences in men who have sex with men rectal sexually transmitted infection uptake.[351] Within these factors, the main barrier for testing is lack of disclosure.[352] If men who have sex with men are unwilling to disclose their sexual behavior, the likelihood of getting tested is low.[353] I explore the relationship between outness and rectal sexually transmitted infection testing.

The objectives of the study were to assess if men who have sex with men are more likely to select the gonorrhea and chlamydia test most representative of their sexual behavior, compared to a test less representative of their behavior; and if outness is related to the decision to select a rectal vs urethral test. Research on men who have sex with men sexual behavior does not often account for patient factors. The study may shed light on how sexual behavior and outness may affect gonorrhea and chlamydia test provision, improving men who have sex with men sexually transmitted infection testing efforts.

Methods

Study Design and Participants

I conducted secondary analysis of baseline data from a cross-sectional survey collected through an randomized controlled trial that sought to improve on sexually transmitted infection testing rates in men who have sex with men from December 2018 - January 2019 in China.[351] This randomized controlled trial is henceforth referred to the parent randomized controlled trial, from which I drew data to conduct secondary analysis to evaluate how outness can affect sexually transmitted infection test uptake. The parent randomized controlled trial was conducted in Guangzhou at two sites, and Beijing in a single site. All randomized controlled trial sites provided free HIV testing and were administered by men who have sex with men community-based organizations. Sites were selected based on men who have sex with men input, provided free HIV and syphilis testing for men who have sex with men, and had capacity to deliver sexually transmitted infection testing services during the study period. All sites were staffed with a mix of men who have sex with men volunteers, nurses, and public health staff, with no physicians. Blood draws, testing, results reporting, and test follow-up were handled by site-based staff. Sites followed similar procedures. The inclusion criteria was that subjects were assigned male sex at birth and identified as male, >16 years of age, reported anal intercourse with other men, did not have a gonorrhea and chlamydia test in the past year, did not previously participate in the study and were willing to provide a mobile number or WeChat ID (popular Chinese mobile application) for sexually transmitted infection results notification. The study was approved by the Human Subjects Committee at the University of North Carolina at Chapel Hill (IRB 18-2142), Southern Medical University Dermatology Hospital

(China) and Yale University. The parent randomized controlled trial[351] was registered on ClinicalTrials.gov (NCT03741725). Written informed consent was obtained from all participants.

Procedures

All testing sites offered gonorrhea and chlamydia tests to men who have sex with men waiting for free HIV and syphilis testing. After a short introduction to the gonorrhea and chlamydia test, participants decided whether to receive testing. After obtaining informed consent, I conducted patient interviews (survey instrument in Appendix) from all men approached about a gonorrhea and chlamydia test, even if they declined testing. I developed the survey for study purposes. Men who have sex with men were surveyed about their sexual history, sexually transmitted infection testing history, sexual behavior, and sociodemographic variables. Men who have sex with men were offered gonorrhea and chlamydia tests and were given a choice to get tested either at rectal or urethral sites but not both, because of limits to free testing at the clinics. While guidelines generally suggest triple site testing (urethral, rectal, pharyngeal),[354] this is not always possible in resource limited settings, such as this study. I thus provide implications generalizable to other resource-scarce settings. With men who have sex with men limited to a single test, I can understand the relationship between disclosure of sexual behavior and test choice. Men who have sex with men were told that the urethral test was appropriate for those preferring insertive anal intercourse, while the rectal test was for those preferring receptive anal intercourse---given that gonorrhea and chlamydia infections can be site-specific.[355] There was no unique choice specific to versatile behavior. Men who have sex with men could

select to receive both tests but would have to pay 150RMB (USD21). Men were told that their information would be kept confidential and gonorrhea and chlamydia test results sent after a week. Program organizers updated respondents of test results through WeChat. HIV, syphilis and gonorrhea and chlamydia tests were conducted in the clinic and the results recorded. Participants with positive test results were counselled and directed to hospital resources to receive paid treatment and follow-up care. Due to resource limitations, I was not able to pay for participant treatment, but note that Chinese sexually transmitted infection treatment is relatively affordable.[356] These tests would likely not have been done if the study had not happened, as Chinese men who have sex with men have low gonorrhea and chlamydia testing rates.[339] The parent randomized controlled trial increased gonorrhea and chlamydia testing rates and reduced cost, with the control being the community standard of care.[351]

The question on disclosure was as follows: "In the past, have you told anyone about your sexuality or sexual history with men?" The following options were provided: (1) "Yes, my long-term female partner/wife"; (2) "Yes, my family members"; (3) "Yes, my friends"; (4) "Yes, my healthcare providers"; (5) "No one". Options four and five were coded as binary variables to detail sexual behavior disclosure to health providers and non-specific disclosure respectively. Option five captures disclosure in a non-specific sense i.e. Anyone and is associated with improved health outcomes.[357] Option four indicates disclosure to health providers, which is key to receiving appropriate healthcare,[306] more so than the other group-specific disclosure options. For example, men out to their healthcare provider are more likely to get HIV testing compared to those out to their family.[308] Although

participants attended a specialized men who have sex with men testing clinic, this does not reflect their disclosure to their primary care or other health providers. There is significant stigma around men who have sex with men sexual behavior in China[358] and thus men may be comfortable going to a men who have sex with men-centric health provider, yet not be out to their primary health provider. For example, while men were out within the context of the health clinic in the study, 35% were not out to anyone and 80% were not out to their primary health provider. Given the high rates of non-disclosure outside the testing clinic, I suggest that broader non-disclosure may affect in-study outcomes.

Statistical analysis

To analyze study data I used inferential statistical methods. First, a probit model with sample selection was used to assess the relationship between receiving a rectal sexually transmitted infection test and various sexual behaviors (receptive, insertive, versatile). Then, I used a probit model with sample selection to assess the relationship between receiving a rectal sexually transmitted infection and sexual behavior disclosure/outness (non-specific disclosure, disclosure to health provider). I used STATA 13.0. All models included demographics, socioeconomic measures, and sexual history as controls. Further information about statistical methods is in Appendix. $P<0.05$ was considered significant.

Results

Table 1 Participants characteristics

Variable	Mean (SD)
Age	28.10 (7.10)
Number of male partners last three months	2.30 (2.98)
	%
Gonorrhea test site	
-rectal	43.9
-urethal	56.1
	n=114
Sexual behavior	
-receptive	31.8
-insertive	37.8
-versatile	30.4
	n=283
Yearly income, $	
-<2690.88	11.5
-2690.88 - 5381.64	9.0
-5381.64 - 8,969.40	14.9
-8969.40 - 14351.04	26.4
->14351.04	38.2
	n=288
Experienced sexually transmitted infection symptoms	
-no	11.2
-yes	88.8
	n=285
HIV test frequency	
-<once every two years	16.9
-once a year	23.0
-once every six months	28.1
-once every three months	26.3
-monthly	5.8
	n=278
Previous HIV test	
-no	9.0
-yes	91.0
	n=288

Frequency of condomless anal intercourse last three months	
-0% condom use	6.0
-<50% condom use	10.3
->50% condom use	29.5
-100% condom use	54.3
	n=234
Out to someone (Non-specific disclosure)	
-no	35.1
-yes	64.9
	n=288
Out to health provider (Disclosure to health provider)	
-no	79.5
-yes	20.5
	n=288
Gonorrhea test result	
-negative	98.3
-positive	1.7
	n=114
Chlamydia test result	
-negative	93.7
-positive	6.3
	n=114

Table 2 Multivariate analyses of men who have sex with men propensity to select the rectal test compared to the urethral test, in line with sexual behavior

Variable	Marginal Effects (95% CI)	*P*	Marginal Effects (95% CI)	*P*	Marginal Effects (95% CI)
Sexual behavior	Receptive		Insertive		Versatile
Dependent variable: Rectal test					
Insertive	-	-	-0.51 (-0.59, -0.44)	< .001	-
Receptive	0.45 (0.34, 0.57)	< .001	-	-	-
Versatile	-	-	-	-	0.006 (-0.18, 0.19)
Age	0.006 (-0.001, 0.013)	.12	0.004 (-0.009, 0.018)	.52	0.003 (-0.012, 0.019)
Income	0.012 (-0.036, 0.060)	.64	0.050 (-0.027, 0.128)	.2	0.05 (-0.05, 0.14)
Number of male partners last three months	-0.022 (-0.042, -0.001)	.04	-0.019 (-0.035, -0.002)	.03	-0.01 (-0.04, 0.01)
Frequency of condomless anal intercourse last three months	0.12 (-0.031, 0.28)	.12	0.37 (0.17, 0.57)	< .001	0.26 (-0.13, 0.65)
Non-specific disclosure	-0.08 (-0.19, 0.03)	.16	-0.093 (-0.34, 0.15)	.46	0.12 (-0.1, 0.33)
Disclosure to health provider	0.04 (-0.11, 0.18)	.6	-0.041 (-0.29, 0.20)	.74	-0.046 (-0.29, 0.20)
N	85		85		85
Predicted mean for receiving a rectal test	0.33		0.41		0.32

Note: Marginal effects of probit with sample selection (outcome equation results shown). Confidence interval (CI) estimated using jackknife with clustering by sites and within-site groups. Receptive: Compared to men who have sex with men not indicating the receptive role, men who have sex

with men indicating the receptive role are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Insertive: Compared to men who have sex with men not indicating the insertive role, men who have sex with men indicating the insertive role are less likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Versatile: Compared to men who have sex with men not indicating the versatile role, men who have sex with men indicating the versatile role have no gonorrhea and chlamydia test preference.

Table 3 Multivariate analyses of men who have sex with men propensity to select the rectal test compared to the urethral test, in line with non-specific disclosure and disclosure to health provider

Variable	Marginal Effects (95% CI)	*P*	Marginal Effects (95% CI)	*P*
Type of disclosure	Non-specific disclosure		Disclosure to health provider	
Dependent variable: Rectal test				
Insertive	-	-	-	-
Receptive	0.58 (0.5, 0.66)	< .001	0.58 (0.53, 0.64)	< .001
Versatile	0.26 (-0.23, 0.78)	0.29	0.26 (0.12, 0.41)	< .001
Age	0.01 (-0.01, 0.02)	.45	0.01 (-0.01, 0.02)	.35
Income	0.03 (-0.04, 0.1)	.47	0.02 (-0.04, 0.08)	.54
Number of male partners last three months	-0.02 (-0.1, 0.05)	.51	-0.03 (-0.06, 0.002)	.07
Frequency of condomless anal intercourse last three months	0.23 (0.06, 0.4)	.01	0.23 (0.1, 0.36)	.001
Non-specific disclosure	-0.08 (-0.32, 0.15)	.49	-	-
Disclosure to health provider	-	-	-0.04 (-0.25, 0.17)	.72
N	85		85	
Predicted mean for receiving a rectal test	0.4		0.41	

Note: Marginal effects of probit with sample selection (outcome equation results shown). Confidence interval (CI) estimated using jackknife with clustering by sites and within-site groups. Non-specific disclosure: Compared to those not out to anyone, those out to someone are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Disclosure to health provider: Compared to those not out to their health provider, those out to their health provider are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test.

Table 4 Multivariate analyses of versatile men who have sex with men propensity to select the rectal test compared to the urethral test, in line with non-specific disclosure and disclosure to health provider

Variable	Marginal Effects (95% CI)	*P*	Marginal Effects (95% CI)	*P*
Type of disclosure	Non-specific disclosure		Disclosure to health provider	
Dependent variable: Rectal test				
Insertive	-	-	-	-
Receptive	0.61 (0.52, 0.70)	< .001	0.56 (0.46, 0.67)	< .001
Versatile	0.36 (0.23, 0.48)	< .001	0.15 (0.03, 0.26)	.01
Age	0.004 (-0.01, 0.01)	.46	0.005 (0.001, 0.01)	.01
Income	0.03 (-0.02, 0.08)	.24	0.02 (-0.02, 0.05)	.39
Number of male partners last three months	-0.03 (-0.06, 0.003)	.08	-0.03 (-0.05, -0.01)	.01
Frequency of condomless anal intercourse last three months	0.2 (0.09, 0.32)	.001	0.19 (0.05, 0.33)	.01
Non-specific disclosure	-0.2 (-0.36, -0.05)	.01	-	-
Versatile*non-specific disclosure	0.27 (0.06, 0.48)	.01	-	-
Disclosure to health provider	-	-	-0.16 (-0.29, -0.04)	.01
Versatile*disclosure to health provider	-	-	0.29 (0.06, 0.53)	.01
N	85		85	
Predicted mean for receiving a rectal test	0.41		0.39	

Note: Marginal effects of probit with sample selection (outcome equation results shown). Confidence interval (CI) estimated using jackknife with clustering by sites and within-site groups. Non-specific disclosure: Compared to versatile men who have sex with men not out to someone, versatile men who have sex with men who are out to someone (disclosed sexual identity) are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Disclosure to health provider: Compared to versatile men who have sex with men not out to their health provider, versatile men who have sex with men out to their health provider are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test.

Table 1S Outness, Sexual Behavior and Gonorrhea and Chlamydia Test Choice Among Chinese men who have sex with men

Variable	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*	Coefficients (95% CI)	*P*
	Receptive		Insertive		Versatile		Non-specific disclosure		Disclosure to health provider		Versatile men who have sex with men-Non-specific disclosure		Versatile men who have sex with men-Disclosure to health provider	
Outcome stage. Dependent variable: Rectal test														
Insertive	-	-	-2.12 (-3.58, -0.82)	.003	-	-	-	-	-	-	-	-	-	-
Receptive	1.98 (0.94, 3.03)	.001	-	-	-	-	3.04 (-2.79, 8.87)	.29	3.13 (1.7, 4.56)	<.001	3.3 (2.11, 4.48)	<.001	3.24 (1.64, 4.85)	.04<.001
Versatile	-	-	-	-	0.02 (-0.55, 0.6)	.95	1.38 (0.18, 2.58)	.03	1.41 (0.24, 2.57)	.02	1.92 (1.13, 2.71)	<.001	0.86 (0.02, 1.69)	1
Age	0.03 (-0.01, 0.06)	.09	0.02 (-0.04, 0.08)	.55	0.01 (-0.04, 0.06)	.71	0.03 (-0.04, 0.09)	.42	0.031 (-0.04, 0.1)	.38	0.02 (-0.04, 0.08)	.47	0.03 (0.01, 0.06)	.02
Income	0.05 (-0.17, 0.28)	.66	0.22 (-0.2, 0.64)	.3	0.13 (-0.15, 0.42)	.34	0.13 (-0.4, 0.67)	.61	0.11 (-0.26, 0.47)	.56	0.26 (-0.13, 0.46)	.34	0.09 (-0.14, 0.32)	.42
Number of male partners last three months	-0.1 (-0.2, 0.01)	.07	-0.08 (-0.16, -0.002)	.04	-0.04 (-0.11, 0.03)	.27	-0.13 (-0.75, 0.5)	.69	-0.15 (-0.33, 0.03)	.1	-0.14 (-0.32, 0.04)	.12	-0.17 (-0.36, 0.01)	.06
Frequency of condomless anal intercours	0.56 (-0.22, 1.31)	.15	1.6 (0.38, 2.82)	.01	0.76 (-0.29, 1.81)	.15	1.2 (-0.89, 3.33)	.25	1.22 (0.38, 2.06)	.01	1.09 (0.35, 1.83)	.01	1.08 (-0.1, 2.07)	.03

e last three months														
Non-specific disclosure	-0.34 (-0.88, 0.19)	.2	-0.4 (-1.65, 0.85)	.52	0.35 (-0.28, 0.98)	.27	-0.44 (-1.54, 0.66)	.42	-	-	-1.09 (-1.96, -0.22)	.02	-	-
Versatile* non-specific disclosure	-	-	-	-	-	-	-	-	-	-	1.45 (0.29, 2.61)	.02	-	-
Disclosure to health provider	0.17 (-0.52, 0.89)	.62	-0.18 (-1.32, 0.97)	.76	0.13 (-0.62, 0.89)	.72	-	-	-0.21 (-1.45, 1.03)	.73	-	-	-0.95 (-1.67, -0.23)	.01
Versatile* disclosure to health provider	-	-	-	-	-	-	-	-	-	-	-	-	1.7 (0.37, 3.04)	.02
Selection stage. Dependent variable: Test uptake														
Insertive	-	-	-0.08 (-0.44, 0.28)	.67	-	-	-	-	-	-	-	-	-	-
Receptive	0.03 (-0.31, 0.38)	.85	-	-	-	-	0.06 (-0.36, 0.49)	.76	0.06 (-0.33, 0.46)	.76	0.057 (-0.35, 0.46)	.77	0.05 (-0.32, 0.43)	.77
Versatile	-	-	-	-	0.56 (-0.15, 1.27)	.78	0.09 (-0.33, 0.52)	.65	0.07 (-0.36, 0.5)	.73	0.3 (-0.34, 0.94)	.34	-0.08 (-0.56, 0.41)	.75
Age	0.03 (0.002, 0.06)	.04	0.03 (-0.002, 0.07)	.06	0.03 (-0.003, 0.07)	.07	0.03 (-0.001, 0.07)	.06	0.03 (-0.01, 0.07)	.1	0.03 (-0.003, 0.06)	.07	0.03 (-0.01, 0.06)	.1
Income	-0.16 (-0.32, 0.003)	.05	-0.16 (-0.34, 0.02)	.08	-0.16 (-0.34, 0.02)	.08	-0.16 (-0.33, 0.02)	.08	-0.15 (-0.32, 0.03)	.1	-0.14 (-0.32, 0.03)	.1	-0.14 (-0.31, 0.02)	.09

Number of male partners last three months	0.05 (-0.07, 0.17)	.38	0.06 (-0.07, 0.18)	.36	0.05 (-0.07, 0.17)	.36	0.06 (-0.07, 0.18)	.35	0.06 (-0.07, 0.18)	.35	0.06 (-0.07, 0.18)	.37	0.06 (-0.06, 0.17)	.34
Frequency of condomless anal intercourse last three months	-0.41 (-1.56, 0.73)	.46	-0.43 (-1.57, 0.7)	.44	-0.42 (-1.53, 0.7)	.45	-0.41 (-1.56, 0.73)	.47	-0.42 (-1.53, 0.68)	.44	-0.41 (-1.7, 0.89)	.53	-0.41 (-1.62, 0.81)	.5
HIV test frequency	-0.01 (-0.21, 0.19)	.94	-0.004 (-0.23, 0.22)	.97	-0.003 (-0.24, 0.23)	.98	-0.000 (-0.22, 0.22)	1.0	-0.003 (-0.22, 0.21)	.98	-0.009 (-0.22, 0.21)	.93	0.003 (-0.21, 0.22)	1
Previous HIV test	1.01 (0.37, 1.65)	.003	1.03 (0.38, 1.67)	.003	1.04 (0.41, 1.68)	.002	1.04 (0.38, 1.7)	.003	0.97 (0.36, 1.59)	.003	1.12 (0.5, 1.73)	.001	0.96 (0.33, 1.59)	.004
Possible sexually transmitted infection	0.60 (-0.03, 1.23)	.06	0.6 (-0.09, 1.28)	.09	0.56 (-0.15, 1.27)	.12	0.62 (-0.05, 1.28)	.07	0.62 (-0.07, 1.3)	.07	0.63 (-0.06, 1.32)	.07	0.63 (-0.04, 1.3)	.07
Symptoms Non-specific disclosure	0.22 (0.19, 0.63)	.28	-	-	0.24 (-0.23, 0.7)	.31	0.27 (-0.19, 0.73)	.24	-	-	0.09 (-0.52, 0.7)	.76	-	-
Versatile* non-specific disclosure	-	-	-	-	-	-	-	-	-	-	0.62 (-0.67, 1.9)	.33	-	-
Disclosure to health provider	0.19 (-0.28, 0.66)	.42	0.11 (-0.45, 0.66)	.7	0.11 (-0.43, 0.64)	.68	-	-	0.21 (-0.33, 0.75)	.43	-	-	0.06 (-0.56, 0.68)	.85
Versatile* disclosure to health provider	-	-	-	-	-	-	-	-	-	-	-	-	0.61 (-1.03, 2.25)	.45

Site														
-site 2	-0.61 (-1.18, -0.03)	.04	-0.69 (-1.93, 0.55)	.26	-0.7 (-1.93, 0.53)	.25	-0.68 (-1.88, 0.53)	.26	-0.66 (-1.85, 0.54)	.27	-0.68 (-1.87, 0.51)	.25	-0.66 (-1.56, 0.24)	.14
-site 3	-0.18 (-0.59, 0.24)	.39	-0.3 (-1.45, 0.84)	.6	-0.29 (-1.39, 0.82)	.6	-0.28 (-1.41, 0.85)	.61	-0.28 (-1.4, 0.84)	.61	-0.29 (-1.4, 0.82)	.6	-0.26 (-1.07, 0.56)	.53
Arm														
-pay-it-forward	1.36 (0.71, 2.01)	<.001	1.31 (0.57, 2.04)	.001	1.29 (0.52, 2.05)	.25	1.34 (0.61, 2.06)	.001	1.31 (0.59, 2.04)	.001	1.38 (0.66, 2.09)	.001	1.3 (0.64, 1.97)	<.001
-pay-what you-want	0.99 (0.32, 1.68)	.01	0.97 (0.18, 1.78)	.02	1.02 (0.27, 1.77)	.01	0.97 (0.2, 1.75)	.02	0.96 (0.17, 1.76)	.02	1 (0.2, 1.8)	.02	0.95 (0.17, 1.737)	.02
N	85		85		85		85		85		85		85	

Note: Coefficients of probit with sample selection. Confidence interval (CI) estimated using jackknife with clustering by sites and within-site groups. Receptive: Compared to men who have sex with men not indicating the receptive role, men who have sex with men indicating the receptive role are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Insertive: Compared to men who have sex with men not indicating the insertive role, men who have sex with men indicating the insertive role are less likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Versatile: Compared to men who have sex with men not indicating the versatile role, men who have sex with men indicating the versatile role have no gonorrhea and chlamydia test preference; Non-specific disclosure: Compared to those not out to anyone, those out to someone are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Disclosure to health provider: Compared to those not out to their health provider, those out to their health provider are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Versatile men who have sex with men-Non-specific disclosure: Compared to versatile men who have sex with men not out to someone, versatile men who have sex with men who are out to someone (disclosed sexual identity) are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test; Versatile men who have sex with men-Disclosure to health provider: Compared to versatile men who have sex with men not out to their health provider, versatile men who have sex with men out to their health provider are more likely to select the rectal gonorrhea and chlamydia test, compared to the urethral test.

431 men were approached intending to test for HIV and syphilis. After exclusion criteria and decision to participate, 301 men were enrolled, and sexually transmitted infection test uptake was 40%. Seven men chose to get both tests and were dropped from the analysis. As I am exploring whether sexual behavior is related to the choice of rectal over urethral testing, those who took both tests were not a focus of the analysis. Forty-four % (50/114) chose the rectal gonorrhea and chlamydia test and 56% (64/114) picked the urethral gonorrhea and chlamydia test. Among the randomized controlled trial participants, 35% (187/288) had disclosed sexual behavior to someone (non-specific disclosure) and 21% (59/288) of men had disclosed sexual behavior to their health provider. Five men who have sex with men were diagnosed with gonorrhea (urethral - two, rectal - three) and 19 with chlamydia (urethral - six, rectal - 13). I present descriptive statistics in Table 1.

Using three separate models, I explored if men who have sex with men made a test choice in line with their indicated sexual behavior. Table 2 indicated that receptive sexual behavior was associated with 45.2% (95%CI=33.8, 56.5) increased likelihood for selecting a rectal test. Insertive sexual behavior was related to 51.1% (95%CI=-58.7, -43.5) decreased likelihood for selecting the rectal test. Finally, versatile sexual behavior was not significantly associated with selecting a rectal test, possibly indicating that versatile men who have sex with men have no preference for a rectal gonorrhea and chlamydia test.

I then explored disclosure and likelihood to select the rectal gonorrhea and chlamydia test. Table 3 indicated that there was no significant relationship between non-specific disclosure or disclosure to one's health provider and selecting a rectal gonorrhea and chlamydia test. Table 4 indicated that, for versatile men who have sex with men, non-specific disclosure was

associated with a 26.8% (95%CI=6.1, 47.5) increased likelihood of selecting the rectal gonorrhea and chlamydia test, compared to the urethral test. I also found that for versatile men who have sex with men, disclosure to one's health provider was associated with a 29.4% (95%CI=6.3, 52.6) greater likelihood for selecting the rectal gonorrhea and chlamydia test, compared to the urethral test. These results were visualized in Figure 1, focusing on the interaction effects between disclosure and versatile sexual behavior. While being versatile alone was not significantly associated with rectal test uptake, once non-specific disclosure or disclosure to health providers comes into the picture, the model suggested a large and significant increase in rectal test uptake. Note that this was a marginal effect, controlling for sociodemographics, sexual history and medical history relevant to sexually transmitted infection testing.

Discussion

I first demonstrated that men who have sex with men selected tests in line with their preferred sexual behavior. I then indicated that versatile men who have sex with men out to a non-specific individual or one's health provider (outside the study context) had increased likelihood for selecting the rectal gonorrhea and chlamydia test, compared to the urethral test. The findings are in line with past research and reinforce the need to screen men who have sex with men for sexually transmitted infections through a full scope of transmission routes, ensuring no sexually transmitted infections are undiagnosed. I detailed how patient factors such as sexual behavior and outness may affect gonorrhea and chlamydia test provision in a clinical setting.

Many men who have sex with men in the sample with indications for rectal sexually transmitted infection testing did not receive it. This is consistent with research in China and globally. A China-based study found a higher prevalence of rectal chlamydia infection (24.4%) compared to urethral infection (5.3%).[359] Similar findings were indicated in several other studies, where rectal prevalence of sexually transmitted infections was greater than the urethral prevalence.[326] Other global studies indicated similar findings. Among asymptomatic men screened for chlamydia, 9.8% were positive for rectal infection vs 2.3% for a urethral infection. However, the same study reported higher prevalence of urethral gonorrhea (5.0%) vs rectal gonorrhea (3.0%).[360] Other studies indicated higher rates of rectal sexually transmitted infection infections compared to urethral infections.[361] Rectal sexually transmitted infections were associated with an increased risk for HIV seroconversion.[362] A retrospective men who have sex with men cohort study found that greater than two prior rectal gonorrhea or chlamydia infections were associated with eight times greater risk of HIV conversion.[328] Findings indicated there could be a large number of missed infections and underestimation of sexually transmitted infection prevalence. Undetected and consequently untreated cases may exacerbate the Chinese men who have sex with men sexually transmitted infection epidemic.[363] I extended previous research suggesting the importance of rectal sexually transmitted infection testing in men who have sex with men. Men who have sex with men in marginalized contexts and resource limited settings may need to receive a combined rectal, urethral, and pharyngeal gonorrhea and chlamydia test, as pharyngeal gonorrhea and chlamydia testing is also recommended for men who have sex with men.[364] However, when resources are scarce, as per the study, stigma-free settings may allow for providing a single test most appropriate to sexual behavior.

Finally, I found that men who have sex with men who had disclosed their sexual behavior to someone (non-specific disclosure) or their healthcare provider (outside the study context) were more likely to select rectal sexually transmitted infection testing compared to urethral testing. Past China research indicated that larger disclosure networks were associated with greater propensity of HIV testing.[308] Increased probability of never testing for HIV or syphilis was associated with non-disclosure to anyone or health professionals.[365] The odds of disclosure to a healthcare professional was greater for men who have sex with men who had received a sexually transmitted infection or HIV test.[366] In global literature, disclosure to healthcare providers was associated with HIV and sexually transmitted infection testing among young men who have sex with men.[367] Closeted men who have sex with men were less likely to have tested for HIV compared to out men who have sex with men.[306] Being completely out or even disclosure to a healthcare provider is clearly key to receiving sexually transmitted infection and HIV testing, as Chinese men who have sex with men often express fear of being ostracized because of their sexual behavior, a common barrier preventing testing.[368] When men who have sex with men are given a choice between a rectal or urethral test, it is possible that patient factors affect test selection decision. I extend the literature to suggest that disclosure can improve testing outcomes.

Limitations

This work has limitations. First, other unmeasured factors, such as knowledge levels about sexually transmitted infections and site of sexually transmitted infection symptom (urethral or rectal), may have driven selection of the urethral gonorrhea and chlamydia test. I partially addressed this by controlling for previous HIV test, HIV test frequency, and possible sexually

transmitted infection symptoms in estimating the decision to test, but not the choice between the tests (since these measures are not site specific). I also conducted the analysis including education level as a control but excluded it from the final analysis due to near collinearity with income. I did not consider how the psychological effects of testing would affect results. Sexually transmitted infection testing can be viewed as a form of commitment in a relationship[369] or cause significant distress.[370] Further work can model this through a survey item or qualitative techniques. Second, the gonorrhea and chlamydia test randomized controlled trial was conducted at sites catered to men who have sex with men sexually transmitted infection testing. Such site selection may have limited analysis to men who have sex with men connected with community-based organizations and already interested in HIV testing.[371] Despite limited generalizability to hospitals and other provider settings, the results remain relevant since specialized community men who have sex with men clinics remain major providers of testing in China[372] and globally[373] where patient factors drive health outcomes. As participants would have to pay an additional amount to take both tests, it could be that some selected a single test due to lack of funds. I utilized income as a control to account for this concern. Due to resource limitations, I was unable to offer rectal and urethral testing to all participants and then determine the number of mismatches between a positive test at a particular site and sexual behavior (e.g. Men who have sex with men reporting insertive sexual behavior but with a positive rectal test). Future research will incorporate such a study design.

Conclusion

Greater efforts are needed to ensure that patient factors do not adversely affect men who have sex with men testing outcomes. Sexual behavior and outness may affect gonorrhea and

chlamydia testing provision. Apart from clinicians, community-based efforts may reduce stigma-based barriers to testing.

Blocking and being blocked on gay dating apps: Implications for online sexual health interventions from a study of Chinese men who have sex with men

This section is currently under review at Sexual Health, with Marcus Alexander and Laura Forastiere et. al as co-authors.

Introduction

Although most men who have sex with men in China do not disclose their sexual orientation to anyone,[374] there is a rich and expanding digital social life for these men.[375,376] The world's largest gay social networking app, Blued, is based in China and provides news, health services, shopping, and gaming.[375,376] Blocking, both being blocked and blocking someone, are in-app antisocial ties produced when men who have sex with men use gay apps. Blocking someone is when users select a function on an app to prevent another user from contacting them and being blocked is when someone is prevented from contacting another user.[377] Users may block others because of harassment, lack of attractiveness, screening for time-wasters, racism, perceived HIV risk, privacy and safety concerns.[377–380] Blocking is associated with increased anxiety, distress, isolation;[377,378] and HIV risk.[379] Blocking behaviors can cascade through social networks[381,382] and thus the correlates of blocking warrant future study. Moreover, while the role of social networks in the spread of positive health-related behaviors is well understood,[383,384] less is known about how antisocial ties affect health. We note that blocking is not always antisocial, but can be protective of abusive or harassing behavior.[379]

App-based health interventions among men who have sex with men are becoming increasingly common,[385,386] but several features on such apps, such as blocking, and their public health implications are not well understood. Such understudied features may have unintended

consequences on men who have sex with men sexual networks and HIV risk.[379] While studies on blocking and men who have sex with men health outcomes have been conducted in other nations, albeit limited and mostly using qualitative techniques,[378,379] no such study has been conducted in China, despite its large men who have sex with men population[56] and relationship between Chinese men who have sex with men gay app use and health outcomes.[387] I characterized the determinants of blocking among Chinese men who have sex with men, to better understand blocking and its association with health outcomes. As Chinese men who have sex with men are a marginalized community, understanding potential correlates of marginalization is key to mitigating reduced health outcomes.

Methods

Study design and participants

I conducted a quasi-experimental study among men who have sex with men in Guangzhou, China that sought to promote male partner testing through social network-based distribution of HIV self-test kits in a cohort study, where index participants were offered HIV self-test kits and asked to distribute kits to their social network alters. Alters are index men's social contacts who received HIV self-testing kits. Men who have sex with men were recruited from May 2019 to December 2019 through a social media account run for men who have sex with men-centric studies via advertisements within the account, and through a men who have sex with men-friendly clinic at the Guangdong Provincial Center for Skin Diseases and Sexually Transmitted Infection Control via approaching participants who came for sexually transmitted infection testing. Men who have sex with men were first recruited for the treatment arm and once recruitment for the treatment arm had been completed, men who have sex with men

were recruited for the control arm. Participants interested in HIV testing at the clinic could book appointments online or enroll in the study at the clinic. Men who have sex with men were screened for the following criteria: 1) aged ≥ 18 years; 2) born biologically male; 3) ever had sex with men; 4) willing to provide phone number and willing to be surveyed at baseline and follow-up. Eligible participants were provided with study information, such as, potential risks, benefits, procedures, and outcomes. Participants unable to provide informed consent were excluded. A baseline survey was administered to eligible participants via a QR code they could scan and thereby complete the survey on their mobile device.

Survey items

I collected participants' baseline data such as, sociodemographic characteristics, sexual behavior, HIV testing history, social network data and blocking behavior (survey instrument in Appendix). Survey instrument was not validated but had been used multiple times in past studies.[321,334,388] Sexual behavior items included number of male partners in the last three months, and main sexual role. Examples of sexual behavior items were: In the past three months, with approximately how many different male sexual partners did you have anal sex?; your main sexual role is (pick one) insertive/receptive/both. To represent sexual behavior disclosure to family and medical professional, I used the following item: If you have told others about your sexuality or sexual history with men, who are they?. This item had the following options: medical professionals; family members; friends with no sexual relationship; coworkers; employers; other. I recoded the *medical professionals* option into a binary variable representing sexual behavior disclosure to medical professionals. I similarly recoded the *family members* option to a binary variable representing sexual behavior disclosure to one's family.

Social network survey items included name generator and descriptor questions to measure degree (number of people whom you have a social tie to) and weighted degree (degree weighted by the frequency of contact).[389] Degree was based on the sum of people listed in the question: Besides your family members, who are the people you spend your free time with? (list up to five). For example, if someone listed four people to the indicated question, their assigned degree was four. Weighted degree was based on the following item: How often do you contact the indicated person? This item had the options: Once a year; once every 6 months; once a month; once a week; daily. I treated this as an ordinal variable (scale of 1-5) and summed the item across each alter listed in the degree question. For example, if someone had a degree of four and contacted each person once a month, the weighted degree was 3+3+3+3=12. These items were based on validated instruments used to measure social network characteristics.[389]

Blocking items included likelihood of engaging in blocking, both directed (blocking someone or getting blocked) and undirected (blocking someone or getting blocked were treated collectively as undirected blocking behavior. 0=participant neither was blocked or blocked someone, 1=participant blocked someone or was blocked), and level of distress caused by being blocked (see below for details). The time frame for all blocking items was since inception i.e. Had men ever blocked someone? Examples of questions were: Have you ever blocked someone on a Blued?; Have you ever been blocked by someone else on Blued?. I did not ask why participants blocked someone e.g blocking someone was not necessarily a response to being blocked, harassed, or stigmatized. To identify the distress of being blocked in relation to other life events, I used the Gay Life Events Scale,[390] where participants had to rate being

blocked in relation to a serious illness. With the Gay Life Events Scale, I compared being blocked to events such as: You were harassed because you were gay; you find out your partner has AIDS; you failed an important exam; you had to work more hours in the office.

Ethical review

Participant anonymity was maintained during the entire project. No identifying information was collected. Institutional Review Board approval was obtained from the Dermatology Hospital of Southern Medical University (GDDHLS-20180503) and the University of North Carolina at Chapel Hill (18-1358).

Statistical analysis

I calculated descriptives (Table 1) using data obtained from all men who have sex with men surveyed. I modeled blocking behavior (undirected blocking behavior, blocking someone, being blocked) using multivariate logistic regression and reported adjusted odds ratio estimates for each independent variable. Covariates represented sexual behavior (sexual role, number of male partners in the past three months, condom use, disclosure of men who have sex with men sexual behavior to family, disclosure of men who have sex with men sexual behavior to medical professional, prior HIV test), participant social network structure (degree, weighted degree), and sociodemographic categories (income, age). The Income variable was denominated in the survey as RMB/month and I converted it to USD/year for clarity. Degree and weighted degree were calculated as indicated in the Survey Items section, and all other variables were used unaltered from the survey instrument. Analysis was conducted in R.[217]

Missing data

There was significant missing data on sexual role, condom use, number of social ties, and number of sexual partners so I did not use these as control variables for regression analyses. There was also significant missing data on variables used in our analysis, constraining the dataset. Complete case analysis was used as this technique generally remains unbiased, attains precision similar to or superior to multiple imputation, and has high statistical coverage when data is missing at random, as per this dataset.

Results

Table 1: Participant characteristics for 208 Chinese men who have sex with men, collected in a quasi-experimental study in Guangzhou, China

Variable	Mean (SD)
Age	27.9 (7.1)
Number of male partners in the past three months	1.7 (1.1)
Degree	2.3 (1.1)
Weighted degree	8.5 (4.2)
	%
Yearly income (USD/year)	
Less than USD36,000	20.7
USD36,000 - USD72,000	35.1
USD72,000 - USD120,000	30.8
More than USD120,000	13.5
	n=208
Condom use	
Never used	5.7
Occasionally (Less than half of the time)	7.4
Often used (More than half of the time)	24.6
Every time	62.3

	n=122
Sexual behavior disclosure to family	
Yes	22.9
No	77.1
	n=166
Sexual behavior disclosure to medical professional	
Yes	66.3
No	33.7
	n=166
Prior HIV test	
Yes	83.7
No	16.4
	n=208
Sexual role	
Insertive	42.6
Receptive	20.5
Versatile	36.9
	n=122
Undirected blocking behavior	
Yes	74.6
No	25.4

	n=181
Blocked by someone	
Yes	46.4
No	53.6
	n=181
Blocked someone	
Yes	62.4
No	37.6
	n=181

Table 2: Comparative distress from being blocked by someone, for 208 Chinese men who have sex with men, collected in a quasi-experimental study in Guangzhou, China.

Variable	Mean (SD)
Comparative distress from being blocked by someone [a]	
Harassed because you were gay	6.1 (6.1)
Partner has AIDS	11.7 (8.0)
Failed an important exam	10.0 (6.5)
Had to work more hours in the office	7.3 (5.8)

Note: A Being blocked by someone has been given a value of 10 on a scale of 0 (no emotional distress) to 20 (maximum emotional distress). If the event is more distressing, participants chose a number more than 10, and less than 10 if otherwise. If equal in distress, they chose the number 10.

Table 3: Multivariate analysis of blocking among 208 Chinese men who have sex with men, collected in a quasi-experimental study in Guangzhou, China

Variable	adjusted odds ratio (95% CI) [a]	P	adjusted odds ratio (95% CI)	P	adjusted odds ratio (95% CI)	P
	Undirected blocking behavior		**Blocked someone**		**Blocked by someone**	
Income	1.02 (0.33, 1.71)	0.004	1.84 (1.21, 2.46)	p<0.001	0.71 (0.06, 1.36)	0.033
Age	0.98 (0.87, 1.09)	p<0.001	0.95 (0.87, 1.03)	p<0.001	1.02 (0.92, 1.11)	p<0.001
Sexual role						
Insertive	-	-	-	-	-	-
Receptive	0.20 (1.26, 2.77)	0.817	0.72 (-0.50, 1.93)	0.249	0.40 (-0.86, 1.65)	0.534
Versatile	0.10 (-1.42, 1.52)	0.903	0.33 (-0.79, 1.44)	0.566	0.14 (-1.00, 1.29)	0.806
Number of male partners in the past three months	2.02 (1.26, 2.77)	p<0.001	1.10 (0.62, 1.56)	p<0.001	1.87 (1.29, 2.46)	p<0.001
Condom use	0.97 (0.30, 1.64)	0.005	0.79 (0.19, 1.39)	0.010	0.82 (0.23, 1.41)	0.007
Degree	1.05 (-0.22, 2.32)	0.106	2.01 (0.92, 3.11)	p<0.001	1.29 (0.20, 2.40)	0.021
Weighted degree	1.05 (0.73, 1.37)	p<0.001	0.83 (0.56, 1.10)	p<0.001	0.90 (0.62, 1.17)	p<0.001
Sexual behavior disclosure to family	2.66 (1.28, 4.04)	p<0.001	1.52 (0.44, 2.59)	0.006	1.67 (0.53, 2.80)	0.005
Sexual behavior disclosure to medical professional	1.35 (0.21, 2.50)	0.021	1.52 (0.50, 2.55)	0.004	1.06(0.00, 2.12)	0.051
Prior HIV test	1.98 (0.09, 3.87)	0.040	1.69 (0.11, 3.27)	0.037	7.90 (5.86, 9.95)	p<0.001
Intervention	1.82 (0.68, 2.98)	0.002	1.77 (0.80, 2.75)	p<0.001	1.15 (0.11, 2.18)	0.031
N	94		94		94	

Note: I estimated all adjusted odds ratios with logistic regression models. Adjusted Odds Ratios account for intervention assignment. Adjusted odds ratio=adjusted odds ratio.

Sociodemographic characteristics

Two hundred and eight men who have sex with men enrolled in the study. I conducted complete case analysis on a final sample of 94 men who have sex with men. I presented descriptive statistics in Table 1. Men who have sex with men had a mean age of 27.9 years (SD=7.1) and mean of 1.7 (SD=1.1) sexual partners in the last three months. Participants had a mean of 2.3 social ties (SD=1.1) and a mean weighted degree of 8.5 (SD=4.2). Men who have sex with men generally fell into two yearly income groups: USD36,000 - USD72,000 (35.1%) and USD72,000 - USD120,000 (30.8%). In the last three months, most men who have sex with men (62.3%) used condoms every time during anal sex with men. Most had not disclosed sexual behavior to their family (77.1%) but had disclosed sexual behavior to their medical professional (66.3%). Most had a prior HIV test (83.7%) and an insertive main sexual role (42.6%). Blocking was a common behavior. Most men who have sex with men (75%) had engaged in undirected blocking behavior in their lifetime i.e. They had blocked someone or had been blocked. About 62% had blocked someone in their lifetime and 46% had been blocked in their lifetime. Data was not collected on recent blocking e.g. six months.

Using an instrument derived from Gay Life Events Scale, I identified the distress of being blocked in relation to other life events (see Table 2). Being blocked seemed similar in distress to failing an important exam, but more distressing than getting harassed for being gay or having to work more hours in the office.

Multivariate analyses of blocking correlates among Chinese men who have sex with men

Men who used condoms were 21% (adjusted odds ratio= 0.79, 95%CI=0.19, 1.39) less likely to block someone and 18% (adjusted odds ratio=0.82, 95%CI= 0.23, 1.41) less likely to get blocked. Men with more social ties were more likely to block someone and get blocked. Each additional social tie increased the chance of blocking someone by 101% (adjusted odds ratio=2.01, 95%CI=0.92, 3.11) and the chance of being blocked by 29% (adjusted odds ratio=1.29, 95%CI= 0.20, 2.38). Older men were more likely to get blocked (see Table 3). Each year increase in age was associated with a 2% increase in getting blocked (adjusted odds ratio=1.02, 95%CI= 0.92, 1.11).

Discussion

I found that blocking other men was common on gay social media apps and getting blocked was as distressful as failing an exam (see Table 2). Men using condoms blocked less and were less likely to get blocked. Men with more social ties, such as friends or co-workers, were more likely to block someone and get blocked. Older men were more likely to be blocked compared to younger men. There is limited empirical research on blocking,[378,379] and none on the public health implications of blocking. Blocking is likely associated with men who have sex with men HIV risk[379] and other health outcomes but its correlates are unclear. Moreover, studies on blocking are predominantly conducted in high income nations, but not in low- and middle-income nations such as China, where there is a large men who have sex with men HIV burden.[391]

Getting blocked was as distressful as failing an exam. Past research related blocking to mental distress among men who have sex with men.[392,393] Mental distress is related to reduced health outcomes,[394] indicating the importance of studying blocking.

Men using condoms blocked less and were less likely to get blocked. Findings suggest a mechanism by which online behaviors related to blocking could impact social and sexual networks. Those who block less may feel the need to use condoms more frequently, with the same men who have sex with men viewing reduced blocking and increased condom use as morally appropriate behaviors.[395]

Men with more social ties, such as friends or co-workers, were more likely to block someone and get blocked. Past work indicated that having more social ties was associated with a greater amount of negative social ties.[396] I expand on previous work by detailing a similar relationship within a men who have sex with men sample. Having many friends is related to more negative social ties on other online networks,[397] which may explain the findings. While having more friends is related to improved health,[398] increased social ties may be linked to negative outcomes on gay apps. Larger online and offline men who have sex with men social networks were associated with risky sexual behavior,[399] and blocking may also be a similar negative consequence of a larger network.

Older men were more likely to be blocked compared to younger men. Past work suggested that older men were not preferred on gay dating apps,[377,393] younger men who have sex with men were more likely to use such apps,[400,401] and there was some preference on apps for contacting men in the same age group.[393] Blocking could be used to select potential partners by attractiveness,[378] and with age being a barometer of attractiveness among men who have

sex with men,[402] older men who have sex with men may be blocked for perceived unattractiveness. Alternatively, given the preference for same age partners,[393] the age gap between men who have sex with men may result in younger men blocking older men.

Overall, with more detailed epidemiological data, I suggest that future work expand on the indicated correlates of blocking. While I am uncertain on the direction of causality, designing interventions on gay dating apps to target certain behaviors and demographic groups may minimize blocking. An example of such an intervention may be sanctioning users who block excessively within a certain time frame, a technique previously used on social media to reduce racism.[403] By curtailing blocking, we may be able to reduce risky sexual behaviors and improve health outcomes among subsets of men who have sex with men.[378,379] On the policy front, I suggest that regulatory organizations ensure that blocking on gay dating apps does not facilitate increased men who have sex with men HIV risk.

Limitations

Unmeasured factors, such as time of blocking event and reciprocal blocking may have driven the results. I did not ask why participants blocked someone e.g blocking someone was not necessarily a response to being blocked. Participants might have reported lower amounts of blocking than experienced, especially since men may not know if they were blocked. I was unable to control for such effects but plan future study to use data drawn directly from apps rather than relying on participant self-report. I did not ask participants why they engaged in blocking and future qualitative work can detail the underlying factors behind blocking. The high rate of missing data may have biased the results, and future research can ensure a higher response rate using techniques such as emailing follow-ups and a providing a larger cash

incentive. Data was collected at sites catered to men who have sex with men sexually transmitted infection testing. Such site selection may have limited the sample to men who have sex with men connected with community-based organizations and perhaps biased the results.

Conclusions

Blocking other men was common on gay social media apps and getting blocked was as distressful as failing an exam. Age, condom use, and number of social ties may be associated with antisocial behavior, with implications for the design of online sexual health interventions.

Improving HIV Self-testing Social Network Interventions: The Role of Sexual Behavior Disclosure among Chinese Men who have Sex with Men

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Introduction

There is growing evidence to support social network-based interventions for sexual minorities.[308,404] Social network characteristics and structures influence individual-level behavior and HIV transmission.[300,405] Thus, social network analysis is key to HIV interventions. Social network analysis can identify intervention targets and pathways,[406] and has been used to detail the relationship between social networks and HIV prevention behavior, like condom use.[407] Several studies also related social network analysis to HIV testing. In a study of undiagnosed HIV-infected individuals in the United States, researchers used social networks to achieve a 5% positivity rate.[408] In a Chinese study of men who have sex with men, those with a larger same-sex disclosure network were more likely to have received HIV testing.[308] To further improve social network-based HIV testing, some studies combined social network analysis with HIV self-testing, successfully implemented globally.[409,410] HIV self-testing is where individuals self-collect specimens and then conduct and read tests themselves.[411] HIV self-testing may overcome issues around low testing rates, especially among men who have sex with men, via increasing privacy, convenience and anonymity.[412,413]

While social network-based interventions are important to mitigate the spread of HIV, it is not clear how we can optimize such interventions.[300] There also remain several issues with

social network HIV-testing. For example, most studies tend to be conducted in high-income nations,[300] despite the HIV burden being mostly in low- and middle-income countries.[414] In addition, many studies tend to be unlinked (where the relationship between members in the social network is unknown),[415] with a need for more data on linked HIV testing distribution networks, possibly improving HIV surveillance and testing efforts.[416]

About half of Chinese men who have sex with men had never received HIV testing and 62% had not been tested in the past year.[372] HIV self-testing augmented by social network techniques, may expand HIV testing among men who have sex with men.[324] When conducting social network-based HIV self-testing interventions among men who have sex with men, the characteristics of the initial participant, also called *seed* or *index* participant, are important, as some index participants are better able to reach alters for testing compared to others.[417] Alters are index men's social contacts who receive HIV self-testing kits. Disclosure of men who have sex with men sexual behavior is positively associated with both HIV testing uptake[387,418,419] and referral of alters to testing among Chinese men who have sex with men.[420] Disclosure of sexual behavior may thus relate to index men who have sex with men HIV self-testing kit distribution.

In partnership with a larger team, I conducted a quasi-experimental study among men who have sex with men in Guangzhou, China, that evaluated the use of HIV self-testing in testing men who have sex with men alters for HIV. Index men who have sex with men were provided HIV self-testing to distribute to their alters. Alters could upload test results through an online system monitored by the research team. The purpose of this analysis was to examine the

relationship between index sexual behavior disclosure and the number of HIV self-testing kits distributed and completed.

Methods

Study design and participants

The parent quasi-experimental study conducted among men who have sex with men in Guangzhou, China sought to promote male partner testing through social network-based distribution of HIV self-testing kits, where index participants were offered HIV self-test kits and asked to distribute kits to their social network alters. Men who have sex with men were recruited from May 2019 to December 2019 through a social media account run for men who have sex with men-centric studies via posts within the account, and through a men who have sex with men-friendly clinic at the Guangdong Provincial Center for Skin Diseases and Sexually Transmitted Infection Control via approaching participants who came for sexually transmitted infection testing.

Participants interested in HIV testing could book appointments online or enroll at the clinic. Men who have sex with men were screened for the following criteria: 1) aged ≥ 18 years; 2) born biologically male; 3) ever had sex with men; 4) willing to provide phone number and willing to be surveyed at baseline and follow-up. Eligible participants were provided with study information, such as, potential risks, benefits, procedures, and outcomes. A baseline survey was administered to eligible participants via a QR code they could scan and thereby complete the survey on their mobile device.

Upon survey completion within the treatment arm, participants were given up to five HIV self-test kits and encouraged to distribute the kits to their social network over one

month. Instruction materials were included with each kit. Participants could return for more kits and received RMB20 ($3) for baseline survey completion. Tests included instructions and a list of Centers for Disease Control and Prevention clinics where confirmatory testing could be sought. The alter of each index participant received RMB20 ($3) when they uploaded the test result to study team through an online system. The online system was a platform where participants could upload HIV self-testing results. Alters were aware that they would receive money upon test report. Each participant received RMB20 ($3) when his alters submitted the test result.

Survey items

I collected participants' data such as: sexual behavior disclosure; treatment arm outcomes; socio-demographic characteristics; previous HIV testing history; number of social ties. Sexual behavior disclosure items included whether the participants had disclosed their sexual behavior to their family or healthcare providers. The survey item for sexual behavior disclosure was: If you have told others about your sexuality or sexual history with men, who are they? This item had the following options: medical professionals; family members; friends with no sexual relationship; coworkers; employers; other. I recoded the medical professionals option into a binary variable representing sexual behavior disclosure to healthcare providers. I similarly recoded the family members option to a binary variable representing sexual behavior disclosure to one's family. I used three treatment arm outcomes, as follows. Successful receipt of test results uploaded by alters was a binary variable (0=alters of an index did not upload any test results from the HIV self-testing kits given to that index; 1=at least one alter of the index uploaded a test result). Number of kits requested by index

participant was a count variable representing the number of HIV self-testing kits each index received-index participants could obtain additional kits if they wanted. Number of test results successfully uploaded by alters was a count variable indicating the number of test results uploaded by the alters of an index. Previous HIV testing history item was: Prior to this self-test, have you tested for HIV before? Number of social ties was based on the sum of people listed in the question: Besides your family members, who are the people you spend your free time with? (list up to five). For example, if someone listed four people for the indicated question, their assigned number of social ties was four.

Ethical review

Participant confidentiality was maintained during the entire study. No identifying information was collected. Institutional Review Board approval was obtained from the Dermatology Hospital of Southern Medical University (GDDHLS-20180503) and the University of North Carolina at Chapel Hill (18-1358).

Statistical analysis

I calculated descriptives (Table 1) using data obtained from all men who have sex with men surveyed in the treatment arm. I used logistic regression for analyzing successful receipt of test results uploaded by alter, and negative binomial regression models for number of kits requested by index participant and number of test results successfully uploaded by alters. I used forms of sexual behavior disclosure (disclosure to family, disclosure to healthcare provider) as key independent variables. All models included socio-demographic characteristics (age, income) and HIV testing history (prior HIV test) as control variables, reporting adjusted odds ratios or adjusted incidence rate ratios for each independent variable. Income variable

was denominated in the survey as RMB/month and I converted it to USD/year for clarity. Analysis was conducted in R.

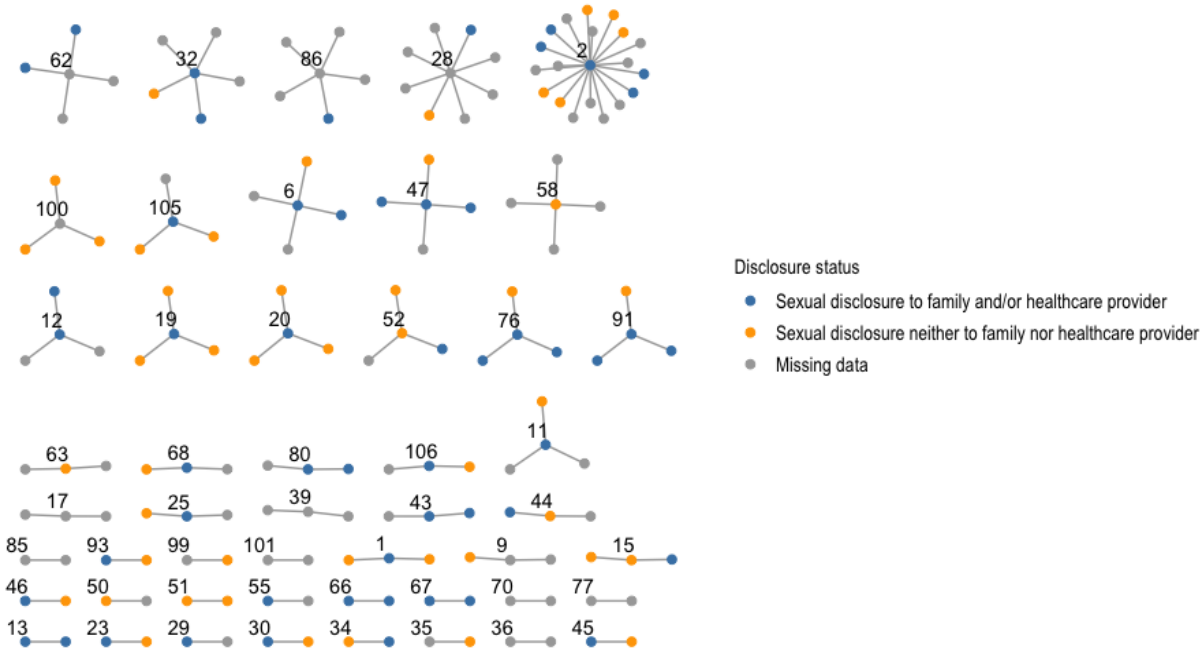

Fig 1. Self-reported social ties of index men who have sex with men collected from the treatment arm of a quasi-experimental study in Guangzhou, China for 106 Chinese men who have sex with men (index), and 143 Chinese men who have sex with men (alters) reached by index participants. Numbers (1-106) correspond to 106 index participants who initiated HIV self-testing distribution (see Table 1 for characteristics of index and alters). Index men who have sex with men are ordered from top to bottom based on number of social ties reported.

Table 1: Participant characteristics for 106 Chinese men who have sex with men (index), collected from the treatment arm of a quasi-experimental study in Guangzhou, China, and 143 Chinese men who have sex with men (alters) reached by index participants

	Index	Alter
Variable	**Mean (SD)**	**Mean (SD)**
Age	27.0 (5.3)	24.1 (5.0)
Number of male partners in the past 6 months	1.9 (1.2)	1.6 (1.0)
Number of social ties	2.3 (1.1)	1.3 (0.6)
	%	**%**
Sexual behavior disclosure to healthcare provider		
Yes	69.0	32.1
No	31.0	67.9
	n=84	n=84
	missing=21%	
Sexual behavior disclosure to family		
Yes	23.8	8.9
No	76.2	91.1
	n=84	n=79
	missing=21%	
Yearly income (USD/year)		
Less than USD36,000	23.6	39.4
USD36,000 - USD72,000	34.0	29.2
USD72,000 - USD120,000	32.1	20.4
More than USD120,000	10.4	10.9
	n=106	n=137
	missing=0%	
Sexual role		
Insertive	47.7	35.8
Receptive	23.1	35.8
Versatile	29.2	28.3
	n=65	n=53
	missing=40%	

Condom use		
Never used	4.6	7.5
Occasionally (Less than half of the time)	9.2	9.4
Often used (More than half of the time)	21.5	20.8
Every time	64.6	62.3
	n=65	n=53
	missing=40%	
Prior HIV test		
Yes	78.3	68.6
No	21.7	31.4
	n=106	n=137
	missing=0%	

Table 2: Multivariate analysis of sexual behavior disclosure and successful receipt of test results uploaded by alters, for 106 Chinese men who have sex with men (index), collected from the treatment arm of a quasi-experimental study in Guangzhou, China

Variable	adjusted odds ratio[1] (95% CI)	P
Sexual behavior disclosure to family	3.59 (2.00, 4.78)	p<0.001
Sexual behavior disclosure to healthcare provider	1.33 (0.20, 2.45)	0.021
Age	0.90 (0.81, 1.00)	p<0.001
Income	1.89 (1.29, 2.45)	p<0.001
Prior HIV test	0.90 (-0.54, 2.33)	0.220
N	94	

[1] I estimated all adjusted odds ratios with logistic regression models. Adjusted Odds Ratios account for baseline age, income, and prior HIV test. Adjusted odds ratio=adjusted odds ratio.

Table 3: Multivariate analysis of sexual behavior disclosure and treatment arm outcomes for 106 Chinese men who have sex with men (index), collected from the treatment arm of a quasi-experimental study in Guangzhou, China

Variable	Adjusted incident risk ratio[1] (95% CI)	P	Adjusted incident risk ratio (95% CI)	P
	Number of kits requested by index participant		Number of test results successfully uploaded by alters	
Sexual behavior disclosure to family	1.46 (1.18, 1.73)	p<0.001	2.87 (2.13, 3.61)	p<0.001
Sexual behavior disclosure to healthcare provider	0.90 (0.61, 1.20)	p<0.001	1.33 (0.54, 2.13)	0.001
Age	0.99 (0.97, 1.01)	p<0.001	0.93 (0.86, 0.99)	p<0.001
Income	1.03 (0.89, 1.18)	p<0.001	1.53 (1.12, 1.94)	p<0.001
Prior HIV test	0.97 (0.59, 1.34)	p<0.001	1.35 (0.24, 2.47)	0.018
N	78		78	

[1] I estimated all adjusted incident rate ratios with negative binomial regression. Adjusted incident rate ratios account for baseline age, income, and prior HIV test.

Missing data

There was significant missing data on sexual role, condom use, number of social ties, and number of sexual partners so I did not use these as control variables for regression analyses. There was also significant missing data on variables used in our analysis, constraining the dataset. Complete case analysis was used as this technique generally remains unbiased, attains precision similar to or superior to multiple imputation, and has high statistical coverage when data is missing at random, as per this dataset.

Results

Sociodemographic and behavior characteristics

A hundred and six index men who have sex with men enrolled in the treatment arm and 143 men who have sex with men alters successfully uploaded their test results. I presented descriptive statistics in Table 1. Index men who have sex with men had a mean age of 27.0 years (SD=5.3), mean of 1.9 (SD=1.2) sexual partners in the last six months and mean of 2.3 (SD = 1.1) social ties. Index men who have sex with men generally fell into two annual income groups: USD36,000 - USD72,000 (34.0%) and USD72,000 - USD120,000 (32.1%). In the last three months, most index men who have sex with men (64.6%) reported using condoms every time during anal sex with men. Most index men who have sex with men had a prior HIV test (78.3%) and had an insertive main sexual role (47.7%). About 24% of index men who have sex with men had disclosed their sexual behavior to their families and 69% to healthcare provider. Overall, index men who have sex with men had higher disclosure of men who have sex with men sexual behavior compared to their alters. For alters, 9% had disclosed their sexual behavior to their families, and 32% to their healthcare provider. Index men had a greater mean number of social ties compared to their alters, contradicting the friendship paradox.[421]

Index men who have sex with men social ties

I detailed the self-reported social ties of index men who have sex with men (see Figure 1). All index men who have sex with men who reported ≥four social ties had disclosed their sexual behavior to their family and/or healthcare provider. Based on this observation, a larger self-reported social network may be positively related to sexual behavior disclosure.

Index men who have sex with men HIV self-testing kit distribution characteristics

Index men who have sex with men who disclosed their sexual behavior to their family or healthcare provider were 259% (adjusted odds ratio=3.59, 95%CI= 2.40, 4.78, p<.001) or 33% (adjusted odds ratio=1.33, 95%CI= 0.20, 2.45, p=.021) more likely to have alters upload completed test results, respectively (see Table 2). Index men who have sex with men who disclosed their sexual behavior to their family were more likely to request (adjusted incident rate ratio=1.46, 95%CI= 1.18, 1.73) a larger number of HIV self-testing kits (see Table 3). Similarly, index men who disclosed their sexual behavior to their family (adjusted incident rate ratio=2.87, 95%CI= 2.13, 3.61, p<.001) or healthcare provider (adjusted incident rate ratio=1.33, 95%CI= 0.54, 2.13, p=.001) were more likely to yield an increase in number of test results successfully uploaded by alters.

Discussion

I found that index men who have sex with men who disclosed sexual behavior tended to request more HIV self-testing kits and yield an increase in completed tests by alters. Previous work on HIV self-testing kit distribution applied social network techniques to improve kit uptake,[422] but there is limited empirical research on selecting index men who have sex with men to optimize testing coverage. The strength of this study is that I measured the actual number of HIV self-testing kits collected by index men who have sex with men and alters' submitted test results, instead of relying on self-report. Such outcome measurement is key to demonstrating the importance of selecting index participants who have disclosed their men who have sex with men sexual behavior, thus optimizing interventions.

Men who have sex with men who disclosed their sexual behavior tended to request multiple HIV self-testing kits. In the United States and China, men who have sex with men disclosure was associated with increased HIV testing.[367,423] While studies related disclosure to increased HIV testing, there is limited research around behavior disclosure and HIV self-testing kit request. Findings indicated that index men who have sex with men who had disclosed their sexual behavior tended to have a larger social network,[337] possibly explaining why they requested more kits.

men who have sex with men who disclosed sexual behavior were more likely to have alters upload completed tests. As above, United States and China research indicated that disclosure was related to increased HIV testing,[367,423] but there was limited work on behavior disclosure and alters completing tests. It may be that men who have sex with men who had disclosed sexual behavior sought those who had not disclosed their sexual behavior, to provide support,[424] perhaps influencing alters to upload completed tests.

A few index men who have sex with men were responsible for most alters' completed tests. Similar research among United States men who have sex with men indicated that some men who have sex with men reached most of the alters for HIV testing.[425] Among Chinese men who have sex with men, most alters were reached by a handful of index men who have sex with men.[426] I provide further insight around social network interventions in LMICs, indicating that such interventions may need to be designed around a select group of index participants to optimize testing coverage.

To optimize testing coverage within HIV testing social network interventions, I suggest that men who have sex with men who have disclosed their sexual behavior be selected as index

participants, as they may obtain more HIV self-testing kits and result in more completed tests by alters. Future work can expand on the use of other characteristics to improve upon social network-based HIV testing interventions. On the policy arc, reducing the stigma around sexual behavior disclosure in China[427] may aid overall HIV self-testing use rates.

Limitations

I did not ask participants the reasons for sexual behavior disclosure and future research can detail underlying factors. Data was collected at sites catered to men who have sex with men sexually transmitted infection testing. Such site selection may have limited the sample to men who have sex with men connected with community-based organizations and perhaps more likely to engage in sexual behavior disclosure, as indicated by the sample's greater levels of sexual behavior disclosure to healthcare providers, compared to past research (16.3%).[366] The high rate of missing data may have biased the results, and future research can ensure a higher response rate using techniques such as emailing follow-ups and a providing a larger cash incentive.

Conclusions

Index men who have sex with men who disclosed sexual behavior tended to request more HIV self-testing kits. Similarly, index men who disclosed their sexual behavior tended to yield an increase in number of test results successfully uploaded by alters. Findings have implications for the development of social network-based interventions for key populations.

Conclusion: Chapter Two

I first described factors associated with contribution amounts in a gonorrhea and chlamydia testing program for men who have sex with men. Expression of altruism may be linked to certain sexual behaviors and can promote contributions toward public health initiatives especially in stigmatized settings. I then detailed the association between men who have sex with men community-centric behaviors and contribution towards another's sexually transmitted infection testing cost. I found that increased support for community-centric behaviors was associated with greater pay-it-forward contribution in the sexually transmitted infection testing environment. I suggested that community-centric behaviors may be associated with a reduction in testing service cost that would otherwise be associated with fees. I then evaluated whether men who have sex with men selected a sexually transmitted infection test (urethral vs rectal) appropriate for their sexual behavior (insertive and/or receptive role in anal sex). I proposed that not disclosing sexual identity to treatment providers may lead to missed diagnoses and under-reporting of men who have sex with men rectal sexually transmitted infections. I also detailed the correlates of antisocial behavior on the world's largest gay dating app among Chinese men who have sex with men. I suggested that age, condom use, and number of social ties may be associated with antisocial behavior, with implications for the design of online sexual health interventions. Finally, I assessed if same-sex sexual behavior disclosure of Chinese men who have sex with men was related to number of HIV self-testing kits requested, and number of test results successfully uploaded by alters in a network-based HIV self-testing intervention. Findings had implications for the development of network-based interventions for key populations.

Stigma is common among Chinese men who have sex with men,[428] often leading to reduced participation in HIV/AIDS and other sexually transmitted infection testing programs.[428] While stigma and other systemic factors reduce test uptake, findings seem to indicate that men who have sex with men do participate in testing and can aid peers in getting tested. Even in environments that are inimical to a men who have sex with men identity, men who have sex with men still seek testing and encourage others to do so. Such findings are encouraging on two fronts. Firstly, despite systemic factors eroding the agency that marginalized communities face, marginalized populations still find ways to mitigate poor health outcomes. Given the risk borne from an environment hostile toward men who have sex with men,[429] men engage in altruistic behaviors toward each other. Secondly, the cohesiveness and reacquiring of agency in the men who have sex with men environment could act as a platform for other marginalized communities. For example, almost half of United States HIV infections are concentrated in the Black community.[430] Black populations in the United States have faced poorer health outcomes[431] and discrimination,[432] but even in such environments, Black faith leaders may increase uptake of HIV prevention strategies.[433] Such strategies are relatively novel in Black communities and perhaps drawing lessons from the Chinese men who have sex with men environment could produce synergies that reduce risk and thus alleviate poor health outcomes in a range of marginalized communities.

Even in the Chinese men who have sex with men environment where being out can result in reduced wellbeing,[434] findings indicate that disclosure of sexual identity seems to improve sexually transmitted infection testing outcomes. These results suggest that a more supportive environment for Chinese men who have sex with men may relate to better health outcomes.

In addition, while the studies were conducted in men who have sex with men-friendly environments, there was stigma around certain men who have sex with men roles or identities. Thus, support is likely essential to men who have sex with men both in the broader public space and men who have sex with men-only environments. Destigmatization of men who have sex with men identities could thus facilitate the promotion of sexually transmitted infection testing and reduce risk and poor health outcomes.

Chapter 3: Social Support and Medication for Opioid Use Disorder

This chapter will detail a systematic review exploring how social support is associated with medication for opioid use disorder treatment outcomes. Through this chapter, I hope to provide insight on a key public health strategy in combating the opioid epidemic.[435,436]

The Role of Social Support on Treatment Outcomes regarding Medication for Opioid Use Disorder: A Systematic Review

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Introduction

Increasing access to medications for opioid use disorder is a key public health strategy in combating the opioid overdose epidemic.[435] Medication for opioid use disorder has several benefits such as decreases in mortality, increases in treatment adherence, decreases in heroin use, and augmented health, social and criminal justice.[437,438] World Health Organization recommendations indicate that access to medication for opioid use disorder is key to treatment for opioid use disorder.[439] Medication for opioid use disorder refers to several medications, but primarily opioid agonist medications, like methadone and buprenorphine, but also opioid-antagonist medications such as naltrexone.[440] Although medication for opioid use disorder models are the most efficacious evidence-based treatment for opioid use disorder,[441] there remains a high percentage of patients with unfavorable treatment outcomes.[442] Greater understanding of how social support functions with respect to medication for opioid use

disorder treatment outcomes may improve treatment outcomes. Social support are the kinds of support, such as assistance or help, that people receive from friends, family, peers and neighbors, paid or unpaid, in their social network.[443]

Although clinical delivery characteristics, baseline substance use behaviors, comorbid mental health or substance use disorders and patient demographics influence treatment outcomes,[444] less research has focused on how social support is associated with treatment outcomes. Novel treatment paradigms, such as open access models, have gone a long way in decreasing barriers to treatment and improving engagement, but there is still unexplained variability in patient engagement and therefore an opportunity for improvement.[445]

Observational and experimental studies have shown that phenomena as diverse as cooperation, obesity, drug use, smoking, alcohol use may be associated with social networks.[388,446] Thus, it seems highly likely that social support is significant in understanding patterns of substance use, help-seeking, and adherence. A previous systematic review detailed psycho-social interventions and medication for opioid use disorder,[447] but there is limited research around the role of social support on medication for opioid use disorder treatment outcomes.

The study objective was to review existing scientific evidence on the following research question: For medication for opioid use disorder patients (population), what influence does social support have on medication for opioid use disorder (intervention) treatment outcomes (outcome)? This systematic review sought to provide policymakers, administrators, practitioners, and researchers with a systematic and reproducible strategy to query the literature around the role of social support on medication for opioid use disorder treatment outcomes.

With a larger team, I reviewed evidence under two themes, derived from medication for opioid use disorder outcomes: Treatment retention/Adherence, Drug use/Abstinence. Within these themes, I divided studies by the following forms of social support: Family, Peer, Combined family, and peer, General.

Methods

I conformed to frameworks and standard tools of the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P)[448,449] and Synthesis without meta-analysis (SWiM) guidelines.[450] The protocol was pre-registered on PROSPERO (CRD42018095645) on May 24, 2018.

Search strategy

I searched online indexes, references in previous reviews/guidelines, and Clinicaltrials.gov. For more details on search strategy and inclusion/exclusion criteria, see Appendix.

Outcomes

Primary outcomes were 1) medication for opioid use disorder treatment outcomes e.g. Medication adherence, program retention; 2) opioid use, defined as the percentage of urine samples negative for opioids or self-reported drug use. Not all the studies included adhered to these definitions. There were variations and differing definitions for individual studies.

Data extraction, review methods, quality assessments and data synthesis

I utilized a standardized template to extract data from each study. I searched online indexes, references in previous reviews/guidelines, and Clinicaltrials.gov. In addition, I consulted content experts. I conducted a systematic review of the literature using the databases of PubMed, MEDLINE, Embase, PsycINFO and Sociological Abstracts (see Appendix for

search strategy). I searched literature from inception through Feb 2020. Studies written in English, conducted in humans, mentioned medication for opioid use disorder in the title or abstract, included social support were considered for inclusion. Additional studies were identified by scanning reference lists of previous literature reviews and other studies. To reduce publication bias, I included a broad range of studies. The ClinicalTrials.gov library was searched to identify potentially qualifying studies that have not led to published results. I obtained additional papers through consultation with experts and authors, targeted searches of thematic journals, technical reports, conference proceedings and national databases.

Specialist journals

Addiction, Addiction Research & Theory, Addictive Behaviors, American Journal of Addictions, Addiction Science and Clinical Practice, Drug and Alcohol Dependence, Drug and Alcohol review, Drugs: Education, Prevention and Policy, European Addiction Research, International Journal of Drug Policy, Journal of Addiction Medicine, Journal of Addiction and Offender Counselling, Journal of Alcohol and Drug Education, Journal of Drug Issues, International Journal of Mental Health and Addiction, Addictive Disorders and Their Treatment, Journal of Substance Abuse, Journal of Substance Abuse and Treatment, Journal

of Substance Use, Substance Abuse: Research and Treatment, Substance Abuse Treatment, Prevention and Policy and Substance Use & Misuse.

Inclusion/Exclusion criteria

I included studies that meet the following criteria:

Randomized controlled trials, quasi-experimental studies and observational studies published in peer-reviewed journals; other scientific publications (e.g. Scientific Monographs); non-peer reviewed journals and grey literature (technical reports, conference papers).

Participants sought treatment for opioid use or met criteria for opioid abuse, opioid dependence, or opioid use disorder.

One or more variants of medication for opioid use disorder are offered (e.g. Methadone, buprenorphine, naltrexone).

The study reported social support (e.g. Family/partner/friend/peer/neighbor support, social network interventions as interventions or as predictors for the outcome.

The study reported adherence to medication for opioid use disorder as an outcome e.g. Medication adherence, program retention. There will be no restrictions on study design, population, or comparator (if included). Studies excluded from review will be case reports, reviews, systematic literature reviews, qualitative studies, opinion pieces, editorials, comments, news articles, and letters.

Data extraction

I utilized a standardized template to extract data from each study. I extracted general information (e.g. Year, setting) and methods (e.g. Design, duration), variant of medication for

opioid use disorder (e.g. Methadone, buprenorphine, naltrexone), and results specific to each outcome (e.g. Treatment adherence, self-reported drug use, urine drug screen). Endnote, a bibliographic software, was used to store, organize and manage all references.[451] Covidence was used to manage the screening phases.[452]

Review methods, quality assessments and data synthesis

With collaborators, in groups of two, we conducted study selection. A standardized template was pre-piloted independently, in groups of two, all relevant data was extracted. We resolved disagreements in study selection and data extraction through discussion. A third author stepped in when necessary for a final arbitration of any disagreements that occurred. In groups of two, we independently evaluated quality assessments and outcomes for each study and reached consensus via discussion. When consensus was not reached, a third reviewer made final decisions. Quality assessments for experimental studies were conducted using criteria from the Cochrane Handbook and similarly described the quality of observational studies.[449]

I assessed possible bias arising from low or differential follow-up rates, as losses to follow-up may have more negative outcomes than included subjects. I considered potential bias in self-report data due to social acceptability. For experimental studies, assessment included level of randomization, rates of attrition in the experimental group, use of intention-to-treat analysis and how group-level baseline differences were dealt with. For observational studies, bias assessment centered on group similarity (e.g. Matching), selection-bias and baseline differences possibly influencing outcomes (e.g. Severity of dependence), and on analyses (e.g. Multivariate logistic regression) adjusting for pre-study group differences. I assessed risk of bias at the study

level or specific outcome level. I detailed whether biases were likely to exaggerate or under-estimate the reported treatment effect.

In non-randomized studies, systematic bias may occur between different strata of social support. This was a general problem with observational studies because parsing between causal relationships around social support and severity of treatment outcomes is complex. Inclusion of data from unpublished studies may reduce risk of publication bias. I used a structured narrative format to synthesize the literature, organized by research question and thematic focus. Within the social support themes, family social support refers to studies that incorporated patient's partner or other family members. Peer social support connotes studies that involved peers, friends, or other patients. Combined family and peer social support indicate studies that involve both family and peer social support. General social support refers to broad, non-specific social support .

Results

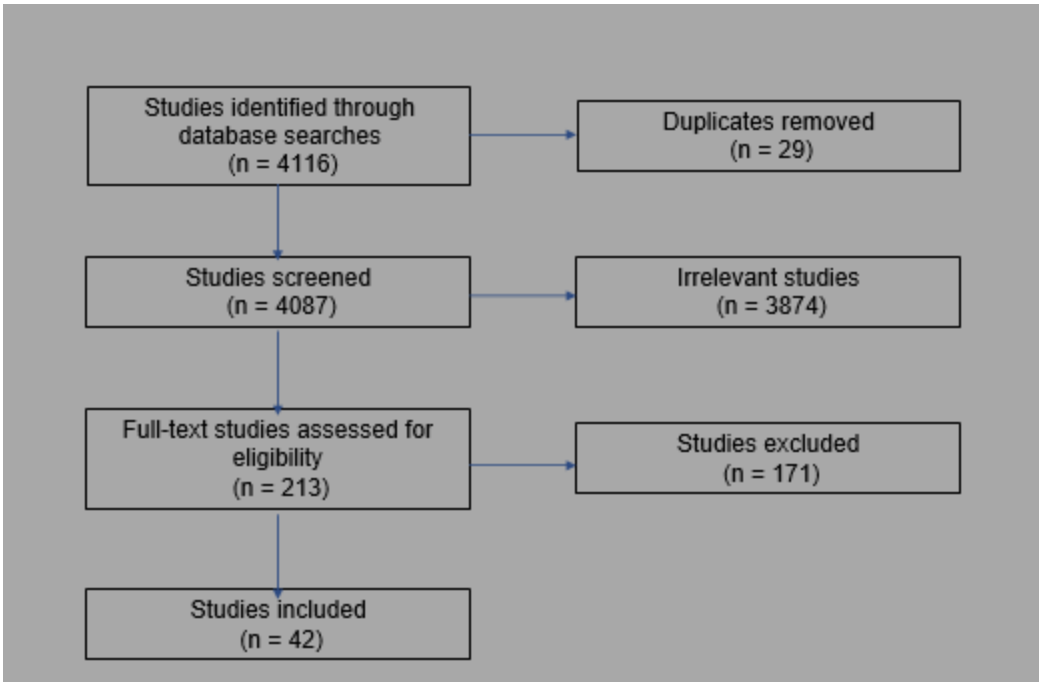


Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analsys (PRISMA) flow diagram of study selection

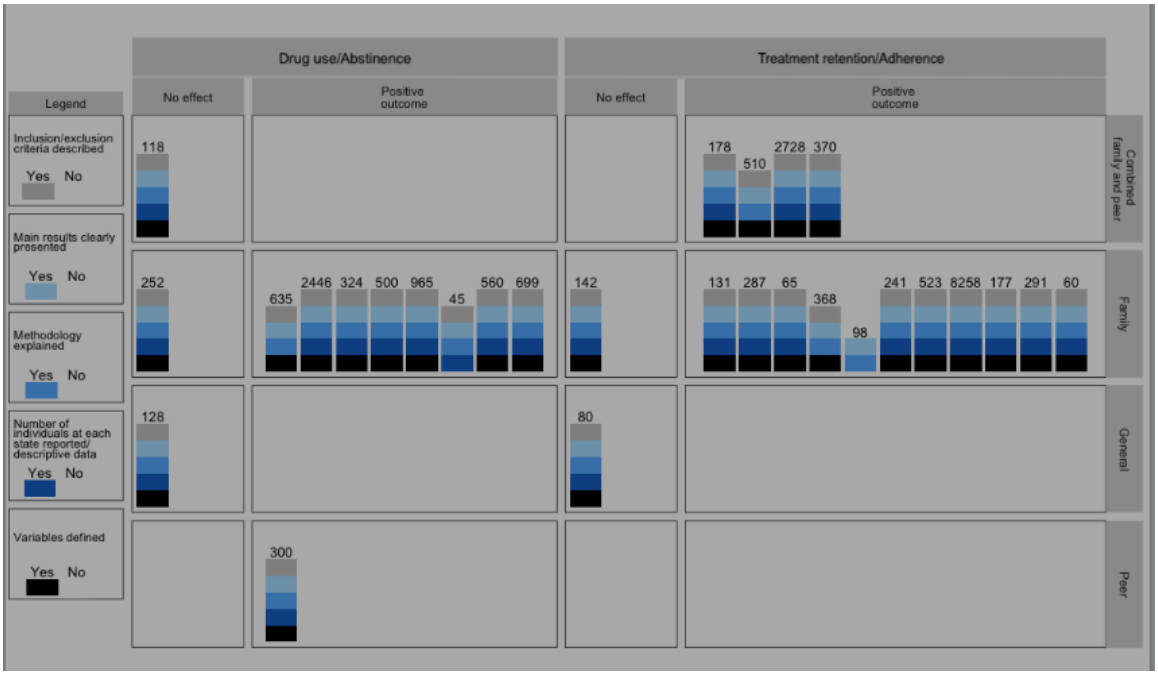


Figure 2. Evidence for observational studies regarding the role of social support on treatment outcomes for medication for opioid use disorder. A supermatrix covering all study outcome categories (columns) and forms of social support (rows) by change in the outcome of interest. Each study is represented by a stacked bar. The height of each component corresponds to a quality score representing the suitability of study design with respect to five quality measures: Description of inclusion/exclusion criteria, clear presentation of main results, explanation of methodology, presence of descriptive data and definition of variables. Each bar is annotated with the sample size.

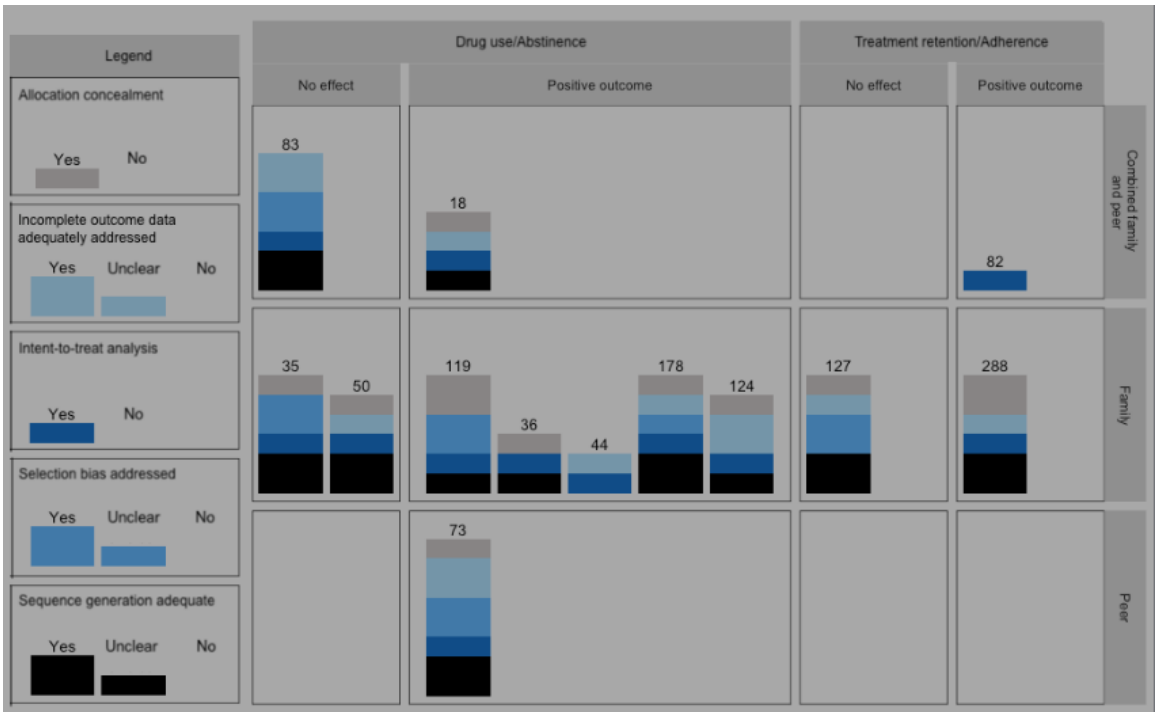


Figure 3. Evidence for experimental studies regarding the role of social support on treatment outcomes for medication for opioid use disorder. A supermatrix covering all study outcome categories (columns) and forms of social support (rows) by change in the outcome of interest. Each study is represented by a stacked bar. The height of each component corresponds to a quality score representing the suitability of study design with respect to five quality measures: Allocation concealment, addressing of incomplete outcome data, intent-to-treat analysis, addressing of selection bias and adequate sequence generation. Each bar is annotated with the sample size

Table 1: Quality of Experimental Studies						
Study	*Sequence generation adequate*	*Allocation concealment*	*Baseline data/ selection bias*	*Incomplete outcome data adequately addressed*	*Intent-to-treat analysis*	*Other limitations discussed by authors*
Fals-Stewart and O'Farrell, 2003	Unclear	Unclear	Groups comparable	Yes: Multiple imputation	No	Naltrexone pharmacotherapy intervention not fully standardized or manually driven. Complacence measured by self-reports. Key secondary outcomes (family relationship function and HIV-risk) behaviors not measured. Poor generalizability due to study sample characteristics and low rate of study participation.
Fals-Stewart et al., 2001	Unclear	Unclear	Groups comparable	No: 5 participants who did not complete treatment were excluded	No	Small sample size. Recall bias from strategy used for scheduling interviews with patients. Underreporting due to stigma and impact of opioid dependence. Bias from retrospective data collection, lack of blinding and the use of proxy informants.
Gu et al., 2013	Yes: Block randomization	Adequate: Central allocation	Groups comparable	Unclear: Attrition from methadone maintenance treatment service was	No	Small sample size. Sample overrepresented males. Assessment of family interaction processes limited by self-reporting measures.

				primary outcome		
Kidorf, 2018	Unclear	Unclear	Groups comparable	Unclear	No	Not indicated
Rothenberg et al., 2002	No randomization	None: No randomization	No randomization, selection bias possible	No: Participants who failed to complete treatment were removed from the trial	No	Inadequate accounting for potential change in family and peer relations as a result of treatment participation.
Yandoli et al., 2002	Unclear	Adequate: Central allocation	Groups comparable	Follow-up groups not comparable: High attrition at second follow up leading to differences between treatment groups.	Yes	Temporal ambiguity due to cross-sectional design. Recall bias and social desirability bias due to self-reporting. Underreporting of heroin use as the urine morphine test could only detect use in the past seven days rather than the 30 day period of self-reporting. Poor generalizability as drug-using patterns and economic situations differ across other provinces,
Carroll et al., 2001	Yes: Urn randomization program	Unclear	Yes: Groups differed significantly on baseline intensity of opioid use	Unclear: High attrition after detoxification	Yes	Retrospective study. Not randomized.

Catalano et al., 1997	Yes: Block randomization	Unclear	Groups comparable	No: Missing data mentioned, but method of addressing omitted	Yes	Results produced at post-test only show immediate effects after intervention, not overall efficacy. Bias from sole examination of parent differences post-test. Does not study molecular processes of family change that produce observed findings.
Catalano et al., 1999	Yes: Block randomization	Unclear	Groups comparable	Unclear	Unclear	Retrospective study. Follow-up data unavailable. Generalizability depends on the skills of NCM caring for patients.
Day et al., 2018	Yes: Independent randomization algorithm	None: Open trial	Groups comparable	Yes: High attrition in experimental group addressed with high recruitment in experimental group	Yes	Organizational barriers. Discontinuity in staff delivering treatment. Inadequate recruitment for outcome measurement.
Hojjat et al., 2017	Yes: Computerized random numbers	Unclear	Groups comparable	Unclear: No missing data reported	No	Patients in cohort experiments other interventions not captured by study.
Roozen et al., 2003	No randomization	None: No randomization	Groups comparable	Unclear	No	Not indicated

Scherbaum et al., 2005	Yes: Simple randomization via coin flip	Unclear	Groups comparable	Yes: Missing data addressed by following the last observation carried forward principle	Yes	Recall bias from a longer recall period during non-attendance episode. Reporting bias from self-reporting. Underreporting of attendance and non-attendance episodes due to inclusion of only the most recent pair, and exclusion of non-attendance duration. Poor generalizability due to study location limitations.

Table 2: Quality of Observational Studies						
Study	*Methodology explained*	*Inclusion/exclusion criteria described*	*Variables defined*	*Number of individuals at each state reported/descriptive data*	*Main results clearly presented*	*Limitations / bias discussed by authors*
Anton et al., 1981	Yes	Yes	Yes	Yes	Yes	Not a randomized study due to unavailability or unwillingness of patients to participate. Poor generalizability due to small proportion of addicts with families willing to participate in therapy sessions.
Cerovecki et al., 2013	Yes	Yes	Yes	Yes	Yes	Sample size of deceased group too small to determine association between mortality risk and other factors. Recall bias from interview scheduling. Underreporting due to the stigma of opioid dependence. Bias from retrospective data collection, lack of blinding and the use of proxy informants.
Chaudhry et al., 2012	Yes	Yes	Yes	Yes	Yes	Retrospective study. Small sample size.
Davila Torres, 2011	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to old age of study sample.

Day et al., 2013	Yes	Yes	Yes	Yes	Yes	Cross-sectional study design obscures causal inferences between network support factors and continuing drug use. Poor generalizability due to the exclusion of social support, environment, and developmental upbringing.
Feng et al., 2018	Yes	Yes	Yes	Yes	Yes	Baseline limited to making causal inferences due to randomized controlled trial source. Bias from self-reporting. Weak measure of family members' support on methadone maintenance treatment from a single-item question.
Gogineni et al., 2001	Yes	Yes	Yes	Yes	Yes	Not randomized. Results not confirmed by toxicology Cross-sectional study design obscures causal inference between continued injection and social relationships. Measured of important constructs based on single survey questions with limited response formats.
Grey et al., 1986	Yes	Yes	Yes	Yes	Yes	Small sample size without cross-validation.
Gu et al., 2014	Yes	Yes	Yes	Yes	Yes	Reporting bias from self-reporting. Failure to study all episodes of attendance and non-attendance. Inadequate recording of non-attendance period. Limited generalizability because participants were recruited from two methadone maintenance treatment clinics from one city.

Heinz et al., 2009	Yes	Yes	Yes	No	Yes	Reliance on one dichotomous measure as a proxy for relationship closeness. Lack of information on partner substance use. High selective attrition leading to more unhappily married individuals dropping out of treatment. Insufficient sample of married individuals for outcome comparison. Bias in lack of differentiation between single participants without a significant other and with a significant other but without a close and personal relationship.
Hikmayani et al., 2012	Yes	No	No	No	Yes	N/A
Hoang et al., 2015	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to selection bias in sample for wealthier, more motivated individuals with more stable families. Sample disproportionately male. Bias from loss to follow-up.
Hoang et al., 2018	Yes	Yes	Yes	Yes	Yes	Unverified information obtained from methadone maintenance treatment clinical records. Overestimation of concurrent heroin use due to high level of missing data. Biased from loss of patients to follow-up. Missing data limit analysis on association between psychiatric comorbidities and concurrent heroin use.

Lee et al., 2015	Yes	Yes	Yes	Yes	Yes	Temporal ambiguity from cross-sectional study design. Recall bias and social-desirability due to self-reporting. Inconsistency in drug use assessment tools affected verification of status. Self-reporting for the past 30 days and urine test (limited to past 7 days) gave inconsistent assessments. Poor generalizability because of specific geographic focus of study.
Lin et al., 2011	Yes	Yes	Yes	Yes	Yes	Cross-sectional study design limited causal inferences. Poor generalizability due to modesty of drug use in study sites.
Lin et al., 2013	Yes	Yes	Yes	No	Yes	Poor generalizability due to specificity of study group.
Lundgren et al., 2007	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to expansive insurance coverage and treatment programs of study location.
Monico et al., 2015	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to over-representation of African Americans with access to BMT clinics.
Mutasa, 2001	Yes	Yes	No	Yes	Yes	Statistical short-fall due to small sample numbers.

Nguyen et al., 2017	Yes	Yes	Yes	Yes	Yes	Recall bias due to self-reporting. Poor generalizability as sampling method was limited to mountainous settings. Cross-sectional design obscured causal relations between methadone maintenance treatment adherence and determinants.
Sarasvita et al., 2012	Yes	Yes	Yes	Yes	Yes	Invalid predictors of retention for longer studies due to six-month observation period.
Shen et al., 2018	Yes	Yes	Yes	Yes	Yes	Cross-sectional study design hinders causal inference. Social desirability and recall biases due to self-reporting. Underestimation of heroin use prevalence due to the 7-day detection limit of urine tests. Unrobust measure of social network functionality function due to assessment form a single question. Poor generalizability of the study due to location.
Smith, 2002	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to homogeneity of sample (same gender and shared military history). Fully male sample. Limited follow-up interviews due to compromised power to detect significant findings.
Tang, 2016	Yes	Yes	Yes	Yes	Yes	Social desirability bias through under-reporting drug use and availability of comprehensive psychological counseling to methadone maintenance treatment clients Poor generalizability due to study location.

Torrens et al., 1996	Yes	Yes	Yes	Yes	Yes	Retention rate in Spain influenced by long-term methadone policy. Poor generalizability of study to countries with greater experience with methadone maintenance.
Tran et al., 2018	Yes	Yes	Yes	No	Yes	Cross-sectional design obscured causal associations between adherence and its determinants. Recall bias from self-reporting. Sample size too small due to convenience sampling. Poor accuracy of medication adherence measurement due to self-reporting.
Wasserman et al., 2001	Yes	Yes	Yes	Yes	Yes	Short follow-up period limited detection of independent effects. Single instrument used to measure social support. Undercounting of social network participants due to restriction to household members only. Study cannot make causal inferences about social support and abstinence.
Yang et al., 2013	Yes	Yes	Yes	Yes	Yes	Poor generalizability due to limited geographic location of study participants.
Zhu et al., 2018	Yes	Yes	Yes	Yes	Yes	Recall bias due to self-reporting opioid use. Potential correlates associated with opioid abstinence not measured. Statistical significance of difference between abstinent and non-abstinent groups needs to be further ascertained

Table 3: Synthesis						
Outcome	*Significance of outcome*	*Study*	*Form of social support*	*medication for opioid use disorder drug used*	*Intervention (if any)*	*Possible impact of bias on treatment effect, if any (understate, exaggerate, no effect, unclear)*
Drug use/Abstinence	Positive outcome at P < 0.05	Zhu et al., 2018	Family	Buprenorphine, Methadone	Methadone treatment vs. Buprenorphine/Naloxone	Exaggerate
		Shen et al., 2018	Family	Methadone		Unclear
		Kidorf, 2018	Combined family and peer	Methadone		Unclear
		Hoang et al., 2018	Family	Methadone		
		Feng et al., 2018	Family	Methadone		
		Monico et al., 2015	Peer	Buprenorphine		
		Hoang et al., 2015	Family	Methadone		
		Lin et al., 2011	Family	Methadone		
		Heinz et al., 2009	Family	Methadone		
		Scherbaum et al., 2005	Peer	Methadone	Methadone treatment vs. Psychotherapy + Methadone treatment	Exaggerate

		Roozen et al., 2003	Family	Naltrexone	Community reinforcement approach + Naltrexone therapy	Unclear
		Fals-Stewart and O'Farrell, 2003	Family	Naltrexone	Behavioral family counseling + Individual naltrexone treatment vs Individual-based naltrexone treatment	Unclear
		Yandoli et al., 2002	Family	Methadone	Family therapy + SCT vs "Low contact" + SCT vs Standard clinic treatment (SCT)	Exaggerate
		Mutasa, 2001	Family	Methadone		
		Fals-Stewart et al., 2001	Family	Methadone	Individual counseling + Methadone treatment vs. Couples therapy + Individual counseling + Methadone treatment	Exaggerate
		Catalano et al., 1999	Family	Methadone	Focus on families	Unclear
	No effect	Day et al., 2018	Combined family and peer	Methadone	Treatment as usual vs. Social behavior and network therapy	Understate

		Hojjat et al., 2016	Family	Methadone	Group family training + Methadone therapy vs. Methadone therapy	Unclear
		Day et al., 2013	Combined family and peer	Buprenorphine, Methadone	Network drug use + General support	Unclear
		Wasserman et al., 2000	General	Methadone		
		Gogineni et al., 2000	Family	Methadone		
		Catalano et al., 1997	Family	Methadone	Standard methadone treatment vs. Standard methadone treatment + Supplemental parenting program	Unclear
Treatment Retention/Adherence	Positive outcome at $P < 0.05$	Tran et al., 2018	Combined family and peer	Methadone		
		Nguyen et al., 2017	Family	Methadone		
		Tang, 2016	Family	Methadone		
		Gu et al., 2014	Family	Methadone		
		Yang et al., 2013	Combined family and peer	Methadone		

		Gu et al., 2013	Family	Methadone	Individual + Family-based counseling	Exaggerate
		Cerovecki et al., 2013	Family	Methadone		
		Sarasvita et al., 2012	Combined family and peer	Methadone		
		Hikmayani et al., 2012	Family	Methadone		
		Lundgren et al., 2007	Family	Methadone		
		Rothenberg et al., 2002	Combined family and peer	Naltrexone	Behavioral naltrexone therapy	Unclear
		Lin et al., 2013	Family	Methadone		
		Lee et al., 2015	Family	Methadone		
		Davila Torres, 2011	Family	Methadone		
		Torrens et al., 1996	Combined family and peer	Methadone		

		Grey et al., 1986	Family	Naltrexone and Methadone		
		Anton et al., 1981	Family	Naltrexone		
	No effect	Chaudhry et al., 2011	Family	Naltrexone		
		Smith, 2002	General	Methadone		
		Carroll et al., 2000	Family	Naltrexone	Standard naltrexone treatment vs. Naltrexone treatment + CM vs. Naltrexone treatment + CM + Significant other involvement	Unclear

Included studies

Results from the study selection process are indicated in Figure 1 and general study characteristics displayed in the Appendix. Systematic searches yielded 4116 papers imported for screening, with 4087 studies screened for review (29 duplicates, see Figure 1). Screening yielded 213 articles for full-text review by two independent reviewers. Forty-two studies were deemed relevant to the review, summarized in Table 1. Thirteen were experimental studies, 29 were observational studies. The United States (18) and China (seven) were the most represented nations. Treatment and comparison groups were all drawn from opioid-dependent populations. Thirty interventions involved maintenance on methadone, six involved naltrexone, three involved methadone or buprenorphine, one involved methadone or LAAM (levo-alpha-acetyl-methadol), one involved naltrexone and methadone combination therapy, and one involved just buprenorphine. Tables 1 and 2 indicate the quality of experimental and observational studies.

Quality assessments

Tables 1 and 2 indicate the quality of experimental and observational studies. For experimental studies, allocation concealment was rarely reported and its impact on bias was not clear. The quality ratings for observational studies were overall high. I indicated relevant evidence for observational (see Fig 2) and experimental studies (see Fig 3) across treatment retention/adherence and drug use/abstinence outcomes, for each variety of social support with a harvest plot.[453] Twenty four observational studies met all five criteria.[454–476] Four observational studies met four criteria.[466,477–479] Observational studies on treatment retention/adherence, compared to drug use/abstinence, were more likely to fulfil the criteria

for quality of execution, with fourteen treatment retention/adherence studies meeting all five criteria.[464–476,480] No experimental studies met all five criteria. Two experimental studies met four criteria, both of which addressed drug use/abstinence.[481,482] The remaining studies in this review met between zero and three criteria.

Treatment retention/adherence

Twenty studies reported treatment retention/adherence as a medication for opioid use disorder outcome. Three were experimental[483–485] and 17 were observational.[464–476,479,480,486,487] Seventeen studies indicated that social support was related with improved medication for opioid use disorder treatment retention/adherence.[464–467,469–475,480,484–487] There was one randomized controlled trial which improved treatment retention/adherence.[484] Most statistically significant results involved family social support , with a few studies focused on combined family and peer social support . There was a single study on general social support with statistically significant results and no studies on peer social support that demonstrated statistically significant results.

Family social support

Eleven of 14 studies exploring family social support within the treatment retention/adherence outcome demonstrated significant improvements in treatment retention/adherence[467,470–475,480,484,486,487] and three had no significant change.[468,469,483] Improvements in treatment outcome were found in both experimental[467,484] and observational studies.[470–475,480,486,487] In one of the experimental studies, differences between control and treatment groups were large.[484] The study reported lower estimated probability of attrition at Month 12 [0.35 (control) vs. 0.55 (treatment)], higher median number of days of attendance [Month 6: 147 vs. 91 days; end-

date: 225 vs. 142 days].[484] The researchers evaluated the relative efficacy of a combination of a psycho-social intervention and standard of care medication for opioid use disorder versus standard of care on methadone attrition and treatment attendance. Family members provided support (e.g. Recognizing participant improvement in daily life after starting medication for opioid use disorder) during the family-centric sessions of the interventions. In the other experimental study,[467] some participants received multiple family therapy and the standard therapy, with the rest only receiving the standard therapy which included counseling, psychotherapy, and outreach. Multiple family therapy sought to build and strengthen family ties, support parents and partners in monitoring patient behavior, among other goals. For the observational studies, living with one's children, good family relationships and higher levels of perceived family support were associated with improved medication for opioid use disorder outcomes.[473–475] Conversely, absence of family support and living in an unstable relationship were related to reduced medication for opioid use disorder outcomes.[480,486]

Combined family and peer social support

All five studies exploring combined family and peer social support within the treatment retention/adherence outcome indicated significant outcomes.[464–466,479,485] Improvements in treatment outcome were found in one experimental study[485] and four observational studies.[464–466,479] The experimental study, applying behavioral naltrexone therapy, reported a positive correlation between length of time in treatment, and adherence and opiate-free urine samples.[485] Behavioral Naltrexone Therapy was delivered over a six-month period in weekly and network therapy sessions, comprised of Relapse Prevention, Community Reinforcement Approach and Network Therapy. For the observational studies, positive family relationships,

no communication with former drug-taking peers and disclosing one's health issues to friends were associated with retention.[466,479]

General social support

Only one study explored general social support .[476] The results were statistically non-significant.

Drug use/abstinence

Twenty-two studies reported drug use/abstinence as a medication for opioid use disorder outcome. Ten were experimental[481,482,488–494] and 12 were observational.[454–463,477,478] Multiple studies indicated that social support was related with reduced drug use/abstinence.[455,457–461,463,477,478,481,490–495] Several randomized controlled trials demonstrated the role of social support in decreasing drug use/abstinence.[481,490–493,495] The most detailed variant was family social support , with a few studies exploring combined family and peer social support , peer social support and general social support .

Family social support

Thirteen of 16 studies exploring family social support within the drug use/abstinence outcome demonstrated significant improvements in treatment retention/adherence.[455,457–461,477,478,490,491,493,495,496] Improvements in outcome were indicated in experimental studies[490,491,493,495,496] and observational studies.[455,457–461,477,478] Two of the experimental studies reported large differences between control and treatment groups. The first study[493] reported a higher proportion of drug-free patients six and twelve months in both intervention groups (22% and 15% for family therapy) compared to the standard treatment group (5% and 0%) and low contact group (8% at both marks). The researchers evaluated the efficacy of family

therapy compared to a ``low contact'' intervention and standard psychotherapy. All groups also received medication for opioid use disorder. The family intervention comprised of up to sixteen sessions and involved the patient's family or partner. Sessions were based on the discussion of family relationships and medication for opioid use disorder. The low contact treatment comprised of monthly, standardized 30-minute interviews for up to 12 months. Standard treatment involved supportive counselling and the delivery of information related to managing drug use. In the other experimental study,[495] patients were assigned to a supplemented medication for opioid use disorder treatment with 33 sessions of family training and 9 months of home-based case management, or the control group with standard medication for opioid use disorder. Family training focused on relapse prevention and coping, anger management and child development. For the observational studies, increased social support[461] and having a spouse or child in one's social network[460,497] were associated with reduced drug use and abstinence. Conversely, factors such as family conflict,[478] interactions with drug-using friends[455,478] and low family support[487] were associated with poorer treatment outcomes.

Peer social support

There were two studies, both significant, which explored peer social support within the drug use/abstinence outcome.[463,481] In the experimental study based in Germany, participants were assigned to medication for opioid use disorder or medication for opioid use disorder and group psychotherapy. Patients in the psychotherapy group demonstrated less drug use than control subjects.[481] Psychotherapy centered on the patient's understanding of situations

predisposing drug use. In the observational study, narcotics anonymous meeting attendance in the past six months was associated with drug abstinence.[463]

General social support

A single study explored general social support within the drug use/abstinence outcome.[462] Results were non-significant.

Combined family and peer social support

Only one study that explored combined family and peer social support within the drug-use/abstinence outcome had results that were statistically significant.[498] The remaining two did not demonstrate significant results.[454,482] In the significant experimental study,[498] individuals who inject drugs were recruited from a community needle exchange group and a medication for opioid use disorder program. Patients attended a weekly community support group with a drug-free family or friend and participated in weekly community activities to expand drug-free social support. Results indicated reductions in heroin use (27 vs. 17 days/month), intravenous drug use (27 days vs. 20 days/month) and number of injections (123 vs. 48 injections/month).

Synthesis

Table 3 synthesizes the 42 studies per theme and outcome indicating positive treatment effects or no effect. Table 3 also indicates whether biases may have understated or over-reported treatment effects. Figure 4 displays the studies by social support variant and statistical significance. Evidence is not consistent for either outcome, although studies mostly support the conclusion that social support improves medication for opioid use disorder treatment outcomes. Table 3 also summarizes whether biases might understate or exaggerate treatment effects, if any. This information is derived from Table 1. For experimental studies, bias was

considered likely to understate positive outcomes in one study, to exaggerate in four and unclear in the remaining eight studies. The most common source of bias for experimental studies was the lack of intent-to-treat analysis and recall bias and reporting bias may also play a role.

Discussion

In this systematic review, I present a current and comprehensive synthesis of the published literature on the role of social support on medication for opioid use disorder treatment outcomes. I examined the effect of social support on two medication for opioid use disorder treatment outcomes: Treatment retention/adherence; Drug use/abstinence. I detailed several observational and experimental studies over a range of social support variants. Overall, social support is significantly associated with improved medication for opioid use disorder treatment outcomes. Quality of observational studies was overall high, but quality of experimental studies was much lower. A previous review explored psycho-social interventions and medication for opioid use disorder,[447] but there is limited work around social support on medication for opioid use disorder outcomes. I thus extend the literature by detailing the role of social support on medication for opioid use disorder outcomes, broadening the scope of social networks on health outcomes.

While studies indicated that social support was associated with improved treatment outcomes, there were several studies (21%) which did not indicate a significant relationship.[454,456,462,468,476,482,483,488,489] Given the large proportion of non-significant findings, more research is necessary to establish the relationship between social support and medication for opioid use disorder treatment outcomes. Comparing treatment outcomes, six out of 22

(28%) studies were not significant for drug use/abstinence vs three out of 20 (15%) for treatment retention/adherence. I was unable to conduct a meta-analysis due to variations within outcomes. Family social support was the most common variant of social support detailed across both outcomes. It is not clear why other forms of social support were not similarly studied, despite their likely importance. Compared to the control arms, the treatment arms for studies focused on family social support network tended to have large improvements in treatment outcome. Given the role of families in substance use outcomes,[499] further research can detail family social support on treatment outcomes.

Treatment retention/adherence

Several studies indicated that social support was associated with augmented medication for opioid use disorder treatment retention/adherence.[464–467,469–475,479,480,484–487] There was only a single randomized controlled trial which improved treatment retention/adherence.[484] Most studies with statistically significant results involved family social support , with a few studies centered on combined family and peer social support . There was a single study on general social support with statistically significant results and no studies on peer social support with statistically significant results. Given the relationship between families and medication for opioid use disorder treatment outcomes,[498,500] the focus on family social support and treatment outcomes is understandable. However, the number of studies detailing family social support and medication for opioid use disorder treatment retention is still scarce. Despite the substantial scholarship on peer effects and substance use,[501,502] there are no studies exploring peer social support on its own, and treatment retention/adherence. Thus, it is not clear if certain forms of social support are more effective at improving treatment retention/adherence

or there is reporting bias, or some other effect involved. Future studies can explore if certain variants of social support are more effective than others at improving medication for opioid use disorder treatment retention/adherence. Overall, social networks are associated with treatment retention/adherence.[464,503] Thus, social support interventions are a critical research gap that may improve treatment retention/adherence.

Some studies suggest that family social support is related to improved medication for opioid use disorder treatment retention/adherence.[467,484,486,487] The randomized controlled trial conducted by Gu et al. (2013) in China provides strong evidence in this regard.[484] However, there are only two experimental studies detailing family social support and treatment retention/adherence.[467,484] Evidence is clearly lacking around family social support interventions around treatment retention/adherence. As family-related factors are related to substance use outcomes,[499] studies on family social support and medication for opioid use disorder outcomes are a clear gap in the scholarship. A few studies suggest that combined family and peer social support were associated with improved medication for opioid use disorder treatment retention/adherence.[464–466,479,485] However, there was only one experimental study in this area[485] and a total of five studies. The United States-based experimental study detailed the use of significant other and peer support to improve naltrexone adherence.[485] As with family social support , research around the combined role of family and peer social support is limited within medication for opioid use disorder treatment retention/adherence. As a mix of family and peer social support are critical to medication for opioid use disorder treatment outcomes,[465] scholarship in this area is important. However, it is not clear if social support interventions that centers on either the family or peers are more effective than

interventions which have some combination of both. A single study detailed general social support on medication for opioid use disorder treatment retention/adherence.[476] This United States-based study detailed that the perception of or orientation toward non-specific social support did not contribute significantly to the predicted length of time in treatment. It is not clear if general social support affects medication for opioid use disorder treatment retention/adherence as evidence is lacking in this area. Most research on social networks and substance use tend to center on specific alters such as family members and peers,[456,504] but it may be possible that generalized social support has an effect on treatment outcomes. Future research can detail if general or more specific forms of social support make a greater difference to treatment retention/adherence.

Drug use/abstinence

There is evidence that social support was associated with drug use/abstinence as a medication for opioid use disorder outcome.[455,457–461,463,477,478,481,490–495] Several randomized controlled trials demonstrated the role of social support in increasing drug use/abstinence as a medication for opioid use disorder outcome.[481,490,491,493,495,496] The bulk of studies detailed family social support , with a few studies exploring combined family and peer social support , peer social support and general social support . Like the relationship between treatment retention/adherence and social support, I expected several studies focusing on family social support but noted the lack of studies on peer social support. Overall, the number of studies per variant of social support was limited, indicating a clear research gap.

Several studies indicated that family social support contributed to improved medication for opioid use disorder treatment outcomes around drug use/abstinence.[456,488,495] An randomized

controlled trial conducted in the Netherlands provides strong evidence in this regard.[496] However, there were only seven experimental studies in this area[455,457–461,477,478,496] and of these, two did not demonstrate significant results.[456,488] Evidence is limited and somewhat mixed around family social support and drug use/abstinence-related treatment outcomes, and there is a stark gap in the scholarship. Given the relationship between family social support and medication for opioid use disorder outcomes,[480,486] future research can detail if family social support consistently improves outcomes around drug use/abstinence. There were two observational studies which indicated that peer social support related to improved treatment outcomes around drug use/abstinence.[463,481] While there is some evidence around peer social support and treatment outcomes surrounding drug use/abstinence, literature is still scarce, indicative of a literature gap. The lack of research is surprising, given the broader literature on peer effects and substance use.[505,506] Three studies indicated that combined family and peer social support were associated with augmented treatment outcomes around drug use/abstinence.[454,482,494] Of these three, only one (an observational study) indicated significant results. As with treatment retention/adherence, it is not clear if combined family and peer social support is more effective at improving treatment outcomes, compared to interventions focused on peer or family social support. As peer and family social support , acting individually, have effects on treatment outcomes,[463,496] interventions combining peer and family social support may be more effective. There is a clear literature gap, with more studies, especially experimental research, needed in this area. There was a single, non-significant, observational study detailing general social support and treatment outcomes around drug use/abstinence.[462] While there is some research on more specific forms of social support on medication for opioid use disorder outcomes,[460,461,493] generic social support seems understudied. As with

treatment retention/adherence, it was not clear if general vs specific social support is more effective at improving treatment outcomes. There is an evident lack of research on general social support in this area.

Limitations

Most of the studies had key methodological concerns. I emphasized more robust study designs and assessed the probable impact of bias to compensate for methodological weaknesses. Possible sources of bias are: Group baseline differences; selection bias; attrition bias; differential rates of follow-up. Selection bias may exaggerate or under-report treatment effects. If rates of attrition are relatively high or greater in untreated groups, there may be a possibility that treatment effects are overestimated if participants lost to follow-up have greater negative outcomes. A few studies in this review conducted analysis to control for bias through multivariate analysis and/or comparison of losses to follow-up with those followed-up. Attempts to account for biases may not always be successful and I thus assessed the risk of biases (see Table 3), providing an assessment of probable impact of bias on various outcomes. Limitations also arose from differences in methods of reviewed studies, making it more complex to assess or synthesize all studies under the same rubric. The details provided on methods and analysis was highly varied, possibly leading to fluctuations in the confidence level of results.

While evidence was generally scarce within both outcomes and within individual variants of social support, some themes were severely understudied. For example, there was only a single (non-significant) study exploring general social support within drug use/abstinence treatment outcomes.[462] Thus, while I indicated that social support was associated with improved

medication for opioid use disorder treatment outcomes, I cannot say whether specific variants of social support were related to treatment outcomes. Moreover, there were no studies which detailed forms of social support apart from family, peer, combined family and peer, and general social support. For example, there seemed to be no research on social support from authority figures. The role of employer social support may be important to treatment outcomes given the role of workplace authority figures in the lives of medication for opioid use disorder patients.[507]

Conclusion

The main strength of the study is the quality assessment of the content and provision of broad summaries of the literature. I detailed the population, intervention and outcomes included, along with data extraction methods and search strategy. I also centered on the specific variants of social support on medication for opioid use disorder treatment outcomes. Although evidence is limited, social support likely improves a range of medication for opioid use disorder treatment outcomes. Interventions around social support could potentially augment medication for opioid use disorder treatment outcomes, possibly playing a role in mitigating the opioid epidemic. Some kinds of social support may be more efficacious than others in improving treatment outcomes, e.g. Family social support vs peer social support . Despite the variety of outcomes and social support, I suggest the key role of social support on broad medication for opioid use disorder outcomes.

Conclusion: Chapter Three

I indicated the results of a systematic review on the influence of social network interactions on medication for opioid use disorder treatment outcomes. I detailed literature on the role of family, peer, and general social support on medication for opioid use disorder treatment outcomes. Most studies, many of which were randomized controlled trials, indicated that social support may improve medication for opioid use disorder treatment outcomes. Given that evidence is still limited on the role of social support on medication for opioid use disorder treatment outcomes, I suggest future research centering on social support and integration of social support interventions into medication for opioid use disorder treatment programs to improve treatment outcomes.

Medication for opioid use disorder and opioid use disorder are heavily stigmatized, often reducing likelihood of seeking treatment.[136,508] Socioeconomic marginalization is associated with opioid use disorder,[509] with factors such as union decline associated with overdose rates.[510,511] Even with the marginalization and stigma associated with opioid use disorder, medication for opioid use disorder patients still seek treatment. This reclamation of agency draws parallels with previous chapters, where marginalized men who have sex with men seek testing at risk to themselves. However, even though medication for opioid use disorder patients overcome significant hurdles in seeking treatment, medication for opioid use disorder treatment outcomes can still be improved. While patients can overcome some aspects of marginalization and retain agency to enter treatment, the effects of disadvantage persist and affect treatment outcomes. Thus, echoing previous chapters, mitigating stigma and marginalization could facilitate improved wellbeing of opioid use disorder patients.

Conclusion

In the first chapter, I detailed a range of cannabis-centric studies. First, I detailed cannabis usage preferences among United States cannabis users. I put forth that frequent cannabis use may increase risk of health harms and highlighted the need to minimize problematic use. I also detailed if sociodemographic indicators were associated with increased likelihood for cannabis-related emergency department admissions in New York City. Results may suggest that cannabis use further burdens marginalized groups. I then investigated large cannabis firms' motivations for participating in the cannabis space. I suggested that policymakers be aware that non-profits and for-profits both seek to expand cannabis access and consider the groups as a unified whole.

With increasing proliferation of cannabis use, marginalized communities are likely to bear a greater burden of poor health outcomes. Some communities face a lack of agency through the processes of marginalization but still attempt to retain some level of agency by engaging in risk reduction practices, drawing parallels to the broad chapters of my thesis. Some large firms in the cannabis space are likely contributing to increases in cannabis use. However, all firms are not solely focused on increasing cannabis consumption. Some firms are cognizant about the demographic groups disproportionately affected by drug use and seek to use the cannabis industry to reduce risk and enhance agency for marginalized communities. Such firms are usually founded by individuals from marginalized communities.[512]

By virtue of retailing a stigmatized and federally illegal product, cannabis firms are marginalized from the broader firm space. Cannabis firms incur a range of costs due to federal illegality, such as increased banking fees and greater premiums from service providers. Firms attempting

to recoup these costs may provide poor occupational environments and employment benefits for their employees, worsening marginalization of entry-level workers.[513,514] Thus, marginalization on the firm level may be transferred to marginalization faced by employees, possibly resulting in reduced health outcomes. My results suggest that some firms are aware of the negative effects the cannabis industry can have and thus strive toward equitable working conditions and health outcomes. Workers in the cannabis space have also attempted to organize for improved conditions, augmenting health outcomes and mitigating risk.[515] In line with the broader themes of this document, workers are marginalized in the cannabis space, but seek agency by organizing and reducing marginalization and health risks.

In the second chapter I explored sexually transmitted infection testing in the Chinese men who have sex with men environment. I first detailed factors associated with sexually transmitted infection testing. Expressions of altruism may promote contributions toward public health initiatives in marginalized communities. In the same vein, I detailed the association between men who have sex with men community-centric behaviors and contributions toward others' sexually transmitted infection testing. I proposed that community-oriented behaviors may be related with a reduction in testing service costs. I also evaluated whether men who have sex with men selected a sexually transmitted infection test appropriate for their sexual behavior. I suggested that disclosing sexual identity to treatment providers can improve men who have sex with men sexually transmitted infection prevalence estimates. I also detailed the correlates of antisocial behavior on the world's largest gay dating app among Chinese men who have sex with men. I suggested that age, condom use, and number of social ties may be associated with antisocial behavior, with implications for the

design of online sexual health interventions. Finally, I assessed if same-sex sexual behavior disclosure of Chinese men who have sex with men was related to number of HIV self-testing kits requested, and number of test results successfully uploaded by alters in a network-based HIV self-testing intervention. Findings had implications for the development of network-based interventions for key populations.

China has the world's largest men who have sex with men population. Despite repeals against legal persecution, discrimination against the broader lesbian, gay, bisexual, and transgender population still exists.[57] Lesbian, gay, bisexual, and transgender discrimination is a barrier to preventing sexually transmitted infections, such as HIV.[58] A recent survey led by the UN Development Program and the Beijing lesbian, gay, bisexual, and transgender Center indicated that 11% of heterosexual participants were unable to accept lesbian, gay, bisexual, and transgender family members and more than 10% of respondents did not believe that lesbian, gay, bisexual, and transgender individuals should be allowed to raise children.[56] Such sentiments and the associated legislation results in marginalization and stigma, wresting agency from the lesbian, gay, bisexual, and transgender community. Even within such sites of limited agency, several Chinese organizations have campaigned for lesbian, gay, bisexual, and transgender rights, increasing the social visibility of the community, and reducing discrimination. For example, in 2018, a group of Chinese artists protested against sexual orientation conversion efforts.[60,516] Several lesbian, gay, bisexual, and transgender groups in major Chinese cities launched a campaign to support Li Yinhe, a sociologist pushing for a same-sex marriage law in China.[517,518] In 2008 and 2009, a group of Beijing lesbian, gay, bisexual, and transgender activists had a Valentine's Day same-sex marriage event.[517] More

recently in 2013, some Chinese lesbian, gay, bisexual, and transgender began seeking out lawyers and legal professionals who would be willing to represent clients in China's first series of lesbian, gay, bisexual, and transgender rights litigation.[519] Similarly, my results suggest that while men who have sex with men are marginalized in China, men who have sex with men still seek sexually transmitted infection testing and are willing to contribute anonymously to other men who have sex with men. Although men who have sex with men often face marginalization and incur poorer health outcomes, many men who have sex with men work with their communities to improve overall wellbeing and reduce health risks.

In the final chapter I detailed those various forms of social support may influence medication for opioid use disorder treatment outcomes. Failure to implement successful social support programs within medication for opioid use disorder treatment settings may represent an important missed opportunity to engage patients at risk of treatment failure.

Illicit opioid use and poor medication for opioid use disorder treatment outcomes may be related to marginalization and loss of agency.[508,510,511] While opioid use disorder can affect anyone, the opioid crisis has predominantly affected those from the most marginalized areas of the United States.[520] Opioid use disorder rates among people who earn less than $20000 a year are three times higher than those who make more than $50000.[521] In 2016, individuals under the poverty line were more likely to have misused opioids and have an opioid use disorder in the past year compared to individuals above the poverty level.[522] Increases in county unemployment rates predicted increases in opioid death rates.[523] Per-capita opioid-related hospital stays and emergency department visits are higher and have increased at higher rates in low-income communities compared to high-income communities.[524] Opioid prescriptions

are also negatively correlated with labor force participation.[525] In addition, there is a negative relationship between prescriptions and economic opportunity, where counties with worse economic prospects having a greater prevalence of substance use and opioid prescriptions.[522] Those on Medicaid are more likely to be prescribed opioids, at higher doses and longer durations, possibly resulting in greater risk of dependence.[526–528] Those with mental illness and childhood trauma are overrepresented among people prescribed opioids and overdoses.[529–532] Medicaid recipients are also less likely to have access to medication for opioid use disorder. There are a range of barriers that further marginalize medication for opioid use disorder patients. Some communities oppose medication for opioid use disorder treatment in their neighborhoods and officials have attempted to make medication for opioid use disorder sites illegal in some areas.[533]

The increased overdose mortality among middle-aged white Americans may be due to increasing economic challenges and psychological stresses.[534] Environmental and social stresses likely contribute to opioid use disorder. Solitary animals demonstrate greater opioid self-administration compared to animals housed together.[535,536] Socially dominant male monkeys demonstrate less cocaine self-administration compared to their lower-ranked or solitary counterparts.[537] In addition, compared to rodents housed in environments with multiple opportunities for play, exploration and exercise, rodents housed in environments with fewer opportunities for play, exploration and exercise are more sensitive to the reward effects of heroin.[538] While animal models may be highly simplified, they may indicate that marginalization and loss of agency within human environments may increase risk for substance use.[520]

Various forms of marginalization appear related to opioid use disorder and further impact opioid use disorder treatment outcomes. Marginalization increases the health risks of opioid use disorder patients and repudiates agency. However, even within this sphere of limited agency, individuals with opioid use disorder and the broader people who use drugs community engage in various activities to reduce risk and retain some agency. Through needle exchanges and similar environments, some opioid use disorder patients build a sense of community.[539] Such community-based initiatives have resulted in people who use drugs unions that seek to alleviate stigma around people who use drugs and opioid use disorder.[539] Even within sites of marginalization and health risks, marginalized individuals still seek to reduce risk and preserve some agency. On a broader scale, there are governmental initiatives that seek to mediate risk and marginalization for medication for opioid use disorder patients. Significant federal funds have been allocated to improving access to medication for opioid use disorder in rural and underserved areas.[522] Similarly, grants have been allocated to identify child welfare practices which may mitigate the impact of parental substance use, and interventions are ongoing to increase economic self-sufficiency of opioid use disorder patients eligible for the Temporary Assistance for Needy Families program.[522] My findings in the opioid space indicate that social support provided by family and peers can improve upon treatment outcomes and that medication for opioid use disorder patients from marginalized communities face lowered levels of social support . Despite the stigma against medication for opioid use disorder and opioid use disorder, patients seek to reduce risk and retain agency, drawing parallels to the broad themes of my thesis.

In previous chapters, I indicated that marginalization could worsen health outcomes in the Chinese men who have sex with men community. Similarly, compared to heterosexual communities, United States lesbian, gay, bisexual, and transgender communities were more likely to have misused prescription opioids and have opioid use disorder.[529] Lesbian, gay, bisexual, and transgender communities live with high levels of discrimination and stigma, which can disrupt one's psychological processes. Such stigma can become internalized and some may turn to opioids to cope.[540,541] Lesbian, gay, bisexual, and transgender individuals may also be exposed to opioids in medical settings at disproportionate rates, compared to heterosexuals.[542] For example, opioid therapy is often prescribed to transgender people post-surgery, who also report increased prevalence of chronic pain.[543,544] Opioid use may also have deleterious effects in a sexual context. Non-medical opioid use among men who have sex with men is associated with condomless sexual intercourse and other possibly less safe sexual behaviors.[545,546] Medication for opioid use disorder may have unwanted interactions with antiretroviral therapy taken by those living with HIV.[547] Fear of unwanted side effects may deter lesbian, gay, bisexual, and transgender individuals from engaging in medication for opioid use disorder. Opioid use disorder can also co-occur with posttraumatic stress disorder.[548] Post-traumatic stress disorder in lesbian, gay, bisexual, and transgender populations can arise from sexual violence and hate crimes. The themes I have indicated thus do not exist mutually exclusive of each other but overlap to possibly worsen marginalization. A men who have sex with men identity can worsen marginalization and as indicated, opioid use disorder can intersect with marginalized sexual identities to widen inequality. While marginalization strips agency from men who have sex with men medication for opioid use disorder patients, such individuals still manage to retain some level of agency. Men who have

sex with men have organized their own Narcotics Anonymous groups to mitigate the effects of opioid use disorder.[549,550] Thus, even with the twin effects of marginalization around opioid use disorder and a men who have sex with men identity, patients still seek to reduce risk around their health behaviors.

I indicated how marginalized communities improve their health outcomes and retain agency through mechanisms such as solidarity and social support. I detail a set of specific cases where marginalized communities can benefit from a sense of togetherness, viewed as positive by broader society. When this argument is extended to other marginalized communities, not all cases result in positive outcomes. There are many marginalized communities where increases in solidarity and agency are a concern. For example, white nationalist groups consider themselves marginalized[551] and solidarity in such groups often troubles law enforcement agencies. Some white Americans feel victimized and stigmatized because of their ethnicity. They perceive traditionally marginalized ethnic groups as being the oppressors.[551] Another example is the *pro-ana* (pro-anorexia) community. Anorexia is an eating disorder and patients may benefit from social support .[552] However, some online communities of anorexia patients reinforce social dynamics that encourage anorexia instead of promoting recovery.[553] Pro-ana communities exchange tips on how to maintain potentially harmful behaviors.[554,555] Patients engaging in such communities face reduced self-esteem and increased negative affect in the short and long term.[556,557] In opposition to the pro-ana community, there exists the *Fat Acceptance Movement*. The movement challenges claims about the relationship between body weight and health, and promotes respect for those who are overweight.[558] Women in this community gain self-acceptance and emancipation from dieting, among other benefits.[558–560]

However, the fat acceptance movement has been accused of promoting obesity and weight gain.[561,562] *Gang Stalking* is another example parallel to the pro-ana community. Gang Stalking is a perceived form of systematic intimidation perpetuated by an individual or organization, usually identified as the government or a large corporation.[563] Individuals who believe they are gang stalked call themselves *Targeted Individuals* or TIs. Such individuals who set out to find out more about Gang Stalking on the internet are informed that they are neither crazy nor delusional.[563,564] Those who deny Gang Stalking as a real phenomenon are labelled close-minded or naïve, creating a closed echo chamber.[565] Much like the pro-ana community, increased participation in Gang Stalking communities may result in reduced treatment seeking for a medical condition, in this case Delusional Disorder.[563,566]

Given the amorphous nature of marginalization, not all marginalized communities are constant and stable. For example, as United States HIV rates of new infections decrease,[567] communities of individuals with HIV will similarly decrease. Existing communities of those with HIV may thus face reduced levels of social support which could further exacerbate marginalization. Similarly, as smoking cessation behaviors spread through a social network, smokers become increasingly forced to the peripheries of the network.[384] Thus, medical advances and similar phenomena can possibly increase marginalization in communities exemplifying strong solidarity.

Unlike the above example in the smoking case, marginalized behavior may not always be at the peripheries of a network. For example, risk of current smoking was greater among popular students in schools with high smoking prevalence than among popular students in schools with low smoking prevalence.[568,569] Smoking also enhanced popularity in adolescent social

networks.[570] Similarly, perceived popularity in adolescent peer groups predicted bullying[571] and powerful bullies were perceived to be more popular and better liked.[572] In line with the perceived social status of marginalized behaviors, lower status individuals may seek to engage in such behaviors. In the smoking case, there may be an ebb and flow around marginalization. Marginalized youth may pick up smoking to attain status in a social network, but later be marginalized when members of their social network give up smoking.

Apart from seeking social status, there are other reasons why individuals would engage in marginalized behaviors. Given the sense of support and belonging found within certain marginalized communities, it is possible that non-marginalized individuals may seek to somehow *marginalize* themselves to attain some sense of community. *Bug chasing*, where physiologically healthy, HIV-negative men who have sex with men seek seroconversion by engaging in unprotected anal intercourse with HIV-positive men who have sex with men fits this description.[573] Bug chasers report gaining a HIV infection as a rite of passage and initiation into a community from which one can never be exiled.[574] Some HIV negative men who have sex with men feel they have been cast aside as potential sexual partners and seek a newly renewed sense of community.[575–577] For bug chasers, the HIV-positive men who have sex with men population may appear to have significantly stronger bonds of community and cohesiveness compared to the broader men who have sex with men population.[578] Some HIV-positive men will refuse to have unprotected intercourse with bug chasers and only seek out other HIV-positive men who have sex with men.[574] This may create a closed community of HIV-positive men who have sex with men, who share a sense of camaraderie and kinship, further creating a sense of alienation among bug chasers.

As with the above cases, how does one decide when to encourage agency within marginalized communities? Perhaps we can foster agency in communities that face poor health outcomes. Such definitions would include communities described in the empirical sections of this thesis, but also include pro-ana communities. Refining the argument further, we can facilitate agency in communities where improvement in agency would result in improved health outcomes. If we enhance togetherness in HIV-positive men who have sex with men communities, would it further alienate bug chasers and increase their numbers? There are likely no clear demarcations or indicators when we should tackle health concerns in marginalized communities. This dissertation favors marginalized communities that broader academia has agreed upon as needing improvements in health outcomes. However, men who have sex with men and individuals with substance use disorders were not always viewed as deserving of medical treatment by the medical establishment. While we currently malign pro-ana and Gang Stalking communities, academic opinion toward them could change in the future. Such questions are pertinent when designing policy solutions for health outcomes within marginalized communities. I suggest carefully considering when to foster agency in marginalized communities, for even in scorned communities such as white nationalists, there may be higher rates of opioid use disorder[579,580] that require addressing.

While the topics covered in this thesis are broad, they share a thematic arc. Low sexually transmitted infection testing uptake, opioid use disorder and cannabis use are issues often disproportionately faced by marginalized communities. Establishing marginalization as the causal factor behind these concerns is often complex, but there is significant work indicating that problematic patterns of drug use and poor sexual health outcomes are engendered by

marginalization. Drawing together research from several arenas, I establish a clear strand of reasoning. Marginalization is associated with conditions inimical to health and well-being, creating a host of health risks. Such marginalization limits the agency of affected communities. However, even within these sites of marginalization, men who have sex with men seek testing and opioid use disorder patients seek medication, mitigating health risks borne from marginalization. I advance that marginalized communities are not completely helpless considering reduced health outcomes, indicating how some communities reclaim agency. Finally, I indicated other cases where fostering agency in marginalized communities needs to be carefully considered.

Appendix

Chapter 1: Cannabis Use Patterns at the Dawn of United States Cannabis Reform

Regarding mixing cannabis with tobacco, participants were asked whether they used tobacco mixed with cannabis in the last 12 months, with Never and Yes provided as response options. Concerning how soon after the participant woke up and had their first joint on the day they used cannabis, the selections of Immediately within 5 minutes, Within less than an hour, Within 1-4 hours, Within 5-12 hours and After more than 12 hours were provided. For normal daily cannabis use, participants were asked to select the weight, from a dropdown list of 29 weights, starting at 50mg and gradually increasing to the final selection of >20g. Regarding the number of hours spent stoned in a session, participants were asked to select from a dropdown list of 24 options, increasing in one-hour increments to the last option of 24 Hours. For the number of days cannabis was used in the last 12 months, participants keyed in their answer in a box provided. Participants were asked how long before bed they had their last joint, with the following options: Last thing before bed, 1-2 hours before bed, 3-4 hours before bed and More than 4 hours before bed. Concerning the most common way participants used cannabis, the following options were provided: Smoked in a joint (rolled cannabis cigarette) with tobacco, Smoked in a joint without tobacco, Smoked in a blunt (cigar that has been hollowed out and filled with cannabis) with tobacco, Smoked in a blunt without tobacco, Smoked in a pipe with tobacco, Smoked in a pipe without tobacco, Smoked in a bong/water pipe with tobacco, Smoked in a bong/water pipe (filtration device generally used for smoking cannabis) without tobacco, Bucket bong (method of consuming smokable substances such as cannabis, using two containers), Hot knife (method of smoking cannabis with two knife blades),

Vaporizer (device used to vaporize cannabis for inhalation), Eaten in food, Tincture/drank as tea, and Medical spray. For the preferred preparation of cannabis in the last year, participants could select the following: High potency herbal cannabis, Resin/hash (drug made from the resin of the cannabis plant), Normal weed/bush/pressed, Edibles (food product that contains cannabinoids), Kief (resinous trichomes of cannabis that may accumulate in containers), Oil, and Butane Hash Oil (oil extracted from cannabis using butane as a solvent). Prior to analysis, the variable regarding the time of first joint in a day was categorized into >60mins and <60mins of waking, to model time to first cigarette. The variable regarding the grams of cannabis used per session was recoded into a continuous variable, and the >20g value was recoded as 21 grams. On average, there are about 0.32 grams of cannabis in a joint 172. For ease of interpretation, the age variable was recoded into a categorical variable with intervals of ten years each, and consecutive age groups representing less than 5% of the sample were subsumed into a larger group (41-79 years) for clearer interpretation.

Chapter 1: Correlates of Cannabis-related emergency department Visits in New York City

An unintentional emergency department visit were those where I excluded International Classification of Diseases for self-inflicted injury, injury purposely inflicted by other persons, injury undetermined whether accidentally or purposely inflicted, poisoning by adverse effects, poisoning by underdosing, and International Classification of Diseases codes for substance abuse detoxification and additional codes which conveyed services and procedures billed for outpatient visits rather than emergency department visits described using revenue codes for drug and alcohol rehabilitation and procedure codes. International Classification of Diseases codes refer to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems, a medical classification list by the World Health Organization. The International Classification of Diseases contains codes for diseases, symptoms, abnormal findings, complaints, social circumstances and external causes of injury or diseases (see www.icd10data.com for more information).

Based on the presence of cannabis and other drugs, I divided the data into two categories using the relevant International Classification of Diseases codes: 1) cannabis-related (cannabis was identified, possibly with one or more other psychoactive drugs); 2) non-cannabis related, where no cannabis was involved. A cannabis-related diagnosis was assigned with the following codes: F12 and T407. International Classification of Diseases codes with two integers represent a range of codes. For example, F12 represents codes like F12.1, F12.12 and F12.15. Codes with three digits, like T407, represent specific diagnoses, such as cannabis poisoning. Other psychoactive drugs included alcohol, cocaine, heroin, stimulants

(methamphetamine/amphetamine), hallucinogens (3,4-methylenedioxymethamphetamine, phencyclidine, d-lysergic acid diethylamide and miscellaneous hallucinogens), opiates/opioids and sedatives/benzodiazepines.

The alcohol, opioid, cocaine, anxiety disorder, mood disorder and schizophrenia and other psychotic disorders variables were assigned using the relevant International Classification of Diseases codes. I assigned an alcohol-related diagnosis using the following International Classification of Diseases codes: F10, K70, E52, Y90, G621, I426, K292, E244, E512, G721, K852, K860, G312, R780, T510, T519, O354 and O993. For an alcohol-related diagnosis, conditions arising from overconsumption of alcohol were included, like alcoholic liver disease (K70). Opioid-related International Classification of Diseases codes were as follows: F11, T400, T401, T402, T403, T404 and T406. Cocaine-related International Classification of Diseases codes were the following: F14 and T405. The Substance Abuse and Mental Health Services Administration Mental Health Client Level Data report[581] was used to assign the anxiety disorder, mood disorder and schizophrenia and other psychotic disorders variables.

Demographic characteristics of patients in the Statewide Planning and Research Cooperative System dataset included age (13-17, 18-24, 25-34, 35-44, 45-54, 55-64, 65-84), sex (male, female), ethnicity (White non-Hispanic, Black non-Hispanic, Hispanic, Other) and zip code. I used zip code to assign participants to neighborhood poverty levels, measuring neighborhood socioeconomic status. The following neighborhood poverty levels were assigned, based on percent residents living below the federal poverty line: <5%, 5% to <10%, 10% to <20%, 20% to <30%, 30 to <40% and ≥40%.[582] The 2012-2016 American Community Survey definitions were used to define poverty levels. Examples of admission case types based on

International Classification of Diseases codes include substance related disorders (intoxication, dependence, abuse), limb fractures and other admission types.

Chapter 2: Community-centric Behaviors and Chinese Men who have Sex with Men

A. Sociodemographics

The next set of questions will ask you to provide some information about yourself.

A1. Age: ____ years old

A2. Nationality

1. Han Chinese 2. Other _____

A3. Current marital status:

1. Never married
2. Engaged or Married
3. Separated or divorced
4. Widowed

A4. Highest level of completed education:

1. Elementary
2. Middle school
3. High school or vocational school
4. Bachelor or associate degree
5. Above bachelor's degree

A5. What is your occupation?

o Student
o Civil servant
o Farmer
o Labor worker (blue collar)
o Office worker (white collar)
o Seller/service staff
o Technician
o Unemployed
o Other_____

A6. What is your total individual **monthly** income from all sources?

1. <1500 RMB/month
2. 1500-3000 RMB/month
3. 3001-5000 RMB/month
4. 5001-8000 RMB/month
5. >8000 RMB/month

A7. What is your gender identity?

1. Male
2. Female
3. Transgender
4. Unsure/Other

A8. What is your sexual orientation?

1. Homosexual
2. Bisexual
3. Heterosexual
4. Unsure/Other

B. Sexual behaviors

The next set of questions will ask you about your sexual behaviors with other men.

B1. What is your role during anal sex?

1. Mostly receptive (bottom)

2. Mostly insertive (top)
3. Half and half (versatile)

B2. In the past 3 months, how many sex partners have you had? (Number)

____
partners

B3. In the past 3 months, have you had anal sex?
1. Yes
2. No (Skip to B5)

B4. In the past 3 months, when you had anal sex, how frequently did you use condoms?

1. 0% condom use
2. Less than 50% condom use
3. More than 50% condom use
4. 100% condom use

B5. In the past 3 months, have you had condomless vaginal sex?
1. Yes
2. No

B6. In the past 3 months, have you had condomless oral sex?
1. Yes
2. No

B7. In the past, have you told anyone about your sexuality or sexual history with men? (Select all that apply)
1. Yes, my long-term female partner/wife
2. Yes, my family members
3. Yes, my friends
4. Yes, my healthcare providers
5. Yes, others:_____
6. No one

C. Clinical Information

C1. Do you have any symptoms that you are worried may be due to a sexually transmitted infection?
1. Yes. Symptoms: _____
2. No

C2. Have you ever tested for HIV in the past?
1. Yes
2. No (Skip to C5)

C3. When was the last time you tested for HIV? (If cannot recall exactly, please estimate)
Year:_____Month:_____Day:_____

C4. In the last two years, how frequently did you get tested for HIV?
1. Less than once every two years
2. Once a year
3. Once every six months
4. Once every three months
5. Monthly

C5. Today, did you agree to get tested for gonorrhea and chlamydia?
1. Yes (Go to C6)
2. No (Go to C7)

C6 (Pay-it-forward arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)
1. "Pay It Forward" allowed for discounted testing
2. "Pay It Forward" allowed paying kindness forward to community members
3. Recent symptoms

4. Recent high-risk sexual behavior
5. Testing site's staff told me to get tested
6. A friend told me to get tested
7. Other _____

C6 (Pay-what-you-want arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)

1. "Pay What You Want" allowed for discounted testing
2. Recent symptoms
3. Recent high-risk sexual behavior
4. Testing site's staff told me to get tested
5. A friend told me to get tested

Other _____

C6 (Standard of care arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)

1. Because the research staff introduced gonorrhea and chlamydia testing
2. Recent symptoms
3. Recent high-risk sexual behavior
4. Testing site's staff told me to get tested
5. Other _____

C7. If you did NOT agree to testing for gonorrhea and chlamydia today, why NOT? (select all that apply)

1. I don't know anything about gonorrhea or chlamydia
2. I don't want to know if I have gonorrhea or chlamydia
3. I don't need to get tested
4. Too much of a hassle
5. Too expensive
6. I am worried about confidentiality
7. I am afraid of pain/ discomfort
8. I don't want to leave sample today
9. I am embarrassed to get tested in front of my friend/partner
10. I am afraid that my results will be positive
11. Other _____

D. Community Engagement

The next set of questions asks about your experiences with men who have sex with men-related causes, events and organizations in your community.

D1. Have you ever participated in online forums or discussions on social media (ie. Weixin, Weibo, Twitter, or other on-line communities) about issues related to the men who have sex with men community?

o Yes
o No

D2. Are you aware of any ongoing men who have sex with men-related community events?

o Yes
o No

D3. Have you ever encouraged someone to use men who have sex with men-related community resources, such as free HIV and syphilis testing services?

o Yes
o No

D4. Have you ever attended men who have sex with men-related community events?

o Yes
o No

D5. Have you ever donated to men who have sex with men-related causes, events, or organizations? (other than today)

o Yes

o No

D6. Have you ever volunteered for men who have sex with men-related causes, events, or organizations?
o Yes
o No

E. Community Connectedness

The following set of questions asks about your feelings toward the men who have sex with men. Here, "men who have sex with men community" broadly refers to the collective of individuals and community organizations that have an interest in men who have sex with men-related issues.

E1. You feel that you are a part of the men who have sex with men community.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

E2. Participating in the men who have sex with men community is a positive thing for you.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

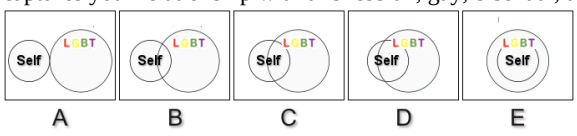
E3. You are proud of the men who have sex with men community.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

E4. It is important for you to be an advocate for the men who have sex with men community.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

E5. If you and your peers work together, the problems in the men who have sex with men community can be solved.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

E6. You really feel that any problems faced by the men who have sex with men community are also your own problems.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

E7. The diagram below is designed to represent your relationship ("Self") with lesbian, gay, bisexual, and transgender as a group ("lesbian, gay, bisexual, and transgender"). Please indicate your relationship by selecting the option that best captures your relationship with this lesbian, gay, bisexual, and transgender as a group.



F. Social Cohesion

F1. You can count on other men who have sex with men in your group of friends if you need to borrow money.
o Strongly Agree
o Agree
o Disagree
o Strongly Disagree

F2. You can count on other men who have sex with men in your group of friends if you need to talk about your problems.
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

F3. You can count on other men who have sex with men in your group of friends if you need somewhere to stay.
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

F4. The group of men who have sex with men with whom you socialize with is an integrated group.
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

F5. You can trust the majority of the men who have sex with men you know.
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

F6. In general, men who have sex with men in your group of friends in the area where you live only worry about themselves
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

F7. In general the men who have sex with men you socialize with are always arguing amongst each other
- o Strongly Agree
- o Agree
- o Disagree
- o Strongly Disagree

G. Pay-It-Forward Participation (Pay-it-forward arm only)

G1. Today, you came to testing:
1. By yourself (Skip to G3)
2. Accompanied by someone else

G2. How would you describe your relationship to the person accompanying you?
1. Sex partner
2. Men who have sex with men peer
3. Non-men who have sex with men peer
4. Family
5. Other, specify:____

G3. Did you choose to contribute any amount of money?
1. Yes
2. No

G4. What determined your contribution amount?
1. One's own financial situation
2. Normal price of testing
3. Quality of testing service
4. Estimate of how much others contributed
5. Feel bad if not pay anything
6. Other, specify:_____

G5. What do you believe are the main benefits to participating in the pay-it-forward program? (select all that apply)

1. I can receive discounted GC/CT test
2. I can experience warm glow through receiving donated testing
3. It reduces my sexually transmitted infection risk by making my community healthier
4. It can help more men who have sex with men get tested
5. It allows someone to help me, and then I can help someone else
6. Other _____

G. Pay-What-You-Want Participation
(Pay-what-you-want arm only)

G1. Today, you came to testing:

1. By yourself (Skip to G3)
2. Accompanied by someone else

G2. How would you describe your relationship to the person accompanying you?

1. Sex partner
2. Men who have sex with men peer
3. Non-men who have sex with men peer
4. Family
5. Other:____

G3. Did you choose to contribute any amount of money?

1. Yes
2. No

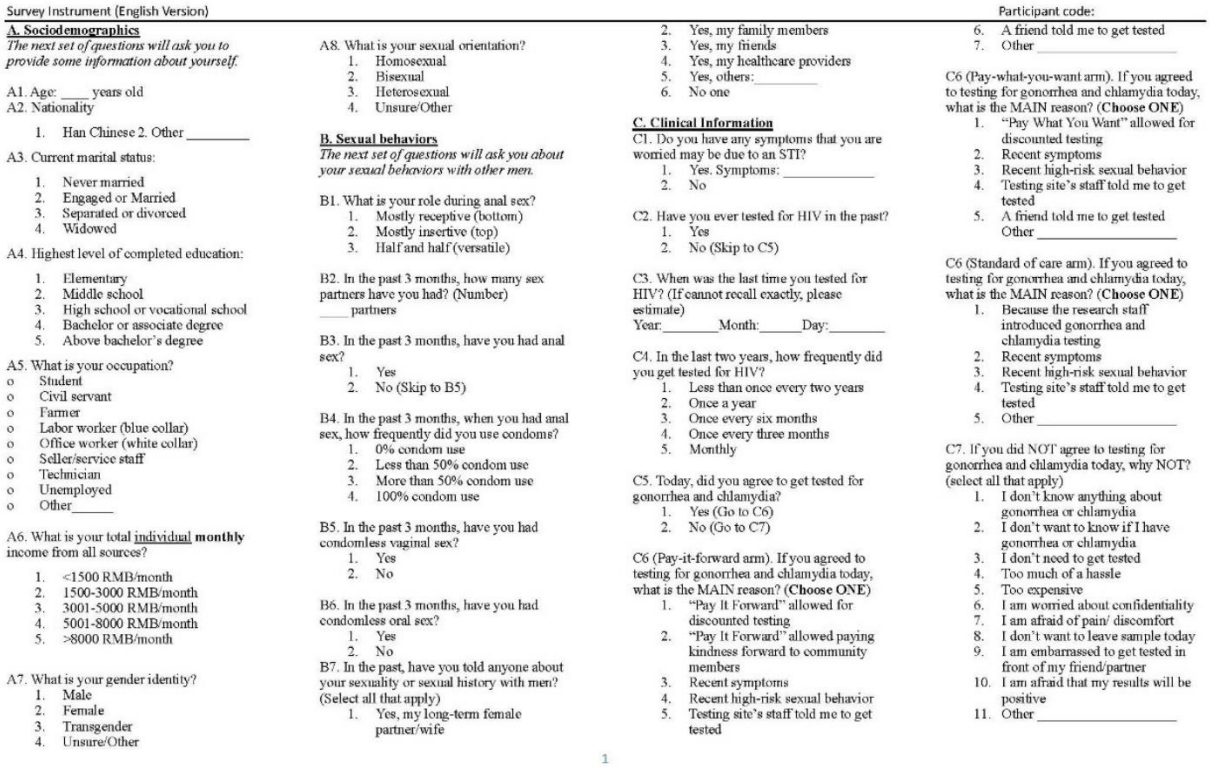
G4. What determined your contribution amount?

1. One's own financial situation
2. Normal price of testing
3. Quality of testing service
4. Estimate of how much others contributed
5. Feel bad if not pay anything
6. Other:_____

G5. What do you believe are the main benefits to participating in the pay-it-forward program? (select all that apply)

1. I can receive discounted GC/CT test
2. I can experience warm glow through receiving discounted testing
3. It reduces my sexually transmitted infection risk by making my community healthier
4. It can help more men who have sex with men get tested
5. It allows men who have sex with men to have more control over testing price
6. Other _____

Chapter 2: Lack of Sexual Behavior Disclosure May Distort sexually transmitted infection Testing Outcomes



Survey Instrument (English Version)

Participant code:

A. Sociodemographics

The next set of questions will ask you to provide some information about yourself.

A1. Age: ____ years old

A2. Nationality

1. Han Chinese 2. Other _____

A3. Current marital status:

1. Never married
2. Engaged or Married
3. Separated or divorced
4. Widowed

A4. Highest level of completed education:

1. Elementary
2. Middle school
3. High school or vocational school
4. Bachelor or associate degree
5. Above bachelor's degree

A5. What is your occupation?

o Student
o Civil servant
o Farmer
o Labor worker (blue collar)
o Office worker (white collar)
o Seller/service staff
o Technician
o Unemployed
o Other_____

A6. What is your total individual **monthly** income from all sources?

1. <1500 RMB/month
2. 1500-3000 RMB/month
3. 3001-5000 RMB/month
4. 5001-8000 RMB/month
5. >8000 RMB/month

A7. What is your gender identity?

1. Male
2. Female
3. Transgender
4. Unsure/Other

A8. What is your sexual orientation?

1. Homosexual
2. Bisexual
3. Heterosexual
4. Unsure/Other

B. Sexual behaviors

The next set of questions will ask you about your sexual behaviors with other men.

B1. What is your role during anal sex?

1. Mostly receptive (bottom)
2. Mostly insertive (top)
3. Half and half (versatile)

B2. In the past 3 months, how many sex partners have you had? (Number)

____ partners

B3. In the past 3 months, have you had anal sex?

1. Yes
2. No (Skip to B5)

B4. In the past 3 months, when you had anal sex, how frequently did you use condoms?

1. 0% condom use
2. Less than 50% condom use
3. More than 50% condom use
4. 100% condom use

B5. In the past 3 months, have you had condomless vaginal sex?

1. Yes
2. No

B6. In the past 3 months, have you had condomless oral sex?

1. Yes
2. No

B7. In the past, have you told anyone about your sexuality or sexual history with men? (Select all that apply)

1. Yes, my long-term female partner/wife
2. Yes, my family members
3. Yes, my friends
4. Yes, my healthcare providers
5. Yes, others:_____
6. No one

C. Clinical Information

C1. Do you have any symptoms that you are worried may be due to an STI?

1. Yes. Symptoms: _____
2. No

C2. Have you ever tested for HIV in the past?

1. Yes
2. No (Skip to C5)

C3. When was the last time you tested for HIV? (If cannot recall exactly, please estimate)

Year:_____Month:_____Day:_____

C4. In the last two years, how frequently did you get tested for HIV?

1. Less than once every two years
2. Once a year
3. Once every six months
4. Once every three months
5. Monthly

C5. Today, did you agree to get tested for gonorrhea and chlamydia?

1. Yes (Go to C6)
2. No (Go to C7)

C6 (Pay-it-forward arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)

1. "Pay It Forward" allowed for discounted testing
2. "Pay It Forward" allowed paying kindness forward to community members
3. Recent symptoms
4. Recent high-risk sexual behavior
5. Testing site's staff told me to get tested
6. A friend told me to get tested
7. Other _____

C6 (Pay-what-you-want arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)

1. "Pay What You Want" allowed for discounted testing
2. Recent symptoms
3. Recent high-risk sexual behavior
4. Testing site's staff told me to get tested
5. A friend told me to get tested
Other _____

C6 (Standard of care arm). If you agreed to testing for gonorrhea and chlamydia today, what is the MAIN reason? (**Choose ONE**)

1. Because the research staff introduced gonorrhea and chlamydia testing
2. Recent symptoms
3. Recent high-risk sexual behavior
4. Testing site's staff told me to get tested
5. Other _____

C7. If you did NOT agree to testing for gonorrhea and chlamydia today, why NOT? (select all that apply)

1. I don't know anything about gonorrhea or chlamydia
2. I don't want to know if I have gonorrhea or chlamydia
3. I don't need to get tested
4. Too much of a hassle
5. Too expensive
6. I am worried about confidentiality
7. I am afraid of pain/ discomfort
8. I don't want to leave sample today
9. I am embarrassed to get tested in front of my friend/partner
10. I am afraid that my results will be positive
11. Other _____

1

Study design

The randomized controlled trial was designed to evaluate the comparative effectiveness of Pay-it-Forward and Pay-what-you-Want against the standard of care for increasing gonorrhea/chlamydia test uptake in men who have sex with men. Pay-it-forward consists of telling participants that their test was paid for by another men who have sex with men and

asking the participant how much they would like to contribute to the next participant.[321] Pay-what-you-Want is a pricing strategy where consumers select a desired amount for a particular product or service.[583] In a solely monetary sense, pay-as-you-what is similar to pay-it-forward pricing where consumers select the price for a good or service.

However, pay-as-you-what and pay-it-forward vary socially. In pay-as-you-what, the consumer pays for themselves, while in pay-it-forward, the consumer pays for someone else. Comparing pay-as-you-what and pay-it-forward can provide insight on whether participants are engaging in testing solely because it is free or if there are community-based effects of altruism involved. Participants were randomly assigned into clusters within the study arms. A cluster is a group of ten eligible men who arrived one after another at the study sites and decided to participate. Cluster randomization was utilized to minimize intervention contamination to account for men who have sex with men who turned up in pairs and to simplify processes undertaken by site staff. Men who have sex with men in the same cluster were collectively assigned to the same study arm. Similarly, those who arrived with partners were placed in the same study arm. Randomized controlled trial randomization sequence was designed through STATA 15.[331] For the pay-it-forward arm, participants were told the experiment was for promoting gonorrhea/chlamydia test uptake and that the standard price of a gonorrhea/chlamydia test was 150RMB (USD22). They were offered a free test and told it was paid for by another men who have sex with men. In the pay-as-you-what introduction, men who have sex with men were told the standard gonorrhea/chlamydia test price was 150RMB (USD22). Men who have sex with men were told that they could first receive a free gonorrhea/chlamydia test and then decide the amount to pay. Participants were told that payment and receiving a gonorrhea/chlamydia test was voluntary and the payment amount was up to the participant.

Men who have sex with men assigned to the SOC arm received the same gonorrhea/chlamydia test information through a pamphlet and no further details. Those in the SOC arm were told that the standard price of the gonorrhea/chlamydia test was 150RMB (USD22). 101 were allocated to the pay-it-forward arm, 100 to the pay-as-you-what arm and 100 to the SOC arm across the three testing sites. Within the randomized controlled trial, gonorrhea/chlamydia test uptake was 56%, 46%, and 18% respectively.

Model specification

I analyzed the data using probit models with sample selection. Test uptake (selection stage) was operationalized as a dichotomous variable indicating whether men had selected the gonorrhea/chlamydia test. In the outcome stage, the variable of interest was choice of rectal gonorrhea/chlamydia test. Standard errors were calculated with a jackknife estimator, using 30 jackknife samples that accounted for the study design. Statistical analyses were conducted using Stata version 15.0.38. $P<.05$ was considered statistically significant. The first-stage model applies a probit model to represent a measure of the propensity of a participant to choose a gonorrhea/chlamydia test on the basis of factors believed to be related to the decision to test. The first model's assessment of the probability of the gonorrhea/chlamydia test choice is then applied in the second stage to adjust the estimates produced from a probit model to account for the effect of selection bias. To effectively use this approach, I had to develop an understanding not only of factors that influenced selection of the rectal gonorrhea/chlamydia test but also of factors that affected the decision to engage in the gonorrhea/chlamydia test/test uptake. Formally, I can write the two models as follows:

$$Y_1^* = \boldsymbol{\alpha}_1^T \mathbf{Z} + \boldsymbol{\alpha}_2^T \mathbf{W} + \boldsymbol{\alpha}_3^T \mathbf{X} + u_1, \qquad Y_1 = \begin{cases} 1 & \text{if} \quad Y_1^* > 0 \\ 0 & \text{if} \quad Y_1^* \leq 0 \end{cases}$$

$$Y_2^* = \boldsymbol{\beta}_1^T \mathbf{W} + \boldsymbol{\beta}_1^T \mathbf{X} + u_2, \qquad Y_2 = \begin{cases} 1 & \text{if} \quad Y_2^* > 0, Y_1 = 1 \\ 0 & \text{if} \quad Y_2^* \leq 0, , Y_1 = 1 \end{cases}$$

where Y_1^* represents the decision to test and Y_2^* represents the decision to select the rectal gonorrhea/chlamydia test as unobserved latent variables. **Z** is the set of instruments used to adjust for selection, **W** is the set of variables of interest for which I wish to infer the effect on the outcome Y_2, and **X** is the set of controls for the outcome model. **Z** were included in the selection stage but not the outcome stage: Whether participant had experienced sexually transmitted infection symptoms prior to the gonorrhea/chlamydia test, Previous HIV test, HIV test frequency, Site, Arm. These variables likely influenced test uptake but not gonorrhea/chlamydia test choice and were generally not associated with gonorrhea/chlamydia test choice. **W**: Top, Bottom, Versatile, Out to anyone, Out to health provider. Inclusion of W was dependent on the hypothesis of interest. **X**: Age, Income, Number of male partners in last three months, Frequency of condomless anal intercourse.

Given the relatively small number of participants both versatile and out, I was limited in the number of controls to include. I thus did not include controls co-linear with reported variables (e.g. Marital status, education). Regarding the sexually transmitted infection symptoms variables, participants were not asked where on the body symptoms were observed, just whether they had symptoms. Thus, the symptoms variable may affect test uptake but not rectal

gonorrhea/chlamydia test choice, perhaps indicative of a strong instrument. The Arm variable varies the attractiveness of testing but does not affect rectal gonorrhea/chlamydia test choice, perhaps indicating its strength as an instrument.

Chapter 3: The Role of Social Support on Treatment Outcomes regarding Medication for Opioid Use Disorder: A Systematic Review

The following is an example of the PubMed search strategy:

((("buprenorphine, naloxone drug combination"[MeSH Terms] OR "naltrexone"[MeSH Terms] OR "methadone"[MeSH Terms] OR "opiate substitution treatment"[MeSH Terms] OR "opioid-related disorders"[MeSH Terms] OR "medication assisted therapy"[tw] OR "medication assisted therapies"[tw] OR Naltrexone[tw] OR Methadone[tw] OR Celupan[tw] OR Trexan[tw] OR ReVia[tw] OR Nemexin[tw] OR Nalorex[tw] OR Antaxone[tw] OR "EN 1639A"[tw] OR Vivitrol[tw] OR Suboxone[tw] OR "Buprenorphine Naloxone"[tw] OR Methadone[tw] OR Dolophine[tw] OR Metadol[tw] OR Symoron[tw] OR Methadose[tw] OR Phenadone[tw] OR Physeptone[tw] OR Phymet[tw] OR Amidone[tw] OR Methaddict[tw] OR "Methadone Maintenance Treatment"[tw] OR "Opiate Substitution Treatments"[tw] OR "Opioid Substitution Treatment"[tw] OR "Opioid Substitution Treatments"[tw] OR "Opioid Substitution Therapy"[tw] OR "Opioid Substitution Therapies"[tw] OR "Opiate Replacement Therapy"[tw] OR "Opiate Replacement Therapies"[tw] OR "Opioid Replacement Therapy"[tw] OR "Opioid Replacement Therapies"[tw]) AND ("social support"[MeSH Terms] OR "community health services"[MeSH Terms] OR "community networks"[MeSH Terms] OR "spouses"[MeSH Terms] OR "friends"[MeSH Terms] OR "family"[MeSH Terms] OR "societies"[MeSH Terms] OR "residence characteristics"[MeSH Terms] OR "social support"[tw] OR "social supports"[tw] OR "social network"[tw] OR "social networks"[tw] OR "support system"[tw] OR "support systems"[tw] OR Spouse[tw] OR Spouses[tw] OR Partner[tw] OR Partners[tw] OR Friend[tw] OR Friends[tw] OR Society[tw] OR

Community[tw] OR Communities[tw] OR Peer[tw] OR Peers[tw] OR Family[tw] OR Families[tw] OR Husband[tw] OR Husbands[tw] OR Wife[tw] OR Wives[tw] OR co-worker[tw] OR co-workers[tw] OR coworker[tw] OR coworkers[tw] OR neighbor[tw] OR neighbors[tw] OR Neighborhood[tw] OR Neighborhoods[tw] OR Neighbourhood[tw] OR neighbourhoods[tw])) NOT (("buprenorphine, naloxone drug combination"[MeSH Terms] OR "naltrexone"[MeSH Terms] OR "methadone"[MeSH Terms] OR "opiate substitution treatment"[MeSH Terms] OR "medication assisted therapy"[tw] OR "medication assisted therapies"[tw] OR Naltrexone[tw] OR Methadone[tw] OR Celupan[tw] OR Trexan[tw] OR ReVia[tw] OR Nemexin[tw] OR Nalorex[tw] OR Antaxone[tw] OR "EN 1639A"[tw] OR Vivitrol[tw] OR Suboxone[tw] OR "Buprenorphine Naloxone"[tw] OR Methadone[tw] OR Dolophine[tw] OR Metadol[tw] OR Symoron[tw] OR Methadose[tw] OR Phenadone[tw] OR Physeptone[tw] OR Phymet[tw] OR Amidone[tw] OR Methaddict[tw] OR "Methadone Maintenance Treatment"[tw] OR "Opiate Substitution Treatments"[tw] OR "Opioid Substitution Treatment"[tw] OR "Opioid Substitution Treatments"[tw] OR "Opioid Substitution Therapy"[tw] OR "Opioid Substitution Therapies"[tw] OR "Opiate Replacement Therapy"[tw] OR "Opiate Replacement Therapies"[tw] OR "Opioid Replacement Therapy"[tw] OR "Opioid Replacement Therapies"[tw]) AND ("social support"[MeSH Terms] OR "community health services"[MeSH Terms] OR "community networks"[MeSH Terms] OR "spouses"[MeSH Terms] OR "friends"[MeSH Terms] OR "family"[MeSH Terms] OR "societies"[MeSH Terms] OR "residence characteristics"[MeSH Terms] OR "social support"[tw] OR "social supports"[tw] OR "social network"[tw] OR "social networks"[tw] OR "support system"[tw] OR "support systems"[tw] OR Spouse[tw] OR Spouses[tw] OR Partner[tw] OR Partners[tw] OR Friend[tw] OR Friends[tw] OR Society[tw] OR

Community[tw] OR Communities[tw] OR Peer[tw] OR Peers[tw] OR Family[tw] OR Families[tw] OR Husband[tw] OR Husbands[tw] OR Wife[tw] OR Wives[tw] OR co-worker[tw] OR co-workers[tw] OR coworker[tw] OR coworkers[tw] OR neighbor[tw] OR neighbors[tw] OR Neighborhood[tw] OR Neighborhoods[tw] OR Neighbourhood[tw] OR neighbourhoods[tw]))

Study characteristics related to design of study, medication for opioid use disorder drug used, target population, outcome, number of participants, follow-up, and conclusions										
Author, date	*Ref*	*Location*	*Study Design*	*medication for opioid use disorder drug used*	*Population*	*Outcomes*	*Sample characteristics (N, % male, age, ethnicity)*	*Form of social support*	*Follow-up*	*Conclusions*
Anton et al., 1981	[38]	United States	Observational, retrospective study	Naltrexone	Opioid dependent self-referred patients	Naltrexone maintenance for three months or more	Total N: 65 Naltrexone + HIP N: 40 % male: 85 Mean age: 26.9 Ethnicity: 42.5% White; 57.5% Black Naltrexone + HIP + MFT N: 25 % male: 96 Mean age: 24.8 Ethnicity: 72% White; 28% Black	Family	1 year	Higher retention rate for patients treated with multiple family therapy (MFT) than those who did not receive MFT.
Carroll et al., 2001	[30]	United States	randomized controlled trial	Naltrexone	Opioid dependent patients who had completed outpatient detoxification	Compliance with naltrexone treatment	N: 127 % male: 76 Mean age: 32 Ethnicity: 77% White	Family	unclear	Patients who attended at least 1 family counselling session had better results for those under the significant other (SO) than those in the contingency management (CM) group with regards to retention, compliance, and drug use outcomes.

Catalano et al., 1997	[51]	United States	randomized controlled trial	Methadone	Opioid dependent parents who had been in methadone treatment for a minimum of 90 days and have one or more children between the ages of 3 and 14 years old living with them at least 50% of the week	Parent self-reported drug-use	N: 35 % male: 25 Mean age: 35.36 Ethnicity: 77% White; 18% Black; Mixed/Other: 5%	Family	3 years	Parents in the experimental group (Standard methadone treatment + supplemental parenting program) who had lower levels of opiate use than subject in standard methadone treatment group.
Catalano et al., 1999	[52]	United States	randomized controlled trial	Methadone	Opioid dependent parents who had been in methadone treatment for a minimum of 90 days and have one or more children between the ages of 3 and 14 years old living with them at least	Self-reported frequency of use of marijuana, cocaine, opiates and drug use in previous month	N: 178 % male: 26.7 Mean age: 35.4 Ethnicity: 77% White	Family	3 years	Parents in experimental group who did a parent skills training and home-based case management to reduce parents' risk for relapse had lower levels of opiate use than control subjects.

					50% of the week					
Cerovecki et al., 2013	[43]	Croatia	Observational, prospective study	Methadone	Opioid dependent patients treated in family medicine settings	Fatal outcome risk factors like quality of relationships and continuation of drug use during previous therapeutic attempts	N: 287 % male: NA Mean age: NA Ethnicity: NA	Family	12 years	Increased fatal outcome for patients with more unstable relationships and loss of continuity of care
Chaudhry et al., 2012	[48]	UK	Observational, retrospective study	Naltrexone	Opioid dependent patients who had successfully completed detoxification	Treatment retention	N: 142 % male: 93.7 Mean age: NA Ethnicity: 25.4% White; 70.4% Asian; 4.2% Other	Family	10 years	Parental supervision of naltrexone administration was a predictor of long-term retention in treatment.

Davila Torres, 2011	[47]	United States	Observational, retrospective study	Methadone	Latino opioid dependent patients	Retention and treatment program completion	N: 291 % male: 66.7 Mean age: NA Ethnicity: NA	Family	1 year	Successful treatment completion associated with living in stable housing and higher perceived physician/nurse support.
Day et al., 2013	[71]	UK	Cross-sectional analysis	Buprenorphine, Methadone	Opioid dependents	Heroin use in the previous month	N: 118 % male: 79 Mean age: 35.5 Ethnicity: 73% White; 14% South Asian; 4% Black, 8% Mixed	Combined family and peer	6 months	Substance use involvement of heroin using social network was higher amongst patients who had used heroin in the past month.
Day et al., 2018	[58]	UK	randomized controlled trial	Methadone	Opioid dependent individuals who had been prescribed methadone or buprenorphine for the past 12 months and had reported heroin use on one or more days 28 days prior to beginning of the study	Number of days of heroin use in the past month	N: 83 % male: 79 Mean age: 35.5 Ethnicity: 73% White; 14% South Asian; 4% Black; 8% Mixed	Combined family and peer	1 year	No significant differences were found between the 3 intervention arms in primary or secondary outcome measures: Treatment as usual (TAU; Brief Social Behavior and Network Therapy (BSBNT) ± TAU or Personal Goal Setting (PGS) ± TAU)

Fals-Stewart and O'Farrell, 2003	[53]	United States	randomized controlled trial	Naltrexone	Opioid dependent individuals living with at least one parent/spouse/intimate partner/family member willing to participate and did not have a current substance use disorder or meet Diagnostic and Statistical Manual of Mental Disorders-III-R criteria for schizophrenia, bipolar disorder, or psychosis	Percentage of opioid-free urines	N: 124 % male: 100 Mean age: 32.9 Ethnicity: 66% White; 26% Black; 3% Hispanic; 5% Other	Family	4 years	Male opioid-dependents living with a family member with a family-based naltrexone compliance contract produced better outcomes during treatment.

Fals-Stewart et al., 2001	[54]	United States	randomized controlled trial	Methodone	Opioid dependent male partners who had been married for at least 1 year or in a stable common-law relationship for at least 2 years who had to refrain from seeking additional substance abuse treatment except for self-help meetings like Alcoholics Anonymous	Urine tests	N: 36 % male: 100 Mean age: 38.1 Ethnicity: 18% White; 15% Black; 3% Hispanic	Family	4 years	Patients who received BCT reported greater reductions in drug use severity and family and social problems from baseline to post treatment than patients receiving standard MM treatment.
Feng et al., 2018	[61]	China	Observational, retrospective study	Methadone	Opioid dependent patients enrolled in methadone clinic	Self-reported heroin use or a positive urine morphine test result	N: 2446 % male: 79.2 Mean age: NA Ethnicity: NA	Family	1 year	Higher heroin use concurrent with treatment for patients with family members with history of heroin use.

Gogineni et al., 2001	[60]	United States	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Continued opioid use	N: 252 % male: 56 Mean age: 40.3 Ethnicity: 64% White; 22% Black; 9% Latino/Hispanic; 2% Native American; 3% Other	Family	None	Patients with substance-using live-in partners or drug-using social relationships had higher drug use.
Grey et al., 1986	[36]	United States	Observational, prospective study	Naltrexone and Methadone	Opioid dependent patients who had been opiate-free for 7 days prior to treatment (for naltrexone) and opiate dependents for at least 1 year for methadone maintenance treatment	Retention (number of required clinic appointments kept)	N: 60 % male: 73.3 Ethnicity: 58.3% White; 11.7% Black; 30.0% Hispanic	Family	3 months	Drug abuse was correlated significantly with perceived family support.
Gu et al., 2013	[31]	China	randomized controlled trial	Methadone	Heroin dependent patients recently admitted to the three participating methadone maintenance	Attrition from the methadone maintenance treatment service, which was defined as a failure to visit	N: 288 % male: 92 Mean age: NA Ethnicity: 98.9% Han	Family	1 year	Patients who received a combination of psycho-social intervention with the standard of-care (SOC) methadone maintenance treatment service as compared to that of the SOC methadone maintenance treatment service alone showed lower likelihood of attrition.

					treatment clinics	the methadone maintenance treatment clinic consecutively for at least 1 month immediately prior to the study's completion date				
Gu et al., 2014	[41]	China	Case-crossover design	Methadone	Opioid dependent patients	Methadone maintenance clinic nonattendance	N: 131 % male: 88 Mean age: NA Ethnicity: NA	Family	1 month	Increased nonattendance at methadone maintenance treatment clinics for patients with interpersonal conflicts with family, financial difficulty and with worry about police arrest.
Heinz et al., 2009	[62]	United States	Observational, retrospective study	Methadone	Opioid dependent patients with a history of cocaine use	Positive urinalysis tests for cocaine and opiates	N: 635 % male: 54.1 Mean age: 39.2 Ethnicity: 39.5% White; 59% Black; Other: 1.5%	Family	6 years	Reduced cocaine and heroin use for married participants who reported a close relationship with one's partner.
Hikmayani et al., 2012	[42]	Indonesia	Observational, prospective study	Methadone	Heroin dependent patients	Retention rate in methadone management treatment clinics	N: 98 % male: NA Mean age: 31.6 Ethnicity: NA	Family	1 year 6 months	Low retention significantly associated with absence of family support.

Hoang et al., 2015	[63]	Vietnam	Observational, prospective study	Methadone	Opioid dependent patients	Concurrent heroin use after methadone treatment initiation	N: 965 % male: 98.1 Mean age: 34.4 Ethnicity: NA	Family	10 months	Increased continued use of heroin after methadone maintenance treatment with likelihood of family conflict.
Hoang et al., 2018	[64]	Vietnam	Observational, retrospective study	Methadone	Opioid dependent patients	Concurrent heroin use after methadone treatment initiation	N: 500 % male: 96.8 Mean age: NA Ethnicity: NA	Family	5 years	Increased odds of concurrent heroin use during treatment for patients with no emotional support from family or financial stability.
Hojjat et al., 2017	[50]	Iran	randomized controlled trial	Methadone	Individuals with a substance dependent husband with no history of drug dependence	Relapse rate	Total N: 50 Control % male: NA Mean age: 32.7 Ethnicity: NA Experimental % male: NA Mean age: 30.2 Ethnicity: NA	Family	1 year two months	Harm reduction education in families of patients undergoing methadone maintenance treatment can be effective on their marital satisfaction and treatment retention.
Kidorf, 2018	[59]	Unclear	randomized controlled trial and Single group design	Methodone	Opioid dependent individuals recruited from a community syringe exchange or from a methadone	Rate of alcohol and other drug use	N: 18 % male: NA Mean age: NA Ethnicity: NA	Combined family and peer	unclear	Patients with drug-free community support benefited from it clinically.

					maintenance program					
Lee et al., 2015	[46]	Taiwan	Observational, prospective study	Methadone	Heroin dependent patients enrolled in methadone maintenance treatment clinic	Treatment retention	N: 177 % male: 76.9 Mean age: 37.15 Ethnicity: NA	Family	unclear	Increased expressed emotion between family members and patients is linked to retention.
Lin et al., 2011	[65]	China	Cross-sectional study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Self-reported drug use and urine tests	N: 560 % male: 84.1 Mean age: 33 Ethnicity: NA	Family	7 months	Perceived family support associated with improved health and negatively correlated with concurrent substance abuse
Lin et al., 2013	[45]	Taiwan	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Retention rate in methadone maintenance treatment clinics	N: 368 % male: 86.4 Mean age: 37.2 Ethnicity: NA	Family	1 year	Perceived higher family support predicted a lower risk of methadone maintenance treatment dropout

Lundgren et al., 2007	[39]	United States	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Longest consecutive stay in methadone maintenance treatment clinic	N: 8258 % male: 65.7 Mean age: 36.5 Ethnicity: 68.6% White; 25.9% Latino; 5.5% Black	Family	6 years	Patients who resided with children, were younger and had no public health insurance were more likely to stay in methadone maintenance treatment for 6 months or less.
Monico et al., 2015	[70]	United States	Observational, prospective study	Buprenorphine	African American opioid dependent patients	Treatment retention and long-term abstinence	N: 300 % male: 60 Mean age: 46.2 Ethnicity: 100% Black	Peer	3 & 6 months	12-step meeting during the first 6 months of methadone maintenance treatment associated with superior abstinence outcomes.
Mutasa, 2001	[66]	UK	Observational, prospective study	Methadone	Opioid dependent individuals living within catchment area	MST noncompliance (misuse drugs)	N: 45 % male: 66.7 Mean age: NA Ethnicity: 88.89% White; 6.67% South Asian; 4.44% Black	Family	unclear	Medication noncompliance was associated with social company availability, family-related conflicts and peer association.
Nguyen et al., 2017	[44]	Vietnam	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Treatment adherence	N: 241 % male: NA Mean age: NA Ethnicity: NA	Family	4 months	Patients who were reminded by family members by mobile phone to adhere to treatment were more likely to do so.

Roozen et al., 2003	[55]	Netherlands	randomized controlled trial	Naltrexone	Opioid dependent patients	Abstinence for a 6-month treatment period	Naltrexone N: 24 % male: 87 Mean age: 30.5 Ethnicity: NA Methadone N: 20 % male: 82 Mean age: 29.9 Ethnicity: NA	Family	3 years	Patients who received a combination of naltrexone and CRA (community reinforced approach) had better outcomes than those with traditional treatment.
Rothenberg et al., 2002	[32]	United States	Prospective study	Naltrexone	Opioid dependent individuals with a significant other who could commit to participating in treatment	Retention in treatment	N: 82 % male: 77 Mean age: 33.6 Ethnicity: 64% White; 25% Hispanic; 11% Black	Combined family and peer	unclear	Poorer outcomes for patients who used methadone regularly at baseline than heroin only.
Sarasvita et al., 2012	[40]	Indonesia	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Duration of treatment in days	N: 178 % male: 90 Mean age: 27.2 Ethnicity: 32.6% Javanese; 16.3% Sudanese; 4.5% Bataknese	Combined family and peer	1 year 6 months	Patients with family support and with less peer support were less likely to drop out.

Scherbaum et al., 2005	[57]	Germany	randomized controlled trial	Methadone	Opioid dependent patients	Drug use	N: 73 % male: 73 Mean age: 30 Ethnicity: NA	Peer	2 1/2 years	A reduction in drug use was observed in the intervention (psychotherapy) group and but this was only observed at the 6-month follow up but not by the end of the study.
Shen et al., 2018	[67]	China	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Positive urinalysis tests for heroin use	N: 324 % male: 76.9 Mean age: 45.2 Ethnicity: 83% Han	Family	1 year	Patients with a spouse, child or who had a close family member were less likely to have positive urine tests for heroin.
Smith, 2002	[49]	United States	Observational, prospective study	Methadone	Male veteran literate opioid dependents individuals	Length of time in treatment was not predicted by social support, buut interaction of perceived social support and orientation towards social support predict therapeutic alliance (adherence)	N: 80 % male: 60 Ethnicity: 60% Black; 38.8% White; 1.2% Latino	General	12 weeks	Retention as measured by length of time in treatment

Tang, 2016	[37]	China	Observational, prospective study	Methadone	Opioid dependent patients with a history of quitting attempts	Treatment adherence	N: 523 % male: 75.9 Mean age: 38.5 Ethnicity: NA	Family	9 months	Patients are more likely to engage in sexual activity, have stronger family relationships, and experience improved health status post-treatment.
Torrens et al., 1996	[33]	Spain	Observational, prospective study	Methadone	Opioid dependent patients	Retention rate	N: 370 % male: 66 Mean age: 29.6 Ethnicity: NA	Combined family and peer	2 years 10 months	Patients living with family or stable partners had higher rates of retention.
Tran et al., 2018	[34]	Vietnam	Observational, prospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Self-reported medication adherence	N: 510 % male: 98.4 Mean age: 36.6 Ethnicity: NA	Combined family and peer	5 months	Low rate of methadone maintenance treatment non-adherence associated with job stability, engagement in self-care, and active participation of partners, family, and friends in the treatment process.
Wasserman et al., 2001	[69]	United States	Observational, prospective study	Methadone	Opioid dependent patients with at least 1 month enrollment in methadone or LAAM maintenance	Biochemciallly confirmed opiate and cocaine abstinence	N: 128 % male: 55 Mean age: 45 Ethnicity: 50% White	General	unclear	Having social networks with less drug users (abstinence specific structural support) correlated with reduced drug use and demoralization for cocaine abstinence but not opiate abstinence. There was no effect for general support.

Yandoli et al., 2002	[56]	UK	randomized controlled trial	Methadone	Patients with at least six months' duration of opioid dependence who agreed to be seen with their partner/family during treatment if required	Frequency of opiate use (allocated as opiate free, occasional users, regular users)	N: 119 % male: 63 Mean age: 28.2 Ethnicity: NA	Family	14 months	Family therapy produced significantly more drug-free subjects than standard treatment at six months and at twelve months.
Yang et al., 2013	[35]	China	Observational, retrospective study	Methadone	Opioid dependent patients enrolled in methadone maintenance treatment clinic	Retention rate in methadone maintenance treatment clinic	N: 2728 % male: 72.8 Mean age: 36.4 Ethnicity: NA	Combined family and peer	4 years 9 months	Protective factors for methadone maintenance treatment retention were: Strong relationships with family, living on support of family or friends and not communicating with former drug taking peers in the past month.
Zhu et al., 2018	[68]	United States	Observational, retrospective study	Buprenorphine, Methadone	Opioid dependent patients	Long-term opioid abstinence (at least 5 years)	N: 699 % male: 65.2 Mean age: 37.4 Ethnicity: NA	Family	3 years	Long-term abstinence was positively associated with greater social support.

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