7-31-2020

Chemsex Screening and Intervention Training for Urban Primary Care Providers

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CHEMSEX SCREENING AND INTERVENTION TRAINING FOR URBAN PRIMARY CARE PROVIDERS

A Thesis Presented to
The Faculty of the School of Medicine
Yale University

In Candidacy for the degree of
Master of Medical Science

2020

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ABSTRACT

Chemsex, defined as the use of drugs before or during sex to enhance and facilitate the experience, is increasingly prevalent in urban populations of men who have sex with men. Chemsex is associated with higher risks of sexually transmitted infections including HIV, and it has negative effects on mental health and productivity. However, chemsex is under- or un-addressed in most primary care practices, and chemsex users rarely present to specialists in addiction medicine. We hypothesize that an integrative, multimodal training program for urban primary care providers in chemsex identification and harm reduction will increase the proportion of male patients screened for chemsex. We propose a stepped-wedge cluster randomized trial to measure baseline prevalence of screening and determine the effect of training on the relative risk of screening. Screening and appropriate safety counseling can stem the progression of the epidemic and reduce the burden of consequences associated with chemsex.

CHAPTER ONE - INTRODUCTION

1.1 Background

1.1.1 Chemsex Proliferation and Associated Risks

Chemsex can be defined as the use of drugs before or during sexual experiences in order to facilitate or enhance the experience[1]. Typical substances identified in the literature associated with chemsex include crystal methamphetamine, gamma hydroxybutyric acid (GHB), gamma butyrolactone (GBL), and less frequently inhaled nitrates ("poppers"), phosphodiesterase-5 inhibitors (Viagra), and 3,4-Methylenedioxy methamphetamine ("ecstasy") [2]. Chemsex is a distinct form of recreational drug use, with its own culture and language allowing users to communicate, source drugs, and plan meetings openly on apps and social platforms. For this reason some postulate that chemsex has been expanding in communities of men who have sex with men (MSM) in the age of gay social apps like Grindr and Scruff which enable these interactions[3,4]. Chemsex itself has several pseudonyms both in literature and online, and is commonly referred to as "sexualized drug use" or "party and play."

The 56 Dean St. Clinic in London, a premier sexual and gender minority health center specializing in chemsex research and treatment, define chemsex as being associated with prolonged sex, extreme sexual practices, multiple partners, disinhibition, unpredictable drug interactions, inexperienced injection use, poor condom use, poor antiretroviral adherence, frequent sexually transmitted infections (STI), and psychosis[5]. Regardless of the source of the definition there is general consensus that chemsex is associated with high risk sexual behavior and high rates of HIV and STI transmission[1,2]. In particular its associations with serodiscordant sex, condom-less sex, and group sex

make chemsex of particular concern for HIV transmission, and it likely contributes to the disproportionate burden of HIV transmissions affecting MSM[6,7]. The marathon nature of chemsex afforded by use of substances like methamphetamines is thought to facilitate transmission due to the ensuing rectal trauma of extended sessions and group sex activities, as well as the lack of pain or fatigue perception[6]. Additionally, the culture of early exposure of young gay males to chemsex online and associated inexperienced drug use contributes to sexual risk behavior and HIV seroconversion in young MSM[5,8].

1.1.2 Epidemiology of Chemsex

Estimating the true prevalence of chemsex within both national and international MSM communities has proven difficult, and there is a great deal of heterogeneity in the literature in terms of subject recruitment, sample size, and estimations[2]. In general studies of MSM reporting to sexual health clinics or presenting to care with an STI estimated relatively high prevalence, though perhaps an overestimate of the characteristics of the whole community[2]. New landmark research comparing heterosexual, bisexual, and homosexual men and women has provided invaluable insight. Across all groups chemsex was prevalent, however it was significantly higher in homosexual men[9]. Specifically, homosexual and bisexual men had statistically significant higher rates of use of cocaine, methamphetamines, GHB/GBL, MDMA, Mephedrone, phosphodiesterase inhibitors, inhaled nitrates, and ketamine as evidenced by Table 1.[9]

	Men				χ^2 between orientations within men
	Heterosexual	Homosexual	Bisexual	Total men	
Alcohol	6,966 (60.2%) [1]	710 (58.0%) [1]	551 (58.5%) [1]	8,227 (58.5%) [1]	$\chi^2 = 3.041$, $P = .219$
Cannabis	4,535 (39.2%) [2]	322 (26.3%) [2]	367 (39%) [2]	5,224 (37.0%) [2]	$\chi^2 = 78.465$, $P < .001$
Cocaine	1,172 (10.1%) [4]	173 (14.1%) [6]	88 (9.3%) [4]	1,433 (10.2%) [4]	$\chi^2 = 20.242$, $P < .001$
GHB/GBL	83 (0.7%) [9]	120 (9.8%) [8]	16 (1.7%) [9]	219 (1.6%) [9]	$\chi^2 = 582.407$, $P < .001$
Ketamine	233 (2%) [6]	62 (5.1%) [9]	29 (3.1%) [7]	324 (2.3%) [7]	$\chi^2 = 47.014$, $P < .001$
MDMA	1748 (15.1%) [3]	262 (21.4%) [3]	169 (17.9%) [3]	2,179 (15.5%) [3]	$\chi^2 = 36.141$, $P < .001$
Mephedrone	132 (1.1%) [8]	52 (4.2%) [10]	15 (1.6%) [10]	199 (1.4%) [10]	$\chi^2 = 74.980$, $P < .001$
Methamphetamine	150 (1.3%) [7]	134 (10.9%) [7]	27 (2.9%) [8]	311 (2.2%) [8]	$\chi^2 = 467.445$, $P < .001$
Poppers	80 (0.7%) [10]	238 (19.4%) [4]	47 (5%) [6]	365 (2.6%) [6]	$\chi^2 = 1525.796$, $P < .001$
Viagra	543 (4.7%) [5]	214 (17.5%) [5]	78 (8.3%) [5]	835 (5.9%) [5]	$\chi^2 = 325.375$, $P < .001$
Total number of people in this group	11,577	1,225	942	14,050	

Table 1. Chemsex Prevalence A tabulation created by Lawn W, Aldridge A, Xia R, Winstock AR (2019) of the percent of participants that reported "Yes, I have had sex while on this drug in the last 12 months" stratified by self-reported sexuality.[9]

Use of methamphetamine, GHB/GBL, and poppers represented the greatest difference between MSM and heterosexual men, and the researchers concluded both that chemsex was a significant problem in MSM and that targeted measures for this group were warranted[9]. Variation in use patterns differ by country, further complicating confluence in literature reviews. In the United States it is likely that crystal methamphetamine represents the drug contributing most to chemsex, however polydrug use is also reported to be common[8,10].

1.1.3 Barriers and Opportunities in Treatment

As a problem there are three dynamics to chemsex that make it difficult to address: chemsex users do not view themselves as addicts and often do not present to care in addiction medicine or psychiatry[11-13]; use is thought to be fed by minority stress and internalized homophobia meaning potential solutions require an intersectional approach[14,15]; and there are no pharmacologic treatments for addiction to methamphetamines or GHB/GBL[10,16].

There is no single answer in the literature to why chemsex users differ in self-perception as compared to the prototypical patient seen in addiction care settings. It is suggested that chemsex users may be more likely to have steady employment and social support, making them less likely to have a pathological view of their substance use[11]. One way this dissonance can be explained is through the cultural concept of the "weekend warrior", a homosexual man with a stable, potentially high paying job who only participates in chemsex activities on the weekends. Such men present to society as successful and in control, however the danger lies when chemsex use crosses over into the work week, an unpredictable event trending towards an unstable spiral. The stereotype of the "circuit queen," as well as culturally defined space also prove useful in attempting to understand the variant perspective of chemsex users. The element of defined space is pertinent to consider in both describing chemsex ecosystems, and modeling interventions[17]. Specifically, it is important to note the relationship between chemsex and the typified "gay scene," urban districts with high concentrations of gay men, nightlife, and sex venues: clubs, saunas, and cruise bars[13]. Regardless of the

syndemics at play, the cognitive dissonance between self-perception, experienced risk, and quality of life has been verified in the data. In a UK study, more than half of gay chemsex users reported feeling that their drug use had no negative impact on their life despite evidence that an increasing number experienced both social and sexual health consequences[6]. Additionally, even for those who do seek help, typical addiction medicine and psychiatry practitioners may be ill equipped to assist these patients as usage patterns are distinct from opiate users—the population of substance users receiving the most attention from practitioners at this juncture[18].

To the second dynamic, there are described societal pressures that have created the disparity in prevalence such that chemsex is most prevalent in MSM by wide margins[9,19]. The association-between substance use and various psychosocial factors affecting MSM is well documented: these factors include minority stress, experienced discrimination, and internalized homophobia[20-22]. Social determinants of health have similar negative outcome associations for other marginalized identities, such as racial minorities[23]. Therefore, having multiple identities and their related forms of discrimination increases the odds of having a substance use disorder—a claim supported by multivariate analyses [24].

While no pharmaceutical interventions exist for methamphetamine or GHB/GBL addiction, harm reduction efforts as well as behavioral and community interventions exist and have been proven effective[12,25,26]. Pre-exposure prophylaxis (PrEP) has been proven to be an effective strategy to reduce the risk of HIV seroconversion in chemsex users[27,28]. Safety counseling in an environment free of discrimination has also been shown to be an effective and attractive option for people who participate in chemsex [18].

1.2 Statement of the problem

As chemsex users rarely present to addiction specialists, and harm reduction in chemsex requires a holistic approach that addresses the syndemics of discrimination of and minority stress, it is a topic well suited to primary care. However, primary care providers lack the knowledge to screen and identify chemsex users, and provide appropriate safety counseling. This demonstrates a need to educate primary care providers, specifically those practicing in or near urban "gay centers," in chemsex screening, identification, and intervention. However, no current research exists demonstrating the effect of an educational training program for practicing primary care providers on relevant outcomes such as rates of screening for chemsex behaviors in male patients.

1.3 Goals and Objectives

The goal of our study is to determine if an integrative, multimodal training program on screening for chemsex behaviors, identifying users, and providing safety counseling is an effective strategy to improve the rate of chemsex behavior screening in urban primary care clinics in New York City. We also aim to determine baseline chemsex screening prevalence in urban primary care practices. Utilizing a cohort stepped-wedge cluster randomized design, our primary objectives will be to:

1. Form a statistical estimate of the baseline prevalence of chemsex screening in urban primary care clinics in New York City.

2. Determine if a multimodal training program has a significant effect on the relative risk of chemsex screening in male patients as compared to control periods.

Our secondary objectives are to:

1. Determine if the intervention increases the proportion of male patients who receive chemsex safety counseling.
2. Determine if the intervention increases the proportion of male patients with a documented sexual history.

1.4 Hypothesis

There will be a statistically significant increase in the proportion of male patients receiving chemsex screening during the intervention periods by urban primary care providers who have completed an integrative, multimodal training program as compared to the control periods.

1.5 Definitions

Training Program: The integrative, multimodal training program is a continuing medical education style activity inclusive of print material, interactive online resources and case based learning activities, and an in-person didactic and patient role play session.

Chemsex behaviors: Behaviors relating to the use of drugs before or during intercourse to enhance or facilitate the sexual experience. Enhancement through the elevation of pleasure sensations and/or duration of intercourse, and facilitation by anxiolysis and lowered inhibition.

Safety Counseling: Dialogue between patient and provider about harm reduction opportunities based on a patient's specific needs, risks, and patterns of drug use.

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CHAPTER TWO - LITERATURE REVIEW

2.1 Introduction

Review of the current literature demonstrates that there are no studies or reviews on educating primary care providers on chemsex nor the effects of interventions on rates of chemsex behavior screening or relevant patient outcomes. Chemsex itself is a novel topic with the majority of articles published after 2015. While we cannot present research on the association between provider education and chemsex screening rates, we can present research on key points that guide our study rationale, namely:

1. Articles that describe a need in primary care for sexual and gender minority (SGM) health education.
2. Descriptive articles on screening rates in men who have sex with men.
3. Articles demonstrating that multimodal continuing medical education (CME) programs increase screening rates.

The first two topics demonstrate the need and novelty of our proposed experiment, while the last informs our approach in developing an intervention and plan for analysis.

We utilized Ovid Medline and Scopus to conduct a comprehensive literature search in December of 2019. We placed no restrictions on date of publication or language due to the novelty of our topic and scarcity of articles. Article titles and abstracts were reviewed to determine relevance and significance. In Scopus, keywords and synonyms we used in our search included: chemsex, sexualiz(s)ed drug use, party and play, sexualized drug taking, sexualized drug abuse, substance linked sex, and screening. Our secondary search included the key terms: continuing medical education, graduate medical education, screening rates, screening, prevention, behavioral intervention, primary care,

men who have sex with men, and sexual and gender minorities. Terms were recombined in novel ways to broaden scope, and the search within feature was utilized to find articles relevant to our study. Reference lists of select publications were also reviewed for relevant studies. In Ovid Medline subject headings identified and utilized were: medical education and graduate medical education. Chemsex, prevention, and screening rates were utilized along with subject headings to refine the search. Articles included in our literature review proved relevant to one of three aforementioned foci, and can be categorized as reviews, descriptive studies, experimental studies, and educational studies.

In addition to our comprehensive literature review, we conducted a supplementary search on Scopus for the purpose of describing the protocol, benefits, and disadvantages of stepped-wedge cluster randomized trials as they are a relatively uncommon design. Search terms used included stepped-wedge cluster randomized trial in combination with sample size, advantages, disadvantages, and protocol.

2.2 Review of Relevant Literature

2.2.1 Primary Care and Sexual and Gender Minority Health

Eleven articles were identified that describe the current state of sexual and gender minority (SGM) health knowledge and competency in primary care settings. There were six cross sectional surveys, one review article, three descriptive articles, and one experimental pre-post design study. The majority of articles were published within the past five years, which is important as large public health campaigns targeting health disparities have begun within the past decade, necessitating recent data to describe current needs. Despite social progress, all eleven articles described a lack of SGM health

knowledge as well as deficits in provider competence and confidence in caring for these patients. This section details a foundational need to educate primary care providers in SGM health including chemsex, a topic considered novel to this subject area.

Three cross sectional survey studies assessed primary care provider SGM health knowledge in the context of describing barriers associated with PrEP prescribing. One study reported that providers who provided care to patients with HIV were more likely to have knowledge of PrEP and SGM health, suggesting a role for provider interest in SGM health competency[1]. Another study surveyed patients instead of providers, and found that providers likely needed training not just in SGM health content but in providing culturally sensitive care to MSM and other SGM[2]. The third study supported these findings, but of note, the study specifically targeted providers in North Carolina making it less generalizable to providers in the Northeastern United States[3]. In sum, all three studies concluded that the largest barrier to PrEP prescription was a lack of provider knowledge.

A cross sectional survey of primary care providers in 2019 found that while 78% of providers felt comfortable treating SGM patients, they had deficits in health knowledge, proper screening and clinical management, and culturally competency relating to SGM patients[4]. Another study of SGM health knowledge in residents found similar deficits that were equivalent across residency years, demonstrating that these topics are often not covered in standard graduate medical training[5].

Multiple articles have detailed unique clinical considerations and the importance of targeted preventative health measures in MSM populations. Specifically, there is a described need for more provider education and organizational support[6], as well as a

need to improve preventative health screening rates and the sexual health care of MSM in primary care settings[7]. A cross sectional survey of MSM looking at primary care provider rates of recommended preventative services found that provider knowledge of sexual behaviors was key, and that educational efforts should be aimed at both providers and MSM to improve communication[8].

One cross sectional survey asked sexual health practitioners about their perceived needs for chemsex services, education on chemsex, and clinical management training. The researchers found that practitioners in surveyed clinics were aware of chemsex, and that there was a demand for more training regardless of the services the clinic currently offered[9]. This particular study was conducted in the United Kingdom, which limits its generalizability to the United States. However, the study supports that chemsex falls under the scope of general medicine and sexual health. A literature review investigating methods to address chemsex in MSM found that essential to getting patients to disclose chemsex behaviors was provider knowledge on chemsex and SGM health[10]. Additionally, the article purported the role of primary care providers who are able to open communication with patients about chemsex in connecting these MSM to services and offering safety counseling. This sentiment was echoed in an older descriptive article that argued the vital importance of the sexual history in managing the clinical care of patients who participate in chemsex[11].

2.2.2 Screening in Men Who Have Sex with Men

Ten articles were identified pertaining to sexual health and drug use screening in MSM in primary care settings. Five of the articles specifically looked at screening in HIV positive MSM, a sub-population that is better studied than HIV negative MSM. Overall

studies found a link between sexual risk behaviors and drug use, as well as a deficit in preventative sexual health screenings in MSM despite increased STI prevalence in this population.

A retrospective cohort analysis of HIV positive MSM in the Study to Understand the Natural History of HIV and AIDS (SUN) trial looked at the relationships between screening, STIs, and drug use in primary care. The researchers found that having an STI was associated with recreational drug use, especially polysubstance use and chemsex substance use[12]. The original prospective cohort of the SUN trial was HIV positive men seen in primary care in five US cities. The researchers concluded that in HIV primary care better screening and substance use management was needed[12]. A prospective survey and drug toxicology study in HIV positive inpatients found high prevalence of drug use and higher likelihood of drug-related admissions as compared to a HIV negative control group[13]. Additionally, in the study cohort chemsex substances including amphetamines, GHB/GBL, and ketamine were exclusively found in MSM with high prevalence, warranting formal screening and referral processes for HIV positive inpatients[13]. However, this study was conducted in the United Kingdom where providers practice within an integrated health system that has greater awareness of chemsex. Therefore, the generalizability may be limited, and there is a potential for bias.

In a retrospective cohort study again looking at HIV positive MSM, researchers found a high prevalence of substance use, as well as co-occurring mood and anxiety disorders that were under-identified in primary care[14]. Another study in HIV positive men similarly reported a high prevalence of STIs and substance use including chemsex, supporting the need for improved screening and inclusion of chemsex into the standard

sexual history[15]. A retrospective cohort study with a large sample size of urban-residing HIV positive MSM seen in primary care found that over 50% of subjects had used substances within the past three months, including over 20% who used crystal methamphetamine, a chemsex substance[16]. This study however did not address frequency of use, which is relevant both for management purposes as well as future research.

A literature review examining drug and alcohol screening found that screening, treatment, and referrals for drug use were plausible and beneficial in primary care settings[17]. A cross sectional study of primary care providers found low rates of syphilis screening in MSM patients, and provider educational needs regarding STIs in MSM[18]. Specifically, researchers found women were more likely to receive screening and testing despite the fact that syphilis primarily affects MSM[18]. A cross sectional study of Black MSM in Washington DC found that rates of preventative screenings were lower in regular primary care centers than in community health centers[19].

Two cross sectional studies assessed general STI screening in MSM. One study set in Massachusetts found that STI screening rates were low, there was a high prevalence of risky sexual behavior, and that MSM who identify as bisexual had an increased risk of not receiving appropriate screening [20]. The other study looked at a larger set of data from the US overall and found that STI screening in MSM nearly met the Center for Disease Control and Prevention (CDC) goal of once annually, but with large gaps along key demographics and risk behaviors, warranting more targeted screening practices[21].

2.2.3 Continuing Medical Education Activities to Improve Screening Rates

Nineteen articles evaluating the effects of educational interventions on preventative screening were identified. Interventions designed to improve screening varied between studies in terms of length, online versus in-person, interactive versus didactic, and knowledge assessment format. The success of interventions on improving preventative screening was wide ranging with some studies reporting no significant effect, and others large increases. The majority of articles assessed continuing medical education (CME) style activities. While there was great variability regarding study design, prevention topic, and activity, themes emerged guiding the creation of future interventions.

A literature review on educational interventions to improve rates of chlamydia screening compared the effectiveness of different educational intervention designs and reported a comprehensive meta-analysis. The authors found that singular activities such as distributing printed educational materials or holding a didactic CME activity produced only modest improvements, if any[22]. The most effective interventions were multimodal, using combinations of distributing printed materials for patients and providers, in-person provider outreach activities, digital reminders, and didactic CME activities[22].

Another literature review examining interventions to increase colorectal cancer screening in African Americans purported that interventions that addressed the populations' self-risk perception and increased provider confidence provided the most promise[23]. The generalizability of that review to our study may be limited given its specificity in terms of population and screening. Similarly, another article described a non-randomized controlled study of a multimodal media and provider education campaign to increase colorectal cancer screening in Vietnamese Americans[24]. Given the

cultural specificity of the described interventions, the study's results are unlikely to be generalizable to another culture and screening topic.

One randomized controlled trial and one prospective cohort study specifically looked at the effect of stand-alone one hour CME activities on screening. Both found that a CME activity alone had no statistically significant effect on screening[25,26]. Neither trial included a true control group; the one-hour CME activities in both cases were compared to a more effective intervention: a patient mailer or a digital provider reminder. The aim of both studies was to increase colorectal cancer screening, which generally remains a difficult goal due to low patient acceptability and interest[27]. Despite these threats to study validity, taken in context with the evidence presented in the reviews, it is likely that a brief CME activity alone is not enough to change provider behaviors.

Three randomized controlled trials utilized digital technology in their interventions. Digital interventions described in these trials included both standard CME style online-modules, as well as longitudinal case-based learning and practice question models. All three studies reported positive results; however, the study utilizing a standard CME module reported only a decreased slope of screening decline in the intervention group[28]. While the study concluded that it favorably influenced provider screening rates, the failure to show a statistically significant improvement from baseline screening rate supports the theme that stand alone CME activities have minimal effects on screening rates. The other digital intervention studies reported much more favorable results, with one study reporting improved knowledge outcomes compared to standard education[29]. The third study reported results demonstrating that a digital education intervention was not only equivalent in effect to in-person training in terms of knowledge gains, but lead to

a statistically significant practice change, in this case rate of guideline-directed pharmacotherapy prescription[30]. This practice change was in comparison to both the in-person training and the no-intervention control group, supporting the utility of interactive online CME style activities in affecting screening rates.

Six experimental studies with no control group comparisons reported favorable outcomes using various educational interventions. One study looked at pre and post self-reported pharmacotherapy prescriptions rates after a brief educational intervention. The investigators found that the intervention had a positive effect on prescription rates[3]. Considering that the study had providers self-report the outcome and there was no control group, the study validity must be questioned. Additionally, in the post-intervention survey less providers responded, and it is likely that those who did had an interest in the study topic, which could have introduced selection bias into the results. Two studies examined the effect of education programs in combination with tools including screening forms. Both studies reported promising results in improving STI screening in MSM, demonstrating a benefit in including screening tools in educational interventions aimed at increasing preventative screening in MSM[31,32]. Another study examined the effect of a digital education intervention on LGBT health knowledge and provider confidence, and found the intervention produced a positive result[33]. A similar pre-post test study found that case-based CME improved provider LGBT health knowledge[5]. Without a control the generalizability of this study is limited; however, it adds to the library of studies using online interventions to target screening and knowledge goals in minority health disparities. Finally, another study with a robust pre-post experimental design analyzed the effect of skills-based CME on five different preventative screening topics. The

investigators stratified the data across different clinical settings (urgent care, primary care, women's health) and found that across all settings the CME activities increased the risk of screening[34]. The study included a large sample size, and reached statistical significance for all outcomes. However, the study's biggest threat to validity is that it did not include a control.

Three other non-randomized controlled trials examined the effect of CME and video learning on screening rates. The first study found that a systematic approach to developing a quality CME produced a significant increase in screening and referral rates six months post intervention[35]. While including a control and having longer follow-up periods produced quality data, this study is markedly older than any others included in our search, making its generalizability to contemporary medicine of concern. Another study investigating a CME activity for sleep problems found that the intervention was effective at both increasing screening and improving treatment rates[36]. While the study showed strong results between intervention and control on relevant outcomes, the study measured its outcomes via patient report. Patient report avoids bias from providers self-reporting their own positive practices however, it is not as objective as chart review or other concrete measures that prevent the introduction of bias. It is worth noting that in a study comparing chart review to patient report in measuring preventative screening in resident physicians, patient report was accurate except in vaccination and smoking[37]. Given that these topics carry social stigma, it is likely that patient report is an accurate measure of screening except in cases where the topic is vulnerable to social desirability bias. The final non-randomized controlled study found that a video training on social determinants of health led to a statistically significant increase in screening of two out of

six measured social determinants of health[38]. One of the patient outcomes, free formula distribution, also reached statistical significance post intervention[38]. While the study did not reach statistical significance on all their outcomes, the results suggest educational videos can have a positive effect on screening rates.

2.3 Review to Identify Possible Confounding Variables

Six articles were identified related to identifying potential confounding variables for our proposed study. Three articles described characteristics of primary care providers with the potential for confounding. A cross sectional survey found that female sex, teaching hospital affiliation, urban location, and having a systematic approach to screening sexual behavior were associated with provider identification of MSM[39]. As ascertainment of sexual behavior is the first step in providing appropriate screening, it follows a homogenous sample with aligning characteristics could cause positive confounding. A literature review describing the best methods for providers to assess for chemsex found that provider communication skills were linked to patient disclosure[10]. A cross-sectional study found that 80% of surveyed providers were concerned that collecting sexual orientation and gender identity routinely would offend patients[40]. Thus communication skills and provider bias are also potential confounders.

A retrospective cohort study evaluated the effect of housing status on risk of sexual health screening in HIV positive MSM. The researchers found that homelessness, irrespective of time spent in care was associated with a decreased risk of preventative screening[41]. A cross sectional study of young adult gay men in New York City found that attending school and having insurance were positive factors related to seeing a primary

care provider[42]. Overall, SGM status was associated with less access to primary care, with fear of being outed and unknowledgeable providers described as specific concerns in this population[42]. Another cross sectional study linked disclosure of sexual orientation to rates of appropriate screening[8]. In sum, patient characteristics with the potential risk for confounding include housing status, socioeconomic status, healthcare access, fear of discrimination, and disclosure of orientation to providers.

2.4 Review of Relevant Methodology

2.4.1 Overview of Stepped-Wedge Cluster Randomized Trial Design

Once a novel study design, stepped-wedge cluster randomized trials (SW-CRT) have grown in popularity in contemporary research due to their unique advantages. Because the SW-CRT was a new methodology to us, we decided to conduct a literature review on its use to be certain that it was the best approach for our study. Therefore, we are including the result of this review in this chapter as opposed to the following chapter on methodology. In the latter, we "pick up on" the information gained from our literature review and specifically describe how we use the SW-CRT in our research design.

In a published literature review of contemporary trials, the majority studied educational interventions aimed at evaluating the relationship between training and behavioral change[43]. A SW-CRT is unique in that in the course of the study, all clusters experience an initial control period followed by a transition to an intervention period at different stepped time points[43]. The control in the SW-CRT is made of the same cluster, but at an earlier time period. As the design allows for within cluster comparison, there is less variance in treatment effect[44]. A literature review of the advantages and

disadvantages of the SW-CRT reported that the design is best for pragmatic trials of interventions that are both likely to be beneficial and unlikely to cause harm, such as interventions aimed at promoting preventative screening[45]. Additional benefits of the design include that it reduces the need for stringent inclusion/exclusion criteria allowing for a better estimate of an intervention's real world effect; it better accounts for temporal effects on an intervention; there is better differentiation of intervention effect from standard of care; and there are logistical benefits such as a smaller number of clusters required compared to parallel designs[45,46].

As compared to standard parallel cluster randomized trials, the SW-CRT has unique limitations and considerations. Multiple studies have detailed that the design is more vulnerable to participant drop out and loss to follow up, making *a priori* suspicion of any adverse effects associated with an intervention a relative contraindication[44,45]. Depending on the length of each time period, measurement burden on participants and researchers is important to consider[44]. Additionally, blinding is not possible and there is a greater risk of contamination within the cluster data[45]. Given these considerations it is important to carefully evaluate the suitability of a SW-CRT over a parallel design based on study aims and characteristics of the proposed intervention.

2.4.2 Sample Size in Stepped Wedge Cluster Randomized Trials

Multiple studies have documented the difficulties of sample size calculations in SW-CRT designs as well as a lack of proper reporting of sample size and analysis methodology[43,46,47]. When considering different approaches to the sample size calculation, it is likely that simulation-based methods are the most dynamic and utilitarian approach[48]. In simulation-based calculations of sample size it is necessary to

calculate a correction factor using parameters of the study design including number of cross over points, and number of measurement points per cross over[49]. In our study, we have opted to conduct a simulation-based calculation[47,49-52]. The parameters and methodology of our sample size calculation are described in detail in Chapter Three.

2.4.3 Intervention and Outcome Variables

Section 2.2.3 describes in detail the literature on the designs of various educational training programs and their efficacy in improving knowledge scores and screening rates. Based on our comprehensive literature review, an integrated, multimodal educational intervention is likely to have the highest chance of success in improving rates of chemsex screening. Specifically, a multimodal intervention should include skills based exercises and role play[34]; use tools like screening forms[31,32]; include videos and online components[28,30,38] ; and use email and chart reminders to increase provider participation[53,54]. In a literature review of sexual health screening in primary care, interventions that used monomodal educational interventions were found to be less effective at positively altering provider behavior[22].

The majority of studies included in section 2.2.3 measured outcomes in terms of proportion of patients screened before and after intervention. Methods to determine these proportions included provider report[55], patient survey[38], and chart review[30]. A study specifically comparing chart review against patient survey found that patients under-reported screening for sensitive topics, in this case vaccination and smoking cessation[37]. Given the sensitivity of our subject, it is vulnerable to social desirability bias. As electronic record systems that support de-identified review are ubiquitous in large urban

health networks, chart review is likely the most appropriate and objective option for our study.

Proportions in the studies in section 2.2.3 were compared before and after intervention using simple statistical tests like chi squared[3] or Fishers exact test[30]. However, there is no validated absolute difference in screening rate that is clinically meaningful for our study population, setting, or screening topic in the literature. As it would be inappropriate to pick an arbitrary difference (e.g., change in proportion screened), and pre-determining a significant effect is important for the sample size simulation and ensuring proper study power, with guidance from a statistician experienced in SW-CRT, we decided to operationalize our data as a relative risk (RR=proportion screened during active intervention/proportion screened during control period). Specifically, we took guidance from a robust study analyzing the effect of interactive CMEs on five types of preventative screening in primary care to formulate our power calculation and variable operationalization[34]. This study was set in primary care, used a multimodal educational intervention, and looked at drug and sexual health preventative screening making it an appropriate model based on our study goal and objectives. The exact methodology of our power calculation and variable operationalization are described in detail in Chapter Three.

2.5 Conclusion

Overall, there is a body of evidence and expert opinion that confirms a lack of sexual and gender minority health knowledge in primary care, including MSM chemsex behaviors. There is also evidence that preventative screening rates in MSM populations

are low, and that provider education can have a positive impact on rates of preventative screening. Our study rationale then follows that an educational intervention aimed at primary care providers can improve the rate of chemsex behavior screening. A stepped wedge cluster randomized design is uniquely suited to this task as we are analyzing a novel topic and the design allows us to calculate a precise baseline prevalence in our study population, as well as get a better sense of our intervention's real world effect. Furthermore, minimal exclusion criteria for providers are necessary for the design, and the direct comparison of the same group between control and intervention will allow for a better analysis of the intervention's effect. Additional advantages of the design are described in section 2.4.1. While there are no biomedical interventions for chemsex[56], screening represents the next step in an appropriately addressing this epidemic.

2.6 References

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CHAPTER 3: METHODS

3.1 Study Design

This is a cohort stepped wedge cluster randomized control trial. Outcomes will be assessed by tabulating simple frequencies of study variables from review of regular patient charting and converting them into proportions of all male patients for analysis. In this study each clinic (k=18) will be a cluster, and clusters will be stratified by three geographic locations. Implicit bias and attitudes will be assessed upon enrollment and at the end of the twelve month study period to control for possible confounding using the Harvard Implicit Association test and the Gay Affirmative Practice Scale (Appendix A). A four month planning and recruitment period will precede phase one of the study.

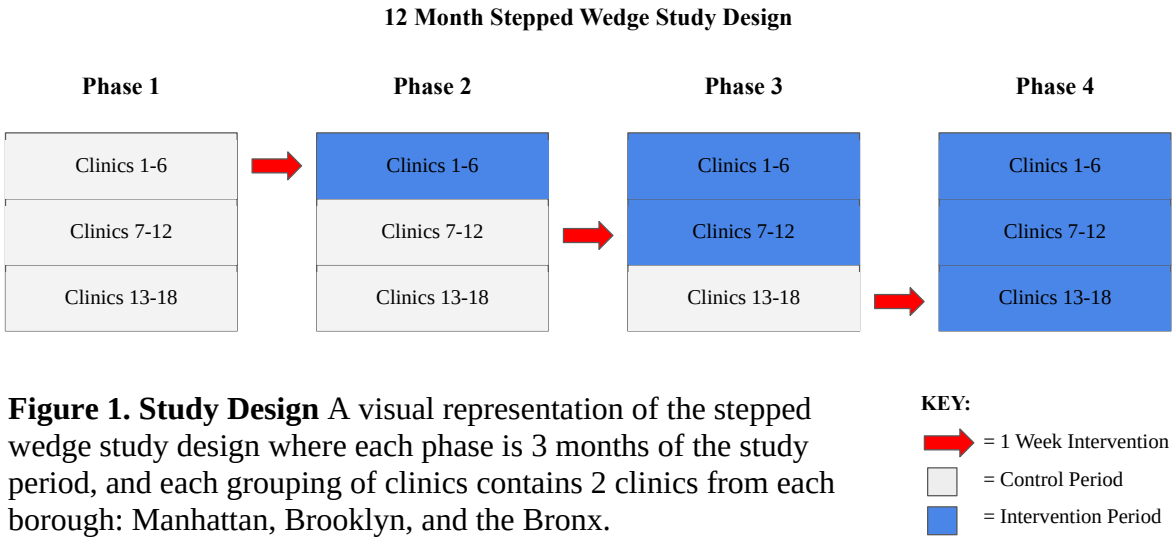

Figure 1. Study Design A visual representation of the stepped wedge study design where each phase is 3 months of the study period, and each grouping of clinics contains 2 clinics from each borough: Manhattan, Brooklyn, and the Bronx.

3.2 Study Population and Sampling

Eighteen large primary care practices operating on electronic medical record systems that support deidentified chart review will be selected by convenience and

willingness to participate. Large practices will be defined as practices with ten or more providers. Six clinics will be chosen from each of the three New York City boroughs included in our study: Manhattan, Brooklyn, and the Bronx. These boroughs were selected as they contain large healthcare conglomerates and "gay centers" or areas with concentrations of gay oriented nightlife. The study population will be participating health care providers at each of the study clinics. As patient-level outcome information collected from the study population will be anonymized and aggregated into counts screened – for example – among the total number of male patients seen during a study phase (every 3 months) - no informed consent from patients will be necessary. The intervention will be administered at the primary care provider level (physician associates, nurse practitioners, and physicians), among providers volunteering for the study in the eighteen participating primary care practices.

Inclusion criteria for participants will include the following: (1) Hold an active medical license and be in good standing; (2) be employed full time at a participating primary care center located in Manhattan, Brooklyn, or the Bronx; (3) self-report providing direct patient care to an average of at least five patients per eight hour work period; (4) provide care to male patients. The purpose of these criteria are to ensure that outcomes are not diluted by care practitioners who serve part time in administrative roles, or who have minimal patient panels. Requiring active licensure and full time employment provides basic quality control, as all such participants must have completed an accredited health professional training program in order to achieve licensure. As the study intervention focuses on screening a subpopulation of male patients, a substantial portion

of a given provider's patient panel must be male in order to measure the intervention's effect.

We will also collect provider-level information with regard to prior self-reported completion of a sexual and gender minority educational training program, such as a concentration course at a health professional school, LGBTQ+ health learning conference, or an online certificate program. This information will be used in the sensitivity analyses of the outcomes of interest, to examine whether in addition to the active intervention period, health care provider's experience might also have a positive effect on screening.

3.3 Subject Protection and Confidentiality

Prior to the start of the study, all details and required documents will be submitted to the Yale University Institutional Review Board, including a waiver of all consent and waiver of privacy authorization. Our study falls under category five expedited review. Review of patient medical records will solely be to measure the number of male patients, tabulate frequencies of provider documentation of chemsex screening, sexual history taking, and chemsex safety counseling. No identifiable information will be collected on any patients, and chart review will utilize electronic medical record systems allowing for de-identified review. The study will meet criteria for waiver of consent as it poses minimal risk and does not affect the welfare or rights of the patient. Reviewers will be using redacted charts without name, age, address, or other identifying information, and will receive training to only review encounters for documentation of study variables. Reviewers will only record simple frequencies associated with a de-identified provider

number. Patients will not be subject to any special tests, harm, or alterations in standard care as the study is a provider level intervention. De-identification of patient charts, protection of protected health information, and reviewer training will meet the standards required for a waiver of authorization and HIPAA privacy requirements.

Informed consent will be obtained from all providers that agree to participate in this study (Appendix B). Participants will be assured that no identifying information will be collected, and that no data will be reported back to their employer. At the end of the study period all of each provider's chart notes dated within the twelve month study period will be grouped and randomly assigned a number. Attitude surveys, and implicit associations tests will also be grouped with the assigned number. Investigators and chart reviewers will be blinded to the identity of the providers. After completion of the study and assignment of numbers to providers, no list of participants will be kept by the investigators, nor will any such list be published. Additionally, lists of participating providers will not be distributed to employers.

All hard copy consent forms will be stored in a secure, pass-coded location in a locked filing cabinet accessible only to the principal investigator. At the conclusion of the study all sensitive documents will be disposed of properly to ensure participant privacy and anonymity.

3.4 Recruitment

Providers will be recruited from the eighteen convenience selected large primary care practices in Manhattan, Brooklyn, and the Bronx. Generalist primary care practices with more than ten providers, inner city location, and electronic medical record systems

that support de-identified review will be contacted to participate in the study. Practices located in or near "gay districts," defined as districts with a concentrated volume of gay nightlife venues, will be preferred. Providers will be voluntarily recruited by posters hung in staff work rooms, direct emails, and inclusion on employer communications like newsletters. Recruitment will be facilitated by collaboration with administrative leaders at participating practices. All providers interested in participating will be directed to take an online eligibility survey (Appendix C) to determine eligibility and provide contact information for further communications and acquisition of informed consent. Recruitment communications will not detail the subject matter of the intervention to prevent the introduction of bias. Communications will only state that providers must commit to a one week educational training at some time during the twelve month study period. Recruitment will take place over the four-month planning and recruitment period preceding the twelve-month, four-phase study period.

3.5 Study Variables and Measures

The independent variable will be completion of a multimodal training program. Chapter Two reviews in detail the literature supporting multimodal interventions. Our health care provider level intervention will include print materials and screening forms (Appendix D), online resources (Appendix E), interactive online content, and a three hour in-person training session including review of supportive materials, didactic presentations, and interactive case based and patient role play activities (Content Blueprint Appendix F). All parts of the intervention will be completed within one week.

The timing of the training intervention will vary between clinics based on their placement within the stepped wedge design.

In our study, the exposure variable has two levels: (1) control period, where outcomes are observed under standard clinical practice, and (2) active intervention period where, once a practice is switched to receive intervention, volunteer health care providers will start participating in our training program and will then begin utilizing their acquired knowledge and skills in their practice.

Our primary outcomes are (1) baseline prevalence of chemsex screening in urban primary care clinics in New York City, expressed as proportion of chemsex screening among the population of male patients seen at a clinic during the first phase of our study (first 3 months); and (2) change in the rate of chemsex screening in male patients between the control and active intervention periods. Our secondary outcomes are (1) change in the rate of chemsex safety counseling among male patients screened positive during chemsex screening between the control and active intervention periods; and (2) change in the proportion of male patients with a documented sexual history between the control and active intervention periods.

Study variables will be measured by review of regular patient charting. We will use proportion of all male patients and not proportion of men who have sex with men to prevent possible confounding by differences in accuracy and rates of identification of men who have sex with men between the intervention and the control periods.

3.6 Assignment of Intervention and Blinding

Blinding of the intervention is not possible for researchers or the participants. Our study will use a stepped wedge design over a twelve month period (Figure 1). Clinics will be randomized into groups of six, made up of two clinics each from Manhattan, Brooklyn and the Bronx. Depending on which group their clinic is allocated to, participants will receive the intervention either three, six, or nine months after the initiation of the study period.

3.7 Adherence

Completion of the in-person portion of the training program will be verified by sign in and sign out at the beginning and end of the training. Completion of pre and post tests for the online learning, and completion of responses to online patient cases will also be verified to assure providers in the intervention group completed the training program.

3.8 Data Collection

Data will be tabulated from deidentified electronic chart review at the end of the twelve month study period. All visit notes from participating providers will be collected from the start of the study period through the last day of the study period twelve months later. For each deidentified provider reviewers will tally the total number of male patients seen during each phase of the study period, as well as the total documented instances of chemsex screening, chemsex safety counseling, and sexual history taking in male patient chart notes. The data will be clustered by clinic, and stratified into groups by burrow location, and categorized by study period (intervention or control). Implicit Bias tests and attitude surveys collected at enrollment and at the completion of the study period will be

associated with the provider number for the purpose of bias and attitude analysis and controlling of possible confounding.

3.9 Sample Size Calculation

As described in Chapter Two SW-CRT are not common, and therefore, there is no standardized closed-form analytical formula for sample size. In order to obtain a sample size and ensure the study is adequately powered we propose the following approach: Using the literature to guide us in estimating baseline prevalence and setting our effect size, we will calculate a sample size estimate. After phase one of our study we will then conduct a precise simulation-based sample size and power calculation as discussed below, using the references from section 2.4.2.

For the purpose of our preliminary sample size calculation we set an effect size of a 1.18 relative risk (RR=1.18) of screening, based on a study of the effects of interactive CME on multiple preventive screenings in the primary care setting that was most similar to our study in terms of intervention and aims[1]. Additionally, for the purposes of estimating baseline prevalence of screening (P2), we used a range of 0.05 (based on a study in a similar urban setting that found approximately 5% of patients are MSM[2]) to 0.30 (the reported proportion of patients screened for drug use in a literature review of drug screening in primary care[3]). We set statistical power at 90%, and significance level at 5% (two-sided alpha=0.05). We then conducted a sensitivity analysis for the smallest detectable proportion of screened male patients during the active intervention period (P1). Figure 2 shows the range of detectable values for P1, varying the number of male patients seen in a clinic during the study (m: from 10 patients to 100 patients), varying the

measure of within-clinic correlation in the outcome across time (IntraClass Correlation, ICC: from 0.01 to 0.10), and using 18 clusters (k=18 clinics), with 6 clinics being switched from the control to active intervention period during 3 steps (see Figure 1). For example, in Figure 2f, if the baseline prevalence of screening is 30% (P2=0.30) and ICC is 0.08, a sample of 18 clusters in a complete stepped-wedge cluster-randomized design with 4 time periods (including the baseline), 3 steps, 6 clusters (clinics) switching from control to active treatment at each step, and an average of 40 subjects per cluster with an average of 10 subjects per cluster per time period (for a total sample size of N=720 subjects) we will have 90% power to detect a difference between proportions of 0.06 (RR=1.18). The test statistic used is the two-sided Wald Z-Test.

We will revisit sample size at the end of the first phase in which all clusters will have finished the control period. At that time we will implement a series of simulations, using the same methods described above, to estimate a more precise sample size with adequate power to be able to detect the desired effect size of RR=1.18. Set variables in this simulation procedure will include the number of clusters (k=18 clinics) and time points (J= 4 three-month periods, meaning 3 steps or switches from control to active intervention), the average number of male patients seen in a clinic during phase I (m/4), and an estimated ICC and P2 from phase I. Our statistical power will remain at 90% and we will reject the null hypothesis of no difference in screening rate between the control and active intervention periods (H0: RR=1) at the two-side alpha of 0.05.

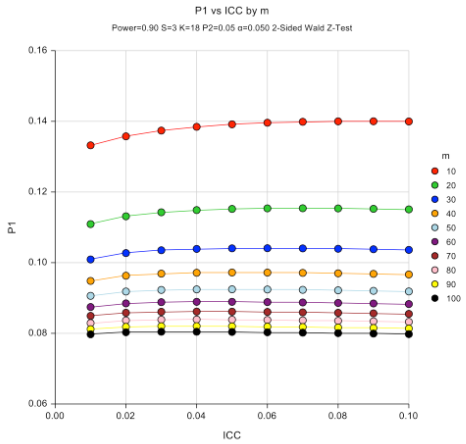

Figure 2a: Baseline Screening Prevalence, P2=0.05

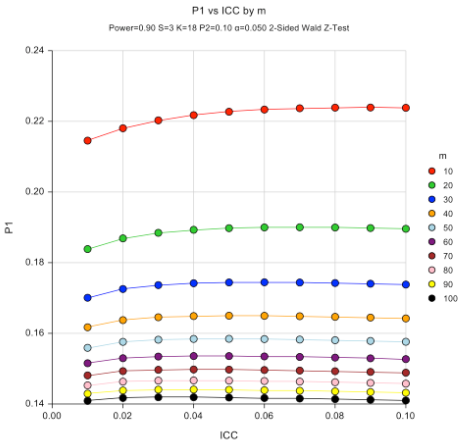

Figure 2b: Baseline Screening Prevalence, P2=0.10

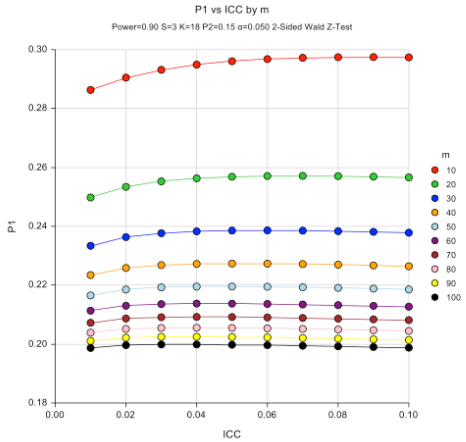

Figure 2c: Baseline Screening Prevalence, P2=0.15

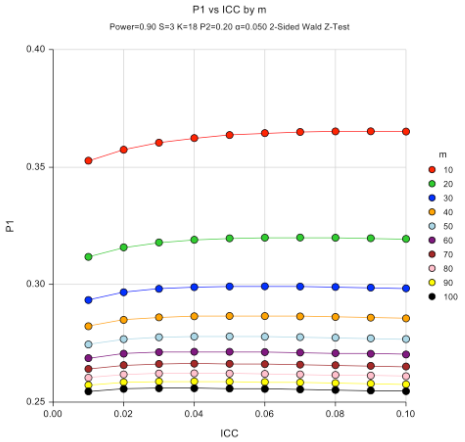

Figure 2d: Baseline Screening Prevalence, P2=0.20

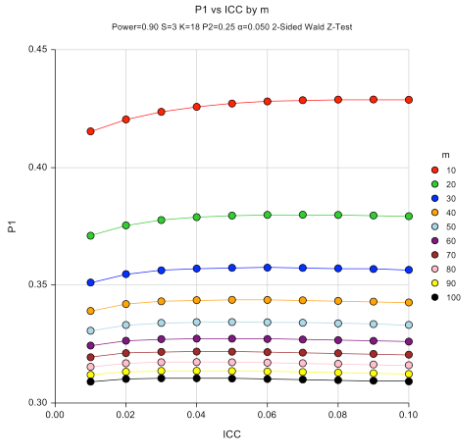

Figure 2e: Baseline Screening Prevalence, P2=0.25

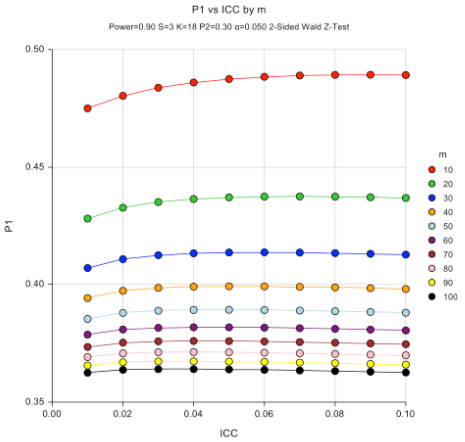

Figure 2f: Baseline Screening Prevalence, P2=0.30

Figure 2. P1 Sensitivity Analysis Range of smallest detectable proportion of screened male patients during the active intervention period (P1) where set power is 0.90, significance level is 5% (two-sided alpha=0.05), m is the number of male patients seen in a clinic during the study, ICC is IntraClass Correlation in the outcome across time, k=18 is the 18 clinics/clusters, and s=3 is the 3 steps at which 6 clinics are switched from control to active intervention period at 3-month interval staggered time points.

3.10 Analysis

Statistical analysis software will be used to analyze the collected data. Percentages will be calculated for each provider and data will be compiled and clustered by clinic, stratified by geographic region (Manhattan, Brooklyn, or the Bronx), and categorized by temporal study phase (intervention or control). A baseline prevalence of chemsex screening, expressed as a percent of all male patients with a confidence interval will be calculated using phase one data from the entire study sample, all eighteen clinics. We will use generalized linear mixed effects modeling (GLMM), to model $g(E(Y_{ilj}=1|X_i,b_{0i,}\ b_{0l}))$, which is the transformed probability (rate) of screening in a clinic *i* (*i*: 1…,*k*=18), for a health care provider (*l*:1,…,*p*), at time *j* (*j*:1,2,3,4 time periods), with the main effect of time period *j* (X_{2ij}), and the time-varying covariate X_{1ij}{1=Active intervention during a study phase, 0=Placebo during a study phase}. The actual models will be implemented on the aggregated counts of screens per clinic-per provider-per study phase, with an offset variable equal to the natural log of the number of male patients seen during a time period *j* in clinic *i* by health care provider *l*, and the link function g(.) for the mean response being 'log', so that we can obtain the estimate of relative risk (RR). We will incorporate a random intercept for each clinic (b_{0i}) and each provider (b_{0l}), which will allow us to estimate an ICC, in order to characterize the variability in the outcome of

interest across the different clinics (and across different providers). We will also conduct a per protocol analysis, including only data from providers who completed training.

By exponentiating the estimated parameter for the effect of treatment (X_{1ij}), we will obtain an estimated relative risk with surrounding 95% confidence intervals for the effect of the intervention on screening rate (i.e., proportion screened is actually the same as screening rate). Our secondary outcomes will be analyzed in similar fashion to the primary outcomes.

Scores from the Harvard Implicit Association test and Gay Affirmative Practice scale will be aggregated and compared between clinics, and the three geographic regions (Manhattan, Brooklyn, and the Bronx) using linear mixed effects models (LME), which is similar to GLMM but the outcome of interest is a continuous variable, so the link function will be Identity. This variable will also be used in the sensitivity analysis for the primary outcome model, but including it as a health-care provider level covariate.

3.11 Timeline and Resources

The planning and recruitment period will commence January 1, 2021 and will finish on April 30, 2021. The study period will begin on May 3, 2021 and continue until May 2, 2022. Phase one will end July 31, 2021. Phase two will begin August 1, 2021 and end October 31, 2021. Phase three will begin November 1, 2021 and end January 30, 2022. Phase four will begin January 31, 2022, and end May 3, 2022. The Intervention, including online learning, print materials distribution, and in-person sessions, will take place the first week of phases two through four for the assigned clinics.

The principle investigators will be John Encandela, PhD and Jona Tanguay, PA-SII. The study will be based out of the Yale School of Medicine with support from the Dean's Advisory Council on LGBTQI+ affairs and Veronika Shabanova, PhD from the department of Biostatistics. In-person training modules will be facilitated by Jona Tanguay, and participating practices will need to provide a classroom or break room for the training. A portable projector setup will be required for the in-person training sessions. A Yale Qualtrics account will be used to issue the eligibility survey, attitude surveys, as well as pre and post tests for the online content. An Information Technology professional will be needed to help translate the online learning content into an interactive format. The study will also require two research assistants to serve as chart reviewers, assist with data entry and analysis, and assist with communication with participating primary practice sites. Office space within the School of Medicine or Public Health will be required for the research assistants and principal investigators.

3.12 References

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CHAPTER FOUR: CONCLUSION

4.1 Advantages and Disadvantages

A strength of our proposed study is the novelty of its topic and design. Chemsex is a relatively well described problem, yet there is a large gap in medical literature relating to interventions to address the epidemic in everyday clinical care. While community efforts have value and efficacy as described in Chapters One and Two, there is a need in healthcare for chemsex education so that MSM can access the care, testing, and safety information they need. The design of our study, a SW-CRT, is also uncommon though not novel in terms of published literature. Design specific advantages are described in section 2.4.1. A number of studies have validated the use of the stepped wedge cluster randomized design for low-risk educational interventions aimed at preventative screening and behavioral change[1,2]. Considering our proposed goal and objectives, the design is thus well suited.

The complicated analysis inherent in the SW-CRT is considered by some to be a limitation[1]. However contemporary guidance aiming to simplify the analysis have laid out effective frameworks[3]. A further step to our analysis might have been to obtain clinic-level screening rates across study phases for all health care providers (not just those who were consented for this study) at each clinic to assess whether training a few providers can have a disseminating effect on clinics as a whole. However, this would have added an additional layer to the study that might go beyond the resources and time allotted, which are extensive. Should the study be expanded in the future or subsequent studies follow our framework, this aspect could be included.

Our design is superior to the many pre-post studies described in section 2.2.3 in that it has a control. As each cluster is its own control, the design is advantageous over parallel designs where such a precise level of control matching is unattainable. Additionally, our study protocol allows us to calculate an exact baseline prevalence across all clusters. However, our study like other SW-CRT is more vulnerable to being underpowered or failing to reach sample size[4]. To minimize this issue we employed a complex simulation procedure as described in Chapters Two and Three. Should the study fail to reach proper power after phase one the design is flexible and the study could either be conducted as a pilot or phase one could be extended and recruitment reopened.

The setting of our study is very specific, utilizing primary care centers only in three boroughs of New York City. While this a logical choice given the association of chemsex with "gay districts," which was discussed further in Chapter One, it risks sacrificing generalizability for the sake of utility. Our study focuses on districts that are likely to have a high concentration of men who have sex with men, especially MSM who might attend gay night life venues and participate in chemsex based simply on geographic availability. It follows then that the results of this study would be generalizable to other American cities with known "gay districts" and "gay scenes" such as San Francisco, Chicago, Boston, Washington DC, and Los Angeles. This gives our study utility to guide primary care practices in urban locations. However, at the same time it makes the generalizability of the study to suburban and rural areas low given the differences in culture, population density, and primary care provision. Furthermore, studies have described lower levels of sexual and gender minority (SGM) health knowledge and competence in primary care providers in the Southern United States[5].

Baseline differences in provider knowledge of chemsex and drug use in SGM populations may thus be an additional barrier to the generalizability of this study to other regions of the United States. It is also likely our study may be limited in its generalizability to other countries due to structural differences in health systems. However, as this will be the first study to focus on primary care providers and chemsex prevention, the study may serve as a model for others to expand upon in other systems and geographies.

Our study focuses specifically on men who have sex with men as studies have demonstrated chemsex is more prevalent in this population in comparison to heterosexual men and women[6]. However, heterosexual people still can and do participate in chemsex[6]. Transgender individuals are left out of the literature entirely, even though the prevalence of chemsex and related harms are likely similar or higher in transgender females as compared to MSM[7]. Though we do not include these populations in our study, future research may be indicated to better describe chemsex in these populations and determine appropriate interventions. Our study design might be instructive for these future studies.

4.2 Public Health Significance

There is a wealth of literature that describes health disparities affecting sexual and gender minorities. In research and in public health campaigns the focus primarily has been on addressing HIV in MSM. Substance use and substance use disorders are disproportionately prevalent in MSM and other sexual and gender minorities. Chemsex is a form of substance use distinct from the alcohol and opioid use disorders that primary care providers are trained in handling. Primary care providers, especially those in urban areas, are uniquely positioned to make a difference in this epidemic as they are the ones

who communicate and build therapeutic alliances with these patients in everyday practice. However in order to make a difference, providers need to know about these behaviors and have the information and competence to intervene. Should our study produce positive results, it would make a case for standardizing chemsex screening in urban primary care. Additionally, if effective our training program could be offered to primary care practices across all major American metropolitan areas. Increasing appropriate primary care intervention could substantially improve the disproportionate burden of chemsex on MSM communities and improve their productivity. Given the associations between chemsex and STIs/HIV, our intervention also has the potential to reduce the incidence and prevalence of these diseases in MSM which has positive ramifications for people of all sexual and gender identities.

4.3 References

1. Zhan Z, Van Den Heuvel ER, Doornbos PM, et al. Strengths and weaknesses of a stepped wedge cluster randomized design: Its application in a colorectal cancer follow-up study. *Journal of Clinical Epidemiology.* 2014;67(4):454-461.
2. Beard E, Lewis JJ, Copas A, et al. Stepped wedge randomised controlled trials: Systematic review of studies published between 2010 and 2014. *Trials.* 2015;16(1).
3. Campbell MJ, Hemming K, Taljaard M. The stepped wedge cluster randomised trial: what it is and when it should be used. *Medical Journal of Australia.* 2019;210(6):253-254.
4. Eichner FA, Groenwold RHH, Grobbee DE, Oude Rengerink K. Systematic review showed that stepped-wedge cluster randomized trials often did not reach their planned sample size. *J Clin Epidemiol.* 2019;107:89-100.
5. Clement ME, Seidelman J, Wu J, et al. An educational initiative in response to identified PrEP prescribing needs among PCPs in the Southern U.S. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV.* 2018;30(5):650-655.
6. Lawn W, Aldridge A, Xia R, Winstock AR. Substance-Linked Sex in Heterosexual, Homosexual, and Bisexual Men and Women: An Online, Cross-Sectional "Global Drug Survey" Report. *The journal of sexual medicine.* 2019;16(5):721-732.
7. Goldsmith D, Hillyard M. The lack of focus on trans women in a themed issue of the International Journal of Drug Policy on sexualised drug use. *International Journal of Drug Policy.* 2019;68:1-2.

APPENDICES

A. Gay Affirmative Practice Scale

GAY AFFIRMATIVE PRACTICE SCALE (GAP)

This questionnaire is designed to measure clinicians' beliefs about treatment with gay and lesbian clients and their behaviors in clinical settings with these clients. There are no right or wrong answers. Please answer every question as honestly as possible.

Please rate how strongly with you agree or disagree with each statement about treatment with gay and lesbian clients on the basis of the following scale:

SA = Strongly agree
A = Agree
N = Neither agree nor disagree
D = Disagree
SD = Strongly disagree

1. In their practice with gay/lesbian clients, practitioners should support the diverse makeup of their families. _____
2. Practitioners should verbalize respect for the lifestyles of gay/lesbian clients. _____
3. Practitioners should make an effort to learn about diversity within the gay/lesbian community. _____
4. Practitioners should be knowledgeable about gay/lesbian resources. _____
5. Practitioners should educate themselves about gay/lesbian lifestyles. _____
6. Practitioners should help gay/lesbian clients develop positive identities as gay/lesbian individuals. _____
7. Practitioners should challenge misinformation about gay/lesbian clients. _____
8. Practitioners should use professional development opportunities to improve their practice with gay/lesbian clients. _____
9. Practitioners should encourage gay/lesbian clients to create networks that support them as gay/lesbian individuals. _____
10. Practitioners should be knowledgeable about issues unique to gay/lesbian couples. _____
11. Practitioners should acquire knowledge necessary for effective practice with gay/lesbian clients. _____
12. Practitioners should work to develop skills necessary for effective practice with gay/lesbian clients. _____
13. Practitioners should work to develop attitudes necessary for effective practice with gay/lesbian clients. _____
14. Practitioners should help clients reduce shame about homosexual feelings. _____
15. Discrimination creates problems that gay/lesbian clients may need to address in treatment. _____

Please rate how frequently you engage in each of the behaviors with gay and lesbian clients on the basis of the following scale:

A = Always
U = Usually
S = Sometimes
R = Rarely
N = Never

16. I help clients reduce shame about homosexual feelings. _____
17. I help gay/lesbian clients address problems created by societal prejudice. _____
18. I inform clients about gay affirmative resources in the community. _____
19. I acknowledge to clients the impact of living in a homophobic society. _____
20. I respond to a client's sexual orientation when it is relevant to treatment. _____
21. I help gay/lesbian clients overcome religious oppression they have experienced based on their sexual orientation. _____
22. I provide interventions that facilitate the safety of gay/lesbian clients. _____
23. I verbalize that a gay/lesbian orientation is as healthy as a heterosexual orientation. _____
24. I demonstrate comfort about gay/lesbian issues to gay/lesbian clients. _____
25. I help clients identify their internalized homophobia. _____
26. I educate myself about gay/lesbian concerns. _____
27. I am open-minded when tailoring treatment for gay/lesbian clients. _____
28. I create a climate that allows for voluntary self-identification by gay/lesbian clients. _____
29. I discuss sexual orientation in a non-threatening manner with clients. _____
30. I facilitate appropriate expression of anger by gay/lesbian clients about oppression they have experienced. _____

Scoring instructions: Using the chart below, please give each answer the indicated number of points. After all questions have been answered, add up the total number points. Higher scores reflect more affirmative practice with gay and lesbian clients.

Items 1–15	Items 16–30	Points
Strongly agree	Always	5
Agree	Usually	4
Neither agree nor disagree	Sometimes	3
Disagree	Rarely	2
Strongly disagree	Never	1

B. Informed Consent Form

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Deidentified Provider Study
Principal Investigator (the person who is responsible for this research): Jona Tanguay, PA-S (Jona.tanguay@yale.edu)
Phone Number: 203-510-0005

Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to determine the effect of a multimodal continuing medical educational program on select patient outcomes
- Study procedures will include: participation in training program that will require no more than 10 hours of your time, including 3 hours of in person attendance.
- The study may have no benefits to you. The study may benefit your patients, and improve some select patient outcomes.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because you are a practicing primary care provider in Manhattan, Brooklyn, or the Bronx in one of the participating primary care centers.

Who is paying for the study?
Yale University School of Medicine

What is the study about?
The effect of a multimodal continuing medical education training program on select patient outcomes.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen: you will be randomly assigned to a group and you will be asked to complete an educational training program during one week of August 2021, November 2021, or February 2022. This will include an in person training session that is 3 hours long, as well as self-study online modules, quizzes, videos, and resources. The program should take no longer than 10 hours of your time total, and is confined to one week. You will also be asked to take surveys and implicit association tests at the beginning and end of the study period. During the study

period of May 3rd 2021 to May 3rd 2022 data will be collected from your patient charts using de-identified review.

What are the risks and discomforts of participating?
The study will pose no risks to your patients or to your employment. Your identity and participation will be kept confidential. The trainings contain sensitive topics, and you may experience mild discomfort. The trainings do not contain obscenity, or offensive content. The trainings do not advocate for any off label uses of drugs, or practices outside of standard medical procedure.

How will I know about new risks or important information about the study?
We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?
The study may provide you with useful tips for your practices that will help you better meet the needs of your patients.

How can the study possibly benefit other people?
This study may improve our understanding of how to address public health issues at the level of primary care. It may also benefit your patients If it improves the care they receive.

Are there any costs to participation?
If you take part in this study, you will not have to pay for any services, supplies, study materials or procedures. You will not be required to miss any work time, however during the week of the educational activities you will be asked to stay beyond the hours of your normal work week. You may also have to pay for additional transportation costs if the activities take place on days you are not scheduled to work.

Will I be paid for participation?
There will be no compensation for participating in this study.

How will you keep my data safe and private?
We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if we learn that you are hurting a child or an older person. At the end of the study all identifiable data will be erased and data will be coded with numbers. We will not publish a list of participants or inform your employer about your participation in this study. During the study any identifiable information will be kept in a locked cabinet in a secure location. All electronic data will be properly encrypted and password protected. When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission. We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission. We will not distribute any identifiable information or contact information for use in future studies.

What Information Will You Collect About Me in this Study?
We will only collect the minimum necessary information about you for this study. This includes basic demographic information on an eligibility survey including questions about

your healthcare training, what kind of role you have in your workplace, and characteristics of your patient panel. Additionally, we will collect surveys and implicit association tests from you twice during this study. Data will also be collected about your clinical practices via de-identified chart review. All of this information will be assigned to a randomized number, so that none of the data we collect after the study begins will be associated with your name or any identifiable markers.

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The study sponsor
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes.

What if I change my mind?

You may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to ***Jona Tanguay, PA-S, 100 Church St. South*** at the Yale University, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study. No new information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not give up any legal rights or benefits.

Not participating or withdrawing later will not harm your relationship with your employer or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. The researchers may withdraw you from participating in the research if necessary.

What will happen with my data if I stop participating?
As stated data collected in this study will be de-identified, meaning that it will not be possible to retrieve your data if you decide to no longer participate.

Who should I contact if I have questions?
Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 203-510-0005.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Appendix C. Provider Eligibility Survey

1. Please choose you practice from the drop down menu…

2. Do you hold a valid medical license in your state of residence?
    a. Yes
    b. No

3. Please select your medical qualification.
    a. MD/DO
    b. APRN
    c. PA-C

4. Are you currently being investigated by your supervising body? Is your license currently suspended? Have you ever been reprimanded or had your practice abilities revoked by your state medical board?
    a. Yes
    b. No

4. Are you a full time clinician in a primary care practice (defined as providing patient care ~40 hours per week)?
    a. Yes
    b. No

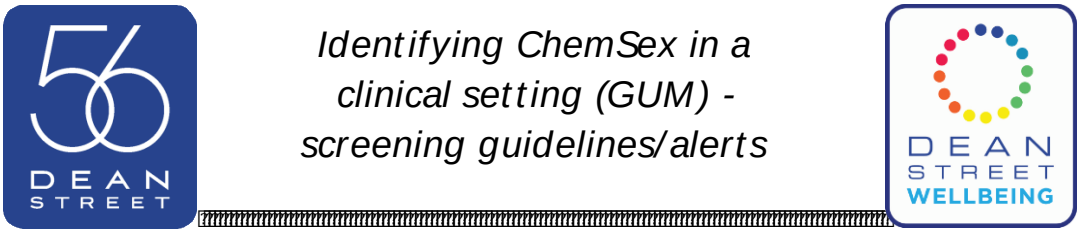
6. Do you spend part of your job time in an administrative role?
    a. Yes
    b. No

7. Do you provide direct patient care to at least five patients every regular work period (8 hours)?
    a. Yes
    b. No

8. Do you provide primary care to male patients?
    a. Yes
    b. No

9. Have you ever completed training in sexual and gender minority or LGBTQ+ health such as a medical school course, an online learning program, or a learning conference?
    a. Yes
    b. No

D. Print Materials for Screening



"Have you used drugs before/during sex in the last 6 months?"

- "If yes, Which? - Mephedrone/GBL/Crystal Methamphetamine?"

(i.e; emphasis on the recreational drugs that are associated with greater sexual disinhibition/sexual risk-taking).

- "If yes - Did you inject?"

(To highlight those needing needles/injecting advice, and to alert non-sexually transmitted infection risks).

- Finally a question that could trigger a call to action/reflection

(Examples; 'Are you happy with your level of drug use?', 'When did you last have sober sex?", " do you feel your drug use is negatively impacting your sex life or general wellbeing?"

Clinicians are encouraged to be particularly alert to the following risks;

- High number of sexual partners per ChemSex episode
- High frequency of ChemSex episodes
- Long gaps between GUM/HIV screens/poor engagement with GUM/HIV/HCV appointments
- Consistently poor condom use when using Chems
- High number of STIs in last 6 months/multiple reinfections of HCV
- High frequency of PEP presentations (if HIV-ve)
- Seroconversion symptoms, that might be disguised as a drug 'high' or a drug 'comedown'
- HIV+ve but not on treatment
- Consistently poor antiretroviral adherence if HIV+ve (enough to increase infectiousness/jeopardize viral suppression)
- Dependent GBL use (daily, beyond 7 consecutive days) which can be associated with potentially fatal withdrawal symptoms if use is discontinued suddenly.

56 Dean Street Survey

- We're running this survey to find out about the use of recreational drugs by our users.
- We would really appreciate it if you'd answer these questions.
- The answers will be used to help us improve our service.
- It's completely anonymous, your answers won't be traceable back to you.
- You do not have to complete the survey if you do not want to.
- Your answers will not affect the care you are given today.

Age _____

My Sex is _ Male _ Female _ Other (please specify) _____

Do you have sex with _ Men _ Women _ Both

What is your HIV status? _ Negative _ Positive _ I don't know

In the last 6 months have you used Post Exposure Prophylaxis (PEP)? _ Yes _ No _ I don't know

If yes, was this following sex whilst using drugs? _ Yes _ No

If HIV positive, and on treatment, do you sometimes forget to take your HIV medicines when high/on drugs?

_ Yes _ No

In the last 6 months have you used any of the following drugs before, or during sex? (please tick all that apply)

- _ Cocaine (Coke, Charlie)
- Ketamine (K, Auntie K)
- _ GBL/GHB (G, Gina)
- _ Crystal Meth (Tina, T, Ice)
- _ Mephedrone (Meph)
- _ Other _____
- _ None

If you have used any drugs in the last 6 months, please answer the questions over leaf.

How frequently have you used recreational drugs in the last 6 months? (Please circle)

Once	Once a month or less	A few times a month	Once a week	More than once a week	Daily

How strongly do you agree/disagree with the following statements: (please circle)

I enjoy taking drugs

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

I know how to use drugs in a safe way

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

If I wanted advice about my drug use I would know where to go

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

I feel like my drug use is having a negative effect on my sex life

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

I am more likely to have sex without a condom when I'm high/on drugs

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Does not apply to me

When I use drugs I do things sexually that I wouldn't do sober

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Does not apply to me

I am able to enjoy sex without using drugs

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree

If you wanted advice about your drug use, where would you prefer to get this?(Please Tick)

- □ My GP practice
- □ A standard drug service
- □ A specialist gay/lesbian/bisexual/trans* counselling service?
- □ A Sexual Health Clinic
- □ Somewhere else (Tell us where) _____

Thank you. Now put this questionnaire in the box on the reception desk, or hand to a member of staff.

E. Chemsex Online Resource Guide

- 56 Dean St London Clinic: https://dean.st/for-professionals/
  - Provider tools and resources including:
    - Informational videos on chemsex, risk assessment, and harm reduction
    - Care plans
    - Motivational Support tools
    - Chemsex first aid information
    - Patient Information
    - Print-outs for Patients
- National LGBT Health Education: https://www.lgbthealtheducation.org/#learn
  - Educational CME
  - Videos
  - Webinars
  - Conference Talks
- GGD Amsterdam: https://www.ggd.amsterdam.nl/english
  - Information on chemsex, STIs, and MSM health concerns
  - Descriptions of specialized MSM services and chemsex services
- Engage Montreal, CA: https://www.engage-men.ca/
  - Relevant literature
  - Oral presentations and slide show presentation on chemsex
    - Resource pages and sample services

F. Didactic Session Content Blue Print

- Chemsex Content Review
  - Epidemiology
  - Contextualization, partner finding, and significance of culturally defined spaces and roles
  - Review of chemsex substances and their effects
  - Review of appropriate harm reduction interventions and principles of harm reduction and safety counseling
- Chemsex Screening
  - How to utilize the sexual history and screening tools
  - Review of colloquial chemsex language
  - Creating a safe space, neutralizing stigma, and initiating patient centered safety discussions
- Resource Review
  - Review of supplementary online resources as well as required interactive online curriculum to be completed
- Interactive Learning
  - Patient-provider discussion role plays
  - Patient case based problem solving
  - Systems level creative problem solving cases
- Wrap up and Q&A

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