A narrative systematic review of sexualised drug use and sexual health outcomes among LGBT people

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Abstract

Introduction: Chemsex is a specific form of sexualised drug use (SDU) that is an emerging public health issue among men who have sex with men (MSM). Although the recent focus on chemsex is a reflection of the associated harms it is important to understand SDU more broadly and its associations with risk behaviours. Additionally, some of the reasons suggested for MSM engagement in SDU are also likely to apply to women who have sex with women (WSW) and trans people. The aim of this review was to investigate SDU, including chemsex, among lesbian, gay, bisexual and trans (LGBT) people internationally in relation to sexual health outcomes (HIV status, STI diagnosis, condom use).

Methods: Papers that were published between January 2010 and June 2020 reporting SDU in MSM, WSW, or trans people were identified through Medline, PsycINFO, CINAHL Plus and Web of Science. Results were synthesised using a narrative approach.

Results: The search identified 2,710 publications, of which 75 were included in the final synthesis. The majority of studies measured SDU among MSM (n=71), and four studies measured SDU among trans people. Research into SDU had been conducted in 55 countries and 32 countries had recorded the use of a chemsex drug among MSM, although the drugs used to define chemsex varied. Among studies that researched MSM, SDU was most commonly investigated in relation to condomless anal intercourse (n=42), followed by HIV prevalence (n=35), and then STI diagnoses (n=27). Drug use was generally associated with sexual health outcomes, but particularly in chemsex studies.

Conclusions: SDU research is lacking among WSW and trans people, despite trans women having a high HIV prevalence. Among MSM, most drugs were associated with sexual health outcomes, and therefore it is important to include both chemsex drugs and other drugs in SDU research.

Keywords: LGBT people; sexualised drug use; chemsex; systematic review; sexual health

Introduction

Sexualised drug use (SDU) is a term used to refer to sexual activities whilst under the influence of a wide range of drugs and substances, such as cannabis, amyl nitrates (poppers), and crystal methamphetamine and has been a topic of research among men who have sex with men (MSM) for some time (Bourne, 2012; Leigh & Stall, 1993). Chemsex (sometimes referred to as 'party and play') is a particular form of SDU whereby men engage in sex with other men for long periods of time with multiple sexual partners, typically taking one or more of crystal methamphetamine, γ-hydroxybutyrate/ γ-butyrolactone (GHB/GBL), methedrone, cocaine and/or ketamine immediately before or during sex to facilitate and enhance the sexual experience (Bourne, Reid, Hickson, Torres Rueda, & Weatherburn, 2014). Chemsex has become a public health issue over the last decade. Clinicians (Stuart, 2013) and men who engage in chemsex (Ahmed et al., 2016) report that this may be due to an increase in the number of people engaging in this behaviour, with geospatial networking apps and online sites used to meet sexual partners likely to have enabled this increase (Ahmed et al., 2016; Stuart, 2013).

Chemsex has been associated with injecting drug use and sexual risk behaviours such as condomless anal intercourse (CAI) and a greater number of CAI partners (Bourne et al., 2014; Glynn et al., 2018; Hegazi et al., 2017), as well as with a greater likelihood of sexually transmitted infection (STI) diagnoses and human immunodeficiency virus (HIV) (Gilbart et al., 2015; Glynn et al., 2018; Hegazi et al., 2017; Hibbert, Brett, Porcellato, & Hope, 2019a). The broader sexualised use of drugs among MSM has been a topic of research for much longer, due to the potential for HIV acquisition from both injecting drug use and CAI sometimes facilitated by drug use (Halkitis, Parsons, & Stirratt, 2001; Mattison, Ross, Wolfson, Franklin, & HNRC Group, 2001; Stall & Purcell, 2000). Although there is no agreed definition of chemsex or even of drugs associated with chemsex, people may engage

in a variety of forms of SDU that encompasses what may be categorised as chemsex as well as other forms of SDU. However, due to the recent focus on chemsex, SDU more broadly has received less attention, even though it incorporates a much wider range of drug use behaviours and therefore may be more common.

A narrative systematic review of international quantitative and qualitative chemsex literature found that chemsex among MSM (defined as taking methamphetamine, mephedrone, GHB/GBL, cocaine or ketamine before or during sex) was associated with high sexual risk and HIV prevalence (Maxwell, Shahmanesh, & Gafos, 2019). Additionally, a systematic review investigating international prevalence of SDU among MSM found the most commonly reported sexualised drugs were methamphetamines, GHB/GBL and amyl nitrates (poppers), and that SDU was associated with increased sexual risk (Tomkins, George, & Kliner, 2019). A literature review investigating prevalence of both chemsex (defined as taking methamphetamine, GHB/GBL and mephedrone before or during sex) and SDU (defined as use of illicit drugs before or during sexual activity) in the United Kingdom (UK) found the prevalence of both varied across studies (Edmundson et al., 2018). The reviews identify that both SDU and chemsex are associated with sexual risk, and that the definitions of chemsex and SDU vary between studies. A recent UK study found that those MSM who engaged in SDU have a greater likelihood of a STI diagnosis and more anal intercourse partners than those who had not engaged in SDU, and among those who had engaged in SDU, those who engaged in chemsex (defined as the use of crystal methamphetamine, GHB/GBL, ketamine, mephedrone) had a greater likelihood of an STI diagnosis and more anal intercourse partners (Hibbert, Brett, Porcellato, & Hope, 2019b). Therefore, those engaging in chemsex may be engaging in greater sexual risk behaviours than those who engage in other forms of SDU.

Research investigating SDU among MSM has mostly been conducted in Western countries, and the term chemsex is typically used in a Western context (Bourne & Weatherburn, 2017), but SDU, including the sexualised use of drugs associated with chemsex, has also been observed internationally (Bourne, 2012; Maxwell et al., 2019; Tomkins et al., 2019). Due to the nature of researching SDU, studies tend to be cross-sectional, making causation hard to infer. Causation is also hard to infer when researching SDU due to the large number of potentially confounding factors that could also impact on sexual health outcomes (e.g. relationship status, number of sexual partners). Despite this, Leigh and Stall (1993) categorised the possible ways of measuring and analysing SDU into global associations, situational associations, and event-level associations. Global association is where general drug use is measured over a specific period (e.g. in the past 12 months), and sexual behaviour is also measured over a specific period, and an analysis between the two is conducted. Situational association is where the drug use is measured in relation to sex over a specific period, and sexual behaviour is also measured over a specific period, and an analysis between the two is conducted. Event-level associations are where drug use and sexual behaviour are asked about for a specific sexual event (e.g. the last time you had sex whilst using a drug, did you use a condom?). This is particularly important when investigating SDU, including chemsex, as drug use and sex are both linked, so a valid measurement needs to account for this (by using situational or event-level associations) rather than to explore global associations.

Some of the factors that have been suggested as motivations for MSM engaging in SDU, including chemsex, such as internalised homophobia and HIV stigma (Weatherburn, Hickson, Reid, Torres-Rueda, & Bourne, 2017), may apply to SDU among other lesbian, gay, bisexual and transgender (LGBT) people. This is particularly pertinent for trans women who have a high global estimate of HIV prevalence (Baral et al., 2013). However, less is known

about SDU among trans women and if it is associated with the same sexual risk as MSM. Additionally, SDU has been observed among women who have sex with women (WSW) (Hibbert, Porcellato, Brett, & Hope, 2019), but comparatively little research has been conducted in this group.

Therefore, the primary aim of this review was to:

- Investigate the associations between SDU and specific health outcomes (HIV status, STI diagnoses and CAI) among LGBT people.

Secondary aims of this review were to:

- Investigate how representative research into SDU in relation to health outcomes is of the whole LGBT population.
- Analyse what methods are used to explore the relationship between SDU and health outcomes (global association, situational association or event-level association).
- Assess which countries have reported SDU among LGBT people, and in particular, which countries have reported the sexualised use of a drug associated with chemsex.

Method

The systematic review was designed and reported following the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2010), with the protocol registered at PROSPERO International Register of Systematic Reviews prior to commencing the review (ID CRD42018084366). The PECO framework (Population, Exposure, Comparison, Outcome) (Methley, Campbell, Chew-Graham, McNally, & Cheraghi-Sohi, 2014) was used to form the search strategy where the population was LGBT people (MSM, WSW, and trans people); exposure was SDU; comparison was between those engaging in SDU and those who were not; and the outcome was HIV, STI diagnoses, or CAI. These outcomes were decided upon

due to preliminary searches identifying these outcomes as commonly measured in relation to SDU and chemsex. The analysis between SDU and HIV, STI diagnoses, or CAI was classified as global, situational, or event level associations. Due to the difficult nature of attributing HIV and STI transmission to specific sexual events, only the measurement of CAI could be classified as an event-level association. Studies that measured HIV and STIs by self-report and/or laboratory tests were included in the review.

Suitable search terms were obtained from systematic reviews on similar topics (Choi, Wong, & Fong, 2017; Vosburgh, Mansergh, Sullivan, & Purcell, 2012). A preliminary search was then conducted using these terms on MEDLINE, with relevant articles retrieved to identify additional search terms. Search terms were grouped into three concepts: "LGBT terms", "Drug terms", and "Sex terms" (Table 1),so that searches used the string: "LGBT terms" AND "Drug terms" AND "Sex terms". The search string was used to search MEDLINE, PsycINFO, CINAHL Plus, and Web of Science (EBSCO MEDLINE from 1879 to 30th June 2020, ProQuest PsycINFO from 1806 to 30th June 2020, EBSCO CINAHL Plus from 1981 to 30th June 2020, Web of Science Core Collection from 1900 to 30th June 2020). Where studies were not published in English, an attempt to find a translation was made. A period limit of 1st January 2010 to 30th June 2020 (inclusive) was imposed due to the end date of a previous systematic review on a similar topic (Vosburgh et al., 2012), although that systematic review was specific to MSM engaging in SDU and event-level condom use. A limit was also set on the period of data collection (January 2010-June 2020) to ensure that the review represented recent patterns of SDU. An attempt to find grey literature from relevant community organisations and public health organisations was made, but no reports provided sufficient detail to be included.

Chemsex drugs were defined as the '4 chems' (crystal methamphetamine, GHB/GBL, ketamine and mephedrone) as in Schmidt et al. (2016), and are commonly accepted as drugs

associated with chemsex (Bourne et al., 2014). SDU and their health related outcomes were grouped into three categories: global association, situational association, and event-level associations (Leigh & Stall, 1993).

Four stages were used to identify studies: identification, screening, eligibility and inclusion (Moher et al., 2010). A data extraction form with quality assessment was adapted from The Cochrane Public Health Group Data Extraction and Assessment Template, The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies, and the Center for Evidence-Based Management (CEMa) critical appraisal checklist for surveys. This form was created using online survey software Qualtrics (www.qualtrics.com). Cross-tabulated data on drug use and outcomes (HIV status, STI diagnoses, condom use) were extracted, and where underlying data were not available, the unadjusted odds ratios were extracted. There was not enough homogeneity in the data in terms of time duration of drug use or sexual risk factor (i.e. ever, the last 12 months, the last three months), as well as in terms of the populations studied (i.e. MSM living with HIV only, sex workers, young MSM, Black MSM only) for meta-analyses to be conducted. Additionally, it was not possible to control for confounding variables (e.g. age, number of sexual partners, sexuality, relationship status) due to the variability in the confounding variables reported in the studies. Screening and eligibility was conducted by two researchers independently (MH and AH) and a third researcher (VD) was used for any disagreements. Data extraction was completed by one researcher (MH), and then checked by a second researcher (AH). Quality assessment was conducted by two researchers independently (MH and AH), and a third researcher was used for any disagreements (VD).

Table 1 about here

Inclusion criteria:

1. A measure of drug use and sexual health risk (HIV status, STI diagnoses, CAI) within the same population.
2. An association analysis conducted between the drug behaviour and the sexual behaviour and/or health risk.
3. Population studied included a sexual and/or gender minority population.
4. Studies published and data collected in the date range January 2010 to June 2020 (inclusive).

Exclusion criteria:

1. Articles not published in English and no translation available.
2. Studies including children (aged equal to or less than 15 years).
3. Studies that are not relevant to the research question (e.g. heterosexual populations only, comparisons with heterosexual people, medical drug trial studies).
4. Qualitative research.

Results

The search yielded 2,710 unique citations, of which 1,658 were excluded during title and abstract screening and 977 during full-text review, leaving 75 studies eligible for data extraction (Figure 1). The majority of studies were cross-sectional (n=67), six studies were cohort studies, and two were case-control studies. A list of included studies can be found in Supplementary Material 1.

Figure 1 about here

The 75 included studies spanned across 55 countries, of which 71 researched MSM and 4 researched trans women (Supplementary Material 2). No studies examining SDU among WSW or trans men/non-binary people met the inclusion/exclusion criteria. The countries of included studies in which SDU had been studied among MSM or trans women or both are shown in Figure 2, as well as the countries where a study had examined the use of one or more chemsex associated drugs (crystal methamphetamine, GHB/GBL, ketamine, or mephedrone) among MSM.

Figure 2 about here

Men who have sex with men

Over one quarter of studies among MSM were conducted in the United States of America (USA) (n=20), and around a quarter were conducted in the UK (n=16). The most commonly studied drug among MSM was cannabis (n=34), followed by amyl nitrates/poppers (n=29), crystal methamphetamine (n=18), erectile dysfunction drugs (EDD) (n=15), cocaine (n=13), ecstasy (n=10), GHB/GBL (n=11), and ketamine (n=8). Less common drugs were mephedrone (n=3), heroin (n=2), amphetamine (n=1), and crack cocaine (n=1). The time period for measuring drug use ranged from the last anal sex event (n=6) to lifetime use (n=3), with the most common recall period being six months (n=20).

Around one third of studies (n=23) grouped drugs into chemsex/party drugs. The specific drugs grouped as chemsex/party drugs varied considerably, but GHB/GBL were included in all chemsex groups, and crystal methamphetamine was included in 21 out of 23

chemsex groups (Table 2). Fourteen of the studies used situational association analyses to investigate the sexual health outcome and the remaining nine used global association analyses. At least one of the drugs associated with chemsex had been investigated in the majority of countries (n=32/54, Figure 2).

Table 2 about here

HIV prevalence was the outcome examined in 35 studies, 27 studies examined STI incidence, and CAI was the most common health outcome examined (n=42). . Table 3 displays the breakdown of outcomes studied in relation to specific drugs and how many studies found a significant bivariate association between drug use and the outcome investigated.

Table 3 about here

HIV prevalence

Among the 35 studies that investigated HIV prevalence, ten measured HIV status using a laboratory test, the remaining 25 asked participants to self-report their HIV status. The majority of studies conducted global association analyses (n=26) and nine conducted situational association analyses. The most common drug category investigated in relation to HIV prevalence was poppers use (n=14) with around 70% of studies finding a bivariate association between poppers use and HIV prevalence. Chemsex drugs grouped were investigated in relation to HIV prevalence in thirteen studies and 77% of studies found

bivariate associations between chemsex drug use and HIV prevalence. For chemsex drugs that were investigated independently, four out of the seven studies investigating crystal methamphetamine use and HIV prevalence found a bivariate association. Four studies were found that investigated either GHB/GBL or ketamine and two found bivariate associations with HIV prevalence (50%). Two studies investigated mephedrone and HIV prevalence and both found a bivariate association, although both studies investigated among MSM who use drugs only and three out of the four studies that investigated EDDs found a bivariate association with HIV prevalence.

STI diagnoses

Among the 27 studies investigating STI diagnoses in relation to drug use, 16 conducted global association analyses, 10 conducted situational association analyses and one study conducted both global and situational association analyses. Most studies grouped STIs for their investigations (n=17). Seven of these groups investigated associations between drug use and bacterial STIs only (chlamydia, gonorrhoea, lymphogranuloma venereum (LGV), syphilis), whilst others included herpes, genital warts, and blood borne viruses such as hepatitis A, B, and C as well as newly acquired HIV (See Supplementary Material 2). Over half (n=15) of the studies measured STI diagnoses using laboratory tests, whilst the remaining 12 studies used self-report methods. The recall period for self-reported STI diagnoses was most commonly 12 months (n=8), whilst two studies had a recall period of three months, one study had a recall period of six months, and one study did not report the recall period.

The most commonly researched drug in relation to STI diagnoses were chemsex drugs grouped (n=14), and in the majority of studies (n=11) this was in relation to grouped STI diagnoses. One study each investigated chemsex drugs in relation to shigella, hepatitis C and

gonorrhoea, and all bivariate associations between chemsex drugs and STI diagnoses were significant. Poppers were the second most commonly researched in relation to STI diagnoses (n=11). Six studies investigated poppers use in relation to syphilis diagnoses, all of which were conducted in China, with two of these studies finding bivariate associations. All four studies that conducted bivariate association analyses between poppers use and grouped STI diagnoses found associations, and one study investigated poppers use in relation to Shigella diagnoses and found a bivariate association.

Condomless anal intercourse (CAI)

Among the 42 studies investigating CAI, 22 studies conducted global association analyses, 14 conducted situational association analyses, five conducted event-level association analyses, and one study conducted both global and situational association analyses depending on the drug of interest. The recall period for CAI ranged from event-based (n=6) to 12 months (n=7), with the most common recall period being three months (n=13). The most commonly researched drug in relation to global and situational analyses for CAI was cannabis (n=19), with around 40% of studies (n=8) finding a bivariate association between cannabis use and CAI. All 11 studies that investigated chemsex drugs grouped found bivariate associations when analysing CAI and over three quarters of studies (n=13/16) that investigated poppers use and CAI found a bivariate association.

Among the five studies that used event-level associations, all three studies investigating crystal methamphetamine, EDDs, GHB/GBL, and poppers found bivariate associations between drug use and CAI. One study found bivariate associations between cannabis use, ecstasy use and CAI among HIV positive partners only, whilst the remaining three studies that investigated event-level associations between cannabis use, ecstasy use and

CAI found no association. One study investigated each cocaine and ketamine use in relation to CAI and both found no association.

Trans women

Among the four studies that researched trans women, a range of drugs were investigated (cocaine, crack cocaine, crystal methamphetamine, heroin, and poppers). Three studies conducted global association analyses and one study conducted a combination of global and situational analyses. Two studies were conducted in the USA, one in Brazil, and one in Vietnam. A bivariate association was found between crystal methamphetamine (n=1) and condomless sex. One study investigated a possible association between poppers use and condomless sex, but found no association. One study found a situational association between cocaine and HIV status, although two studies did not find this association when conducting global association analyses. One study found an association between methamphetamine use and HIV status. No association was found between heroin use (n=1) and HIV status or syphilis diagnosis.

Quality assessment of the included studies

The majority of studies had an overall rating of moderate (n=31/75, 41%), 28 studies (33%) were rated as weak, and 16 (21%) were rated as strong. The weakest sections tended to be the reporting of withdrawals and dropouts, where 34 studies (45%) were rated as weak, and confounders, where 20 studies (27%) were rated as weak.

Discussion

This systematic review firstly assessed the extent to which SDU has been studied among LGBT people in relation to sexual health outcomes, and it found that the vast majority of research has been conducted among MSM. A smaller number of studies had been conducted among trans women; however, no studies were found that reported on SDU in relation to sexual health outcomes among trans men or WSW. Whilst a few studies were found among trans women, due to the potentially high risk of HIV among trans women (Baral et al., 2013), further studies are needed to explore SDU and its related sexual and health implications among trans women.

It should be noted that some studies among WSW were found, but they were not included in this review because they compared WSW with heterosexual women, and therefore data were not available for health outcomes exclusively for WSW. These few studies identified that WSW may be more likely to use ketamine (Heinsbroek, Glass, Edmundson, Hope, & Desai, 2018), as well as cannabis and cocaine (Bauer, Jairam, & Baidoobonso, 2010) compared to heterosexual women, but drug use was not measured in a sexual context. One study did find that lesbian and bisexual women were more likely to engage in SDU (Estrich, Gratzer, & Hotton, 2014), but data were not available exclusively for WSW with regards to sexual risk and SDU. Recent research has indicated an association between SDU among WSW and greater sexual risk (Hibbert, Porcellato, et al., 2019), but further event-level research among WSW is warranted. Narrowing the search criteria to sexual health outcomes may have limited the number of possible studies found in relation to WSW, as the reasons for engagement and effects on sexual health may be different for WSW (Hibbert, Porcellato, et al., 2019). However, due to bisexual women possibly being more likely to engage in SDU (Estrich et al., 2014; Hibbert, Porcellato, et al., 2019), research regarding sexual health behaviours like condom use and STI diagnoses may be warranted.

Whilst there was some research regarding SDU among trans women, further research is needed due to the suspected high-risk of HIV transmission. Additionally, no studies indicated they included trans men and non-binary people. Where trans men do identify as MSM, they are most often not included in analyses among men. Therefore, further research is needed among trans people in general, to understand if SDU exists, and if so, whether it is associated with sexual risk.

Associations between SDU among MSM and/or trans women have been studied in 55 countries, but due to the inclusion and exclusion criteria used in this review, not all countries which have examined SDU among LGBT people may have been identified. Additionally, the use of at least one of the drugs associated with chemsex among MSM has been observed in 32 of these countries spanning North America, Europe, Asia, and Australasia. Although chemsex was first documented within the UK and has been researched in other Western countries (Bourne & Weatherburn, 2017), this behaviour has been observed internationally, and therefore more international research is needed, particularly in countries with high prevalence of HIV among MSM. Similar to a literature review of SDU and chemsex in the UK (Edmundson et al., 2018), it was found that the definition of chemsex varied greatly, but GHB/GBL was included in all chemsex definitions. This may be because the drugs used for chemsex differ internationally, or that research had been conducted before a definition which drugs used specifically for sex, constituted as chemsex. A consensus of what drugs constitute as chemsex may be hard to reach due to emerging new drugs, local availability of specific drugs, or personal preferences for the type of drugs used for chemsex. Therefore, an international definition of what drugs constitute as chemsex may not be appropriate and instead more local definitions may be more suitable. Although the lack of an international definition may limit cross-cultural comparisons, because of the sexual risk associated with chemsex, defining chemsex with regards to sexual behaviour may be equally or if not more

important, and trying to commonly define chemsex as a particular use of drugs may be too simplistic. However, it is useful to see which drugs are common internationally, so harm reduction and drug safety information can be shared across countries.

It is of note that nearly all drugs were associated with greater sexual risk, regardless of the drug or outcome in question, similar to previous systematic reviews regarding chemsex, SDU and MSM (Maxwell et al., 2019; Tomkins et al., 2019), but causation cannot be inferred from these analyses. For some of the more commonly used, and more socially accepted substances, such as poppers and cannabis, the associations found may in part be due to people taking these substances also being more likely to use other substances (which they may not always disclose). It is unclear the influence that polydrug use may have on these findings. For example, whether individuals who use multiple drugs during the same sexual encounter are considered to engage in greater risk taking. When considering global associations, individuals may use multiple drugs in a variety of different contexts, some of which are specific to a sexual context. However, in these situations, drug use outside a sexual context could be associated with a sexual health outcome via proxy. Therefore, there is a need to move away from global associations when investigating SDU and sexual health associations.

Certain patterns of drug use, such as chemsex, may be associated with HIV prevalence, STI diagnoses and CAI more than other patterns of drug use, which has been suggested by previous research (Hibbert, Brett, et al., 2019a). The variation found in this review regarding the definition of what drugs constitute as chemsex may be because sex under the influence of the drugs used in chemsex may lower inhibitions and therefore impact on behaviour to a greater extent than other types of SDU, or social norms associated with chemsex may influence risk taking. Additionally, it could be that grouping drugs creates a more powerful analysis due to a greater number of observations included, and therefore this is why chemsex appears to be associated with greater risk.

There were similar associations between event-level analyses and global and situational associations for condom use, but a large number of studies relied on global associations of drug use and health outcomes, even when aiming to research chemsex, which is by definition use in a sexual context. Therefore, if future research is aiming to investigate SDU, situational and event-level analyses should be used for a potentially more accurate measurement. Another limitation identified in the research was the variability in the recall period for reporting drug use and sexual health behaviours. Whilst lifetime use of drugs may be important for drugs that are typically injected when investigating blood borne viruses, for more recent sexual behaviours, the usefulness of lifetime drug use is questionable. Therefore, studies should aim to have more recent recall periods for both drug use and sexual behaviours. Due to the nature of researching SDU being mostly cross-sectional, causation cannot be inferred, regardless of the measurement method chosen. It is possible that other factors influence associations between drug use and sexual risk behaviours, for example, those who take drugs and have CAI may just be less risk averse.

Strengths and limitations

A limitation of this review is that there may be a publication bias in the data, suggested by most studies finding an association with the health outcome researched. An attempt was made to find grey literature on the topic, however no reports or publications were found where information had not already been published in peer-review journals, or that met the inclusion/exclusion criteria. Additionally, it was not possible to control for confounding variables that may influence drug use and HIV, STI diagnoses and condom use, such as age and sexual identity, due to the heterogeneity among control variables in multivariable analyses. Collating data is also difficult due to different window periods of measurement (e.g. three months/six months/twelve months), and variability in the grouping of drugs associated with sex. In terms of quality, one third of studies were given an overall quality assessment

rating of weak. Due to the various sub-categories in this review, it was deemed inappropriate to exclude studies rated as weak, which may have impacted the findings.

This review focused specifically on HIV, STI diagnoses, and CAI due to these outcomes being commonly researched in relation to SDU. However, this does ignore other sexual health factors that may be related to SDU such as pre- and post-exposure prophylaxis (PrEP/PEP) use, as well as possible psychological associations. Despite this, the finding that SDU among MSM was associated with HIV prevalence, STI diagnoses and CAI is still important when considering service delivery, as well as harm reduction services, due to potentially confounding factors a person may experience (i.e. drug harms, living with HIV, greater sexual risk taking).

Conclusion

For the majority of drugs examined, drug use appears to be associated with living with HIV, STI diagnoses, and CAI among MSM. However, the measurement of SDU often relied on global associations between drug use and risk, so may be subject to misclassification bias. Therefore, more accurate measurements of SDU, such as situational or event-level analyses, should be used. Definitions of what constitutes chemsex drugs varied across studies, making conclusions with regards to associated risks with chemsex difficult. The definition of what constitutes chemsex drugs may be even more difficult when considering the behaviour internationally, as the availability of certain drugs will differ across countries, depending upon legal categorisation and common illicit drug markets. Further research is needed regarding SDU among WSW and trans people to assess the occurrence of SDU and any possible impact on sexual risk.

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Table 1. Results generated from each search term used for each database, June 2020.

Database	Keywords			Articles retrieved
	LGBT terms	Drug terms	Sex terms	
Medline	Homosexuality (MH) Homosexuality, female (MH) Homosexuality, male (MH) Homosexual* Gay Lesbian* Bisexual* Transexual* Transsexual* Transgender* Trans Transgender persons (MH) Genderqueer "Non binary" "Men who have sex with men" "Sexual minorit*" Sexual minorities (MH) LGBT*	Substance-related disorders (MH) "Substance use" Alcohol drinking (MH) Alcohol "Drug use" Chemsex "Party and play" Marijuana GBL GHB Ecstasy Cocaine Crack Methamphetamine Methadone Poppers "Amyl nitrate*" Ketamine Viagra "Erectile dysfunction drug*" "Sildenafil Citrate" (MH)	"Sexual health" Reproductive health (MH) "Sexual behavior" "Sexual behaviour" Sexual behavior (MH) "Sexual risk" Risk-taking (MH) Unsafe sex (MH) "Unsafe sex"	1,858
PsycINFO	Homosexuality (SH) Homosexuality, female (SH) Homosexuality, male (SH) Homosexual* Gay Lesbian* Bisexual* Transexual* Transsexual* Transgender* Trans Transgender persons (SH) Genderqueer "Non binary" "Men who have sex with men" "Sexual minorit*" Sexual minorities (SH) LGBT*	Substance-related disorders (SH) "Substance use" Alcohol drinking (SH) Alcohol "Drug use" Chemsex "Party and play" Marijuana GBL GHB Ecstasy Cocaine Crack Methamphetamine Methadone Poppers "Amyl nitrate*" Ketamine Viagra	"Sexual health" Reproductive health (SH) "Sexual behavior" "Sexual behaviour" Sexual behavior (SH) "Sexual risk" Risk-taking (SH) Unsafe sex (SH) "Unsafe sex"	1,445

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CINAHL Plus	Homosexuality (MH) Homosexuality, female (MH) Homosexuality, male (MH) Homosexual* Gay Lesbian* Bisexual* Transexual* Transsexual* Transgender* Trans Transgender persons (MH) Genderqueer "Non binary" "Men who have sex with men" "Sexual minorit*" Sexual minorities (MH) LGBT*	Substance-related disorders (MH) "Substance use" Alcohol drinking (MH) Alcohol "Drug use" Chemsex "Party and play" Marijuana GBL GHB Ecstasy Cocaine Crack Methamphetamine Methadone Poppers "Amyl nitrate*" Ketamine Viagra "Erectile dysfunction drug*" "Sildenafil Citrate" (MH)	"Sexual health" Reproductive health (MH) "Sexual behavior" "Sexual behaviour" Sexual behavior (MH) "Sexual risk" Risk-taking (MH) Unsafe sex (MH) "Unsafe sex"	727
Web of Science	Homosexual* Gay Lesbian* Bisexual* Transexual* Transsexual* Transgender* Trans Genderqueer "Non binary" "Men who have sex with men" "Sexual minorit*" LGBT*	Substance-related disorders "Substance use" Alcohol "Drug use" Chemsex "Party and play" Marijuana GBL GHB Ecstasy Cocaine Crack Methamphetamine Methadone Poppers "amyl nitrate*" Ketamine Viagra "Erectile dysfunction drug*" "Sildenafil Citrate"	"Sexual health" "Sexual behavior" "Sexual behaviour" "Sexual risk" "Risk-taking" "Unsafe sex"	1,357

MH – Medical Subject Heading (MeSH). SH – Subject Heading

Table 2. Summary of drugs included in chemsex definitions

Drug or drugs included in chemsex definitions	**N (n=23)**
Crystal methamphetamine	21
GHB/GBL	23
Ketamine	12
Mephedrone	20
Grouped	
Crystal methamphetamine, GHB/GBL, mephedrone	20
Crystal methamphetamine, GHB/GBL, ketamine, mephedrone	11

Table 3. Bivariate associations found in studies investigating drug use in relation to HIV prevalence, STI diagnoses, and condom use among MSM.

	HIV prevalence (n=35)				STI diagnoses (n=27)*				Condomless anal intercourse (n=42)*					
	Global (n=26)		Situational (n=9)		Global (n=17)		Situational (n=11)		Global (n=23)		Situational (n=15)		Event (n=5)	
Drugs investigated	N sig. (%)	N total	N sig. (%)	N total	N sig. (%)	N total	N sig. (%)	N total	N sig. (%)	N total	N sig. (%)	N total	N sig. (%)	N total
Amphetamine	-	-	-	-	-	-	0 (0%)	1	-	-	0 (0%)	2	-	-
Cannabis	4 (57%)	7	1 (50%)	2	1 (20%)	5	1 (50%)	2	4 (25%)	12	4 (57%)	7	1 (25%)	4
Cocaine	1 (25%)	4	-	-	0 (0%)	2	1 (100%)	1	4 (80%)	5	0 (0%)	3	0 (0%)	1
Crack cocaine	-	-	-	-	-	-	-	-	1 (50%)	2	-	-	-	-
Crystal methamphetamine	4 (57%)	7	-	-	5 (83%)	6	-	-	4 (67%)	6	2 (100%)	2	3 (100%)	3
Ecstasy	1 (25%)	4	-	-	0 (0%)	1	1 (100%)	1	-	-	1 (33%)	3	1 (25%)	4
Erectile Dysfunction Drugs (EDDs)	2 (67%)	3	1 (100%)	1	2 (100%)	2	1 (100%)	1	3 (60%)	5	1 (50%)	2	3 (100%)	3
GHB/GBL	2 (50%)	4	-	-	2 (67%)	3	1 (100%)	1	1 (100%)	1	-	-	3 (100%)	3
Heroin	1 (100%)	1	-	-	-	-	-	-	-	-	0 (0%)	1	-	-
Ketamine	2 (50%)	4	-	-	0 (0%)	2	1 (100%)	1	-	-	-	-	0 (0%)	1
Mephedrone	2 (100%)	2	-	-	0 (0%)	1	-	-	-	-	-	-	-	-
Poppers	9 (69%)	13	1 (100%)	1	5 (56%)	9	2 (100%)	2	11 (92%)	12	2 (50%)	4	3 (100%)	3
Chemsex grouped	4 (67%)	6	6 (86%)	7	5 (100%)	5	9 (100%)	9	3 (100%)	3	8 (100%)	8	-	-

Note: Studies measured multiple drugs for the same outcomes, therefore column totals do not add up to the total number of studies

*One study included both global and situational associations so is counted in both sub-total

Figure 1. Flow diagram of the identification process.

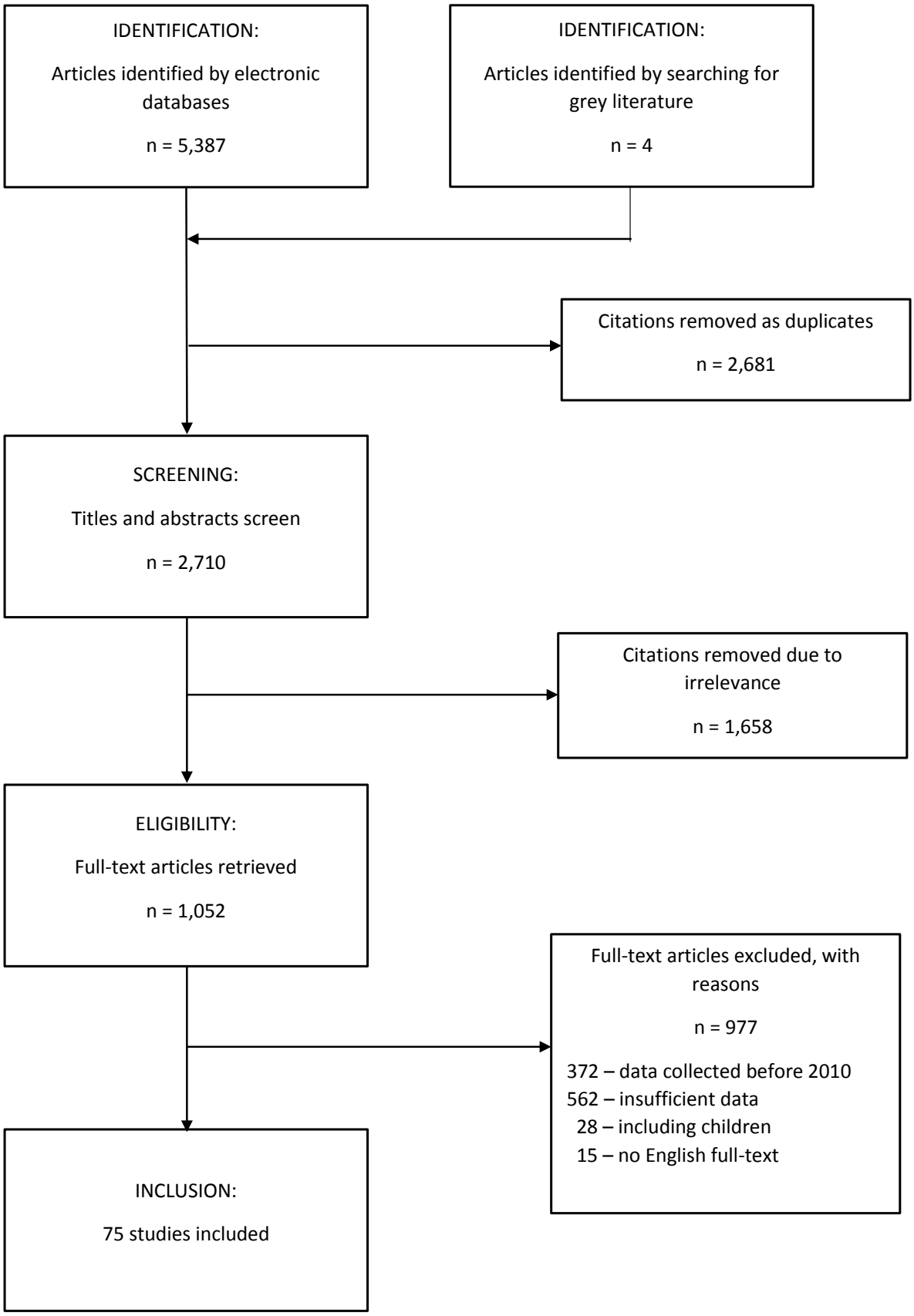
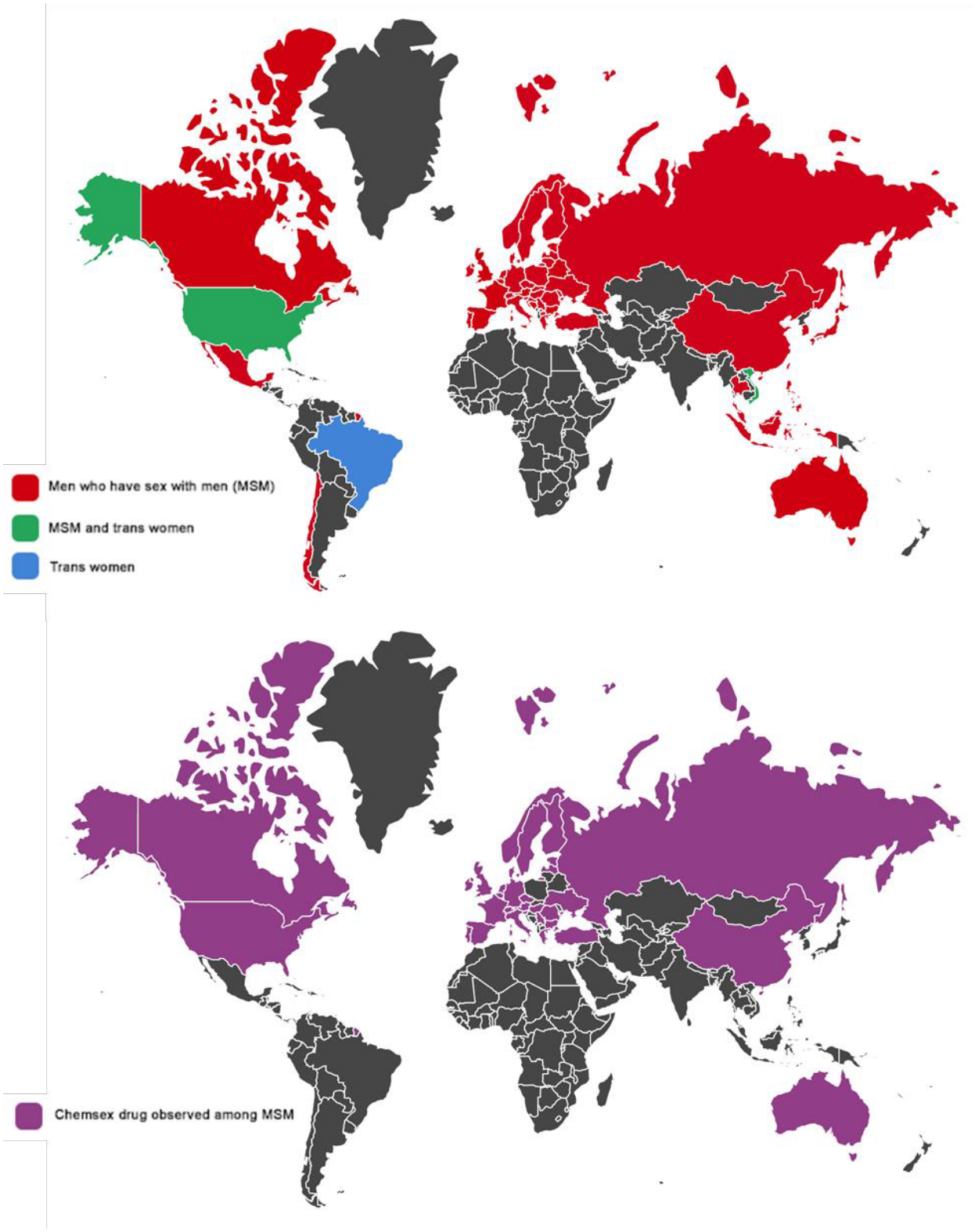


Figure 2. Map of countries with studies on sexualised drug use among men who have sex with men (MSM), trans women, or both, and those that have reported chemsex drug use included in the review.



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Heroin	1 (100%)	1	-	-	-	-	-	-	-	-	0 (0%)	1	-	-
Ketamine	2 (50%)	4	-	-	0 (0%)	2	1 (100%)	1	-	-	-	-	0 (0%)	1
Mephedrone	2 (100%)	2	-	-	0 (0%)	1	-	-	-	-	-	-	-	-
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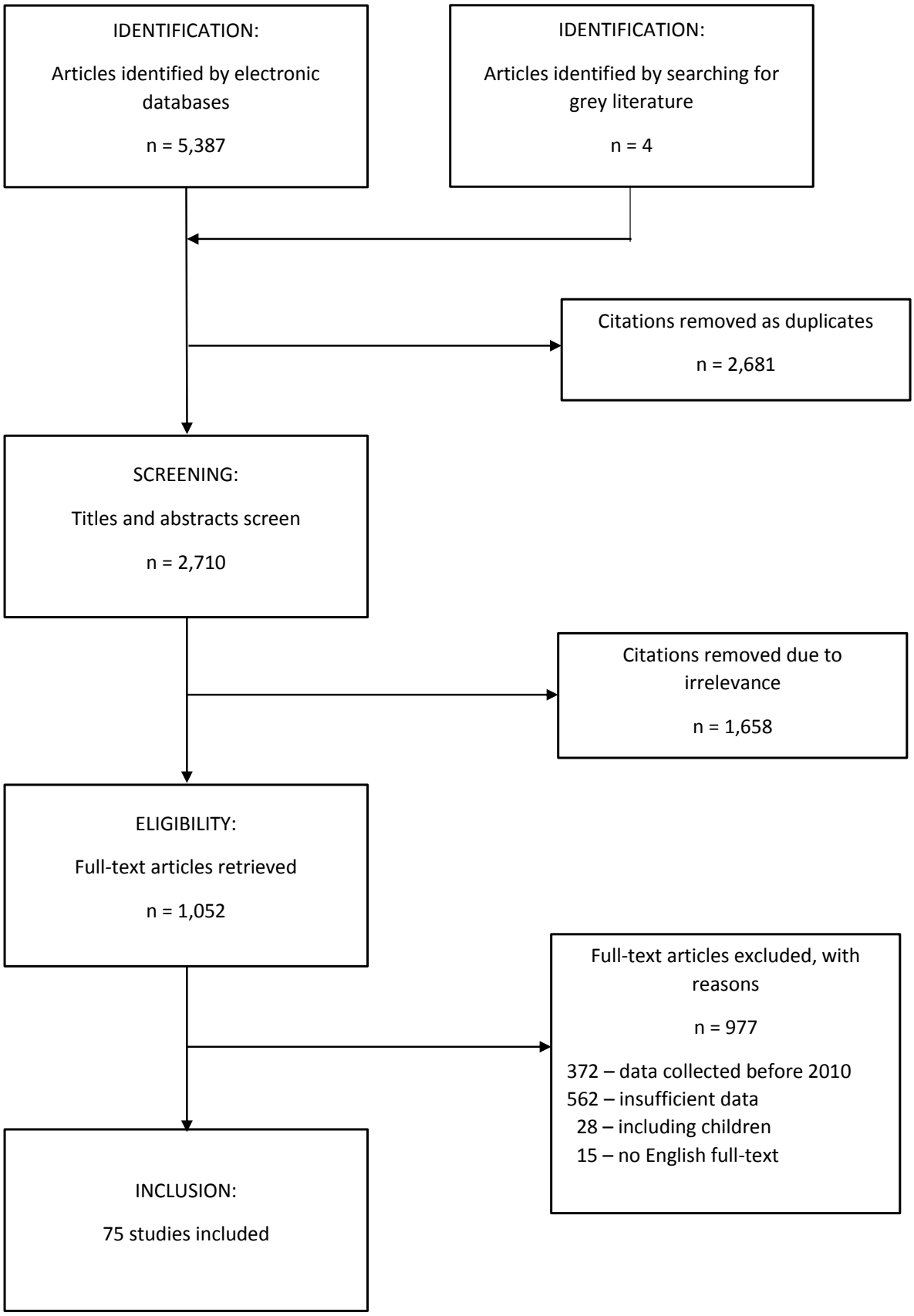

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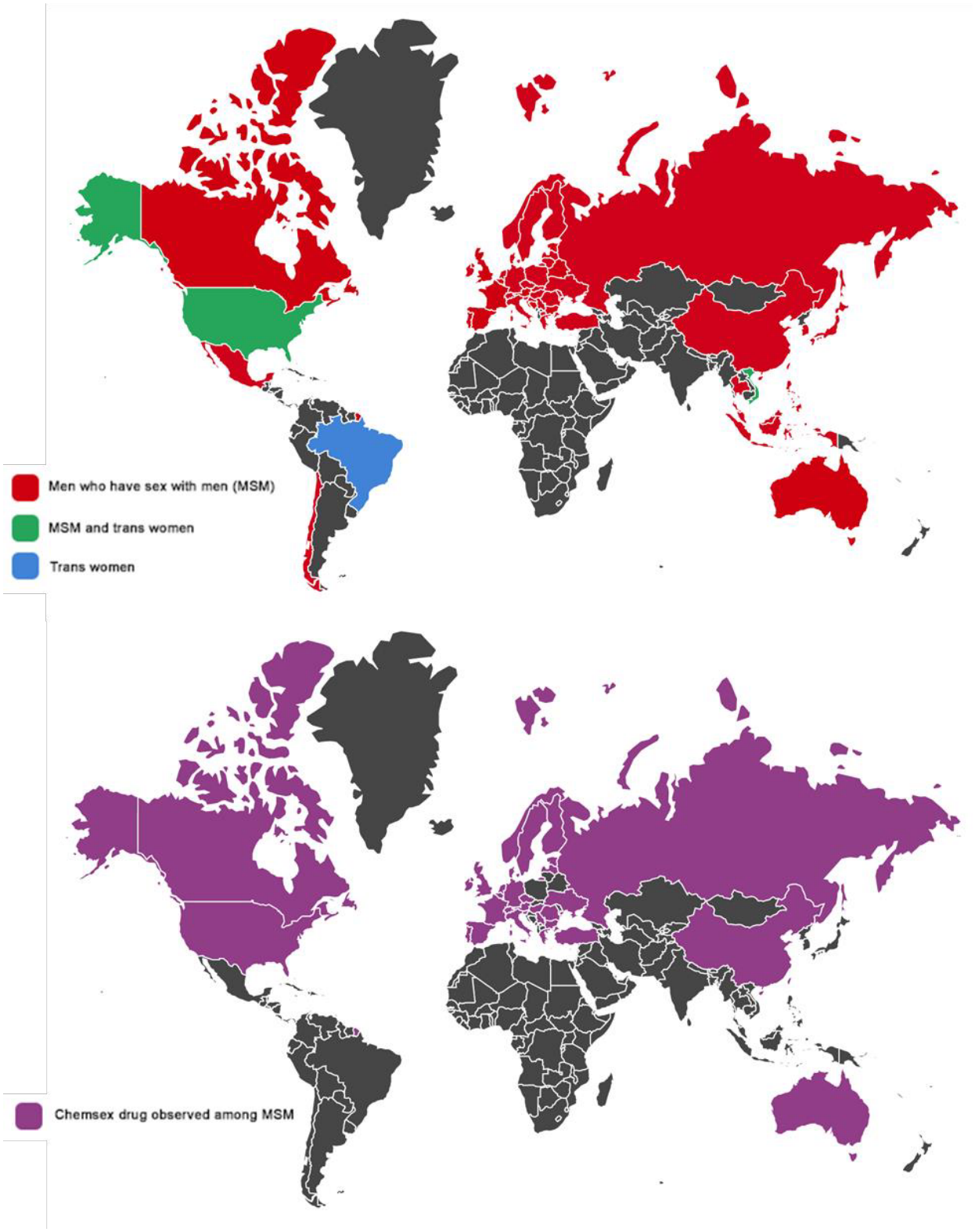

figure 2

Click here to access/download;Figure(s);Figure 2 bandw.png

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2-3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6-7, Table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7, Figures 3-6

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5-7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplementary information
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-11, Figures 2-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-11, Figures 2-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Supplementary information
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8-11, Figures 2-6
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-16
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	n/a

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Included Studies

Barrett, P., O'Donnell, K., Fitzgerald, M., Schmidt, A. J., Hickson, F., Quinlan, M., . . . Igoe, D. (2019). Drug use among men who have sex with men in Ireland: Prevalence and associated factors from a national online survey. *The International Journal On Drug Policy, 64*, 5-12. doi:10.1016/j.drugpo.2018.11.011

Barron-Limon, S., Semple, S. J., Strathdee, S. A., Lozada, R., Vargas-Ojeda, A., & Patterson, T. L. (2012). Correlates of unprotected anal sex among men who have sex with men in Tijuana, Mexico. *BMC Public Health, 12*(433).

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Bowden-Jones, O., Whitelock, C., Abdulrahim, D., Hemmings, S., Margetts, A., & Crawford, M. (2017). Prevalence of HIV risk-related drug use and sexual activity among men who have sex with men attending a specialist UK club drug clinic. *Drugs and Alcohol Today, 17*(1), 50-59. doi:10.1108/dat-01-2017-0001

Card, K. G., Lachowsky, N. J., Cui, Z., Shurgold, S., Armstrong, H. L., Rich, A. J., . . . Hogg, R. S. (2017). An Event-Level Analysis of the Interpersonal Factors Associated With Condomless Anal Sex Among Gay, Bisexual, and Other Men Who Have Sex With Men (MSM) With Online-Met Partners. *AIDS Education And Prevention: Official Publication Of The International Society For AIDS Education, 29*(2), 154-174. doi:10.1521/aeap.2017.29.2.154

Chen, H. L., Yang, Y., Huang, Y. L., Dai, Y. X., & Zhang, J. X. (2018). Prevalence of poppers use and its sexual risks among men who have sex with men in southwestern China: a cross-sectional study. *BMC Public Health, 18*. doi:10.1186/s12889-018-6010-8

Chou, F. Y., Armstrong, H. L., Wang, L., Bacani, N., Lachowsky, N. J., Patterson, T. L., . . . Moore, D. M. (2019). A longitudinal analysis of cannabis use and mental health symptoms among gay, bisexual, and other men who have sex with men in Vancouver, Canada. *Journal Of Affective Disorders, 247*, 125-133. doi:10.1016/j.jad.2019.01.015

Colby, D., Nguyen, N. A., Le, B., Toan, T., Thien, D. D., Huyen, H. T., . . . Stall, R. (2016). HIV and Syphilis Prevalence Among Transgender Women in Ho Chi Minh City, Vietnam. *AIDS And Behavior, 20*(3), 379-385.

Colyer, S. P., Lachowsky, N. J., Cui, Z., Zhu, J., Armstrong, H. L., Taylor, M., . . . Moore, D. M. (2018). HIV treatment optimism and crystal methamphetamine use and initiation among HIV-negative men who have sex with men in Vancouver, Canada: A longitudinal analysis. *Drug And Alcohol Dependence, 185*, 67-74. doi:10.1016/j.drugalcdep.2017.12.004

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Supplementary material 2

First author	Year of study	Countries	Type of study	Sample size	Type of analysis	Drugs measured	Chemsex definition	Drug recall period	HIV measurement	STI measurement (recall period)	STI definition	CAI recall period	Quality assessment rating
Men who have sex with men (MSM)													
Barrett	2019	Ireland	Cross sectional study	3090	Global association	Poppers, Chemsex	Crystal mephampetamine, GHB/GBL, ketamine, or mephedrone	12 months	HIV self report				Weak
Barron-Limon	2012	Mexico	Cross sectional study	260	Situational association	Cannabis, Amphetamine , Cocaine, Ecstasy, Heroin, Poppers		12 months				12 months	Strong
Blomquist	2020	United Kingdom of Great Britain and Northern Ireland (England)	Cross sectional study	3922	Situational association	Chemsex	Crystal methamphetamine, GHB/GBL, ketamine, or mephedrone	12 months	HIV self report			3 months	Moderate
Bowden-Jones	2017	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	407	Global association	Mephedrone , Crystal methampetamine		Primary drug of abuse	HIV self report				Moderate
Card	2017	Canada	Cohort study	774	Event-level association	Cannabis , Ecstasy, GHB/GBL , Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		Event based				Event based	Weak
Chen	2018	China	Cross sectional study	1122	Global association	Poppers		Ever	HIV self report	Self report (not stated)	gonorrhoea, condyloma acuminata or syphilis	12 months	Weak
Chou	2019	Canada	prospective cohort study	583	Global association	Cannabis		Weekly in the last 3 months	HIV self report				Moderate
Colyer	2018	Canada	Prospective behavioural cohort study	497	Global association	crystal methamphetamine		6 months		Self report (6 months)	unspecified	6 months	Moderate
Curtis	2020	United Kindgom (England)	Cross-sectional study	1644	Situational association	Chemsex	Crystal methamphetamine, GHB/GBL, ketamine, or mephedrone	12 months		Self report (12 months)	Chlamydia, gonnorohoea, syphilis, Lymphogranuloma venereum, Hep C, genital warts, genital herpes, pubic lice, non-specific urethritis, scabies, unspecified other STI	12 months	Weak
Daskalopoulou	2014	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	2248	Global association	Cannabis , Cocaine, Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		3 months				3 months	Moderate
Drückler	2018	The Netherlands	Cross-sectional study	4925	Situational association	Chemsex	Crystal methamphetamine, GHB, or mephedrone	6 months	Diagnostic test	Diagnostic test	Bacterial STI (chlamydia, gonorrhea, LGV, and/or infectious syphilis)	not stated	Strong
Duan	2017	China	Cross sectional study	1935	Global association	Cocaine, Crystal methampetamine, Poppers		6 months	Diagnostic test	Diagnostic test	Syphilis		Moderate
Eaton	2015	United States of America	Cross sectional study	544	Global association	Cocaine, Ecstasy, Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		6 months	HIV self report				Strong
Eaton	2016	United States of America	Cross sectional study	271	Global association	Cannabis		3 months	Diagnostic test				Strong
Evers	2019	The Netherlands	Cross sectional study	250	Situational association	amphetamine, cannabis, cocaine, ecstacy, ghb/gbl, Ketamine, poppers, Viagra or other erectile dysfunction drug, Chemsex	Cocaine, crystal methampetamine, designer drugs, ecstasy, GHB/GBL, ketamine, mephedrone, or speed	6 months		Diagnostic test	Chlamydia, syphilis, gonorrhoea, Hepatitis B newly aquired HIV		Strong
Feinstein	2019	United States of America	Cohort study	763	Situational association	Cannabis		6 months				6 months	Moderate

Fernandez-Rollan, Stuardo Ávila, and Strömdahl (2020)	2019	Chile	Cross sectional study	246	Situational association	Amphetamine, Cannabis, cocaine, poppers, ecstasy		6 months				6 months	Weak
FISHER	2013	United States of America	Cross sectional study	489	Global association	Cannabis , Ecstasy, GHB/GBL , Ketamine (Vitamin K, K, Special K), Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		2 days	HIV self report				Weak
Frankis	2018	Ireland,United Kingdom of Great Britain and Northern Ireland	Cross sectional study	2328	Situational association	Chemsex	Crystal methamphetamine, mephedrone, GHB/GBL, Ketamine	12 months	HIV self report			12 months	Moderate
Gilbart	2015	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	42	Global association	Chemsex	Crystal meth, mephedrone, GHB/GBL	Not stated	HIV self report				Weak
Girometti	2019	United kingdom (England)	Cross sectional study	60	Situational association	Chemsex	crystal meh, ghb/gbl, mephedrone	6 months	HIV self report				Weak
Glynn	2018	Ireland	Cross sectional study	486	Situational association	Chemsex	ketamine, GHB/GBL, crystal meth, mephedrone, cocaine, NPS and other stimulants (including speed/amphetamine/ecstasy /eros/nexus/ smiles)	12 months	HIV self report	Self report (12 months)	Chlamydia, syphilis, gonorrhoea	event based	Strong
Goddard	2019	Australia	Prospective cohort study	617	Global association	crystal methamphetamine		6 months		Diagnostic test	Anal gonorrhoea, Syphilis		Weak
Goedel	2016	United States of America	Cross sectional study	174	Global association	Cannabis		3 months				3 months	Weak
Gonzalez-Baeza	2018	Spain	Cross sectional study	742	Situational association	Chemsex	mephedrone or similar cathinones, 3,4-methylenedioxy-Nmethylamphetamine (MDMA), crystal methamphetamine, amphetamines, GHB/GBL, ketamine, or cocaine	12 months		Diagnostic test	Syphilis, Gonorrhoea, Chlamydia, Hepatitis C	Self report 6 months	Moderate
Gorbach	2019	United states of America	Cohort study	512	Global association	cannabis		6 months	HIV self report	Diagnostic test	Chlamydia, Gonorrhea, or Early Syphilis		Weak
Halkitis	2012	United States of America	Cross sectional study	199	Global association	Cannabis , Poppers		30 days				30 days	Weak
Hambrick	2018	France	Cross-sectional study	580	Global association	poppers		3 months	HIV self report	Self report (12 months)	STI gonorrhoea, chlamydia, syphilis, herpes simplex virus (HSV), human papillomavirus (HPV) or Hepatitis C	3 months	Weak
Hammoud	2017	Australia	Cross sectional study	2250	Global association	Viagra or other erectile dysfunction drug or other erectile dysfunction drug		6 months	HIV self report			6 months	Moderate
Hammoud	2018	Australia	Cross sectional study	3190	Global association	GHB/GBL		6 months	HIV self report			6 months	Moderate
Hammoud	2020	Australia	Cross-sectional study	1367	Global association	crystal methamphetamine		6 months	HIV self report			6 months	Moderate
Hassan	2018	United states of America	Cross-sectional study	395	Global association	Cannabis		3 months		Diagnostic test	Rectal Chlamydia and Gonorrhoea		Strong
He	2014	China	Cross sectional study	200	Situational association	Poppers		6 months		Diagnostic test	Syphilis		Weak
Heinsbroek	2018	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	299	Global association	Heroin, Ketamine (Vitamin K, K, Special K), Mephedrone		12 months	Diagnostic test				Weak
Hibbert	2019	United Kingdom	Cross-sectional study	1648	Situational association	Chemsex	Crystal methamphetamine, GHB/GBL, ketamine, or mephedrone	12 months	HIV self report	Self report (12 months)	Chlamydia, Gonorrhoea, Genital warts, Herpes, LGV (Lymphogranuloma venereum), Shigella, Syphilis, Hepatitis C	12 months	Strong

Hightow-Weidman	2020	United states of America	Cross sectional study	134	Global association	Cannabis		ever				3 months	Strong
Kahler	2015	United States of America	Cross sectional study	109	Global association	Cannabis		30 days				30 days	Weak
Kecojevic	2015	United States of America	Cross sectional study	191	Global association, Situational association	cannabis, ectasy, cocaine, crystal meth, Viagra or other erectile dysfunction drug		6 months				6 months	Moderate
Kelly	2014	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	178	Event-level association	Cannabis		Event based				Event based	Weak
Kelly	2016	United States of America	Cross sectional study	445	Global association	Cannabis		30 days				3 months	Moderate
Kenyon	2018	Belgium	Cross sectional study	1529	Global association	cannabis, Chemsex	Amphetamines, cocaine, ecstasy, GHB	6 months	Diagnostic test				Moderate
Kohli	2019	United Kingdom	Cross sectional study	16065	Global association	crystal meth, ghb/gbl, mephedrone, Chemsex	Crystal methamphetamine, GHB/GBL, or mephedrone	12 months		Self report (12 months)	gonorrhoea: crystal meth S, ghb/gbl S, mephedrone S, chemsex S		Moderate
Kramer	2016	Austria,Belarus,Belgium,Bosnia and Herzegovina,Bulgaria,Croatia,Cyprus,Czech Republic,Denmark,Estonia,Finland,France,Germany,Greece,Hungary,Ireland,Italy,Latvia,Lithuania,Luxembourg,Malta,Netherlands,Norway,Poland,Portugal,Republic of Moldova,Romania,Russian Federation,Serbia,Slovakia,Slovenia,Spain,Sweden,Switzerland,The former Yugoslav Republic of Macedonia,Turkey,Ukraine,United Kingdom of Great Britain and Northern Ireland	Cross sectional study	91477	Global association	Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug, Chemsex	Amphetamines, cocaine crystal methamphetamine, ecstasy, GHB, ketamine, or mephedrone	4 weeks				12 months	Moderate
Kupprat	2017	United States of America	Cross sectional study	169	Global association	Cannabis		30 days				30 days	Weak
Lachowsky	2016	Canada	Cross sectional study	436	Event-level association	Cannabis , Ecstasy, GHB/GBL , Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		Event based				Event based	Moderate
Latini	2019	Italy	Cross sectional study	354	Global association	Chemsex	crystal meth, GHB/GBL, mephedrone	12 months	Diagnostic test	Self report (12 months)	gonorrhoea, syphilis, chlamydia, non-gonococcal urethritis and hepatitis A, B and C	12 months	Strong
Li	2014	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	639	Situational association	Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		12 months	HIV self report			12 months	Moderate
Li	2014	China	Cross sectional study	400	Global association	Poppers		3 months	HIV self report	Self report (3 months)	Syphilis	3 months	Strong
Martinez	2017	United States of America	Cross sectional study	240	Global association	Cannabis		3 months				3 months	Weak
Melendez-Torres	2017	United Kingdom of Great Britain and Northern Ireland	Cross sectional study	6742	Event-level association	Cannabis , Cocaine, Ecstasy, GHB/GBL , Ketamine (Vitamin K, K, Special K), Crystal methampetamine, Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug		Event based				Event based	Weak
Mitchell	2016	United States of America	Cross sectional study	722	Situational association	Cannabis , Poppers , Viagra or other erectile dysfunction drug or other erectile dysfunction drug, Chemsex	Ecstasy, GHB, or ketamine	3 months				Event based	Moderate
Morgan	2016	United States of America	Cross sectional study	1185	Situational association	Cannabis		12 months	HIV self report			6 months	Weak
Pufall	2018	United Kingdom (england and wales)	Cross sectional study	392	Situational association	Chemsex	Crystal methamphetamine, GHB/GBL, ketamine, or mephedrone	12 months		Self report (12 months)	Chlamydia, gonorrhoea, syphilis	12 months	Moderate