### Syndemic conditions and their measurement

We identified 46 different syndemic conditions in the 94 quantitative studies we included : depression or depressive symptoms (N = 76), intimate partner violence [IPV] (N = 45), substance use (N = 43), childhood sexual abuse [CSA] (N = 34), polysubstance use (N = 26) , binge drinking (N = 22), sexual compulsivity (N = 19), alcohol use disorder [AUD] (N = 18), suicidal thoughts and/or attempts (N = 16), sexual risk behaviors (N = 15), experiences of violence (N = 15), anxiety (N = 14), substance use disorder [SUD] (N = 13), alcohol use (N = 12), discrimination (N = 10), post-traumatic stress disorder [PTSD] (N = 34), chemsex (N = 7), loneliness (N = 6), incarceration (N = 5), unstable housing (N = 5), tobacco use (N = 5), general mental distress (N = 5), low social support (N = 4), low self-esteem (N = 4), internalised homophobia (N = 3), exchange sex (N = 3), sexually transmitted infections [STI] (N = 3), childhood abuse (N = 3), intravenous drug use [IDU] (N = 2), poverty (N = 2), unemployment (N = 2), poor healthcare access (N = 2), involuntary subordination (N = 2), HIV diagnosis (N = 2), hostility (N = 2), stress (N = 2), experience of trauma (N = 2), school bullying (N = 1), sleep disturbance (N = 1), cognitive escape (N = 1), attention deficit hyperactivity disorder [ADHD] (N = 1), impulsivity (N = 1), hypersexuality (N = 1), alexithymia (N = 1), poor physical health (N = 1) and frequenting gay social venues (N = 1).

We chose to distinguish alcohol use disorder, binge drinking and alcohol use instead of merging them in a broad “alcohol-related syndemic condition”. Some authors also considered “heavy drinking”[[22](#ref-Martinez2016a),[23](#ref-martinez2020)] or “heavy alcohol use”[[24](#ref-Mimiaga2015b)] but we chose to aggregate these conditions under “binge drinking” for clarity. Similarly, we distinguished substance use, substance use disorder, intravenous drug use, polysubstance use, marijuana use, tobacco use and chemsex since they differ in potential harm and context of use.

Despite the important number of syndemic conditions studied in the literature, the impact of the seminal study by Stall et al.[[1](#ref-Stall2003)] is striking as the conditions in this paper (depression, IPV, CSA and polysubstance use) are among the five most studied conditions in the field. Furthermore, 91% of the quantitative studies included in our review consider at least one of the four conditions studied by Stall and colleagues as part of a syndemic.

In order to better understand the connections between the syndemic conditions in the studies we elaborated a network plot (Figure [4](#SyndemicNetwork)). Nodes represent the syndemic conditions studied in the literature and edges are drawn between two nodes when two conditions are studied in the same research paper. Furthermore, edges between nodes are thicker as the two conditions are frequently studied together.

In this graph, we divided each conditions into 4 categories : mental health (e.g. depression, anxiety, PTSD), social conditions (e.g. substance use, loneliness), structural conditions (e.g. unemployment, healthcare access) and physical health (e.g. STI, HIV) . When viewing this graph, it is readily apparent that structural syndemic conditions and physical health-related syndemic conditions are way less central than social syndemic conditions and mental health-related syndemic conditions.

Regarding the edges of the network, we identified 337 pairs of syndemic conditions. However, nearly half of these pairs of conditions (N = 157) appear in only one research paper. On the other hand , the most studied pairs of syndemic conditions were depression and IPV (N = 37), depression and substance use (N = (N = 33), depression and CSA (N = 29), depression and polysubstance use (N = 24) and IPV and CSA (N = 24).

We also computed centrality indices for this network, namely degree centrality, the sum of weight in the network, closeness centrality, the inverse of the total length of the paths from a node to all other nodes, and betweennness, the number of shortest path passing through a node[[25](#ref-opsahl2010)].  
Because the weight of the nodes in this network corresponds to the number of studies in which the syndemic conditions appear, degree centrality of each node does is nearly perfectly correlated to the number of studies in which the syndemic condition was studied (r(44) = 0.99, p<0.01).  
Closeness centrality and betweenness centrality are also strongly correlated to the number of studies (r(44) = 0.8, p<0.01 and r(44) = 0.76, p<0.01 respectively). Interestingly, the betweenness centrality of unstable housing is notably high given the low number of studies taking this syndemic condition into account (N = 5). Betweenness centrality can be seen as the extent of brokerage a node can exert on a network.[[26](#ref-zweig2016)] Moreover, the three structural syndemic conditions “unstable housing”, “incarceration” and “poverty” are mostly connected between each others. In other words, in syndemic literature, unstable housing acts as a bridge, notably between the two aforementioned structural syndemic conditions and the rest of the syndemic conditions. Indeed, unstable housing as been studied alongside 15 other syndemic conditions : depression, substance use, IPV, binge drinking, sexual compulsivity, IDU, CSA, polysubstance use, incarceration, poverty, unemployment, discrimination, poor healthcare access, alcohol use and violence.

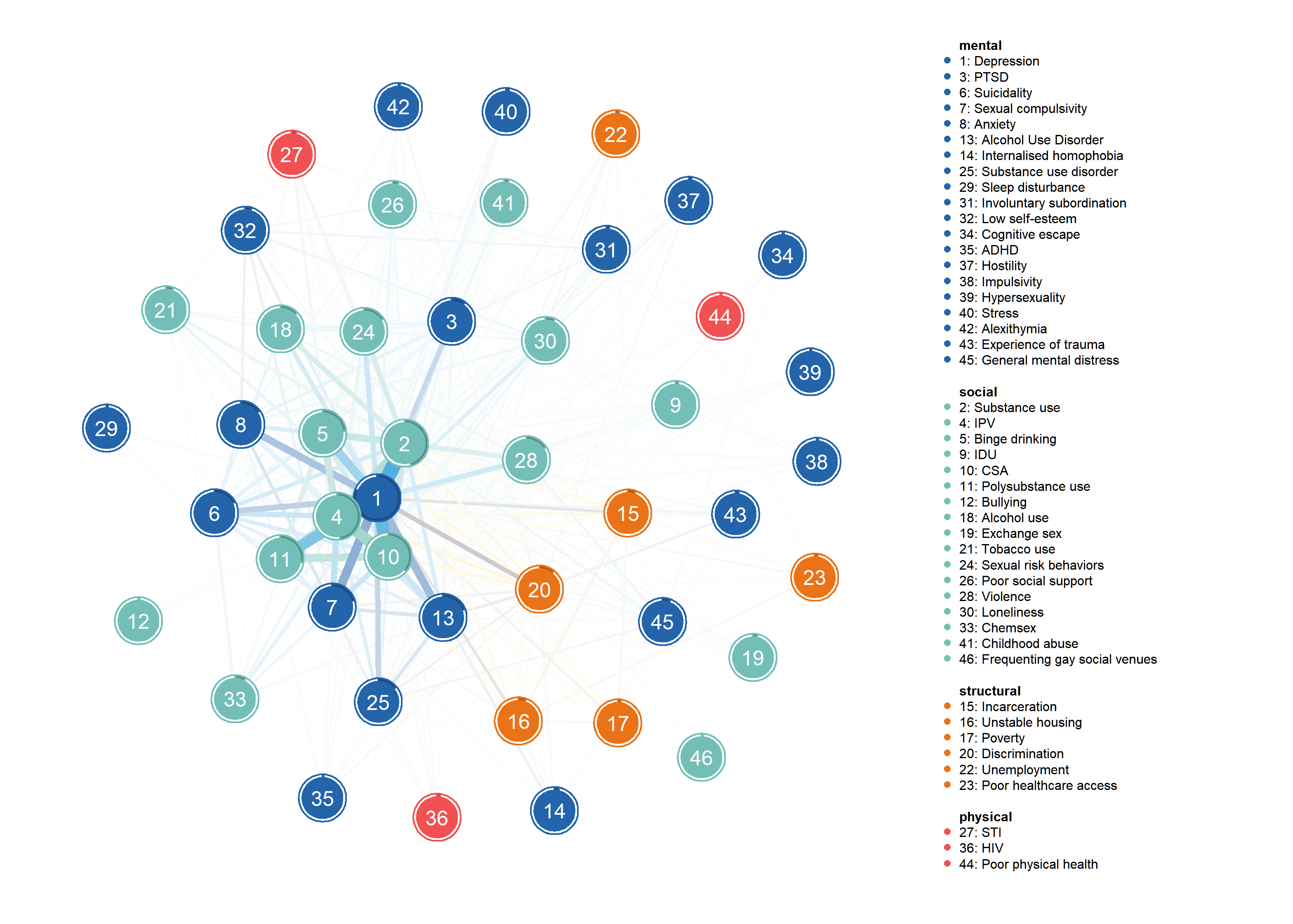


Figure 4: Network of the syndemic conditions studied in quantitative research. The centrality of the nodes gives an indication on the importance of the condition in the literature, the most studied conditions being the most central. Moreover, each node is circled by a pie chart of their frequency in the review. The thickness of the edges linking two nodes depends on the number of studies in which the two conditions were studied together.

The other part of our research question was to examine the way the syndemic conditions were studied in the literature. For the most often studied syndemic conditions, we found an important variability in their measurement. Different authors used different scales or criteria and, even when the same scale or criteria was used, the cutoff or reference period differed among studies. For the sake of brevity, we will not provide a detailed description of the measurement method of the syndemic conditions represented in less than 10% of our studies sample.

For depression, 20 different scales or criteria were used among the 76 studies in which this condition was studied.  
66 studies used scales while 10 studies used criteria to assess the presence of depression or depressive symptoms among the participants. The most used scales were the full Center for Epidemiologic Studies-Depression scale [CESD] (N = 24) and the 10-items version of this scale [CESD-10] (N=10), the 9-items version of the Patient Health Questionnaire [PHQ-9] (N=8) and the Beck Depression Inventory [BDI-II] (N = 5).  
Cutoff for these scales varied the most for the CESD (range : 16 to 27) and the PHQ-9 (range : 5 to 15).  
When a scale was not used, the most frequent criteria to assess the presence of depression was the participant being on medication for depression in the past 12 months (N = 4).  
Table S1 summarizes every scales, criteria and cutoff used in the measurement of depression as well as the references of the studies.

For IPV, 5 types of intimate partner violence were identified : physical violence (N = 36), sexual violence (N = 21), psychological violence (N = 23), gay-related violence (e.g. threats of revealing the partner’s sexual orientation ; N = 3) and HIV-related violence (e.g. threats of disclosing the partner’s serologic status ; N = 1). Reference period varied from past month to lifetime.  
Furthermore, 7 studies used a scale to assess the presence of IPV : the HITS scale (N = 3) the Revised Conflict Tactics Scale [CTS2] (N= 3) and a scale developed by the authors of the study, assessing physical and psychological violence[[27](#ref-Yu2013)].  
Table S2 summarizes every combination of IPV, reference periods, scales and cutoff used as well as the references of the studies.

For substance use, we looked at the class of substances explicitly screened by the authors and the reference period used. The most frequently screened class of substance was stimulants (i.e. cocaine/crack, amphetamines ; N = 37), followed by depressants (i.e. GHB/GBL, benzodiazepines without prescriptions ; (N = 19), opioids (i.e. opioids misuse and ecstasy ; N = 19), marijuana (N = 17), ecstasy /MDMA (N = 17), hallucinogens (i.e. ketamine, psilocybine, phencyclidine ; N = 17), inhalants (nitrous oxyde, Popper ; N = 13) and new psychoactive substances (i.e. synthetic cannabinoids, cathinones ; N = 3).  
Reference period ranged from past month to lifetime.  
Table S3 summarizes every class of substances screened and reference period as well as the references of the studies.

For CSA, we identified 13 different definitions and 3 scales among the 34 studies. The various definitions differed on the age at which the sexual intercourse occurred to be qualified as childhood sexual abuse, the age gap between the victim and the perpetrator and the need for the sexual intercourse to be unwanted. The most frequent definition was Finkelhor’s definition[[28](#ref-finkelhor1994)] : any sexual experience before 13 years old with someone at least 5 years older or any sexual experience between 13 and 17 years old with someone at least 10 years older (N = 7).  
Table S4 summarizes every definition and scales as well as the references of the studies.

For polysubstance use, 17 studies considered there were polysubstance when 3 or more class of substance use were used while 9 studies defined polysubstance use as more than one class of substance use. Moreover, 4 studies excluded marijuana from the class of substances screened and 1 study excluded stimulants, because stimulants were already screened in another syndemic condition.  
Table S5 summarizes every definition of polysubstance use and the references of the studies.

For binge drinking, we identified 6 different thresholds for binge drinking, differing on the number and frequency of binge drinking episodes. The threshold ranged from one episode in the past 12 months to more than one episode per week, every week in the past 12 months.  
Table S6 summarizes every definition and reference period used as well as the references of the studies.

Measurement of sexual compulsivity was surprisingly standardized, compared to the rest of the most frequently studied syndemic conditions. Nearly every study used the Kalichman’s Sexual Compulsivity Scale, with cutoff ranging from 20 to 26, except for two studies using the Compulsive Sexual Behavior Inventory[[29](#ref-Herrick2013),[30](#ref-Dyer2012)] and one study using a scale devised by the authors[[31](#ref-Wang2017)].

For AUD, we identified 4 different definitions. 8 studies used the full Alcohol Use Disorder Identification Test (AUDIT-10),[[32](#ref-tomori2018)–[39](#ref-scheer2021)] 4 studies used the 3-items version of this screening test (AUDIT-C),[[5](#ref-Perry),[40](#ref-Chakrapania)–[42](#ref-sullivan2020)] 5 studies used the CAGE questionnaire[[43](#ref-Zhang2019)–[47](#ref-Safren2018)] and one study used clinical diagnosis based on the DSM-IV criteria[[21](#ref-Mustanski2017)].

Regarding suicide, 6 studies considered only suicidal thoughts[[21](#ref-Mustanski2017),[39](#ref-scheer2021),[44](#ref-Biello2016),[46](#ref-Mimiaga2015),[48](#ref-lee2020),[49](#ref-Halkitis2015)] , 5 studies considered both suicidal thoughts and suicide attempts[[18](#ref-ferlatte2018),[50](#ref-McDaid2019a)–[53](#ref-Halkitis2013)] and 3 studies considered only suicide attempts[[54](#ref-ocleirigh2018)–[56](#ref-Pantalone2018)] . Furthermore, one study used the Positive and Negative Suicide Ideation scale (PANSI)[[57](#ref-oginni2019)] and one study used the Suicide Behaviors Questionnaire-Revised (SBQ-R)[[20](#ref-ng2020)].

A number of behaviors have been used to define sexual risk behaviors as a syndemic condition. The most widely used of these criteria is condomless anal sex (N = 11)[[8](#ref-chandler2020),[16](#ref-Mustanski2014),[34](#ref-semple2017),[49](#ref-Halkitis2015),[58](#ref-Wu2018)–[64](#ref-blondeel2021)], followed by the number of partners (N = 7)[[8](#ref-chandler2020),[16](#ref-Mustanski2014),[34](#ref-semple2017),[58](#ref-Wu2018)–[60](#ref-Li2016),[64](#ref-blondeel2021)] . The condomless anal sex criteria has been refined in three studies, two of them taking into account the type of partner (regular versus casual)[[65](#ref-Friedman2015),[66](#ref-friedman2016)] and one, the serologic status of both partners[[67](#ref-Ferlatte2015)].  
Other criteria such as condomless oral sex[[49](#ref-Halkitis2015),[62](#ref-Halkitis2013a),[63](#ref-Storholm2011)] , condomless vaginal sex[[61](#ref-eaton2013)], STI diagnosis[[8](#ref-chandler2020)], engagement in sex work[[8](#ref-chandler2020)] and sexual intercourse with a HIV positive partner[[8](#ref-chandler2020)] have been used. Finally, one study used the Kalichman’s Sexual Sensation Seeking Scale to assess the propensity of participants to engage in novel or risky sexual stimulation.[[68](#ref-Wim2014a)]

For violence 11 studies looked at sexual violence, 10, at physical violence and 5 at psychological violence. One Indian study also took into account sexual and physical harassment by the police[[69](#ref-Chakrapani2017)].  
Table S7 summarizes every combination of violence studied, the reference period as well as the reference of the studies.

Several types of anxiety disorder were studied : generalized anxiety disorder (N = 7), social phobia (N = 5) and panic disorder (N = 3). The type of anxiety disorder screened was not specified in 5 studies.  
8 different criteria were used to assess the presence of an anxiety disorder among the 14 studies considering anxiety as a syndemic condition. The most frequent criteria was a score equal or greater than 10 on the 7-items version of the Generalized Anxiety Disorder screening test (GAD-7 ; N = 4).  
Table S8 summarizes every combination of anxiety disorder studied, the criteria or scale used and the cutoff or reference period, as appropriate, as well as the references of the studies.

SUD was screened through a clinical diagnosis based on the DSM-IV[[2](#ref-buttram2015),[19](#ref-Kurtz2012),[70](#ref-Batchelder2019),[71](#ref-carrico2018)], mention of substance abuse in the electronic medical record[[72](#ref-Byg2016)] or the participant thinking he should reduce his substance use[[73](#ref-Ferlatte2014)]. Several screening test were also used : the Drug Use Disorder Identification Test (DUDIT)[[33](#ref-Morrison2018a),[36](#ref-tan2016),[37](#ref-achterbergh2021)], the Texas Christian University Drug Screen (TCUDS)[[43](#ref-Zhang2019),[74](#ref-OLeary2014b)], the Mini International Neuropsychiatric Interview (MINI)[[47](#ref-Safren2018)] and the 10-items Drug Abuse Screening Test (DAST-10)[[75](#ref-chuang2018)].

Outside of binge drinking and alcohol use disorder, which represents two distinct syndemic conditions, we aggregated three aspects of alcohol use studied in syndemic literature to form a generic “alcohol use” syndemic condition : alcohol consumption[[27](#ref-Yu2013),[49](#ref-Halkitis2015),[53](#ref-Halkitis2013),[57](#ref-oginni2019)], alcohol use until intoxication[[4](#ref-Halkitis2012),[52](#ref-Guadamuz2014),[63](#ref-Storholm2011)] and early alcohol use[[76](#ref-Hirshfield2015)].

Finally, for discrimination, there were as many criteria as there were research papers studying this condition. Most of the studies only considered discrimination based on sexual orientation, except for two studies examining racist discrimination[[14](#ref-dyer2020),[77](#ref-turpin2020)], one study examining HIV-based discrimination[[75](#ref-chuang2018)] and one study who did not distinguish discrimination based on sexuality, race/ethnicity or any other factor[[22](#ref-Martinez2016a)].

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# Supplementary Materials

Table S1: Summary of the studies including depression or depressive symptoms as a syndemic condition and the criteria used to screen this condition

| **Use of a scale or a criteria** | **Number of studies** | **Scale or criteria used** | **Number of studies** | **Cutoff used** | **References** |
| --- | --- | --- | --- | --- | --- |
| Scale | 66 | CESD | 24 | 16 | **Zhang et al. 2019** |
| **Morrison et al. 2018** |
| **Wang et al. 2017** |
| **Friedman et al. 2016** |
| **Tulloch et al. 2015** |
| **Friedman et al. 2015** |
| **Herrick et al. 2014** |
| **Herrick et al. 2013** |
| **Dyer et al. 2012** |
| **Tan et al. 2016** |
| **Ng et al. 2020** |
| 22 | **Vanden Berghe et al. 2014** |
| 23 | **Wang et al. 2018** |
| **Parsons et al. 2017** |
| **Hart et al. 2017** |
| **Li et al. 2016** |
| **Starks 2014** |
| **Jie et al. 2012** |
| **Parsons et al. 2012** |
| **Stall et al. 2003** |
| 27 | **Carrico et al. 2018** |
| Continuous | **Hugh Klein 2011** |
| **Turpin et al. 2020b** |
| **Dyer et al. 2020** |
| CESD-10 | 10 | 10 | **Chandler et al. 2020a** |
| **Ogunbajo et al. 2019** |
| **Chandler et al. 2020b** |
| **Martinez et al. 2016** |
| **Biello et al. 2016** |
| **Mimiaga et al. 2015a** |
| **Biello et al. 2014** |
| **Shuper et al. 2020** |
| **Chandler et al. 2020c** |
| **Sullivan and Eaton 2020** |
| PHQ-9 | 8 | 10 | **Zepf et al. 2020** |
| **Nostlinger et al. 2020** |
| **Harkness et al. 2019** |
| **Tomori et al. 2018** |
| 15 | **McDaid et al. 2019** |
| 5 | **Chakrapani et al. 2020** |
| **Safren et al. 2018** |
| Having at least 5 positive items in addition to the depressed mood and/or loss of interest items | **Harkness et al. 2018** |
| BDI-II | 5 | 16 | **Halkitis et al. 2012** |
| 17 | **Pitpitan et al. 2016** |
| Continuous | **Semple et al. 2017** |
| **Halkitis et al. 2015** |
| **Halkitis et al. 2013** |
| Depression subscale of the Brief Symptom Inventory | 4 | 0.5 (raw-score) | **Parsons et al. 2015** |
| 0.8 (raw score) | **Muñoz-Laboy et al. 2018** |
| 65 (T-score) | **Starks et al. 2016** |
| Not specified | **Moeller et al. 2011** |
| PHQ-2 | 3 | 3 | **Walters et al. 2020** |
| **Hirshfield et al. 2015** |
| **Santos et al. 2014** |
| PHQ-8 | 3 | 10 | **Blashill et al. 2020** |
| Continuous | **Lee et al. 2020a** |
| **Lee et al. 2020b** |
| HADS | 2 | 10 | **Card et al. 2018** |
| 8 | **Achterbergh et al. 2021** |
| Zung Self Rating Depression Scale | 2 | 0.5 | **Jiang et al. 2020** |
| 40 | **Oginni et al. 2019** |
| BDI-FS | 1 | 7 | **Chakrapani et al. 2017** |
| CESD-12 | 1 | 10 | **Yu et al. 2013** |
| CESD-5 | 1 | 1 | **O'Leary et al. 2014** |
| CESD-SF | 1 | 13 | **Mimiaga et al. 2015b** |
| The Depression Symptom Scale (DSS-9) | | | **Friedman et al. 2014** |
| Criteria | 10 | Being on medication for depression in the last 12 months | | | **Ferlatte et al. 2015** |
| **Brandstrom and Pachankis 2018** |
| **Ferlatte et al. 2018b** |
| Clinical diagnosis based on the DSM-IV | | | **Batchelder et al. 2019** |
| **Mustanski et al. 2017** |
| During the past 12 months having felt so sad or hopeless almost every day for 2 weeks in a row that the respondent stopped doing some usual activities | | | **Turpin et al. 2020a** |
| **Mustanski 2014** |
| Feeling snap and unable to snap out of it for most of the time or being in treatment for depression | | | **Ferlatte et al. 2014** |
| Medical diagnosis of depression in the EMR | | | **Byg et al. 2016** |
| Self-report of a medical diagnosis | | | **Reisner et al. 2016** |

Table S2: Summary of the studies including intimate partner violence as a syndemic condition and the criteria used to screen this condition

| **Use of a scale or a criteria** | **Number of studies** | **Type(s) of violence screened or scale used** | **Number of studies** | **Reference period or cutoff used** | **References** |
| --- | --- | --- | --- | --- | --- |
| Criteria | 38 | physical IPV, sexual IPV, psychological IPV | 12 | Past year | **Oginni et al. 2019** |
| Past 6 months | **Turpin et al. 2020b** |
| Past 5 years | **Biello et al. 2016** |
| **Starks et al. 2016** |
| **Mimiaga et al. 2015a** |
| **Parsons et al. 2015** |
| **Stall et al. 2003** |
| **Achterbergh et al. 2021** |
| Lifetime | **Lee et al. 2020a** |
| **Safren et al. 2018** |
| **Mustanski et al. 2007** |
| **Dyer et al. 2020** |
| physical IPV, psychological IPV | 8 | Past 5 years | **Starks 2014** |
| **Herrick et al. 2013** |
| **Dyer et al. 2012** |
| **Parsons et al. 2012** |
| Past 12 months | **McDaid et al. 2019** |
| **Ferlatte et al. 2018a** |
| Not specified | **Jie et al. 2012** |
| Lifetime | **Walters et al. 2020** |
| physical IPV | 7 | Past month | **Mustanski 2014** |
| Past 4 months | **Eaton et al. 2013** |
| Past 12 months | **Chandler et al. 2020a** |
| **Chandler et al. 2020b** |
| **Chandler et al. 2020c** |
| Lifetime | **Tomori et al. 2018** |
| **Tulloch et al. 2015** |
| physical IPV, sexual IPV | 6 | Past 6 months | **Mustanski et al. 2017** |
| Lifetime | **Turpin et al. 2020a** |
| **OCleirigh et al. 2018** |
| **O'Leary et al. 2014** |
| **Ng et al. 2020** |
| **Reisner et al. 2016** |
| physical IPV, sexual IPV, psychological IPV, gay-related IPV | 2 | Past 5 years | **Jiang et al. 2020** |
| Lifetime | **Chuang et al. 2018** |
| Not specified | 2 | Not specified | **Byg et al. 2016** |
| Lifetime | **Beymer et al. 2016** |
| physical IPV, sexual IPV, psychological IPV, gay-related IPV, HIV-related IPV | 1 | Past month | **Wu Elwin 2018** |
| Scale | 7 | HITS | 3 | Continuous | **Lee et al. 2020b** |
| 11 | **Zepf et al. 2020** |
| **Blashill et al. 2020** |
| CTS2 | 3 | Responding yes to at least one item | **Parsons et al. 2017** |
| Not specified | **Zhang et al. 2019** |
| Continuous | **Pantalone et al. 2018** |
| Authors' scale (physical and psychological) | 1 | continuous | **Yu et al. 2013** |
| Physical intimate partner violence: 36 studies ; 80% of studies with IPV as a syndemic condition | | | | | |
| Psychological intimate partner violence: 23 studies ; 51% of studies with IPV as a syndemic condition | | | | | |
| Sexual intimate partner violence: 21 studies ; 47% of studies with IPV as a syndemic condition | | | | | |
| Gay-related intimate partner violence: 3 studies ; 7% of studies with IPV as a syndemic condition | | | | | |
| HIV-related intimate partner violence: 1 studies ; 2% of studies with IPV as a syndemic condition | | | | | |

Table S3: Summary of the studies including substance use as a syndemic condition and the substances specifically screened in the studies

| **Type of substances screened** | **Number of studies** | **Reference period** | **References** |
| --- | --- | --- | --- |
| stimulants | 6 | Past month | **Zepf et al. 2020** |
| Past 6 months | **Mimiaga et al. 2015b** |
| **Herrick et al. 2013** |
| **Dyer et al. 2020** |
| Past 3 months | **Harkness et al. 2019** |
| **Harkness et al. 2018** |
| stimulants, ecstasy, hallucinogens, depressants | 4 | Past 4 months | **Moeller et al. 2011** |
| Past 12 months | **Ferlatte et al. 2015** |
| **Ferlatte et al. 2018a** |
| **Ferlatte et al. 2018b** |
| stimulants, marijuana, opioids | 3 | Past month | **Semple et al. 2017** |
| Past 3 months | **Wu Elwin 2018** |
| Lifetime | **Oginni et al. 2019** |
| stimulants, ecstasy, hallucinogens, marijuana, depressants, opioids, inhalants | 3 | Past month | **Halkitis et al. 2015** |
| **Halkitis et al. 2013** |
| Past 3 months | **Storholm et al. 2011** |
| stimulants, opioids | 2 | Past 6 months | **OCleirigh et al. 2018** |
| **Tomori et al. 2018** |
| not\_specified | 2 | Past month | **Biello et al. 2014** |
| Past 12 months | **Santos et al. 2014** |
| marijuana | 2 | Past month | **Blashill et al. 2020** |
| Lifetime | **Perry et al. 2019** |
| stimulants, marijuana, inhalants | 1 | Past 4 months | **Eaton et al. 2013** |
| stimulants, marijuana | 1 | Past month | **Mustanski 2014** |
| stimulants, inhalants | 1 | Past 3 months | **Sullivan and Eaton 2020** |
| stimulants, hallucinogens, marijuana, depressants, inhalants | 1 | Lifetime | **Shuper et al. 2020** |
| stimulants, hallucinogens, depressants, opioids, inhalants | 1 | Past 3 months | **Lee et al. 2020a** |
| stimulants, hallucinogens, depressants, opioids | 1 | Past month | **Lee et al. 2020b** |
| stimulants, hallucinogens, depressants, NPS, opioids | 1 | Lifetime | **Ogunbajo et al. 2019** |
| stimulants, hallucinogens, depressants, NPS | 1 | Past 3 months | **Nostlinger et al. 2020** |
| stimulants, ecstasy, opioids, inhalants | 1 | Past 6 months | **Dyer et al. 2012** |
| stimulants, ecstasy, NPS, opioids | 1 | Lifetime | **Turpin et al. 2020a** |
| stimulants, ecstasy, marijuana, depressants, opioids | 1 | **Yu et al. 2013** |
| stimulants, ecstasy, marijuana | 1 | **Li et al. 2016** |
| stimulants, ecstasy, inhalants | 1 | Past 12 months | **Beymer et al. 2016** |
| stimulants, ecstasy, hallucinogens, marijuana, depressants, opioids | 1 | Past month | **Hugh Klein 2011** |
| stimulants, ecstasy, hallucinogens, marijuana, depressants | 1 | Past 12 months | **Mustanski et al. 2007** |
| stimulants, ecstasy, hallucinogens, depressants, opioids, inhalants | 1 | Lifetime | **Pitpitan et al. 2016** |
| stimulants, ecstasy, hallucinogens, depressants, opioids | 1 | Past 3 months | **Herrick et al. 2014** |
| stimulants, ecstasy, hallucinogens, depressants, inhalants | 1 | Past 4 months | **Guadamuz et al. 2014** |
| stimulants, depressants, opioids, inhalants | 1 | Past 6 months | **Turpin et al. 2020b** |
| marijuana, opioids | 1 | Past 12 months | **Chakrapani et al. 2019b** |
| marijuana, inhalants | 1 | Past month | **Halkitis et al. 2012** |
| Stimulants : cocaine/crack, amphetamine (37 studies ; 86%) | | | |
| Ecstasy (17 studies ; 40%) | | | |
| Hallucinogens : ketamine, psilocybine, phencyclidine (17 studies ; 40%) | | | |
| Marijuana (17 studies ; 40%) | | | |
| Depressants : GHB/GBL, benzodiazebines (19 studies ; 44%) | | | |
| NPS : New Psychoactive Substances : synthetic cannabinoids, cathinones (3 studies ; 7%) | | | |
| Opioids : opioids misuse, heroin (19 studies ; 44%) | | | |
| Inhalants : nitrous oxyde, Popper : (13 studies ; 30%) | | | |

Table S4: Summary of the studies including childhood sexual abuse as a syndemic condition and the criteria used to screen this condition

| **Use of a scale or a criteria** | **Number of studies** | **Scale or criteria used1** | **Number of studies** | **Cutoff used** | **References** |
| --- | --- | --- | --- | --- | --- |
| Definition | 28 | Finkelhor definition | | | **Lee et al. 2020a** |
| **Blashill et al. 2020** |
| **Lee et al. 2020b** |
| **Harkness et al. 2019** |
| **Safren et al. 2018** |
| **Harkness et al. 2018** |
| **Mimiaga et al. 2015b** |
| Any unwanted sexual experience before 18 years old | | | **Semple et al. 2017** |
| **Biello et al. 2016** |
| **Starks et al. 2016** |
| **Mimiaga et al. 2015a** |
| **Biello et al. 2014** |
| **Ng et al. 2020** |
| Any unwanted sexual experience before 17 years old with someone at least 10 years older | | | **Parsons et al. 2015** |
| **Starks 2014** |
| **Parsons et al. 2012** |
| **Stall et al. 2003** |
| Any unwanted sexual experience before 15 years old | | | **OCleirigh et al. 2018** |
| **Reisner et al. 2016** |
| Having experienced unwanted sexual activity with someone older at 16 years old or younger | | | **Parsons et al. 2017** |
| Having experienced sexual abuse as a child | | | **Eaton et al. 2013** |
| Any unwanted sexual experience before 17 years old | | | **Martinez et al. 2016** |
| Any unwanted sexual experience before 16 years old with someone at least 5 years older | | | **Jie et al. 2012** |
| Any unwanted sexual experience before 16 years old | | | **Tomori et al. 2018** |
| Any unwanted sexual experience before 13 years old | | | **Mustanski et al. 2017** |
| Any sexual experience before 13 years old with someone at least 4 years older | | | **Muñoz-Laboy et al. 2018** |
| Any sexual experience before 12 years old, any unwanted sexual experience between 12 years old and 16 years old or any sexual experience with an adult or someone at least 5 years older before 16 years old | | | **Jiang et al. 2020** |
| Any sexual experience before 11 years old, any unwanted sexual experience between 11 years old and 17 years old or any sexual experience with someone at least 4 years older before 17 years old | | | **Wu Elwin 2018** |
| Scale | 6 | CTQ Sexual Abuse subscale | 3 | 5 | **Perry et al. 2019** |
| **Hart et al. 2017** |
| 13 | **Carrico et al. 2018** |
| WSHQ-CSA | 2 |  | **Zhang et al. 2019** |
| **O'Leary et al. 2014** |
| Sexual abuse subscale of the Childhood Maltreatment Interview Schedule - Short Form (CMIS-SF) | 1 | Endorsement of any one item | **Pantalone et al. 2018** |
| 1Finkelhor definition : any sexual experience before 13 years old with someone at least 5 years older or any sexual experience between 13 and 17 years old with someone at least 10 years older (Finkelhor 1994) | | | | | |

Table S5: Summary of the studies including polysubstance use as a syndemic condition and the criteria used to screen this condition

| **Number of substances to qualify as polysubstance use** | **Number of studies** | **Inclusion of marijuana in the substances count** | **Reference period** | **References** |
| --- | --- | --- | --- | --- |
| At least 3 categories of substance use | 16 | Marijuana not included | Past month | **Blashill et al. 2020** |
| Past 3 months | **Chandler et al. 2020a** |
| **Chandler et al. 2020b** |
| Past 12 months | **Pantalone et al. 2018** |
| Marijuana included | Past 6 weeks | **Parsons et al. 2015** |
| Past 6 months | **Card et al. 2018** |
| **Tulloch et al. 2015** |
| **Stall et al. 2003** |
| Past 4 months | **Muñoz-Laboy et al. 2018** |
| Past 3 months | **Harkness et al. 2019** |
| **Harkness et al. 2018** |
| **Parsons et al. 2017** |
| **Starks 2014** |
| **Parsons et al. 2012** |
| Past 2 months | **Hirshfield et al. 2015** |
| Past 12 months | **Reisner et al. 2016** |
| More than one category of substance use | 9 | Marijuana not included | Past 3 months | **Walters et al. 2020** |
| **Hart et al. 2017** |
| Marijuana included | Past 6 months | **Mustanski et al. 2017** |
| **Friedman et al. 2016** |
| **Friedman et al. 2015** |
| **Jie et al. 2012** |
| Past 3 months | **Starks et al. 2016** |
| **Scheer et al. 2021** |
| **Chandler et al. 2020c** |
| At least 3 categories of substance, excluding stimulants | 1 | Marijuana included | Past 6 months | **Mimiaga et al. 2015b** |

Table S6: Summary of the studies including binge drinking as a syndemic condition and the criteria used to screen this condition

| **Number of episodes to qualify as binge drinking** | **Number of studies** | **Reference period** | **References** |
| --- | --- | --- | --- |
| At least one episode | 12 | Past month | **Blashill et al. 2020** |
| **Martinez et al. 2020** |
| **Martinez et al. 2016** |
| **Herrick et al. 2014** |
| Past 6 months | **Mustanski et al. 2017** |
| **Jie et al. 2012** |
| **Dyer et al. 2012** |
| **Reisner et al. 2016** |
| **Dyer et al. 2020** |
| Past 3 months | **Lee et al. 2020a** |
| **Wu Elwin 2018** |
| Past 12 months | **Zepf et al. 2020** |
| At least one per week, every week | 4 | Past 3 months | **Harkness et al. 2019** |
| **Harkness et al. 2018** |
| Past 12 months | **Mustanski et al. 2007** |
| **Ferlatte et al. 2018b** |
| At least one per month | 2 | Past 12 months | **Chandler et al. 2020a** |
| **Chandler et al. 2020b** |
| More than one per week, every week | 2 | Past 12 months | **Brandstrom and Pachankis 2018** |
| **Ferlatte et al. 2018a** |
| At least 3 episodes | 1 | Past month | **Mustanski 2014** |
| Having at least 4 drinks everyday or at least 6 drinks on a typical drinking day | 1 | Not specified | **Mimiaga et al. 2015b** |

Table S7: Summary of the studies including violence as a syndemic condition and the criteria used to screen this condition

| **Type(s) of violence screened** | **Number of studies** | **violence\_period** | **References** |
| --- | --- | --- | --- |
| sexual | 5 | Past 4 months | **Eaton et al. 2013** |
| Lifetime | **Turpin et al. 2020a** |
| **Guadamuz et al. 2014** |
| **Biello et al. 2014** |
| **Mustanski et al. 2007** |
| physical, sexual, psychological | 4 | Past 12 months | **Friedman et al. 2014** |
| Lifetime | **Pitpitan et al. 2016** |
| **Buttram et al. 2015** |
| **Kurtz et al. 2012** |
| physical, sexual | 2 | Past 12 months | **Chakrapani et al. 2019b** |
| Lifetime | **Zepf et al. 2020** |
| physical | 2 | Past 12 months | **Chandler et al. 2020c** |
| Lifetime | **Brandstrom and Pachankis 2018** |
| physical, sexual harassment by police, physical harassment by police | 1 | Not specified | **Chakrapani et al. 2017** |
| physical, psychological | 1 | Past 12 months | **Santos et al. 2014** |
| Physical violence: 10 studies ; 22% of studies with violence as a syndemic condition | | | |
| Psychological violence: 5 studies ; 11% of studies with violence as a syndemic condition | | | |
| Sexual violence: 11 studies ; 24% of studies with violence as a syndemic condition | | | |
| Physical harassment by the Police: 1 studies ; 2% of studies with violence as a syndemic condition | | | |
| Sexual harassment by the Police: 1 studies ; 2% of studies with violence as a syndemic condition | | | |

Table S8: Summary of the studies including anxiety as a syndemic condition and the criteria used to screen this condition

| **Type of anxiety disorder screened, if specified** | **Number of studies** | **Criteria or scale used** | **Number of studies** | **Reference period or cutoff used** | **References** |
| --- | --- | --- | --- | --- | --- |
| not specified | 5 | Being on medication for anxiety | 2 | Past 12 months | **Ferlatte et al. 2015** |
| **Ferlatte et al. 2018b** |
| BSI | 1 | Not specified | **Moeller et al. 2011** |
| Self-report of having an anxiety disorder | 1 |  | **Reisner et al. 2016** |
| HADS | 1 | 8 | **Achterbergh et al. 2021** |
| generalized anxiety disorder | 4 | GAD-7 | 4 | 10 | **McDaid et al. 2019** |
| **Wang et al. 2018** |
| **Wang et al. 2017** |
| **Li et al. 2016** |
| social phobia, panic disorder, generalized anxiety disorder | 3 | MINI-SPIN, PHQ | 2 |  | **Harkness et al. 2019** |
| **Harkness et al. 2018** |
| Clinical diagnosis based on the DSM-IV | 1 | **Batchelder et al. 2019** |
| social phobia | 2 | SPIN | 2 | 19 | **Lee et al. 2020a** |
| **Safren et al. 2018** |