AMERICAN UNIVERSITY OF BEIRUT

IMPACT OF SUBSTANCE USE DISORDERS ON SELF- AND OTHER-DIRECTED VIOLENCE AN INTEGRATED MODEL APPROACH

by
ELIAS FAWZI GHOSSOUB

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AN ABSTRACT OF THE THESIS OF

Elias Fawzi Ghossoub for Master of Science
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Title: Impact of Substance Use Disorders on Self- and Other-Directed Violence: An Integrated Model Approach

Background: In 1996, the World Health Organization (WHO) published its resolution WHA49.25, declaring violence to be a "leading worldwide public health concern". Judging by current available data, it remains so. Questions persist regarding the typology of violence, its determinants and predictors, and its management and treatment. Several explanatory models have addressed these questions separately for self-directed (i.e. suicide) and other-directed (i.e. interpersonal/assaultive) violent behavior and have found similarities in risk and predisposing factors. Substance (alcohol and illicit drugs) use has been identified as an independent environmental risk factor for perpetration of both types of violence through different mechanisms, including the mediating effect of impulsivity. Given that extensive epidemiological, clinical and neurobiological research has shown that self- and other-directed violence share similarities in predispositions and stressors, one important question stands out: what are the determinants of directionality, i.e. choosing the target of the violent behavior? To answer this question, an integrated conceptualization of violence is required.

Hypotheses: Our hypotheses are: (1) alcohol use disorder's association with overall violence will be stronger than that of drug use disorders; (2) drug use disorders will act as a "force of direction" towards interpersonal violence as it will significantly increase the odds of assault compared to suicide attempts; (3) cannabis use disorder will act as a "force of direction" towards interpersonal violence as it will significantly increase the odds of assault compared to suicide attempts; (4) age will modify the association between alcohol and drug use disorders, and suicide attempts, assaults and overall violence, with the association being strongest among youth.

Objectives: Our objectives are: (1) to measure the association between alcohol and/or drug use disorders and different types of violence (attempted suicide and assault) as well as violence as a whole (attempted suicide and/or assault) in an integrated model approach; (2) to assess the effect of socio-demographic, psychosocial and clinical control variables on the association between alcohol and/or drug use disorders and the type of violence.

Methods: Data were obtained from the National Survey on Drug Use and Health pooled across survey years 2008–2014, with a combined sample of 270227 respondents aged 18 years or above. We computed our dependent variables using self-reported history of a suicide attempt (self-directed) and/or of attacking someone with the intent for serious injury

(other-directed) during the past twelve months. The four categories were: no violence, self-directed (SDV), other-directed (ODV), and combined violence (CV). We computed our substance use disorder variables using modified DSM-4 criteria to better align the diagnoses with DSM-5 criteria. The categories of our main exposure variable were: no substance use disorder (NSUD), alcohol use disorder alone (AUDa), drug use disorder(s) alone (DUDa), alcohol and drug use disorders (ADUD). The categories of our second exposure variable were: no cannabis use disorder, positive cannabis use disorder (CUD). We first conducted bivariate analyses for the independent and control variables with the dependent variables. The associations were measured using the adjusted F test which is a Chi-Square statistic adjusted for complex samples. We determined statistical significance using two-sided tests at the alpha level cut-off of 5% and we used Bonferroni's correction method to adjust for multiple testing. We then used multinomial logistic regression models to estimate the odds ratios of (1) having alcohol and/or drug use disorders and (2) having cannabis use disorder for (1) each violence category compared to no violence and (2) other-compared to self-directed violence, while controlling for relevant socio-demographic, psychosocial and clinical variables. We then stratified the analyses according to age strata (18-25, 26-49 and 50 years of age or above) to explore whether age modifies the magnitude or the associations.

Results: AUDa was significantly associated with overall violence, but not significantly more so than DUDa after adjusting for confounders [aOR_{AUDa} = 2.38 (2.16-2.63) vs. aOR_{DUDa} = 2.01 (1.77-2.27)]. Having ADUD tripled the odds of committing any type of violence [aOR_{ADUD} = 3.72 (3.36-4.12)]. Individuals with DUDa were up to two times more likely to commit ODV compared to SDV [aOR_{DUDa} = 1.45 (1.03-2.04)], while individuals with AUDa were not likely to commit one over the other [aOR_{AUDa} = 1.19 (0.89-1.59)]. CUD was associated with a significantly increased risk of committing ODV [aOR_{CUD} = 1.47 (1.31-1.66)] and CV [aOR_{CUD} = 2.20 (1.41-3.43)], but not SDV. CUD was positively associated with perpetration of ODV compared to SDV, but that association was marginally non-significant after adjusting for confounders [aOR_{CUD} = 1.29 (0.97-1.71)]. After stratifying according to age, we found that among 18-25 year olds, AUDa was more strongly associated with committing overall violence compared to DUDa [aOR_{AUDa} = 2.42 (2.18-2.69) vs. aOR_{DUDa} = 1.77 (1.57-2.01)] and DUDa and CUD significantly increased the odds of perpetrating ODV compared to SDV [aOR_{DUDa} = 1.55 (1.15-2.07) and aOR_{CUD} = 1.27 (1.00-1.60)]. We thus rejected our first and third hypotheses and accepted our second and fourth hypotheses.

Conclusions: The integrated model of violence is a scientifically relevant model to establish the nature and the magnitude of violence risk factors. The associations of alcohol, drug and cannabis use disorders with violent behavior depend on the type of violence and are modulated by age. Further research is needed to identify longitudinal predictors of directionality of violence and to design better preventive and therapeutic strategies targeting specific violent behaviors.

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To Rita

my anchor

CHAPTER I:
INTRODUCTION

In 1996, the World Health Organization (WHO) published its resolution WHA49.25, declaring violence to be a "leading worldwide public health concern" (WHO, 1996). Judging by current available data, it remains so (WHO, 2002, 2014a, 2014b).

Violence is defined as "the intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation" (WHO, 2002). For operational purposes, the WHO has elected to divide types of violence according to two major axes (WHO, 2002):

- The identity of the target:
    - Self.
    - Interpersonal, which is inflicted on either children, partners, elderly, acquaintances or strangers.
    - Collective, defined as "violence inflicted by larger groups such as states, organized political groups, militia groups and terrorist organizations".
- The nature of the act:
    - Physical.
    - Sexual.
    - Psychological.
    - Deprivation or neglect.

In our thesis, the terms "violence", "physical violence" and "aggression" are interchangeable. We do not explore psychological or sexual violence or neglect, nor do we discuss non-suicidal self-injury or suicidal ideations. While collective violence can be motivated by social, political or economic agendas, self-directed or interpersonal violence are more frequently attributed to inter- or intra-personal motivations. These motivations are more accessible to early detection and intervention, which may contribute to reducing the burden of these violent behaviors. We will therefore focus on suicidal (i.e. "self-directed") behavior and interpersonal (i.e. "other-directed" and "assaultive") violent behavior.

In 1990, the WHO's Global Burden of Disease estimated the age-standardized rates (per 100000 population) of self-directed violence (self-harm) at 61.2 (60.6-61.8), assault by firearm at 48.2 (44.0-50.7) and assault by sharp object at 111.8 (107.2-115.6) (G. B. o. D. S. Collaborators, 2015). By 2013, only the rates of self-harm had significantly dropped (by around 28%) (G. B. o. D. S. Collaborators, 2015). Furthermore, self-harm and interpersonal violence continue to have a significant burden worldwide (as measured by the Disability-Adjusted Life Year DALY[1] metric) despite declining trends in the developed regions since 1990 (Haagsma et al., 2016).

Violence is associated with important financial costs in addition to negative physical consequences. The bill was estimated at billions of US dollars per year in terms of health care costs and lost work productivity (WHO, 2002). One study found that in 1992, gunshot wounds cost around 126 billion USD while cut/stab wounds cost around 177 billion USD in the United States of America (USA) alone (Miller & Cohen, 1997). Intimate

[1] DALY is "an indicator of the time lived with a disability and the time lost due to premature mortality" (Murray, 1994).

partner violence against women was estimated to cost around 5.8 billion USD in the USA in 1995 (Max, Rice, Finkelstein, Bardwell, & Leadbetter, 2004). In 2008, the total cost per-murder in the USA was estimated to be close to 9 million USD (McCollister, French, & Fang, 2010). Completed suicides and suicide attempts' costs reached 93.5 billion USD in the USA in 2013 (Shepard, Gurewich, Lwin, Reed, & Silverman, 2016).

Twenty-one years since the publication of resolution WHA49.25, questions persist regarding the typology of violence, its determinants and predictors, and its management and treatment. Several explanatory models have addressed these questions separately for self-directed (i.e. suicide) and other-directed (i.e. interpersonal/assaultive) violent behavior and have found similarities in risk and predisposing factors. A number of neurobiological and environmental factors have been implicated: among the former, impulsivity is a key determinant for both types of violent behavior. Furthermore, substance (alcohol and illicit drugs) use has been identified as an independent environmental risk factor for perpetration of both self-directed and other-directed violence through different mechanisms (WHO, 2002).

Given that extensive epidemiological, clinical and neurobiological research has shown that self-directed and other-directed violence share similarities in diathesis and stressors, one important question stands out: what are the determinants of choosing the target of the violent behavior?

To answer this question, an integrated conceptualization of violence is required. However, very few models (Lubell & Vetter, 2006; O'Donnell, House, & Waterman, 2015; Plutchik, van Praag, & Conte, 1989; Prabha Unnithan, Huff-Corzine, Corzine, & Whitt, 1994) have adopted such an approach. We are of the opinion that analyzing suicidal and

assaultive behavior in the same population through an integrated model of violence can shed some light on the determinants of directionality, i.e. the chosen target of the violent behavior.

Our thesis explores the association between substance use disorders and self- and other-directed physical violence in an integrated model, based on publically-available databases from 2008 through 2014, of yearly household surveys of nationally representative samples of the United States (US) non-institutionalized general population, the National Survey on Drug Use and Health (NSDUH). Our framework will adopt a unified assessment strategy for the outcome by relying on self-reported intentionality to engage in physically violent behavior towards self (i.e. attempted suicide) and towards others (i.e. assault). Our framework will also measure the presence of the exposure, i.e. substance use disorders, by assessing clinically-based criteria over the past year. We believe that a uniform and consistent conceptualization of the exposure, the outcome and the confounders in our analyses will make our results more robust.

By identifying specific associations between different types of substance use disorders and violent behaviors, we can devise targeted interventions for preventive purposes at the primary, secondary and tertiary levels.

Before discussing our methodology and exposing our results, we will first provide a quick epidemiological and conceptual overview of substance use disorders. Then, we will review for each of self-directed and other-directed violence the biological mechanisms, the risk factors and the protective factors. Afterwards, we will develop the evidence supporting the association between substance use and violent behavior, with emphasis put on alcohol and cannabis use. Then we will review the etiological concepts behind self-directed and

interpersonal violence and introduce the integrated model approach to violence. We will then detail the knowledge gap in the literature and accordingly detail our research questions, hypotheses and objectives in this thesis.

CHAPTER II:
BACKGROUND

A. An Overview of Substance Use Disorders

1. Classification of Substance Use Disorders

a. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a semiological classification of mental illnesses that provides a standardized diagnostic framework for clinicians and researchers alike, in the USA and worldwide (Hasin et al., 2013). Its current (fifth) edition (DSM-5) was published in 2013 by the American Psychiatric Association (APA).

The DSM-5 defines a substance use disorder by a "cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems" (APA, 2013). The substances included are (APA, 2013):

- Alcohol.
- Cannabis.
- Hallucinogens (phencyclidine and other kinds of hallucinogens).
- Inhalants.
- Opioids.
- Sedatives, hypnotics or anxiolytics.
- Stimulants (including cocaine, amphetamine-like substances and other kinds of stimulants).

- Tobacco.
- Others.

Diagnostic criteria for use disorders are uniform across all substances with a few exceptions (APA, 2013):

- Impaired control:
    - Using the substance in larger amounts or over a longer period of time than intended.
    - Expressing a continuous desire to decrease or cut down use.
    - Spending a lot of time trying to obtain, use and recover from the substance effects.
    - Craving, i.e. “intense desire or urge for the drug”.
- Social impairment:
    - Failing to perform at work, at school or at home.
    - Continuously using the substance despite secondary social and interpersonal problems.
    - Decreasing or abandoning activities because of use.
- Risky use:
    - Continuously using the substance in physically dangerous situations.
    - Persistently using the substance despite health-related repercussions.
- Pharmacological criteria:

- Tolerance, i.e. “requiring a markedly increased dose of the substance to achieve the desired effect or a markedly reduced effect when the usual dose is consumed”.
- Withdrawal, i.e. “a syndrome that occurs when blood or tissue concentrations of a substance decline in an individual who had maintained prolonged heavy use of the substance”. This criterion is not included for hallucinogen and inhalant use disorders.

The diagnosis of a substance use disorder is made when at least two of the above eleven criteria are fulfilled over the course of the past twelve months (APA, 2013). The use of “substance use disorder” instead of “addiction” as a diagnostic term is preferred and more scientifically relevant (APA, 2013).

b. Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, Text Revised

The DSM, Fourth Edition, Text Revised (DSM-4-TR) recognized substance use disorders as two separate entities (APA, 2000; Hasin et al., 2013):

- Substance dependence, defined as fulfilling at least three of the following criteria:
  - Using the substance in larger amounts or over a longer period of time than intended.
  - Expressing a continuous desire to decrease or cut down use.
  - Spending a lot of time trying to obtain, use and recover from the substance effects.
  - Decreasing or abandoning activities because of use.

- Persistently using the substance despite health-related repercussions.
- Tolerance.
- Withdrawal. This criterion is not included for cannabis, hallucinogen and inhalant use disorders.

- Substance abuse, defined as fulfilling at least one of the following criteria, without fulfilling diagnostic criteria for substance dependence:
  - Continuously using the substance in physically dangerous situations.
  - Continuously using the substance despite secondary social and interpersonal problems.
  - Failing to perform at work, at school or at home.
  - Having substance-related legal problems.

c. Comparison between DSM-4-TR and DSM-5 Substance Use Disorder Diagnostic Criteria

Substantive research in substance use disorders led to implementing several changes in diagnostic criteria in DSM-5 (Hasin et al., 2013):

- Combining DSM-4-TR criteria for substance abuse and dependence into one use disorder.
- Refining the general diagnostic criteria by dropping the "legal problems" criterion and adding the "craving" criterion.

- Refining the "cannabis use disorder" diagnostic criteria by adding the "withdrawal" criterion.
- Replacing "nicotine dependence" with "tobacco use disorder", diagnosed in a similar way as other substance use disorders.

For the purposes of our thesis, we used the term "substance" as an umbrella term for "alcohol and drugs". The term "drug(s)" refers to the following illicit drug(s): cannabis, stimulants (including cocaine, crack, amphetamines…), hallucinogens (such as phencyclidine), inhalants, opioids (including heroin, prescription pain relievers…) tranquilizers[2] and sedatives. We did not refer to tobacco or nicotine as a "substance" or a "drug" and we did not include tobacco use disorder in our analyses.

2. Epidemiology of Substance Use

a. Worldwide

Substance use is a global public health concern. The WMH's lifetime prevalence estimates of any DSM-4 substance use disorders vary between 1.3% in Italy and 15.0% in the Ukraine, numbers that are likely to be under-estimates (Kessler et al., 2007). The United Nations Office on Drugs and Crime (UNODC) reports that in 2014, approximately 1 in 20 adults worldwide have used at least one drug, with an estimated 29 million individuals suffering from drug use disorders (UNODC, 2016). Cannabis is the most-widely used drug worldwide, with a stable annual global prevalence of 3.8% since 1998 (UNODC, 2016). In

[2] Tranquilizers are "central nervous system depressant drugs classified as sedative-hypnotics" (CBHSQ, 2016).

2016, the WHO's GBD project published global and national aggregate data pertaining to alcohol and drug use in 2015 (G. R. F. Collaborators, 2016):

- Close to 11% of men and 5% of women are exposed to alcohol use while less than 1% of both men and women are exposed to drug use.
- Compared to 1990, only women's exposure to alcohol use has decreased significantly (13.1%), whereas global exposure to drug use has substantially increased by approximately 30%.
- Around 2750000 deaths (a 6% increase since 2005) were attributed to substance use: suicide and homicide accounted for approximately 5% and 2% of those deaths, respectively.
- Substance use is the fifth leading risk factor for men and the twelfth for women, accounting for 6.6% and 2.0% of disease burden.
- Both alcohol and drug use have been among the leading behavioral risk factors for global disease burden for the last thirty years or so, with alcohol use disorder responsible for around 13% of DALYs attributable to alcohol use, and drug use disorders (opioid, cocaine, amphetamine, cannabis and other) responsible for more than 60% of DALYs attributable to drug use.

A majority of adults diagnosed with substance use disorders report onset of use in adolescence and the earlier the onset of use, the higher the likelihood of developing a disorder (Lynskey, Agrawal, & Heath, 2010; Peiper, Ridenour, Hochwalt, & Coyne-Beasley, 2016). Most substance use disorders' age of onset is below 25 years (Peiper et al., 2016).

b. USA

As per the WHO's GBD project, drug use and alcohol use are respectively the sixth and seventh leading risk factors in terms of DALYs (G. R. F. Collaborators, 2016).

The prevalence of alcohol and drug use disorders is reportedly on the rise. Recent data indicates that the lifetime and twelve-months prevalence of DSM-V alcohol use disorder 29.1% and 13.9% respectively (B. F. Grant et al., 2015) while the lifetime and twelve-months prevalence of any DSM-V drug use disorder were 9.9% and 3.9% respectively (B. F. Grant et al., 2016). Earlier studies reported more conservative numbers: lifetime prevalence of 8% for alcohol use disorders and 2-3% for drug use disorders (Merikangas & McClair, 2012). Furthermore, alcohol and drug use disorders were more prevalent among men and youth and were mostly comorbid with each other and with nicotine use disorder (B. F. Grant et al., 2015; B. F. Grant et al., 2016; Kendler, Prescott, Myers, & Neale, 2003).

Cannabis use disorder was by far the most prevalent among drug use disorders (lifetime 6.3% and twelve-months 2.5%) with a male-to-female ratio close to 2:1 (B. F. Grant et al., 2016). It is estimated that around 9% of those exposed to cannabis use develop a use disorder, with the prevalence reaching 50% if cannabis use was on a daily basis (Volkow, Hampson, & Baler, 2017). The recent legalization of cannabis use in some states and the increasing potency of cannabis [i.e. increased concentration of Delta9-TetraHydroCannabinol (THC)] has reportedly led to a rise in cannabis-related health care use, accidents and deaths (UNODC, 2016). Moreover, 2009-2012 trends show a rise in the

number of cannabis users simultaneous with a decrease of the number of cannabis users seeking treatment for problematic use (UNODC, 2016).

3. Conceptual Model of Substance Use Disorders

Complex interactions between genetic factors and unique (and to a lesser extent, common) environmental factors are responsible for the etiology of substance use disorders (Hines, Morley, Mackie, & Lynskey, 2015; Kendler, Myers, & Prescott, 2007; Merikangas & McClair, 2012). Current evidence points to the presence of non-specific and substance-specific genetic risk factors towards developing addiction (Bierut, 2011; Kendler et al., 2007; Kendler et al., 2003; Koob & Le Moal, 2001; Merikangas & McClair, 2012), as well as prenatal and postnatal exposure to stress (Koob & Le Moal, 2001) playing an important role.

The integration of neurobiological and psychological models that have conceptualized the development of addiction is essential to fully understand this cornerstone feature of substance use disorders (Koob & Le Moal, 1997). The widely-accepted model of substance use disorders conceptualizes substance use disorders from the perspective of allostasis, defined as "the process of achieving stability through change" (Koob & Le Moal, 2001). This stability is "not within the normal homeostatic range" (Koob & Le Moal, 2001). Indeed an allostatic state is defined as "a state of chronic deviation of the regulatory system from its normal (homeostatic) operating level" (Koob & Le Moal, 2001) and allostatic load is the "cost to the brain and body of the deviation accumulating over time, and reflecting in many cases pathological states and accumulation of damage" (Koob & Le Moal, 2001).

This model identifies three key stages of addiction: binge-intoxication, withdrawal-negative affect and preoccupation-anticipation (Koob & Le Moal, 1997). In the binge-intoxication stage, there is positive reinforcement of drug intake through activation of the mesocorticolimbic dopamine system which involves the ventral tegmental area and the nucleus accumbens (Koob et al., 2014). The withdrawal-negative affect stage is characterized by loss of motivation, physical and emotional pain, irritability and dysphoria, symptoms which are central to the negative reinforcement of drug intake (Koob et al., 2014). Moreover, withdrawal from chronic substance use leads to a rise in the reward threshold, manifested by subsequent increased administration of the substance (Koob, 2008). The activation of the brain stress systems, including the corticoid and the norepinephrine systems, is key to the withdrawal-negative affect stage (Koob, 2008; Koob et al., 2014; Sarnyai, Shaham, & Heinrichs, 2001). The activation of the HPA axis leads to activation of the extrahypothalamic stress system in the prefrontal cortex and extended amygdala, mediated by the Corticotropin-Releasing Factor (CRF), a polypeptide which controls biological responses to stressors (Koob et al., 2014); this cascade stimulates the release of norepinephrine in the locus coeruleus (Koob & Le Moal, 2001), and dynorphin, a neuropeptide ligand for the kappa opioid receptor, which decreases the activity of the mesocorticolimbic dopamine system (Koob, 2008; Koob et al., 2014). The CRF system activation seems to mediate anxiety-like symptoms in substance use withdrawal, while the dynorphin system activation mediates depression-like symptoms in withdrawal (Koob et al., 2014). Furthermore, research has shown that during withdrawal, in addition to decreased activity of the mesocorticolimbic dopamine system, there is decreased dopamine functioning in the brain, leading to dysfunction of the prefrontal regions of the brain,

including the orbitofrontal cortex and cingulate gyrus (Koob et al., 2014; Volkow, Fowler, & Wang, 2003). The brain stress systems activation can persist in periods of abstinence (long after withdrawal) and increase vulnerability to craving (which corresponds to the preoccupation-anticipation stage) and relapse of use triggered by environmental factors (Koob et al., 2014; Koob & Le Moal, 2001; R. J. Smith & Aston-Jones, 2008).

The repetitive activation of the brain reward and stress systems leads to the progression from initial drug use to substance use disorder in vulnerable individuals: repetitive use shifts the burden of brain stress activation from the HPA to the extrahypothalamic CRF system through neuroadaptation, which leads to dysfunction in the prefrontal cortex, which in turns leads to impairment in executive function and loss of control, further fueling the drug addiction cycle (Koob & Le Moal, 2001). It is fair to say at this point that the progression from initial substance intake to substance use disorder leads to a motivational shift in using the substance, from seeking reward and pleasure (positive reinforcement) to avoiding aversive withdrawal symptoms (negative reinforcement); this shift is illustrated by the simultaneous progressive decreased activation of the brain reward system and overactivation of the brain stress systems (Koob & Le Moal, 2001).

Thus substance use disorders induce an allostatic state, leading to progressive activation of the brain stress systems and decreased functioning of the mesocorticolimbic system, with subsequent compulsive drug-taking and loss of control over this behavior and the development of illness and pathology (Koob et al., 2014; Koob & Le Moal, 2001).

The allostasis model of substance use disorders is not substance-specific and has been constructed through research on alcohol among others (Koob, 2014; Koob et al., 2014; Koob & Le Moal, 2001). Additional evidence point to a substantial role the hypothalamic

CRF system plays in reinforcing the acute alcohol effects (Sarnyai et al., 2001) and the norepinephrine system plays in mediating alcohol withdrawal and the negative reinforcement of alcohol addiction (Koob, 2014). Only recently did molecular research find evidence that endocannabinoids and the active ingredient of cannabis, THC, stimulate the ventral tegmental area and the nucleus accumbens, which are key areas of the reward system, and thus increase dopamine in these areas (Gardner & Vorel, 1998; Koob & Le Moal, 2001; Lupica, Riegel, & Hoffman, 2004). Activation of the endocannabinoid system, of which THC is a ligand, has been implicated in substance-seeking behavior for alcohol and cannabis amongst others (Covey, Wenzel, & Cheer, 2015; Volkow et al., 2017). Furthermore, cannabis use primes the endocannabinoid system to the rewarding effects of other drugs, including alcohol, thus increasing the risk of subsequent polysubstance use (hence it being labeled as a "gateway drug") (Volkow et al., 2017).

Chronic administration of THC has been shown to blunt the dopamine reward system (Covey et al., 2015). Added to that, withdrawal from chronic cannabis use has been shown to activate the CRF system (Caberlotto, Rimondini, Hansson, Eriksson, & Heilig, 2004; Rodriguez de Fonseca, Carrera, Navarro, Koob, & Weiss, 1997), which has been implicated in the pathophysiology of substance use disorders, as detailed above. All this evidence supports the relevance of cannabis use disorder as a pathology of great interest and implications to further understanding addiction (Covey et al., 2015; Lupica et al., 2004).

B. Self-Directed Violence

1. Definitions

As per the WHO, self-directed violence is divided into suicidal behavior, which includes suicidal ideations, attempts and completed suicides, and self-mutilation which does not include intent to kill oneself (WHO, 2002). Suicide is defined as "the deliberate act of killing oneself" (Patel et al., 2016) while suicide attempt is defined as the "engagement in potentially self-injurious behavior in which there is at least some intent to die" (Nock, Borges, Bromet, Cha, et al., 2008). Other terms to describe non-fatal suicide behavior are "deliberate self-harm" and "parasuicide" (WHO, 2002). For the purposes of this thesis, we will refer to completed suicide and fatal suicidal behavior as "suicide" and non-fatal suicidal behavior as "attempted suicide".

2. Epidemiology

a. Worldwide

i. Suicide

Suicide is a global public health concern due to its significant morbidity and mortality across different socio-economic and cultural regions (WHO, 2014b).

In 2012, it was estimated that the global age-standardized suicide rate is 11.4 per 100000 population, with around 804000 suicide deaths reported (WHO, 2014b). Suicides account for more than 50% of global violent deaths (WHO, 2014b).

ii. Attempted Suicide

The WHO's World Mental Health Surveys determined the twelve-months prevalence of suicide ideations, plans and attempts to be around 2.0-2.1%, 0.6-0.7% and 0.3-0.4% respectively (Borges et al., 2010), while the lifetime corresponding prevalence were even higher (9.2%, 3.1% and 2.7% respectively) (Nock, Borges, Bromet, Alonso, et al., 2008).

b. USA

i. Suicide

In the USA, there seems to be an increasing trend in suicide fatalities: the age-standardized rate increased from 9.8 per 100000 in the year 2000 to 12.1 per 100000 in 2012, a 24.2% increase (WHO, 2014b). Firearm suicide rates were estimated to be eight times higher than in other high-income countries (Grinshteyn & Hemenway, 2016) and represented close to two-thirds of total deaths by firearms in 2012 (Wintemute, 2015).

ii. Attempted Suicide

Estimates for twelve-months prevalence of suicide ideations (2.1-10.0%), plans (0.7-7.0%) and attempts (0.2-2.0%) point towards a possible higher burden of suicide, although the variation in the reported rates might be due to methodological differences in the studies (Nock, Borges, Bromet, Cha, et al., 2008).

3. Neurobiological Basis

Most studies have focused on the serotonin system's key role in suicidal behavior. Genetic studies have identified that dysfunctions in serotonin-related genes promote suicidal behavior through shared pathways with mood disorders but also through suicide-specific pathways (Brezo et al., 2010; Mirkovic et al., 2016). Structural and functional imaging studies have determined alterations to several brain areas, including the medial prefrontal cortex, the anterior cingulate, the dorsolateral prefrontal cortex, the orbitofrontal cortex, the insula, the amygdala, the striatum and the thalamus, to be correlated with attempted suicide; these brain areas are connected through serotonergic circuitry emerging from the dorsal raphe nucleus (van Heeringen & Mann, 2014). The medial prefrontal cortex has been shown to modulate the dorsal raphe nucleus activity in response to stress (Amat et al., 2005) and thus to promote behavioral control of stress and resilience (Maier, Amat, Baratta, Paul, & Watkins, 2006). Alterations to serotonergic circuitry among the aforementioned brain areas lead to reduced efficiency of decision-making processes and emotional control and a heightened sensitivity to rejection (van Heeringen & Mann, 2014), outcomes which have been correlated with the display of suicidal behavior (Richard-Devantoy, Berlim, & Jollant, 2014; Richard-Devantoy, Turecki, & Jollant, 2016). Recent research has also implicated the role of noradrenergic dysfunction as a pathophysiological mechanism in suicide: suicide victims have depleted synaptic norepinephrine in the locus coeruleus (Ordway, 1997) and a significantly lower density of noradrenergic neurons in that nucleus (Arango, Underwood, & Mann, 1996). Furthermore, low levels of the noradrenaline metabolite 3-methoxy-4-hydroxphenylglycol (MHPG) in the cerebrospinal fluid (CSF) have been found to significantly predict a serious suicide attempt within the

next twelve months in depressed individuals (Galfalvy et al., 2009). Finally, hyperactivity of the Hypothalamic-Pituitary-Adrenal (HPA) axis and subsequent excessive cortisol release in response to stress have been found to predict suicide attempts in depressed youth (Jokinen & Nordstrom, 2009) and elderly (Jokinen & Nordstrom, 2008). However, caution should be exercised regarding the suicide predictive value of such biomarkers as a recent meta-analysis showed that, after accounting for publication bias, only cytokines and low levels of fish oil nutrients significantly predicted suicide (B. P. Chang et al., 2016).

4. Risk Factors

Risk factors for suicidal behavior have been studied extensively in order to provide a framework for prevention. Age, sex, socioeconomic status and psychiatric comorbidities have been consistently found to be associated with suicidal behavior (Nock, Borges, Bromet, Alonso, et al., 2008; Nock et al., 2009; WHO, 2014b).

a. Socio-Demographic Parameters

i. Suicide

One of the major variables modulating suicide rates is sex, with men reportedly 3 times more likely to kill themselves than women (WHO, 2014b). However, there are large regional variations to the male-to-female ratio, mostly between high-income countries (3.5 in 2012) and low to middle income countries (1.6 in 2012). In the USA, the age-standardized male suicide rate was estimated to be 19.4 in 2012, and the female rate to be 5.2, with a male-to-female ratio of 3.73 (WHO, 2014b).

It has been well established that suicide varies by age, with rates reportedly being lowest in children and adolescents younger than 15 years of age and highest in the elderly aged 70 and above (WHO, 2014b). But the age-by-sex patterns of suicide completers differ by region as well as by time.

Between 2000 and 2003, 25 countries out of 62 witnessed a significant increase in male suicide rates with increasing age, while 27 countries witnessed such an increase in female suicide rates and 17 countries had a significant increase in both rates with increasing age (Shah, 2007). In Australia between 2004 and 2013, male suicide rates decreased in age cohorts 20-34 years then increased in midlife and peaked in age cohorts above 70 years, while female suicide rates were comparatively significantly lower across all age-groups and did not show substantive variations between age-groups (Burns, 2016). In the USA, a 28.4% increase in suicide rates was reported between 1999 and 2010 among middle-aged men and women (Mann & Kuehn, 2014), especially those of white or American Indian/Alaska Native ethnicities (Sullivan, Annest, Luo, Simon, & Dahlberg, 2013). Suicide rates of men between 10 and 24 years of age decreased significantly from 1994 to 2007 whereas corresponding female suicide rates decreased significantly from 1994 to 2001; both rates then significantly increased from 2007 to 2012 (Sullivan, Annest, Simon, Luo, & Dahlberg, 2015).

The age-by-sex patterns of suicide seem to be influenced by demographic and socio-economic factors. Differences in suicide rates between rural and urban areas have been reported to vary depending on the study region (Patel et al., 2016), but a significant amount of evidence points towards rurality being a risk factor of suicide due to higher levels of social isolation and demographic changes (Singh & Siahpush, 2002; Wilkinson &

Israel, 1984). The 2008 economic crisis was found to negatively affect suicide rates, especially among men between 45 and 64 years of age in North and South American countries (S. S. Chang, Stuckler, Yip, & Gunnell, 2013). Increased unemployment subsequent to this economic crisis have been associated to increases in suicide rates (De Vogli, Marmot, & Stuckler, 2013; Stuckler, Basu, Suhrcke, Coutts, & McKee, 2009, 2011) especially in low socio-economic European countries (Karanikolos et al., 2013), but unemployment rates' association with completed suicides was not universal (S. S. Chang et al., 2013; Laanani, Ghosn, Jougla, & Rey, 2015; Miret et al., 2014). Socio-economic status, including educational level, was found to have an inverse relationship with suicide rates across most of Europe and the USA (Lorant, Kunst, Huisman, Costa, & Mackenbach, 2005). In the USA, educational level and marital status was significantly associated with an increased risk of suicide only among men, while family size and employment status had a significant inverse relationship with risk of suicide for both men and women (Denney, Rogers, Krueger, & Wadsworth, 2009). Male and female suicide rates were higher in rural areas compared to urban areas, with the rural-urban disparity widening for men over time (Singh & Siahpush, 2002). Further explanations to the male-to-female ratio variations in suicide include different cultural expectations of men and women, as well as different attitudes in dealing with adversity and seeking mental health care (Canetto & Sakinofsky, 1998; WHO, 2014b). An added complexity to the understanding of suicide risk among populations is the global evidence supporting the existence of a birth cohort effect, i.e. that certain birth cohorts are more likely to experience suicide compared to others, as well as a period effect, i.e. time period-specific factors that influence suicide rates (Chauvel, Leist, & Ponomarenko, 2016; Phillips, Robin, Nugent, & Idler, 2010); both of these effects might

not be as influential for rates of suicide attempts (Kessler, Berglund, Borges, Nock, & Wang, 2005).

ii. Attempted Suicide

Similarly to suicide completers, there are age-by-sex patterns to suicide attempters that interact differently with socio-economic factors. Around 60-70% of those who commit self-harm are below 35 years of age (Hawton et al., 2015). Unemployment was found to predict serious suicidal attempts only in men in their forties while single marital status and ill health predicted such attempts only in women in their twenties (Fairweather-Schmidt, Anstey, Salim, & Rodgers, 2010). The 2008 economic crisis appears to have a differential impact on the rates of self-harm between men and women in England (Hawton et al., 2016). In the USA, it has been consistently reported that suicide completers were more likely to be male, adolescent or middle-aged, of White Non-Hispanic or Native American ethnicities, whereas suicide attempters were more likely to be female, younger, unmarried, unemployed and of lower educational level (Nock, Borges, Bromet, Cha, et al., 2008). Male-to-female ratio of suicide attempters seems to increase with increasing age (Hawton & Harriss, 2008a). While risk factors for suicide attempts and completed suicides overlap considerably (Beautrais, 2001; Shah, 2009), an important discriminating factor in youth appears to be differences in methods adopted by men compared to women (Beautrais, 2003). As a matter of fact, men are more likely to have a higher intent to die and to use more lethal methods to commit suicide (Nock, Borges, Bromet, Cha, et al., 2008).

A prior suicide attempt is associated with a repeat non-fatal attempt and a repeat fatal attempt (Carroll, Metcalfe, & Gunnell, 2014; Fedyszyn, Erlangsen, Hjorthoj, Madsen,

& Nordentoft, 2016; Schmidtke et al., 1996; Yoshimasu, Kiyohara, & Miyashita, 2008); while the former association is modulated by the study region, the survey methods and prevalence of prior self-harm within the population surveyed, the latter one is modulated by age, sex and method used to self-harm (Carroll et al., 2014; Fedyszyn et al., 2016). Overall, for each suicide death there are about 20 attempts reported (Patel et al., 2016), but there are considerable variations as per age-by-sex patterns. The ratio was found to be around five times higher for females than for males (87.9 vs. 18.7), with this difference decreasing with increasing age and with suicidal intent highest in elderly above 60 years of age (Hawton & Harriss, 2008b; Schmidtke et al., 1996). Attempting suicide is a major risk factor for completed suicide, as suicide rates were a hundred times higher in those with a prior attempt compared to the general population (Hawton, Zahl, & Weatherall, 2003). The risk of completed suicide after a non-fatal attempt was found to be higher in males, with increasing age and with increasing length of follow-up (Hawton et al., 2003). But a history of multiple attempts yielded a considerably higher risk for females (Zahl & Hawton, 2004).

b. Psychiatric Disorders

A major risk factor for suicidal behavior is the presence of a psychiatric disorder. Several mental illnesses have been found to significantly predict suicidal behavior (Nock, Borges, Bromet, Cha, et al., 2008; Patel et al., 2016; Swanson, McGinty, Fazel, & Mays, 2015). As per the WHO's Global Burden of Disease, psychiatric disorders (including substance use disorders) were responsible for more than 62% of the DALYs attributed to suicide in 1990 and in 2010 (Ferrari et al., 2014). Family psychiatric and suicide history was also reported to be associated with suicidal behavior (Mok et al., 2016; Nock, Borges,

Bromet, Cha, et al., 2008; Pawlak et al., 2013). Substance use disorders are highly comorbid with mood and anxiety disorders (Conway, Compton, Stinson, & Grant, 2006; B. F. Grant et al., 2015; B. F. Grant et al., 2016; B. F. Grant et al., 2004; Lai, Cleary, Sitharthan, & Hunt, 2015) and schizophrenia (Volkow, 2009). Comorbid substance use disorders with a psychiatric disorder significantly increased the associated risk of attempted suicide (Carra, Bartoli, Crocamo, Brady, & Clerici, 2014; Dharmawardene & Menkes, 2016; Sher et al., 2008) and suicide (Nordentoft, Mortensen, & Pedersen, 2011). In this section, we will not discuss substance use disorders' association with suicidal behavior, as it will be explored in a later section.

i. Suicide

Around 90% of those who died by suicide had a mental illness at the time they committed the act (Cavanagh, Carson, Sharpe, & Lawrie, 2003), although these prevalence numbers seem to vary according to study region and publication year (Cho, Na, Cho, Im, & Kang, 2016; Milner, Sveticic, & De Leo, 2013). Among a variety of socio-economic, demographic, familial and psychiatric factors, a previous hospitalization for management of a psychiatric disorder was the strongest predictor for suicide in Denmark, accounting for 40.3% of the attributable risk for suicide, significantly more so in women than in men (Qin, Agerbo, & Mortensen, 2003; Qin & Nordentoft, 2005).

The absolute risk of suicide associated was 7.77% for men and 4.78% for women with bipolar disorder, 6.67% for men and 3.77% for women with unipolar affective disorders, and 6.55% for men and 4.91% for women with schizophrenia; comorbid self-harm doubled the risk (Nordentoft et al., 2011). Suicide risk seems to increase with the

number of psychiatric disorders diagnosed (Blasco-Fontecilla, Rodrigo-Yanguas, Giner, Lobato-Rodriguez, & de Leon, 2016; Conner et al., 2013; Nock et al., 2009; Nordentoft et al., 2011).

ii. Attempted Suicide

Psychiatric disorders' association with suicide attempts is more controversial. While depression and anxiety significantly predicted non-fatal self-harm in most studies (Hawton, Saunders, Topiwala, & Haw, 2013; Kessler, Borges, & Walters, 1999), some found this association to be modified by age and sex (Fairweather-Schmidt et al., 2010). Comorbid anxiety and personality disorders did not yield an additional risk of non-fatal self-harm in people with mood disorders compared to controls (Pawlak et al., 2013). Those who attempted suicide were more likely to be diagnosed with depressive and behavioral symptoms compared to those who self-harmed with no intent to die (Nock & Kessler, 2006). In Spain, depression with or without comorbid anxiety significantly increased the odds of attempted suicide but anxiety alone did not yield such an effect (Miret et al., 2014).

Results from the WMH surveys show conflicting results, depending on whether psychiatric illnesses are diagnosed within the last twelve months of the attempt or not. All lifetime DSM-IV diagnoses were positively associated with suicide attempts in all regions: mood disorders were the strongest predictors in developed countries whereas impulse-control disorders and post-traumatic stress disorder were the strongest predictors in developing countries (Nock et al., 2009). Associations with twelve-months diagnoses were less impressive, with notably conduct disorder predicting planned suicide attempts among ideators in both developed and developing countries and substance use disorders increasing

the odds of suicide attempts among ideators in developing countries seven-fold (Borges et al., 2010).

5. Protective Factors

Protective factors against suicide have been less studied (Nock, Borges, Bromet, Cha, et al., 2008). Religiosity, measured through religious affiliation and/or service attendance, has been shown to be inversely correlated with rates of suicide attempts, but not suicide ideations (Lawrence, Oquendo, & Stanley, 2016). While social isolation (feeling lonely, living alone…) is a strong predictor of suicidal behavior across different age groups (Trout, 1980; Van Orden et al., 2010), perceived social support was found to protect against both ideations (Kleiman, Riskind, & Schaefer, 2014) and attempts (Kleiman & Liu, 2013).

C. Other-Directed Violence

1. Definitions

Other-directed or interpersonal violence is defined as "the intentional use of physical force or power, threatened or actual, against another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation" (WHO, 2002). For the purposes of our thesis, the term "interpersonal violent behavior" is interchangeable with the term "assaultive behavior"; the outcomes of this behavior can be either fatal (homicide) or non-fatal.

2. Epidemiology

a. Worldwide

i. Homicide

Interpersonal violence is as much of a global public health issue as suicide. While in the year 2000, an estimated 520000 individuals died by homicide, corresponding to a global age-adjusted rate of 8.8 per 100000 population (WHO, 2002), an estimated 475000 died similarly in 2012 (at a global rate of 6.7 per 100000), showing around a 16% drop (WHO, 2014a). Intimate partner violence is believed to contribute to around 14% of global homicides (Stockl et al., 2013).

ii. Assault

The WHO's Global Burden of Disease identified a significant drop in the prevalence of assaults between 1990 and 2013 (in the range of 20-50%) but the rates of sequelae secondary to assault by firearms and sharp objects remained unchanged (G. B. o. D. S. Collaborators, 2015). Women, children and the elderly bear most of the burden associated with non-fatal assault injuries (WHO, 2014a). It is estimated that around 30% of women worldwide have experienced violence at the hands of their partners (Devries et al., 2013). There are culturally and regionally different perceptions of what is "acceptable" physical punishment for children (Lansford et al., 2015; WHO, 2002). The WHO has deemed that all corporal punishment is a form of abuse, subsequent to a United Nations Human Rights convention (Child, 1989) but only 51 countries so far have enacted laws outlawing all forms of corporal punishment (Children, 2017). Research has shown that use of physical punishment is a risk factor for subsequent abuse (Lansford et al., 2015). These

differing regional and cultural views pertaining to corporal punishment do not translate to worldwide prevalence differences of child physical abuse (Stoltenborgh, Bakermans-Kranenburg, van Ijzendoorn, & Alink, 2013; WHO, 2002); prevalence estimates range between 0.3-22.6%, depending on the survey methodology used (Stoltenborgh et al., 2013). Elderly physical abuse contributed to an additional risk of death given the vulnerability of this age group (WHO, 2002); the worldwide prevalence of elder physical abuse ranges between 0.1-11.7% (Sooryanarayana, Choo, & Hairi, 2013).

b. USA

i. Homicide

USA homicide rates were around seven times higher than those in other high-income countries (Grinshteyn & Hemenway, 2016). In 2015, the homicide rate in the USA was estimated to be at 5.0 per 100000, whereas the rate of aggravated assault was at 240.0 (Investigation, 2015). In 2012, more than 1700000 individuals were treated in emergency departments for injuries secondary to assault (WHO, 2014a). Intimate partner violence accounted for 9-16% of total homicides (Stockl et al., 2013). Firearms were used in almost 70% of homicides committed in 2012 (Wintemute, 2015) and firearm homicide rates were around 25 times higher (49 times higher in the 15-24 years age group) than in other high-income countries (Grinshteyn & Hemenway, 2016). For the past decade or so, firearm homicide rates have been relatively stable (Wintemute, 2015).

ii. Assault

The prevalence of intimate partner violence ranged between 20-30% (Dicola & Spaar, 2016). Up 46.3% of children in the USA have reported being subjected to physical assault within twelve months of being surveyed (Finkelhor, Turner, Ormrod, & Hamby, 2009) while 3.7-5.0% of children reported being physically abused by a caregiver (Finkelhor, Turner, Shattuck, & Hamby, 2013, 2015). The prevalence of elderly physical abuse was estimated to be around 1.1-1.8% (Acierno et al., 2010; Rosay & Mulford, 2017). In a 2015 survey of the population aged 12 years and above, rates of assault were reported to be around 15 per 1000, rates of domestic violence (including intimate partners and family members) around 4 per 1000, rates of stranger violence around 7 per 1000 and rates of violent crime with subsequent injury around 5 per 1000 (Truman & Morgan, 2016).

3. Neurobiological Basis

There is a significant amount of literature addressing the neurobiology of hetero-aggressive behavior as a whole, focusing on the role of genetic, environmental and epigenetic mechanisms (Tuvblad & Baker, 2011; Waltes, Chiocchetti, & Freitag, 2016). Inconsistencies in findings might be due to studies being conducted on populations having different types of hetero-aggression (Rosell & Siever, 2015). Research has shown that at least half of the variance in hetero-aggressive behavior is explained by genetic factors and a substantial proportion is explained by unique (non-shared) environmental factors (Veroude et al., 2016). Type of aggression, methodological differences, and age, but not sex of the subjects, seem to modulate the weight of the contribution of genetic and environmental factors (Tuvblad & Baker, 2011). Frontal lobe dysfunction leads to exaggerated and

uninhibited emotional responses and behaviors, rigidity and deficits in executive functioning, consequences which increase the propensity to engage in violent behavior (Brower & Price, 2001; Hawkins & Trobst, 2000). Structural and functional imaging studies have directly implicated dysfunctional connectivity between the prefrontal cortex (the orbitofrontal and anterior cingulate cortices in particular) and subcortical structures, such as the amygdala and the striatum (Rosell & Siever, 2015). Alterations in the serotonin system seem to be responsible for altered connectivity between the prefrontal cortex and the amygdala (Pavlov, Chistiakov, & Chekhonin, 2012; Robinson et al., 2013; Rosell & Siever, 2015; Stanley et al., 2000). Dysfunction of the dopamine system and the dysregulation of the interaction between testosterone and cortisol have also been implicated in the neurobiology of aggression (Pavlov et al., 2012; Rosell & Siever, 2015), particularly in reactive aggression (Waltes et al., 2016).

4. Risk Factors

Research on overall criminal behavior has established that adult offenders have a history of aggressive behavior during childhood and adolescent years, much like juvenile offenders (Beckley et al., 2016). Hence risk factors (and protective factors, explored later on) for criminal behavior across all ages, including assaultive behavior, comprise a cluster of factors which play a role during childhood and adolescence years (Beckley et al., 2016).

a. Socio-demographic Parameters

i. Homicide

Homicide rates vary according to age, sex, race and ethnicity and region (WHO, 2014a). Around 80% of homicide victims and 95% of homicide perpetrators are men (UNODC, 2014). Men are four times more likely than women to die by homicide (10.8 per 100000 vs. 2.5 in 2012) with rates peaking among men aged between 15 and 29 years (18.2 per 100000 in 2012). More than 50% of victims of homicide are below 30 years of age (UNODC, 2014). One third of female deaths by homicide occur secondary to intimate partner violence (Stockl et al., 2013). Infanticide/neonaticide rates vary between 2.1 and 7.0 per 100000 in high-income countries (Porter & Gavin, 2010) and global children homicide rates were estimated to be 8 per 100000 in 2012 (Devakumar & Osrin, 2016). Homicide rates in individuals aged 60 years and above were among the lowest compared to other age groups (4.5 per 100000) (WHO, 2014a).

In the USA, the male-to-female ratio in homicide rates is close to 4 (8.7 vs 2.3 in 2012) (WHO, 2014a). In 2012, intimate partner violence contributed to up to 50% of female homicide rates (Stockl et al., 2013). Homicide rates vary significantly according to race: in 2012, firearm homicide rates were consistently higher for Black men and women across the lifespan, with rates among Black men aged 20-29 years were five and twenty times higher than rates among Hispanic and White men respectively (Wintemute, 2015).

ii. Assault

Public health research has focused on identifying risk factors of perpetrating specific types of interpersonal violence, with several factors being consistently associated

across studies. Young age, unemployment, ethnic or racial minority status, relationship status were associated with perpetrating intimate partner violence across all ages (Capaldi, Knoble, Shortt, & Kim, 2012). Around 60-65% of elderly victims of physical abuse report that the assault was perpetrated by their intimate partners (Pillemer & Finkelhor, 1988; Rosay & Mulford, 2017). More than 70% of children were reportedly being physically abused by their biological parents, 70% of whom were 26 years of age or older (Sedlak et al., 2010). Parental unemployment and younger age, parental intimate partner violence, higher family size and lower socioeconomic status (Stith et al., 2009), as well as ethnic or racial status (Lee, Guterman, & Lee, 2008; Sedlak et al., 2010), were correlated with perpetrating child physical abuse.

Childhood exposure to violence (witnessed or incurred) was found to be a risk factor for perpetration of violence in adulthood (WHO, 2002). Violent interpersonal behavior during early adolescence was a significant predictor of such behavior in adulthood (Reingle, Jennings, & Maldonado-Molina, 2012), which concords with the repeatedly tested notion that past violent behavior is the best predictor of future violent behavior (Bushman et al., 2016). Individual-level (neurocognitive deficits), family-level (poor family bonds) and community level (peer and social rejection, cultural acceptance of violence) are significant risk factors of perpetrating interpersonal violent behavior among youths (Bushman et al., 2016).

Sex did not stand out as a consistent risk factor of perpetrating any type of interpersonal violence (Capaldi et al., 2012; Lee et al., 2008; Pillemer, Burnes, Riffin, & Lachs, 2016; Sedlak et al., 2010), although men were more likely to inflict serious injury

(Lee et al., 2008; Sedlak et al., 2010; WHO, 2014a); one notable exception is the fact that women are more likely to commit infanticide/neonaticide (Porter & Gavin, 2010).

b. Psychiatric Disorders

Psychiatric disorders and mental distress, and substance use (alcohol and drugs) were consistently found to be major determinants of perpetrating interpersonal violence: (Amstadter et al., 2011; Capaldi et al., 2012; Lee et al., 2008; Mallory et al., 2016; Pillemer et al., 2016; Porter & Gavin, 2010; Sedlak et al., 2010; UNODC, 2014; Whittington et al., 2013; WHO, 2002, 2014a).

A lifetime diagnosis of a psychiatric disorder, including bipolar disorder (OR = 3.72), unipolar depression (OR = 1.73), and anxiety disorder (OR = 1.29), was found to significantly increase the odds of interpersonal violent behavior among a cohort aged 15 years or older, after controlling for socio-demographic factors (Pulay et al., 2008). Individuals diagnosed with bipolar disorder consistently reported significantly higher rates of physical aggression display than individuals with other psychiatric illnesses and healthy controls across four years of follow-up, especially when in an acute mood episode (Ballester et al., 2014). A diagnosis of psychotic disorder (including schizophrenia) was associated with up to a seven-fold increase in male violence and twenty-nine-fold increase in female violence compared to the general population (Fazel, Gulati, Linsell, Geddes, & Grann, 2009); the risk of interpersonal violence in individuals with psychosis was found to increase over time (Fazel, Wolf, Palm, & Lichtenstein, 2014). Women with depression were more at risk of perpetrating intimate partner violence (Capaldi et al., 2012). Elder abuse perpetrators were more likely to have psychological distress, depression and anxiety

(Pillemer et al., 2016). Family history of psychiatric diseases and of substance use was found to substantially increase the risk of violent offending (Mok et al., 2016). Parental and personal comorbidities between psychiatric disorders and with substance use disorders further increase the risk of interpersonal violence (Fazel et al., 2009; Fazel et al., 2014; Mok et al., 2016; Pulay et al., 2008). Serious mental illness without comorbid substance use disorders did not significantly predict display of violent behavior among US adults (Elbogen & Johnson, 2009). The risk of interpersonal violence in individuals with substance use was similar to the risk in individuals diagnosed with psychotic disorders and comorbid substance use, and higher than the risk in individuals diagnosed with psychotic disorders only (Fazel et al., 2009). Alcohol use concurrent with depressive symptoms significantly increased the risk of future assault in subjects diagnosed with depression, but less so than alcohol use alone (S. Yang, Mulvey, Loughran, & Hanusa, 2012). The association between substance use and perpetrating interpersonal violence will be explored in a later section.

5. Protective Factors

Protective factors for interpersonal violence have been less researched (Bushman et al., 2016). Strong family ties, high socio-economic status, positive experiences at school (academic and social) and living in a non-violent community were deemed protective factors against perpetrating interpersonal violence among youth (Losel & Farrington, 2012). Low peer delinquency (Bernat, Oakes, Pettingell, & Resnick, 2012), close parental and school bonds (Todd I. Herrenkohl et al., 2003; Piquero, Farrington, Welsh, Tremblay, & Jennings, 2009) and attending religious services (Todd I. Herrenkohl et al., 2003) in

adolescence protected against interpersonal violence in early adulthood. Moreover, having close family ties and peer support during childhood protected against the perpetration of intimate partner violence in adulthood (Greenman & Matsuda, 2016). Having strong social relationships protects against perpetrating elder abuse (CDC, 2016).

D. Substance Use Disorders and Violent Behavior

The relationship between substance use and suicidal behavior is best understood in a framework that incorporates the following two dimensions: directionality and temporality (Bagge & Sher, 2008; Borges & Loera, 2010). The former explores whether the substance use directly causes suicidal behavior or vice-versa or whether there is a spurious correlation between the two due to confounders; the latter refers to the proximity of the association between substance use and suicidal behavior, which can vary from minutes and hours (proximal) to days, months and years (distal) (Bagge & Sher, 2008).

The association between substance use and interpersonal violent behavior is three-dimensional: “psychopharmacological”, “economic compulsive” and “systemic” (Goldstein, 1985). Psychopharmacological violence relates to the direct and indirect biological effects of the short- or long-term use of a substance on the individual, leading to the display of interpersonal violent behavior (Goldstein, 1985; UNODC, 2014). Economic compulsive violence relates to the exhibition of such behavior by the individual in order to acquire funding for substance use (Goldstein, 1985). Finally, systemic violence pertains to the violent interaction style within the realm of drug production, distribution and use (Goldstein, 1985; UNODC, 2014). Early research indicates that approximately three-quarters of substance use-related homicides is systemic, while psychopharmacological

violence accounted for 14% and 8% of homicides are multidimensional (Goldstein, Brownstein, & Ryan, 1992).

Substances can be proximal psychopharmacological risk factors of interpersonal violence through intoxication and distal risk factors (due to chronic use) through neurotoxic effects and withdrawal effects (Hoaken & Stewart, 2003).

For the purposes of this thesis, we will hence discuss the evidence behind the psychopharmacological association between substance use and violent behavior as a proximal risk factor (acute use) and a distal risk factor (chronic use or use disorder).

1. Empirical Evidence

a. Suicidal Behavior

Although substantial evidence supports the association of substance use with suicidal behavior (Darvishi, Farhadi, Haghtalab, & Poorolajal, 2015; Ferrari et al., 2014; McGinty, Choksy, & Wintemute, 2016; Nock et al., 2009; Patel et al., 2016; Poorolajal, Haghtalab, Farhadi, & Darvishi, 2016; Schneider, 2009), the nature of this association is complex and is likely modulated by different biological, psychological and/or socioeconomic factors (Borges & Loera, 2010; McGinty et al., 2016). The GBD project recently published the epidemiological evidence supporting a causal relationship between substance use and self-harm: only one prospective observational study was found demonstrating a causal relationship between drug use and self-harm (G. R. F. Collaborators, 2016). However a causality between substance use and suicidal behavior was deemed biologically plausible and no evidence to a causality in the opposite direction was found (G. R. F. Collaborators, 2016).

Substance use is highly prevalent among suicide completers. Approximately 82% of suicide decedents had positive blood alcohol concentrations and almost a quarter of the decedents were deemed intoxicated (G. S. Smith, Branas, & Miller, 1999). Among those who committed suicide by means other than overdose in Australia, at least 40% of cases tested positive for alcohol and at least 20% for illicit drugs, the most common of which was cannabis (10.5% of cases) (Darke, Duflou, & Torok, 2009). Furthermore, cases that tested positive for alcohol and/or an illicit drug were more likely to be young, male and have a history of alcohol and/or drug use (Darke et al., 2009). A meta-analysis of psychological autopsy studies found that substance use disorders were strongly associated with completed suicide [Odds Ratio (OR) = 5.24] (Yoshimasu et al., 2008). Substance use disorders were found to increase the risk of suicide among women who had a psychiatric hospitalization but not among men; that risk was found to decline slowly after treatment and recovery in contrast to the risk attributed to mood and psychotic disorders (Qin & Nordentoft, 2005).

i. Alcohol Use

The evidence supporting the association between alcohol use and suicide is strong (Borges & Loera, 2010; Darvishi et al., 2015). Alcohol use disorder more than doubled the odds of suicidal ideations, attempts and deaths (Darvishi et al., 2015) and alcohol dependence was associated with a ten-fold increase in the odds of death by suicide (Ferrari et al., 2014). Acute alcohol use and alcohol use disorder have both been found to independently increase the risk of attempted suicide up to ten and four times respectively (Borges & Loera, 2010; Conner, Bagge, Goldston, & Ilgen, 2014; Darvishi et al., 2015; Nock et al., 2009). Furthermore, alcohol drinking was associated with a higher likelihood

of using firearms as a means for suicide and of suffering a self-inflicted firearm injury (Branas, Han, & Wiebe, 2016).

ii. Drug Use

The evidence behind the association between drug use and suicide has caveats. There is no evidence associating acute drug use with suicidal behavior (Borges & Loera, 2010). A recent meta-analysis that included cohort, cross-sectional and case-control studies, found that drug use disorders significantly increased the odds of suicidal ideations and attempts but not completed suicides (Poorolajal et al., 2016). In another meta-analysis that only included longitudinal prospective cohort studies, drug use disorders significantly predicted suicide deaths and self-reported suicide attempts but the three included studies were of low quality (McGinty et al., 2016). A lifetime diagnosis of drug use disorders significantly increased the odds of suicide attempts among the general population (three- to four-fold) but not among those endorsing suicidal ideations (Nock et al., 2009).

There is very limited evidence as to the association between suicide and specific types of drugs used, and whether this association is modulated by age and sex (McGinty et al., 2016; Poorolajal et al., 2016). Psychostimulant (cocaine and amphetamines) and opioid dependence were respectively associated with an eight- and seven-fold increase in the odds of completed suicide (Ferrari et al., 2014). Available data suggests that opioid use disorder (McGinty et al., 2016; Wilcox, Conner, & Caine, 2004) and intravenous drug use (Wilcox et al., 2004) are predictors of mortality by suicide. This association between opioid use and completed suicide might be explained by the higher likelihood of use of firearms by this population as a suicide method (Sheehan, Rogers, & Boardman, 2015).

Data pertaining to cannabis use's association with suicide is not consistent. Lifetime cannabis use disorder was found to increase the odds of attempting suicide among subjects diagnosed with bipolar disorder (Carra et al., 2014) and a six-months diagnosis of cannabis use disorder was associated with self-harm in patients with severe mental illness (Dharmawardene & Menkes, 2016). An old prospective general population cohort study failed to find an association between past-year cannabis use and self-reported suicide attempts (Petronis, Samuels, Moscicki, & Anthony, 1990). Recent meta-analytic evidence highlights the low quality and high heterogeneity of the data addressing this issue but points to the temporality of cannabis use being instrumental in predicting suicidal behavior: chronic cannabis use significantly predicted attempted or completed suicide in the general population, whereas acute use did not (Borges, Bagge, & Orozco, 2016). Another meta-analysis similarly found that cannabis use disorder in the general population was associated with attempted suicide (OR = 1.60) (Poorolajal et al., 2016).

b. Other-Directed Violence

Substance use is a major risk factor for perpetrating interpersonal violence (Boles & Miotto, 2003; Darke, 2010). Even though the majority of individuals who use alcohol and drugs do not engage in violence, a substantive proportion of offenders have been linked to substances (Boles & Miotto, 2003). Alcohol and drug use disorders are responsible for the striking majority of the burden of interpersonal violent behavior in the USA population (Pulay et al., 2008). Around 80% of homicide offenders in Finland and 50% of offenders in Sweden were found to be intoxicated with alcohol while perpetrating the act; more than 70% of Finnish male and female offenders were intoxicated with alcohol in cases of

intimate partner homicide (UNODC, 2014). Close to 20% of Finnish offenders and male Swedish offenders were under the influence of drugs (often combined with alcohol) while committing homicide (UNODC, 2014). Lifetime substance use disorders increased the odds of interpersonal violent behavior six-fold among a cohort aged 15 years or older; nicotine dependence, alcohol abuse and dependence and illicit drug use and dependence each alone doubled the odds of engaging in assaultive behavior (Pulay et al., 2008). In another cohort of individuals aged 18 years or older, lifetime diagnoses of alcohol use disorder, drug use disorders and nicotine dependence were significantly associated with interpersonal violence, with ORs equal to 4.39, 2.94 and 2.37 respectively (Harford, Yi, & Grant, 2013). In the Dunedin birth cohort, individuals diagnosed with alcohol or cannabis dependence were significantly more likely to commit violence than controls (Arseneault, Moffitt, Caspi, Taylor, & Silva, 2000).

i. Alcohol Use

Alcohol is the substance whose association to interpersonal violence is the most studied (Boles & Miotto, 2003; Darke, 2010) The rate and volume of alcohol drinking seems to be positively associated with the risk of interpersonal violence (Fitterer, Nelson, & Stockwell, 2015) and seems to be the determining factor in increased rates of violence in individuals with alcohol use disorder (A. Beck, Heinz, & Heinz, 2014). Alcohol's effect on committing intimate partner violence was found to be modulated by sex, race and ethnicity, and socio-economic status (Caetano, 2003; Capaldi et al., 2012; Field & Caetano, 2003, 2004). The association between alcohol and interpersonal violence is not straightforward because not only is it modulated by biological determinants (age, sex, personality traits…),

but also by social, cultural and environmental factors such as the drinking setting and the cultural expectations of occurrence of violence (Boles & Miotto, 2003; Fitterer et al., 2015; Leonard, Quigley, & Collins, 2003).

ii. Drug Use

The evidence supporting the association of drug use disorders and psychopharmacological interpersonal violence is not as compelling: a meta-analysis of prospective cohort studies found no association between drug use and perpetration of such violence in moderately biased studies that controlled for alcohol use and socio-economic factors (McGinty et al., 2016). An early review found that non-regular use of marijuana might dampen aggressive behavior whereas chronic use might increase the risk of engaging in violent behavior because of neurotoxicity (Reiss & Roth, 1993). A meta-analysis of cross-sectional studies found a mild-to-moderate association between male marijuana use and male-to-female perpetration of intimate partner violence (Moore et al., 2008). There were no longitudinal studies assessing the association between cannabis use disorder and committing violence (McGinty et al., 2016). However, evidence suggests that cannabis withdrawal increases the likelihood of interpersonal violence, especially within the first week of abstinence (Hoaken & Stewart, 2003; Moore et al., 2008). Self-reported use of marijuana at 15 years of age but not at the age of 18, significantly predicted involvement in violence at 19 years of age after controlling for socio-demographic variables and antecedents of violent behavior (Brady, Tschann, Pasch, Flores, & Ozer, 2008). Self-reported past-month marijuana use predicted violence perpetration from adolescence to early adulthood, but it failed to predict violence perpetration in adulthood (Lim & Lui,

2016). Furthermore, self-reported marijuana use in adolescence and early adulthood ("consistent use") predicted perpetration of intimate partner violence later in adulthood (Reingle, Staras, Jennings, Branchini, & Maldonado-Molina, 2012). Past-year self-reported frequent marijuana use in adolescence did not consistently predict occurrence of violence, especially after controlling for socio-demographic factors and concurrent use of other drugs (Wei, Loeber, & White, 2004). Self-reported frequent marijuana use among Black adults significantly predicted self-reported conviction for attempted homicide and weapons offenses but not with assault, completed homicide and gang fighting, within two and a half years of use (Friedman, Glassman, & Terras, 2001). Self-reported lifetime (Green, Doherty, Stuart, & Ensminger, 2010) and past-year (Pedersen & Skardhamar, 2010) cannabis use was not found to be associated with criminal conviction for violent offenses.

2. Neurobiological Evidence

Twin studies have demonstrated the presence of a common genetic factor to substance use disorders and both externalizing disorders[3] and, to a lesser extent, internalizing disorders[4] (Lynskey et al., 2010).

The neurobiological mechanisms of alcohol-related aggression are well studied. Acute alcohol intoxication's association to violence seems to be mediated by a heightened emotional response to perceived threats through overactivation of the amygdala, disrupted cognitive control and executive dysfunction through alteration of the prefrontal cortex, and

[3] Externalizing disorders comprise disorders with prominent impulsive and behaviorally disruptive symptoms and substance use (APA, 2013).

[4] Internalizing disorders comprise disorders with prominent anxiety, depressive and somatic symptoms (APA, 2013).

increased sensation-seeking through activation of the dopamine system in the striatum (A. Beck et al., 2014; Boles & Miotto, 2003; Darke, 2010; Hoaken & Stewart, 2003). Furthermore, heavy alcohol use reduced the functional connection between the amygdala and the prefrontal cortex (Gorka, Fitzgerald, King, & Phan, 2013), a dysfunction also correlated with aggressive behavior as discussed above. Chronic alcohol use has also been shown to impair both the serotonin and the dopamine systems, with subsequent dysfunction in the amygdala, prefrontal cortex and striatum, leading to increased impulsivity, disinhibition and executive dysfunction (A. Beck et al., 2014).

The neurobiological link between cannabis use and hetero-aggressive behavior is less studied (Moore et al., 2008). Acute intoxication (Crean, Crane, & Mason, 2011; Howard & Menkes, 2007) as well as chronic use (Crean et al., 2011) might increase impulsivity through disruption of prefrontal cortex function. Recent systematic reviews found evidence for chronic cannabis use impairing several cognitive functions such as memory, attention, decision-making and psychomotor function, with acute use also impairing response inhibition (Broyd, van Hell, Beale, Yucel, & Solowij, 2016; Crean et al., 2011). Chronic THC exposure leads to down-regulation of the endocannabinoid receptors type 1 (CB1-R) in the amygdala, prefrontal cortex and hippocampus (Volkow et al., 2017), which might be one of the mechanisms of increased aggression as knock-out mice for CB1-R displayed more aggressive behavior than mice which had a functional CB1-R (Rodriguez-Arias et al., 2013). Cannabis use's potentiation of interpersonal violent behavior might depend on the individual's vulnerability, personality traits and social network (Brady et al., 2008; Friedman, Terras, & Glassman, 2003).

E. Conceptual Models of Violent Behavior

1. A Brief Introduction to Decision-Making: Volition and Impulsivity

While decision-making capacity is common to humans and animals (Shadlen & Kiani, 2013), the capacity for voluntary action, one form of decision-making, is human-specific (Haggard, 2008). Indeed, "most adult humans have a strong feeling of voluntary control over their actions, and of acting 'as they choose'" (Haggard, 2008).

Volition is best modeled as a set of three of decisional processes in order to execute a behavior (Haggard, 2008):

- "Early whether decision": it is modulated by the individual's processing of external sensory input and/or internal drives and needs, and the individual's motivation to act upon the input.
- "What decision": it involves the selection of a goal and the selection of an action to be performed towards achieving that target. Brain correlates include the prefrontal, premotor and parietal cortices.
- "Late whether decision": it determines whether the selected action is executed or not, in response to external of internal inputs. Brain correlates include the prefrontal cortex and the insula.

Volitional behavior is accompanied by the subjective experience of a conscious intention "causing" the behavior (Haggard, 2008). Although the contribution of "consciousness" to decision-making is hotly debated in the scientific community, research has identified neurobiological correlates (including the prefrontal cortex, the supplementary

motor area and the amygdala) and models to explain the emergence of consciousness of sensory inputs and volitional triggering of behaviors (Grossberg, 2016).

Impulsivity is defined as "the tendency to act without foresight" (Bevilacqua & Goldman, 2013). Impulsive individuals are predisposed to rapidly acting in response to internal and/or external stimuli without sound appreciation of the negative consequences of the act on themselves and/or others (Fineberg et al., 2014). One model for impulsivity involves two functionally contrasting brain circuits (Fineberg et al., 2014):

- The "Drive", which motivates the behavior.
- The "Inhibitory Control", which stops the behavior.

Extensive research has demonstrated that impulsivity is a heterogeneous construct modulated by different biological and environmental factors, with a prominent role attributed to dysfunctions in the serotonin and dopamine systems (Bevilacqua & Goldman, 2013; Dalley & Roiser, 2012).

Impulsivity can be subdivided into two broad and distinct categories:

- Rapid-Response Impulsivity, defined as "a tendency toward immediate action that is out of context with the present demands of the environment, and which occurs with diminished forethought" (Hamilton, Littlefield, et al., 2015). Brain correlates include (Hamilton, Littlefield, et al., 2015):
    - Drive circuit includes the ventral striatum.
    - Inhibitory control circuit includes the pre-supplementary motor, supplementary motor and pre-motor areas as well as the inferior frontal, ventrolateral prefrontal and parietal cortices and insula.

- Choice Impulsivity, defined as "tendencies to select smaller-sooner rewards over larger-later rewards" (Hamilton, Mitchell, et al., 2015). Brain correlates include (Hamilton, Mitchell, et al., 2015):
    - Drive circuit includes the ventral striatum.
    - Inhibitory control circuit includes the medial prefrontal and anterior cingulate cortices.

Therefore, excessive impulsivity impacts decision-making capacities (Dalley & Roiser, 2012; Fineberg et al., 2014).

2. Self-Directed Violence

Researchers have struggled to conceptualize suicidal behavior in order to identify treatment pathways and/or prevent it. The French sociologist Emile Durkheim was among the first to study suicide in the context of society and defined four types that result from imbalances of social integration and moral regulation: egoistic, altruistic, anomic and fatalistic (Durkheim, 1897). Although his case study relied on aggregate data, his findings and conclusions about suicide have been replicated and continue to be widely accepted (Condorelli, 2016; Nordentoft, 2007). However, this model does not include the biological determinants of suicide.

The stress-diathesis model is one well-evidenced conceptual model that "posits that suicide is the result of an interaction between state-dependent (environmental) stressors and a trait-like diathesis or susceptibility to suicidal behavior, independent of psychiatric disorders" (van Heeringen & Mann, 2014). In other words, suicidal behavior in a person

results from the interplay between stress generated by psychosocial events and a biological susceptibility within that person.

3. Other-Directed Violence

Interpersonal violent (hetero-aggressive) behavior is not a homogeneous construct (Rosell & Siever, 2015; Waltes et al., 2016) and is classically divided into two subtypes:

- Reactive, defined as "aggressive response to a perceived threat or provocation" (Waltes et al., 2016). Correlates include childhood physical abuse, attention difficulties, impulsivity, depression, anxiety and social isolation (Rosell & Siever, 2015; Tuvblad, Raine, Zheng, & Baker, 2009).
- Proactive, defined as "planned antisocial behavior that anticipates a reward or dominance over others" (Waltes et al., 2016). Correlates include callousness, physical violence and violent offending, delinquency, psychopathy, leadership qualities and sense of humor (Rosell & Siever, 2015; Tuvblad et al., 2009).

Although reactive and proactive hetero-aggression are highly correlated and comorbid, there is sufficient evidence supporting that these two types of hetero-aggression are distinct pathophysiological and clinical constructs (Dickson et al., 2015; Raine et al., 2006; Rosell & Siever, 2015; Y. Yang, Joshi, Jahanshad, Thompson, & Baker, 2016). However, research has mostly concentrated on reactive aggression (Rosell & Siever, 2015). Given the ongoing debate regarding whether hetero-aggressive behavior is a mental health issue, it is not surprising that it has received less attention from the scientific community than suicide (Asherson & Cormand, 2016).

4. Towards an Integrated Model of Violence

a. Socio-Psychological Evidence

In the tradition of sociologists Henry Morselli and Enrico Ferri in nineteenth century Europe and Andrew F. Henry and James F. Short in the 1950s, Prabha Unnithan, Huff-Corzine, Corzine and Whitt have argued for an integrated explanatory model of violence, arguing for studying suicide and homicide as "two sides of one coin" rather than as two separate independent entities (Prabha Unnithan et al., 1994).

The model "conceptualizes suicide and homicide as two alternative channels in a single stream of lethal violence" (Prabha Unnithan et al., 1994). It thus identifies two sets of causal factors for violence within a population (Prabha Unnithan et al., 1994):

- "Forces of production", responsible for the production of total lethal violence. Total lethal violence is measured through the Lethal Violence Rate (LVR), which is the sum of the suicide and homicide rates. These causal factors originate from social and environmental sources of frustration such as negative life events, economic difficulties and other sources of stress.
- "Forces of direction", responsible for the direction of violence, i.e. for choosing between suicide and homicide. The choice between one and the other is measured through the Suicide-Homicide Ratio (SHR), which is the suicide rate divided by

the LVR. These culture-specific factors influence one's interpretation of the "causes" behind one's frustrations based on attribution theory[5]:

- Internal attributional style: attributing the cause of frustrations to oneself in a global and stable manner leads to learned helplessness and hopelessness and a tendency towards suicide.
- External attributional style: attributing the cause of frustrations to others in a global and consistent manger leads to a tendency towards homicide.

The model described above relied heavily on research carried out by psychologists and psychiatrists studying suicide from a behavioral, cognitive and emotional perspective. Sigmund Freud (Freud et al., 1956-1974) and Karl Menninger (Menninger, 1938) had already argued that auto- and hetero-aggressive impulses in an individual stem from similar frustrations. Aaron T. Beck singled out cognitive distortions such as the egocentric bias, catastrophizing, dichotomous thinking and causal attributional biases as the sources of anger and aggression that is either directed towards the self or others depending on the perception of the cause of distress (A.T. Beck, 1999; A. T. Beck, 2008).

Prabha-Unnithan's model fits in the framework of the stress-diathesis model described in an earlier section: the "forces of production" are best categorized as "stress" factors whereas "forces of direction" are best categorizes as "diathesis" elements in that model (Prabha Unnithan et al., 1994). It has been empirically shown that internal negative attributional (inferential) styles and hopelessness are diathesis elements that predispose to

[5] "Attribution theory deals with how the social perceiver uses information to arrive at causal explanations for events. It examines what information is gathered and how it is combined to form a causal judgment" (Fiske & Taylor, 1991)

displaying suicidal behavior when confronted with stress (Liu, Kleiman, Nestor, & Cheek, 2015; van Heeringen & Mann, 2014).

Most sociological studies used country-level mortality data and correlated it to several macro-level variables including unemployment, income inequality, poverty rate, urbanization, immigration, availability of health care, religion, divorce rates, alcohol consumption, ethnicity, race, gender and age (Batton, 1999; Chon, 2013; Jorgensen, 2007; Prabha Unnithan et al., 1994). Results were largely mixed as there was evidence of a period effect (Batton, 1999) and a spatial effect (Jorgensen, 2007) modulating the associations.

However, researchers argue that studies using individual-level data should show that individuals committing suicidal or homicidal acts experience similar levels of frustration, but react differently to those frustrations based on whether they attribute blame to themselves (self-directed violence) or others (interpersonal violence) (Prabha Unnithan et al., 1994).

The integrated socio-psychological approach to violence had the merit of conceptually expanding the framework of the stress-diathesis model from suicide to violence as a whole, a direction that has been supported by medical researchers (Ferguson & Dyck, 2012).

b. Clinical Evidence

There is widespread evidence to a common predisposition to self-directed and interpersonal violence. A recent systematic review into the co-occurrence of both types of violence found that, regardless of the methodology used, they are positively associated (correlation ranging between 0.12 and 0.62), and that displaying one behavior increases the

risk of displaying the other, with a co-occurrence prevalence above 20% in most studies (O'Donnell et al., 2015). Most of the included studies in that review were carried on a psychiatric population (O'Donnell et al., 2015). This finding is further supported by the identification of several common risk factors for self-directed and interpersonal violence (Plutchik, 1995). As discussed in previous sections, having a psychiatric disorder or a substance use disorder is associated with auto- and hetero-aggressive behavior; the magnitude of this association was modulated by different socio-demographic factors such as age, gender and socio-economic factors.

The "Two-Stage Model of Countervailing Forces" was one such model that relied on the premise that "any [violent] event is a vectorial resultant of the interaction of opposing forces" over two stages (Plutchik et al., 1989). It argued that aggressive impulses are a common denominator between self-directed and interpersonal violence and that they are generated by "triggers" such as the perception of a threat or a challenge or the feeling of loss of control (Plutchik et al., 1989). At the first stage, these impulses are subjected to "amplifiers" (psychiatric disorders, physical symptoms, access to means, tolerance towards violence…) and "attenuators" (traits of timidity, close family network…) and the probability of it turning to a violent behavior depends on the "vectorial resultant of the presence of these opposing or countervailing forces" (Plutchik et al., 1989). At the second stage, the "goal" of the violent behavior is selected, depending on another set of forces (Plutchik et al., 1989):

- Self: risk factors include depression, hopelessness, recent psychiatric symptoms, life problems…

- Others: risk factors include impulsivity, legal issues, recent stress, menstrual problems in women…

Plutchik's model echoes Prabha-Unnithan's sociological model but relies on individual-level data to identify factors of production of violence (forces of production) and factors of direction of violence (forces of direction). However, Plutchik's model suffers from a lack of clarity in defining some factors and the lack of inclusion of neurobiological correlates.

Another model developed by Marc Hillbrand was more exhaustive as it included biological (dysfunctional serotonin system…), psychological (impulsivity, anger, modeling effects, negative affect, depression and hopelessness, substance use…) social (exposure to violence in the media, access to means, poor social support, unemployment…) and cultural factors as common predisposing factors to both types of violence (Hillbrand, 2001). Psychological factors such as mood lability, modeling effects and projective defenses and the availability of a victim were considered as forces of direction (Hillbrand, 2001).

Although Hillbrand's model included biological factors, its focus was mainly on the forces of production of violence rather than on determinants of its directionality.

c. Neurobiological Evidence

The socio-psychological and clinical overlap in self-directed and interpersonal violence is further supported by neurobiological studies. As reviewed in earlier sections, genetic and, to a lesser extent, environmental factors play a role in engaging in both behaviors. Important evidence implicate serotonin transporter gene, monoamine oxidase A gene (MAOA) and catechol O-methyltransferase gene (COMT) polymorphisms in

predisposing to auto- and hetero-aggressive behavior (Savitz, Cupido, & Ramesar, 2006). We have also reviewed that dysfunctions in the prefrontal cortex, amygdala and striatum as well as alterations in the serotonin, dopamine and brain stress systems are associated with suicidal and interpersonal violent behavior. Studies addressing both types of behavior have confirmed the association with a dysfunctional serotonin system (Golden et al., 1991; Mann, 2003; Oquendo & Mann, 2000; Turecki, 2005; Zouk et al., 2007) and a dysfunctional prefrontal cortex (Mann, 2003). As discussed in earlier sections, these correlates have been implicated in both types of violent behavior and substance use disorders.

5. Common Diathesis for Violence: The Example of Impulsivity

Given the evidence, some researchers have argued for conceptualizing self-directed and interpersonal violence as two phenomena sharing a common diathesis or etiological factors (Lubell & Vetter, 2006; O'Donnell et al., 2015). Impulsivity seems to be one such factor.

Current evidence highlights the mediating role of impulsivity in manifesting violent behavior (Bevilacqua & Goldman, 2013; Turecki & Brent, 2016). There is substantial evidence linking impulsivity to hetero-aggressive behavior (Archer & Webb, 2006; E.S. Barratt, 1994; E. S. Barratt, Stanford, Dowdy, Liebman, & Kent, 1999; Seroczynski, Bergeman, & Coccaro, 1999). Impulsive-aggressive traits were found to be positively associated with suicidal behavior in non-psychiatric populations (Gvion & Apter, 2011; Savitz et al., 2006) and in patients with mood disorders (Grunebaum et al., 2006; Mann et al., 2008; Mann, Waternaux, Haas, & Malone, 1999; Oquendo et al., 2004;

Oquendo et al., 2000) and schizophrenia (Mann et al., 1999; McGirr & Turecki, 2008). Impulsive-aggressive traits strongly predicted suicide among youth after controlling for psychiatric disorders and other confounders (McGirr et al., 2008; Turecki & Brent, 2016).

As reviewed earlier, neuroimaging correlates of impulsivity overlap with those of self-directed and other-directed violence. Furthermore, dysfunctions in the serotonin and dopamine brain systems are heavily implicated in the pathophysiology of impulsivity (Dalley & Roiser, 2012). Genes associated with violent behavior (MAOA, COMT, serotonin transporter among others) have also been found to be associated with impulsivity (Bevilacqua & Goldman, 2013; Fineberg et al., 2014; Khadka et al., 2014; Turecki & Brent, 2016).

However, it is unlikely that impulsivity is the sole biological factor predisposing to all types of violent behavior. Just as proactive and reactive (impulsive) hetero-aggressive behavior are most likely to be distinct phenomena, some suicides, such as those committed by the elderly, are not mediated by impulsivity (Turecki, 2005).

6. Common Stressors for Violent Behavior: Substance Use Disorders

Within the framework of the proposed stress-diathesis model of violence, substance use disorders are relevant stressors contributing to both self-directed and interpersonal violence, as already discussed in previous sections. As mentioned earlier, individuals with a particular diathesis who are subjected to stressors produce certain kinds of behavior. For example, adverse childhood experiences predispose to both types of violence in all ages through the mediating effect of impulsivity (Brodsky et al., 2001; Felitti

et al., 1998; T. I. Herrenkohl & Jung, 2016; Liu et al., 2015; Mok et al., 2016; O'Donnell et al., 2015; WHO, 2002). Substance use disorders seem to act similarly.

Impulsivity has been found to be a predictor, a consequence and a perpetuator of substance use (Aragues, Jurado, Quinto, & Rubio, 2011; Coccaro et al., 2016; de Wit, 2009; Fineberg et al., 2014; J. E. Grant & Chamberlain, 2014; Leung et al., 2017). Crucially, in individuals with substance use disorders, impulsive traits are associated with hetero-aggressive and suicidal behavior (Borges et al., 2016; Borges & Loera, 2010; Haw, Houston, Townsend, & Hawton, 2001; Hoaken & Stewart, 2003; Koller, Preuss, Bottlender, Wenzel, & Soyka, 2002; Sher et al., 2005; Sher et al., 2008; Tremeau et al., 2008). The use of a violent method predicted the presence of impulsive-aggressive traits, lifetime history of aggression and substance use disorders among suicide decedents (Dumais et al., 2005).

The evidence points to shared causal and predisposing processes to impulsivity, substance use, suicidal behavior and interpersonal violence: impulsivity, through impairing decision-making capacity, appears to be a mediating factor between substance use and auto- and hetero-aggressive behavior especially among youth (Fineberg et al., 2014; Turecki, 2005).

F. Knowledge Gap

Despite extensive research (reviewed in part above) about self-directed and interpersonal violence over the past decades, a lot of questions remain unanswered, probably because of a lack of a uniform evidence-based conceptual approach to violence (Ferguson & Dyck, 2012; Lubell & Vetter, 2006; O'Donnell et al., 2015; Prabha Unnithan

et al., 1994). As already discussed, multiple risk and protective factors have been identified; however, current models of suicide and interpersonal violence have failed to reliably and accurately predict occurrence of events (Quinlivan et al., 2016; Whittington et al., 2013). Given the burden of violence, it is crucial to further explore the pathophysiology of violent behavior in order to identify predictive factors and design avenues for treatment.

An integrated model approach to violence can help bridge that gap (Hillbrand, 2001; Lubell & Vetter, 2006; O'Donnell et al., 2015; Prabha Unnithan et al., 1994).

We have extensively reviewed that self-directed and interpersonal violence share common risk factors and frequently co-occur; however, caveats persist:

- The models elaborated have either relied on macro-level data (Prabha Unnithan et al., 1994) or data from populations with psychiatric disorders (Plutchik et al., 1989). General population data on risk and protective factors for self-directed and interpersonal physical violence is sparse. Results from studies on specific populations (psychiatric inpatients/outpatients, forensic population among others) are rarely generalizable.
- The models elaborated have failed to accurately identify "Forces of direction" probably due to methodological issues and failure to include biomarkers. Conversely, neurobiological research has mainly focused on identifying biomarkers of aggression as a whole and rarely addressed the question of whether there are biomarkers that discriminate self-directed from interpersonal violence.

Within the framework of a stress-diathesis model of violence, questions persist as to the factors that determine the choice of target of violent behavior. To the best of our knowledge, a neurobiological "force of direction" has yet to be identified.

As we already discussed, substance use disorders are strongly associated with self-directed and interpersonal violence. However, several methodological concerns are raised in addressing this association:

- Cross-sectional study designs.
- Selection bias: patients with psychiatric disorders, patients who sought treatment and have health records, forensic patients…
- Most studies relied on self-reported use of substances rather than on a diagnosis of substance use disorders.
- Most studies focus on victims rather than perpetrators of interpersonal violence.
- Lack of controlling for potential confounders.

To the best of our knowledge, there have been very few studies that have assessed substance use disorders as forces of direction of violence.

Harford and his colleagues (Harford et al., 2013), using data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 2, compared socio-demographic characteristics and prevalence of lifetime DSM-4 psychiatric disorders (including alcohol and drug use disorders and nicotine dependence) among those surveyed according to four groups:

- No violence.

- Self-directed violence: reported lifetime antecedents (since the age of 15 years) of death wishes or suicidal ideations or attempts.
- Other-directed violence: reported having had lifetime antecedents of starting fights, injuring someone on purpose or using weapons.
- Combined violence: reported having had lifetime antecedents of both self- and other-directed violence.

The NESARC population (Wave 2) consisted of the adult non-institutionalized household-based survey of the US population (N = 34653 respondents). Harford and colleagues reported that around 16% of the population surveyed reported engaging in any type of violence. Women constituted the majority of those reporting self-directed violence while men were the majority of those reporting other-directed and combined violence. Mood disorders and anxiety disorders predicted self-directed as opposed to other-directed violence while male sex, older age, Black race, Hispanic ethnicity, substance use disorders and certain personality disorders predicted the opposite (Harford et al., 2013).

After controlling for age, sex, race/ethnicity and other lifetime psychiatric disorders, the odds were the following (Harford et al., 2013):

- Alcohol Use Disorder:
    - Other-directed vs. no violence: OR = 4.39 [99% Confidence Interval (99%CI) = 2.89-6.69].
    - Self-directed vs. no violence: OR = 1.36 (99%CI = 1.15-1.62).
    - Combined vs. no violence: OR = 3.16 (99%CI = 1.96-5.12).
    - Self- vs. other-directed violence: OR = 0.31 (99%CI = 0.20-0.48).

- Drug Use Disorders:
    - Other-directed vs. no violence: OR = 2.94 (99%CI = 2.16-4.010.
    - Self-directed vs. no violence: OR = 1.86 (99%CI = 1.49-2.31).
    - Combined vs. no violence: OR = 4.81 (99%CI = 3.11-7.49).
    - Self- vs. other-directed violence: OR = 0.63 (99%CI = 0.45-0.88).

Using school-based data of the Youth Risk Behavior Survey in the USA, Harford and colleagues (Harford, Yi, & Freeman, 2012) examined the correlation between past-month alcohol binge-drinking with past-year violent behavior according to the following typology:

- No violence.
- Self-directed violence: reported past-year antecedents of suicide attempts.
- Other-directed violence: reported past-year antecedents of being involved in a physical fight.
- Combined violence: reported having had past-year antecedents of both self- and other-directed violence.

The study included N = 43172 high-school students, with 24% of them reporting having engaged in any type of violence (Harford et al., 2012). Males and youth were more prevalent among those reporting other-directed and combined violence while female students were more prevalent among those engaging in self-directed violence; male students were four times more likely than their female counterparts to engage in other-directed rather than self-directed violence (Harford et al., 2012).

After controlling for age, sex, race/ethnicity, self-reported past-year depression and self-reported past-month smoking, cannabis and cocaine use and self-reported lifetime heroin, methamphetamines and steroids use, the authors found that past-month drinking and binge drinking was associated with increased odds of commission of any type of violence (Harford et al., 2012). Furthermore, students of binged alcohol more three times or more over the past month were at increased risk of engaging in other-directed violence compared to self-directed violence (Harford et al., 2012):

- Binge drinking 3-9 times: OR = 1.77 (99.75%CI = 1.13-2.79).
- Binge drinking 10 times or more: OR = 3.48 (99.75%CI = 1.59-7.65).

In another youth-based study using data from the National Survey on Drug Use and Health (NSDUH), Harford and colleagues (Harford, Chen, & Grant, 2016) investigated the association between the number of DSM-4 substance use disorder (alcohol, cannabis and other illicit drug use disorders) criteria and violence among youth aged 12-17 years sampled between 2008-2013, according to the following typology:

- No violence.
- Self-directed violence: reported past-year antecedents of suicide attempts while being depressed or antecedents of mental health treatment subsequent to suicidal ideations or attempts.
- Other-directed violence: reported past-year antecedents of assault with the intent of seriously hurting the other person.
- Combined violence: reported having had past-year antecedents of both self- and other-directed violence.

After controlling for age, sex, race/ethnicity, family income, nicotine dependence and legal involvement, the results were (Harford et al., 2016):

- A diagnosis of alcohol use disorder was associated with significantly increased odds of committing any type of violence compared to no violence and significantly increased odds (up to two times) of committing other- vs self-directed violence.
- A diagnosis of cannabis use disorder was associated with significantly increased odds of committing any type of violence compared to no violence, but did not significantly discriminate between other- and self-directed violence.
- A diagnosis of drug use disorders (excluding cannabis) was associated with significantly increased odds of committing any type of violence compared to no violence and significantly increased odds (up to two times) of committing self- vs other-directed violence.

The aforementioned studies have the benefited of exploring the association of substance use and different types of violence within the same population, adopting an integrated model framework. Those studies are cross-sectional and thus cannot establish causality between substance use and violence. They also have other limitations including merging suicidal ideations with attempts (Harford et al., 2016; Harford et al., 2013) using different time frames of studied variables (Harford et al., 2012; Harford et al., 2013), non-adjusting for socio-economic status (Harford et al., 2012; Harford et al., 2013), psychiatric disorders (Harford et al., 2016; Harford et al., 2012), and household size and protective factors such as religious beliefs (Harford et al., 2016; Harford et al., 2012; Harford et al.,

2013). Furthermore, all three of those studies did not assess the differential effect of the combination of alcohol and drug use disorders on violence.

We will build on Harford's work in order to explore whether alcohol and drug use disorders have a differential association with different forms of violence among adults.

G. Research Questions

We will address the following research questions:

- Does substance use disorders' association with violence differ according to the type of substance? How can this association change when controlled for socio-demographic, psychosocial and clinical variables?
- Does substance use disorders' association with violence differ according to the type of violence? How can this association change when controlled for socio-demographic, psychosocial and clinical variables?
- How do these associations vary across different age groups?
- What are the sets of variables leading to the modification of the association between substance use disorders and the type of violence which can be used in preventive interventions?

H. Hypotheses

1. (Hyp1): alcohol use disorder is more strongly associated with violence than drug use disorders

We hypothesize that although alcohol use disorders and drug use disorders will each be associated with increased odds of perpetration of all types of violence (acting as

"forces of production"), alcohol use disorder's association with violence will be stronger than that of drug use disorders. This hypothesis will be labeled (Hyp1).

2. ***(Hyp2): drug use disorders are associated with an increased risk of other- versus self-directed violence.***

We hypothesize that drug use disorders will act as a "force of direction" towards interpersonal violence as it will significantly increase the odds of assault compared to suicide attempts. This hypothesis will be labeled (Hyp2).

3. ***(Hyp3): cannabis use disorder is associated with an increased risk of other- versus self-directed violence.***

We hypothesize that cannabis use disorder will act as a "force of direction" towards interpersonal violence as it will significantly increase the odds of assault compared to suicide attempts. This hypothesis will be labeled (Hyp3).

4. ***(Hyp4): age is a risk-modifier of the association between alcohol use disorder and violence, and drug use disorder and violence.***

We hypothesize that age will modify the association between alcohol and drug use disorders, and suicide attempts, assaults and overall violence, with the association being strongest among youth. This hypothesis will be labeled (Hyp4).

I. Objectives

The objectives of our thesis are:

- To measure the association between alcohol and/or drug use disorders and different types of violence (attempted suicide and assault) as well as violence as a whole (attempted suicide and/or assault) in an integrated model approach.
- To assess the effect of socio-demographic, psychosocial and clinical control variables on the association between alcohol and/or drug use disorders and the type of violence.

CHAPTER III:
METHODS

A. Data Source and Population

The present thesis aims to address the above research questions and hypotheses by employing publicly available data from the population-based National Survey on Drug Use and Health (NSDUH) in the USA, retrieved from the Inter-university Consortium for Political and Social Research (ICPSR) (ICPSR, 2017). The NSDUH is "an annual nationwide survey involving interviews with approximately 70,000 randomly selected individuals aged 12 and older" (SAMHSA, 2017a). It is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), an agency in the U.S. Department of Health and Human Services (DHHS), and is under the supervision of SAMHSA's Center for Behavioral Health Statistics and Quality (CBHSQ) (SAMHSA, 2017a). The NSDUH survey aims to provide national estimates on the use of alcohol, various types of illicit drugs and tobacco products and on the prevalence of mental illness in the USA (SAMHSA, 2017a).

The NSDUH survey uses a multistage area probability sampling technique in each of the fifty states and the District of Columbia, in order to select a nationally-representative sample of the non-institutionalized, household-based civilian population aged 12 years and older (ICPSR, 2017) (refer to Appendix 1 for further details on sampling procedure). Participants are interviewed face-to-face by a professional interviewer in their households, answering computer-assisted questions providing socio-demographic data and substance use and mental health data (ICPSR, 2017). Each interview has its own code number;

participants' identifiers are never recorded in order to ensure full confidentiality of data (SAMHSA, 2017a).

For the purposes of our thesis, we are pooling data from consecutive cross-sectional NSDUH surveys from:

- 2008 (United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a).
- 2009 (United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015b).
- 2010 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, & Quality, 2015a).
- 2011 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, & Quality, 2015b).
- 2012 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, & Quality, 2015c).
- 2013 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, & Quality, 2015d).
- 2014 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, & Quality, 2016).

Yearly response rates varied between 71% and 76% (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016;

United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a, 2015b).

Several variables were imputation-revised or logically-edited in order to minimize missing data and inconsistencies (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016; United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a, 2015b). Details about the methodology of each survey are available in the yearly methodological resource books (SAMHSA, 2017b).

All of these public-use data files have been treated to further protect the privacy of respondents: all variables that could potentially be used as identifiers have been either encrypted, substituted or removed (such as state identifiers) (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016; United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a, 2015b). Furthermore, these files do not include the total number of original respondents because of a subsampling step used in the procedures of disclosure protection: the public-use files include 391753 records out of 477896 respondents from 2008 to 2014 (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016; United States Department of, Human Services. Substance, & Mental Health Services Administration.

Office of Applied, 2015a, 2015b). We analyzed the data of the 270227 adult respondents (aged 18 years or older) from 2008 to 2014.

B. Measures

1. Dependent Variables

(V) is the dependent variable measuring violence. It is a composite categorical variable constructed based on answers provided by the respondents to the following two questions:

- (1) Addressing self-directed violence: "*During the past 12 months, did you try to kill yourself?*". Valid answers were dichotomous:
    - No = 0.
    - Yes = 1.
- (2) Addressing interpersonal violence: "*During the past 12 months, how many times have you attacked someone with the intent to seriously hurt them?*". Valid answers were dichotomized in the following manner:
    - None = 0.
    - One or more times = 1.

The categories of (V) are:

- No violence reported in the past twelve months => Non-Violent (NV): (1) = 0 AND (2) = 0.
- At least one suicide attempt reported and no physical assault reported => Self-Directed Violence (SDV): (1) = 1 AND (2) = 0.

- At least one physical assault reported and no suicide attempt reported => Other-Directed Violence (ODV): (1) = 0 AND (2) = 1.
- At least one suicide attempt and one physical assault reported => Combined Violence (CV): (1) = 1 AND (2) = 1.

For the purposes of addressing hypothesis (Hyp1), we computed the variable (V') with the following categories:

- No violence reported in the past twelve months: (1) = 0 AND (2) = 0.
- Any violent behavior reported in the past twelve months: (1) = 1 OR (2) = 1.

2. Independent Variables

(U) is the independent variable measuring substance use disorders.

The NSDUH surveys from 2008 until 2014 assess the following substances: tobacco, alcohol, cannabis, cocaine, crack, stimulants, hallucinogens, inhalants, heroin, prescription pain relievers, tranquilizers, and sedatives (CBHSQ, 2016). Substances assessed that we included in (U) are: alcohol, cannabis, cocaine, crack, stimulants, hallucinogens, inhalants, heroin, prescription pain relievers, tranquilizers, and sedatives. NSDUH have used the DSM-4 criteria for the diagnoses of past-year substance abuse and dependence, with the following differences (CBHSQ, 2016):

- NSDUH assessed crack use separate from cocaine use, heroin and pain reliever use separately (opioid use in DSM-4) and tranquilizer use separate from sedative use.

- NSDUH did not assess tranquilizer and nicotine withdrawal; the cut-off for positive sedative withdrawal symptoms was “one” instead of “two”.
- NSDUH did not assess past-year nicotine dependence but measured past-month cigarette dependence using two different scales. Given the different time scales, cigarette dependence was not included in our analyses.

The diagnostic criteria for substance abuse and substance dependence between DSM-4 and NSDUH overlap extensively (CBHSQ, 2016). Changes implemented in DSM-5 (explored in an earlier section) have led to a re-evaluation of the NSDUH diagnostic algorithms’ validity (refer to Appendix 2 for a comparison between DSM-4, DSM-5 and NSDUH criteria for substance use disorder). As a matter of fact, NSDUH does not assess craving nor cannabis withdrawal and includes “the legal criterion” for substance abuse diagnosis (CBHSQ, 2016).

In order to better align NSDUH’s algorithms with DSM-5 criteria for substance use disorders, and based on SAMHSA’s suggestions (CBHSQ, 2016) and previous studies using the same data (Harford et al., 2016), the past-twelve months diagnostic criteria for substance use disorders were assessed through combining DSM-4 substance abuse and dependence criteria and dropping the legal criterion. The variables upon which the assessment is based are:

- (1) *Was there a month or more when you spent a lot of your time getting or using the substance?*
    - No = 0.
    - Yes = 1.

- (2) *Was there a month or more when you spent a lot of your time getting over the effects of the substance you used?*
    - No = 0.
    - Yes = 1.
- (3) *Were you able to keep to the limits you set on substance use or did you use more than you intended to?*
    - No = 0.
    - Yes = 1.
- (4) *Did you need to use more substance than you used to in order to get the effect you wanted?*
    - No = 0.
    - Yes = 1.
- (5) *Did you notice that using the same amount of substance had less effect on you than it used to*?
    - No = 0.
    - Yes = 1.
- (6) *Were you able to cut down or stop using the substance every time you wanted or tried to?*
    - No = 0.
    - Yes = 1.
- (7) *Did you continue to use the substance even though you thought this was causing you to have problems with your emotions, nerves, or mental health?*

    - No = 0.
    - Yes = 1.

- (8) *Did you continue to use the substance even though you thought this was causing you to have physical problems?*
    - No = 0.
    - Yes = 1.
- (9) *Did substance use cause you to give up or spend less time doing important activities?*
    - No = 0.
    - Yes = 1.
- (10) *Did you have one or more of these symptoms at the same time that lasted for longer than a day after you cut back or stopped using the substance?* [the specific number and type of listed withdrawal symptoms varied by substance]
    - No = 0.
    - Yes = 1.
- (11) *Did substance use cause you to have serious problems at home, work or school?*
    - No = 0.
    - Yes = 1.
- (12) *Did you regularly use substance and then do something where substance use might have put you in physical danger?*
    - No = 0.

    - Yes = 1.

- (13) *Did you have any problems with family or friends that were probably caused by substance use?*
    - No = 0.
    - Yes = 1.
- (14) *Did you continue to use the substance even though you thought this caused problems with family or friends?*
    - No = 0.
    - Yes = 1.

A diagnosis of substance use disorder is deemed positive if, for any one substance, two or more of the below criteria are fulfilled:

- (1) = 1 OR (2) = 1.
- (3) = 0.
- (4) = 1 OR (5) = 1.
- (6) = 0.
- (7) = 1 OR (8) = 1.
- (9) = 1.
- (10) = 1 [available for the following substances: alcohol, pain relievers, heroin, cocaine, sedatives and stimulants].
- (11) = 1.
- (12) = 1.
- (13) = 1 AND (14) = 1.

We categorized the substance use disorders according to the following variable nomenclature:

- Alcohol Use Disorder (AUD): variable (A).
    - No = 0.
    - Yes = 1.
- Cannabis Use Disorder (CUD): variable (C).
    - No = 0.
    - Yes = 1.
- Drug (cannabis, cocaine, crack, stimulants, hallucinogens, inhalants, heroin, prescription pain relievers, tranquilizers, and/or sedatives) Use Disorder(s) (DUD): variable (D).
    - No = 0.
    - Yes = 1.
- Drug Use Disorder(s) excluding Cannabis Use Disorder: (D) – (C) = (B).
    - No = 0.
    - Yes = 1.

Hence, the categories of (U) are:

- No Substance Use Disorder (NSUD) reported in the past twelve months: (A) = 0 AND (D) = 0.
- Alcohol Use Disorder alone (AUDa) reported: (A) = 1 AND (D) = 0.
- Drug Use Disorder(s) alone (DUDa) reported: (A) = 0 AND (D) = 1.
- Alcohol and Drug Use Disorders (ADUD) reported: (A) = 1 AND (D) = 1.

C. Control Variables

1. Age

The NSDUH includes a categorical variable *Age Category Recode (6 Levels)* with the following age-group categories (in years): 12-17; 18-25; 26-34; 35-49; 50-64; 65 or older. Since our study focuses strictly on the adult population, we recoded this variable and excluded the 12-17 category. The categories of our variable are:

- 18-25.
- 26-49.
- 50 or older.

2. Sex

The NSDUH includes a categorical variable *Imputation-Revised Gender*, and we included it in our analysis. It has the following categories:

- Male.
- Female.

3. Race/Ethnicity

The NSDUH contains a categorical variable *Race/Hispanicity Recode (7 Levels)* with the following categories: NonHisp [Non-Hispanic] White; NonHisp Black/Afr Am [Black/African-American]; NonHisp Native Am/Ak Native [Native American / Alaska Native]; NonHisp Native HI/Other Pac Isl [Native Hawaiian or Other Pacific Islander];

NonHisp Asian; NonHisp more than one race; Hispanic. We computed a new variable based on the aforementioned variable with the following categories:

- Non-Hispanic White.
- Non-Hispanic Black/African-American.
- Hispanic.
- Others.

4. Marital Status

The NSDUH includes a categorical variable *Imputation Revised Marital Status* with these categories: married; widowed; divorced or separated; never been married; respondent is <= 14 years old. Given that our thesis focuses on adults, we recoded this variable and excluded the last category. The categories of our variable are:

- Married.
- Widowed.
- Divorced or separated.
- Never been married.

5. Household Type

Each participants' household composition is documented in the survey according to two variables: *Recode – Imputation-Revised Number of Persons in Household* and *Imputation-Revised – Number of Respondent's Family Members in Household*. Both of these variables have six categories: one; two; three; four; five; six or more people/family

members in household. We used these two variables to compute a variable that measured household size according to the following categories:

- Single-Person Household.
- Family Household: household includes family members only.
- Non-Family Household: household includes exclusively non-family members.
- Mixed Household: household includes family and non-family members.

6. Education Level

The NSDUH contains a categorical variable *Education Recode* with these categories: less than high school; high school graduate; some college; college graduate; 12 to 17 year olds. Since our study focuses strictly on the adult population, we recoded this variable and excluded the 12-17 category. The categories of our variable are:

- Less than high school.
- High school graduate.
- Some college.
- College graduate.

7. Past Year Employment

The NSDUH asked respondents about employment status in the past week prior to the survey, largely adopting the United States Bureau of Labor Statistics' Current Population Survey's definitions (BLS, 2017). Based on the information provided, the NSDUH classified adult respondents as either employed full time, employed part time,

unemployed and other (including not in labor force) in the variable *Imputation Revised Employment Status 18+* (12-17 year olds were assigned a skip code). Participants surveyed deemed part of the labor force were asked the following question: *during the past twelve months, was there ever a time when you did not have at least one job or business*. Answers provided were either "yes" or "no". Participants who reported having no job over the past week and who did not make specific efforts to find work, and participants who were disabled, or were keeping house full-time, or were in school/training, or were retired or did not have a job for any other reason were deemed not part of the labor force and were thus assigned a skip to the aforementioned question. We assessed employment over the past year by recoding the variable *Past 12 Months, Time With No Job* according to the following categories:

- Yes = Yes (i.e. time with no job in past year).
- No = No (i.e. continuous employment over the past year).
- Legitimate Skip = Not in Labor Force.

Our variable's categories are:

- Continuous.
- Intermittent.
- Not in Labor Force.

8. Personal Income Level

The NSDUH survey includes a categorical variable *Recode – Imputation-Revised Respondent's Total Income* with the following categories: less than 10000$ (including

loss); 10000-19999$; 20000-29999$; 30000-39999$; 40000-49999$; 50000-74999$; 75000$ or more. We recoded this variable into another one to be included in the analyses, with its categories determined according to the 33rd percentile:

- Less than 10000$.
- 10000-29999$.
- 30000$ or more.

9. Area of Residence

The NSDUH survey includes a categorical variable *County Metro/Non-Metro Status (3-Level)* with the following categories:

- Large metropolitan area.
- Small metropolitan area.
- Non-metropolitan area.

This variable is based on the United States Department of Agriculture's Economic Research Service's rural-urban classification which distinguishes metropolitan counties by the population size of their metropolitan area (above or below one million persons) and non-metropolitan counties by their level of urbanization and proximity to metropolitan areas (ERS, 2013). Metropolitan areas stand for urban areas whereas non-metropolitan areas correspond to rural areas (ERS, 2016). Since the 2003 and 2013 Rural-Urban Continuum Codes have used the same methodology, they are considered to be directly comparable (ERS, 2013). This comparability allows us to use this variable across the different NSDUH surveys from 2008 until 2014. We included this variable in our analyses.

10. Religiosity

Participants were asked whether their agreed with the statement *Your religious beliefs influence how you make decisions in your life*. Answers were provided according to a four-point Likert scale (strongly disagree; disagree; agree; strongly agree).

We recoded the variable *My Religious Beliefs Influence My Decisions* according to the following categories:

- Strongly Disagree = No.
- Disagree = No.
- Agree = Yes.
- Strongly Agree = Yes.

Our variable's categories are:

- No.
- Yes.

11. Past Year Tobacco Use

NSDUH participants were asked about whether they use tobacco products (smoking cigarettes, cigars or pipes, chewing tobacco, using smokeless tobacco or snuff) and, if they did, how recent was their use (within the past month, within the past year, within the past three years or beyond the past three years). A dichotomous variable *Any Tobacco – Past Year Use* was recoded to measure whether the participant used any tobacco product in the past year prior to the survey or not (i.e. never smoked or stopped smoking

before the past year). The variable *Any Tobacco – Past Year Use* has the following categories:

- Did not use in the past year.
- Used within the past year.

We included this variable in our analyses.

12. Psychiatric Disorder

The NSDUH survey includes a statistical prediction model of mental illness. "Adults with a serious mental illness" are defined by SAMHSA as (SAMSHA, 1993):

- Persons aged 18 and over, who currently or at any time during the past year, have had diagnosable mental, behavioral, or emotional disorder of sufficient duration to meet diagnostic criteria specified within DSM-III-R that has resulted in functional impairment, which substantially interferes with or limits one or more major life activities.
- These disorders include any mental disorders (including those of biological etiology) listed in DSM-III-R or their ICD-9-CM equivalent (and subsequent revisions), with the exception of DSM-III-R "V" codes, substance use disorders, and developmental disorders, which are excluded unless they co-occur with other diagnosable serious mental illness.
- All of these disorders have episodic, recurrent, or persistent features; however, they vary in terms of severity or disabling effects. Functional impairment is defined as difficulties that substantially interfere with or limit role functioning in

one or more major life activities, including basic daily living skills (e.g., eating, bathing, dressing); instrumental living skills (e.g., maintaining a household, managing money, getting around the community, taking prescribed medication); and functioning in social, family, and vocational/educational contexts.

- Adults who would have met functional impairment criteria during the referenced year without benefit of treatment or other support services are considered to have serious mental illnesses.

Currently, SAMHSA uses the following mental illness categories (CBHSQ, 2014):

- Any Mental Illness (AMI):
    - Serious Mental Illness (SMI): at least one DSM-4 diagnosis (excluding substance use and developmental disorders) and severe impairment as estimated by a Global Assessment of Functioning (GAF) score equal to or below 50.
    - Moderate Mental Illness (MMI): at least one DSM-4 diagnosis (excluding substance use and developmental disorders) and moderate impairment as estimated by a GAF score between 51 and 59.
    - Low Mental Illness (LMI): at least one DSM-4 diagnosis (excluding substance use and developmental disorders) and mild impairment as estimated by a GAF score equal to or above 60.
- No Mental Illness: no DSM-4 diagnosis of a psychiatric disorder.

The predictive model designed to screen for AMI (and SMI) includes input from the following measures of (CBHSQ, 2014):

- Past-year Kessler-6 (K6) scale.
- World Health Organization Disability Assessment Schedule (WHODAS) scale.
- Suicidal ideations in the past year.
- Major depressive episode in the past year.
- Age.

However, this model (included in the NSDUH) has been shown to overestimate the prevalence of mental illness in the population surveyed (CBHSQ, 2014). Furthermore, SAMHSA has recommended not to use the mental illness variables in analyses incorporating suicide variables (ideations, plans or attempts) (CBHSQ, 2014), which is the case of our current analysis. Therefore, we will use an alternative prediction model, as recommended by SAMHSA (CBHSQ, 2015). Since the *Age* variable is not available in a continuous form in the public-use NSDUH files (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016; United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a, 2015b), we will adopt the statistical model (labeled Y3) to screen for AMI. It includes the following predictors: the past-year K6 scale and the WHODAS scale (CBHSQ, 2015).

a. K6 Scale

The K6 scale is a dimensional scale of non-disorder-specific psychological distress, a measure that usually evaluates a set of cognitive, behavioral, emotional and psychophysiological symptoms and which was shown to be elevated among people with psychiatric disorders, irrespective of the type of the disorder (Kessler et al., 2002). Using a five-point Likert scale (all of the time = 4 points; most of the time = 3; some of the time = 2; a little of the time = 1; none of the time = 0) individuals respond to six questions assessing depressed mood, hopelessness, restlessness, fatigue, worthlessness and nervousness during the last month and during the worst month in the past year (Kessler et al., 2002). The K6 scale has been shown to have strong psychometric properties across populations with different socio-demographic characteristics and to reliably discriminate individuals in the community with a DSM-4 psychiatric disorder (not including substance use disorders) from those who don't (Kessler et al., 2002; Kessler et al., 2003; Kessler et al., 2010): at a cut-off score of 13 (out of 24), it had a sensitivity of 36%, a specificity of 96% and a total classification accuracy of 92% for SMI (Kessler et al., 2003). In the USA, data from the WMH survey showed that worst month in the past year K6 scale detected around 89% of SMI (Kessler et al., 2010).

The NSDUH survey includes the variable *Worst K6 Total Score In Past Year* which is based on the adult respondent's worst total K6 score over the past year (during the last month or during the worst month in the past year prior to the survey). Values range between 0 and 24. A calibration analysis of the K6 scale in the NSDUH found that an alternative scoring version is a better fit for predicting mental illness (Aldworth et al., 2010). The *Alternative Worst K6 Total Score* variable was computed by assigning the value

0 if the *Worst K6 Total Score In Past Year* variable was equal to or below 7 and a value of 1 to 17 if that variable had a corresponding value of 8 to 24.

We thus included the *Alternative Worst K6 Total Score* variable, labeled from here then on (K), in our statistical prediction model for mental illness.

b. WHODAS scale

The WHODAS scale measures impairment and disablement secondary to all illnesses (Rehm et al., 1999). The NSDUH includes an abbreviated and validated eight-item version of this scale (Novak, Colpe, Barker, & Gfroerer, 2010). Participants are asked about the difficulties they had during their worst month in the past year in the following activities: remembering to do things they needed to do, concentrating on doing something important when other things were going on around them, going out of the house and getting around on their own, dealing with people they did not know well, participating in social activities, taking care of household responsibilities, taking care of daily responsibilities at work or school, and getting daily work done as quickly as needed (CBHSQ, 2014). Respondents provided answers using a four-point Likert scale (severe difficulty = 3 points; moderate difficulty = 2; mild difficulty = 1; no difficulty/refuse to answer = 0) (Novak et al., 2010).

The NSDUH survey includes the variable *WHODAS Total Score* which computes the total score (range from 0 to 24) of the eight provided answers. However, a calibration analysis of the WHODAS scale in the NSDUH found that an alternative scoring method is a better fit for predicting mental illness (Aldworth et al., 2010). For the variable *Alternative WHODAS Total Score, WHODAS Total Score* items that scored 2 or 3 were assigned the

score of 1 whereas the items that scored 0 or 1 were assigned the score of 0, yielding a score range from 0 to 8.

We included the *Alternative WHODAS Total Score* variable, labeled from here then on (W), in our statistical prediction model for psychiatric illnesses.

c. Computed Variable

SAMHSA provides a mathematical model to estimate psychiatric disorders among the NSDUH population using the five aforementioned predictor variables and recommends using the same equation for Y3 (CBHSQ, 2015). Therefore we will compute a variable (AMI) based on the following equation (CBHSQ, 2015):

$$AMI = \frac{1}{1 + e^{\left[-\left(-5.9726644+\left(0.0873416 \times (K)\right)+ \left(0.3385193 \times (W)\right)\right)\right]}}$$

At the cut point of 0.0282057278, the Y3 model accurately predicted AMI in 73% of cases (area under the curve: 0.733) with a sensitivity of 56.4% and a specificity of 90.3%, faring equally well compared to the complete predictive model; moreover, SAMHSA found Y3 to exhibit low bias levels and error rates (CBHSQ, 2015).

We computed the variable (M) based on dichotomizing (AMI) according to the recommended cut point 0.0282057278 (CBHSQ, 2015). The categorical variables are:

- Below 0.0282057278 = no psychiatric disorder.
- Equal to or above 0.0282057278 = positive psychiatric disorder.

13. Past Year Mental Health Treatment

Adult participants in the NSDUH survey were asked about whether they received treatment for mental health issues (not substance-related) during the past year. Included treatment modalities were inpatient hospitalization, outpatient follow-up (mental health clinic, medical clinic, psychotherapist, day hospital…) and medication intake. We used the following dichotomous variable *Received Any Mental Health Treatment in the Past Year*, with the following categories:

- Yes.
- No.

14. Past Year Substance Use Treatment

Participants in the NSDUH survey who reported lifetime use of any substance were asked about whether they received treatment targeting their substance use. They were asked whether they received such treatment in a "specialty facility" (hospital, mental health center, rehabilitation center) during the past year. We used the following NSDUH dichotomous variables in our analyses:

- *Received Treatment at a Specialty Facility for Alcohol – Past Year*:
    - No.
    - Yes.
- *Received Treatment at a Specialty Facility for Illicit Drugs – Past Year*:
    - No.
    - Yes.

15. Juvenile Substance Use

NSDUH participants who reported using any substance were asked about age of onset of use. In order to control for juvenile substance use, we used the following dichotomous variables (depending on the analysis):

- *First Used Alcohol Prior to Age 18*:
    - Yes.
    - No.
- *First Used Illicit Drugs Prior to Age 18*:
    - Yes.
    - No.
- *First Used Marijuana* [Cannabis] *Prior to Age 18*:
    - Yes.
    - No.
- *First Used Illicit Drugs Other Than Marijuana* [Cannabis] *Prior to Age 18*:
    - Yes.
    - No.

16. Survey Year

We computed a survey year variable in the pooled data file to account for the period effect. Its categories are:

- 2008.

- 2009.
- 2010.
- 2011.
- 2012.
- 2013.
- 2014.

D. Analysis Plan

We conducted the analyses using the *Complex Samples* module in the Statistical Package for Social Sciences (SPSS) version 21. This module allowed us to account for the complex survey design by using the sample design variables *Analysis Stratum* (VESTR: variance estimation [pseudo] stratum) and *Analysis Replicate* (VEREP: variance estimation [pseudo] replicate within stratum). Since we pooled data from 2008 through 2014, we adjusted sample weights by computing a variable (We) according to the following formula, as recommended (United States Department of, Human Services. Substance, Mental Health Services Administration. Center for Behavioral Health, et al., 2015a, 2015b, 2015c, 2015d; United States Department of et al., 2016; United States Department of, Human Services. Substance, & Mental Health Services Administration. Office of Applied, 2015a, 2015b):

$$(We) = \frac{Person - Level\ Analysis\ Weight}{Number\ of\ Years\ of\ Combined\ Data} = \frac{Final\ Person - Level\ Sample\ Weight}{7}$$

We tabulated all variables and presented their frequencies (in percent) according to different levels of the substance use disorders variable (U). We made sure there was no multicollinearity between variables by using Pearson's bivariate correlation test. We then

conducted bivariate analyses for the independent and control variables with the dependent variables (V') and (V). The associations were measured using the adjusted F test which is a Chi-Square statistic adjusted for complex samples. We determined statistical significance using two-sided tests at the alpha level cut-off of 5% and we used Bonferroni's correction method to adjust for multiple testing. We then entered the independent variables in a multivariate logistic model with the set of control variables that were significant in bivariate analyses and we adjusted the models to reach the best fit for each analysis. We then calculated the adjusted OR (aOR) and its corresponding 95%CI.

To address the first hypothesis (Hyp1), we regressed the dependent variable (V') on the independent variable (U) while controlling for relevant variables (cf. Figure 1).

To address the hypothesis (Hyp2), we regressed the dependent variable (V) on the independent variable (U) while controlling for relevant variables (cf. Figure 2).

To address the hypothesis (Hyp3), we regressed the dependent variable (V) on the independent variable (C) while controlling for relevant confounders, including past year comorbid alcohol use disorder [variable (A)] and past year comorbid drug use disorder [variable (B)] (cf. Figure 3).

To address the hypothesis (Hyp4), we regressed the dependent variables (V') and (V) on the independent variables (U) and (C) in each of the age groups. We controlled for relevant confounders pertaining to each sub-analysis (cf. Figures 4.1, 4.2 and 4.3).

CHAPTER IV:
RESULTS

A. Sample Characteristics

1. Total Sample

The total sample of adults in the NSDUH surveys from 2008 through 2014 includes 270227 adults [Population Size Estimate (PSE) = 232414058], distributed across survey years almost evenly as shown in Table 4.1.

Table 4.2 provides the weighted distribution of the sample characteristics in the total sample as well as in the valid sample included in the analyses of (V). Close to 15% of the adult population surveyed were 18-25 year olds, with the rest equally divided between 26-49 year olds and 50 year olds or above. Male-to-female ratio was close to even [Prevalence (P) of females = 51.8%]. The sample was racially and ethnically diverse, with around 67% identifying as Non-Hispanic Whites, 14% as Hispanic and 12% as Non-Hispanic Blacks.

A majority of those surveyed were married (P = 53.1%), were continuously employed over the past year (P = 57.2%) and lived in a household exclusively with family members (P = 78.8%) at the time of questioning. High school dropouts constituted less than 15% of the total sample. Close three-quarters of those surveyed reported that religion played an important role in their decision-making.

One-third confirmed use of tobacco products over the last year. Around 8.5% of the total population had a positive alcohol use disorder (AUD) diagnosis whereas 4.4% had one or multiple drug use disorders (DUD). Only 2.5% of the sample had cannabis use

disorder (CUD). Juvenile substance use was highly prevalent: almost half reported alcohol use, while a quarter reported any drug use and cannabis use.

Around 5% of the population were estimated to have a psychiatric disorder during the past year. Only a minority of the population surveyed reported past year mental health treatment (P = 14.1%) and substance use treatment (P < 1%). Further details are reported in Table 4.2.

2. Sample Characteristics by Exposure: Substance Use Disorders (U)

Based on the criteria we outlined in the Methods section, 6.8% of the population surveyed had an alcohol use disorder alone (AUDa), 2.7% had a drug use disorder(s) alone (DUDa), and 1.7% had both disorders (ADUD). There were significant group differences for all variables, with $p<0.001$. Full details are displayed in Table 4.3.

More than half of the respondents with AUDa were 26-49 year olds and more than half of those who had ADUD were 18-25 year olds. Two-thirds of each group of users were male. Non-Hispanic Blacks were significantly more prevalent among DUDa and ADUD subgroups.

A significant proportion of users had “never been married” at the time of questioning. Around 16% of respondents in DUDa and ADUD were college graduates, less so than respondents in AUDa and NSUD. A higher proportion of positive substance use disorder respondents had intermittent employment over the past year and more than 40% of respondents in DUDa and ADUD had low income levels.

Past year tobacco use and juvenile substance use were preponderant among all positive substance use categories.

Between 10 and 20% of substance use disorder respondents were estimated to have a psychiatric disorder over the past year and more than a quarter of those diagnosed with DUDa or ADUD received mental health treatment over the same time frame.

3. Prevalence of Violence among Exposed Respondents

As shown in Figures 5 through 7, more than 80% of respondents with any substance use disorder were classified as Non-Violent (NV) over the past year. However, violence is more prevalent in those who have a positive substance use disorder compared to those who don't. Figure 5 shows that around 4.9% of those with a positive alcohol use disorder have reported Other-Directed Violence (ODV) and around 1.5% have reported Self-Directed Violence (SDV). By contrast, 7.7% and 2.0% of those with a drug use disorder have reported ODV and SDV respectively. Figure 6 illustrates that although the prevalence of violence is increased among AUDa and DUDa, it is even higher in ADUD: 11.1% reported ODV, 3.0% reported SDV and 1.2% reported Combined Violence (CV). More than 10% of those with CUD have reported violence over the past year, predominantly ODV (cf. Figure 7).

B. Comparison between Violent and Non-Violent Subgroups

Of the total sample surveyed, only 1.7% (PSE = 4017689) reported past year suicidal attempt and/or assault. As detailed in Table 4.4, the violent group is strikingly different from the non-violent group: bivariate analyses show that all independent and control variables (except *Area of Residence*) have significantly different distributions between those two subgroups.

18-25 year olds (P = 44.1%), males (P = 56.9%), Non-Hispanic Blacks (P = 20.9%), Hispanics (P = 17.8%) and "never been married" people (P = 59.5%) were significantly more prevalent among those who committed any type of violence compared to those who haven't.

A significant majority of violent respondents have not had a college education, have not had continuous employment and have earned less than 30000 USD over the past year. Only 57.6% of them reported that religious beliefs influence their decisions.

Close to two-thirds of violent respondents reported past year use of tobacco products. Almost half of the violent group had a substance use disorder (P = 44.9% vs. 10.6%; adjusted F = 2212.475; $p<0.001$): 18.5% had AUDa, 11.4% had DUDa and 14.9% had ADUD. A significantly high proportion of violent respondents had cannabis use disorder (P = 16.6% vs. 2.2%; adjusted F = 4288.459; $p<0.001$). A significant majority of the violent group reported alcohol, drug and cannabis use prior to age 18.

Close to a quarter of those who reported past year violent behavior are estimated to have a positive psychiatric diagnosis (P = 25.7% vs. 5.0%; adjusted F = 2289.688; $p<0.001$). A third of this group has received mental health treatment over the past year, while only 5% have received substance use treatment. However, treatment-seekers were significantly more prevalent among the violent group compared to the non-violent group.

1. Self-Directed, Other-Directed and Combined Violence vs. None

The exclusion of missing values led to the inclusion of a subsample of 268839 adults (PSE = 231365447) in the violence typology analyses, as shown in Table 4.5:

- Non-Violent (NV): unweighted sample size (N) = 259914; PSE = 227373377; P = 98.2%.
- Self-Directed (SDV): N = 1944; PSE = 1014525; P = 0.4%.
- Other-Directed (ODV): N = 6571; PSE = 2836342; P = 1.2%.
- Combined (CV): N = 410; PSE = 141203; P = 0.1%.

Compared to NV, the SDV (P = 33.2%), ODV (P = 47.5%) and CV (P = 55.6%) subgroups included significantly higher proportions of 18-25 year olds. While the sex distribution did not differ between SDV, CV and NV, males were the majority in ODV (P = 62.8%). The proportions of Non-Hispanic Blacks were significantly higher in the ODV and CV subgroups compared to NV.

Compared to NV, SDV, ODV and CV included significantly greater proportions of "never been married" and high school dropout respondents and significantly lower proportions of respondents who were continuously employed over the past year, who earned 30000 USD or above and who reported religiosity.

Past year tobacco use was highly prevalent among all subgroups. Substance use disorders (U) were significantly more prevalent across SDV, ODV and CV subgroups (adjusted F = 727.397; $p<0.001$). In the SDV subgroup, 17.7% had AUDa, 8.4% had DUDa and 11.6% had ADUD. Proportions were higher in the ODV subgroup with 18.9% having AUDa, 12.4% DUDa and 15.2% ADUD and even higher in the CV subgroup: 18.3% had AUDa, 15.1% had DUDa and 33.2% had ADUD.

CUD was also significantly more prevalent among the three subgroups compared to NV [P(SDV) = 10.4%, P(ODV) = 17.9%, P(CV) = 32.2%, P(NV) = 2.2%; adjusted F = 1370.889; $p<0.001$].

Finally, a higher proportion of respondents in SDV, ODV and CV were estimated to have had a psychiatric disorder in the past year [P(SDV) = 41.9%, P(ODV) = 18.4%, P(CV) = 53.6%, P(NV) = 4.9%; adjusted F = 1096.109; $p<0.001$) and to have sought mental health or substance use treatments.

2. Self- vs. Other-Directed Violence

Adjusted bivariate analyses have revealed a few differences in characteristics between SDV and ODV. The proportion of 18-25 year olds was significantly higher among ODV. The male-to-female ratio is 0.7:1 in SDV and 1.7:1 in ODV. There were no distribution differences in race/ethnicity between the two subgroups.

Almost two-thirds of ODV identified as "never been married", a proportion significantly greater than in SDV. There were no differences in household types, education level, past year employment, income level and religiosity between the two subgroups.

The prevalence of AUDa, DUDa and ADUD was similar between SDV and ODV. However, the prevalence of CUD was significantly higher among ODV. The prevalence of juvenile substance use was not different between the two subgroups.

Also, significantly higher proportions of SDV respondents were estimated to have had a psychiatric disorder over the past year, and to have sought mental health treatment. But the proportions of past year substance use treatment seekers were similar between the two subgroups.

C. Association of Substance Use Disorders and Overall Violence

As shown in Table 4.6, all three categories of substance use disorders are independently associated with commission of any type of violence:

- AUDa: OR_{AUDa} = 4.55, 95%CI = (4.18-4.95).
- DUDa: OR_{DUDa} = 7.29, 95%CI = (6.45-8.23).
- ADUD: OR_{ADUD} = 16.60, 95%CI = (15.25-18.06).

The ORs for all three categories gradually decreased after adjusting for confounding variables. In the best-fit model [McFadden's Pseudo R Square (R^2) = 0.196], AUDa's association with overall violence was stronger than that DUDa's association, but not significantly so:

- [aOR_{AUDa} = 2.38, 95%CI = (2.16-2.63)] vs. [aOR_{DUDa} = 2.01, 95%CI = (1.77-2.27)].

ADUD significantly increased the likelihood of any type of violence compared to AUDa or DUDa: aOR_{ADUD} = 3.72, 95%CI = (3.36-4.12).

D. Association of Substance Use Disorders and Subtypes of Violence

As detailed in Table 4.7, AUDa and DUDa significantly increased the odds of perpetuating SDV, ODV and CV, even after adjusting for confounding variables. ADUD was even more strongly associated with each of those subtypes.

A positive drug use disorder was associated with significantly higher crude odds of perpetuating other- vs. self-directed violence [OR_{DUDa} = 1.71, 95%CI = (1.29-2.27)],

whereas a positive alcohol use disorder diagnosis was not [OR_{AUDa} = 1.24, 95%CI = (0.95-1.63)]. Comorbid alcohol and drug use disorders also yielded significantly higher odds of perpetuating ODV: OR_{ADUD} = 1.51, 95%CI = (1.21-1.90). All three associations were maintained in the adjusted best-fit model (McFadden's R^2 = 0.189):

- aOR_{AUDa} = 1.19, 95%CI = (0.89-1.59).
- aOR_{DUDa} = 1.45, 95%CI = (1.03-2.04).
- aOR_{ADUD} = 1.34, 95%CI = (1.03-1.76).

E. Association of Cannabis Use Disorder and Subtypes of Violence

As shown in Table 4.8, a positive diagnosis of cannabis use disorder is associated with self-directed, other-directed and combined violence compared to none. However, after adjusting for confounders, the best-fit model (McFadden's R^2 = 0.190) yielded significant associations with ODV [aOR_{CUD} = 1.47, 95%CI = (1.31-1.66)] and CV [aOR_{CUD} = 2.20, 95%CI = (1.41-3.43)] only.

While CUD was associated with an increased risk of ODV compared to SDV [OR_{CUD} = 1.88, 95%CI = (1.50-2.37)], that association remained positive but was non-significant in the best-fit model: aOR_{CUD} = 1.29, 95%CI = (0.97-1.71).

F. Effect of Age on the Association of Substance Use Disorders and Violence

1. Effect of Age on the Association of Substance Use Disorders and Overall Violence

The odds of committing overall violence varied according to age groups as shown in Table 4.9. Positive diagnoses of AUDa and of DUDa yielded significantly increased

odds of perpetuating violence among 18-25 year olds and 26-49 year olds but not in the elderly group, even after adjusting for confounders.

Among 18-25 year olds, the association between AUDa and violence was significantly stronger than the association between DUDa and any type of violence in the best-fit model (McFadden's $R^2 = 0.145$):

- [$aOR_{AUDa} = 2.42$, 95%CI = (2.18-2.69)] vs. [$aOR_{DUDa} = 1.77$, 95%CI = (1.57-2.01)].

The association of co-occurring alcohol and drug use disorders with overall violence was even stronger: $aOR_{ADUD} = 3.34$, 95%CI = (2.99-3.73).

Among 26-49 year olds, this subgroup of substance users also had significantly higher odds [$aOR_{ADUD} = 4.11$, 95%CI = (3.31-5.11)] of committing any type of violence compared with alcohol use disorder [$aOR_{AUDa} = 2.43$, 95%CI = (2.05-2.89)] or drug use disorder [$aOR_{DUDa} = 2.40$, 95%CI = (1.91-3.02)] alone. Overall, the odds of perpetuating violence were similar between these two age categories in each of the substance use categories.

Among the 50 year olds or above, only ADUD yielded significantly higher odds of committing violence in the best-fit model (McFadden's $R^2 = 0.119$): $aOR_{ADUD} = 7.04$, 95%CI = (3.60-13.78).

2. Effect of Age on the Association of Substance Use Disorders and Subtypes of Violence

We have excluded the CV subtype from this analysis due to low sample size. Results are displayed in Table 4.10. All substance use categories significantly increased the

odds of perpetrating self-directed and other-directed violence in the three age categories. But after adjusting for confounders, results differed depending on the age category.

Among 18-25 year olds, DUDa did not significantly increase the odds of SDV compared to NV in the best-fit model (McFadden's $R^2 = 0.140$). All other associations between substance use categories and SDV or ODV were significant.

Among 26-49 year olds, AUDa, DUDa and ADUD were significantly associated with committing SDV and ODV in the best-fit model (McFadden's $R^2 = 0.172$).

In the 50 year olds or above category, DUDa did not significantly increase the odds of committing SDV or ODV in the best-fit model (McFadden's $R^2 = 0.123$). AUDa was strongly associated with committing SDV but not ODV. Comorbid alcohol and drug use disorders were strongly associated with both subtypes of violence.

The effect of age on the directionality of violence is displayed in Table 4.11. Only among 18-25 year olds did all categories of substance use disorders significantly increase the odds of committing other- vs. self-directed violence:

- $aOR_{AUDa} = 1.44$, 95%CI = (1.17-1.87).
- $aOR_{DUDa} = 1.55$, 95%CI = (1.15-2.07).
- $aOR_{ADUD} = 1.44$, 95%CI = (1.11-1.87).

Among 50 year olds or above, AUDa was significantly associated with SDV compared to ODV: $aOR_{AUDa} = 0.32$, 95%CI = (0.11-0.96).

3. Effect of Age on the Association of Cannabis Use Disorder and Commission of Other- vs. Self-Directed Violence

We have excluded the CV subtype from this analysis because of low sample size. As displayed in Table 4.12, CUD was associated with ODV but not with SDV across all three age groups in the best-fit model.

A positive cannabis use disorder diagnosis was significantly associated with perpetration of other- vs. self-directed violence only among 18-25 year olds. The best-fit model (McFadden's $R^2 = 0.142$) yielded an $aOR_{CUD} = 1.27$, 95%CI = (1.003-1.60). More details are shown in Table 4.13.

G. Other Correlates of Directionality of Violence

1. Unstratified Analyses

Several socio-demographic, psycho-social and clinical factors were significantly correlated to directionality of violence (ODV vs. SDV) in our multinomial logistic regression analyses of (V) on (U). Men were up to two times more likely than women to commit ODV than SDV. Odds of committing ODV were greater among high school dropouts compared to college graduates. While positive history of juvenile drug use was significantly associated with ODV compared to SDV, juvenile alcohol use was not. Respondents who were estimated to have had a psychiatric disorder and who received mental health treatment over the past year were more likely to commit SDV than ODV.

Multinomial logistic regression analyses of (V) on (C) yielded a similar profile of correlates with one exception: positive history of juvenile cannabis use was significantly associated with ODV compared to SDV but juvenile drug use other than cannabis was not.

In both analyses, household type, past year employment, personal income level, religiosity and past year substance use treatment were not significantly correlated with committing ODV vs. SDV.

2. Stratified Analyses

a. 18-25 Years Old Age Group

In our regression analyses of (V) on (U) and on (C), the odds of committing ODV vs. SDV were higher for men compared to women and for low- compared to high-income respondents. Juvenile use of alcohol and drugs (including cannabis) were associated with higher odds of committing ODV. On the other hand, respondents who were estimated to have had a psychiatric disorder and who received mental health or alcohol use treatment over the past year were more likely to commit SDV than ODV. Interestingly, respondents who reported that religion influences their decision-making had significantly greater odds of committing ODV compared to SDV.

b. 26-49 Years Old Age Group

In our regression analyses of (V) on (U), men were no more likely than women to commit ODV compared to SDV. Respondents who were married or were divorced or separated were more likely to commit SDV than ODV compared to those who "never were married" at the time of the survey. Juvenile use of alcohol was associated with committing ODV while juvenile drug use was not. Having a psychiatric disorder and receiving mental health or drug use treatment over the past year were associated with greater odds of committing SDV.

There were two key differences in our regression analyses of (V) on (C): juvenile use of all substances and past year substance use treatment were not associated with directionality of violence.

c. 50 Years Old or Above Age Group

We found very few correlates of directionality of violence in this age group. In our regression analyses of (V) on (U), greater odds of committing SDV compared to ODV were associated with past year intermittent employment, past year mental health treatment and juvenile history of alcohol use. A positive psychiatric diagnosis was not associated with directionality of violence.

By comparison, we found that past year intermittent employment was not correlated with directionality of violence in our regression analyses on (V) on (C).

CHAPTER V:
DISCUSSION

A. Summary of Findings

The overarching goal of this thesis was to examine the association between substance use disorders and self- and other-directed violence within an integrated model of violence. We hypothesized that by using this conceptualization, we can identify differential effects of substances on the production of violence and the directionality (self- vs. other-) of violence, that are independent of the effects of other key risk factors. We also hypothesized that the magnitude of these effects will be inversely proportional to age, highlighting the biological complexity of the association between substance use disorders and violence and the need for early prevention to reduce the burden of both the exposure and the outcome.

In (Hyp1), we hypothesized that alcohol use disorder is more strongly associated with overall violence than drug use disorders. Our analysis showed that after controlling for confounders, AUDa's association with violence was numerically higher but statistically similar to DUDa's association with violence. Of significance was the finding that comorbid alcohol and drug use disorders tripled the odds of committing violence, significantly more so than AUDa and DUDa. We thus rejected (Hyp1) and accepted our null hypothesis that alcohol use disorder and drug use disorder's associations with overall violence are equal.

In (Hyp2), we hypothesized that drug use disorders alone are associated with an increased risk of other- vs. self-directed violence. Our analysis showed that individuals with DUDa were up to two times more likely to commit other-directed violence compared to

self-directed violence, while individuals with AUDa were not likely to commit one over the other. Individuals with ADUD were also more likely to commit other- vs. self-directed violence. We therefore accepted (Hyp2).

In (Hyp3), we hypothesized that cannabis use disorder is associated with an increased risk of other- vs. self-directed violence. After adjusting for confounders, our analysis showed that CUD was associated with a significantly increased risk of committing other-directed violence and combined violence, but not self-directed violence. CUD was positively associated with perpetration of other-directed violence compared to self-directed violence, but that association was marginally non-significant after adjusting for confounders. We therefore rejected (Hyp3) and accepted the null hypothesis that cannabis use disorder is not associated with an increased risk of other- compared to self-directed violence.

In (Hyp4), we hypothesized that age is an effect modifier of the association between alcohol use disorder and violence and drug use disorder and violence. We stratified each of our analyses addressing the aforementioned three hypotheses according to three age groups: 18-25 year olds, 26-49 year olds and 50 year olds or above.

We found that AUDa was more strongly associated with committing any type of violence than DUDa among 18-25 year olds; these two associations were equally significant among 26-49 year olds and equally non-significant among 50 year olds or above. ADUD's association with violence was strongly significant in all three age groups.

We also found that ADUD significantly increased the odds of committing self-directed and other-directed violence in all three age groups. DUDa was not associated with self-directed violence among 18-25 year olds and AUDa was associated with self-directed

violence among 50 year olds or above. All three substance use disorder categories increased the risk of self- and other-directed violence among 26-49 year olds. AUDa, DUDa and ADUD significantly favored other-directed compared to self-directed violence only among 18-25 year olds.

Added to that, we found that cannabis use disorder's association with violence was also modulated by age. It significantly increased the odds of committing other- vs. self-directed violence only among 18-25 year olds.

Overall, we found enough evidence to support and accept (Hyp4).

Finally, we explored the socio-demographic, psychosocial and clinical correlates of the association between substance use disorders [(U) and (C)] and other- vs. self-directed violence. We found that having a psychiatric disorder and undergoing mental health treatment were significantly correlated with committing self- vs. other-directed violence in almost all of our models. Among the youth, male sex, low income, juvenile history of alcohol or drug use and religiosity were significantly correlated with perpetrating other- vs. self-directed violence.

B. Profiles of Substance Users

Our twelve-months prevalence of alcohol use disorder was lower compared to another US general population survey (B. F. Grant et al., 2015) while the prevalence of drug use disorder and cannabis use disorder were pretty similar (B. F. Grant et al., 2016). The socio-demographic and clinical characteristics of our substance user subsamples AUDa, DUDa and ADUD are similar to those reported in the literature (Stinson et al., 2005): young age, male sex and "never been married" status were more prevalent in all

three user subsamples, Non-Hispanic Black respondents were more prevalent among DUDa, and low education and income levels were more prevalent among DUDa and ADUD. Furthermore, a smaller proportion of substance users lived in family households, a finding that possibly reflects the negative impact substance use has on family dynamics (Lander, Howsare, & Byrne, 2013). The functional impact of substance use is demonstrated by the higher prevalence of intermittent employment over the past year among users. Predictably (Gmel et al., 2013), significantly lower proportions of respondents with substance use disorders (compared to non-users) reported that their religious beliefs influenced their decision-making. A striking majority of substance users also used tobacco products over the past year, a finding already supported in the literature (John, Hill, Rumpf, Hapke, & Meyer, 2003). AUDa, DUDa and ADUD subgroups had, in increasing order, higher percentages of respondents with a psychiatric disorder, who reported juvenile alcohol and drug use and who sought mental health and substance use treatment. These findings are in line with previous reports in the literature regarding higher comorbidity with psychiatric disorders (Arnaout & Petrakis, 2008; Bucholz, 1999; Compton, Thomas, Stinson, & Grant, 2007; B. F. Grant et al., 2004; Hasin, Stinson, Ogburn, & Grant, 2007), higher likelihood of juvenile substance use (Arnaout & Petrakis, 2008; Peiper et al., 2016) and higher likelihood of seeking treatment (Arnaout & Petrakis, 2008; Stinson et al., 2005). Taken together, our findings suggest that the overall profiles of respondents with substance use disorders is similar to what has been described in the literature.

C. Substance Use Disorders as Forces of Production of Violence

It has been well established that substance use disorders are associated with increased risk of aggressive behaviors towards the self and towards others. However, as we have detailed in our literature review, the strength of the independent association between substance use and violence has been confounded by several issues, including the lack of uniformity in defining the exposure (i.e. substance use), the outcome (i.e. violent behavior), the population (general, offenders, decedents…) and the confounding factors.

We have clearly demonstrated that both alcohol and drug use disorders are independently associated with an increased risk of overall violence within the same general adult population. We have also clearly shown that, even after adjusting for confounders, alcohol use disorder only, drug use disorder only and combined alcohol and drug use disorders are significantly associated with self-directed, other-directed and combined violence, with differing effect margins. We hypothesized that alcohol use disorder will be more strongly associated with perpetration of violence given the extensive research documenting this association and the wider availability of this substance compared to others. However, drug use disorders had an equally strong association with violent behavior (across all subtypes) despite its lower prevalence in the sampled population. This effect could be explained by a larger potency of illicit drugs to induce violent behavior or by the added exposure to drug markets which is a known risk factor for violence (Pulay et al., 2008).

The association between substance use disorders and violence was magnified when alcohol and drug use disorders were comorbid. While previous research underlined the association of co-occurring alcohol and drug use disorders with suicide (Arnaout &

Petrakis, 2008) and other-directed violence (Korcha et al., 2014), our findings suggest that alcohol and drug use might have a synergistic effect on the production of violence: further research should identify which drugs interact with alcohol in increasing violence (Cherpitel, Martin, Macdonald, Brubacher, & Stenstrom, 2013).

D. Substance Use Disorders as Forces of Direction of Violence

One of the main questions our project set out to answer focused on determinants of the directionality of violence: self vs. other. We found that drug use disorders and co-occurring alcohol and drug use disorders increased the odds of directing violence towards others rather than towards the self. This association remained significant even after controlling for multiple socio-demographic and clinical confounders.

Previous research using the integrated model of violence framework led to different results. Harford and his team (Harford et al., 2013) found that alcohol use disorders and drug use disorders were both associated with increased likelihood of other- vs. self-directed violence among adults; however that study did not explore the risk associated with alcohol and drug use combined and did not control for psycho-social confounders. A second study by Harford (Harford et al., 2016) used NSDUH data and showed an increased risk of other- vs. self-directed violence for alcohol use disorder as per DSM-5 criteria and a lower risk for drug use disorders (also as per DSM-5 criteria) among 12-17 year olds. This study was also limited by the lack of controlling for psycho-social factors as well as psychiatric diagnoses.

So far, explanatory theories of the directionality of violence have relied on psychological constructs such as personality traits and attributional styles. Anger was found

to be correlated with other-directed violence but not self-directed violence among men while anhedonia predicted self- vs. other-directed violence among men and women; hostility predicted both types of violence in women (Sadeh, Javdani, Finy, & Verona, 2011). Hostile attributional bias[6] among juveniles and adults was regularly shown to be positively correlated with other-directed aggressive behavior (Dodge, 2006; Dodge et al., 2015; Yeager, Miu, Powers, & Dweck, 2013) and this correlation was found to be moderated by impulsivity traits (Chen, Coccaro, & Jacobson, 2012). Negative attitudes and biases about oneself promote hopelessness and helplessness and consequently suicidal behavior (A. T. Beck, 2008; van Heeringen & Mann, 2014): for example, a deficient self-serving bias[7], characterized by the internal causal attribution of negative events, is believed to be a key contributing factor (Mezulis, Abramson, Hyde, & Hankin, 2004). The neurobiological processes by which people give causal attributions to other people's behavior have been extensively studied and involve the supratemporal sulcus, the temporal poles, the anterior cingulate and the dorsolateral and medial prefrontal cortices (Mason & Morris, 2010). Recent research has found that hostile attributional bias might be correlated with increased amygdala activity (Choe, Shaw, & Forbes, 2015) and that a dysfunctional self-serving bias is correlated with fronto-limbic dysfunction (Seidel et al., 2012) and increased activation of the inferior parietal lobule (Hao et al., 2015). Furthermore, one study implicated the fronto-temporo-parietal network in internal and external causal attributions (Seidel et al., 2010).

[6] Hostile attributional bias is defined as the tendency "to interpret unambiguous social stimuli as displays of hostility" (Nasby, Hayden, & DePaulo, 1980).

[7] Self-serving bias is defined as the tendency "to attribute one's successes to personal characteristics, and one's failures to factors beyond one's control" (Fournier, 2016).

Taken together, this evidence seems to indicate that, even though self- and other-directed violence have overlapping diatheses and stressors (as we demonstrated in our literature review), specific neural circuits might be involved in determining directionality of violence. Having said that, alcohol and drugs might regulate these circuits (acutely and chronically) and differentially affect the directionality of aggressive urges. But in order to better understand the role of substances in promoting violent behavior, research should focus on substance-specific associations rather than lump all substances in one or two (alcohol and drugs) categories as there is evidence supporting substance-specific alterations of gene expression patterns (Lehrmann & Freed, 2008).

E. Cannabis Use Disorder and Violence

We have detailed in our literature review the mixed evidence regarding the association of cannabis and self- and other-directed violence. In our study, we found that cannabis use disorder significantly increased the odds of perpetrating other-directed and combined violence, but not self-directed violence. This is a substantial finding as both of these associations were identified in nationally representative US sample and remained significant after adjusting to other substance use, socio-demographic and clinical factors. Also, there is evidence that CUD favored other- vs. self-directed violence, although this association was marginally non-significant in the overall sample (further discussion in the next section). CUD is thought to promote aggression through decreasing prefrontal response inhibition (Broyd et al., 2016; Crean et al., 2011) and down-regulation of CB1-R in the amygdala, prefrontal cortex and the hippocampus (Volkow et al., 2017). These effects are modulated by THC and become more prominent as the potency of cannabis

increases (UNODC, 2016). Added to that, CUD withdrawal activates the extrahypothalamic stress system in the prefrontal cortex and extended amygdala (Caberlotto et al., 2004; Rodriguez de Fonseca et al., 1997), regions that have been implicated in aggressive behavior. All of these mechanisms have been implicated in self- and other-directed violence but there is some evidence that might explain the tendency to aggress others rather than oneself: volunteers with no substance use disorders were found to have increased hostile attributional bias and impulsivity within two days of use of cannabis compared to days when no cannabis was used (Ansell, Laws, Roche, & Sinha, 2015). We might argue that individuals with CUD exhibit higher levels of hostile attributional bias due to circuit-specific modulating effects, putting them more at risk to engage in other- vs. self-directed violence.

F. Age: Effect Modifier of the Association between Substance Use Disorders and Violence

Given that substance use causes brain changes (de Wit, 2009; Koob et al., 2014; Lehrmann & Freed, 2008), it is fair to assume that the magnitude of these changes depend on, among other factors, the age of the user. While a review of normal neurodevelopment and brain maturation is beyond the scope of our study, it is important to mention that the morphological and functional development of the frontal cortex occurs between late childhood and early adulthood (Marsh, Gerber, & Peterson, 2008). This process is highly sensitive to its neurobiological environment and can be modulated and affected by factors such as substance use (Arnsten & Rubia, 2012; Wetherill & Tapert, 2013). As a matter of

fact, animal studies have shown short-term and long-term neurobehavioral changes secondary to early use of alcohol and cannabis (Spear, 2016).

These age-dependent substance-induced neurobiological modifications might explain our results which found significantly strong associations between all substance use disorder categories and the commission of overall violence among 18-25 and 26-49 year olds. Interestingly, we found AUDa, DUDa, ADUD and CUD to significantly increase the odds of other- vs. self-directed violence only among 18-25 year olds. Although the prevalence of use disorders was highest among the youth, this does not fully explain the observed effects, given that AUDa significantly increased the odds of self- vs. other-directed violence among the elderly despite a comparatively low prevalence in this group (refer to Appendix 3 for more information regarding the weighted distribution of sample characteristics across age groups). Moreover, we found that a history of juvenile substance use was highly prevalent among respondents with a substance use disorder across all age groups (refer to Appendix 4) and that juvenile substance use was a significant correlate of the association between substance use disorders and perpetrating violence mainly among 18-25 and 26-49 year olds. Taken all together, these findings highlight the compounded risk of early substance use associated with developing substance use disorders across the lifespan and committing violent behavior in developmentally-sensitive periods.

G. Strengths and Limitations

Our work has several strengths. We used pooled cross-sectional weighted data from a nationally representative survey of the US general population in order to maximize our sample size and raise confidence in our findings. We used homogeneous definitions of

self-directed violence (i.e. attempted suicide) and other-directed violence (i.e. assault) in order to increase comparability of categories within our outcome variables. Although NSDUH data used DSM-4 criteria to define substance use disorders, we coded exposure variables that are closer to DSM-5 criteria and are thus more scientifically relevant. Furthermore, our work was able to detect associations between specific substance use disorders and specific subtypes of violent behaviors within an integrated model of violence, and after controlling for a wide array of relevant socio-demographic, psycho-social and clinical factors. We were also able to demonstrate the variability of these associations according to age, further highlighting the need for preventive efforts targeting the youth. Using the integrated model of violence has allowed us to quantify and compare these associations in the same population and therefore has provided more solid information on the burden of specific substance use disorders and argued for the potential benefits of substance-specific research, in the same vein as the research on alcohol. In addition to that, the integrated model of violence has shown its benefits in its ability to identify common risk factors for self- and other-directed violence and, most importantly, specific determinants of directionality of violence (self- or other).

However, our work has a number of limitations. First, although we coded our exposure variables to further resemble DSM-5 criteria, they do not fully comply: the NSDUH did not include a "withdrawal criterion" for some substances, including cannabis. This might have led to an underestimation of the prevalence and the impact of substance use disorders in our population and might explain differences in prevalence with other studies that relied on validated DSM-5 diagnostic tools (B. F. Grant et al., 2015; B. F. Grant et al., 2016). The *Drug Use Disorder(s) alone* category in our variable (U) included

individuals who had one and/or multiple drug use disorders. Future research should assess drug-specific effects to further understand their contribution to the burden of violence.

Second, despite the fact we pooled seven consecutive years of cross-sectional data, we had to adjust our analyses due to low sample sizes in some categories: for example, we had to exclude the *Combined Violence* category in order to carry our age-stratified analyses. As a consequence of low sample size, some of our models had low fit, especially among the elderly age category.

Third, although the categories of our variable (V) had homogeneous constructs in terms of the intentionality of the behavior and the physical nature of the act, there were several relevant missing factors pertaining to the self- and other-directed violent behaviors. We did not include violence of a strictly sexual or psychological nature and neglect was not evaluated. Also, we were unable to assess the social context of the behavior, or whether it was pre-meditated or impulsive, or what means were used to commit it. Hence our results have limited generalizability and might only apply to impulsive physically violent behaviors given the shared diathesis with substance use disorders. Furthermore, we didn't have information regarding juvenile history of abuse which is known to be a predisposing factor to commit violence (WHO, 2002).

Fourth, our assessment for the presence of a psychiatric disorder relied on an equation derived from two scores of psychological distress (K6 scale) and functional impairment (WHODAS scale) rather than on structured diagnostic tools for psychiatric disorders. Our tool had "moderate agreement[8]" (Landis & Koch, 1977) with the full NSDUH tool (which we could not use as we mentioned in our literature review). Given its

[8] Cohen's kappa = 0.450.

low sensitivity, it is highly possible that we underestimated the prevalence of psychiatric disorders among our sample and therefore we couldn't fully account for their mediating effect on displaying violent behavior.

Fifth, survey data is subject to several biases, most important of which is recall bias as participants were asked symptoms and behaviors over the past twelve months. Poor recall might explain the finding that respondents who did not fulfill substance use disorder criteria reported having had substance use treatment over the past year. Selection bias also limits the generalizability of our results because the NSDUH is a household survey and excludes institutionalized and homeless individuals.

Finally, since our work relied on pooled cross-sectional data and hence is unable to establish causality between substance use disorders and violence. Future longitudinal prospective studies are needed to determine psychopharmacological causality between specific substance use disorders and violent behavior, within an integrated model approach.

CHAPTER VI:
CONCLUSIONS

A. Theoretical Implications

Throughout our work we have shown that using the integrated model of violence as a conceptual framework to study physically violent behavior is scientifically relevant and valuable. We were able to identify specific substance use disorders to be "correlates of directionality" of violence, lending support to Plutchik's two-stage model (Plutchik et al., 1989) and giving evidence for its generalizability to the household general population. We were also able to identify age as a major effect modifier in the association between use disorders and different types of violence.

The WHO typology of violence (WHO, 2002), while useful, is a semiological categorization and does not rely on neurobiological evidence. However, by adopting the integrated model, we will be able to pinpoint common ("forces of production") and discriminatory ("forces of direction") etiological mechanisms and thus categorize violent behavior from a neurobiological perspective.

Whereas "fractional" approaches are the rule when it comes to violence research, integrated approaches are predominant in substance use research. Unified models of addiction such as the allostatic model (Koob et al., 2014) are not comprehensive models of the psychoactive effects of all substances. Yet a significant amount of substance use research lumps substances together ("illicit drugs" for example), masking the potentially disparate behavioral effects of individual substances. In this framework, an association between substance use disorders and a certain outcome is an association between addictive

behavior and this outcome. Our work has highlighted the scientific relevance of substance-specific research: identifying neurobiological correlates of individual substance use disorders' associations with specific behaviors (such as self- or other-directed violence) can shed light on the mechanisms of these behaviors.

We believe that adopting the two frameworks we described above will also help researchers develop targeted preventive and/or therapeutic interventions.

B. Practical Implications

Our work has shown that alcohol, drug and cannabis use disorders are associated with violent behavior especially among youth, highlighting the need to design substance use and violence prevention strategies targeting the youth.

The WHO's latest reports on worldwide prevention of suicide and interpersonal violence (WHO, 2014a, 2014b) acknowledged that although efforts are being made, they still come short of the standards required. There is a lack of population-based data to inform local policymakers and preventive policies are not widely implemented. Strategies addressing substance use are not universally applied.

Efforts tackling harmful alcohol use are increasing: taxation, sales-restricting measures and drink-driving countermeasures are the most common and were shown to be effective strategies in reducing youth self- and other-directed violence (WHO, 2014a, 2014b). Other effective strategies to deter from drug use include school-based mentoring and countermeasures against global drugs trade (WHO, 2014a). Promoting access to health care for individuals with substance use disorders is necessary given the stigma associated

with seeking mental health care and because it increases recovery (UNODC, 2016; WHO, 2014a, 2014b).

Cannabis is the most trafficked and used drug in the world (UNODC, 2016) and one of the most largely debated public health issues pertains to its harms and benefits (Volkow et al., 2017). In our study, cannabis use disorder was independently associated with perpetration of other-directed violence, most notably among youth. Far from taking sides on whether to legalize cannabis use or not, we advocate for fact-based public information campaigns about the risks of cannabis and the availability of substance use disorder treatment options.

C. Future Research

There are several uncharted avenues that need exploration. First of all, longitudinal prospective studies of subjects from childhood to early adulthood are needed in order to establish whether there are causal relationships between different substance use disorders and violent behavior. Such studies would need to not only rely on self-report of violent events (self- or other- directed), but also on standardized measurement tools of aggression and impulsivity, and validated diagnostic tools of substance use and psychiatric disorders. Prospective studies including genetic and brain imaging data as well as data about adverse childhood events are needed in order to construct stress-diathesis models for production and for direction of violence. These models might be age and/or sex-specific as suggested by our analyses. Longitudinal prospective studies can thus be powerful resources of information to build reliable and accurate predictive tools of future violent behavior, which are lacking to this day (Warden, Spiwak, Sareen, & Bolton, 2014; Whittington et al., 2013).

Second of all, interventional studies targeting violent dispositions are needed. Recent reviews have highlighted the lack of effective "anti-suicide" pharmacological agents and the need for additional randomized controlled trials (Al Jurdi, Swann, & Mathew, 2015). Most reviews addressing management of other-directed violence have focused on violence in mental illness (Citrome & Volavka, 2014; Meyer, Cummings, Proctor, & Stahl, 2016). Therefore, more randomized controlled interventional studies are needed targeting violent behaviors in the general population.

Third of all, further trials are needed to address the management of substance use disorders. It is reported that only 1/6 of those with a drug use disorder are undergoing treatment (UNODC, 2016) and that overall relapse rates of substance use disorders range between 40-60% (McLellan, Lewis, O'Brien, & Kleber, 2000). Prevention and treatment of adolescent substance use disorders should be a research priority as glaring gaps remain (Hammond, 2016). Much like violence, substance use is a public health issue with wide repercussions: addressing this issue is linked to achieving sustainable development[9] (UNODC, 2016; WHO, 2002).

Finally, one promising therapeutic avenue might involve targeting impulsivity as a symptom and thus indirectly promoting substance use and violence prevention/management.

[9] As per the United Nations, there are five areas of development: social development, economic development, environmental sustainability, peaceful just and inclusive societies and partnership (UNODC, 2016).

ILLUSTRATIONS

Figure 1: Model Testing (Hyp1)

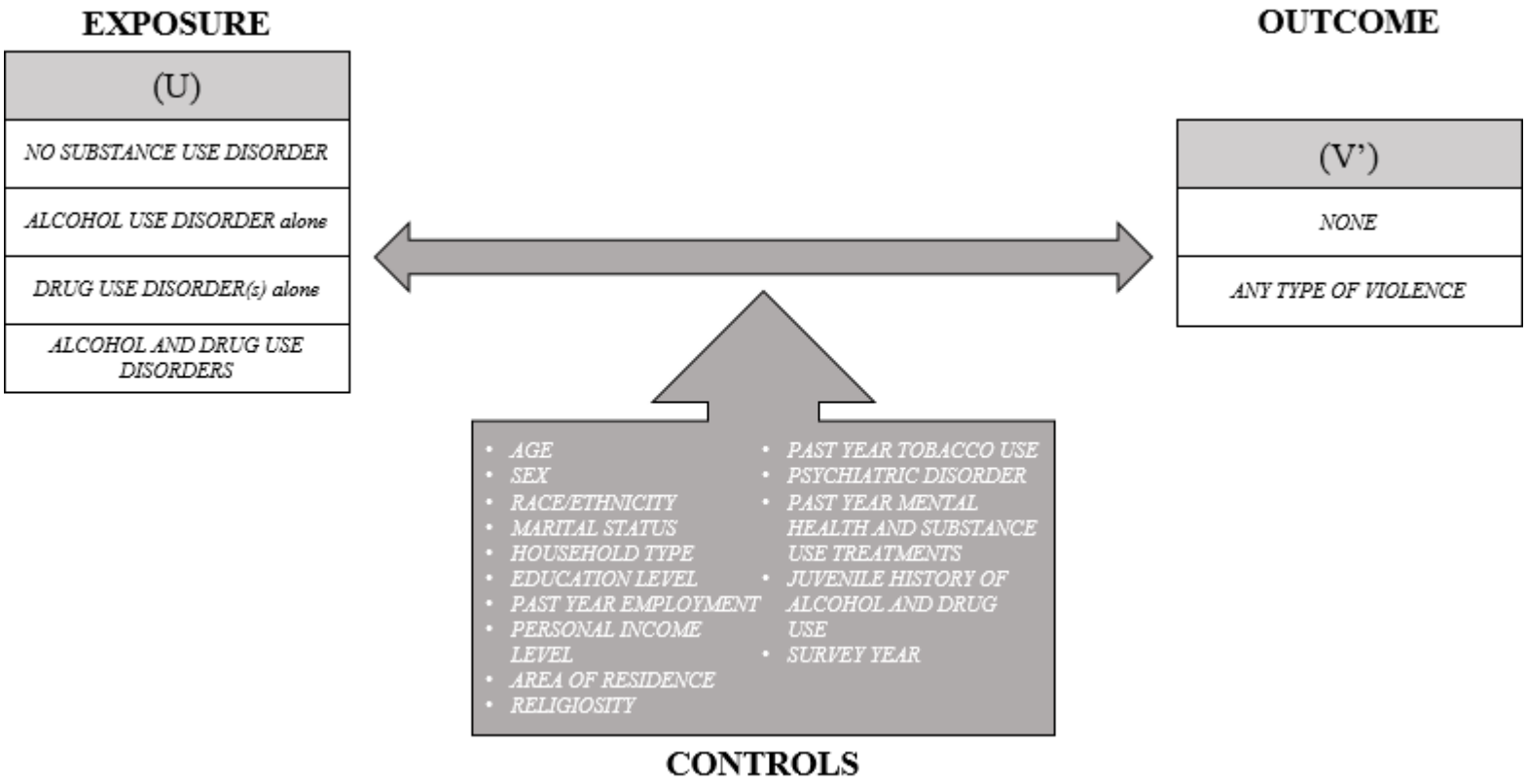


Figure 2: Model Testing (Hyp2)

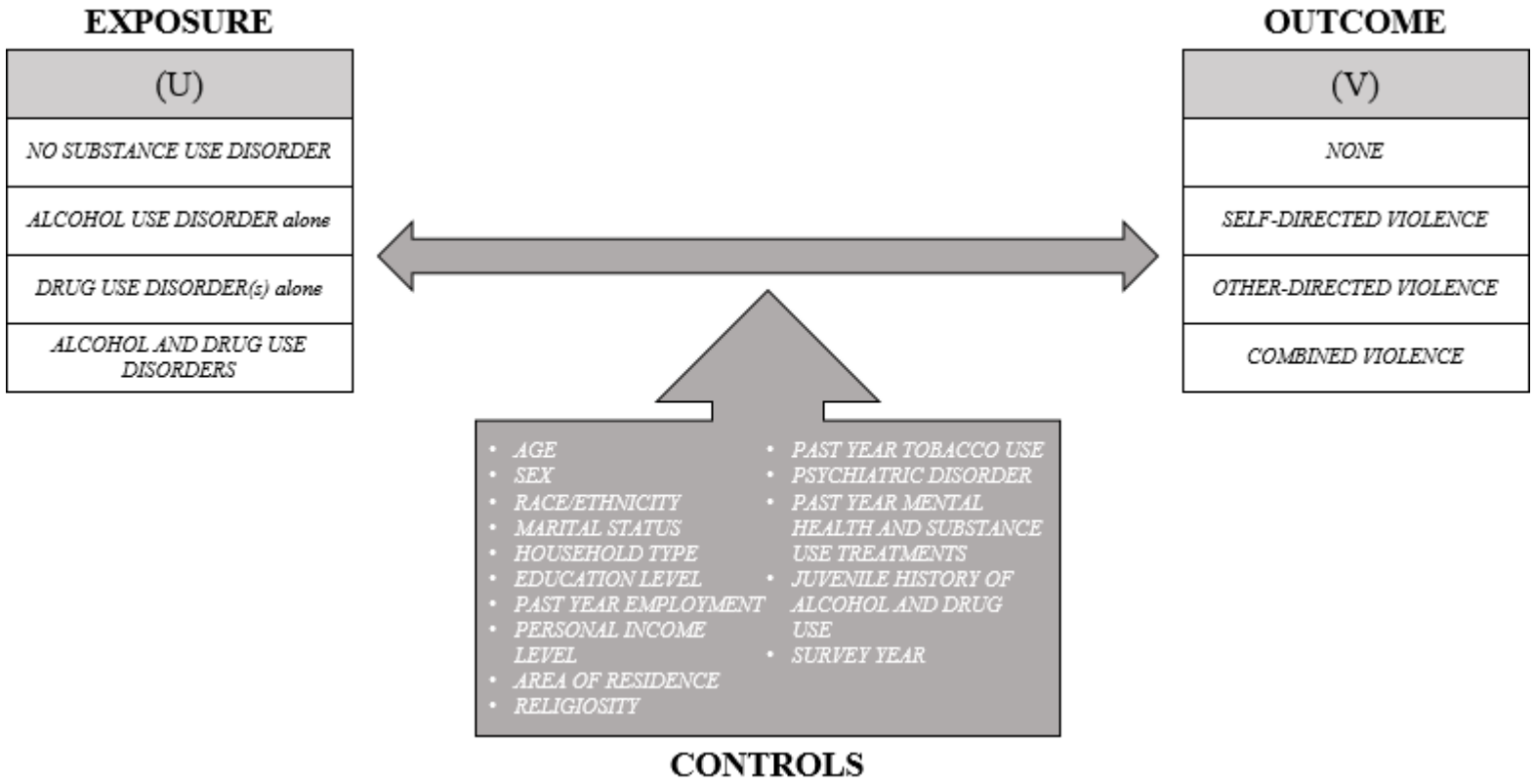


Figure 3: Model Testing (Hyp3)

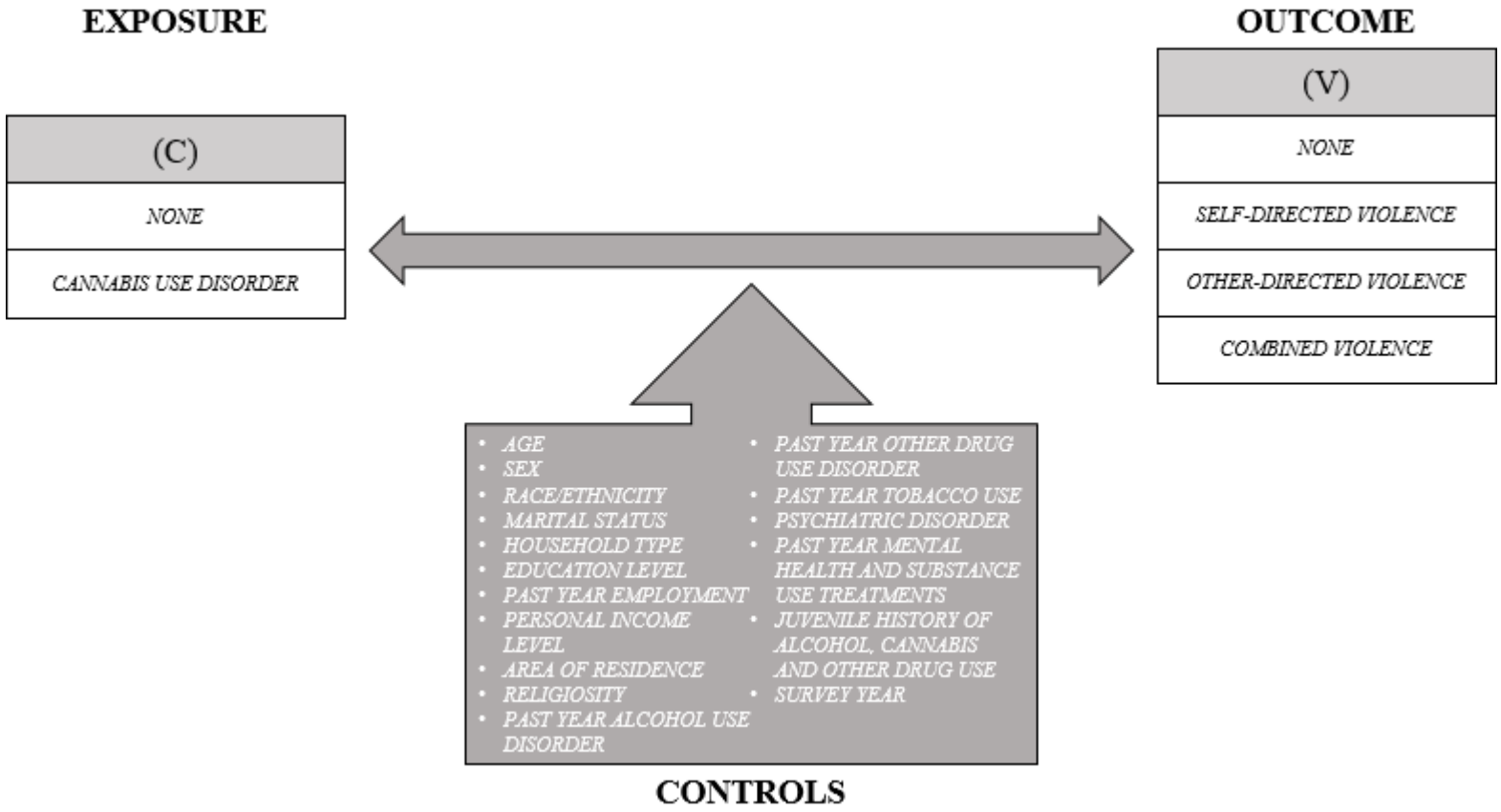


Figure 4.1: Models Testing (Hyp4): Age-Stratified Model Testing (Hyp1)

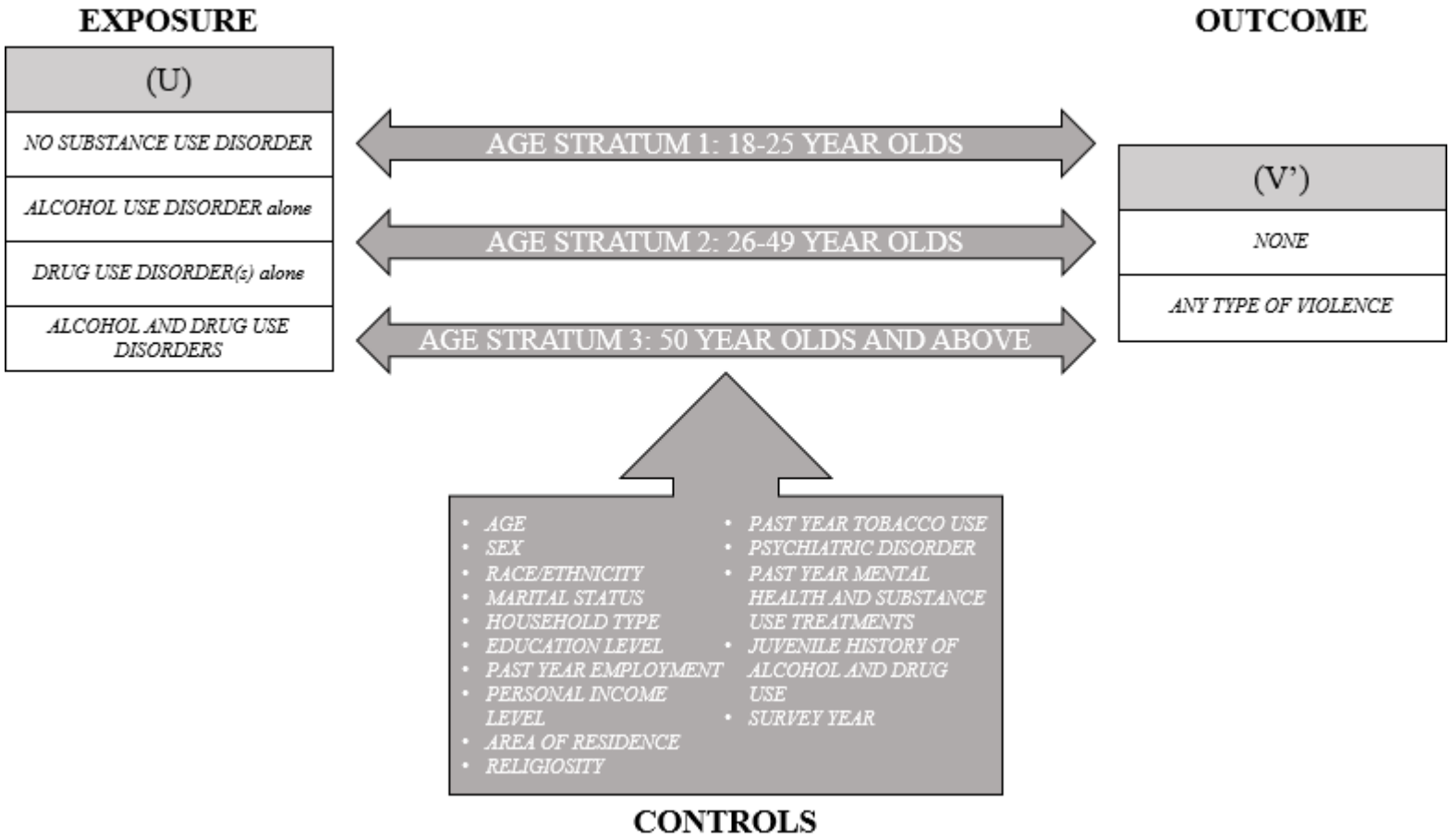


Figure 4.2: Models Testing (Hyp4): Age-Stratified Model Testing (Hyp2)

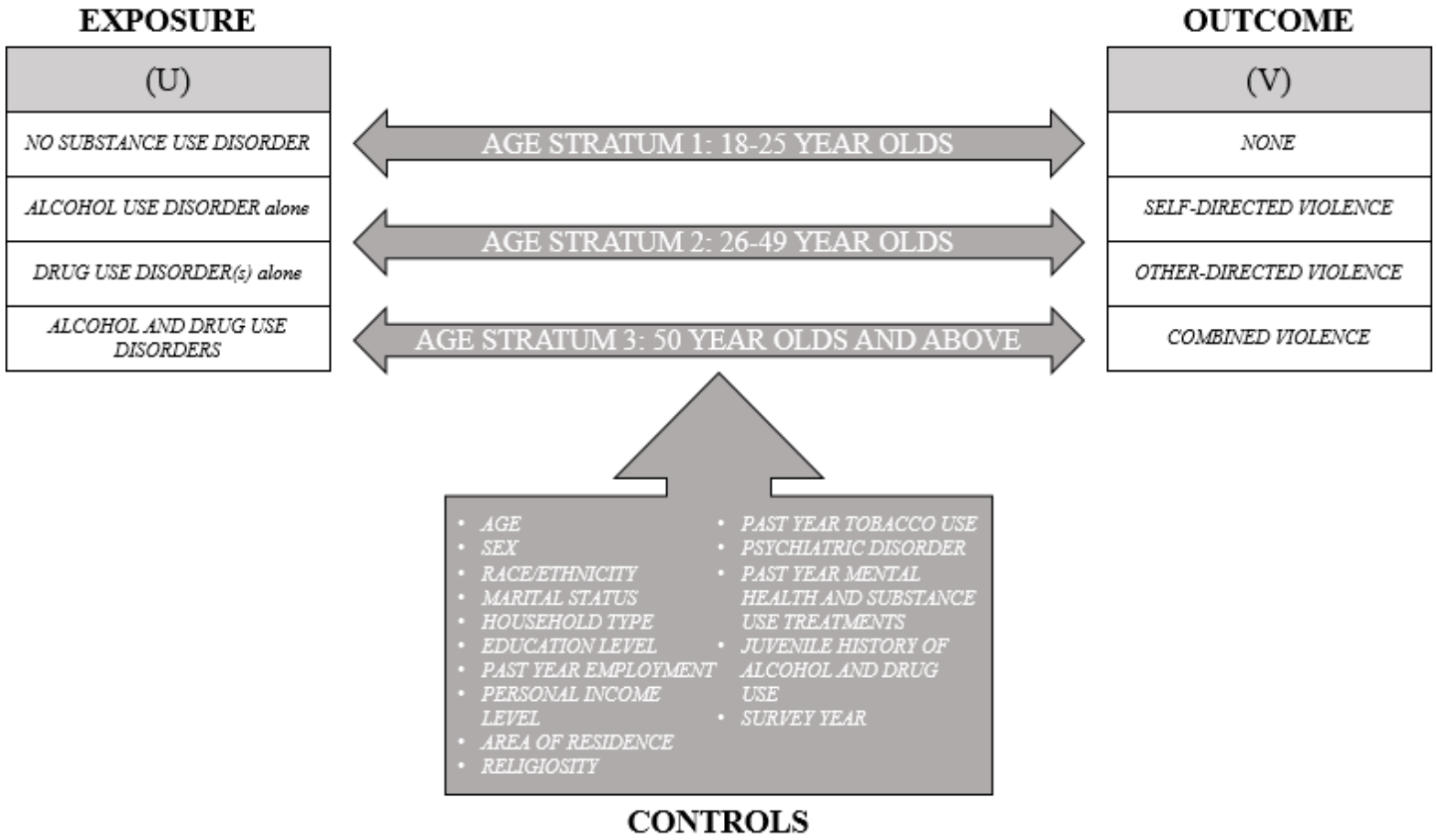


Figure 4.3: Models Testing (Hyp4): Age-Stratified Model Testing (Hyp3)

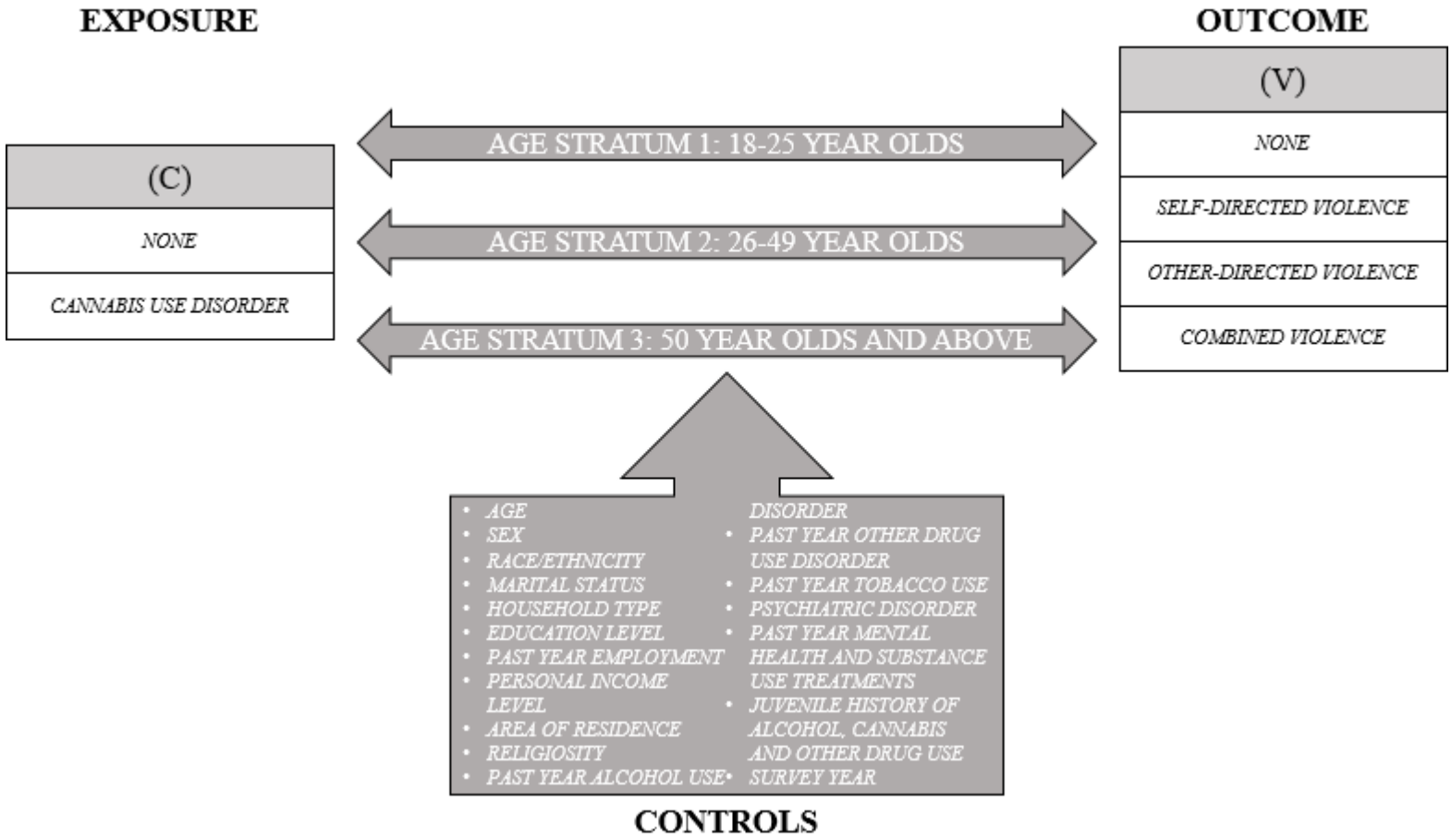
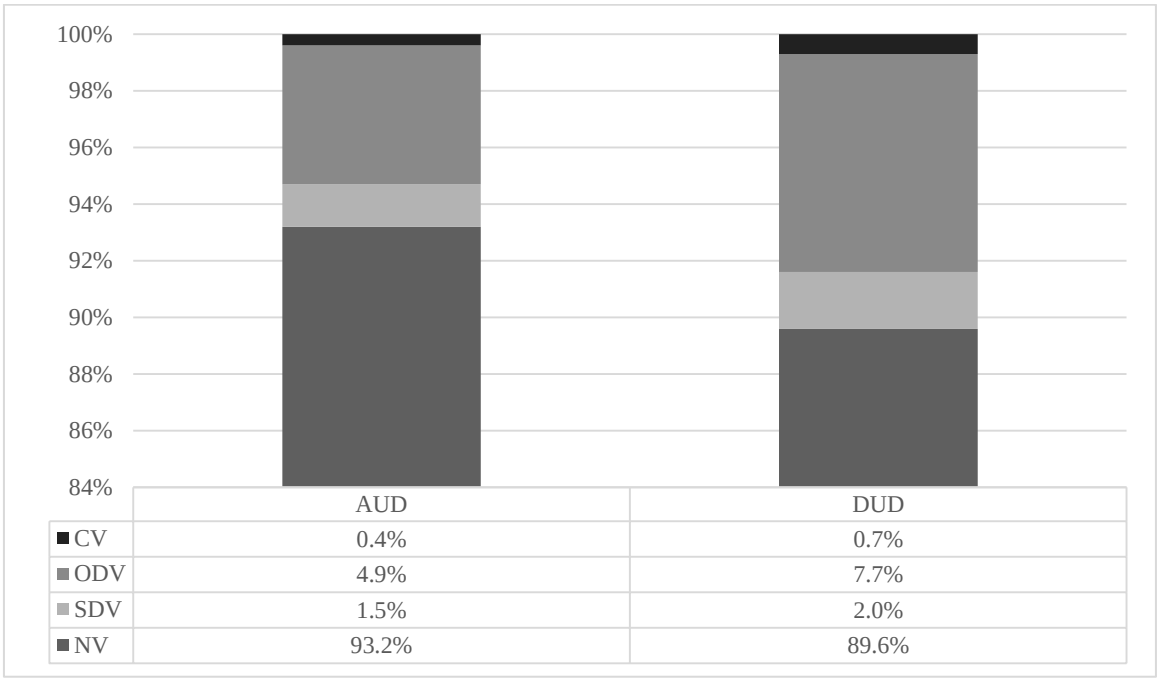


Figure 5: Weighted distribution of violence subtypes (V) by alcohol (A) and drug (D) use disorders

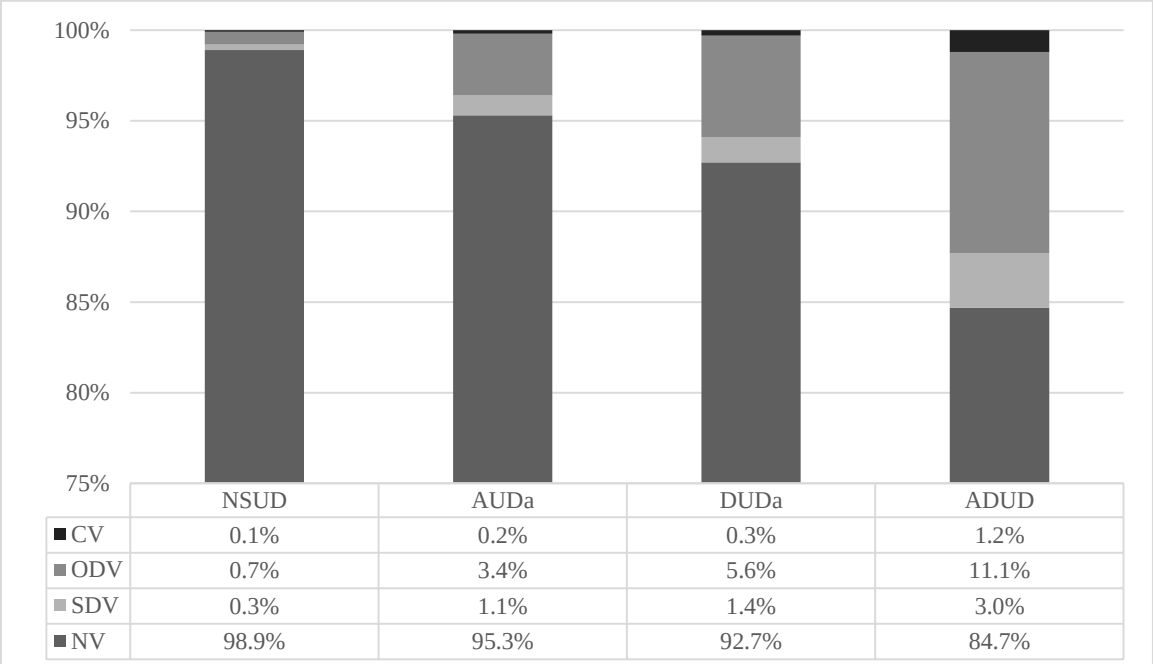


	AUD	DUD
CV	0.4%	0.7%
ODV	4.9%	7.7%
SDV	1.5%	2.0%
NV	93.2%	89.6%

AUD: Alcohol Use Disorder; DUD: Drug Use Disorder(s).

NV: Non-Violent; SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence.

Figure 6: Weighted distribution of violence subtypes (V) by substance use disorder categories (U)

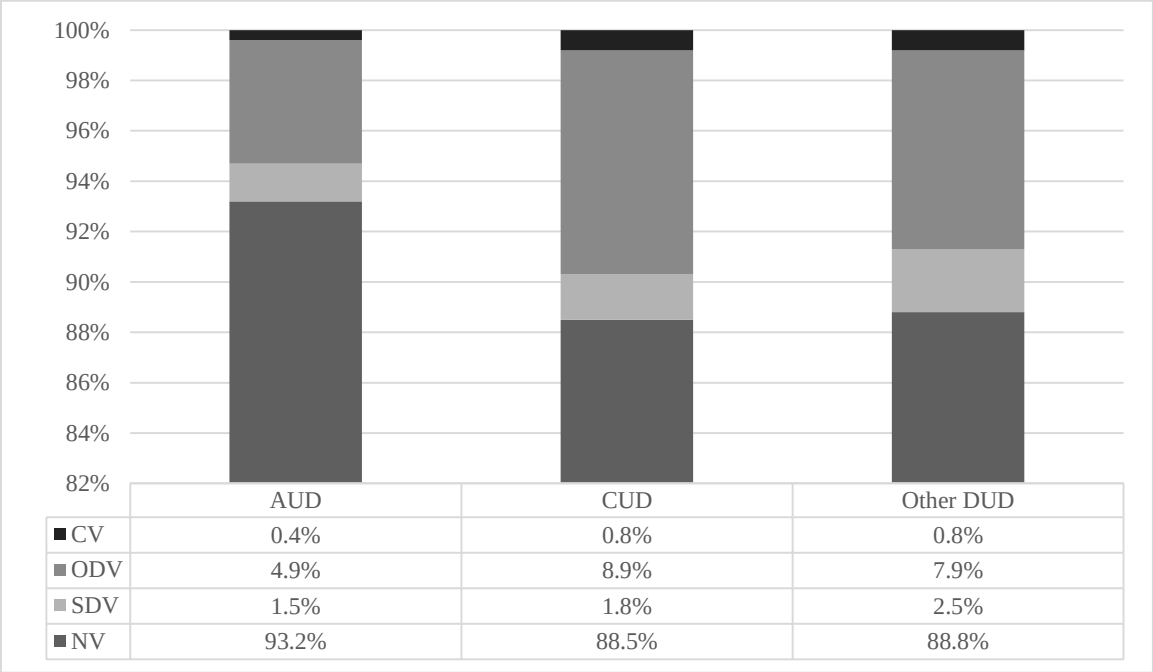


	NSUD	AUDa	DUDa	ADUD
CV	0.1%	0.2%	0.3%	1.2%
ODV	0.7%	3.4%	5.6%	11.1%
SDV	0.3%	1.1%	1.4%	3.0%
NV	98.9%	95.3%	92.7%	84.7%

NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

NV: Non-Violent; SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence.

Figure 7: Weighted distribution of violence subtypes (V) by alcohol (A), cannabis (C) and other drug (B) use disorders



	AUD	CUD	Other DUD
CV	0.4%	0.8%	0.8%
ODV	4.9%	8.9%	7.9%
SDV	1.5%	1.8%	2.5%
NV	93.2%	88.5%	88.8%

AUD: Alcohol Use Disorder; CUD: Cannabis Use Disorder; DUD: Drug Use Disorder(s).

NV: Non-Violent; SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence.

TABLES

Table 4.1: Weighted distribution of the sample across survey years

Survey Year	N	PSE	P (SE)
2008	37504	32131823	13.8 (0.1)
2009	37707	324580178	14.0 (0.1)
2010	38919	32753225	14.1 (0.1)
2011	39133	33232186	14.3 (0.1)
2012	37869	33589182	14.5 (0.1)
2013	37424	33928405	14.6 (0.1)
2014	41671	34321159	14.8 (0.1)
Total	**270227**	**232414058**	**100 (0.0)**

N: unweighted sample size; PSE: Population Size Estimate; P: Prevalence in percent; SE: Standard Error in percent.

Table 4.2: Weighted prevalence estimates in percent of total sample characteristics

Characteristic	Total Sample (N=270227; PSE=232414058)	Total Valid Sample Included in (V) (N=268839; PSE=231365447; P_{TS}=99.5%)
	P (SE)	P (SE)
Age in years		
18-25	14.7 (0.1)	14.7 (0.1)
26-49	42.5 (0.2)	42.5 (0.2)
50 or above	42.8 (0.2)	42.8 (0.2)
Sex		
Male	48.2 (0.2)	48.2 (0.2)
Female	51.8 (0.2)	51.8 (0.2)
Race/Ethnicity		
Non-Hispanic White	67.0 (0.2)	67.1 (0.2)
Non-Hispanic Black	11.6 (0.2)	11.6 (0.2)
Hispanic	14.4 (0.1)	14.4 (0.1)
Other	7.0 (0.1)	6.9 (0.1)
Marital Status		
Married	53.1 (0.2)	53.1 (0.2)
Widowed	6.0 (0.1)	6.0 (0.1)
Divorced or Separated	13.9 (0.1)	13.9 (0.1)
Never Been Married	27.0 (0.2)	26.9 (0.2)
Household Type		
Single-Person	12.5 (0.1)	12.5 (0.1)
Family	78.8 (0.2)	78.8 (0.2)
Non-Family	4.9 (0.1)	4.9 (0.1)
Mixed	3.9 (0.1)	3.9 (0.1)
Education Level		
Less Than High School	14.4 (0.1)	14.3 (0.1)
High School Graduate	30.1 (0.2)	30.1 (0.2)
Some College	26.2 (0.2)	26.2 (0.2)
College Graduate	29.3 (0.2)	29.4 (0.2)
Past Year Employment		
Continuous	57.2 (0.2)	57.2 (0.2)
Intermittent	7.9 (0.1)	7.9 (0.1)
Not in Labor Force	34.9 (0.2)	34.8 (0.2)

Personal Income Level in USD		
Less than 10000	24.3 (0.1)	24.2 (0.1)
10000-29999	33.1 (0.2)	33.1 (0.2)
30000 or Above	42.5 (0.2)	42.6 (0.2)
Area of Residence		
Large Metro	53.6 (0.3)	53.6 (0.3)
Small Metro	30.3 (0.3)	30.3 (0.3)
Non-Metro	16.1 (0.2)	16.1 (0.2)
Religiosity	71.4 (0.1)	71.4 (0.1)
Past Year Tobacco Use	33.9 (0.2)	33.8 (0.2)
AUD	8.5 (0.1)	8.5 (0.1)
DUD	4.4 (0.1)	4.4 (0.1)
CUD	2.5 (0.0)	2.5 (0.0)
Other DUD	2.5 (0.0)	2.5 (0.0)
Substance Use Disorders (U)		
NSUD	88.8 (0.1)	88.8 (0.1)
AUDa	6.8 (0.1)	6.8 (0.1)
DUDa	2.7 (0.0)	2.7 (0.0)
ADUD	1.7 (0.0)	1.7 (0.0)
Psychiatric Disorder	5.3 (0.1)	5.3 (0.1)
Past Year Mental Health Treatment	14.1 (0.1)	14.1 (0.1)
Past Year Substance Use Treatment		
Alcohol	0.6 (0.0)	0.6 (0.0)
Drugs	0.6 (0.0)	0.6 (0.0)
Juvenile Alcohol Use	49.3 (0.2)	49.4 (0.2)
Juvenile Drug Use	27.6 (0.1)	27.6 (0.1)
Cannabis	25.1 (0.1)	25.1 (0.1)
Any Other Drug	12.7 (0.1)	12.7 (0.1)

N: unweighted sample size; PSE: Population Size Estimate; P_{TS}: Proportion of the Total Sample; P: Prevalence in percent; SE: Standard Error in percent; AUD: Alcohol Use Disorder; DUD: Drug Use Disorder(s); CUD: Cannabis Use Disorder; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

Table 4.3: Weighted prevalence estimates in percent of sample characteristics by substance use disorder category

Characteristic	AUDa (N=24907; PSE=15820617; P=6.8%)	DUDa (N=12795; PSE=6271927; P=2.7%)	ADUD (N=9209; PSE=3928475; P=1.7%)	NSUD (N=223316; PSE=206393039; P=88.8%)
	P (SE)	P (SE)	P (SE)	P (SE)
Age in years				
18-25	25.2 (0.4)	42.2 (0.7)	52.0 (0.9)	12.4 (0.1)
26-49	50.8 (0.6)	44.8 (0.7)	40.9 (1.0)	41.8 (0.2)
50 or above	24.0 (0.6)	12.9 (0.7)	7.1 (0.7)	45.8 (0.2)
Sex				
Male	62.9 (0.5)	60.7 (0.7)	65.1 (0.8)	46.4 (0.2)
Female	37.1 (0.5)	39.3 (0.7)	34.9 (0.8)	53.6 (0.2)
Race/Ethnicity				
Non-Hispanic White	66.0 (0.5)	67.0 (0.9)	65.9 (0.9)	67.1 (0.2)
Non-Hispanic Black	11.3 (0.4)	14.1 (0.5)	14.3 (0.6)	11.5 (0.2)
Hispanic	16.6 (0.5)	13.2 (0.6)	14.9 (0.6)	14.3 (0.1)
Other	6.1 (0.2)	5.6 (0.4)	4.8 (0.3)	7.1 (0.1)
Marital Status				
Married	37.6 (0.6)	21.5 (0.7)	13.2 (0.7)	56.0 (0.2)
Widowed	2.1 (0.2)	1.6 (0.3)	1.0 (0.2)	6.5 (0.1)
Divorced or Separated	15.9 (0.5)	12.9 (0.6)	11.5 (0.7)	13.9 (0.1)
Never Been Married	44.4 (0.6)	63.9 (0.9)	74.3 (1.0)	23.6 (0.2)
Household Type				
Single-Person	12.4 (0.4)	10.0 (0.5)	10.4 (0.6)	12.6 (0.1)
Family	71.9 (0.5)	70.5 (0.7)	64.0 (0.9)	79.8 (0.2)

Non-Family	10.2 (0.3)	11.5 (0.4)	17.9 (0.7)	4.0 (0.1)
Mixed	5.5 (0.3)	8.0 (0.4)	7.7 (0.5)	3.5 (0.1)
Education Level				
Less Than High School	14.0 (0.3)	19.6 (0.6)	20.1 (0.6)	14.2 (0.1)
High School Graduate	28.9 (0.4)	32.4 (0.7)	32.0 (0.9)	30.1 (0.2)
Some College	29.6 (0.5)	31.5 (0.7)	31.8 (0.8)	25.7 (0.2)
College Graduate	27.6 (0.5)	16.4 (0.6)	16.1 (0.7)	30.1 (0.2)
Past Year Employment				
Continuous	62.0 (0.5)	45.1 (0.8)	44.3 (0.9)	57.4 (0.2)
Intermittent	12.3 (0.3)	18.5 (0.5)	21.7 (0.6)	7.0 (0.1)
Not in Labor Force	25.6 (0.5)	36.4 (0.7)	34.0 (0.9)	35.6 (0.2)
Personal Income Level in USD				
Less than 10000	25.1 (0.4)	41.5 (0.7)	44.8 (0.8)	23.3 (0.1)
10000-29999	33.1 (0.5)	36.5 (0.7)	36.4 (0.9)	33.0 (0.2)
30000 or Above	41.8 (0.5)	22.0 (0.8)	18.9 (0.7)	43.7 (0.2)
Area of Residence				
Large Metro	56.1 (0.6)	56.2 (0.9)	55.5 (0.9)	53.3 (0.3)
Small Metro	30.0 (0.6)	29.9 (0.8)	32.0 (0.8)	30.3 (0.3)
Non-Metro	13.9 (0.3)	13.9 (0.6)	12.4 (0.5)	16.4 (0.2)
Religiosity	61.7 (0.4)	52.4 (0.8)	50.7 (0.9)	73.1 (0.2)
Past Year Tobacco Use	60.9 (0.5)	77.9 (0.8)	87.0 (0.6)	29.5 (0.2)
Psychiatric Disorder	10.2 (0.3)	15.2 (0.6)	20.2 (0.6)	4.4 (0.1)
Past Year Mental Health Treatment	20.4 (0.5)	25.6 (0.7)	28.1 (0.7)	13.0 (0.1)
Past Year Substance Use Treatment				
Alcohol	3.5 (0.2)	1.9 (0.2)	8.3 (0.5)	0.2 (0.0)
Drugs	0.7 (0.1)	7.1 (0.3)	7.9 (0.5)	0.2 (0.0)

Juvenile Alcohol Use	74.7 (0.5)	80.7 (0.7)	89.3 (0.6)	45.7 (0.2)
Juvenile Drug Use	50.9 (0.5)	76.6 (0.7)	83.7 (0.7)	23.2 (0.1)
Cannabis	45.9 (0.6)	71.4 (0.8)	78.7 (0.8)	21.1 (0.1)
Any Other Drug	26.4 (0.4)	47.3 (0.7)	56.5 (0.9)	9.8 (0.1)

AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders; NSUD: No Substance Use Disorder; N: unweighted sample size; PSE: Population Size Estimate; P: Prevalence in percent; SE: Standard Error in percent.

Table 4.4: Weighted prevalence estimates in percent of sample characteristics of violent and non-violent subgroups

Characteristic	Violent (N=8984; PSE=4017689; P=1.7%)	Non-Violent (N=261243; PSE=228396369; P=98.3%)	Test Statistic (Pearson Adjusted F)	P-value
	P (SE)	P (SE)		
Age in years			908.772	<0.001
18-25	44.1 (0.9)	14.2 (0.1)		
26-49	37.7 (0.9)	42.6 (0.2)		
50 or above	18.1 (0.9)	43.2 (0.2)		
Sex			104.368	<0.001
Male	56.9 (0.9)	48.1 (0.2)		
Female	43.1 (0.9)	51.9 (0.2)		
Race/Ethnicity			84.168	<0.001
Non-Hispanic White	54.0 (1.0)	67.2 (0.2)		
Non-Hispanic Black	20.9 (0.7)	11.4 (0.2)		
Hispanic	17.8 (0.8)	14.4 (0.1)		
Other	7.3 (0.6)	7.0 (0.1)		
Marital Status			371.334	<0.001
Married	21.5 (0.9)	53.6 (0.2)		
Widowed	3.8 (0.5)	6.0 (0.1)		
Divorced or Separated	15.2 (0.8)	13.9 (0.1)		
Never Been Married	59.5 (0.9)	26.4 (0.2)		
Household Type			75.543	<0.001
Single-Person	10.7 (0.7)	12.5 (0.1)		
Family	71.9 (0.8)	78.9 (0.2)		
Non-Family	9.6 (0.5)	4.8 (0.1)		
Mixed	7.7 (0.5)	3.8 (0.1)		
Education Level			229.541	<0.001
Less Than High School	28.3 (0.9)	14.2 (0.1)		
High School Graduate	35.8 (0.8)	30.0 (0.2)		
Some College	25.9 (0.9)	26.2 (0.2)		
College Graduate	9.9 (0.7)	29.7 (0.2)		
Past Year Employment			340.793	<0.001
Continuous	37.4 (0.9)	57.5 (0.2)		
Intermittent	17.3 (0.6)	7.7 (0.1)		

Not in Labor Force	45.4 (0.9)	34.7 (0.2)		
Personal Income Level in USD			571.020	<0.001
Less than 10000	46.7 (0.9)	23.9 (0.1)		
10000-29999	36.0 (0.8)	33.1 (0.2)		
30000 or Above	17.3 (0.8)	43.0 (0.2)		
Area of Residence			3.169	0.046
Large Metro	51.8 (0.9)	53.7 (0.3)		
Small Metro	30.9 (0.8)	30.3 (0.3)		
Non-Metro	17.4 (0.6)	16.1 (0.2)		
Religiosity	57.6 (1.0)	71.6 (0.1)	239.332	<0.001
Past Year Tobacco Use	64.4 (0.9)	33.3 (0.2)	1139.363	<0.001
AUD	33.4 (0.7)	8.1 (0.1)	3937.990	<0.001
DUD	26.4 (0.7)	4.0 (0.1)	4338.465	<0.001
CUD	16.6 (0.5)	2.2 (0.0)	4288.459	<0.001
Other DUD	16.3 (0.7)	2.3 (0.0)	2293.779	<0.001
Substance Use Disorders (U)			2212.475	<0.001
NSUD	55.1 (0.8)	89.4 (0.1)		
AUDa	18.5 (0.6)	6.6 (0.1)		
DUDa	11.4 (0.5)	2.5 (0.0)		
ADUD	14.9 (0.5)	1.5 (0.0)		
Psychiatric Disorder	25.7 (0.8)	5.0 (0.1)	2289.688	<0.001
Past Year Mental Health Treatment	33.6 (1.1)	13.8 (0.1)	661.639	<0.001
Past Year Substance Use Treatment				
Alcohol	5.1 (0.5)	0.6 (0.0)	661.501	<0.001
Drugs	5.2 (0.5)	0.5 (0.0)	855.344	<0.001
Juvenile Alcohol Use	68.1 (1.0)	49.0 (0.2)	364.730	<0.001
Juvenile Drug Use	58.7 (0.9)	27.0 (0.1)	1592.685	<0.001
Cannabis	52.3 (1.0)	24.6 (0.1)	1154.657	<0.001
Any Other Drug	36.8 (0.8)	12.3 (0.1)	1867.924	<0.001

N: unweighted sample size; PSE: Population Size Estimate; P: Prevalence in percent; SE: Standard Error in percent; AUD: Alcohol Use Disorder; DUD: Drug Use Disorder(s); CUD: Cannabis Use Disorder; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

Table 4.5: Weighted prevalence estimates in percent of sample characteristics by violence category

Characteristic	SDV (N=1944; PSE=1014525; P=0.4%)	ODV (N=6571; PSE=2836342; P=1.2%)	CV (N=410; PSE=141203; P=0.1%)	NV (N=259914; PSE=227373377; P=98.2%)	Test Statistic (Pearson Adjusted F)	P-value
	P (SE)	P (SE)	P (SE)	P (SE)		
Age in years	[a,b,c]	[c]	[c]		318.258	<0.001
18-25	33.2 (1.5)	47.5 (1.2)	55.6 (3.7)	14.2 (0.1)		
26-49	42.1 (1.9)	36.3 (1.1)	32.1 (4.0)	42.6 (0.2)		
50 or above	24.7 (2.0)	16.2 (1.1)	12.3 (3.8)	43.2 (0.2)		
Sex					73.830	<0.001
Male	41.6[a] (2.0)	62.8[c] (1.0)	46.1 (3.6)	48.0 (0.2)		
Female	58.4 (2.0)	37.2 (1.0)	53.9 (3.6)	52.0 (0.2)		
Race/Ethnicity		[c]	[c]		40.763	<0.001
Non-Hispanic White	60.2 (2.0)	51.9 (1.1)	53.2 (3.4)	67.3 (0.2)		
Non-Hispanic Black	14.9 (1.2)	22.9 (0.8)	24.7 (2.7)	11.4 (0.2)		
Hispanic	15.9 (1.3)	18.6 (1.0)	13.9 (2.3)	14.3 (0.1)		
Other	9.0 (1.6)	6.6 (0.6)	8.2 (1.7)	6.9 (0.1)		
Marital Status	[a,c]	[c]	[c]		143.629	<0.001
Married	26.6 (1.9)	20.3 (1.0)	11.1 (2.4)	53.7 (0.2)		
Widowed	4.0 (0.9)	3.8 (0.7)	3.3 (2.1)	6.0 (0.1)		
Divorced or Separated	22.4 (2.1)	12.3 (1.0)	22.0 (3.7)	13.9 (0.1)		
Never Been Married	47.0 (2.0)	63.7 (1.2)	63.7 (3.7)	26.4 (0.2)		
Household Type	[c]	[c]	[c]		28.646	<0.001
Single-Person	14.0 (1.7)	9.7 (0.9)	6.6 (1.8)	12.5 (0.1)		

Family	68.8 (1.9)	73.1 (0.9)	72.6 (4.1)	78.9 (0.2)		
Non-Family	9.6 (1.1)	9.7 (0.7)	8.9 (2.5)	4.8 (0.1)		
Mixed	7.6 (1.2)	7.5 (0.5)	11.9 (3.1)	3.8 (0.1)		
Education Level	[c]	[c]	[c]		93.498	<0.001
Less Than High School	23.3 (1.7)	29.7 (1.2)	36.6 (3.8)	14.1 (0.1)		
High School Graduate	34.5 (1.6)	36.3 (1.0)	36.0 (3.6)	30.0 (0.2)		
Some College	28.1 (1.9)	25.1 (1.0)	24.9 (3.7)	26.2 (0.2)		
College Graduate	14.1 (1.6)	8.9 (0.7)	2.5 (0.9)	29.7 (0.2)		
Past Year Employment	[c]	[c]	[c]		121.944	<0.001
Continuous	33.4 (1.9)	39.4 (1.1)	24.9 (3.2)	57.6 (0.2)		
Intermittent	16.0 (1.5)	17.6 (0.8)	19.6 (2.5)	7.7 (0.1)		
Not in Labor Force	50.5 (2.0)	43.0 (1.2)	55.5 (3.8)	34.7 (0.2)		
Personal Income Level in USD	[c]	[c]	[c]		178.878	<0.001
Less than 10000	47.3 (2.1)	45.9 (1.1)	57.5 (3.3)	23.9 (0.1)		
10000-29999	34.9 (2.1)	36.7 (1.0)	30.1 (3.1)	33.1 (0.2)		
30000 or Above	17.7 (1.6)	17.4 (0.9)	12.4 (3.0)	43.1 (0.2)		
Area of Residence					1.342	0.244
Large Metro	50.9 (2.1)	52.1 (1.0)	49.6 (3.6)	53.6 (0.3)		
Small Metro	30.7 (1.7)	30.9 (0.9)	34.2 (3.7)	30.3 (0.3)		
Non-Metro	18.4 (1.6)	17.0 (0.7)	16.2 (2.3)	16.1 (0.2)		
Religiosity	61.2[c] (1.9)	56.4[c] (1.1)	54.5[c] (3.8)	71.6 (0.1)	102.132	<0.001
Past Year Tobacco Use	58.5[c] (2.1)	66.0[c] (1.1)	74.7[c] (2.9)	33.3 (0.2)	445.181	<0.001
AUD	29.3[c] (1.7)	34.1[c] (0.9)	51.4[c] (4.3)	8.0 (0.1)	925.277	<0.001
DUD	20.0[b,c] (1.2)	27.5[b,c] (1.0)	48.2[c] (4.1)	4.0 (0.1)	1609.268	<0.001
CUD	10.4[a,b,c] (0.9)	17.9[c] (0.7)	32.2[c] (3.7)	2.2 (0.0)	1370.889	<0.001

Other DUD	14.5[b,c] (1.0)	16.1[c] (0.9)	33.7[c] (3.9)	2.3 (0.0)	991.781	<0.001
Substance Use Disorders (U)	[b,c]	[b,c]	[c]		727.397	<0.001
NSUD	62.3 (1.7)	53.6 (1.1)	33.5 (3.4)	89.4 (0.1)		
AUDa	17.7 (1.6)	18.9 (0.7)	18.3 (3.5)	6.6 (0.1)		
DUDa	8.4 (0.8)	12.4 (0.7)	15.1 (2.9)	2.5 (0.0)		
ADUD	11.6 (0.9)	15.2 (0.6)	33.2 (3.6)	1.4 (0.0)		
Psychiatric Disorder	41.9[a,c] (2.0)	18.4[b,c] (0.9)	53.6[c] (3.9)	4.9 (0.1)	1096.109	<0.001
Past Year Mental Health Treatment	55.6[a,c] (2.2)	24.3[b,c] (1.1)	61.6[c] (3.5)	13.8 (0.1)	458.551	<0.001
Past Year Substance Use Treatment						
Alcohol	7.0[c] (1.2)	4.0[c] (0.5)	11.3[c] (2.8)	0.6 (0.0)	269.347	<0.001
Drugs	6.0[c] (0.9)	4.7[c] (0.5)	8.0[c] (2.4)	0.5 (0.0)	359.795	<0.001
Juvenile Alcohol Use	63.6[c] (2.0)	69.2[c] (1.2)	78.3[c] (3.1)	49.0 (0.2)	140.699	<0.001
Juvenile Drug Use	50.5[b,c] (1.8)	60.7[c] (1.1)	75.9[c] (3.3)	27.0 (0.1)	582.511	<0.001
Cannabis	42.8[c] (1.9)	55.0[c] (1.1)	65.0[c] (3.9)	24.6 (0.1)	441.653	<0.001
Any Other Drug	31.4[c] (1.7)	37.8[c] (1.1)	55.9[c] (4.2)	12.3 (0.1)	588.051	<0.001

SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence; NV: Non-Violent; N: unweighted sample size; PSE: Population Size Estimate; P: Prevalence in percent; SE: Standard Error in percent; AUD: Alcohol Use Disorder; DUD: Drug Use Disorder(s); CUD: Cannabis Use Disorder; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

[a] *Significantly different from "ODV" after adjusting for multiple comparisons (p<0.0083).*

[b] *Significantly different from "CV" after adjusting for multiple comparisons (p<0.0083).*

[c] *Significantly different from "NV" after adjusting for multiple comparisons (p<0.0083).*

Table 4.6: Odds Ratios from multinomial logistic regression analyses of committing any type of violence on substance use disorders

Substance Use Disorders (U)	Commission of Any Type of Violence (V')			
	Unadjusted Model	**Adjusted[a] Model 1**	**Adjusted[b] Model 2**	**Best-Fit[c] Model**
	OR (95%CI)	**aOR (95%CI)**	**aOR (95%CI)**	**aOR (95%CI)**
NSUD (reference)	1.00	1.00	1.00	1.00
AUDa	**4.55 (4.18-4.95)**	**3.55 (3.24-3.89)**	**3.01 (2.73-3.32)**	**2.38 (2.16-2.63)**
DUDa	**7.29 (6.45-8.23)**	**4.69 (4.15-5.31)**	**3.00 (2.65-3.38)**	**2.01 (1.77-2.27)**
ADUD	**16.60 (15.25-18.06)**	**9.79 (8.90-10.77)**	**6.25 (5.63-6.92)**	**3.72 (3.36-4.12)**

OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval; AUD: Alcohol Use Disorder; DUD: Drug Use Disorder; CUD: Cannabis Use Disorder; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

[a] *Adjusted for age, sex, race/ethnicity and survey year.*

[b] *Adjusted for age, sex, race/ethnicity, survey year, marital status, household type, education level, past year employment, personal income level, religiosity and past year tobacco use.*

[c] *Adjusted for age, sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile drug use, past year mental health treatment and past year substance use treatment.*

Significantly different from "NSUD" in ***Bold*** *($p<0.05$).*

Table 4.7: Odds Ratios from multinomial logistic regression analyses of committing different types of violence on substance use disorders

Substance Use Disorders (U)	Commission of Violence (V)							
	SDV vs. NV		ODV vs. NV		CV vs. NV		ODV vs. SDV	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
NSUD (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
AUDa	**3.84 (3.07-4.81)**	**2.09 (1.62-2.70)**	**4.78 (4.30-5.32)**	**2.49 (2.22-2.79)**	**7.40 (4.56-12.02)**	**3.07 (1.84-5.12)**	1.24 (0.95-1.63)	1.19 (0.89-1.59)
DUDa	**4.76 (3.79-5.97)**	**1.49 (1.15-1.93)**	**8.13 (6.99-9.46)**	**2.16 (1.83-2.54)**	**15.87 (10.19-24.70)**	**3.03 (1.74-5.25)**	**1.71 (1.29-2.27)**	**1.45 (1.03-2.04)**
ADUD	**11.51 (9.56-13.86)**	**2.89 (2.29-3.65)**	**17.49 (15.70-19.48)**	**3.88 (3.43-4.39)**	**61.15 (41.97-89.11)**	**9.17 (5.54-15.17)**	**1.52 (1.21-1.90)**	**1.34 (1.03-1.76)**

SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence; NV: Non-Violent; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

[a] Adjusted for age, sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile drug use, past year mental health treatment and past year substance use treatment.

Significantly different from "NSUD" in ***Bold*** *($p<0.05$).*

Table 4.8: Odds Ratios from multinomial logistic regression analyses of committing different types of violence on cannabis use disorder

Cannabis Use Disorder (C)	Commission of Violence (V)							
	SDV vs. NV		ODV vs. NV		CV vs. NV		ODV vs. SDV	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
None (Reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Positive	**5.08 (4.19-6.17)**	1.14 (0.91-1.45)	**9.57 (8.71-10.52)**	**1.47 (1.31-1.66)**	**20.77 (14.83-29.10)**	**2.20 (1.41-3.43)**	**1.88 (1.50-2.37)**	1.29 (0.97-1.71)

SDV: Self-Directed Violence; ODV: Other-Directed Violence; CV: Combined Violence; NV: Non-Violent; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval.

[a] Adjusted for age, sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, past year alcohol and other drug use disorders, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year substance use treatment.

*Significantly different from "None" in **Bold** ($p<0.05$).*

Table 4.9: Odds Ratios from multinomial logistic regression analyses of committing any type of violence on substance use disorders, by age groups

Substance Use Disorders (U)	Commission of Any Type of Violence (V')					
	18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model	Unadjusted Model	Best-Fit[c] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
NSUD (reference)	1.00	1.00	1.00	1.00	1.00	1.00
AUDa	**3.14 (2.86-3.44)**	**2.42 (2.18-2.69)**	**4.27 (3.66-4.98)**	**2.43 (2.05-2.89)**	**2.61 (1.54-4.43)**	1.81 (1.00-3.29)
DUDa	**3.41 (3.05-3.82)**	**1.77 (1.57-2.01)**	**6.77 (5.44-8.41)**	**2.40 (1.91-3.02)**	**5.24 (2.61-10.55)**	2.01 (0.85-4.79)
ADUD	**6.68 (6.13-7.27)**	**3.34 (2.99-3.73)**	**14.66 (12.01-17.89)**	**4.11 (3.31-5.11)**	**26.86 (16.02-45.03)**	**7.04 (3.60-13.78)**

OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

[a] *Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.*

[b] *Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.*

[c] *Adjusted for sex, race/ethnicity, education level, past year employment, religiosity, presence of a psychiatric disorder, past year mental health treatment and past year drug use treatment.*

Significantly different from "NSUD" in ***Bold*** *($p<0.05$).*

Table 4.10: Odds Ratios from multinomial logistic regression analyses of committing self- and other-directed violence* on substance use disorders, by age groups

Substance Use Disorders (U)	Commission of Violence (V)											
	SDV vs. NV						ODV vs. NV					
	18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above		18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model	Unadjusted Model	Best-Fit[c] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model	Unadjusted Model	Best-Fit[c] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
NSUD (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
AUDa	**2.29 (1.85-2.84)**	**1.81 (1.41-2.33)**	**3.37 (2.46-4.62)**	**2.04 (1.43-2.91)**	**5.21 (2.58-10.52)**	**2.98 (1.38-6.46)**	**3.40 (3.07-3.76)**	**2.60 (2.32-2.92)**	**4.69 (3.88-5.66)**	**2.59 (2.11-3.18)**	1.17 (0.54-2.54)	0.97 (0.42-2.24)
DUDa	**2.46 (1.92-3.17)**	1.25 (0.94-1.67)	**4.43 (2.86-6.87)**	**1.64 (1.05-2.57)**	**4.82 (1.53-15.23)**	1.38 (0.35-5.48)	**3.64 (3.21-4.12)**	**1.94 (1.69-2.22)**	**7.76 (5.90-10.21)**	**2.62 (1.92-3.57)**	**5.35 (2.21-12.94)**	2.53 (0.88-7.29)
ADUD	**5.39 (4.40-6.60)**	**2.48 (1.98-3.10)**	**9.82 (7.10-13.58)**	**3.07 (2.04-4.63)**	**24.25 (9.60-61.26)**	**4.48 (1.53-13.14)**	**6.79 (6.11-7.55)**	**3.57 (3.14-4.06)**	**15.98 (12.12-20.94)**	**4.25 (3.29-5.50)**	**22.01 (10.94-44.28)**	**7.52 (2.83-19.95)**

SDV: Self-Directed Violence; ODV: Other-Directed Violence; NV: Non-Violent; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

** The "Combined Violence" category was omitted from the analysis due to low sample size.*

[a] Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.

[b] Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year substance use treatment.

[c] *Adjusted for sex, race/ethnicity, education level, past year employment, religiosity, presence of a psychiatric disorder, juvenile alcohol use, past year mental health treatment and past year drug use treatment.*

Significantly different from "NSUD" in ***Bold*** *(p<0.05).*

Table 4.11: Odds Ratios from multinomial logistic regression analyses of committing other- vs. self-directed violence on substance use disorders, by age groups

Substance Use Disorders (U)	Commission of ODV vs. SDV (V)					
	18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model	Unadjusted Model	Best-Fit[c] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
NSUD (reference)	1.00	1.00	1.00	1.00	1.00	1.00
AUDa	**1.48 (1.17-1.87)**	**1.44 (1.09-1.89)**	1.39 (0.96-2.02)	1.27 (0.85-1.92)	0.23 (0.08-0.63)	**0.32 (0.11-0.96)**
DUDa	**1.48 (1.13-1.92)**	**1.55 (1.15-2.07)**	**1.75 (1.02-3.01)**	1.59 (0.89-2.86)	1.11 (0.27-4.61)	1.84 (0.35-9.54)
ADUD	1.26 (1.00-1.60)	**1.44 (1.11-1.87)**	**1.62 (1.02-2.57)**	1.39 (0.85-2.25)	0.91 (0.30-2.79)	1.68 (0.42-6.66)

SDV: Self-Directed Violence; ODV: Other-Directed Violence; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

** The "Combined Violence" category was omitted from the analysis due to low sample size.*

[a] Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.

[b] Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year substance use treatment.

[c] Adjusted for sex, race/ethnicity, education level, past year employment, religiosity, presence of a psychiatric disorder, juvenile alcohol use, past year mental health treatment and past year drug use treatment.

*Significantly different from "NSUD" in **Bold** ($p<0.05$).*

Table 4.12: Odds Ratios from multinomial logistic regression analyses of committing self- and other-directed violence* on cannabis use disorder, by age groups

Cannabis Use Disorders (C)	Commission of Violence (V)											
	SDV vs. NV						ODV vs. NV					
	18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above		18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
None (Reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Positive	**2.74 (2.24-3.34)**	1.11 (0.88-1.41)	**4.30 (2.94-6.30)**	1.26 (0.83-1.91)	3.03 (0.50-18.38)	0.42 (0.05-3.58)	**3.88 (3.57-4.23)**	**1.41 (1.26-1.58)**	**7.21 (5.72-9.09)**	**1.54 (1.18-2.00)**	**11.48 (5.19-25.38)**	**2.97 (1.15-7.72)**

SDV: Self-Directed Violence; ODV: Other-Directed Violence; NV: Non-Violent; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval.

** The "Combined Violence" category was omitted from the analysis due to low sample size.*

[a] *Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, past year alcohol and other drug use disorders, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.*

[b] *Adjusted for sex, race/ethnicity, education level, past year employment, religiosity, past year alcohol and other drug use disorders, presence of a psychiatric disorder, juvenile alcohol use and past year mental health treatment.*

Significantly different from "None" in ***Bold*** *($p<0.05$).*

Table 4.13: Odds Ratios from multinomial logistic regression analyses of committing other- vs. self-directed violence on cannabis use disorder, by age groups

Cannabis Use Disorder (C)	Commission of ODV vs. SDV (V)					
	18-25 Year Olds		26-49 Year Olds		50 Year Olds or Above	
	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[a] Model	Unadjusted Model	Best-Fit[b] Model
	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)	OR (95%CI)	aOR (95%CI)
None (Reference)	1.00	1.00	1.00	1.00	1.00	1.00
Positive	**1.42 (1.16-1.74)**	**1.27 (1.00-1.60)**	**1.68 (1.03-2.74)**	1.22 (0.72-2.05)	3.78 (0.53-26.88)	7.02 (0.71-69.18)

SDV: Self-Directed Violence; ODV: Other-Directed Violence; OR: Odds Ratio; aOR: adjusted Odds Ratio; 95%CI: 95% Confidence Interval.

** The "Combined Violence" category was omitted from the analysis due to low sample size.*

[a] *Adjusted for sex, race/ethnicity, survey year, marital status, education level, past year employment, personal income level, religiosity, past year tobacco use, past year alcohol and other drug use disorders, presence of a psychiatric disorder, juvenile substance use, past year mental health treatment and past year alcohol use treatment.*

[b] *Adjusted for sex, race/ethnicity, education level, past year employment, religiosity, past year alcohol and other drug use disorders, presence of a psychiatric disorder, juvenile alcohol use and past year mental health treatment.*

Significantly different from "None" in ***Bold*** *($p<0.05$).*

APPENDICES

Appendix I: NSDUH Survey Methodology

Source: United States Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Center for Behavioral Health Statistics & Quality. (2016). National Survey on Drug Use and Health, 2014. Codebook. i-9-32. Retrieved from: http://doi.org/10.3886/ICPSR36361.v1.

Survey Methodology

Like the 1999 to 2013 surveys, the 2014 survey was conducted using CAI methods. This survey also allows for improved state estimates based on minimum sample sizes per state. The target sample size of 67,507 allows SAMHSA to continue reporting adequately precise demographic subgroup estimates at the national level without needing to oversample specially targeted demographics, as was required in the past. The achieved sample size for the 2014 survey was 67,901 individuals.

A coordinated sample design was developed for the 2014 through 2017 NSDUHs. The coordinated design facilitated a 50 percent overlap in third-stage units (area segments [see below]) between each 2 successive years from 2014 through 2017.[8] This design was intended to increase the precision of estimates in year-to-year trend analyses because of the expected positive correlation resulting from the overlapping sample between successive survey years.

The 2014 design allows for computation of estimates by state in all 50 states plus the District of Columbia. States may therefore be viewed as the first level of stratification and as a reporting variable. Compared with previous sample designs, the 2014 through 2017 sample design moves from two to essentially five state sample size groups (lumping Hawaii with the remaining states and the District of Columbia). The 2014 through 2017 surveys have a sample designed to yield 4,560 completed interviews in California; 3,300 completed interviews each in Florida, New York, and Texas; 2,400 completed interviews each in Illinois, Michigan, Ohio, and Pennsylvania; 1,500 completed interviews each in Georgia, New Jersey, North Carolina, and Virginia; 967 completed interviews in Hawaii; and 960 completed interviews in each of the remaining 37 states and the District of Columbia—for a total national target sample size of 67,507. The sample is selected from 6,000 area segments that vary in size according to state.

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[7] Information from the 2010 census suggests that the civilian, noninstitutionalized population includes at least 97 percent of the total U.S. population. See the following reference: Lofquist, D., Lugaila, T., O'Connell, M., & Feliz, S. (2012, April). *Households and families: 2010* (C2010BR-14, 2010 Census Briefs). Retrieved from https://www.census.gov/prod/cen2010/briefs/c2010br-14.pdf

[8] In segments used in 2 successive years, only addresses not sampled in the first year may be included in the second year's sample.

The change in the state sample allocation was driven by the need to increase the sample in the original 43 small states (to improve the precision of state and substate estimates in these states) while moving closer to a proportional allocation in the larger states.

Stratification and Selection of Primary, Secondary, and Tertiary Sampling Units (Census Tracts, Census Block Groups, and Area Segments)

Within each state, sampling strata called state sampling regions (SSRs) were formed. Based on a composite size measure, states were partitioned geographically into roughly equally sized regions. In other words, regions were formed such that each area within a state yielded, in expectation, roughly the same number of interviews during each data collection period. The partitioning divided the United States into a total of 750 SSRs, resulting from 36 SSRs in California; 30 SSRs each in Florida, New York, and Texas; 24 SSRs each in Illinois, Michigan, Ohio, and Pennsylvania; 15 SSRs each in Georgia, New Jersey, North Carolina, and Virginia; and 12 SSRs each in the remaining 38 states and the District of Columbia.

Similar to the 2005 through 2013 surveys, the first stage of selection for the 2014 through 2017 NSDUHs was census tracts. The first stage of selection began with the construction of an area sample frame that contained one record for each census tract in the United States. If necessary, census tracts were aggregated within SSRs until each tract[9] met the minimum dwelling unit[10] (DU) requirement. In California, Florida, Georgia, Illinois, Michigan, New Jersey, New York, North Carolina, Ohio, Pennsylvania, Texas, and Virginia, this minimum size requirement was 250 DUs in urban areas and 200 DUs in rural areas.[11] In the remaining states and the District of Columbia, the minimum requirement was 150 DUs in urban areas and 100 DUs in rural areas. These census tracts served as the primary sampling units (PSUs) for the coordinated 4-year sample.

Before selecting census tracts, additional implicit stratification was achieved by sorting the first-stage sampling units by a CBSA/SES[12] (core-based statistical area/socioeconomic status) indicator[13] and by the percentage of the population who are non-Hispanic and white. From this well-ordered sample frame, 48 census tracts per SSR were selected with probabilities proportionate to a composite size measure and with minimum replacement.

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[9] For the remainder of the discussion, first-stage sampling units are referred to as "census tracts" even though each first-stage sampling unit contains one or more census tracts.

[10] DU counts were obtained from the 2010 decennial census data supplemented with revised population counts from Nielsen Claritas, which is a market research firm headquartered in San Diego, California (see http://www.claritas.com/sitereports/Default.jsp).

[11] The basis for the differing minimum DU requirement in urban and rural areas is that it is more difficult to meet the requirement in rural areas, 100 DUs are sufficient to support one field test and two main study samples in the smaller states, and 200 DUs are sufficient to support three samples in the larger sample states.

[12] CBSAs include metropolitan and micropolitan statistical areas, as defined in the following reference: Office of Management and Budget. (2009, December 1). *OMB Bulletin No. 10-02: Update of statistical area definitions and guidance on their uses*. Retrieved from https://www.whitehouse.gov/sites/default/files/omb/assets/bulletins/b10-02.pdf

[13] The CBSA/SES indicator was defined using 2006-2010 American Community Survey (ACS) estimates, 2010 census data, and the December 2009 CBSA definition. Four categories are defined as follows: (1) CBSA/low SES, (2) CBSA/high SES, (3) non-CBSA/low SES, and (4) non-CBSA/high SES.

For the second stage of selection, adjacent census block groups were collapsed as needed within selected census tracts. Compared with prior years, the selection of census block group is an additional stage of selection that was added to facilitate possible transitioning to an address-based sample (ABS) design in the future. The block groups were required to have the same minimum number of DUs as the census tracts from which they were selected (150 or 250 in urban areas and 100 or 200 in rural areas, according to state). The resulting block groups were then sorted in the order in which they were formed, and one census block group[14] was selected per selected census tract with probability proportionate to a composite size measure.

Because census block groups generally exceed the minimum DU requirement, one smaller geographic area was selected within each sampled census block group. For this third stage of sampling, each selected census block group was partitioned into small geographic areas composed of adjacent census blocks. These geographic clusters of blocks are referred to as *segments* and are the tertiary sampling units (TSUs) for the coordinated sample design. A sample *dwelling unit* in NSDUH refers to either a housing unit or a group quarters listing unit, such as a dormitory room or a shelter bed. To support the overlapping sample design and any special supplemental samples or field tests that SAMHSA might wish to conduct, segments were formed to contain a minimum of 150 or 250 DUs in urban areas and 100 or 200 DUs in rural areas, according to state.

One segment was selected within each sampled census block group with probability proportionate to size. The 48 selected segments then were randomly assigned to a survey year and quarter of data collection.

Selection of Dwelling Units

The primary objective of the fourth stage of sample selection (listing units) was to select the minimum number of DUs needed in each segment to meet the targeted sample sizes for all age groups. For the 2014 through 2017 NSDUHs, each state sample will be allocated to age groups as follows: 25 percent for youths aged 12 to 17, 25 percent for young adults aged 18 to 25, 15 percent for adults aged 26 to 34, 20 percent for adults aged 35 to 49, and 15 percent for adults aged 50 or older. In the 2005 through 2013 NSDUHs, the sample was allocated equally across the 12 to 17, 18 to 25, and 26 or older age groups. The 2014 through 2017 design places more sample in the 26 or older age groups to estimate drug use and related mental health measures more accurately among the aging drug use population. The size measures used in selecting the area segments were coordinated with the DU and person selection process so that a nearly self-weighting sample could be achieved in each of the five age groups. Departures from the self-weighting objective occurred for several reasons, including the following: (a) advance projections on the number of DUs did not accurately reflect the current housing inventory; (b) maximum DU sample sizes were preset to control the interviewer workload and to allow unused addresses to be available for the next year's survey; and (c) the person selection probabilities were constrained so that no more than two individuals could be selected per DU. An iterative sample allocation process was followed to adjust for these additional constraints.

[14] For the remainder of the discussion, second-stage sampling units are referred to as "census block groups" even though each second-stage sampling unit contains one or more census block groups.

In addition, the DU sample allocation in each area segment was adjusted to allow for DU eligibility, for screening nonresponse, and for person nonresponse.

In advance of the survey period, specially trained listers had visited each area segment and listed all addresses for housing units and eligible group quarters units in a prescribed order. Systematic sampling was used to select the allocated sample of addresses from each segment.[15]

Selection of Individuals

During each quarterly survey, field interviewers (FIs) visited each sample address to determine DU eligibility, to list all eligible individuals at the address, to select the sample of individuals to be interviewed, and to conduct interviews. Unlike the 2005 through 2013 NSDUHs, the "half-open" interval (HOI) rule was not implemented in the 2014 NSDUH. This special procedure identified any new (since the time of listing) housing units or any DUs missed during the advance listing process. Any new or missed DUs following immediately after a sample DU and up to, but not including, the next initially listed address in the prescribed order of listing also were included in the sample. Eliminating the HOI rule in 2014 decreased the burden on interviewers and simplified training and the screening process. This decrease in burden outweighed the small amount of coverage afforded by the HOI rule. Because the majority of missed DUs are found on the premises of sampled DUs, the 2014 NSDUH had in place a procedure for checking for and adding missed DUs on the premises of sampled DUs. During the screening interview, FIs asked the screening respondent about other units on the property of the selected DU. If missing from the original list, these DUs also were included in the sample.

The FIs used a handheld computer to record the results of the DU screening process and to select the sample of respondents. They recorded the results of each call, the final eligibility status of the DU, and information on new and missed DUs. If a sample address was an eligible occupied DU, the FIs also conducted a screening interview to identify and roster all survey-eligible individuals residing at the address. When the roster was complete, the computer was programmed to select the sample of individuals to be interviewed using parameters specified for that area segment and a random number specified for that address.

Data collection progress was monitored during each quarterly survey by state. Small reserve samples were held back each quarter so that the assigned sample size could be adjusted if necessary during the course of data collection.

Sample Design Variables

The sample for the 2014 NSDUH was selected using a multistage, deeply stratified sample design. The variables on the full restricted-use analytic data file represent each stage of

[15] This had the effect of creating noncompact clusters (selection from a list), which differ from compact clusters in that not all units within the cluster are included in the sample. Although compact cluster designs are less costly and more stable, a noncompact cluster design was used because it provides for greater heterogeneity of dwellings within the sample. Also, social interaction (contagion) among neighboring dwellings is sometimes introduced with compact clusters. See the following reference: Kish, L. (1965). *Survey sampling*. New York, NY: John Wiley.

sample selection (note that, to ensure the confidentiality of survey respondents, the sample design variables described in this section are not included on the public use file):

Stage 1: The 2014 CAI design includes a sample from each of the 50 states plus the District of Columbia. SSRs were formed within each state based on composite size measures, roughly geographically partitioning the state into equally sized regions. A sample of 48 census tracts was selected within each SSR. Census tracts are considered the PSU and can be identified using the STATE, SSREGION, and SEGID[16] variables. Only eight census tracts per SSR were used for the 2014 sample.

Stage 2: For the second stage of selection, adjacent census block groups were aggregated within selected census tracts as necessary to form the second-stage sampling units. One census block group was selected per sampled census tract. A total of 48 census block groups was selected within each SSR. Census block group can be identified using the STATE, SSREGION, and SEGID variables. Eight census block groups per SSR, one from each sampled census tract, were used for the 2014 sample.

Stage 3: The third stage of sampling consisted of partitioning the selected census block groups into smaller geographic areas, called "segments." Segments are defined by joining contiguous census blocks within each selected census block group and are similar to the units selected at the second stage of selection for the 2005 through 2013 surveys. Segments can be identified on the full restricted-use analytic data file[17] using the SEGID variable.

Stage 4: After census tracts, census block groups, and segments were selected, the fourth stage of selection consisted of selecting DUs within each segment. The DU selection rate was based on the state to which a particular segment belonged. State classification was utilized for computation of eligibility, screener and interview response rates, and expected person yield per DU. State classifications can be identified with the STATE variable, and DUs can be identified with the ENCCASE variable.

Stage 5: At the last stage of selection, individuals were selected within screened DUs based on the age group composition of the DU residents. The person-level variable used to determine the selection included AGE. The full restricted-use analytic data file contains one record representing each responding selected person from stage 5 (67,901 individuals). To protect the confidentiality of these respondents, the full analytic file was treated using a statistical disclosure limitation method while ensuring that the data continue to be representative of civilian members of the noninstitutionalized population in the United States. The resulting public use data file contains 55,271 records.

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[16] One segment was selected from each sampled census block group within each sampled census tract, so the census tract, census block group, and segment can be identified by the SEGID variable.

[17] NSDUH's Restricted-use Data Analysis System (R-DAS) data files are available online at http://www.datafiles.samhsa.gov. R-DAS is an online analytic system that allows analysts to produce cross-tabulations using restricted-use NSDUH data files. Restricted-use microdata are not accessible to analysts, but output from the analyses is available as long as the output does not violate any of the disclosure limitation rules that determine what output may be displayed.

A more detailed explanation of the sample design and sample selection procedures at each stage of the design appears in the *2014 NSDUH Methodological Resource Book*, which will be available in early 2016.[18]

Data Collection and Response Rates

The fieldwork for the 2014 NSDUH was directed by RTI staff members. RTI maintained a field staff of approximately 700 FIs to collect the data.

As noted above, a total final sample of 67,901 CAI interviews was obtained for the 2014 survey. Strategies for ensuring high rates of participation resulted in a weighted screening response rate of 81.94 percent and a weighted interview response rate for the CAI of 71.20 percent.

Throughout the course of the study, respondent anonymity and the privacy of responses were protected by separating identifying information from survey responses. Respondents were assured that their identities and responses would be handled in strict compliance with federal law. As discussed above, the questionnaire itself and the interviewing procedures were designed to enhance the privacy of responses, especially during segments of the interview in which questions of a sensitive nature were posed. Answers to sensitive questions were gathered using ACASI. During the ACASI portions of the interview, respondents listened to prerecorded questions through headphones and entered their responses directly into a computer without interviewers knowing how they were answering. At the conclusion of the ACASI section, the interview returned to the CAPI mode with the interviewer completing the questionnaire. Each respondent who completed a full interview was given $30 in cash as a token of appreciation for his or her time.

A more detailed explanation of NSDUH's data collection procedures appears in the *2014 NSDUH Methodological Resource Book*, which will be available in early 2016.[19]

Sample Weights

The estimates yielded by NSDUH are based on sample survey data rather than on complete data for the entire population. This means that the data must be weighted to obtain unbiased estimates for survey outcomes in the population represented by the 2014 NSDUH. The "final analysis weight" of the i^{th} respondent, say w_i, can be interpreted as the number of sampling units in the NSDUH target population represented by the i^{th} respondent. The sum of the weights over all respondents is used to estimate the size of the total target population:

$$\sum_i w_i = \text{estimated size of target population,}$$

where the summation is over all respondents in the 2014 NSDUH.

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[18] Center for Behavioral Health Statistics and Quality. (in press). *2014 National Survey on Drug Use and Health: Methodological resource book*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

[19] See footnote 18.

Similar to the 2013 NSDUH, three sets of analysis weights at the person level, questionnaire dwelling unit (QDU) level, and person pair level were developed for the 2014 NSDUH. The person-level, QDU-level, and person pair-level analysis weights shared the same first 11 weight components at the screening dwelling unit (SDU) level. In addition to the 11 common weight components, QDU-level and person pair-level analysis weights had several specific weight components, and the final weights are the product of all the weight components. As in the 2013 NSDUH, all of the adults in the 2014 NSDUH sample received the WHODAS questions. Therefore, there was no need to have a separate adult mental health weight in the 2014 NSDUH because the person-level analysis weight could be used to produce the adult mental health estimates.

The person-level analysis weights (ANALWT_C) are the product of 16 weight components. Each weight component accounts for either a selection probability at a selection stage or an adjustment factor adjusting for nonresponse, coverage, or extreme weights. The sum of the weight over all respondents on the data file represents an estimate of the total number of individuals in the target population. In view of the use of weights as expansion factors in forming estimates, the weight can be interpreted as representing the total number of target population individuals each record on the file represents. For variance estimation, suitable software, such as SUDAAN®, should be used to take the sample design into account.[20] Similar to the 2013 NSDUH, the 2014 NSDUH used 2010 census-based population estimates in the poststratification adjustment.

Details of the weight components and the sample weighting procedures appear in the *2014 NSDUH Methodological Resource Book*, which will be available in early 2016.[21]

Organization of the Data File

The file described here is made available as an ASCII file with 3,148 variables and 55,271 observations. *Three program files are made available to read the ASCII file into SAS, SPSS, or Stata. The file also is made available as a SAS transport (CPORT) file, SPSS system file, Stata system file, and ASCII tab-delimited file. All of the data and program files are available from SAMHDA at* http://www.datafiles.samhsa.gov.

The overall organization of the file is shown in the Table of Contents of this document. Edited data from core drug modules make up the first portion of the file. Edited data from the noncore self-administered modules and demographic questions are in later sections. Variables from the noncore section contain missing data; see the section on Standard Code Conventions for a description of the codes given to different types of missing data. For each edited variable, the number of observations assigned a given missing data code is shown in the entry for that variable.

Imputation-revised drug use variables, as well as selected recoded versions of these variables, are included for core drug use variables. These imputed and recoded drug use variables are in separate sections following the edited core drug use variables. The recoded drug use

[20] In SUDAAN, the sample design is specified using the NEST statement. See the following reference: RTI International. (2012). *SUDAAN®, Release 11.0* [computer software]. Research Triangle Park, NC: Author.
[21] See footnote 18.

variables include indicators for lifetime, past year, and past month substance use. The imputation-revised core drug use variables served as the starting point for the recoded core drug use variables. Imputation-revised core and noncore demographic variables also are included toward the end of the codebook. Missing values for all imputation-revised variables from the core drug modules have been imputed using the statistical imputation procedures described below. Imputation indicators are provided for each variable so that users may easily determine whether an observation contains data from the questionnaire or an imputed value. *Where imputed or recoded variables are provided, users are encouraged to use them to produce estimates rather than raw or edited variables from the interview.*

Edited variables from self-administered noncore modules comprise the next major section in the codebook. Intermixed between the noncore and core sections of the codebook are sections of recoded variables. The edited and/or imputed variables are used as source variables for the recoded variables. For example, edited variables from the section of the interview pertaining to symptoms of dependence or abuse (Substance Dependence and Abuse section in this codebook) were used to create recoded summary measures of dependence. Unlike variables in the core sections, however, imputation for missing data generally was not done prior to the recoding of noncore variables. Consequently, noncore recoded variables may still have missing values. The missing data codes contained in the source variables and defined in the Standard Code Conventions section of this codebook introduction are recoded to the standard missing code (.) for recoded variables. It is intended that cases containing these missing codes be excluded from an analysis.

Within the recoded sections of the codebook, detailed information is provided in the variable documentation about how levels of source variables are used to define recoded variables. Note that for recoded variables that include other-specify data or logically assigned data (as defined in the Standard Code Conventions section of this introduction), values may be listed in the documentation that do not exist for the current survey year. Because of fluctuations in the data, source variable values may not exist consistently across years. However, to aid in cross-year analyses, all possible source variable values have been retained in the documentation. For example, a recoded variable may document a "Yes" using both source variable values of 1 = Yes and 3 = Logically Assigned Yes, even if the 3 is not applicable for the current survey year. To alert users, notes have been placed at the top of recoded sections that contain variables that include source values even if they do not apply to the current survey year.

In many instances, the codebook itself also indicates in parentheses the question names that were most relevant for creating an edited variable. In particular, an important feature of the transition to CAI in 1999 was that respondents could be routed to different versions of a question based on prior information from the interview. As much as possible, the codebook shows key source variables that were used in creating edited, imputed, or recoded variables. For example, respondents who initiated use of a drug within 1 year of their current age were asked more

detailed questions about the year and month in which they first used that drug. Depending on their age, date of birth, and interview date, respondents could be routed to one of three possible questions to identify the year in which they first used a drug (e.g., CG04a, CG04b, or CG04c for cigarettes). Similarly, respondents could be routed to one of two possible questions to determine the month in which they first used a drug (e.g., CG04c and CG04d for cigarettes). To facilitate analyses, therefore, responses from these multiple year-of-first-use and month-of-first-use questions were combined into one single year-of-first-use variable and one single month-of-first-use variable for each drug, as shown for the variables CIGYFU and CIGMFU. For the most complete information about the logic for asking questions in the interview, however, data file users should refer to the questionnaire (for details, see this codebook's Introduction).

Usable Cases

A key step in the data processing procedures established the minimum item response requirements in order for cases to be retained for weighting and further analysis (i.e., "usable" cases). These procedures were designed to eliminate cases with unacceptable levels of item nonresponse (i.e., missing data), thereby retaining cases with lower levels of missing data and reducing the amount of statistical imputation needed for any given record.

The usable case criteria established for CAI were based on the completeness of information that respondents provided about their lifetime use or nonuse of different drugs. In CAI, respondents were asked more detailed questions about different drugs only if they reported lifetime use of that drug (or lifetime use of one or more drugs within a broader category, such as hallucinogens) on an initial "gate" question.[22] Consequently, whether a CAI respondent was a lifetime user or nonuser of the drugs of interest could be readily determined by reviewing the respondent's answers to the gate question on lifetime use of that drug (or category of drugs).

The requirements for a CAI record to be considered usable are noted as follows:

1. The lifetime cigarette question (i.e., "Have you ever smoked part or all of a cigarette?") had to have been answered as "yes" or "no." This requirement was set so that lifetime use or nonuse would be fully defined for at least one substance. Consequently, data about lifetime use or nonuse of cigarettes could be used in subsequent statistical imputations for other drugs where lifetime use or nonuse was undefined.

2. Responses to questions on at least nine (9) of the following additional drugs had to contain information about lifetime use or nonuse: (a) chewing tobacco, (b) snuff, (c) cigars, (d) alcohol, (e) marijuana, (f) cocaine (in any form), (g) heroin, (h) hallucinogens,

[22] In all modules except those pertaining to hallucinogens, inhalants, pain relievers, tranquilizers, stimulants, and sedatives, the logic for asking more detailed questions about use of that drug was based on the answer to a single "yes/no" question (e.g., "Have you ever, even once, used marijuana or hashish?"). In the hallucinogens through sedatives modules, the logic for asking more detailed questions about use of that category of drugs was based on respondents' answers to multiple "yes/no" questions about the lifetime use or nonuse of specific drugs within that category (e.g., lifetime use or nonuse of the specific hallucinogens lysergic acid diethylamide [LSD], phencyclidine [PCP], peyote, mescaline, psilocybin/mushrooms, Ecstasy [3,4-methylenedioxymethamphetamine, MDMA], or "any other" hallucinogen).

(i) inhalants, (j) pain relievers, (k) tranquilizers, (l) stimulants, and (m) sedatives. Crack cocaine was not included in the usable case rule because the logic for asking about crack cocaine was dependent upon the respondent having answered the lifetime cocaine question as "yes." Although the CAI instrument also asked about pipe tobacco, this was not included in the usable case rule because there was only one other question about pipe tobacco in addition to the lifetime pipe tobacco use question.[23]

The interview also included follow-up probes for respondents who initially refused to answer a gate question or an entire series of gate questions. Follow-up probes were included in the following modules that were relevant to the usable case rule: cigarettes, chewing tobacco, snuff, cigars, alcohol, marijuana, cocaine, heroin, specific hallucinogens (i.e., LSD, PCP, and Ecstasy [MDMA]), the specific stimulant methamphetamine, and any use of inhalants, pain relievers, tranquilizers, stimulants, or sedatives (if respondents refused all lifetime use questions about these latter five drug categories). If respondents changed their initial refusal to a response of "yes" or "no," they were considered to have provided usable data to that drug's gate information.

For the hallucinogens through sedatives sections, respondents reported about use or nonuse of specific drugs within that category. For these sections, the requirement for reporting of lifetime use or nonuse was considered to have been satisfied if at least one lead lifetime question in the series was answered as "yes" or "no" (e.g., if at least one question in the hallucinogens series was answered as "yes" or "no" for hallucinogens). Similarly, in the inhalants, pain relievers, tranquilizers, stimulants, and sedatives sections, if respondents initially refused to answer all gate questions for a given drug but subsequently answered that drug's follow-up probe as "yes" or "no," they were considered to have satisfied the reporting requirement for that drug.

In addition, the CAI program terminated interviews during the initial demographics questions if respondents were ineligible for the survey (i.e., under age 12 or on active duty in the U.S. military). These ineligible cases by definition did not meet the usable case criteria because the interviews were terminated before the respondents were asked the first cigarette use question.

Logical Editing

For selected key variables, response data were reviewed to identify and address inconsistent data among related variables or to replace missing data with nonmissing values. The routing logic in the CAI instrument reduced the opportunities for respondents to give inconsistent answers by skipping respondents past questions that did not apply to them. The occurrence of inconsistent data was reduced further through the use of consistency checks built into the CAI program that prompted respondents to resolve inconsistencies between related items. Nevertheless, there still were limited situations in which respondents could answer one question in a manner that was inconsistent with their answer to a previous question.

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[23] For a more detailed discussion of the development of the usable case requirements, see the following reference: Kroutil, L., & Myers, L. (2002). Development of editing rules for CAI substance use data. In J. Gfroerer, J. Eyerman, & J. Chromy (Eds.), *Redesigning an ongoing national household survey: Methodological issues* (HHS Publication No. SMA 03-3768, pp. 85-109). Rockville, MD: Substance Abuse and Mental Health Services Administration, Office of Applied Studies.

Logical editing was the first step in processing many of the variables on the file. This procedure used data within a respondent's record to identify and address inconsistencies among related variables within a given module of the interview (e.g., within the hallucinogens section). As part of this procedure, variables were identified that had been legitimately skipped because the condition(s) for asking the questions did not apply.

As a general principle, responses from one module (e.g., hallucinogens) were not used to edit variables in another module (e.g., inhalants).[24] For this reason, data in one module may not be completely consistent with data in other modules. Subsequent discussion about editing in this section focuses on key drug use variables.

Editing Procedure for Drug Use Variables

Logical editing and processing of drug use variables in the tobacco through the sedatives modules first involved identifying whether respondents had ever used or never used the drug of interest. That included situations in which respondents initially refused to answer a question about their lifetime use of a drug but then changed their answer to "yes" or "no" on follow-up. If respondents did not provide sufficient information about their use or nonuse of a particular drug (or drug category), their final status was assigned through statistical imputation procedures. If values pertaining to lifetime use or nonuse of a given drug were changed through the editing procedures, this editing was indicated through special codes that indicated that a response was logically inferred; documentation for these codes includes the phrase "LOGICALLY ASSIGNED." In the hallucinogens, inhalants, pain relievers, tranquilizers, stimulants, and sedatives modules, for example, respondents who did not report lifetime use of a specific drug (e.g., LSD) but specified use of it as "some other drug" were logically inferred to be lifetime users of that drug. In the psychotherapeutics modules (i.e., pain relievers, tranquilizers, stimulants, and sedatives), respondents whose only reported lifetime use involved over-the-counter medications were logically inferred to have never used that particular prescription-type psychotherapeutic drug.

After lifetime use or nonuse of a given drug had been determined, edits of the variables that established when respondents last used a drug of interest were probably the most critical. These edited recency-of-use variables were the precursors for the final, imputed measures that established the prevalence of use in the past 30 days, past 12 months, and lifetime.

The interview included follow-up probes for respondents who were lifetime users of a given drug but did not know or refused to report when they last used it. Respondents who initially did not know when they last used a drug were asked to give their "best guess" of when they last used it. Respondents who initially refused to report when they last used a drug were asked to reconsider answering the question. If respondents changed their initial answer of "don't know" or "refused" in response to these probes, the editing procedures incorporated data from

[24] One exception to the principle of not editing across modules involved situations in which responses in one module governed whether respondents were asked questions in another module. For example, if respondents reported never using heroin but they received substance abuse treatment in the past 12 months, they were not asked questions in the noncore substance treatment module about current or past year treatment for heroin. Consequently, codes could be assigned to indicate that the respondents skipped out of the heroin treatment data because they had never used it.

these probes into the final, edited recency-of-use variables. For example, if respondents initially refused to report when they last used a drug but then reported last using it more than 30 days ago but within the past 12 months, their edited recency indicated use in that period, in the absence of any information that was inconsistent with what they reported in the probe (see below).

Situations were identified and flagged in which there were inconsistencies between a respondent's answer to a drug's recency question (or the answer in a follow-up probe) and other data in that module. For example, it would be inconsistent for a respondent to report last using a drug "more than 12 months ago" but also to report having first used it at his or her current age. These inconsistencies then were addressed by statistically imputing final values for the affected recency variable and the other variable(s) where the data were inconsistent with the respondent's original answer to the recency question.

Again, if values pertaining to the period when respondents last used a drug were changed through the editing procedures, special codes were assigned to indicate that these edits had been done. The documentation for these codes included the phrase "LOGICALLY ASSIGNED." For example, a code of 8 in a drug's recency-of-use variable means "Used at some point in the past 12 months LOGICALLY ASSIGNED." Specifically, if a respondent reported using a drug more than 30 days ago but within the past 12 months but other data suggested that the respondent may have used the drug more recently, this code of 8 indicated that at least it could be inferred that the respondent was a user in the past 12 months (and potentially more recently). Similarly, a code of 9 ("Used at some point in lifetime LOGICALLY ASSIGNED") indicated that the respondent was potentially a user in any period that was asked about for that particular drug, including the past 30 days. In particular, respondents were assigned a code of 9 if they initially answered "don't know" or "refused" to a drug's recency question and continued on follow-up to answer "don't know" or "refused" regarding when they last used it.

Details of the editing procedures for the drug use variables in 2014 will appear in the *2014 NSDUH Methodological Resource Book*, which will be available in early 2016.[25]

Standard Code Conventions

Generally, the following codes have the same (or consistent) meanings across all variables. Exceptions are noted in the documentation for individual variables.

91 or 991 or 9991, etc.	=	NEVER USED [DRUG(s) OF INTEREST]
93 or 993 or 9993, etc.	=	USED [DRUG] BUT NOT IN THE PERIOD OF INTEREST
94 or 994 or 9994, etc.	=	DON'T KNOW
97 or 997 or 9997, etc.	=	REFUSED
98 or 998 or 9998, etc.	=	BLANK (i.e., not answered; not asked the question)
99 or 999 or 9999, etc.	=	LEGITIMATE SKIP

[25] See footnote 18.

The following analogous codes also were assigned as part of the logical editing process:

81 (or 981, 9981, etc.)	=	NEVER USED [DRUG(s) OF INTEREST] Logically assigned
83 (or 983, 9983, etc.)	=	USED [DRUG] BUT NOT IN THE PERIOD OF INTEREST Logically assigned
85 (or 985, 9985, etc.)	=	BAD DATA Logically assigned (i.e., usually inconsistent with other data)
89 (or 989, or 9989, etc.)	=	LEGITIMATE SKIP Logically assigned

The codes of 81, 83, 85, and 89 were given values in the 80s to signify that existing values were overwritten during editing. For example, if a respondent was somehow routed into the youth experiences module but that respondent was subsequently classified as being 18 or older, any answers that the respondent gave in the youth experiences module were overwritten with codes of 89 (or 989, etc.). These codes signify that this adult respondent logically was not eligible to be asked the youth experiences questions.

Codes of 85 (or 985, etc.), 94 (or 994, etc.), 97 (or 997, etc.), and 98 (or 998, etc.) are codes for missing data. In particular, codes of 98 (i.e., blank) could occur in the data for the following reasons:

- the respondent broke off the interview before reaching a particular question or section;
- the CAI program allowed the respondent to hit the ENTER key without providing a response (typically, in situations where respondents were asked to specify something, such as the name of some other drug that they had used); or
- the CAI program skipped the respondent past a question, but there was some uncertainty as to whether the skipped question applied or did not apply to the respondent (e.g., if subsequent questions about a drug were skipped because the respondent did not know whether he or she ever used that drug).

Statistical Imputation

Statistical imputation refers to the substitution of acceptable estimated values for missing values. These imputed values cannot be directly distinguished from nonimputed values. Using statistical imputation, missing data were replaced with nonmissing values for selected variables. These variables can be identified in the codebook by their labels, within which can be found the words "IMPUTATION REVISED." In addition, most imputation-revised variables have names with the prefix "IR." (The imputation-revised employment status variable EMPSTATY is an exception to this rule. Also, although no missing data are possible for gender, the "IR" prefix for IRSEX is maintained for continuity with past years.) Associated indicator variables tell the user which values are imputed and which ones are not. These indicator variables have the words "IMPUTATION INDICATOR" in their labels and are identified with the prefix "II." For some imputation-revised variables, additional imputation indicators are available, identified with the prefix "II2," giving more details about the source of the imputed or logically assigned value.

In most cases, the imputation-revised variable can be traced to a specific question in the questionnaire. However, the imputation-revised variable occasionally corresponds to an edited variable that was derived from several questions in the questionnaire.

With the 2014 survey, the core drug use variables are recency of use, frequency of use in the past 12 months, frequency of use in the past 30 days, and age at first use. Age of first daily cigarette use and binge drinking frequency[26] in the past 30 days are also core drug use variables. Imputation of missing values in these core drug use variables was accomplished using an imputation procedure developed specifically for the survey in 1999 and called predictive mean neighborhood (PMN), which is a combination of model-assisted and nearest neighbor hot-deck imputation methods. The PMN method also was used in the 2014 survey to impute missing values in the core demographic, employment status, immigrant status, income, insurance, and roster-derived household composition variables, as well as variables associated with responding pairs. One group of variables for which the PMN method was not used is nicotine dependence. Instead, a weighted least squares regression was used to obtain continuous predicted means, which in turn were used directly as imputed values for this set of variables. More details on the methods used for imputation appear in the *2014 NSDUH Methodological Resource Book*, which will be available in early 2016.[27]

For all imputation-revised variables except those associated with nicotine dependence, the levels within the variables are limited to the valid responses in the interview itself. If neither editing nor imputation was required for any of these variables, the levels for the edited and imputation-revised variables are the same, with each level corresponding to a valid interview response. If an edited variable has a logically assigned value for which no imputation was required, that logically assigned value was converted to the associated valid interview response in the imputation-revised variable. Finally, levels in the edited variable that do not correspond to a valid interview response indicate that the information available for that respondent was incomplete and, consequently, imputation was required. In the imputation-revised variable, these levels were replaced by imputed values corresponding to valid interview responses, which were made consistent with any preexisting information related to that variable. Examples of levels indicating incomplete information include "bad data," "don't know," and "refused." Also, in the case of recency of use, some levels in the edited variable describe a more general recency than was designated from a valid interview response, which, in the imputation-revised variable, were replaced by imputed values consistent with the general recency level.

Imputation Indicators

For each variable that includes imputed values, concomitant indicator variables distinguish imputed from nonimputed values. These associated variables have names nearly identical to the imputation-revised variables, except that the IR prefix was replaced by an II or an II2. In general, the imputation indicator variables with the II prefix have three levels:

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[26] Binge alcohol use is defined as drinking five or more drinks on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days. Heavy alcohol use is defined as drinking five or more drinks on the same occasion on each of 5 or more days in the past 30 days; all heavy alcohol users are also binge alcohol users.

[27] See footnote 18.

1 = From interview

2 = Logically assigned

3 = Statistically imputed.

These levels indicate whether the imputation-revised variable's value originated from interview responses, was logically assigned in the editing process, or was imputed. In some cases, the skip logic inherent in the CAI prevented a respondent from answering certain questions because of his or her responses to previous questions. For the drug use variables, if a respondent had been skipped out of a question, the response in the imputation-revised variables is coded as "never used" or is coded to indicate that the respondent had not used in the relevant time period. For other variables where this occurred, the imputation-revised variable has a level with a label indicating a legitimate skip. The imputation indicators associated with these variables also have an additional level, which likewise has a label indicating a legitimate skip. Typically, this level is given as 9 (= Legitimate skip), often with an accompanying explanation for the skip.

The variables that have an additional set of imputation indicators, as denoted by the prefix "II2," are IRHOGRP4, EMPSTAT4, EMPSTATY, and the recency and frequency of drug use variables. For IRHOGRP4, the II2 variable is simply a more detailed description of the sources of information for these variables. For EMPSTAT4 and EMPSTATY, the II2 variables provide more details about the constraints on imputed values, where the legitimate skip levels are equivalent to those given by the II variables. The drug use II2 variables are a result of the implementation of the flag-and-impute editing procedures on the recency-of-use data. Greater details on these editing procedures are given in the Logical Editing section in this introduction. With these editing procedures, inconsistent responses in the recency-of-use variables were replaced by more general, consistent responses. Subsequently, the specific responses then were imputed. If the response from a recency-of-use variable was considered partially known, such as past year use of a given drug with the more specific recency unknown, imputed values had to be limited to what was consistent with this incomplete information. The types of partial information available for a given variable are as follows:

8 = Used at some point in the past 12 months LOGICALLY ASSIGNED

9 = Used at some point in lifetime LOGICALLY ASSIGNED

14 = Used more than 12 months ago LOGICALLY ASSIGNED

19 = Used more than 30 days ago LOGICALLY ASSIGNED

29 = Used more than 30 days ago but in the past 3 years LOGICALLY ASSIGNED

39 = Used within the past 3 years LOGICALLY ASSIGNED.

The last four levels (14, 19, 29, and 39) are for tobacco product use only. In the imputation indicator for drug use variables, level 3 indicates statistical imputation, but no detail is given regarding any available partial information. The II2 variable breaks out the II level 3 into the following levels:

3 = Statistically imputed data - lifetime use imputed

4 = Statistically imputed data - edited recency = 9

5 = Statistically imputed data - edited recency = 8

6 = Statistically imputed data - edited recency = 19

7 = Statistically imputed data - edited recency = 14

8 = Statistically imputed data - edited recency = 29

9 = Statistically imputed data - edited recency = 39.

Constraints and Consistency

The imputation of missing values in the core demographics and drug use variables was subject to numerous constraints to ensure that imputed values would be consistent with preexisting, nonmissing values. For multivariate analyses, the imputation-revised variables should be used as long as these variables all come from the core section of the interview. On the other hand, no attempt was made to ensure consistency between the imputation-revised core and noncore variables. Therefore, for analyses of relationships requiring imputation-revised variables from both the core and noncore sections of the interview, simultaneous use of these variables may not be appropriate.

Variance Estimation of Totals

Prevalence rates are the proportions of the population who exhibit characteristics of interest (such as substance use). Let $\hat{p}_d$ represent the prevalence rate of interest for domain d. Then $\hat{p}_d$ would be defined as the ratio

$$\hat{p}_d = \frac{\hat{Y}_d}{\hat{N}_d},$$

where $\hat{Y}_d = \sum_{i \in S} w_i \delta_i y_i$, which represents the estimated number of individuals exhibiting the characteristic of interest in domain d; $\hat{N}_d = \sum_{i \in S} w_i \delta_i$, which represents the estimated population total for domain d; S represents the sample; w_i represents the analysis weight; δ_i represents an indicator variable that is defined as 1 if the ith sample unit is in domain d and is equal to 0 otherwise; and y_i represents an indicator variable that is defined as 1 if the ith sample unit exhibits the characteristic of interest and is equal to 0 otherwise.

The sampling error of an estimate is the error caused by the selection of a sample instead of conducting a census of the population. The sampling error may be reduced by selecting a large sample and/or by using efficient sample design and estimation strategies, such as stratification, optimal allocation, and ratio estimation. The use of probability sampling methods in NSDUH allows estimation of sampling error from the survey data. The standard errors (SEs, which are the square roots of the variances) are used to identify unreliable estimates and to test for the statistical significance of differences between estimates.

Suitable software packages, such as SUDAAN,[28] can be used to calculate direct estimates of $\hat{Y}_d$ and $\hat{N}_d$ (and, therefore, $\hat{p}_d$) and also can be used to estimate their respective SEs. Although the SEs of estimates of means and proportions can be calculated appropriately in software (such as SUDAAN) using a Taylor series linearization approach, SEs of estimates of totals may be underestimated in situations where the domain size is poststratified to data from the U.S. Census Bureau.

When the domain size, $\hat{N}_d$, is free of sampling error, an appropriate estimate of the SE for the total number of individuals with a characteristic of interest is

$$\mathrm{SE}(\hat{Y}_d) = \hat{N}_d \mathrm{SE}(\hat{p}_d).$$

This approach is theoretically correct when the domain size estimates, $\hat{N}_d$, are among those forced to match their respective U.S. Census Bureau population estimates through the weight calibration process.[29] In these cases, $\hat{N}_d$ is not subject to a sampling error induced by the NSDUH design. For estimated domain totals, $\hat{Y}_d$, where $\hat{N}_d$ is not fixed (i.e., where domain size estimates are not forced to match the U.S. Census Bureau population estimates), this formulation still may provide a good approximation if it can be assumed that the sampling variation in $\hat{N}_d$ is negligible relative to the sampling variation in $\hat{p}_d$. This is a reasonable assumption for many cases in this study.

For various subsets of estimates, the above approach yielded an underestimate of the variance of a total because $\hat{N}_d$ was subject to considerable variation. Because of this underestimation, alternatives for estimating SEs of totals can be implemented.

A "mixed" method approach can be used to improve the accuracy of SEs and to better reflect the effects of poststratification on the variance of total estimates. This approach assigns the method of SE calculation to domains (subgroups for which the estimates were calculated) so that all estimates among a select set of domains with fixed $\hat{N}_d$ were calculated using the formula above, and all other estimates were calculated directly in SUDAAN. The set of domains considered controlled (i.e., those with a fixed $\hat{N}_d$) was restricted to main effects and two-way interactions in order to maintain continuity between years. The use of such SEs did not affect the SE estimates for the corresponding proportions because all SEs for means and proportions are calculated directly in SUDAAN. Table 1 contains a list of domains with fixed $\hat{N}_d$ for the public use file.

[28] See footnote 20.
[29] See footnote 18.

Table 1. Demographic Domains Forced to Match Their Respective U.S. Census Bureau Population Estimates through the Public Use File Weight Calibration Process: 2014

Main Effects	Two-Way Interactions
Age Group	
12-17	
18-25	**Age Group** × **Gender**
26-34	(e.g., Males Aged 12 to 17)
35+	
All Combinations of Groups Listed Above[1]	
Gender	
Male	
Female	
Race/Ethnicity	
Hispanic or Latino	
Not Hispanic or Latino, White	
Not Hispanic or Latino, Black	
Not Hispanic or Latino, Others	

[1] Combinations of the age groups (including but not limited to 12 or older, 18 or older, 26 or older, and 35 or older) also were forced to match their respective U.S. Census Bureau population estimates through the weight calibration process.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2014.

Statistical Significance of Differences

Due to the 2002 NSDUH methodology changes, the 2002 data constitute a new baseline for tracking trends in substance use and other measures. *As noted previously, it is not considered appropriate to make comparisons of the 2002 through 2014 CAI estimates with 2001 and earlier NHSDA estimates to assess changes in substance use over time. If comparisons such as these are made, it is recommended that they be interpreted with caution.* For a more detailed description of the changes to the 2002 NSDUH methodology, see Appendix C of the *Results from the 2002 National Survey on Drug Use and Health: National Findings.*[30]

Customarily, the observed difference between estimates is evaluated in terms of its statistical significance. Statistical significance is based on the *p* value of the test statistic and refers to the probability that a difference as large as that observed would occur due to random variability in the estimates if there were no difference in the prevalence estimates for the population groups being compared. The significance of observed differences is generally reported at the 0.05 and 0.01 levels when the *p* value is defined as less than or equal to the designated significance level.

[30] Office of Applied Studies. (2003). *Results from the 2002 National Survey on Drug Use and Health: National findings* (HHS Publication No. SMA 03-3836, NSDUH Series H-22). Rockville, MD: Substance Abuse and Mental Health Services Administration.

When comparing prevalence estimates, one can test the null hypothesis (no difference between prevalence estimates) against the alternative hypothesis (there is a difference in prevalence estimates) using the standard difference in proportions test expressed as

$$Z = \frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\text{var}(\hat{p}_1) + \text{var}(\hat{p}_2) - 2\,\text{cov}(\hat{p}_1, \hat{p}_2)}},$$

where $\hat{p}_1$ = first prevalence estimate, $\hat{p}_2$ = second prevalence estimate, var($\hat{p}_1$) = variance of first prevalence estimate, var($\hat{p}_2$) = variance of second prevalence estimate, and cov($\hat{p}_1$, $\hat{p}_2$) = covariance between $\hat{p}_1$ and $\hat{p}_2$. Note that the first and second prevalence estimates may take the form of prevalence estimates from two different survey years (e.g., 2013 and 2014, respectively), prevalence estimates from sets of combined survey data (e.g., 2011-2012 annual averages and 2013-2014 annual averages, respectively), or prevalence estimates for populations of interest within a single survey year.

Under the null hypothesis, *Z* is asymptotically distributed as a normal random variable. Therefore, calculated values of *Z* can be referred to the unit normal distribution to determine the corresponding probability level (i.e., *p* value). Because the covariance term between the two estimates is not necessarily zero, SUDAAN[31] may be used to compute estimates of *Z* along with the associated *p* values such that the covariance term is calculated by taking the sample design into account. A similar procedure and formula for *Z* is used for testing between the estimated totals.

When comparing population subgroups defined by three or more levels of a categorical variable, log-linear chi-square tests of independence of the subgroup and the prevalence variables should be conducted first to control the error level for multiple comparisons. If Shah's Wald *F* test (transformed from the standard Wald chi-square and computed in SUDAAN) indicates overall significant differences, the significance of each particular pairwise comparison of interest should be tested using SUDAAN analytic procedures to properly account for the sample design.[32]

If SUDAAN is not available to compute the significance testing, using published estimates can provide similar testing results. When comparing prevalence rates shown with SEs, *t* tests that assume independence for the difference of proportions can be performed and usually will provide the same results as tests performed in SUDAAN. However, where the *p* value is close to the predetermined level of significance, results may differ for two reasons: (1) the covariance term is included in the SUDAAN tests, whereas it is not included in *t* tests that assume independence; and (2) the reduced number of significant digits shown in the published estimates may cause rounding errors in the *t* tests assuming independence.

Although not generated in all NSDUH publications, some publications do include sampling error in the form of 95 percent confidence intervals (CIs). CIs for NSDUH are computed using degrees of freedom (*df*) and critical values of the *t*-distribution, which will

[31] See footnote 20.
[32] See footnote 20.

change dependent on which sample of data is being analyzed. For more information about computing CIs and *df*, see Sections 8 and 6, respectively, in the 2013 statistical inference report.[33] In terms of testing for differences between prevalence rates shown with 95 percent CIs, it is important to note that two overlapping 95 percent CIs do not imply that their rates are statistically equivalent at the 5 percent level of significance.[34]

Use of Sample Weights and Sample Design Variables

Data file users who wish to analyze data from multiple survey years, including 2014 (e.g., 2002 through 2014[35]), should first sort the combined data by the sample design variables VESTR (variance estimation [pseudo] stratum) and VEREP (variance estimation [pseudo] replicate within stratum). These variables then are specified in a software package, such as SUDAAN, to automatically account for the 50 percent overlap between successive years when estimating variances and SEs. The final person-level analysis weight on the data file should be used when analyzing data for any single year or when comparing estimates between years within a combined file containing data from multiple years. However, estimation of the annual average number of individuals who have engaged in a particular behavior based upon pooled data from multiple years requires adjustment to the analysis weights. These adjusted weights would be created as the final weight divided by the number of years of combined data (e.g., the person-level weight divided by 13 for estimates based on the combined 2002 through 2014 data).

If a data file user is interested in generating estimates using some combination of quarter-level data, a sample weight can be created using the person-level analysis weight as follows:

New Weight =	(4/*q*) * Person-Level Analysis Weight	If the record represents a respondent in one of the quarters of interest
=	0	Otherwise, …

where q = total number of quarters in the domain of interest.

For example, if one is interested in generating estimates for the first quarter of 2014, an appropriate sample weight would be constructed as follows:

New Weight =	(4/1) * Person-Level Analysis Weight	If the record represents a respondent in quarter 1
=	0	If the record represents a respondent in quarters 2, 3, or 4.

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[33] Center for Behavioral Health Statistics and Quality. (2015). *2013 National Survey on Drug Use and Health: Methodological resource book (Section 13, Statistical inference report)*. Rockville, MD: Substance Abuse and Mental Health Services Administration.

[34] For additional information, see the following reference: Payton, M. E., Greenstone, M. H., & Schenker, N. (2003). Overlapping confidence intervals or standard error intervals: What do they mean in terms of statistical significance? *Journal of Insect Science, 3*, 34. doi:http://dx.doi.org/10.1673/031.003.3401. Also see the following reference for further details: Schenker, N., & Gentleman, J. F. (2001, August). On judging the significance of differences by examining the overlap between confidence intervals. *American Statistician, 55*(3), 182-186. doi:10.1198/000313001317097960

[35] Changes in the sample design are accounted for in the sample design variables. Therefore, it is appropriate to combine 2002 through 2013 data with data from 2014 and onward.

If one is interested in generating estimates for the first half of 2014 (quarters 1 and 2), an appropriate sample weight would be constructed as follows:

New Weight =	(4/2) * Person-Level Analysis Weight	If the record represents a respondent in quarters 1 or 2
=	0	If the record represents a respondent in quarters 3 or 4.

In years when a split-sample design is implemented, a special weight is developed for the split samples. When analysis with pooled data from multiple years is conducted, analysts should check the documents for that specific year on how to use the analysis weights in order to use a proper analysis weight for the pooled data analysis.

For example, in the 2004 NSDUH, adult respondents aged 18 or older were split approximately evenly, where respondents in sample A were administered the full adult mental health module as it had been administered in 2002 and 2003, and respondents in sample B were administered a short version of the adult mental health module in addition to the adult depression module as it was administered in 2005, 2006, and 2007. Thus, analyses using 2004 data from either the adult mental health module (renamed to the psychological distress module in 2005, 2006, and 2007) or the adult depression module need to be conducted using a different weight variable. For 2004, analyses that include the adult mental health variables for MDE and/or unadjusted SPD should involve the following: (1) Select either sample A or sample B by using the ADLTSAMP variable (ADLTSAMP = 1 corresponds to sample A, and ADLTSAMP = 2 corresponds to sample B) to restrict the analysis to the appropriate half sample; (2) when combining 2004 adult half-sample data with data for survey years that have comparably defined adult mental health variables, the weight variable (SPD analysis weight for 2004 and the person-level analysis weight for the other years in the analysis) should be divided by the total number of years in the analysis.

Confidentiality of Data

To protect the confidentiality of respondents to the 2014 NSDUH, the full analytic file of 67,901 individuals was treated using a statistical disclosure limitation method called MASSC,[36,37,38] which consists of the following four major steps: **M**icro **A**gglomeration, optimal probabilistic **S**ubstitution, optimal probabilistic **S**ubsampling, and optimal sampling weight **C**alibration. All directly identifying information (such as name, phone number, and address) on

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[36] Singh, A. C. (2002). *Method for statistical disclosure limitation* (U.S. Patent Application Pub. No. US 2004/0049517A1). Research Triangle Park, NC: RTI International. The patent was granted in June 2006 (Patent No. US7058638B2).

[37] Singh, A. C., Yu, F., & Dunteman, G. H. (2003). MASSC: A new data mask for limiting statistical information loss and disclosure. In *Proceedings of the Joint UNECE/EUROSTAT Work Session on Statistical Data Confidentiality, Luxembourg* (Working Paper No. 23, pp. 373-394). Geneva, Switzerland: United Nations Statistical Commission and Economic Commission for Europe Conference of European Statisticians, European Commission Statistical Office of the European Communities (EUROSTAT).

[38] Singh, A., Yu, F., & Wilson, D. H. (2004, August). Measures of information loss and disclosure risk under MASSC treatment of micro-data for statistical disclosure limitation. In *Proceedings of the 2004 Joint Statistical Meetings, American Statistical Association, Section on Survey Research Methods, Toronto, Canada* (pp. 4374-4381). Alexandria, VA: American Statistical Association.

the file was eliminated. In addition, census region, state, and other geographic identifiers were removed. Moreover, the household link between respondents from the same household was not included in the public use file.

All of the variables on the file were reviewed for the possibility of identifying a respondent by combining a number of them at one time. Variables considered to have a high potential of personal identification, as well as a high value for analysis, were treated by standard procedures of categorization and top-and-bottom coding. Using the selected key identifying variables, the data were partitioned into risk strata to control for level of treatment in the micro agglomeration step. In addition, two other techniques were used in MASSC to introduce sufficient uncertainty for anyone who attempted to identify an individual and his or her confidential responses. First, on a random basis, a sample of records was drawn, and variables were substituted from a similar donor record. This step, referred to as substitution, introduces uncertainty about the identity of a record in the database. This process makes it difficult for an intruder to be certain that any record corresponds to a specific individual because some of the variables used to identify the record may have come from other individuals. Second, a portion of the records was randomly removed from the file to reduce the probability of determining that any known respondent was in the public use file. This step, referred to as subsampling, introduces further uncertainty about the presence of a target record in the database. The result is that there is a very small probability of identifying an individual from the file.

Substitution and subsampling were done while simultaneously constraining the resultant file to a minimal increase in bias and a minimal decrease in precision for numerous estimates of drug use prevalence across a number of domains. In addition, the weights on the final file were recalibrated to known totals from the full restricted-use analytic file so as to minimize the decrease in precision owing to the two techniques. Under the MASSC framework, both disclosure risk and information loss are controlled and measured simultaneously.

A further disclosure control procedure includes the treatment of the design variables (VESTR and VEREP). These stratum and replicate identifiers were treated by coarsening, substitution, and scrambling. For the 2014 public use file, the variance estimation stratum variable VESTR was aggregated into 50 pseudo-strata due to sample redesign (see the section on Changes to NSDUH for 2014), whereas in 2013 and prior years, there were 60 pseudo-strata. In addition, certain variables were recoded (e.g., by collapsing of rare levels) or locally suppressed (e.g., by setting to missing values) for confidentiality reasons.

A number of variables were reviewed after the above process was completed in order to determine the impact of these techniques on the bias and precision of estimates compared with those from the full (i.e., untreated or restricted-use) file. These variables included both variables for which partial records were substituted and other variables that were not perturbed. In addition, the change in precision in estimates was studied for 340 combinations of 34 domains and 10 response variables (e.g., the combination of past month alcohol use in the 12 to 17 age group). The ratio of the estimates from the full restricted-use file and the public use file was calculated for each domain and response variable combination. The average ratio over the 34 domains for the 10 response variables was within the 0.98 to 1.08 range. Similarly, to assess the decrease in precision, the SE was compared between the public use file and the full restricted-use file. For the 10 response variables, the average increase in SEs over the 34 domains was about

3 to 9 percent, with the exception of STMFLAG (stimulants ever used) and HALFLAG (hallucinogens ever used),which had an average increase in the SEs of about 12 and 13 percent, respectively.

These statistical disclosure limitation methods have been implemented in such a way that the public use file continues to be representative of civilian members of the noninstitutionalized population in the United States.

Public Use File Estimates and Standard Errors

The sampling weights on the public use file were adjusted for subsampling and calibrated with respect to 45 demographic domains. A sublist of the domains that match their respective U.S. Census Bureau population estimates can be found in Table 1 (shown earlier). Note that the domains in Table 1 are different from those in Table B.1 of the report titled *2014 National Survey on Drug Use and Health: Methodological Summary and Definitions*[39] because of different adjustments applied to the weights on the public use file. Survey analysis software can be used with these weights, along with the sample design variables VESTR and VEREP, to estimate various parameters and their SEs. Tables 2 and 3 show prevalence estimates and their SEs for certain demographic domains that were not included in the calibration constraints.

Table 2 shows the ratio of prevalence estimates and SEs from the public use file subsample to the full sample for past month marijuana use, a relatively high prevalence drug. Table 3 shows the same ratios for past year heroin use, a relatively low prevalence drug. The results are shown for seven demographic domains.

Table 2. Past Month Marijuana Prevalence and Standard Error Ratios of the Public Use File Subsample to the Full Sample, by Seven Domains: 2014

Domain	Prevalence Ratio	Standard Error Ratio
Non-Hispanic American Indian or Alaska Native	1.07	0.98
Non-Hispanic Native Hawaiian or Other Pacific Islander	0.98	1.00
Non-Hispanic Asian	0.95	1.14
Non-Hispanic Two or More Races	1.03	0.91
Household with Four Members	0.99	1.05
Household with Five Members	0.99	0.98
Household with Six or More Members	1.00	1.06

Note: *Ratio = (Public use file subsample estimate / Full sample estimate).*

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2014.

[39] Center for Behavioral Health Statistics and Quality. (2015). *2014 National Survey on Drug Use and Health: Methodological summary and definitions.* Retrieved from http://www.samhsa.gov/data/

Table 3. Past Year Heroin Prevalence and Standard Error Ratios of the Public Use File Subsample to the Full Sample, by Seven Domains: 2014

Domain	Prevalence Ratio	Standard Error Ratio
Non-Hispanic American Indian or Alaska Native	1.08	1.06
Non-Hispanic Native Hawaiian or Other Pacific Islander	0.95	0.96
Non-Hispanic Asian	--	--
Non-Hispanic Two or More Races	1.20	1.33
Household with Four Members	1.06	1.19
Household with Five Members	1.12	1.03
Household with Six or More Members	1.04	0.98

Note: *Ratio* = (*Public use file subsample estimate* / *Full sample estimate*). Missing cells are due to a zero-observed prevalence rate in certain race/ethnicity domains.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2014.

Appendix II: Comparison between DSM-4, DSM-5 and NSDUH Criteria for Substance Use Disorder

Source: CBHSQ. (2016). Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health. 6-8. Retrieved from Rockville, MD: https://www.samhsa.gov/data/sites/default/files/NSDUH-DSM5ImpactAdultMI-2016.pdf

Table 2.1 Comparison of DSM-IV, DSM-5, and NSDUH Substance Use Disorder Assessment

Characteristic	DSM-IV	DSM-5	NSDUH
Disorder Class	Substance-related disorders, included only SUDs	Substance-related and addictive disorders class now includes SUDs and gambling disorder (formerly pathological gambling)	Same as DSM-IV
Disorder Types[1]	Abuse and dependence hierarchical diagnostic rules meant that people ever meeting criteria for dependence did not receive a diagnosis of abuse for the same class of substance	SUD, substance abuse and dependence have been eliminated in favor of a single diagnosis, SUD	Same as DSM-IV
Substances Assessed	11 classes of substances assessed, plus 2 additional categories	10 classes of substances assessed, plus 2 additional categories	Modules for 13 substances, plus 2 additional categories
	• Alcohol	• Alcohol	• Alcohol
	• Amphetamine and similar sympathomimetics	• Stimulant use disorder, which includes amphetamines, cocaine, and other stimulants	• Stimulants
	• Caffeine (intoxication only)	• Caffeine (intoxication and withdrawal)	• Not assessed
	• Cannabis (no withdrawal syndrome)	• Cannabis (with withdrawal syndrome)	• Cannabis (no withdrawal syndrome)
	• Cocaine	• Combined with other stimulants (e.g., amphetamines) under stimulant use disorder	• Cocaine
			• Crack
	• Hallucinogens • Phencyclidine and similar arylcyclohexylamines	• Separated into phencyclidine use disorder and other hallucinogen use disorder	• Hallucinogens
	• Inhalants (no withdrawal syndrome)	• Inhalants (no withdrawal syndrome)	• Inhalants
	• Nicotine (dependence only)	• Tobacco	• Cigarette dependence (measured by two non-DSM–based scales), other tobacco products (use only)
	• Opioids	• Opioids	• Heroin
			• Pain reliever
		• Merged with hallucinogens	
	• Sedatives, hypnotics, and anxiolytics	• Sedatives, hypnotics, and anxiolytics	• Sedatives
			• Tranquilizers
	• Other drug abuse/dependence	• Any other SUD	• Other drugs (use only)
	• Polysubstance dependence	• Dropped polysubstance use disorder	• Polysubstance dependence

(continued)

Table 2.1 Comparison of DSM-IV, DSM-5, and NSDUH Substance Use Disorder Assessment (continued)

	DSM-IV	DSM-5	NSDUH
Disorders Assessed	**Substance abuse: One or more symptoms**	**SUD: Two out of 11 criteria clustering in a 12-month period are needed to meet disorder threshold**	**Substance abuse: One or more symptoms in the past year**
	• Recurrent substance-related legal problems	• Dropped	• DSM-IV criterion assessed
	• Recurrent substance use in situations where it is physically hazardous	• Same	• Assessed
	• Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home	• Same	• Assessed
	• Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance	• Same	• Assessed
		• Added: Craving or a strong desire or urge to use the substance	• DSM-5 craving criterion not assessed
	Substance dependence: Three or more symptoms in the same 12-month period (or one symptom if dependence criteria have been met previously in the lifetime)		**Substance dependence: Three or more symptoms in the past year**
	• Substance is taken in larger amounts or over a longer period than was intended	• Same	• Assessed
	• There is a persistent desire or unsuccessful efforts to cut down or control substance use	• Same	• Assessed
	• A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects	• Same	• Assessed
	• Important social, occupational, or recreational activities are given up or reduced because of substance use	• Same	• Assessed
	• Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by substance use	• Same	• Assessed

(continued)

Table 2.1 Comparison of DSM-IV, DSM-5, and NSDUH Substance Use Disorder Assessment (continued)

	DSM-IV	DSM-5	NSDUH
	• Tolerance, as defined by either: (1) a need for markedly increased amounts of substance to achieve intoxication or desired effect or (2) a markedly diminished effect with continued use of the same amount of the substance	• Same	• Assessed
	• Withdrawal, as manifested by either: (1) the characteristic withdrawal syndrome for the substance (excludes Cannabis, Hallucinogens, and Inhalants see Table 2.2) (2) the substance (or a similar substance) is taken to relieve or avoid withdrawal symptoms	• Withdrawal, as manifested by either: (1) the characteristic withdrawal syndrome for the substance (excludes Phencyclidine, Other Hallucinogens, and Inhalants; see Table 2.2) (2) the substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms Note: This criterion is not considered met for those taking opioids, sedatives, hypnotics or anxiolytics, or stimulant medications solely under appropriate medical supervision.	• Assessed, see Table 2.2 for variations from DSM-IV
Severity	No severity criteria	Severity is assessed in terms of the number of symptoms that meet criteria: Mild: two to three symptoms Moderate: four to five symptoms Severe: six or more symptoms	• No severity criteria assessed
Additional Specifications	With or without physiological dependence, early full remission, early partial remission, sustained full remission, sustained partial remission, on agonist therapy, and in a controlled environment	Early or sustained remission and if the person is in a controlled environment where access to the substance is restricted	• Not assessed

DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition; DSM-5 = *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition; NSDUH = National Survey on Drug Use and Health; SUD = substance use disorder.

[1] Table does not include substance/medication-induced disorders with the exception of notations for withdrawal and caffeine intoxication.

Appendix III: Weighted prevalence estimates in percent of sample characteristics by age group

Characteristic	18-25 Year Olds (N=124625; PSE=33874180; P=14.6%)	26-49 Year Olds (N=99163; PSE=98341277; P=42.5%)	50 Year Olds or Above (N=44641; PSE=99008787; P=42.8%)
	P (SE)	P (SE)	P (SE)
Sex			
Male	50.2 (0.2)	49.2 (0.2)	46.5 (0.3)
Female	49.8 (0.2)	50.8 (0.2)	53.5 (0.3)
Race/Ethnicity			
Non-Hispanic White	58.3 (0.3)	61.6 (0.3)	75.6 (0.3)
Non-Hispanic Black	14.2 (0.2)	12.3 (0.2)	10.0 (0.2)
Hispanic	19.7 (0.2)	18.1 (0.2)	8.9 (0.2)
Other	7.9 (0.1)	8.0 (0.2)	5.6 (0.1)
Marital Status			
Married	10.7 (0.1)	58.4 (0.3)	62.5 (0.3)
Widowed	0.1 (0.0)	0.9 (0.0)	13.1 (0.2)
Divorced or Separated	1.6 (0.0)	14.3 (0.2)	17.8 (0.3)
Never Been Married	87.7 (0.1)	26.4 (0.2)	6.6 (0.2)
Household Type			
Single-Person	4.7 (0.1)	7.7 (0.1)	19.9 (0.2)
Family	73.3 (0.4)	83.8 (0.2)	75.8 (0.3)
Non-Family	15.0 (0.4)	4.2 (0.1)	2.1 (0.1)
Mixed	7.0 (0.4)	4.3 (0.1)	2.3 (0.1)
Education Level			
Less Than High School	16.2 (0.2)	12.9 (0.1)	15.1 (0.2)
High School Graduate	34.5 (0.3)	26.6 (0.2)	32.0 (0.3)
Some College	34.6 (0.3)	26.2 (0.2)	23.4 (0.3)
College Graduate	14.7 (0.2)	34.3 (0.3)	29.6 (0.4)
Past Year Employment			
Continuous	47.1 (0.2)	71.7 (0.2)	46.4 (0.3)
Intermittent	20.1 (0.2)	8.3 (0.1)	3.3 (0.1)
Not in Labor Force	32.8 (0.2)	19.9 (0.2)	50.3 (0.3)
Personal Income Level in USD			

Less than 10000	57.5 (0.2)	19.5 (0.2)	17.5 (0.2)
10000-29999	33.7 (0.2)	30.4 (0.2)	35.6 (0.3)
30000 or Above	8.9 (0.1)	50.0 (0.2)	46.8 (0.3)
Area of Residence			
Large Metro	53.9 (0.4)	56.4 (0.3)	50.7 (0.4)
Small Metro	31.4 (0.4)	29.2 (0.3)	30.9 (0.4)
Non-Metro	14.6 (0.2)	14.4 (0.2)	18.3 (0.3)
Religiosity	59.0 (0.2)	68.8 (0.2)	78.2 (0.3)
Past Year Tobacco Use	49.8 (0.2)	39.3 (0.2)	22.9 (0.3)
AUD	17.6 (0.2)	9.7 (0.1)	4.1 (0.1)
DUD	13.6 (0.2)	4.4 (0.1)	1.1 (0.1)
CUD	9.2 (0.1)	2.2 (0.1)	0.4 (0.0)
Other DUD	6.8 (0.1)	2.8 (0.1)	0.7 (0.1)
Substance Use Disorders (U)			
NSUD	74.7 (0.2)	87.4 (0.1)	95.1 (0.1)
AUDa	11.6 (0.1)	8.1 (0.1)	3.8 (0.1)
DUDa	7.7 (0.1)	2.8 (0.1)	0.8 (0.1)
ADUD	5.9 (0.1)	1.6 (0.1)	0.3 (0.0)
Psychiatric Disorder	7.4 (0.1)	6.1 (0.1)	3.7 (0.1)
Past Year Mental Health Treatment	11.5 (0.1)	14.9 (0.2)	14.2 (0.2)
Past Year Substance Use Treatment			
Alcohol	0.8 (0.0)	0.8 (0.0)	0.4 (0.0)
Drugs	1.0 (0.0)	0.8 (0.0)	0.2 (0.0)
Juvenile Alcohol Use	56.4 (0.2)	55.3 (0.2)	41.0 (0.3)
Juvenile Drug Use	40.7 (0.2)	35.4 (0.2)	15.3 (0.2)
Cannabis	36.4 (0.2)	32.6 (0.2)	13.7 (0.2)
Any Other Drug	20.1 (0.1)	16.1 (0.2)	6.7 (0.2)

N: unweighted sample size; PSE: Population Size Estimate; P: Prevalence in percent; SE: Standard Error in percent; AUD: Alcohol Use Disorder; DUD: Drug Use Disorder(s); CUD: Cannabis Use Disorder; NSUD: No Substance Use Disorder; AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders.

Appendix IV: Weighted prevalence estimates in percent of juvenile use of substances by age group and substance use disorder category

Characteristic	AUDa	DUDa	ADUD	NSUD
	P (SE)	P (SE)	P (SE)	P (SE)
		18-25 Year Olds		
Juvenile Alcohol Use	78.3 (0.4)	83.3 (0.6)	91.2 (0.5)	47.5 (0.2)
Juvenile Drug Use	54.7 (0.6)	81.7 (0.6)	86.1 (0.6)	30.6 (0.2)
Cannabis	48.9 (0.6)	77.3 (0.6)	82.2 (0.7)	26.6 (0.2)
Any Other Drug	27.6 (0.5)	48.3 (0.7)	57.5 (0.8)	13.1 (0.2)
		26-49 Year Olds		
Juvenile Alcohol Use	76.0 (0.6)	81.0 (0.9)	87.7 (1.0)	52.0 (0.2)
Juvenile Drug Use	55.0 (0.7)	77.5 (0.9)	81.6 (1.3)	31.4 (0.2)
Cannabis	50.4 (0.8)	72.0 (1.0)	76.6 (1.4)	28.9 (0.2)
Any Other Drug	28.6 (0.6)	47.9 (1.1)	55.6 (1.7)	13.2 (0.2)
		50 Year Olds or Above		
Juvenile Alcohol Use	68.2 (1.2)	71.4 (3.3)	84.4 (4.0)	39.5 (0.3)
Juvenile Drug Use	37.9 (1.2)	56.4 (3.3)	75.2 (3.8)	13.9 (0.2)
Cannabis	33.1 (1.3)	50.7 (3.3)	63.8 (4.8)	12.5 (0.2)
Any Other Drug	20.1 (1.2)	40.7 (3.1)	48.8 (4.4)	5.7 (0.2)

AUDa: Alcohol Use Disorder alone; DUDa: Drug Use Disorder(s) alone; ADUD: Alcohol and Drug Use Disorders; NSUD: No Substance Use Disorder; P: Prevalence in percent; SE: Standard Error in percent.

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