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Commonalities and differences across substance use disorders: phenomenological and epidemiological aspects

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Abstract

Background—Although psychoactive substances vary in many ways, they have important commonalities, particularly in their ability to lead to an addiction syndrome. The field lacks an updated review of the commonalities and differences in the phenomenology of alcohol, cannabis, tobacco, stimulants, opioids, hallucinogens, sedatives/tranquilizers and inhalants and their related substance use disorders (SUD).

Methods—DSM-IV and DSM-5 SUD diagnostic criteria were reviewed, as was evidence from recent epidemiological and clinical research: psychometric studies (test-retest reliability, latent trait analysis); physiological indicators (tolerance, withdrawal); prevalence and age of onset. Information was incorporated from previous reviews, PubMed and Scopus literature searches, and data from large U.S. national surveys.

Results—Empirical evidence in the form of test-retest reliability and unidimensionality supports use of the same DSM-IV dependence or DSM-5 SUD diagnostic criteria across substances. For most substances, the criteria sets were generally most informative in general population samples at moderate-to-severe levels of SUD. Across substances, two criteria (tolerance and use in hazardous situations) were identified as functioning differently in population subgroups. Since substances have different pharmacological effects, withdrawal is assessed using substance-specific symptoms, while tolerance is not; issues remain with the assessment of tolerance. Alcohol, tobacco, and cannabis were consistently identified as the substances with earliest onset of use, highest prevalence of lifetime use, and highest prevalence of lifetime disorder.

Conclusions—Despite differences between psychoactive substances, the generic DSM criteria set appear equally applicable across substances. Additional studies of tolerance and hazardous use will be useful for future nosologies. Alcohol, cannabis, and tobacco are the substances with the greatest public health impact due to the high prevalence and early onset of their use, and the potential all three substances have to lead to addiction.

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Key words or phrases

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Substance use disorders (SUD) are diagnosed by cognitive, behavioral, and physiological symptoms that accompany repeated substance use despite the occurrence of clinically significant problems. The substances include alcohol, cannabis, tobacco, stimulants, opioids, hallucinogens, sedatives/tranquilizers and inhalants. While these substances vary in many ways (e.g., legality, physiological effects, typical ages of onset), they have important commonalities, particularly in their ability to lead to an addiction syndrome. Since an updated review of the commonalities and differences in the phenomenology of these substances is lacking, we review evidence from recent epidemiologic and clinical studies, covering four areas. (1) Diagnostic criteria for SUD; (2) Psychometric evidence: test-retest reliability and latent trait analysis of SUD; (3) Physiological indicators, i.e., tolerance and withdrawal; and (4) Prevalence and age of onset of substance use and SUD.

1. Diagnostic criteria for SUD

The nosology of SUD was initially based on the “alcohol dependence syndrome” (ADS), combining psychological, biological, and sociological processes whereby drinking develops increasingly greater value relative to other behaviors, becoming unresponsive to consequences of use (Edwards and Gross, 1976), a concept generalized to drugs by the World Health Organization (Edwards et al., 1981). The ADS was seen as one axis of a “bi-axial” set of problems, with a secondary axis consisting of adverse consequences (Edwards et al., 1981, Edwards, 1986). The DSM-III-R and DSM-IV diagnosis of substance dependence was similar to the ADS. DSM-IV provided seven dependence criteria dependence, of which three needed to be met within a 12-month period (American Psychiatric Association, 2000). DSM-III-R and DSM-IV attempted to make the secondary axis (consequences, or abuse) orthogonal to dependence, by only diagnosing abuse in the absence of dependence. DSM-IV provided four abuse criteria, with one required for diagnosis (American Psychiatric Association, 2000). These criteria were largely generic across substances, although cannabis, inhalants and hallucinogens did not have a withdrawal criterion, and nicotine lacked an “abuse” category.

A large body of research into the relationship between dependence and abuse criteria showed that across substances, DSM-IV dependence criteria and three of the four DSM-IV abuse criteria indicated one unidimensional condition (Hasin et al., 2013b). Therefore, in DSM-5, the distinction between dependence and abuse was removed, replaced with one combined “substance use disorder” consisting of eleven criteria to diagnose all SUD (Table 1), of which 2 or more criteria within a 12-month period were required (American Psychiatric Association, 2013). A craving criterion (strong desire for the substance) was added, since it fit well with the dependence and abuse criteria across substances (alcohol (Borges et al., 2011; Casey et al., 2012; Castaldelli-Maia et al., 2015; Cherpitel et al., 2010; Hasin et al., 2012; Keyes et al., 2011a; Mewton et al., 2011a; Mewton et al., 2011b; Preuss et al., 2014); stimulants (Gilder et al., 2014; Hasin et al., 2012); tobacco (Chung et al., 2012;

Shmulewitz et al., 2011; Strong et al., 2009; Strong et al., 2012); cannabis, heroin (Hasin et al., 2012); inhalants (Ridenour et al., 2014)), had potential clinical utility, and to enhance consistency with ICD-10 (Hasin et al., 2013b). A withdrawal criterion was added for cannabis given considerable evidence for its existence (Hasin et al., 2013b), and tobacco disorder criteria were aligned with the other substances (American Psychiatric Association, 2013).

2. Psychometric evidence

Test-retest reliability

To produce useful scientific results, a measure's output must be reproducible across independent administrations. Two reviews summarized earlier information on reliability: one for all substance disorders (Hasin et al., 2006) and the other for nicotine dependence (DiFranza et al., 2010). To update results, we searched PubMed and Scopus for (DSM-IV or DSM-5) AND "substance use disorder" AND (reliability or reproducibility), from 2005 or later. English publications through December 2014 were considered and relevant papers were identified from titles and abstracts.

Across substances, DSM-IV dependence showed good to excellent reliability (Pierucci-Lagha et al., 2005, DiFranza et al., 2010, Malison et al., 2011, Hasin et al., 2006), except for hallucinogens and inhalants, which had moderate reliability (Ridenour et al., 2007, Hasin et al., 2006) (Table 2). Similarly, across substances, a combined DSM-IV dependence or abuse category showed good to excellent reliability (Hasin et al., 2006, Pierucci-Lagha et al., 2005, Cottler et al., 2009, Ridenour et al., 2007), except sedatives/tranquilizers (moderate reliability) (Pierucci-Lagha et al., 2005). Dimensional measures of DSM-IV dependence showed good to excellent reliability across substances (Grant et al., 1995, Hasin et al., 1997, Ridenour et al., 2007). DSM-5 SUD reliability was generally good for binary diagnoses (Grant et al., 2015) across substances, while dimensional measures showed good to excellent reliability (Grant et al., 2015). (We comment elsewhere (Hasin et al., 2013a) on methodological reasons that DSM-5 AUD appeared less reliable in one study (Regier et al., 2013)). Additional studies are needed on the reliability of DSM-5 SUD diagnoses in general population and clinical samples.

Latent trait analysis

Latent trait analysis can investigate the relationships between and functioning of indicators (e.g., diagnostic criteria) of a construct that cannot be observed directly (e.g., addiction). For example, factor analysis can determine how many latent factors (or dimensions) best explain underlying correlations between a set of items (diagnostic criteria). For item/criterion sets that form a unidimensional latent trait (one factor), Item Response Theory (IRT) analysis provides further information about the relationship of each criterion to the latent trait, in terms of two parameters, severity and discrimination (Shmulewitz et al., 2011). Item severity is inversely related to prevalence; higher severity is indicated by lower prevalence (only those with a severe trait/disorder will manifest a rare criterion), while higher prevalence indicates low severity. Discrimination indicates how well the item discriminates between individuals with high or low disorder severity. Total discrimination for all criteria in a set

across the severity continuum can show where in that continuum the greatest amount of information is found. Additionally, IRT analysis is used to examine differential item functioning (DIF). DIF indicates if criteria show differential endorsement probabilities by demographic or other characteristics, conditional on underlying trait severity. IRT analysis was the principal method used by the DSM-5 SUD workgroup to examine the relationship of abuse to dependence criteria (Hasin et al., 2013b); this literature now numbers over 50 publications.

IRT studies

PubMed and Scopus were searched for English publications available through December 2014 with the terms “item response theory” AND (DSM-IV or DSM-5) AND the substances (alcohol, cannabis or marijuana, cocaine or stimulants, tobacco or nicotine, opioids or heroin, sedatives or tranquilizers, inhalants, hallucinogens). Based on titles or abstracts, we excluded papers not reporting on DSM-IV or DSM-5 SUD criteria sets or those that used IRT for severity scores (not to investigate psychometric evidence). We also excluded a study with incomplete assessment of abuse criteria (Kuerbis et al., 2013a). “Criteria sets” refer to the 11 criteria for DSM-IV abuse or dependence, or for DSM-5 substance use disorder, with 10 criteria for hallucinogens and inhalants (withdrawal is excluded) (Table 1). Heroin and prescription opioids were considered together because they have the same DSM-5 withdrawal syndrome. As Table 3 shows, many studies covered alcohol or cannabis, with fewer studies of less prevalent substances.

Unidimensionality across substances

The key empirical evidence necessary to consider combining abuse and dependence criteria in DSM-5 was that for all substances, these items exhibit unidimensionality, i.e., they indicate one underlying latent trait (disorder severity). As reviewed previously (Hasin et al., 2013b), evidence across all substances robustly showed that the 11 criteria (7 DSM-IV dependence criteria, 3 DSM-IV abuse criteria, and craving) indicated one underlying latent construct, with dependence and abuse criteria interspersed across the severity continuum. This supported replacing the two DSM-IV disorders (dependence, abuse) with a single combined disorder in DSM-5. More recent IRT studies continue to consistently indicate unidimensionality for alcohol (Castaldelli-Maia et al., 2015; Preuss et al., 2014, Hagman and Cohn, 2013, Kuerbis et al., 2013b, Ehlke et al., 2012, Rose et al., 2012, Edwards et al., 2013, Wu et al., 2013, Derringer et al., 2013), cannabis (Wu et al., 2013, Gizer et al., 2013, Derringer et al., 2013), cocaine and stimulants (Wu et al., 2013, Derringer et al., 2013, Gilder et al., 2014), opioids (Wu et al., 2013), and inhalants (Ridenour et al., 2014). The unidimensionality evidence also supports dimensional SUD severity scales across all substances; such scales are important in both research and clinical work as they provide information beyond a binary diagnosis (Grant et al., 2015, Hasin et al., 2015).

Defining the region of greatest information

IRT analysis estimates “total information”, which quantifies how well the criteria set as a whole discriminates between individuals with high or low disorder severity. The total or aggregate information curve plotted across the severity continuum shows the precision for the criteria set at each value along the severity continuum (Shmulewitz et al., 2011). A ‘flat’

curve shows equivalent information across all severities, while a ‘peaked’ curve indicates more information about the disorder at the severity level where the ‘peak’ occurs. In all studies with information about these curves, they were peaked, indicating greatest information at a specific severity, with two areas of greatest information: either “moderate” (information ‘peak’ from the mean [0] to about 1.5 SDs above the mean) or “moderate-severe” (information ‘peak’ 1.5 to 2.5 SDs above the mean).

Table 3 shows that regions of greatest information varied little by substance (alcohol, cannabis, opioids, hallucinogens, sedatives/tranquilizers, and inhalants). Instead, differences were found mainly by sample type. General (or mixed) samples tended to provide the most information in the moderate-severe end of the severity continuum, and clinical samples tended to provide the most information at more moderate values. While this could appear counter-intuitive, in clinical samples, the prevalence of all criteria is higher than in the general population, seeming to indicate less severity in these high-severity contexts (analogous to educational testing results only from advanced-placement students who all “get the hard ones right”, in contrast to results from entire schools). An exception to this pattern was stimulants. Clinical studies of cocaine showed greatest information at moderate severity (Hasin et al., 2012, Wu et al., 2009a, Langenbucher et al., 2004), while two general studies also showed moderate severity for stimulants (Gilder et al., 2014, Saha et al., 2012); more studies on stimulants are needed.

Differential Item Functioning (DIF)

DIF occurs when an item’s (criterion’s) parameter estimate differs across population subgroups after accounting for subgroup differences in disorder severity. For example, males generally have higher average AUD severity than females and are more likely to endorse AUD criteria; however, at the same levels of AUD severity, males and females should have the same likelihood of endorsing a criterion, unless it functions differently by sex. Although evidence suggests that across substances, DIF in specific criteria would not lead to differential diagnosis of SUD in population subgroups (Hasin et al., 2013b, Derringer et al., 2013), criteria with DIF across substances suggests that these criteria may not work well in specific subgroups. This information can indicate a poorly functioning criterion for sensitivity analyses and can identify criteria requiring adjustment in future nomenclatures.

The most studied DIF was by age, sex, or race/ethnicity, in the severity parameter. We included studies that reported on DIF results for each criterion (Table 4). DIF was examined most frequently for alcohol, with fewer studies for cannabis, stimulants, tobacco, and opioids, one study for hallucinogens, and no studies for sedatives/tranquilizers or inhalants.

DIF by substance (Table 4)

In a majority of studies, alcohol, cannabis, stimulants, tobacco and hallucinogens showed DIF by age, sex or race/ethnicity for the criteria assessing tolerance and use in hazardous situations, and similar results were seen for cannabis in studies using related methods (Agrawal and Lynskey, 2007; Delforterie et al., 2015a). Alcohol and tobacco also showed DIF by age or race/ethnicity for difficulty quitting or controlling use. Alcohol, cannabis,

stimulants, tobacco and opioids showed DIF inconsistently for the criteria assessing withdrawal, time spent, and continued use despite physical/psychological problems.

A few consistent DIF patterns emerged. Tolerance was more likely to be endorsed by younger participants (Table 4, studies 2, 3, 9–11, 15, 22, 25, 26) perhaps because they begin by using less, then increase use to get the desired effect (Chung et al., 2004, Hartman et al., 2008). Hazardous use was more likely to be endorsed by males (studies 1–3, 9, 11, 13, 14, 22, 28; and (Agrawal and Lynskey, 2007; Delforterie et al., 2015a)) and younger participants (studies 3, 9, 10, 15, 24). Hazardous use may be assessing a distinct dimension of SUD liability (Hasin et al., 2012), or a general tendency to disinhibition or antisocial behaviors more prevalent in younger and male participants (Mewton et al., 2011b, Mewton et al., 2010, Martin et al., 2008), warranting further investigation. Quit/control was less likely to be endorsed by younger participants (studies 2, 3, 9, 10, 14, 15, 25, 26), perhaps reflecting that younger individuals may not try to control use. Overall, alcohol is the only substance with a substantial amount of data on criterion level DIF. Little DIF testing was done for craving (all substances), tobacco abuse, or cannabis withdrawal, new in DSM-5, and warranting further study.

Differences for tobacco

Only seven tobacco IRT studies were available (Table 3). In DSM-IV, tobacco dependence could be diagnosed, but not “abuse”. The limited evidence available showed that the abuse criteria were valid and reliable measures of a tobacco use disorder and that the DSM-5 criteria set provided more information and higher prevalence of a use disorder than DSM-IV dependence (Shmulewitz et al., 2013, Shmulewitz et al., 2011, Chung et al., 2012). These findings led to alignment of the DSM-5 tobacco criteria with those for other substances.

Yet, differences between tobacco and other substances remain. First, DSM-5 suggests different operationalization of some criteria (time spent, hazardous use, tolerance (DiFranza et al., 2010); Table 1). Second, studies were inconsistent on the region of the severity continuum covered by the criteria: some general population studies showed greatest information in the moderate range (Strong et al., 2012, Shmulewitz et al., 2011, McBride et al., 2010, Saha et al., 2010), with others in the moderate-severe range (Rose and Dierker, 2010, Strong et al., 2009), with a wider severity range than other substances (Saha et al., 2010, Strong et al., 2012, Strong et al., 2009). No clinical studies reported total information for tobacco. Third, alternate indices of dependence, i.e., Fagerstrom Test for Nicotine Dependence (FTND; (Heatherton et al., 1991)) and related measures, are widely used (Baker et al., 2012; Hughes, 2006). These assess physical dependence (craving, withdrawal, compulsive use) rather than behavioral, social, or health-related consequences of use; thus, FTND and DSM are considered to indicate related but different domains of dependence (Agrawal et al., 2011; Baker et al., 2012). Recent studies suggest that DSM and FTND criteria together provide more information about tobacco use disorders than either measure alone (Agrawal et al., 2011; Strong et al., 2009; Strong et al., 2012). Studies of DSM-5 tobacco use disorder criteria and diagnoses, and their relationship to the FTND, in general population and clinical samples are warranted.

3. Physiological/pharmacological criteria

Sources of information

Definitions of tolerance and withdrawal were taken largely from expert review papers (Gilpin and Koob, 2008, Koob, 2006, Koob and Volkow, 2010, Koob, 2014). Symptoms of tolerance and withdrawal were derived primarily from DSM-5 (American Psychiatric Association, 2013). Additional information was found by searching PubMed and Scopus English publications from human studies, published or available online through December 2014, for “(DSM-IV or DSM-5) AND tolerance”, and selecting relevant publications based on the titles and abstracts.

Tolerance across substances

For all substances, tolerance occurs when the substance no longer affects an individual as strongly as before. When this happens, the individual needs higher doses of the substance to get the same effect (Gilpin and Koob, 2008, Koob, 2006). This is due to cellular and molecular adaptations to counteract or lessen the substance’s effect, since the body is trying to maintain ‘normal’ functioning in the presence of the substance (Koob and Volkow, 2010). These adaptations reduce sensitivity to further substance use. While tolerance can develop for all substances, the precise mechanisms for tolerance differ across substances, based on how the specific substance acts in the body, primarily the central nervous system (American Psychiatric Association, 2013, Koob and Volkow, 2010, World Health Organization, 2004). For example, tolerance may develop through increased metabolism to clear the substance from the body more quickly (e.g., alcohol, tobacco), or reduced receptor reactivity to the substance (e.g., alcohol, sedatives, tobacco, opioids) (World Health Organization, 2004). Tolerance can develop rapidly for some substances (e.g., sedatives, cannabis, amphetamines), and slowly for others (e.g., inhalants) (World Health Organization, 2004).

Concerns about tolerance as a criterion

The DSM changed-based operationalization of tolerance (needing to use more, or less of an effect, than “before”) is considered problematic across substances (Martin et al., 2008). Since assessment is based on initial or “usual” use levels, tolerance can be endorsed with low levels of use, if small amounts were used (Martin et al., 2008) (e.g., increases from 2 to 3 drinks (Chung et al., 2004, Chung et al., 2001)). This may be the reason tolerance is more likely to be endorsed by younger participants. Conversely, tolerance may not be endorsed at high levels of use (or high disorder severity) if initially high levels were used (e.g., alcohol and cannabis (Martin et al., 2006)), and/or if tolerance developed too quickly (Martin et al., 2008). Additionally, prevalence of tolerance varied across substances (Lynskey and Agrawal, 2007, Hasin et al., 2012, Saha et al., 2012). Lastly, tolerance discriminates poorly between those with or without dependence (alcohol, cannabis (Chung et al., 2004, Chung et al., 2001)), or between those with greater or lesser severity (cannabis, cocaine, amphetamines, opioids (Schuckit et al., 1999)), and does not predict clinical course (alcohol (Hasin et al., 2000)). Therefore, further research investigating inclusion of tolerance in the SUD diagnostic set is warranted.

Withdrawal across substances

Substance use, especially heavy use, leads to tolerance. When regular use ceases or is greatly reduced, the blood or tissue concentration of the substance declines and a re-adjustment is necessary. Withdrawal symptoms indicate this process of readjustment. After the body re-adjusts to the absence of the substance, withdrawal symptoms diminish and eventually cease. These symptoms are adverse across substances, and their avoidance can be one reason for continued use. However, withdrawal symptoms are generally life-threatening only for alcohol, sedatives (e.g, benzodiazepines), and opioids (Koob and Volkow, 2010). In DSM-5, withdrawal is included for alcohol, cannabis, stimulants, tobacco, opioids and sedatives/tranquilizers. The withdrawal criterion is considered positive with endorsement of the required number of substance-specific symptoms, or if the substance or a related substance is used to relieve or avoid symptoms.

Withdrawal by substance

Table 5 presents DSM-5 withdrawal symptoms by substance. All substances show symptoms related to emotional distress, such as depressed or dysphoric mood, anxiety, or insomnia, possibly related to common effects of all substances on the brain systems involved with stress and reward (Koob and Volkow, 2010, Koob, 2014). Other symptoms are more specific to pharmacological effects, and thus differ across substances. Sedating substances (alcohol, sedatives/tranquilizers) have similar withdrawal symptoms: nausea, vomiting, hallucinations, psychomotor agitation, seizures, tremors, sweating, and fast pulse rate. Opioids share some of those symptoms (nausea, vomiting, sweating) but also show other symptoms (lacrimation, diarrhea, yawning, fever, muscle aches). Stimulating substances (stimulants, tobacco) share some withdrawal symptoms (increased appetite, restlessness/agitation), but show some different symptoms, such as fatigue for stimulants and irritability/frustration for tobacco. Similarly, the time period for symptoms to develop (after cessation or reduction of use) and then improve differs across substances (Table 5), since that is partially determined by the amount of time after use the substance is generally biologically available. For example, withdrawal from sedating substances tends to develop within several hours to a few days, and can improve within five days to a week, but some symptoms can last for months. In contrast, withdrawal from tobacco tends to begin within one day, and then improve over two to three weeks. Thus, withdrawal is assessed using substance specific symptoms such that overall, the DSM-5 withdrawal criterion should be a similar indicator across the six substances.

Cannabis withdrawal

Withdrawal from cannabis was not included in DSM-IV because of lack of evidence, but was added in DSM-5, after supporting evidence became available (Hasin et al., 2013b). Studies showed that cannabis withdrawal is a reliable and valid diagnosis, with a time-limited course after cessation of cannabis use. It is prevalent in both general and clinical samples, and has clinical significance, since withdrawal was associated with difficulty quitting and worse treatment outcomes. Additionally, cannabis withdrawal fit the unidimensional model of cannabis use disorder criteria (Derringer et al., 2013, Gillespie et

al., 2007, Gizer et al., 2013, Hartman et al., 2008, Langenbucher et al., 2004, Lynskey and Agrawal, 2007, Mewton et al., 2010, Piontek et al., 2011, Wu et al., 2009b, Wu et al., 2013).

Hallucinogen, inhalant withdrawal

DSM-5 does not include withdrawal for hallucinogens or inhalants due to lack of evidence for a clinically significant withdrawal syndrome (American Psychiatric Association, 2013). A few studies on hallucinogens (Gillespie et al., 2007, Cottler et al., 2009) and inhalants (Ridenour et al., 2007, Perron et al., 2011, Ridenour et al., 2014) suggested that withdrawal symptoms were endorsed, showed acceptable reliability and validity, and fit the underlying disorder latent construct. Yet, a distinct set of symptoms remains to be identified for hallucinogens (Cottler et al., 2009) and inhalants (Ridenour et al., 2014); additional research is needed to determine if identification of such a syndrome is possible (Hasin et al., 2013b).

Exception for medical use

Withdrawal and tolerance are often observed among individuals using substances for medical purposes, such as stimulants, opioids, hallucinogens, sedatives/tranquilizers, and, with the advent of medical marijuana laws, cannabis (Table 1). When substances are used appropriately for supervised medical treatment, these criteria do not count as indicators of a SUD (American Psychiatric Association, 2013). These criteria would count towards a diagnosis if the substance was used in ways other than as prescribed, or for non-therapeutic reasons (American Psychiatric Association, 2013). Although conceptually this distinction appears reasonable, empirical evidence that applying this rule improves the reliability or validity of the criteria or disorder diagnosis is lacking; further studies are warranted. In contrast, tolerance and withdrawal always count towards a diagnosis for non-medically approved substances (alcohol, tobacco, cocaine, inhalants).

4. Prevalence and Age of onset of substance use and SUD

Sources of information

Two sources of information were utilized: literature review and data from US national datasets. Searches were conducted in English publications of human studies, initially restricted to publications dated January 2002-December 2014 from Pubmed, Medline, ProQuest, and Scopus, using the following terms: (“age of/at onset/first use/initiation”) and (alcohol or tobacco or nicotine or stimulant or heroin or cocaine or non-medical or opioid or methamphetamine or inhalant or marijuana or cannabis or k2 or spice or sedative or tranquilizer) and (disorder or abuse or dependence). Earlier publications were included when relevant and needed to supplement scant information. Only US studies were included, since many differences (e.g., legality, availability, and acceptability of substance use) should be considered when comparing patterns across countries, which is beyond the scope of this review. Based on title, abstract, or text, studies were included if they were quantitative, their primary focus was substance use, and substance-specific drug use could be differentiated. While alcohol, cannabis, cocaine, and tobacco had a substantial number of studies reporting on age of onset of use/disorder, several substances (inhalants, other stimulants, hallucinogens, tranquilizers/sedatives) yielded few or no studies (Table 6).

To supplement the literature review, we included findings from several U.S. national datasets. For adolescents, prevalence of use of each substance was examined by age in three datasets from 2013: Monitoring The Future (MTF) (Johnston et al., 2014), the National Survey of Drug Use and Health (NSDUH) (Substance Abuse and Mental Health Services Administration, 2014), and the Youth Behavioral Risk Surveillance Survey (YRBS) (Brener et al., 2013). Both MTF and YRBS are nationally representative school-based surveys of adolescents. The NSDUH is a nationally representative household-based survey of the non-institutionalized U.S. population, ages 12 and above. We provide published estimates from MTF (Johnston et al., 2014) and YRBS (Kann et al., 2014); for NSDUH participants age 12–17, prevalence estimates were calculated from the public use dataset using SAS 9.4, adjusting for the complex survey design and sampling weights.

For adults, we examined the median age of onset of use of each substance in two datasets: NSDUH (participants age 18 and older) and Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative survey of the civilian, non-institutionalized U.S. adult population in households and group living quarters, conducted 2001–2002 (Grant et al., 2004). Prevalence and median age of onset of use in the NSDUH were calculated from the public use dataset using SAS 9.4, adjusting for the complex sampling design and using sampling weights. We examined prevalence of use and of DSM-IV substance use disorders (abuse, dependence), and median age of onset of use and of SUD in the NESARC using SUDAAN 11.0.1, adjusting for the multi-stage sampling design and using sample weights. Medians are presented as they are less influenced by extreme outliers.

Adolescents: prevalence of use, age of first use

MTF, YRBS and NSDUH consistently showed that adolescents used alcohol, tobacco, and cannabis earliest and most commonly (Figures 1–3). Similarly, in other published studies of adolescents (Table 6), younger ages of onset were reported for alcohol, tobacco and cannabis (Bracken et al., 2013, Ridenour et al., 2006, Sartor et al., 2013). This consistency is probably related to environmental/ecological factors (availability, legal status, social norms), since the pharmacologic properties and subjective effects of these substances differ considerably. In MTF, YRBS, and NSDUH, inhalants showed early onset, but low prevalence. Cocaine, other stimulants, opioids, and tranquilizers/sedatives showed later onset of use and were less common among adolescents.

Adults: prevalence of use, age of first use

In published studies (Table 6), alcohol, cannabis, and tobacco were the most prevalent substances used. Similarly, both NESARC (Table 7) and NSDUH (Table 8) showed that the prevalence of alcohol, tobacco, and cannabis use was highest, with other substances used less. Overall lifetime substance use was generally higher in NSDUH than NESARC, perhaps due to methodological differences between the studies (self-administered substance use questions in NSDUH, interviewer-administered questions in NESARC) (Grucza et al., 2007). In both the previously published studies (Table 6) and the additional analyses in NESARC (Table 7) and NSDUH (Table 8), among the more prevalent substances, tobacco showed the earliest median age of onset of use, followed by cannabis and alcohol, with onset

generally occurring in early to mid-adolescence. Use of inhalants and hallucinogens began at younger ages, and cocaine, opioids, and sedatives/tranquilizers began at older ages. The only difference between the US national surveys in age of first use was for stimulants, reported as earlier in the NESARC than the NSDUH; the reasons for this are unclear. For a more complete understanding of the time course of substance use, further examination of the trajectories of use patterns over time both at a population level (e.g. secular trends) and at the individual level (e.g. longitudinal) is warranted. Further, alcohol and substance use function within larger cultural contexts (Degenhardt et al., 2008); expansion of international research on onset and prevalence of use is warranted.

Adults: prevalence of disorder by substance, age of onset of SUD

Overall, the most commonly diagnosed DSM-IV SUDs (dependence or abuse) were for alcohol (30.3%), tobacco (in DSM-IV, dependence only; 17.7%), and cannabis (8.2%), consistent with the high prevalence of lifetime use of these substances (Table 7). However, among users, any SUD was most prevalent for cocaine (45.8%), stimulants (43.8%), and cannabis (41.1%), followed by tobacco (37.8%), alcohol (36.6%), opioids (32.0%), hallucinogens (29.2%), sedatives/tranquilizers (26.6%), and inhalants (19.5%). For most substances, the age of onset of SUDs was generally late adolescence through young adulthood, in both NESARC (Table 7) and other published studies (Kalaydjian et al., 2009, Khan et al., 2013, Perron et al., 2009), while nicotine dependence was later, about age 26 (Table 7). Across all substances, initiation of use was generally younger among those diagnosed with SUDs (Table 7), and earlier onset of use was generally associated with higher risk or earlier onset of SUD (Table 6) for alcohol (Hingson et al., 2006, Hingson et al., 2009, Moss et al., 2014), tobacco (Lopez-Quintero et al., 2011, Moss et al., 2014), and cannabis (Haberstick et al., 2014, Le Strat et al., 2014, Moss et al., 2014).

Discussion

Review of psychometric studies identified many important similarities across substances. Test-retest reliability of the diagnoses was similar across substances, suggesting that differences in SUD prevalence across substances are not artifacts of a nosology more applicable to one substance than another. IRT studies showed that for all substances, the criteria sets were reliable measures of the underlying condition (SUD severity), providing robust empirical support for generic SUD criteria. Conceptually, generic criteria were supported by similar features across substances, such as commonalities in the neurobiological mechanisms of addiction (Koob, 2006, Koob and Le Moal, 2001), which lead to common behaviors across substances. Questions about whether the same set of diagnostic criteria would be similarly reliable and applicable across substances (Budney, 2006, Hughes, 2006) are addressed by the information provided in this review. Further, in general population samples, the criteria sets provided information at levels of greater severity, a desirable characteristic when the purpose is to identify people with disease (greater severity). To use the criteria sets to identify individuals *at risk* for developing a SUD, identification of valid and reliable lower severity indicators may be useful. Consistent DIF across substances was identified for two criteria, tolerance and hazardous use, suggesting further investigation into the role of those criteria in the diagnostic criteria set.

Two related issues warrant further comment. First, the most appropriate methodology (IRT) was used consistently to investigate the relationship between dependence and abuse criteria for all substances. Use of a consistent statistical methodology ensured that if results varied, the variation would be due to differences between substances or samples rather than variation in methodology. Having accomplished this task, studies should now investigate the DSM-5 nosology using different methodologies (Hasin, 2015). For example, rest-retest reliability studies are needed. In addition, validity should be evaluated by determining the association of criteria or diagnoses with external validators, including those that are antecedent (e.g., family history), concurrent (which indicate current state) or prospective (which predict prognosis or course). Second, although most IRT studies (Table 3) were in U.S. samples, a number of studies were conducted in other countries, mainly for alcohol (Argentina, Mexico, and Poland (Borges et al., 2011; Borges et al., 2010; Cherpitel et al., 2010); Israel (Shmulewitz et al., 2010); Australia (Mewton et al., 2011a; Mewton et al., 2011b); Australia, Brazil, Canada, Finland, and Japan (Preuss et al., 2014); and Brazil (Castaldelli-Maia et al., 2015)), with two for cannabis (Australia (Mewton et al., 2010) and France (Piontek et al., 2011)) and one for tobacco (Israel (Shmulewitz et al., 2011)). Those studies indicated that the same relationship between dependence and abuse criteria was found in many other countries; unidimensionality results were not limited to U.S. samples. But, in the few studies that investigated criteria functioning between countries, a number of criteria that functioned differently in different countries were identified for alcohol (Borges et al., 2010; Cherpitel et al., 2010) and cannabis (Delforterie et al., 2015a). Further studies should confirm the unidimensionality for all substances across countries, and identify criteria that function differently between countries, to more fully investigate the cross-country applicability of the DSM-5 nosology across substances.

Concerning the physiological criteria, tolerance and withdrawal show many differences and some similarities across substances. First, tolerance can develop for all substances, but problems with operationalization suggest the need for further research into its utility as a SUD criterion. Second, withdrawal can occur for most substances, and a substance-specific set of withdrawal symptoms are necessary. However, further work is needed to determine if withdrawal occurs for hallucinogens and inhalants. Last, tolerance and withdrawal criteria are not considered to indicate a substance use disorder for substances that are used under appropriate medical care (e.g., opioids); research is needed to determine how applying this exception affects diagnostic reliability.

Concerning prevalence and age of onset, alcohol and tobacco use were most prevalent, reflecting their legal status and availability. Cannabis was the most widely used illicit substance. In national surveys, these three substances tended to be used earliest and showed highest prevalence of SUD. Cocaine, stimulants, tranquilizers/sedatives, and inhalants had consistently low prevalence. While age of onset varied somewhat for these substances, it is unclear if this is due to methodological differences in the surveys or differences in secular trends of the age of onset of substance use.

Although the substances have different pharmacological effects, the same SUD or addiction criteria appear to be generally applicable across substances, suggesting an underlying “addictive process” that is common across all substances. This common addictive process is

most likely determined in part by genetic factors, as suggested by shared genetic liability across substances (Agrawal et al., 2012, Krueger et al., 2007), and in part by environmental factors, as suggested by shared risk factors for developing all types of SUDs, such as childhood maltreatment (Afifi et al., 2012, Dube et al., 2003, Keyes et al., 2012) and stressful life events (Sinha, 2001, Sinha, 2008). SUDs are a key feature of the “externalizing” axis of psychiatric disorders, as well as antisocial and conduct disorders (Krueger, 1999, Krueger et al., 2007), suggesting that the underlying liability to substance problems may be related to disinhibition, or the inability to refrain from unsafe behaviors, such as problematic or maladaptive substance use (Crowley, 2006).

However, despite the many commonalities across substances, substance-specific genetic and environmental liability factors (Tsuang et al., 1998, Kendler et al., 2003) indicate that individuals often prefer one substance to others. Understanding how the general liability for substance use or disorders is expressed for a particular substance is important for designing appropriate substance specific prevention or intervention programs. A proposed framework for “addiction specificity” (Sussman et al., 2011) lays out the complex relationships between both individual and group level factors that influence which substance an individual is most likely to use (and develop a SUD). An individual’s initial response to a substance may affect future use or disorder (de Wit and Phillips, 2012); e.g., unpleasant flushing response to alcohol decreases the likelihood of alcohol use disorders (Edenberg, 2007) or stimulating effects of alcohol increase risk (King et al., 2014). While an underlying personality “type” appears more susceptible to addiction in general (e.g., impulsivity, aggressiveness (Krueger et al., 2007)), limited evidence suggests that specific personality types were more likely to use specific substances (Milivojevic et al., 2012, Le Bon et al., 2004, Gerra et al., 2008). Abundant evidence indicates that individuals use substances that are used by others around them (parents, peer group). Group level factors may affect availability or ability to acquire specific substances; one study suggests that individuals using opiates would have used alcohol instead in less-permissive environments (Milivojevic et al., 2012). Sociodemographic variables affect choice of substance (Clark et al., 2012), as do social norms, which may also differ by demographics or cultural groups (Keyes et al., 2011b; Keyes et al., 2011c; Keyes et al., 2012; Shmulewitz et al., 2012). Additional research in this area is necessary to understand how these factors all work together to increase liability to general substance use or disorder (commonalities), and to affect risk for a specific substance use or disorder (differences).

In conclusion, through focusing on four areas of SUD phenomenology and epidemiology, we elucidated commonalities and differences across substances. Overall commonalities in the psychometric properties of the criteria sets and diagnoses justify the use of generic diagnostic criteria across substances, as long as specificity is allowed for withdrawal. Having consistent criteria for all SUDs is simpler for clinicians and researchers than different, substance-specific criteria. We identified key areas of research that could influence future nomenclatures, such as validation of the nosology across substances, whether tolerance and hazardous use should be removed or modified, and whether lower severity criteria should be added to aid in screening for substance use problems in the general population. Key differences in prevalence and age of onset of use and use disorders across substances are important for designing age appropriate prevention and intervention programs. Lastly, with a

clearer picture of the underlying commonalities across substances, the focus can shift to the differences, and to identifying the reasons individuals choose to use a specific substance, in order to be able to provide the most targeted and effective treatment programs.

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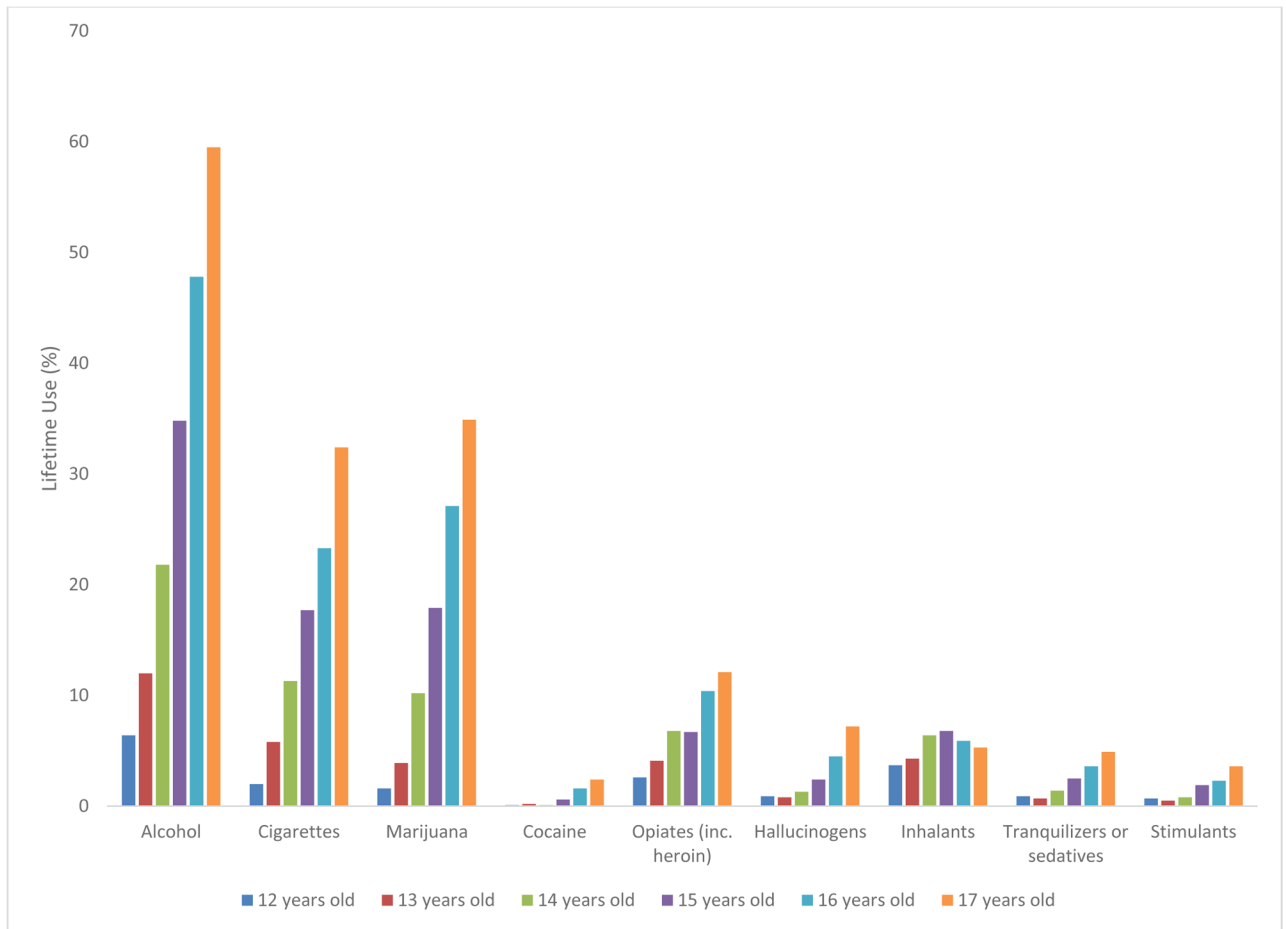


Figure 1.
Substance use among adolescents (12–17), NSDUH 2013 (N = 17,736)

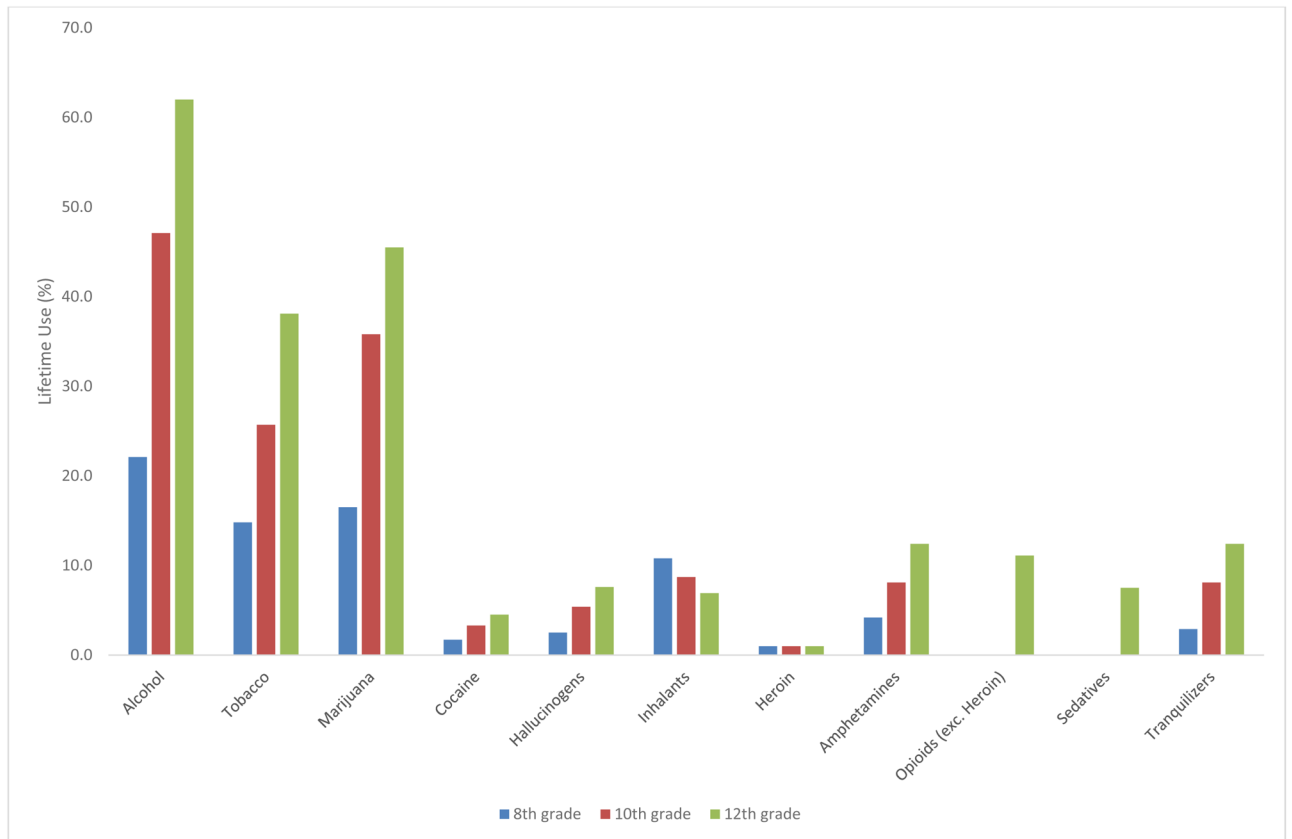


Figure 2.
Substance use by grade, MTF, 2013 (N = 41, 700)

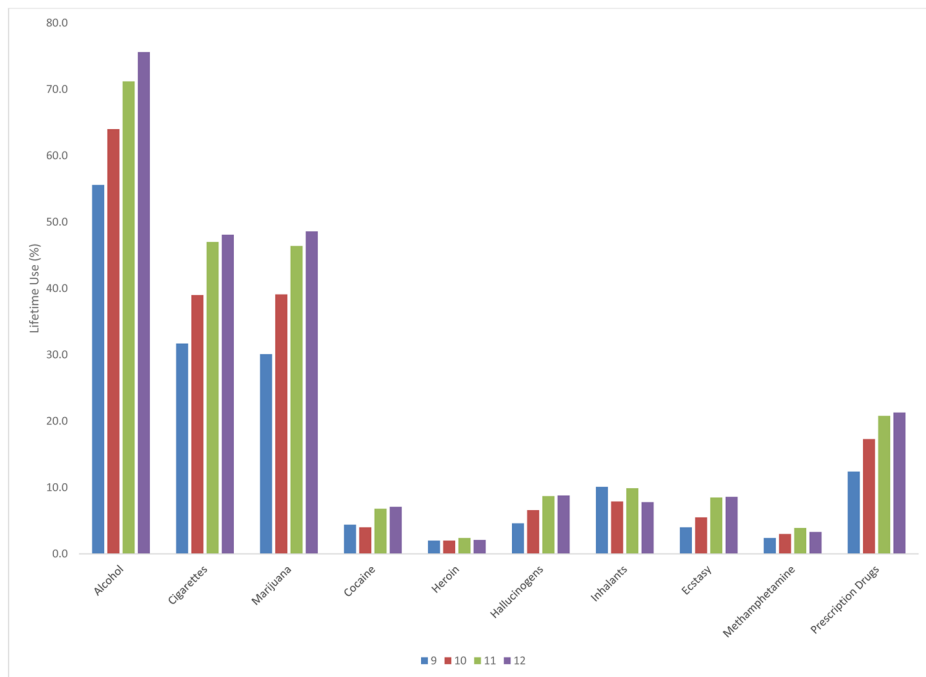


Figure 3. Substance use by grade, YRBS, 2013 (N = 13, 633)

Table 1DSM-5 substance use disorder^a criteria (American Psychiatric Association, 2013)

DSM-5 Criterion	DSM-5 Definition	DSM-5 Substance specific notes	Criterion in DSM-IV ^b ?
Impaired control			
<i>Larger/longer</i>	use substance in larger amounts or over longer period of time than was intended		Dependence
<i>Quit/control</i>	persistent desire to regulate or cut down use, or multiple unsuccessful efforts to quit or decrease use		Dependence
<i>Time spent</i>	lots of time spent obtaining, using or recovering from effects of the substance	Tobacco: often assessed as “chain smoking”; spending lots of time obtaining or recovering is rare	Dependence
<i>Craving</i>	an intense desire or urge for the substance; assessed by asking if had such strong desires for the substances that could not think of anything else		Not included
Social impairment			
<i>Neglect roles</i>	recurrent use resulting in failure to fulfill role obligations at home, work, or school		Abuse
<i>Social/personal</i>	continue to use despite social or interpersonal problems caused or exacerbated by effects of the substance; examples include violent arguments, child abuse, physical fights		Abuse
<i>Activities given up</i>	Important social, occupational, or recreational activities given up or reduced because of use		Dependence
Risky use			
<i>Hazardous use</i>	Recurrent use in situations where it is physically hazardous, such as driving, operating machinery	Tobacco: smoking in bed, around flammable chemicals. This may also apply to other substances that are smoked, such as cannabis, opioids, and stimulants.	Abuse
<i>Physical/psychological</i>	Continue use despite knowing that use causes or exacerbates a persistent or recurrent physical or psychological problem	Specific disorders for different substances, but underlying similarity is the failure to abstain despite substance use causing difficulty	Dependence
Physiological/Pharmacological criteria^c			
<i>Tolerance</i>	Requiring a markedly higher dose to achieve desired effect or markedly lower effect with usual dose	Tobacco: often indicated by no longer feeling nauseous or dizzy with use, or more intense effect the first time used during the day ^d	Dependence
<i>Withdrawal</i>	Substance specific withdrawal symptoms or use of substance or similar substance to avoid or relieve withdrawal symptoms.	Substance specific withdrawal symptoms (Table 5); not included for hallucinogens and inhalants	Dependence

^a A DSM-5 SUD is diagnosed by the presence of 2 or more criteria within 12-months, with severity indicated by number of criteria endorsed: 2–3 (mild), 4–5 (moderate), 6 or more (severe).

^b DSM-IV dependence was diagnosed with the presence of 3 or more criteria occurring within 12-months; abuse was diagnosed with the presence of 1 or more criteria in the absence of dependence, and included a fourth abuse criterion (“continued to use despite legal problems”) that was not included in DSM-5.

^c physiological/pharmacological criteria that develop during the course of appropriate medical treatment do not count towards a SUD diagnosis. These can count towards a SUD diagnosis if the substances are used inappropriately (other than how they are prescribed). Medical usage may be appropriate for the following substances: cannabis (nausea due to chemotherapy, weight loss in AIDs patients); amphetamine or related stimulants (attention-deficit/hyperactivity, narcolepsy, obesity); opioids (analgesics); hallucinogens (emerging use for major depression (Abdallah et al., 2015)); and sedatives/tranquilizers (sleep disorders, anti-anxiety). Medical usage not indicated for alcohol, tobacco, cocaine, or inhalants.

^d Some studies use alternate definitions, such as those based on amount of cigarettes smoked (DiFranza et al., 2010).

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Table 2

Test-retest reliability (kappa) for DSM-IV and DSM-5 substance use disorder (SUD) diagnoses.

	DSM-IV dependence^a	DSM-IV dependence or abuse^b	DSM-5 SUD^c
Alcohol	0.63–0.82 (Hasin et al., 2006); 0.87 (Pierucci-Lagha et al., 2005)	0.70–0.76 (Hasin et al., 2006); 0.83 (Pierucci-Lagha et al., 2005)	0.40 (Regier et al., 2013); 0.60–0.62 (Grant et al., 2015)
Cannabis	0.50–0.94 (Hasin et al., 2006); 0.66–0.69 (Pierucci-Lagha et al., 2005)	0.70–0.78 (Hasin et al., 2006); 0.65–0.71 (Pierucci-Lagha et al., 2005)	0.41 (Grant et al., 2015)
Stimulants-cocaine	0.61–0.99 (Hasin et al., 2006); 0.78–0.92 (Pierucci-Lagha et al., 2005)	0.68–0.91 (Hasin et al., 2006); 0.89–0.97 (Pierucci-Lagha et al., 2005)	0.53 (Grant et al., 2015)
Stimulants-other	0.51–0.92 (Hasin et al., 2006); 0.64–0.66 (Pierucci-Lagha et al., 2005)	0.52–0.56 (Pierucci-Lagha et al., 2005)	0.54 (Grant et al., 2015)
Tobacco	0.60–0.64 (Hasin et al., 2006); 0.63–0.89 (DiFranza et al., 2010); 0.96–0.97 (Pierucci-Lagha et al., 2005)	N/A	0.50–0.87 (Grant et al., 2015)
Opioids	0.59–0.96 (Hasin et al., 2006); 0.97–1.0 (Malison et al., 2011); 0.91–0.94 (Pierucci-Lagha et al., 2005)	0.66–0.80 (Hasin et al., 2006); 0.82–0.88 (Pierucci-Lagha et al., 2005)	0.40–0.47 (Grant et al., 2015)
Hallucinogen	0.49–0.54 (Hasin et al., 2006)	0.69 (Cottler et al., 2009)	Prevalence very low (Grant et al., 2015)
Sedatives/tranquilizers	0.57–0.95 (Hasin et al., 2006); Prevalence very low (Pierucci-Lagha et al., 2005)	0.50–0.56 (Pierucci-Lagha et al., 2005)	Prevalence very low (Grant et al., 2015)
Inhalants	0.47 (Ridenour et al., 2007)	0.76 (Ridenour et al., 2007)	Prevalence very low (Grant et al., 2015)

^aDSM-IV dependence diagnosed by presence of 3 or more dependence criteria occurring together within a twelve month period (American Psychiatric Association, 2000)

^bDSM-IV abuse diagnosed by presence of 1 or more abuse criteria in the absence of dependence; N/A for tobacco (American Psychiatric Association, 2000)

^cDSM-5 substance use disorder diagnosed by 2 or more criteria occurring together within a twelve month period (American Psychiatric Association, 2013)

Table 3

Item Response Theory (IRT) studies on DSM-IV/DSM-5 Substance Use Disorder Criteria (adapted from (Hasin et al., 2013b))

Authors, year	Sample/survey type ^a	Country	Sample size	Diagnostic instrument ^b	Peak information ^c	Unidimensionality shown?
ALCOHOL						
Langenbucher et al. 2004	Adult, clinical	USA	372	CIDI-SAM	Moderate	Yes
Martin et al. 2006	Adolescent, clinical	USA	464	SCID	Moderate	Yes
Saha et al. 2006	Adult, general population (NESARC)	USA	20846	AUDADIS-IV	Moderate-to-severe	Yes
Saha et al. 2007	Adult, general population (NESARC)	USA	20846	AUDADIS-IV	Moderate-to-severe	Yes
Gelhorn et al. 2008	Adolescent, mixed	USA	5587	CIDI-SAM	Moderate-to-severe	Yes
Harford et al. 2009	Adolescent, general population (NSDUH)	USA	133231	Survey-specific instrument	Moderate-to-severe	Yes
Wu et al. 2009b	Adult, clinical	USA	462	DSM-IV checklist	Moderate	Yes (dependence)
Borges et al. 2010	Adult, ER	Argentina, Mexico, Poland, USA	3191	Adapted CIDI	Moderate-to-severe	Yes
Cherpitel et al. 2010	Adult, ER	Arg, Mex, Pol, USA	5195	CIDI	Moderate-to-severe	Yes
Shmulewitz et al. 2010	Adult, general population	Israel	1160	AUDADIS-IV	Moderate-to-severe	Yes
Beseler et al. 2010	Adolescent, general population	USA	353	11-item self report measure (based on DSM criteria)	N/A	Yes
Keyes et al. 2011a	Adult, general population (NLAES)	USA	18352	AUDADIS-IV	Moderate-to-severe	Yes
Borges et al. 2011	Adult, ER	Arg, Mex, Pol, USA	3191	CIDI	N/A	Yes
McCutcheon et al. 2011	Adult, mixed (COGA)	USA	8605	SSAGA	Moderate-to-severe	Yes
Mewton et al. 2011a	Adult, general population (NSMHWB)	Australia	7746	CIDI Version 2.0 (modified)	Moderate-to-severe	Yes
Mewton et al. 2011b	Adolescent, general population (NSMHWB)	Australia	853	CIDI Version 2.0 (modified)	Moderate-to-severe	Yes
Hagman and Cohn 2011	Adolescent, general population	USA	396	Survey-specific instrument	Moderate-to-severe	Yes
Gilder et al. 2011	Adult, general population (American Indians)	USA	530	SSAGA	Moderate	Yes
Hasin et al. 2012	Adult, clinical	USA	543	PRISM	Moderate	Yes
Rose et al. 2012	Adolescent, general population (NSDUH)	USA	9356	Survey-specific instrument	Moderate	Yes

Authors, year	Sample/survey type ^a	Country	Sample size	Diagnostic instrument ^b	Peak information ^c	Unidimensionality shown?
Ehrlke et al. 2012	Adolescent, general population (NSDUH)	USA	4,605	Survey-specific instrument	Moderate-to-severe	Yes
Casey et al. 2012	Adult, general population (NESARC)	USA	22177	AUDADIS-IV	Moderate-to-severe	Yes
Edwards et al. 2013	Adult, general population	USA	7454	SCID	N/A	Yes
Kuehbs et al. 2013	Adult, general population (NSDUH)	USA	3412	Survey-specific instrument	Moderate-to-severe	Yes
Derringer et al. 2013	Adult, mixed	USA	6597	SSAGA, CIDI-SAM	N/A	Yes (dependence)
Hagman and Cohn 2013	Adult, general population (NSDUH)	USA		Survey-specific instrument	N/A	Yes
Wu et al. 2013	Adult, clinical	USA	476	DSM-IV Checklist	N/A	Yes (dependence)
Preuss et al. 2014	Adult, mixed	Australia, Brazil, Canada, Finland, Japan	1424	AUDADIS	N/A	Yes
Castaldelli-Maia et al. 2015	Adult, general (SPMHS)	Brazil	936	CIDI	N/A	Yes
CANNABIS						
Langenbucher et al. 2004	Adult, clinical	USA	262	CIDI-SAM	Moderate	Yes
Martin et al. 2006	Adolescent, clinical	USA	417	SCID	Moderate	Yes
Gillespie et al. 2007	Adult, general population	USA	2337	SCID	N/A	Yes
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	8933	AUDADIS-IV	N/A	Yes
Hartman et al. 2008	Adolescent, mixed	USA	5587	CIDI-SAM	Moderate-to-severe	Yes
Wu et al. 2009b	Adult, clinical	USA	311	DSM-IV checklist	Moderate	Yes (dependence)
Compton et al. 2009	Adult, general population (NESARC)	USA	1603	AUDADIS-IV	Moderate-to-severe	Yes
Mewton et al. 2010	Adult, general population	Australia	722	CIDI	N/A	Yes
Piontek et al. 2011	Adolescent, general population (SHCDDP)	France	3641	M-CIDI	Moderate-to-severe	Yes
Hasin et al. 2012	Adult, clinical	USA	340	PRISM	Moderate	Yes
Wu et al. 2012	Adult, general population (NSDUH)	USA	6917	Survey-specific instrument	Moderate-to-severe	Yes
Gizer et al. 2013	Adult, general population	USA	1134	SSAGA	N/A	Yes
Derringer et al. 2013	Adult, mixed	USA	6597	SSAGA, CIDI-SAM	N/A	Yes (dependence)
Wu et al. 2013	Adult, clinical	USA	316	DSM-IV Checklist	N/A	Yes (dependence)
STIMULANTS						
<i>Cocaine</i>						

Authors, year	Sample/survey type ^a	Country	Sample size	Diagnostic instrument ^b	Peak information ^c	Unidimensionality shown?
Langenbucher et al. 2004	Adult, clinical	USA	225	CIDI-SAM	Moderate	Yes
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	2672	AUDADIS-IV	N/A	Yes
Gillespie et al. 2007	Adult, general population	USA	773	SCID	N/A	Yes
Wu et al. 2009a	Adult, clinical	USA	366	DSM-IV checklist	Moderate	Yes (dependence)
Hasin et al. 2012	Adult, clinical	USA	483	PRISM	Moderate	Yes
Saha et al. 2012	Adult, general population (NESARC)	USA	2528	AUDADIS-IV	Moderate	Yes
Derringer et al. 2013	Adult, mixed	USA	6597	SSAGA, CIDI-SAM	N/A	Yes (dependence)
Wu et al. 2013	Adult, clinical	USA	683	DSM-IV Checklist	N/A	Yes (dependence)
Others (amphetamines, etc.)						
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	2025	AUDADIS-IV	N/A	Yes
Gillespie et al. 2007	Adult, general population	USA	850	SCID	N/A	Yes
Saha et al. 2012	Adult, general population (NESARC)	USA	1750	AUDADIS-IV	Moderate	Yes
Wu et al. 2013	Adult, clinical	USA	166	DSM-IV Checklist	N/A	Yes (dependence)
Cocaine or methamphetamine						
Gilder et al. 2014	Adult, general population (American Indians)	USA	353	SSAGA	Moderate	Yes
TOBACCO						
Strong et al. 2009	Adolescent, general population	USA	296	Survey-specific instrument	Moderate-to-severe	Yes (dependence)
Saha et al. 2010	Adult, general population (NESARC)	USA	7852	AUDADIS-IV	Moderate	Yes (dependence)
Rose and Dierker 2010	Adolescent, general population (NSDUH)	USA	2758	Survey-specific instrument	Moderate-to-severe	Yes (dependence)
McBride et al. 2010	Adult, general population (NESARC)	USA	6185	AUDADIS-IV	Moderate	Yes (dependence)
Shmulewitz et al. 2011	Adult, general population	Israel	727	AUDADIS-IV	Moderate	Yes
Strong et al. 2012	Adolescent, general population	USA	556	Survey-specific instrument	Moderate	Yes (dependence)
Chung et al. 2012	Adolescent, clinical	USA	471	SCID	N/A	Yes
OPIOIDS						
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	2060	AUDADIS-IV	N/A	Yes
Gillespie et al. 2007	Adult, general population	USA	294	SCID	N/A	Yes
Wu et al. 2009c	Adolescent, general population (NSDUH)	USA	1290	Survey-specific instrument	N/A	Yes

Authors, year	Sample/survey type ^a	Country	Sample size	Diagnostic instrument ^b	Peak information ^c	Unidimensionality shown?
Wu et al. 2009 ^a	Adult, clinical	USA	354	DSM-IV checklist	Moderate	Yes (dependence)
Wu et al. 2011	Adult, general population (NSDUH)	USA	2824	Survey-specific instrument	N/A	Yes
Hasin et al. 2012	Adult, clinical	USA	364	PRISM	Moderate	Yes
Saha et al. 2012	Adult, general population (NESARC)	USA	1815	AUDADIS-IV	N/A	Yes
Wu et al. 2013	Adult, clinical	USA	449	DSM-IV Checklist	N/A	Yes (dependence)
HALUCINOGENS						
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	2525	AUDADIS-IV	N/A	Yes
Gillespie et al. 2007	Adult, general population	USA	643	SCID	N/A	Yes
Wu et al. 2010	Adolescent, general population (NSDUH)	USA	1548	Survey-specific instrument	Moderate-to-severe	Yes
Kerridge et al. 2011	Adult, general population (NESARC)	USA	2176	AUDADIS-IV	Moderate-to-severe	Yes
SEDATIVES/TRANQUILIZERS						
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	1896 (sed); 1487 (tran)	AUDADIS-IV	N/A	Yes
Gillespie et al. 2007	Adult, general population	USA	542	SCID	N/A	Yes
Saha et al. 2012	Adult, general population (NESARC)	USA	1609 (sed); 1301 (tran)	AUDADIS-IV	Moderate-to-severe	Yes
INHALANTS						
Lynskey and Agrawal 2007	Adult, general population (NESARC)	USA	728	AUDADIS-IV	N/A	Yes
Perron et al. 2010	Adolescent, clinical	USA	279	DIS-IV	N/A	Yes
Kerridge et al. 2011	Adult, general population (NESARC)	USA	664	AUDADIS-IV	Moderate-to-severe	Yes
Ridenour et al. 2014	Adolescent, young adult	USA	162	CIDI-SAM	N/A	Yes

^a abbreviations used for sample/survey types: NESARC: National Epidemiological Survey on Alcohol and Related Conditions (US); NLAES: National Longitudinal Alcohol Epidemiologic Survey (US); NSDUH: National Survey on Drug Use and Health (US); NSMHWB: National Survey of Mental Health and Well-Being (Australia); SPMHS: São Paulo Megacity Health Survey (Brazil); ER: Emergency Room; COGA: Collaborative Study on the Genetics of Alcoholism (US); SHCDDP: Survey on Health and Consumption during the Day of Defense Preparation (France)

^b abbreviations used for diagnostic instrument: CIDI-SAM: Composite International Diagnostic Interview - Substance Abuse Module; SCID: Structured Clinical Interview for the DSM; AUDADIS-IV: Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; SSAGA: Semi-Structured Assessment for the Genetics of Alcoholism; PRISM: Psychiatric Research Interview for Substance and Mental Disorders

^c area of greatest information: moderate, around the mean of the continuum (0); moderate-to-severe, around 1.5 standard deviations above the mean or higher. N/A indicates that no total information curves were shown or total (aggregate) information was not reported on explicitly in the paper.

Table 4
Differential item functioning (DIF) for DSM-IV/DSM-5 Substance Use Disorder Criteria

Authors, year	Study #	Sex	Age	Race/ethnicity	Criteria tested
ALCOHOL					
Martin et al. 2006	1	D6. Activities given up D7. Physical/Psychological A2. Hazardous Use	Not tested	Not tested	D1-D7 A1-A3
Saha et al. 2006	2	D2. Withdrawal D3. Larger/longer A1. Neglect roles A2. Hazardous use A3. Social/personal	D1. Tolerance D2. Withdrawal D3. Larger/longer D4. Quit/control D5. Time spent D6. Activities given up A1. Neglect roles	D1. Tolerance D3. Larger/longer D4. Quit/control A2. Hazardous use	D1-D7 A1-A3
Harford et al. 2009	3	D7. Physical/Psychological A2. Hazardous use	(by sex) D1. Tolerance D2. Withdrawal D3. Larger/longer D4. Quit/control D5. Time spent D6. Activities given up D7. Physical/Psychological A1. Neglect roles A2. Hazardous use	(by sex) D1. Tolerance D2. Withdrawal D4. Quit/control D6. Activities given up D7. Physical/Psychological A1. Neglect roles A2. Hazardous use	D1-D7 A1-A3
Wu et al. 2009b	4	None	None	None	D1-D7
Borges et al. 2010	5	Not tested	Not tested	D2. Withdrawal D3. Larger/longer D4. Quit/control D5. Time spent A1. Neglect roles A3. Social/personal	D1-D7 A1-A3
Cherpitel et al. 2010	6	Not tested	Not tested	D2. Withdrawal D4. Quit/control A1. Neglect roles	D1-D7 A1-A3 Craving
Shmulewitz et al. 2010	7	A3. Social/personal	None	D1. Tolerance D5. Time spent D7. Physical/Psychological A3. Social/personal	D1-D7 A1-A3
Keyes et al. 2011a	8	None	None	Craving	Craving
Mewton et al. 2011a	9	A2. Hazardous use Craving	D1. Tolerance D4. Quit/control A2. Hazardous use	Not tested	D1-D7 A1-A3 Craving

Authors, year	Study #	Sex (by age) None	Age	Race/ethnicity	Criteria tested
Mewton et al. 2011b	10	D1. Tolerance D4. Quit/control A2. Hazardous use	Not tested	D1-D7 A1-A3 Craving	
Gilder et al. 2011	11	D6. Activities given up A2. Hazardous use	D1. Tolerance A2. Hazardous use	D1-D7 A1-A3	
Hasin et al. 2012	12	None	None	D1-D7 A1-A3 Craving	
Ehlke et al. 2012	13	D1. Tolerance A1. Neglect roles A2. Hazardous use	Not tested	D1-D7 A1-A3	
Casey et al. 2012	14	A2. Hazardous use	D4. Quit/control	D1. Tolerance D4. Quit/control A2. Hazardous use	
Kuerbis et al. 2013	15	D3. Larger/longer A1. Neglect roles	D1. Tolerance D4. Quit/control D5. Time spent D7. Physical/Psychological A2. Hazardous use A3. Social/personal	D1-D7 A1-A3	
Castaldelli-Maia et al. 2015	16	D2. Withdrawal	D2. Withdrawal D4. Quit/control D7. Physical/Psychological craving	D1-D7 A1-A3 Craving	
CANNABIS					
Martin et al. 2006	1	D7. Physical/Psychological A2. Hazardous use	Not tested	Not tested	D1, D3-D7 A1-A3
Wu et al. 2009b	4	None	None	None	D1-D7
Mewton et al. 2010	17	Not tested	None	Not tested	D1-D7 A1-A3
Piontek et al. 2011	18	D1. Tolerance D2. Withdrawal	Not tested	Not tested	D1-D7 A1-A3
Hasin et al. 2012	12	None	D1. Tolerance D5. Time spent D6. Activities given up D7. Physical/Psychological A1. Neglect roles A2. Hazardous use A3. Social/personal craving	None	D1, D3-D7 A1-A3 Craving
Wu et al. 2012	19	D3. Larger/longer D7. Physical/Psychological	Not tested	D1. Tolerance D5. Time spent	D1, D3-D7 A1-A3

Authors, year	Study #	Sex	Age	Race/ethnicity	Criteria tested
Gizer et al. 2013	20	Not tested	Not tested	D2. Withdrawal D7. Physical/Psychological A1. Neglect roles A2. Hazardous use A3. Social/personal	D1-D7 A1-A3
STIMULANTS					
<i>Cocaine</i>					
Wu et al. 2009a	21	None	None	D1. Tolerance D6. Activities given up	D1-D7
Hasin et al. 2012	12	None	None	D1. Tolerance D2. Withdrawal D3. Larger/longer D4. Quit/control D5. Time spent D6. Activities given up D7. Physical/Psychological A1. Neglect roles A2. Hazardous use A3. Social/personal	D1-D7 A1-A3 Craving
<i>Cocaine or methamphetamine</i>					
Gilder et al. 2014	22	D2. Withdrawal A2. Hazardous use	D1. Tolerance	Not tested	D1-D7 A1-A3 Craving
TOBACCO					
McBride et al. 2010	23	Not tested	D2. Withdrawal D4. Quit/control D5. Time spent D6. Activities given up D7. Physical/Psychological	Not tested	D1-D7
Shmulewitz et al. 2011	24	None	A2. Hazardous use	Craving	A1-A3 Craving
Strong et al. 2012	25	Not tested	D1. Tolerance D2. Withdrawal D4. Quit/control	Not tested	D1-D7 Craving
Chung et al., 2012	26	Not tested	D1. Tolerance D3. Larger/longer D4. Quit/control A3. Social/personal	Not tested	D1-D7 A1-A3 Craving
OPIOIDS					
Wu et al. 2009c	27	D2. Withdrawal	None	D5. Time spent D7. Physical/Psychological	D1-D7 A1-A3
Wu et al. 2009a	21	None	None	None	D1-D7

Authors, year	Study #	Sex	Age	Race/ethnicity	Criteria tested
Hasin et al. 2012	12	None	None	None	D1-D7 A1-A3 Craving
HALUCINOGENS					
Wu et al. 2010	28	A2. Hazardous use	A1. Neglect roles	D1. Tolerance D5. Time spent A2. Hazardous use	D1, D3-D7 A1-A3

Notes: Differential item functioning indicates that the criteria show significantly different severity estimates (have different likelihood of endorsement) in the demographic subgroups, at the same level on disorder severity. Criteria are numbered as following: DSM-IV dependence, D1: tolerance; D2: withdrawal; D3: larger/longer; D4: quit/control; D5: time spent; D6: activities given up; D7: physical/psychological; DSM-IV Abuse: A1: neglect roles; A2: hazardous use; A3: social/personal; Craving. The following studies tested DIF for each criterion but only to determine if the criterion DIF led to differential functioning of the entire criteria set, and did not report DIF results for each criterion: alcohol (Saha et al., 2007, Derringer et al., 2013); cannabis (Wu et al., 2009b, Compton et al., 2009, Derringer et al., 2013); stimulants (amphetamines (Saha et al., 2012), cocaine (Saha et al., 2012), Derringer et al., 2013); tobacco (Saha et al., 2010); opioids (Saha et al., 2012); hallucinogens (Kerridge et al., 2011); sedatives/tranquilizers (Saha et al., 2012); inhalants (Kerridge et al., 2011).

Table 5
 Withdrawal characteristics across substances^a. From (American Psychiatric Association, 2013, Hasin et al., 2006).

	Alcohol	Cannabis	Stimulants ^b	Tobacco	Opioids ^c	Sedatives/tranquilizers
Withdrawal symptoms, beginning after cessation of or reduction in heavy or prolonged use^c						
Sleep problems	✓ (insomnia)	✓ (insomnia, disturbing dreams)	✓ (insomnia, hypersomnia)	✓ (insomnia)	✓ (insomnia)	✓ (insomnia)
vivid, unpleasant dreams			✓			
nausea, vomiting	✓				✓	✓
transient visual, tactile, auditory hallucinations	✓					✓
psychomotor changes	✓ (agitation)		✓ (retardation, agitation)			✓ (agitation)
anxiety	✓	✓ (or nervousness)		✓		✓
seizures	✓ (generalized tonic-clonic)					✓ (grandmal)
irritability, anger		✓ (or aggression)		✓ (or frustration)		
Changes in weight/appetite		✓ (decreased appetite, weight loss)	✓ (increased appetite)	✓ (increased appetite)		
restlessness		✓		✓		
lacrimation, rhinorrhea					✓	
diarrhea					✓	
yawning					✓	
Mood changes		✓ (depressed)	✓ (dysphoric)	✓ (depressed)	✓ (dysphoric)	
fatigue			✓			
difficulty concentrating				✓		
<i>physical symptoms</i>						
abdominal pain		✓ Any counted as one symptom (when cause discomfort)				
shakiness/tremors	✓ (hand tremor)					✓ (hand tremor)
sweating	✓autonomic hyperactivity (sweating, fast pulse rate)				✓ pupillary dilation, piloerection, sweating	✓autonomic hyperactivity (sweating, fast pulse rate)
fever					✓	
chills						

	Alcohol	Cannabis	Stimulants ^b	Tobacco	Opioids ^c	Sedatives/tranquilizers
headaches						
Muscle aches					✓	
Number of symptoms required	2	3	3 (one must be dysphoric mood)	4	3	2
Time frame						
Onset	Several hours to a few days	Within one week	Few hours to several days	24 hours	Several minutes to several days (depends on drug type)	Several hours to a few days (depends on drug type)
Duration	4–5 days; anxiety, insomnia, autonomic dysfunction can last 3–6 months	1–2 weeks; sleep problems > 30 days	1–2 weeks (Zoric et al., 2010)	2–3 weeks	One week; chronic symptoms (dysphoria, insomnia) can last for months	Short acting substances, 4–5 days; long acting, a month, can last for several months

^aWithdrawal is not included for hallucinogens or inhalants

^bincludes cocaine, amphetamines and related substances, as in DSM-5

^cincludes heroin, analgesics, others, as in DSM-5; withdrawal can also begin after administration of opioid agonist

Table 6 Epidemiology of substance use and use disorders in the United States; prevalence of use, disorder, age at onset

Authors, Year	Study ^d	Population	N	Lifetime Use (%)	Age of First Use	Prevalence of disorder, relationship of age to disorder ^b
ALCOHOL						
Bracken et al. 2013	Clinical sample	Adolescents	939	N/R	13.2 (mean age)	N/R
Hingson et al. 2006	National survey (NESARC)	Adults (Wave 1)	43093	N/R	9% of users began 14; 17% at 15–16; 32% at 17–18; 15% at 19–20; 28% 21	Earlier drinking onset associated with increased dependence
Hingson and Zha, 2009	National survey (NESARC)	Adults (Wave 2)	39653	N/R	7% of users began 14; 17% at 15–16; 28% at 17–18; 15% at 19–20; 36% 21	Earlier drinking onset associated with increased AUDs
Kalaydjian et al. 2009	National Survey (NCS-R)	Adults	5692	91.7%	16–17 (median)	Age 21, median age for any AUD
Lopez-Quintero et al. 2011	National survey (NESARC)	Adults (ever used alcohol)	28907	100%	8% before 14	Early onset (< 14) not associated with increased dependence; 17% of users met criteria for dependence
Moss et al. 2014	National Survey (Add Health)	Adults (Wave 4)	4245	100%	15.1 (mean)	Earlier drinking onset associated with abuse and dependence
Ridenour et al. 2006	Longitudinal study (CEDAR)	Adolescents	590	N/R	14.6 (mean) 15.0 (median)	Prevalence of dependence: 15% of users
Sartor et al. 2013	Female twin study	Adolescents	3787	79%–88%	15.8 – 16.9 (mean)	AUD symptoms: 30%–39%
Trenz et al. 2012	Community sample (NEURO-HIV Epidemiologic Study)	Adolescents, adults, current drug users	651	71.1% (past 6 months)	13.4–14.6 (mean)	Early onset of drinking predicted injection drug use
CANNABIS						
Flory et al. 2004	Community sample (Project DARE)	Adolescents, young adults	481	N/R	18.5 (mean)	N/R
Haberstick et al. 2014	National longitudinal survey (Add Health)	Young adults	15,500	N/R	N/R	Earlier onset of use associated with increased CUD
Hasin et al. 2008	National survey (NESARC)	Adult frequent cannabis users	2613	100%	16.3 (mean)	N/R
Horey et al. 2012	Clinical sample	Adults in clinical trials for cannabis, cocaine dependence	242	N/R	15.1 (mean)	Mean age at first treatment = 29
Khan et al. 2013	National survey (NESARC)	Adults with a CUD	3297	100%	16.7 (mean)	18.9–19.3 (mean)
Le Strat et al. 2014	National survey (NESARC)	Adults, ever used cannabis	8068	100%	7% < 14; 83% < 21	Early onset of use associated with increased CUD

Authors, Year	Study ^a	Population	N	Lifetime Use (%)	Age of First Use	Prevalence of disorder, relationship of age to disorder ^b
Lopez-Quintero et al. 2011	National survey (NESARC)	Adults, ever used cannabis	7389	100%	14% < 14	Early onset (< 14) associated with decreased dependence; 7% of users met criteria for dependence
Moss et al. 2014	National Survey (Add Health)	Adults (Wave 4)	4245	100%	16 (mean)	Earlier onset of cannabis use associated with increased abuse and dependence
Ridenour et al. 2006	Longitudinal study (CEDAR)	Adolescents	590	N/R	15.7 (mean); 15.5 (median)	Prevalence of dependence: 16% of users
Sartor et al. 2013	Female twin study	Adolescents	3787	44.4%–49.7%	16 (mean)	CUD symptoms: 21.9%–27.9%
Trenz et al. 2012	Community sample (NEURO-HIV Epidemiologic Study)	Adolescent, adults, current drug users	651	52.4% (Past 6-month use)	13.4–15.0 (mean)	Early onset of cannabis use did not predict recent injection drug use
COCAINE						
Bracken et al. 2013	Clinical Sample	Adolescents	939	N/R	15.1 (mean)	N/R
Horey et al. 2012	Clinical Sample	Outpatients enrolled in clinical trials for cannabis or cocaine dependence	242	N/R	20.9 (mean)	34.3 (mean age at first treatment)
Lopez-Quintero et al. 2011	National survey (NESARC)	adults who used cocaine at least once	2259	100%	2% < 14	Early use onset (< 14) associated with decreased dependence; 17% of users met criteria for dependence
Ridenour et al. 2006	Longitudinal study (CEDAR)	Adolescents	590	N/R	18.9 (mean); 18.5 (median)	Prevalence of dependence: 24% of users
Sartor et al. 2014	Clinical sample	Adults	9846	N/R	19.1–22.6 (mean)	22.6–33 (mean)
INHALANTS						
Perron et al. 2009	National survey (NESARC)	adults who used inhalants at least once	664	100%	17.5 (mean); 16.2 (median)	Abuse: 17 (mean); Dependence: 16.8 (mean)
Wu et al. 2008	National survey (NESARC)	Adults	43,093	1.7%	17.5 (mean)	19% of users met criteria for IUD
OPIOIDS						
Ridenour et al. 2006	Longitudinal study (CEDAR)	Adolescents	590	N/R	18.1 (mean) 18.0 (median)	Prevalence of dependence: 21% of users
Sartor et al. 2014	Clinical sample	Adults	9846	N/R	18.5–23.8 (mean)	22.5–31.1 (mean)
TOBACCO						
Lopez-Quintero et al. 2011	National survey (NESARC)	adults who used tobacco at least once	15918	100%	31% < 14	Early onset (< 14) associated with increased dependence; 46% of users met criteria for dependence
Moss et al. 2014	National Survey (Add Health)	Adults (Wave 4)	4245	100%	17 (mean)	Earlier smoking onset (< 14) predicted dependence

Authors, Year	Study ^a	Population	N	Lifetime Use (%)	Age of First Use	Prevalence of disorder, relationship of age to disorder ^b
Ridenour et al. 2006	Longitudinal study (CEDAR)	Adolescents	590	N/R	14.5 (mean); 14.5 (median)	Prevalence of dependence: 8% of users
Trenz et al. 2012	Community sample (NEURO-HIV Epidemiologic Study)	Adolescent, adults, current drug users	651	Past 6-month use: 89.2%	13.7–15.0 (mean)	Early onset of smoking (<15 years) did not predict recent injection drug use

N/R: Not Reported

^a abbreviations used to define the Study type: NESARC: National Epidemiological Survey on Alcohol and Related Conditions (USA); NCS-R: National Comorbidity Survey Replication (USA); Add Health: National Longitudinal Study of Adolescent to Adult Health (USA); CEDAR: Center for Education and Drug Abuse Research (USA); Project DARE: Drug Abuse Resistance Education (US)

^b abbreviation used for disorder type: AUD: any alcohol use disorder (abuse or dependence); CUD: any cannabis use disorder; IUD: any inhalant use disorder

Table 7

Prevalence of lifetime substance use and DSM-IV disorders, age of onset of use and disorders, in Wave 1 of the NESARC (N=43,093)

Substance	% Lifetime Use	Age of First Use		% Lifetime Abuse ^b		Among those with abuse		% Lifetime dependence ^c		Among those with dependence	
		Median	Range (1%-99%)	Whole set	Among users	Median age of first use	Median age of abuse onset	Whole set	Among users	Median age of first use	Median age of dependence onset
Alcohol	82.7	17.8	8-44	17.8	21.5	19.6	17.1	12.5	15.1	16.2	20.4
Cannabis	20.6	16.6	9-37	7.2	34.8	17.5	15.9	1.3	6.3	15.0	17.6
Cocaine	6.2	19.8	13-42	1.8	29.8	20.2	19.3	1.0	16.0	19.7	21.9
Stimulants	4.7	17.4	11-36	1.4	30.1	18.1	17.1	0.6	13.0	16.6	18.7
Tobacco ^a	46.9	15.3	6-31	N/A	N/A	N/A	N/A	17.7	37.8	14.7	26.5
Opioids	4.9	19.4	10-67	1.1	23.5	17.9	17.9	0.4	8.5	18.0	18.4
Sedatives/tranquilizers	5.4	19.4	8-67	1.1	20.3	17.4	17.3	0.3	6.3	17.8	17.9
Inhalants	1.7	16.2	7-36	0.3	17.2	15.7	15.3	0.04	2.3	13.7	14.8
Hallucinogens	5.8	17.3	12-33	1.5	25.0	17.4	16.6	0.2	4.2	15.9	17.5

^aTobacco: cigarette use only, since other forms (cigars, chewing tobacco, snuff) were very rarely used^bDSM-IV abuse diagnosed by presence of 1 or more abuse criteria in the absence of dependence; N/A for tobacco (American Psychiatric Association, 2000)^cDSM-IV dependence diagnosed by presence of 3 or more dependence criteria occurring together within a twelve month period (American Psychiatric Association, 2000)

Table 8

Prevalence of lifetime substance use and age of onset of use and disorders, among adult respondents (age 18 and above), in NSDUH 2013 (N=37,424)

	% Lifetime use	Age at First Use, Median	1% – 99% of age at first use
Alcohol	86.8%	16.3	6 – 32
Cannabis	46.9%	16.5	9 – 41
Cocaine	15.8%	19.7	12 – 44
Stimulants	8.3%	18.4	12 – 45
Tobacco (cigarettes)	66.7%	15.2	6 – 30
Opioids	2.1%	19.9	8 – 54
Sedatives/tranquilizers	9.7%	20.2	11 – 60
Inhalants	8.3%	16.8	7 – 39
Hallucinogens	16.7%	17.7	12 – 41

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