

Assessing cannabis dependence in community surveys: methodological issues

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Abstract

Drug-related social role impairments and social maladaptation are referenced explicitly in the case definitions for drug dependence within DSM-IV-TR. Nonetheless, cases of drug dependence without this type of secondary consequence have been observed in recent epidemiological studies. When an ‘impairment/maladaptation gating’ approach has been taken during recent large-scale psychiatric surveys (for example, to reduce participant fatigue or burden), the net effect may include (a) a reduced number of identified drug dependence cases and (b) biases in the estimates of association linked to the occurrence of drug dependence. In this report, we probe these issues with respect to cannabis dependence, making use of data from the cross-sectional United States National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a household survey of 43,093 adults aged 18 years and over. In this process, we shed light on actual impact of the gating approach mentioned above. Specifically, when we simulated a social impairment/maladaptation ‘gated’ assessment of cannabis dependence, the end result was a very modest reduction in the estimated prevalence of cannabis dependence. It suggested that for every 10 000 general population survey respondents there would be no more than 12 cases of cannabis dependence without the above-referenced impairments/maladaptations. Patterns of association linking suspected background characteristics to the prevalence of cannabis dependence were not appreciably different when the ‘gated’ and ‘ungated’ approaches were applied. In summary, there are reasons to take the ungated approach in detailed research on cannabis use and dependence. Nevertheless, in panoramic mental health surveys, the inefficiency of an ‘ungated’ approach must be balanced against the anticipated yield of cannabis dependence cases who lack social role impairments or socially maladaptive behaviours. Copyright © 2007 John Wiley & Sons, Ltd.

Key words: epidemiological research, psychiatric diagnostic interview, cannabis, dependence

Introduction

Hasin et al. (2005) commented that drug dependence might occur in the absence of drug-related social role impairments or socially maladaptive behaviours. They also provided data, based upon structured diagnostic assessments made according to the American Psychiatric Association’s Diagnostic and Statistical Manual, Fourth Edition Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000), suggesting that the estimated prevalence of drug dependence in the US is somewhat reduced when case ascertainment methods require at least one

drug-related social role impairment or socially maladaptive behaviour before DSM-IV drug dependence can be diagnosed.

Separately, members of our research group have noted that it might now be time to ask whether the apparently chronic and seriously impairing natural history of drug dependence is a consequence of delayed effective clinical intervention. In this way, drug-related social role impairments and social maladaptation would best be regarded as secondary complications in the context of the process of becoming drug dependent (Anthony et al., 2005).

Questions of this type pertain both to case definitions (or 'diagnostic criteria') and to modes of assessment. With respect to case definition, there have been conflicting views about the role of 'impairment' in drug dependence. The World Health Organization's most recent International Classification of Diseases defines drug dependence as a drug-induced state, with no requirement for evidence of associated social role impairments or maladaptation (World Health Organization, 1993). Empirical evidence reported by Hasin et al. (2005) is in this tradition.

In contrast, the American tradition – specifically, the DSM-III – specified impairments in social or occupational functioning as one criterion for certain forms of drug dependence (which included cannabis dependence), as manifest in 'marked loss of interest in activities, loss of friends, absence from work, loss of job, or legal difficulties (other than due to a single arrest for possession, purchase, or sale of an illegal substance)' (American Psychiatric Association, 1980). Of course, for some forms of drug dependence (such as tobacco dependence) there was no requirement for this type of impairment or maladaptation.

Within the more recent DSM-IV and DSM-IV-TR, drug-related maladaptation and impairments are referenced explicitly in the definition of drug dependence (American Psychiatric Association, 2000). Clinically significant impairment is allowed to be exchangeable with a separate clinically significant 'distress' phenomenon, as expressed here: '[Drug dependence is] A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following [criteria] . . .' (p. 197) (American Psychiatric Association, 2000).

With respect to modes of assessment, the earliest standardized interview schedules for epidemiological field research followed the prevailing case definitions and often presumed that drug dependence syndromes would not be present without accompanying social role impairments or socially maladaptive behaviours. For example, in the Diagnostic Interview Schedule, detailed questions on the alcohol withdrawal syndrome and 'benders' were asked only when the drinker had reported difficulties with family, at work, or other related impairments or maladaptation. The logic behind this kind of impairment/maladaptation 'gating' of assessment was (a) that a drinker would not have experienced these signs of serious dependence if impairment or maladaptation had not occurred, and (b) that many

non-dependent drinkers would be annoyed by the line of detailed questioning if all were required to answer all of these questions (L.N. Robins, personal communication). A similar 'gating' logic guided the development of the standardized interview schedule used in the WHO World Mental Health Consortium surveys, which is an adaptation of the original Composite International Diagnostic Interview (R.C. Kessler, personal communication). This type of 'gating' in the assessment of drug dependence often surfaces in panoramic mental health surveys, where the task is to assess many different forms of psychiatric and behavioural disturbances during a single session, within which the drug dependence syndromes are just one of many topics being covered.

Fortunately, there is an 'ungated' approach to assessment of drug dependence, without these 'shortcuts', which allows for examination of dependence symptom profiles (Degenhardt et al., 2002; Hasin et al., 2005). The 'ungated' approach may be preferred in surveys focused primarily upon problems of alcohol and other drug dependence, such as the National Epidemiological Survey on Alcohol and Related Conditions (Grant et al., 2003; Hasin et al., 2005). Clearly, such an 'ungated' approach is essential if research is to be conducted on the possibility that drug-related social role impairments and socially maladaptive behaviour are consequences of drug dependence left untreated for long spans of time, as we have argued elsewhere (Anthony et al., 2005).

Availability of the NESARC public use dataset made it possible to launch an initial inquiry into the characteristics of persons who have met criteria for cannabis dependence but who have reported no drug-related impairments or maladaptation secondary to their cannabis use. The aims of this inquiry were fairly simple, and were organized in order to shed light on what we might find if we were to undertake epidemiological research on the natural history and clinical course of cannabis dependence with and without impairments and maladaptation, in that cannabis use and dependence have emerged as serious public health concerns in the US, Australia, and elsewhere (Grant and Pickering, 1998; Fergusson et al., 2000; Swift et al., 2001; Coffey et al., 2002).

Aims

1. To estimate the prevalence of cannabis dependence, according to 'gated' and 'ungated' assessments

of the syndrome, and to estimate the size of epidemiological sample that might be required in order to identify cases of cannabis dependence that lack cannabis-related impairment and maladaptation, for subsequent investigation of the emergence of secondary impairments and socially maladaptive behaviour.

2. To compare geographical clustering of 'gated' and 'ungated' cannabis dependence within counties and states of the US, given good evidence of local area clustering of cannabis involvement (Bobashev and Anthony, 1998).
3. To examine whether the observed patterns of association of background characteristics with 'gated' cannabis dependence are markedly different from those with 'ungated' cannabis dependence.

Methods

Sample

This study is based upon US data from NESARC, a population-based, face-to-face survey of 43 093 participants aged 18 years and older. The sample was recruited from a prior US Census Supplementary Survey sample (C2SS) that had been interviewed in 2000/1. Participant sampling and interviewing were conducted by the US Census Bureau (Stetser et al., 2002), after pre-screening of households as described below.

Sampling method: NCSS

The Census Bureau's C2SS sample had been recruited from all counties and county equivalents across the US, with over-sampling of communities of size 250 000 or greater. More details of the sampling strategy for that survey are given in detail by Stetser and colleagues (Stetser et al., 2002), but the multistage sampling process they describe is outlined below.

The universe of primary sampling units (PSUs) consisted of 3 142 counties and county-equivalents in the US. The C2SS sample PSUs included 42 counties selected with certainty to serve as comparison counties with the 2000 Decennial Census. The remaining PSUs were included in the 'National Sample': PSUs with a 1996 population of 250 000 or more were selected as self-representing (SR), and all other PSUs were designated as non-self-representing (NSR) and stratified within states by several demographic characteristics including: population and housing growth, education, poverty, housing and rural characteristics, and

Hispanic and Black populations (in some states). From each stratum, two NSR PSUs were selected with a probability that was proportional to the size of the estimated 1996 population (Stetser et al., 2002).

Once the sample PSUs were determined, a 'housing unit' (HU) frame was constructed (Stetser et al., 2002). The unit frame within-PSU sampling occurred in two stages. In stage one, 17.5% of HU were selected; and in stage two, a systematic sample of HU was used to reach the required sample size for that county. The C2SS sample was interviewed between November 2000 and March 2001.

Sampling method: NESARC

The NESARC was intended to contain an overrepresentation of Black and Hispanic participants and it was intended to use the same design as the earlier National Longitudinal Alcohol Epidemiological Survey (NLAES) (Stetser et al., 2002). Identification of the NESARC sample through the C2SS was carried out in a manner that helped to achieve the desired number of Black and Hispanic participants (Stetser et al., 2002).

After completing the N2SS interviews used to secure basic census data, the US Census Bureau selected HU for NESARC sample selection. The NESARC sampling frame was restricted to vacant and occupied non-seasonal HU where there had been a prior response to the Bureau's prior C2SS survey (Stetser et al., 2002). The NESARC sampling frame was designed to exclude seasonally occupied houses, as well as dwelling units that generated a refusal for participation in the C2SS. Neither the C2SS nor NESARC sample included institutionalized, homeless or incarcerated individuals.

Information on race and ethnicity collected from the C2SS was used to sort the cases within each sample PSU into three substrata – Hispanic, Black, and other (all non-Black, non-Hispanic persons and those with missing race/ethnicity data were included here). Sample cases were selected from each substratum according to the desired sample sizes for Black and Hispanic cases.

Representative weights were constructed, which took the following into account: PSU selection probabilities, within-PSU selection probabilities, CAPI subsampling probabilities, and an adjustment for non-response in the C2SS. Housing units were selected proportional to these weights (Stetser et al., 2002). For each HU, field representatives listed persons 18 years and older and randomly selected one designated respondent (DR) from the roster. Persons age 18–24

had a probability of selection that was 2.25 times that of older persons in order to oversample young adults (Stetser et al., 2002).

Recruitment for NESARC took place between August 2001 and April 2002, a minimum of five months and perhaps as many as 18 months after the prior C2SS contact (Stetser et al., 2002). The response rate for eligible housing units in the NESARC has been reported as 81%. Further details on the interview, method and characteristics of the NESARC sample can be found elsewhere in publications by Grant and colleagues (Grant et al., 2001, 2003, 2004).

Measurements

The main response variable under study was case status with respect to recently active cannabis dependence defined by DSM-IV-TR criteria, with both cannabis use and a clustering of at least three manifestations of dependence within the 12 months prior to assessment; we also have combined cases of cannabis dependence with cases of non-dependent cannabis abuse, also defined by DSM-IV-TR criteria. As described above, NESARC assessments were via computer-assisted personal interviews (CAPI), with the 'ungated' approach. For comparative purposes, we simulated the 'gated' approach by recoding cannabis dependence cases as non-cases unless there was evidence of at least one manifestation of cannabis-related social role impairments, socially maladaptive behaviour, or other clinical features under the DSM-IV non-dependent cannabis abuse rubric. Background characteristics, including recently active (past year) DSM-IV-TR alcohol use disorders, were also assessed via CAPI standardized survey questions.

In the NESARC, cannabis dependence and abuse were assessed for all persons reporting cannabis use in the past 12 months. For this project, the following 'dependence' and 'use disorder' categories were generated:

1. Ungated assessment approach:
 - (a) Dependence: this group included all persons meeting criteria for DSM-IV dependence without regard for cannabis-related social impairments or other 'cannabis abuse' clinical features.
 - (b) Use disorders: this included persons meeting criteria for DSM-IV dependence or non-dependent abuse.
2. Gated assessment approach:
 - (a) Dependence: this group only included cannabis dependence cases with at least one clinical feature under the DSM-IV cannabis abuse rubric.
 - (b) Use disorders: this group included the 'gated' cannabis dependence cases, as well as cases of DSM-IV non-dependent abuse.

Analysis

Weighted prevalence estimates and their 95% confidence intervals were derived using Taylor series linearization with SUDAAN Version 9.0, which accommodates field survey samples with self-representing PSUs and accounts for other features of the complex survey sampling design (SAS Institute Inc., 2006). Prevalence estimates (and their 95% confidence intervals) were made according to sex, age group (18–24 years, 25–34 years, 35–44 years and 45 years and older), race-ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), and past year alcohol use disorder. Note that some group categories had to be collapsed due to the very small raw sample sizes for older age groups and some race-ethnicity subgroups. Multiple logistic regressions, which included all background variables in the models, also were run using SUDAAN 9.0, to derive estimates of strength of association (odds ratios).

As an aid to the reader, we have noted when there is overlap in the coverage of 95% confidence intervals for prevalence estimates from the 'gated' and 'ungated' approaches. Although this is not a formal significance test (because these are not independent samples), any overlap in this coverage signifies commonality of the two confidence regions.

Covariate-adjusted estimates of the odds ratios (OR) are presented in order to gauge the degree to which the observed associations are statistically independent from one another; the intent is not to make causal inferences from these cross-sectional data.

In addition to completing multiple logistic regressions described above, we conducted alternating logistic regressions (ALR), which take the survey design effect into account, while estimating a pairwise odds ratio (PWOR) as a statistical measure of geographic clustering at both the state and county levels, which is explicitly modelled (Bobashev and Anthony, 1998; Bobashev and Anthony, 2000; Petronis and Anthony, 2003). The geographic variables used in these analyses

were the PSU and state variables. As in the prevalence estimation and multiple logistic regression analyses described above, these analyses were repeated to allow comparison of results from the 'gated' and 'ungated' approaches.

Alternating logistic regression estimates yield population-averaged or 'marginal' model estimates of clustering when a sample has a multi-level structure; estimates from population-averaged models are related to but are not the same as corresponding estimates from subject-specific multi-level models.

Results

Dependence

Table 1 presents the estimated recently active prevalence of cannabis dependence according to 'ungated' and 'gated' assessments. As can be seen, the use of a 'gated' assessment of dependence resulted in a very slight reduction in the estimated population prevalence of dependence: 0.26%, compared to 0.32% (for a difference of only six cases per 10,000 people). The 95% confidence intervals (CI) for these prevalence proportions do not overlap; they touch one another ('ungated' CI: 0.29%, 0.36%; 'gated' CI: 0.23%, 0.29%).

An estimate was made of the size of the group that met criteria for dependence using 'ungated' assessment, but did not experience cannabis-related social role impairments or other clinical features of DSM-IV non-dependent cannabis abuse. It was estimated that the population prevalence of those meeting criteria for dependence in the absence of clinical features of non-dependent abuse was six per 10,000 (0.06%; 95% CI: 0.03%, 0.12%). Hence, to find 12 such cases in a community survey, one might have to sample and assess 10,000 community residents.

The ALR models did not suggest geographic clustering of cannabis dependence at either the county or state level. This was true for both 'gated' and 'ungated' approaches for cannabis dependence.

The estimated prevalence according to some key background characteristics suggested a slight reduction in prevalence estimates when a 'gated' definition of dependence was used, although in most instances there was overlap of 95% confidence intervals from 'gated' versus 'ungated' approaches (Table 1). The different approaches did not, however, appear to materially affect the associations across the background variables (Table 1). The adjusted ORs (and their 95% CI) were not

appreciably different across sex, age, race-ethnicity, and alcohol use disorders, regardless of the 'gated' versus 'ungated' approach. One exception to this general pattern was a small difference with respect to race: the adjusted OR for non-Hispanic Black persons (compared to non-Hispanic Whites) using the 'gated' approach was 1.98 (95% CI: 1.08, 3.63); for the 'ungated' approach; the OR estimate was 1.59 (95% CI: 0.90, 2.78).

Cannabis-use disorders

Table 2 presents the estimated prevalence and correlates of cannabis use disorders according to the two different assessment approaches. Here, we found no appreciable difference in the estimated population prevalence (and 95% CI) of cannabis-use disorders: 1.39% versus 1.45%, with substantially overlapping 95% confidence intervals. The estimated associations with age, sex, race-ethnicity and past year alcohol use disorders did not differ appreciably across 'gated' and 'ungated' approaches (Table 2).

For 'cannabis-use disorders' (both assessment approaches), there was evidence of statistically robust but quite modest geographical clustering at the county (but not state) level. The PWOR for county level clustering of 'ungated' cannabis-use disorders was 1.20 (95% CI: 1.08, 1.33; $p = 0.0004$), and that for the 'gated' assessment of cannabis-use disorders was 1.14 (95% CI: 1.05, 1.25; $p = 0.0018$).

Discussion

This paper examined the impact of 'gated' assessment of cannabis dependence upon the estimated population prevalence of cannabis dependence and use disorders. It also considered possible biases across key background variables, and variation with respect to geographic clustering.

First, with respect to the estimated prevalence of cannabis dependence and cannabis-use disorders according to 'gated' and 'ungated' approaches, we found no more than a modest difference: 0.32% by the 'ungated' approach and 0.26% by the 'gated' approach. Moreover, the 95% confidence intervals for the 'gated' and 'ungated' prevalence proportions touched; for the cannabis-use disorders estimates, there was appreciable overlap of the intervals. These results suggest that although some persons who meet criteria for DSM-IV dependence do not manifest clinical features of DSM-IV abuse, the size of the underestimates of dependence is relatively small.

Table 1. Estimated prevalence of recently active cannabis dependence by background characteristics, according to 'gated' and 'ungated' approaches. Data from the NESARC surveys, USA, 2001–2002 (unweighted sample size, $n = 43\,093$)¹

	Dependence – ungated approach				Dependence – gated approach ¹					
	%	95% CI ³	Adjusted OR	95% CI	<i>p</i>	%	95% CI ³	Adjusted OR	95% CI	<i>p</i>
<i>Cannabis dependence</i>	0.32	0.29, 0.36		1.06, 2.76	0.0286	0.26	0.23, 0.29		1.06, 2.93	0.0295
Males ($n = 18\,518$)	0.49	0.43, 0.54	1.71		0.0001	0.40	0.35, 0.45	1.76		–
Females ($n = 24\,575$)	0.17	0.14, 0.21	1		–	0.13	0.10, 0.17	1		–
18–24 years ($n = 21\,045$)	1.50	1.32, 1.68	15.32	6.30, 37.24	<0.0001	1.34	1.17, 1.51	14.10	5.30, 37.50	<0.0001
25–34 years ($n = 9090$)	0.38	0.31, 0.45	4.99	1.60, 15.62	0.0064	0.23	0.16, 0.29	3.10	1.02, 9.42	0.0464
35–44 years ($n = 7759$)	0.17	0.13, 0.22	2.59	0.87, 7.73	0.086	0.12	0.07, 0.16	1.93	0.54, 6.85	0.3034
45+ years ($n = 5199$)	0.05	0.02, 0.07	1		–	0.04	0.01, 0.07	1		–
Non-Hispanic White ($n = 24\,507$)	0.30	0.26, 0.33	1		–	0.22	0.19, 0.26	1		–
Non-Hispanic Black ($n = 8245$)	0.43	0.37, 0.49	1.59	0.90, 2.78	0.1059	0.38	0.32, 0.45	1.98	1.08, 3.63	0.0268
Hispanic ($n = 8308$)	0.26	0.23, 0.30	0.69	0.39, 1.24	0.2113	0.25	0.21, 0.29	0.89	0.48, 1.65	0.7055
Other ² ($n = 2033$)	0.57	0.32, 0.82	1.92	0.85, 4.32	0.1132	0.51	0.26, 0.75	2.34	1.00, 5.49	0.0512
Alcohol use disorder ($n = 3327$)	2.60	2.27, 2.93	12.61	6.40, 24.86	<0.0001	2.26	1.95, 2.57	16.34	8.89, 30.02	<0.0001
None ($n = 39\,766$)	0.11	0.09, 0.14	1		–	0.08	0.06, 0.10	1		–

¹Gating refers to the situation where dependence is only assessed if the participant endorses one or more clinical features of DSM-IV non-dependent abuse.

²Note that due to very small numbers, the categories of 'Asian', 'Native American' and other racial groups were combined into 'other'.

³Confidence intervals calculated using Taylor series linearization, adjusting for clustering using sampling strata and primary sampling units.

Table 2. Estimated prevalence of recently active cannabis use disorders by background characteristics, according to 'gated' and 'ungated' approaches. Data from the NESARC surveys, USA, 2001–2002 (unweighted sample size, $n = 43\,093$)¹

	Use disorders – ungated approach				Use disorders – gated approach ¹					
	%	95% CI ³	Adjusted OR	95% CI	p	%	95% CI ³	Adjusted OR	95% CI	p
<i>Cannabis use disorder²</i>	1.45	1.38, 1.52	1.99	1.59, 2.49	<0.0001	1.39	1.32, 1.46	2.01	1.60, 2.53	<0.0001
Males	2.19	2.06, 2.33				2.11	1.97, 2.24			
Females	0.77	0.71, 0.83				0.73	0.67, 0.79			
18–24 years	6.06	5.64, 6.48	13.97	8.96, 21.79	<0.0001	5.91	5.49, 6.33	13.73	8.73, 21.61	<0.0001
25–34 years	1.68	1.57, 1.79	4.36	2.72, 6.98	<0.0001	1.53	1.42, 1.63	3.99	2.48, 6.42	<0.0001
35–44 years	1.05	0.94, 1.17	2.99	1.88, 4.77	<0.0001	1.0	0.89, 1.12	2.88	1.79, 4.65	<0.0001
45+ years	0.27	0.22, 0.32	1	–	–	0.26	0.22, 0.31	1	–	–
Non-Hispanic white	1.40	1.31, 1.49	1	–	–	1.33	1.24, 1.42	1	–	–
Non-Hispanic Black	1.81	1.67, 1.95	1.38	1.03, 1.85	<0.0319	1.77	1.62, 1.92	1.43	1.07, 1.92	0.0181
Hispanic	1.23	1.15, 1.32	0.65	0.49, 0.87	0.0039	1.22	1.13, 1.30	0.69	0.52, 0.92	0.0113
Other ³	1.75	1.45, 2.05	1.23	0.74, 2.03	0.4236	1.69	1.39, 1.99	1.25	0.75, 2.09	0.3787
Alcohol use disorder	9.89	9.23, 10.54	9.03	7.04, 11.58	<0.0001	9.55	8.89, 10.21	9.20	7.31, 11.59	<0.0001
None	0.67	0.63, 0.71	1	–	–	0.63	0.60, 0.67	1	–	–

¹Gating refers to the situation where dependence is only assessed if the participant endorses one or more clinical features of DSM-IV non-dependent abuse.

²Note that for gated dependence assessment, 'cannabis use disorders' is effectively the same as 'cannabis abuse'.

³Note that due to small numbers, the categories of 'Asian', 'Native American' and other racial groups were combined into 'Other'.

⁴Confidence intervals calculated using Taylor series linearization, adjusting for clustering using sampling strata and primary sampling units.

Second, with respect to the size of epidemiological sample that would be required to identify cases of cannabis dependence who lack cannabis-related impairment and maladaptation, the answer is 'a very large number'. Even if we were to accept the upper bound of the 95% confidence limit as a working estimate for a sample size calculation, we would have to assess 10,000 adults in order to identify 12 such cases. It is beyond the scope of most, perhaps all, general population surveys of psychiatric disorders to conduct meaningful analysis with such a small group.

Third, with respect to the pattern of covariate associations, there did not appear to be differential bias across the background variables examined here. Indeed, the odds ratio patterns (and the prevalence estimates) showed little variation across the 'gated' and 'ungated' assessment methods. The one possible exception, with respect to non-Hispanic Blacks in the US, might represent an intriguing lead to social differences of note (for example, perhaps associated with racial profiling or other race-related differences in law enforcement response to cannabis smoking). Nonetheless, the number of cases available to probe into this situation is very small, and a sample much, much larger than the NESARC sample ($n = 43\,093$) would be required to yield a statistically robust probing.

Several study limitations should be acknowledged. First, consider the NESARC sampling frame, which excluded incarcerated and homeless persons; if these inhabitants had been included, what might be the effect on the study estimates? We think it is likely that this group would have an even higher likelihood of social role impairments related to their cannabis use. Second, the NESARC sampling frame also excluded individuals who had previously refused participation in the US Census Bureau survey – such refusers might well have had greater cannabis or other drug involvement; the impact of such a bias on the present study cannot be determined. Finally, the NESARC assessment interview had a lack of specificity with respect to assessment of DSM-IV abuse. Most of the questions assessing social and role impairment (corresponding to DSM-IV abuse symptoms) in the interview schedule did not require recurrent or repeated problems. For example, the question assessing the DSM-IV abuse symptom 3 'Recurrent substance-related legal problems (e.g. arrests for substance-related disorderly conduct)' was worded in the following manner: 'Did you get arrested, held at a police station, or have any problems

because of your cannabis use?' The recurrence issue was not addressed.

Notwithstanding limitations of this type, there are several implications of these findings for future research on cannabis dependence in general and for epidemiological research on the natural history and clinical course of cannabis dependence.

First, it is generally necessary to accumulate 300 to 400 cases in order to produce statistically robust and precise descriptions for many case characteristics. As such, in the US, in order to identify 300 to 400 cases of cannabis dependence without cannabis-related social role impairments and maladaptation, we might have to assemble an adult general population sample of size 300 000 to 400 000 (i.e., roughly five to 10 times larger than the current annual US National Survey on Drug Use and Health; NSDUH). As such, it may be more useful to embed 'ungated' measurement of dependence within the NSDUH, to accumulate such cases over a span of five to 10 years and then to engage these NSDUH participants in the sustained longitudinal follow-up required to characterize natural history and clinical course (crafting a longitudinal elaboration of the current NSDUH cross-sectional design).

Second, whereas these NESARC results on cannabis dependence should be checked and confirmed via independent replications, the comparison of 'gated' versus 'ungated' prevalence estimates suggests that the magnitude of underestimation actually might be quite modest when gauged in relation to the width of the 95% confidence intervals.

Third, a concern about the 'gated' approach might be that case-control comparisons would be contaminated, and studies of associations would be distorted to the extent that the 'gated' approach fails to identify true cases of drug dependence (and leaves them in the 'non-case' category). However, as with the prevalence estimates, the 'gated' and 'ungated' approaches yielded odds ratio estimates of comparable magnitude, with broadly overlapping 95% confidence intervals. No general pattern of distortion is apparent in the set of associations estimated for this initial inquiry, with one exception noted above, which cannot be probed with the material at hand.

Conclusions

For the most thorough studies of drug dependence, there is good reason to choose the 'ungated' option and to allow for the possibility of drug dependence cases

who report no drug-related social role impairment or social maladaptation, even when DSM-IV formulations imply (a) that maladaptation is a necessary feature and (b) that the associated impairments or distress must be 'clinically significant' to meet the diagnostic criteria. The 'ungated' approach is required if we are to probe into the possibility that drug-related impairments and maladaptations are secondary complications of a drug dependence process (Anthony et al., 2005). Nonetheless, studied in cross-section within the US, the adult general population experience with cannabis use appears to be one in which these impairments and maladaptations are occurring in the vast majority of cannabis dependence cases. The exceptions are quite rare – perhaps too rarely detected in most large-scale sample research for any meaningful scientific analysis.

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