Published in final edited form as:
Drug Alcohol Depend. 2009 September 1; 104(0): 147–155. doi:10.1016/j.drugalcdep.2009.04.016.

Extra-medical stimulant dependence among recent initiates

Megan S. O'Brien[a] and **James C. Anthony**[b,*]

[a]University of Kansas School of Social Welfare, Lawrence, KS 66045, USA

[b]Department of Epidemiology, Michigan State University College of Human Medicine, B601 West Fee Hall, East Lansing, MI 48824, USA

Abstract

New estimates for the risk of becoming stimulant dependent within 24 months after first extra-medical (EM) use of a stimulant drug compound are presented, with a focus on subgroup variations in this risk (e.g., alcohol dependence, male–female differences). The study estimates are derived from a representative sample of United States residents ages 12 and older (n = 166,737) obtained from the 2003 to 2005 National Surveys on Drug Use and Health. A total of 1700 respondents were found to have used stimulants extra-medically for the first time within 24 months prior to assessment. Approximately 5% of these recent-onset EM users had become stimulant dependent since onset of EM use. As hypothesized, alcohol dependence cases were found to have experienced an excess risk of becoming stimulant dependent soon after onset of stimulant drug use; there was no robust male–female difference in risk. Independently, initiates who had used multiple types of stimulants extra-medically, and methamphetamine users, were more likely to have become stimulant dependent soon after onset of use; by comparison, EM users of methylphenidate (Ritalin®) were less likely to have developed rapid-onset dependence. These epidemiologic findings help quantify a continuing public health burden associated with new onsets of extra-medical stimulant use in the 21st century.

Keywords

Stimulants; Dependence; Methylphenidate; Logistic regression; Epidemiology; Recent-onset

1. Introduction

In this study the main aim is to estimate the risk of becoming stimulant dependent soon after onset of extra-medical stimulant drug use among community residents of the United States (US). The construct of 'extra-medical' (EM) stimulant use is one this research group, among

*Corresponding author. janthony@msu.edu (J.C. Anthony).

Contributors

JCA conceptualized study approach and finalized all analyses and manuscript drafts. MSO completed all statistical analyses and early drafts.

Conflict of interest

Dr. O'Brien has received compensation as a contractor for Glaxo Smith Kline, and Dr. Anthony received an honorarium from Mead-Johnson on the topic of NIH research career development.

others, has relied upon for more than 15 years (e.g., see Anthony et al., 1994); it refers to consuming stimulants outside the boundaries of medically prescribed indications for use, in larger amounts than the prescription indicated, or for longer spans of time; it does not refer to stimulants when they have been used exactly as prescribed. The EM construct also encompasses the use of stimulant compounds for purposes such as 'getting high' or to enhance performance (except when prescribed for performance enhancement—e.g., nootropic effects). The main theoretical proposition under study involves a hypothesis that pre-existing alcohol problems might convey excess risk of relatively rapid-onset of stimulant dependence, soon after EM use starts. This inference is supported by theory as well as prior cross-sectional survey evidence that linked heavy drinking with occurrence of extra-medical psychostimulant drug use (e.g., see Furr et al., 2000).

In this study, the sample is epidemiological in nature, with sampling of US communities, and residents of dwelling units within those communities, and with a range that includes residents of homeless shelters. The survey assessment of stimulant dependence involved a standardized schedule of items that tapped the drug dependence criteria listed in the American Psychiatric Association's fourth edition of its Diagnostic and Statistical Manual (DSM-IV; APA, 1994), with specific questions about whether stimulants accounted for the clinical features of dependence. There also was a standardized assessment of age of first extra-medical use of a stimulant compound. This information has allowed us to estimate the risk of becoming dependent on CNS stimulant compounds within a relatively brief interval of time after onset of such use, with resulting estimates for stimulant drugs that can be compared directly to our research group's prior estimates for risk of becoming dependent soon after onset of cocaine use, hallucinogen use, and cannabis use (e.g., see Chen et al., 2005; O'Brien et al., 2005; Stone et al., 2007). In this report we focus upon extra-medical use of stimulants because the survey assessment did not include questions about legally prescribed stimulant use when the compounds are used exactly as prescribed; in Section 4 we discuss this feature of the survey data as a limitation that can and should be remedied in future research.

During calendar year (CY) 2005, in the US, an estimated 2.4–2.9 million individuals age 12 or older used a stimulant extra-medically on at least one occasion (point estimate = 2.7 million, or 1.1% of the US population age 12 years and older), and 409,000 or 0.2% of the US population met criteria for stimulant dependence, but we should note that some experts judge that the NSDUH produces an under-count of the more serious cases of stimulant dependence (Rawson and Condon, 2007) and we return to this topic in our discussion of study limitations. Although the frequency of extra-medical stimulant use may have stabilized or even declined during the past few years, the large number of new stimulant users each year is of concern. Calendar year 2005 has been fairly representative of recent years of the 21st century. During 2005, approximately 296,000 individuals initiated EM stimulant use for the first time before the 18th birthday and an additional 155,000 used stimulants for the *first* time between the ages of 18 and 21 years (Tables 4.10A, 4.11A; (OAS, 2006)). If prior estimates hold true, this means that each year of recent years, the stimulant dependence caseload among 12–21 year olds in the US increases by roughly 451 new stimulant dependence cases (9 new cases per week), not counting the cases of stimulant

dependence that might arise after taking psychostimulants exactly as prescribed and within the boundaries of medically prescribed use.

Concern about extra-medical use of stimulants is not restricted to the US. Rehm et al. (2005) studied 'problem amphetamine or opiate use' in countries of the European Union and Norway, and used multiple methods to estimate prevalence between 1995 and 2000. Estimates of problem amphetamine use ranged between 3 and 5% for Denmark, Finland and Sweden (2005). In the New Zealand National Household Drug Survey from 2003, an estimated 9.0% had initiated extra-medical stimulant use; 4% had used in the year prior to assessment (Wilkins et al., 2006). A study of Nigerian youths found that 6–7% of 10–19 year olds had become EM users of amphetamine or ephedrine (Abdulkarim et al., 2005).

Against a backdrop of this type of evidence, there actually is very little epidemiological research on the risk of becoming dependent upon stimulant compounds within or outside the boundaries of medical practice. Nonetheless, if the epidemiological patterns of stimulant dependence risk follow the observed patterns of stimulant use, we might expect to find excess occurrence of stimulant dependence among males, Whites, American Indians, younger age cohorts, and users of alcohol and other drugs (Herman-Stahl et al., 2006; Huang et al., 2006; Wu et al., 2007). Studying 'prevalence' or 'being' a case of stimulant dependence (as opposed to incidence or risk of becoming a case), Wu and Schlenger analyzed data from the 1995–1998 National Household Surveys on Drug Abuse (NHSDA), and found greater prevalence of stimulant dependence among female stimulant users as compared to males (2003). In contrast, Huang et al. (2006) analyzed data from the 2001 to 2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), and found no male–female differences in prevalence of stimulant dependence among EM stimulant users—perhaps traceable to recently publicized methodological problems resulting in NESARC under-counting of illegal drug use (Grucza et al., 2007). For this reason, the present investigation seeks to throw more light on the issue of male–female differences in risk of becoming stimulant dependent once EM stimulant use has started, in addition to the more primary focus upon our hypothesis about alcohol-associated risk of stimulant dependence.

We should reiterate that the research approach used in this study is exactly the same as the one used by O'Brien and Anthony (2005) in estimation of the risk of becoming cocaine dependent soon after onset of EM cocaine use. After our initial work on cocaine dependence, Chen and colleagues (2005) applied the same approach when studying risk of cannabis dependence among recent-onset cannabis users; Stone et al. (2007) have done so with respect to risk of hallucinogen dependence among new hallucinogen users. By holding the research approach constant, we make it possible to compare the risk estimates for each individual group of psychoactive drug compounds. As such, we note that an estimated 5–6% of EM cocaine users have been found to develop cocaine dependence within 12–24 months after onset of cocaine use (O'Brien and Anthony, 2005). By comparison, the corresponding risk estimates for cannabis are in a range of 1–2%, and the estimates for the hallucinogen drugs (including the mixed stimulant-hallucinogen MDMA) are under 1% (Chen et al., 2005; Stone et al., 2007). The new estimates for psychostimulant drug compounds will be evaluated in relation to these estimates, with an expectation that the resulting risk estimates

might be closer to the 5–6% values observed for cocaine compounds, given similarities of subjective effects and some overlap in the neuropharmacological activity, metabolism, and biotrans-formation of compounds within the general psychostimulant drug group.

2. Methods

2.1. Participants

Data from this study are from the public use data files of the National Surveys on Drug Use and Health (NSDUH) from CY 2003, 2004, and 2005 (aggregate sample size, $N = 166,737$). Each year, this cross-sectional epidemiological survey is constructed to seek a nationally representative sample of non-institutionalized US citizens, aged 12 years and older. Multi-stage sampling procedures have been used to obtain a sample of dwelling units (e.g., households and homeless shelters) and individuals within each dwelling. Whereas the NSDUH oversamples youths, this oversampling is counterbalanced in the analysis steps via the use of inverse sampling probability weights. Study participants were given the opportunity to decline participation, and provided consent in accord with an Institutional Review Board approved protocol. The weighted participation level for designated respondents sampled during calendars years 2003–2005 was approximately 77% (OAS, 2004, 2005, 2006).

2.2. Assessment

The NSDUH survey assessment in recent years has involved an audio-enhanced computer-assisted self-interview (ACASI). After a NSDUH field research staff member introduces the survey and completes the consent process, there is a private ACASI assessment session, typically within or near the dwelling unit. During this session, a fixed sequence of standardized pre-worded and pre-coded survey questions is presented visually on the laptop screen and aurally via headphones, and the participant keys responses that provide information about drug experiences and other personal characteristics under study: age, sex, race–ethnicity, marital status, education, and family income. Size of Metropolitan Statistical Area is encoded by the NSDUH survey team in their preparation of public use data sets.

2.3. Key response variable and covariates

Stimulant use—Midway through the assessment session, each NSDUH respondent was asked first about extra-medical (EM) use of three specific classes of stimulant compounds: (1) methamphetamine (crank, crystal, ice, or speed), Desoxyn®, or Methedrine®; (2) amphetamines, Benzedrine®, Biphetamine®, Fastin®, or phentermine; and (3) Ritalin® or methylphenidate. Respondents also were asked whether they had used any of these compounds extra-medically: Cylert®, Dexedrine®, dextroamphetamine, Didrex®, Eskatrol®, Ionamin®, Mazanor®, Obedrin-LA®, Plegine®, Preludin®, Sanorex®, and Tenuate®. If they indicated that they had consumed any of these drugs extra-medically, they were asked which one(s). Respondents also were asked to name any other prescription stimulants they might have used extra-medically. Subsequent standardized items elicited information about age of first use, year of first use, and cumulative number of days used in the past 12 months.

2.3.1. Methamphetamine involvement—In 2003–2004, each participant was asked a series of standardized questions about EM use of "Methamphetamine, Desoxyn, or Methedrine that was not prescribed for you or that you took only for the experience or feeling it caused? Methamphetamine is also known as crank, crystal, ice or speed." In 2005 an additional question was added to address a possible misunderstanding about methamphetamine: "Methamphetamine, also known as crank, ice, crystal meth, speed, glass, and [by] many other names, is a stimulant that usually comes in crystal or powder forms. It can be smoked, "snorted," swallowed or injected. Have you ever, even once, used methamphetamine?" (Ruppenkamp et al., 2006). Thereafter, information about age of first use, etc. was gathered.

Other aspects of extra-medical drug use were assessed as follows. *Route of administration* was assessed by the question: "Have you ever, even once, used a needle to inject Methamphetamine, Desoxyn, or Methedrine when it was not prescribed for you or that you took only for the experience or feeling it caused?" *Past-year other drug use* has been measured via standardized items for cannabis, hallucinogen, inhalant, and cocaine use, subsequently recoded by the NSDUH research team. For example, hallucinogen use was assessed through a series of questions about use of LSD, PCP, Peyote, Mescaline, Psilocybin, and 'Ecstasy' (MDMA) and recoded by NSDUH into past-year use of any hallucinogen. *Other drug use*: other drug use among stimulant users is the norm, especially heavy alcohol consumption as noted by Furr and colleagues (2000) and confirmed by others (Agrawal et al., 2006; Huang et al., 2006; Raimo et al., 2000; Wu and Schlenger, 2003). As such, our analyses included a covariate term for the NSDUH DSM-IV indicator of alcohol dependence as evaluated in terms of the Diagnostic and Statistical Manual of Mental Disorders–fourth edition (1994).

2.3.2. Recent-onset stimulant use—The focus of this inquiry is upon a rapid transition from onset of extra-medical stimulant drug use to the occurrence of a DSM-IV stimulant dependence syndrome. As such, recent-onset stimulant users can be identified via a NSDUH-derived variable that designates individuals who had started extra-medical use of one or more of the stimulant drugs within 24 months of the date of assessment. Here, the label 'recently active past-onset' is assigned to active users who do not qualify as recent-onset users; these users started EM stimulant use more than 24 months before assessment and continued to use at least one of these compounds during the 12 months prior to assessment.

The guiding conceptual model is one in which we might expect to see stimulant dependence develop among a small proportion of recent-onset EM stimulant users, but with subgroup variation in risk, as explained below and in our prior papers in this series on relatively rapid onset of the drug dependence syndromes soon after onset of extra-medical drug use (Chen et al., 2005; O'Brien and Anthony, 2005; Stone et al., 2007, 2006).

2.3.3. Drugs used prior to use of the NSDUH stimulant compounds—We assessed the number of drugs used before initiation of these stimulant compounds in order to control for a possible susceptibility to become stimulant dependent that might occur as a result of prior drug exposures. To create this crude index, for each of 10 other drug

categories assessed in the NSDUH (i.e., tobacco, alcohol, cocaine/crack, heroin, cannabis, inhalants, pain relievers, anxiolytics, hallucinogens, and sedative-hypnotics), a value of '1' is given when a stimulant user had ever used that drug and the age of first use was prior to the age of onset of stimulant use. Based upon the value obtained from these 10 drug categories, "number of drugs used prior to using stimulants" was then derived by adding the values, with a ranged from 0 to 10. (See Stone et al., 2007 for our research group's original application of this same approach.)

2.3.4. Stimulant dependence assessment—All recently active stimulant users were asked seven questions that map onto the seven clinical features of DSM-IV designated stimulant dependence (APA, 1994). Individuals whose stimulant experiences during the 12 months prior to assessment had included at least three clinical features were identified by the NSDUH research team as stimulant dependent (dependence = 1); those who did not meet dependence criteria or had never used stimulants were coded '0'.

2.4. Data analyses

After inspection of sample characteristics, we applied the sampling weight and post-stratification adjustment factor to estimate the distributions of extra-medical stimulant experience within the total population under study, prior to coverage of the EM stimulant experience of recent-onset users or recently active past-onset users. To estimate the risk of rapid development of stimulant dependence soon after onset of EM stimulant use, STATA 9.0 survey commands were used in contingency table analysis and to conduct multiple logistic regressions in which we regressed the logit-transformed odds of becoming stimulant dependent upon the covariates of interest (StataCorp, 2005). Subsequent exploratory analyses involved repeating the above analyses but adding covariate terms for the specific stimulant(s) being used, with EM users of methylphenidate only (e.g., Ritalin®) as the reference group against which to gauge the stimulant dependence risk experience for EM users of the other specifically named compounds (e.g., methamphetamine). This approach for estimation of relative risk (RR) is exactly the approach that we have previously used to estimate variations in the risk of (a) becoming cocaine dependent for recent-onset users of cocaine HCl powder plus crack versus recent-onset users of cocaine HCL powder alone (O'Brien and Anthony, 2005), and (b) becoming hallucinogen dependent for recent-onset users of those who had consumed LSD only, versus recent-onset users of MDMA, psilocybin, mescaline, etc. (Stone et al., 2007).

In these analyses, we introduced dummy-coded covariate terms for the stimulants used, *allowing people to use more than one*, and we included dummy-coded terms for all possible combinations of stimulant drugs. The resulting regression slope estimates for these dummy-coded covariates allow us to estimate risk of becoming stimulant dependent for users of each specifically named stimulant versus the reference group who had tried methylphenidate only, holding constant the use of all other named stimulant drugs (and combinations), and also adjusting for all other sociodemographic characteristics under study. In this manner, the multiple regression approach has been used to estimate the relative risk of becoming stimulant dependent for EM users of each of the named compounds under study, with the risk experience of the EM users of methylphenidate only taken as a reference comparison.

Given the study design and focus on occurrence of a stimulant dependence syndrome among recent-onset EM stimulant users (a relatively rare outcome), the resulting odds ratios (OR) may be interpreted as relative risk (RR) estimates when the covariates of interest are exogenous with respect to the development of stimulant use or dependence (e.g., not likely to be influenced by use or the dependence process). Even when covariates such as level of educational achievement might be endogenous with respect to stimulant use or dependence (i.e., the drug experience might cause premature termination of schooling), the estimated odds ratios can be interpreted as a simple gauge of strength of association between the covariates and the odds of observing stimulant dependence soon after onset of stimulant use. Based upon the available data, we can gauge that the median elapsed time is roughly 12–13 months. A more detailed overview of this technical detail has been provided in O'Brien and Anthony (2005) and Stone et al. (2007).

Finally, it should be mentioned that the NSDUH gathered data on extra-medical use of 12 named stimulant drug compounds under study, plus a residual category for other miscellaneous stimulants. For these analyses, a covariate term has been created for each of the seven stimulant categories in the NSDUH where 1 = used that stimulant *only*. Among the 1700 recent-onset users in this sample, 22% used methamphetamine *only*; 13% used diet pills *only*, 30% used methylphenidate *only* and 12% used other stimulants *only*. For an exploratory analysis of compound-specific risk of stimulant dependence, we classified identifiable prescription stimulant compounds into four categories based on their active ingredients. Group 1 included 105 EM users of Obedrin LA, Eskatrol, Dexedrin, and dextroamphetamine. Group 2 included 6 EM users of Sancrex and Mazanor. Group 3 included 10 EM users of Plegine and Preludin. Group 4 included 497 EM users of Tenuate, Ionamin, Cylert and Didrex (which did not fall into any of the other categories). Covariate terms for all groups were included in the multiple regression analyses to estimate compound-specific relative risk, but the numbers of EM users in groups 2 and 3 were too small to produce interpretable estimates.

3. Results

Within the study sample, an unweighted total of 1700 respondents had started extra-medical stimulant use for the first time within 24 months of interview assessment (i.e., 1.0% of the total sample of 166,737 individuals). As shown in Tables 1 and 2, taking sampling weights and post-stratification adjustment factors into account, we can estimate that 0.4% of the 2003–2005 NSDUH study population qualified as a recent-onset EM stimulant user (95% confidence interval, CI = 0.0038, 0.0045). With these estimates applied to the US population age 12 years and older, roughly one million (910,000–1,100,000) started EM stimulant use during this span of time.

As for the risk of transitioning quite rapidly (within 24 months) from onset of EM stimulant use to full development of a DSM-IV clinical syndrome of stimulant dependence (Table 2), the study estimate is 4.9%—i.e., not too distant from the 5%–6% estimates we reported previously with respect to the transition from first cocaine use to rapid-onset of cocaine dependence (O'Brien and Anthony, 2005). Table 2 presents this estimate, along with other estimates pertinent to the drug involvement of the EM stimulant users.

As noted in Section 1, a major focal hypothesis for this study involved the possibility that individuals with recent alcohol dependence might transition more rapidly into stimulant dependence once EM stimulant use had started, as compared to individuals without recent alcohol dependence. Noted in more detail below, the study evidence supports this hypothesized association: an estimated 3.3% of the study population qualified as cases of alcohol dependence; by comparison, an estimated 16% of the EM stimulant users did so (Table 2). With or without covariate adjustments via multiple logistic regression, the alcohol dependent EM stimulant users were an estimated 3–4 times more likely to become stimulant dependent within 24 months after onset of EM stimulant use, as compared to other EM stimulant users (Table 3: unadjusted and weighted relative risk estimate, uRRw = 3.2; 95% confidence interval, CI = 1.7, 6.0; $p < 0.01$; Table 4: covariate-adjusted and weighted RR estimate, aRRw = 3.4; 95% CI = 1.8, 6.6; $p < 0.001$).

3.1. Sociodemographic characteristics of total sample and sample subsets

In Table 1, a useful set of background associations is seen via a comparison of the 'All persons' column proportions to the corresponding proportions in the 'recently active past-onset users' columns and the 'recent-onset users' columns (see O'Brien and Anthony, 2005). For example, we see that the male–female ratio in the total survey population is 48.4–51.6%. In the 'recently active past-onset users' column, we see the male–female ratio is 56–44%—i.e., an observed excess of males relative to the expected population estimate of the male–female ratio. However, comparison to the values in the recent-onset columns reveals a male female ratio of 41–59%, indicating an observed excess of females. In summary, in this crude contrast, being male is associated with being a recently active (persistent) EM stimulant user, with use carried on from past years, but if anything, would be *inversely* associated with the risk of becoming a recent-onset EM stimulant user.

In similar comparisons for other variables, the recently active past-onset users are found to be younger than the general population (5.3% of these users are between 18 and 20 years of age compared to 15.0% in the overall population); the recent-onset users are younger still (28% in that age group). Persistent and new EM stimulant users are more likely to be White, have lower levels of education, and to have a lower family income. Variation in relation to MSA (Metropolitan Statistical Area) of residence is less pronounced.

3.2. Drug use characteristics of total sample and sample subsets

As shown in Table 2, an estimated 5–6% of the recent-onset EM stimulant users had used any stimulant on at least 100 days during the 12 months prior to assessment, as compared to 28–29% of the recently active past-onset stimulant users. In total, an estimated 29% of the recent-onset stimulant users had consumed stimulants on only 1–2 days in the past 12 months, as compared to the 11% of the recently active past-onset users. The greater accumulated EM stimulant experience is reflected in the larger proportion of past-onset users who had ever used any of the specific stimulants listed in Table 2. A notable exception is the equal proportion of methylphenidate users among past- and recent-onset stimulant users. Past-onset, recently active users were also more likely to have used a needle to inject stimulants for extra-medical reasons (15.8% vs. 1.6% among recent-onset users). These differences in stimulant experience make sense, in that the past-onset users had had more

time during which to accumulate occasions of stimulant use and a more varied drug-taking repertoire (e.g., injecting). Nevertheless, with respect to the number of drugs used extra-medically prior to starting stimulants, the study estimates display no remarkable differences between the past-onset recently active users and the recent-onset users (Table 2).

3.3. Subgroup variation in risk of becoming dependent

We now turn attention to the possibility of other subgroup variations in the experience of the recent-onset stimulant users specifically, seeking answers to the following research question: "Who is becoming stimulant dependent soon after stimulant use starts?" Estimates presented in Tables 3 and 4 indicate an increased risk for becoming stimulant dependent among individuals with stimulant onset under the age of 16 years, as compared to those starting EM stimulant use at a later age (Table 3: uRRw = 3.0; 95% CI = 1.4, 6.1; $p < 0.01$; Table 4: aRRw = 3.1; 95% CI = 1.3, 7.6; $p = 0.014$). In addition, there is an inverse association such that recent-onset EM stimulant users with no prior EM drug involvement were markedly less likely to develop stimulant dependence soon after onset of EM stimulant user, as compared to the other recent-onset EM stimulant users (Table 4: aRRw = 0.1; 95% CI = 0.01, 0.9; $p = 0.043$).

In our study of compound-specific risk of rapid-onset stimulant dependence, we had anticipated an excess risk among users of methamphetamine, and by comparison, lower levels of risk among EM users of medically prescribed stimulant compounds such as methylphenidate. This expectation was borne out in that those with recent-onset EM methamphetamine use was estimated three times more likely to develop rapid-onset stimulant dependence, as compared to recent-onset EM users whose stimulant exposure was restricted to methylphenidate (aRRw = 3.0; 95% CI = 1.5, 6.0; $p = 0.002$; data not shown in a table). Otherwise there were no statistically robust variations in compound-specific risk of developing stimulant dependence within the first 24 months after onset of EM use of these compounds. An association at the margin of conventional statistical significance ($p = 0.075$) was observed in the relative risk estimate for EM users who had combined methylphenidate with EM use of other stimulant compounds. That is, as compared to the EM users of methylphenidate only, these poly-stimulant users of methylphenidate were an estimated 2.5 times more likely to develop rapid-onset stimulant dependence (aRRw = 2.5; 95% CI = 0.9, 6.7; $p = 0.075$; data not shown in a table). We present these values as an aid for future investigations of the compound-specific risk of stimulant dependence. [A detailed table showing these estimates is available upon request to the first author.]

4. Discussion

In brief, this study's estimates are consistent with the idea that an estimated 4.9% (roughly 1 in 20) extra-medical stimulant users develop a clinically recognizable stimulant dependence syndrome within 24 months after first onset of EM stimulant use. Statistically precise, with an unweighted denominator based on the experience of 1700 extra-medical stimulant users, this 4.9% estimate is not too distant from the corresponding 5–6% estimate derived for recent-onset cocaine users, using exactly the same research approach (O'Brien and Anthony, 2005). It is of interest that there is excess risk of rapid-onset stimulant dependence among methamphetamine users, as compared to those with EM use of methylphenidate only

(covariate-adjusted and weighted aRRw = 3.0; $p < 0.05$). Hence, risk of rapid-onset stimulant dependence in association with methamphetamine approaches the elevated risk of rapid-onset cocaine dependence among individuals who start using both cocaine HCL powder and crack-cocaine during the first 24 months after initiation of cocaine use (O'Brien and Anthony, 2005).

Other salient estimates from this study include the threefold excess risk of rapid-onset dependence for individuals who had qualified for the NSDUH/DSM-IV alcohol dependence diagnosis, as compared to other recent-onset users (adjusted weighted aRRw = 3.4; $p < 0.05$). In addition, there was a noteworthy independent association signaling excess risk for the recent-onset EM stimulant users who were under the age of 16 years at the time of starting such use, as compared to those starting at an older age (adjusted RR = 3.1; $p < 0.05$). EM stimulant users with no prior history of using other drugs extra-medically were at lower risk of becoming stimulant dependent soon after onset of EM stimulant use (adjusted RR = 0.1; $p < 0.05$). Consistent with the NESARC evidence on prevalence of being a case of stimulant dependence (Huang et al., 2006), in these NSDUH data on risk of becoming stimulant dependence soon after onset of EM stimulant use, there is no evidence of a male–female difference. No statistically robust associations were found in relation to other demographic or socioeconomic characteristics under study.

Before detailed discussion of these findings, we draw attention to several study limitations that deserve special mention. First, the strength of a common research protocol used in our series of epidemiological investigations makes it possible to compare dependence risk estimates for different types of drug compounds (e.g., estimates for non-cocaine stimulant compounds in this study versus estimates for cocaine, cannabis, and hallucinogens in prior studies). Nonetheless, this common research protocol has all the limitations of self-report survey data on drug use and dependence, which we have discussed in detail elsewhere (e.g., see Anthony et al., 2000, 1994). Second, it is a limitation that the NSDUH approach is one that fails to count stimulant dependence that may occur even when psychostimulants are used exactly as prescribed by a doctor. In the future, NSDUH estimates will be more informative when the assessment protocol is revised to ask about the use of psychostimulants, as prescribed, and not just about extra-medical (and sometimes illegal) use.

Third, our research approach, in effect, is one that takes cross-sectional and retrospective data, and makes a projection to the stimulant dependence risk and RR estimates that might be derived using prospective and longitudinal research designs, which at first might be regarded as superior to this study's estimates. Nevertheless, as noted elsewhere, the claim that risk and RR estimates from new prospective and longitudinal research might be superior is undercut by an already demonstrated fact that sample attrition, over time, degrades the estimates from prospective and longitudinal research designs. In specific, 'heavier' drug users are disproportionately lost to follow-up in prospective and longitudinal studies (e.g., see Ritter, 1988); cross-sectional data often are regarded as inferior to prospective and longitudinal data. Moreover, some experts judge that the NSDUH produces an undercount of diagnosable cases of stimulant dependence (e.g., Rawson and Condon, 2007), but the proposed mechanisms of undercounting appear to surface most prominently in the more

advanced stages of stimulant dependence and when the task is to estimate risk of 'becoming' drug dependent, the cross-sectional design actually might be superior (e.g., see O'Brien and Anthony, 2005, for a more detailed discussion of this topic).

We judge that the time course of stimulant use and dependence is such that some stimulant users might progress to an especially advanced stage of stimulant dependence and become incarcerated or institutionalized within the first 24 months after onset of stimulant use, but that for many stimulant users, disengagement from the NSDUH sampling frame (i.e., migration into an institution) would be much more likely to occur after more time has passed (e.g., after 2–3 years of stimulant use). Nonetheless, we must acknowledge that these empirical estimates for the probability of becoming stimulant dependent within 24 months after onset of stimulant use might be downwardly biased to the extent that the NSDUH undercounts these disengaged cases. We note that this same downward bias might have affected our previously published estimates on probability of becoming dependent on cocaine, hallucinogens, and other drugs as well, perhaps to a similar degree. In that case, then the goal of comparing estimates for one group of drug compounds versus another would not necessarily be compromised, except when the comparison involves a drug compound such as tobacco, with a legal status that does not promote incarceration or entry into in-patient treatment as a consequence of its use.

These and other study limitations are signposts for new and innovative directions in epidemiological research on the risk of becoming drug dependent, as might be undertaken in research that builds from the present study estimates.

Limitations such as the self-report cross-sectional survey character of the study data are counterbalanced by multiple strengths in the research approach. By holding constant the research approach, drug by drug, we can build up a 'comparative' epidemiology of drug dependence that would not be possible if we were to introduce methodological variations from study to study, and from report to report. Our use of the multiple regression method in order to estimate compound-specific excess risk also is a strength because it helps to address the fact that psychostimulant users sometimes are users of multiple stimulant compounds. For example, analyses of 2003 NSDUH data have pointed toward noteworthy male–female variations in *type* of extra-medical stimulant use among young people (Wu et al., 2007), with males more likely to have engaged in EM use of methylphenidate, less likely to have become EM users of diet pill compounds. In consequence, any unadjusted male–female comparison of stimulant dependence risk estimates is confounded by an imbalanced variation in which of the stimulant drug compounds are being used. (Any observed male–female difference of the type seen in Table 1 of this report actually might be attributable to the fact that males and females are using different stimulant drug compounds; any observed compound-specific risk variation might be due to the fact that males are over-represented among methylphenidate users and are under-represented among diet pill users.) The multiple regression approach is one that holds constant covariates, in effect bringing them into balance for estimation purposes. Hence, when estimating the male–female difference, the type of compound is held constant via covariate adjustment. When estimating the compound-specific variations in risk, there is adjustment via a covariate term for sex.

It is clear that continued study of the epidemiology of individual stimulant compounds and the risk of stimulant dependence is warranted, especially when the EM stimulant experience is built on top of a prior history of other drug involvement. For example, an especially provocative finding involves the threefold excess risk observed in association with alcohol dependence. Focused inquiry is required to probe into what might account for the increased vulnerability observed in this study's evidence, which builds from theory about genetic cross-drug susceptibility traits, and prior evidence cited in Section 1 (e.g., Furr et al., 2000).

It is also of interest that EM stimulant users with no prior EM drug involvement whatsoever were at substantially reduced risk of developing rapid-onset stimulant dependence (aRRw = 0.1; $p < 0.05$), and this association was completely independent of the excess risk associated with alcohol dependence. Another way to gauge the strength of this association is to take the inverse of the RR estimate of 0.1 shown in Table 4. Viewed from this perspective, EM stimulant users *with* a prior history of extra-medical use of other drugs are an estimated 10 times more likely to experience rapid-onset stimulant dependence, as compared to those *without* prior history of this type (i.e., RR = 0.1 has the same magnitude of RR = 10.0, gauged as a departure from the null RR = 1.0). In past epidemiological research, when RR estimates of size 10 or greater have been observed, they almost never have been attributable to background confounding factors. Nonetheless, one might speculate about potential confounding by shared genetic susceptibilities or other predispositions such as novelty seeking or harm avoidant personality traits, not yet measured in the NSDUH field research (e.g., see discussion in Furr et al., 2000).

Readers may appreciate our attention to estimation of compound-specific relative risk estimates, in contrast with other studies in which the epidemiological estimates for stimulant dependence have been produced for cocaine and for psychostimulants other than cocaine, but not for individual stimulant compounds (e.g., see Anthony et al., 1994). This study's finding with respect to the methamphetamine–methylphenidate contrast is of interest, in that some scientists have described methylphenidate as a potential '*antidote*' to methamphetamine dependence (Tiihonen et al., 2007).

As documented here, the public health burden represented by stimulant dependence may be considerable. If an estimated one million US residents started extra-medical stimulant use during the time span under study (2003–2005), and if we are correct in our estimate that 4.9% developed stimulant dependence soon after onset of EM stimulant use, then an estimated 49,000 newly incident cases of stimulant dependence arose during that same span of time. This is a rather large number as compared to the current stimulant dependence treatment capacity in the US, even if it is true that many of these individuals become dependent and then remit or recover without treatment. In addition, the relatively rapid onset of stimulant dependence soon after onset of EM stimulant use appears to be an 'equal opportunity' phenomenon, without much risk variation in relation to subgroups defined by sex, race–ethnicity, socioeconomic status, or population density. The observed excess risks associated with alcohol dependence and with use of methamphetamine are noteworthy. If it can be replicated, the observed inverse association between risk of stimulant dependence and the history of no prior extra-medical drug use deserves more thorough probing via new epidemiological studies.

Acknowledgments

Data reported herein come from national survey data collected under the auspices of the Office of Applied Studies, Substance Abuse and Mental Health Services Administration. The views and opinions expressed in this report are those of the authors and should not be construed to represent the views of any of the sponsoring organizations, agencies, or the US government. Finally, we wish to acknowledge pharmacist, Dr. Lanny Sieman, for assistance with classification of stimulant compounds.

Role of funding source

JCA's work on this project was supported by two awards from the National Institute on Drug Abuse (K05DA015799; R01DA016558).

References

Abdulkarim AA, Mokuolu OA, Adeniyi A. Drug use among adolescents in Ilorin, Nigeria. Trop Doct. 2005; 35 (4):225–228. [PubMed: 16354478]

Agrawal A, Grant JD, Waldron M, Duncan AE, Scherrer JF, Lynskey MT, et al. Risk for initiation of substance use as a function of age of onset of cigarette, alcohol and cannabis use: findings in a Midwestern female twin cohort. Prev Med. 2006; 43 (2):125–128. [PubMed: 16697036]

Anthony, JC.; Neumark, YD.; Van Etten, ML. Do I do what I say? A perspective on self-report methods in drug dependence epidemiology. In: Stone, A.; Turkan, JS.; Bachrach, CA.; Jobe, JB.; Kurtzman, HS., editors. The Science of Self-report: Implications for Research and Practice. Lawrence Erlbaum Associates; New Jersey: 2000.

Anthony JC, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. Exp Clin Psychopharmacol. 1994; 2:244–268.

American Psychiatric Association. Diagnostic and Statistical Manual of mental disorders 0-89042-024-6. Washington, DC: Author; 1994.

Chen CY, O'Brien MS, Anthony JC. Who becomes cannabis dependent soon after onset of use? Epidemiological evidence from the United States: 2000–2001. Drug Alcohol Depend. 2005; 79 (1): 11–22. [PubMed: 15943940]

Furr CD, Delva J, Anthony JC. The suspected association between methamphetamine ('ice') smoking and frequent episodes of alcohol intoxication: data from the 1993 National Household Survey on Drug Abuse. Drug Alcohol Depend. 2000; 59 (1):89–93. [PubMed: 10706978]

Grucza RA, Abbacchi AM, Przybeck TR, Gfroerer JC. Discrepancies in estimates of prevalence and correlates of substance use and disorders between two national surveys. Addiction. 2007; 102 (4): 623–629. [PubMed: 17309538]

Herman-Stahl MA, Krebs CP, Kroutil LA, Heller DC. Risk and protective factors for nonmedical use of prescription stimulants and methamphetamine among adolescents. J Adolesc Health. 2006; 39 (3):374–380. [PubMed: 16919799]

Huang B, Dawson DA, Stinson FS, Hasin DS, Ruan WJ, Saha TD, Smith SM, Goldstein RB, Grant BF. Prevalence, correlates, and comorbidity of non-medical prescription drug use and drug use disorders in the United States: results of the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2006; 67 (7):1062–1073. [PubMed: 16889449]

O'Brien MS, Anthony JC. Risk of becoming cocaine dependent: epidemiological estimates for the United States, 2000–2001. Neuropsychopharmacology. 2005; 30 (5):1006–1018. [PubMed: 15785780]

O'Brien MS, Wu LT, Anthony JC. Cocaine use and the occurrence of panic attacks in the community: a case-crossover approach. Subst Use Misuse. 2005; 40 (3):285–297. [PubMed: 15776977]

Office of Applied Studies. Results from the 2003 National Survey on Drug Use and Health: National Findings. Office of Applied Studies; Rockville, MD: Substance Abuse and Mental Health Services Administration; 2004. NSDUH Series H-25, DHHS Publication No. SMA 04-3964

Office of Applied Studies. Results from the 2004 National Survey on Drug Use and Health: National Findings. Office of Applied Studies; Rockville, MD: Substance Abuse and Mental Health Services Administration; 2005. NSDUH Series H-28DHHS Publication No. SMA 05-4062

Office of Applied Studies. Results from the 2005 National Survey on Drug Use and Health: National Findings. Office of Applied Studies; Rockville, MD: Substance Abuse and Mental Health Services Administration; 2006. NSDUH Series H-30, DHHS Publication No. SMA 06-4194

Raimo EB, Smith TL, Danko GP, Bucholz KK, Schuckit MA. Clinical characteristics and family histories of alcoholics with stimulant dependence. J Stud Alcohol. 2000; 61 (5):728–735. [PubMed: 11022813]

Rawson RA, Condon TP. Why do we need an addiction supplement focused on methamphetamine? Addiction. 2007; 102 (suppl 1):1–4. [PubMed: 17493048]

Rehm J, Room R, Van Den Brink W, Kraus L. Problematic drug use and drug use disorders in EU countries and Norway: an overview of the epidemiology. Eur Neuropsychopharmacol. 2005; 15 (4):389–397. [PubMed: 15955677]

Ritter C. Resources, behavior intentions, and drug use: a ten-year national panel analysis. Soc Psychol Quart. 1988; 51 (3):250–264.

Ruppenkamp, J.; Davis, T.; Kroutil, L.; Aldworth, J. 2005 National Survey on Drug Use and Health: Methamphetamine Analysis Report. RTI International; Research Triangle Park: 2006.

StataCorp. Stata Statistical Software: Release 9. 0. StataCorp; College Station, TX: 2005.

Stone AL, O'Brien MS, De La Torre A, Anthony JC. Who is becoming hallucinogen dependent soon after hallucinogen use starts? Drug Alcohol Depend. 2007; 87 (2–3):153–163. [PubMed: 16987612]

Stone AL, Storr CL, Anthony JC. Evidence for a hallucinogen dependence syndrome developing soon after onset of hallucinogen use during adolescence. Int J Methods Psychiatric Res. 2006; 15 (3): 116–130.

Tiihonen J, Kuoppasalmi K, Fohr J, Tuomola P, Kuikanmaki O, Vorma H, et al. A comparison of aripiprazole, methylphenidate, and placebo for amphetamine dependence. Am J Psychiatry. 2007; 164 (1):160–162. [PubMed: 17202560]

Wilkins C, Sweetsur P, Casswell S. Recent population trends in amphetamine use in New Zealand: comparisons of findings from national household drug surveying in 1998, 2001, and 2003. N Z Med J. 2006; 119 (1244):U2285. [PubMed: 17072360]

Wu LT, Pilowsky DJ, Schlenger WE, Galvin DM. Misuse of methamphetamine and prescription stimulants among youths and young adults in the community. Drug Alcohol Depend. 2007; 89 (2–3):195–205. [PubMed: 17257780]

Wu LT, Schlenger WE. Psychostimulant dependence in a community sample. Subst Use Misuse. 2003; 38 (2):221–248. [PubMed: 12625429]

Table 1

Selected sociodemographic characteristics of all persons, and recently active extra-medical users of stimulants, sub-classified in relation to recency of onset of this stimulant use. Data from United States National Surveys on Drug Use and Health, 2003–2005.

	All persons			Recently active past-onset users of stimulant[a]			Recent-onset users of stimulant[b]		
	n	uwtd%	wtd%	*n*	uwtd%	wtd%	*n*	uwtd%	wtd%
All persons	166,737	100.0	100.0	2,359	100.0	100.0	1,700	100.0	100.0
Sex									
Male	80,018	48.0	48.4	1230	52.1	56.3	709	41.7	41.4
Female	86,719	52.0	51.6	1129	47.9	43.7	991	58.3	58.6
Age at interview (in years)[c]									
12–13	18,177	10.9	3.5	65	2.8	1.2	85	5.0	4.0
14–15	18,738	11.2	3.6	140	5.9	2.7	325	19.1	13.9
16–17	18,261	11.0	3.4	302	12.8	6.5	471	27.7	20.1
18–20	21,769	13.1	5.3	555	23.5	15.0	482	28.4	28.0
21–25	33,565	20.1	8.1	851	36.1	25.0	271	15.9	15.6
26–34	16,767	10.1	14.5	202	8.6	19.4	33	1.9	7.6
35 and older	39,460	23.7	61.6	244	10.3	30.2	33	1.9	10.8
Race/ethnicity									
Nonhispanic White	109,040	65.4	69.5	1847	78.3	82.2	1314	77.3	79.0
Nonhispanic Black/African American	20,835	12.5	11.7	76	3.2	3.2	67	3.9	4.0
Hispanic	24,030	14.4	12.9	243	10.3	9.6	172	10.1	11.0
Other	12,832	7.7	6.0	193	8.2	5.0	147	8.7	6.0
Education[c]									
College senior or graduate	21,981	13.2	23.5	207	8.8	13.1	84	4.9	10.5
Some college	31,395	18.8	22.5	585	24.8	26.8	316	18.6	24.0
High school graduate	38,294	23.0	28.5	634	26.9	31.2	298	17.5	19.5
Less than high school graduate	75,067	45.0	25.5	933	39.6	29.0	1002	58.9	46.0
Family income									
0 to $19,999	39,897	23.9	19.5	830	35.2	31.9	474	27.9	25.8
$20,000 to $49,000	61,592	36.9	36	849	36.0	34.8	536	31.5	31.7
$50,000 to $74,999	29,066	17.4	18.3	311	13.2	15.5	297	17.5	17.3

	All persons			Recently active past-onset users of stimulant[a]			Recent-onset users of stimulant[b]		
	n	uwtd%	wtd%	*n*	uwtd%	wtd%	*n*	uwtd%	wtd%
$75,000+	36,182	21.7	26.2	369	15.6	17.8	393	23.1	25.2
Size of Metropolitan Statistical Area									
MSA of 1 million+	62,766	37.6	47.7	692	29.3	40.3	558	32.8	45.7
MSA <1 million	68,398	41.0	35.5	1079	45.7	39.6	765	45.0	37.6
Segment not in MSA	35,573	21.3	16.9	588	24.9	20.1	377	22.2	16.8

Note: "wtd" indicates analysis based on weighted data with Taylor series linearization for variance estimation. Values may not sum to 100% due to rounding.

[a]Recently active use in the past 12 months but with past-onset (i.e., 24+ months before survey assessment date).

[b]Within 24 months of the survey assessment date.

[c]Reflect values at the time of interview.

Table 2

Selected drug use characteristics of all persons and all recently active extra-medical users of stimulants, sub-classified by recency of onset of this stimulant use. Data from United States National Surveys on Drug Use and Health, 2003–2005.

	All persons			Recently active past-onset users of stimulant[a]			Recent-onset users of stimulant[b]		
	n	uwtd%	wtd%	*n*	uwtd%	wtd%	*n*	uwtd%	wtd%
All persons	166,737	100.0	100.0	2,359	100.0	100.0	1,700	100.0	100.0
Occurrence of DSM-IV stimulant dependence syndrome									
Yes, 3+ clinical features	370	0.2	0.1	284	12.0	12.7	79	4.7	4.9
No	166,367	99.8	99.9	2075	88.0	87.3	1621	95.4	95.1
Occurrence of DSM-IV alcohol dependence syndrome									
Yes	7,228	4.3	3.3	608	25.8	23	329	19.4	16.4
No	159,509	95.7	96.7	1751	74.2	77.1	1371	80.7	83.6
Ever used needle for self-administered stimulant injection									
Yes	1,005	0.6	0.7	277	11.7	15.8	32	1.9	1.6
No	165,732	99.4	99.3	2082	88.3	84.2	1668	98.1	98.5
All persons	166,737	100.0	100.0	2359	100.0	100.0	1700	100.0	100.0
Occasions of extra-medical stimulant use (all forms) in past 12 months									
1–2 days	734	0.4	0.2	279	11.8	11.9	455	26.8	29.1
3–11 days	966	0.6	0.3	522	22.1	19.9	444	26.1	26.2
12–100 days	1,299	0.8	0.4	937	39.7	39.4	362	21.3	21.0
101 or more days	729	0.4	0.3	621	26.3	28.8	108	6.4	5.7
Never/not in past year/dk/ref	163,009	97.8	98.8	0	0.0	0.0	331	19.5	18.0
Extra-medical methamphetamine use in lifetime									
Yes	7,190	4.3	4.7	1353	57.5	64.8	518	30.5	30.3
No	159,547	95.7	95.3	1006	42.7	35.2	1182	69.5	69.7
Extra-medical diet pills use in lifetime									
Yes	4,124	2.5	3.4	731	31.0	37.1	336	19.8	21.4
No	162,613	97.5	96.6	1628	69.0	62.9	1364	80.2	78.6
Extra-medical methylphenidate use in lifetime									
Yes	5,187	3.1	1.8	1252	53.1	42.9	784	46.1	41.8
No	161,550	96.9	98.2	1107	46.9	57.1	916	53.9	58.2

	All persons			Recently active past-onset users of stimulant[a]			Recent-onset users of stimulant[b]		
	n	uwtd%	wtd%	*n*	uwtd%	wtd%	*n*	uwtd%	wtd%
Extra-medical use of stimulant group 1 in lifetime									
Yes	1,573	0.9	1.2	370	15.7	15.0	105	6.2	5.7
No	165,164	99.1	98.8	1989	84.3	85.0	1595	93.8	94.3
Extra-medical use of stimulant group 2 in lifetime									
Yes	48	0.0	0.0	19	0.8	0.5	6	0.4	0.3
No	166,689	100.0	100.0	2340	99.2	99.5	1694	99.7	99.7
Extra-medical use of stimulant group 3 in lifetime									
Yes	274	0.2	0.3	59	2.5	2.9	10	0.6	0.4
No	166,463	99.8	99.8	2300	97.5	97.2	1690	99.4	99.6
Extra-medical use of stimulant group 4 in lifetime									
Yes	3,632	2.2	2.3	873	37.0	33.1	497	29.2	28.1
No	163,105	97.8	97.7	1486	63.0	66.9	1203	70.8	71.9
Number of stimulants used extra-medically, in lifetime									
0	152,981	91.8	91.7	–	–	–	–	–	–
1	8,887	5.3	5.3	1105	46.8	47.2	1290	75.9	78.8
2	2,597	1.6	1.6	614	26.0	27.3	269	15.8	14.2
3	1,148	0.7	0.7	308	13.1	12.2	92	5.4	5.0
4	600	0.4	0.4	160	6.8	4.9	31	1.8	1.2
5	319	0.2	0.2	97	4.1	5	10	0.6	0.5
6 or more	205	0.1	0.1	75	3.2	3.5	8	0.5	0.3
Number of other drugs used extra-medically prior to starting stimulants[c]									
0	138,504	83.1	83.4	195	8.3	5.9	85	5.0	5.0
1	16,830	10.1	9.5	234	9.9	7.1	147	8.7	7.8
2	2,141	1.3	1.4	330	14.0	14.5	245	14.1	14.5
3	9,262	5.6	5.7	1600	67.8	72.5	1223	71.9	72.7

Notes: "wtd" indicates analysis based on weighted data with Taylor series linearization for variance estimation. Values may not sum to 100 due to rounding. Metham-phetamine includes methamphetamine, Desoxyn®, or Methedrine®. Diet pills includes prescription diet pills such as amphetamines, Benzedrine®, Biphetamine®, Fastin®, or Phentermine®. Group 1 includes: Obedrin LA®, Eskatrol®, Dexedrin®, dextroamphetamine. Group 2 includes: Sanorex® and Mazanor®. Group 3 includes: Plegine® and Preludin®. Group 4 includes: Tenuate®, Ionamin®, Cylert®, Didrex®, and other stimulants not listed above. Number of stimulants used is calculated from each *individual* stimulant agent. Five cases of recently active past-onset users reported EM use of stimulants but did not report which type of stimulant they used. These 5 cases were too few to form their own group. Rather than exclude them, we added them to the "used only 1 stimulant" group.

[a] Recently active use in the past 12 months but with past-onset (i.e., 24+ months before survey assessment date).

[b] Within 24 months of the survey assessment date.

[c] Included alcohol, tobacco, heroin, crack, hallucinogens, inhalants, cannabis, and extra-medical use of cocaine HCl, pain relievers, anxiolytics, and sedative-hypnotics.

Table 3

Weighted estimated relative risk (RR) for developing stimulant dependence soon after onset of extra-medical stimulant use, without statistical adjustment for covariates.[a] Data from United States National Survey on Drug Use and Health, 2003–2005.

	Number of recent-onset stimulant users	Number of stimulant dependence cases	uRR	95% CI	*p* value
All persons	1700	79	–	–	–
Sex					
Male (ref)	709	23	1.0	–	–
Female	991	56	1.5	0.7, 3.2	0.316
Age of stimulant onset					
15 or younger	562	36	3.0	1.4, 6.1	0.003
16–17	442	20	1.2	0.5, 2.6	0.729
18–20 (ref)	420	12	1.0	–	–
21–25	216	9	1.5	0.5, 4.4	0.482
26 and older	60	2	1.5	0.3, 7.9	0.633
Race/ethnicity					
Nonhispanic White (ref)	1314	67	1.0	–	–
Nonhispanic Black	67	3	0.4	0.1, 2.2	0.396
Hispanic	172	4	0.5	0.1, 1.9	0.291
Other	147	5	0.8	0.2, 2.8	0.775
Education[b]					
College senior or graduate	84	0	–	–	–
Some college	316	14	0.6	0.3, 1.4	0.274
High school graduate	298	11	1.0	0.3, 2.8	0.943
Less than high school grad (ref)	1002	54	1.0	–	–
Family income					
0 to $19,999	474	16	0.5	0.2, 1.1	0.091
$20,000 to $49,000 (ref)	536	33	1.0	–	–
$50,000 to $74,999	297	14	0.7	0.3, 1.7	0.417
$75,000+	393	16	0.6	0.2, 1.6	0.311
Population density					
MSA of 1 million+	558	25	1.3	0.6, 2.7	0.503

	Number of recent-onset stimulant users	Number of stimulant dependence cases	uRR	95% CI	*p* value
MSA <1 million (ref)	765	36	1.0	–	–
Segment not in MSA	377	18	1.3	0.6, 2.7	0.448
Occurrence of DSM-IV alcohol dependence syndrome					
Yes	329	38	3.2	1.7, 6.0	<0.001
No (ref)	1371	41	1.0	–	–
Ever used needle to inject stimulants					
Yes	32	5	2.1	0.6, 8.0	0.276
No (ref)	1668	74	1.0	–	–
Number of drugs used by before stimulant onset					
0	85	1	0.14	0.1, 1.1	0.059
1	147	5	1.2	0.4, 3.5	0.722
2	245	12	0.79	0.3, 2.2	0.648
3 (ref)	1223	61	1.0	–	–

Data based on variance estimates via Taylor Series linearization with statistical adjustment for covariates.

[a] Because schooling and stimulant-injecting may be endogenous covariates (responsive to onset of extra-medical stimulant use), the estimates should be interpreted as odds ratios to gauge the observed strength of association; we do not advocate interpretation of them as relative risk estimates.

[b] Reflect values at the time of interview.

Table 4

Estimated relative risk (RR) for developing stimulant dependence soon after onset of extra-medical stimulant use, with statistical adjustments for all listed covariates.[a] Data from United States National Household Survey on Drug Abuse, 2003–2005.

	aRR	95% CI	*p* value
Sex			
Male (ref)	1.0	–	–
Female	1.5	0.7, 3.0	0.314
Age of stimulant onset			
15 or younger	3.1	1.3, 7.6	0.014
16–17	1.2	0.5, 2.8	0.750
18–20 (ref)	1.0	–	–
21–25	1.3	0.4, 4.3	0.638
26 and older	1.6	0.3, 8.4	0.571
Race/ethnicity			
Nonhispanic White (ref)	–	–	–
Nonhispanic Black	0.4	0.1, 1.9	0.253
Hispanic	0.5	0.1, 1.9	0.286
Other	0.8	0.3, 2.6	0.769
Family income			
0 to $19,999	0.5	0.2, 1.3	0.150
$20,000 to $49,000 (ref)	1.0	–	–
$50,000 to $74,999	0.6	0.2, 1.7	0.364
$75,000+	0.5	0.1, 1.7	0.277
Occurrence of DSM-IV alcohol dependence syndrome			
Yes	3.4	1.8, 6.6	<0.001
No (ref)	1.0	–	–
Ever used needle to inject stimulants			
Yes	2.0	0.4, 10.0	0.398
No (ref)	1.0	–	–
Number of drugs used prior to stimulant onset			
0	0.1	0.1, 0.9	0.043
1	1.0	0.4, 2.8	0.993
2	0.8	0.3, 2.0	0.578
3 (ref)	1.0	–	–

[a] Data based on variance estimates via Taylor Series linearization with statistical adjustment for covariates.