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Prescriptions, Nonmedical Use, and Emergency Department Visits Involving Prescription Stimulants

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ABSTRACT

Objective: Little is known regarding the temporal trends in prescriptions, nonmedical use, and emergency department (ED) visits involving prescription stimulants in the United States. Our aim was to examine these 3 national trends involving dextroamphetamine-amphetamine and methylphenidate in adults and adolescents.

Method: Three national surveys conducted between 2006–2011 were used: National Disease and Therapeutic Index, a survey of office-based practices; National Survey on Drug Use and Health, a population survey of substance use; and Drug Abuse Warning Network, a survey of ED visits. Ordinary least squares regression was used to examine temporal changes over time and the associations between the 3 trends.

Results: In adolescents, treatment visits involving dextroamphetamine-amphetamine and methylphenidate decreased over time; nonmedical dextroamphetamine-amphetamine use remained stable, while nonmedical methylphenidate use declined by 54.4% in 6 years. ED visits involving either medication remained stable. In adults, treatment visits involving dextroamphetamine-amphetamine remained unchanged, while nonmedical use went up by 67.1% and ED visits went up by 155.9%. These 3 trends involving methylphenidate remained unchanged. Across age groups, the major source for nonmedical use of both medications was a friend or relative; two-thirds of these friends and relatives had obtained the medication from a physician.

Conclusions: Trends in prescriptions for stimulants do not correspond to trends in reports of nonmedical use and ED visits. Increased nonmedical stimulant use may not be simply attributed to increased prescribing trends. Future studies should focus on deeper understanding of the proportion of, risk factors for, and motivations for drug diversions.

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The past two decades have witnessed increased public concerns regarding nonmedical use of prescription stimulants,¹ particularly those commonly prescribed for attention-deficit/hyperactivity disorder (ADHD). *Prescription stimulants* refers mainly to methylphenidates and dextroamphetamine-amphetamines, classified as schedule II substances in the Controlled Substances Act due to their high abuse potential.² Nonmedical use of these medications has increased in recent years,^{3–7} particularly among young adults and adolescents.^{8–10} In 2011, 1.1 million Americans aged 12 or older used prescription stimulants nonmedically in the past year.¹¹ According to a Treatment Episode Data Set report, which defined stimulant admissions as treatment episodes primarily resulting from stimulant use (prescription stimulant misuse as well as other stimulants, such as cocaine), the proportion of stimulant admissions that were due to prescription stimulant use increased from 3.6% to 9.2% between 2006 and 2011.¹² Several clinical and social consequences of nonmedical use of these stimulants have been noted, including substance and psychiatric comorbidities, crime, addiction, and cardiovascular adverse outcomes.^{3,5,13–16}

The US Food and Drug Administration (FDA) put a black box warning on dextroamphetamine-amphetamine in 2006 due to cardiovascular risks.¹⁷ There is some evidence that dextroamphetamine-amphetamine prescriptions declined after the FDA warning. In one study, treatment visits for dextroamphetamine-amphetamine declined from 36% in 2004 to 24% in 2008.¹⁸ Nevertheless, emergency department (ED) visits involving ADHD medications tripled from 2005 to 2010.¹⁹ Similarly, calls related to ADHD medication misuse in teenagers rose by 76% on the basis of data from poison control centers.²⁰ Whether prescription trends for specific stimulants are consistent with trends for nonmedical use and associated adverse outcomes (eg, ED visits) remains unknown.

Prescription trends and trends in nonmedical use may vary for different population groups. Although the majority of ADHD medications are prescribed for children and adolescents, most nonmedical prescription stimulant users are young adults.^{3,5–7,21,22} Also, ED visits for nonmedical use of prescription stimulants have shown distinct patterns for adolescents and adults.¹⁹ An improved understanding of nonmedical use of prescription stimulants in these 2 populations would be a valuable step in the development of prevention programs.

The aim of this study was to elucidate these trends and their associations by examining temporal trends in prescriptions, nonmedical use, and ED visits involving dextroamphetamine-amphetamine and methylphenidate among adults and adolescents between 2006 and 2011. We assessed the associations of these

- Treatment visits for dextroamphetamine-amphetamine and methylphenidate decreased over time in adolescents, as did nonmedical use of methylphenidate. In adults, however, both nonmedical use of dextroamphetamine-amphetamine and emergency department visits involving this drug increased.
- In both age groups, the major source of nonmedically used dextroamphetamine-amphetamine and methylphenidate was a friend or relative who obtained the drug through prescriptions from a physician.

trends using 3 nationally representative datasets: National Disease and Therapeutic Index (NDTI), a survey of office-based practices; National Survey on Drug Use and Health (NSDUH), a population survey of substance use; and Drug Abuse Warning Network (DAWN), a survey of emergency department (ED) visits. Additionally, we examined the reported sources of nonmedically used dextroamphetamine-amphetamine and methylphenidate and the reasons for ED visits involving these medications.

METHOD

Samples

Data on prescriptions were obtained from NDTI, a nationally representative audit of office-based physicians conducted by IMS Health (Danbury, Connecticut). The NDTI uses a 2-stage sampling procedure and collects data on patient contacts from approximately 4,300 physicians randomly selected within strata, generating approximately 350,000 annual contact records. We limited our analyses to the approximately 85% of contacts generated through office visits. Our primary unit of analysis was a treatment visit during which dextroamphetamine-amphetamine or methylphenidate was prescribed or continued. There were 26,469 contacts involving ADHD medications for patients 12 years and older, including 18,143 for dextroamphetamine-amphetamine and 8,654 for methylphenidate.

Data on nonmedical use of medications were obtained from NSDUH public data for 2006 to 2011 (N = 338,495). The NSDUH is an annual cross-sectional survey sponsored by the Substance Abuse and Mental Health Services Administration and provides estimates of the prevalence of alcohol and drug use in the household population of the United States. The response rate for household screening ranged from 87% to 91% and for completed participant interviews from 74% to 76% across the 6 years. Detailed information about the sampling and survey methodology of NSDUH is found elsewhere.^{11,23–27} Among the NSDUH 2006–2011 respondents, there were 7,151 nonmedical dextroamphetamine-amphetamine users and 3,197 nonmedical methylphenidate users.

Data on ED visits involving dextroamphetamine-amphetamine and methylphenidate were obtained from DAWN for 2006 to 2011 (N = 1,648,992). DAWN consists of a network of over 250 hospitals that monitor drug-related visits

to hospital EDs. The DAWN data are collected directly from the medical records of patients treated in the EDs. Detailed information about the sampling and survey methodology of DAWN can be found elsewhere.²⁸ Between 2006 and 2011, a total of 9,181 visits involved dextroamphetamine-amphetamine and 2,483 involved methylphenidate.

Assessments

Prescriptions in NDTI were assessed by a treatment visit during which prescription stimulants were prescribed or continued. We focused on 2 groups of medications: dextroamphetamine-amphetamine (including Adderall and Adderall XR) and methylphenidate (including Ritalin, Ritalin SR, Ritalin LA, Concerta, Methylin, Methylin ER, and Metadate). NDTI links each drug therapy to a specific 6-digit taxonomic code capturing diagnostic information similar to the *International Classification of Diseases*, Ninth Revision (ICD-9).

Nonmedical use of dextroamphetamine-amphetamine or methylphenidate in NSDUH was assessed using the following question: “Have you ever, even once, used [drug name] that was not prescribed for you or that you took only for the experience or feeling it caused?” Each question was followed by a question about the time of the most recent use. Those who indicated the last use within 12 months were defined as past-year nonmedical prescription stimulant users.

NSDUH respondents who reported using prescription stimulants nonmedically in the past 30 days were asked a series of questions on how they had obtained these drugs. The sources ascertained included friend/relative source (getting for free, buying from them, or taking without asking), direct physician source (getting from 1 doctor or doctor shopping), illegal source (buying from a drug dealer, buying via the Internet, faking prescription, or stealing from pharmacy, clinic, or hospital), other source (some other way), and multiple sources (more than 2 of the above-mentioned sources). We combined the source variables into 5 larger categories as some of the specific sources were endorsed by very few respondents. Respondents who reported obtaining the stimulant from a friend or relative for free were asked how that friend or relative had obtained the drug (secondary source). Those who reported obtaining the drug either primarily or secondarily from a physician were recorded as having obtained the drug from a physician source.

Information on ED visits in DAWN included medications or substances of abuse that might directly or indirectly have contributed to the visit on the basis of the medical record. We focused on ED visits involving methylphenidate or dextroamphetamine-amphetamine. DAWN also assessed the reasons for the ED visits. We categorized the reasons for ED visits into 5 categories based on a previous DAWN report¹⁹: suicidal attempt, adverse reaction, accidental ingestion, nonmedical use, and other. Nonmedical use in DAWN includes cases who used higher doses, used another person's medication, or had drug abuse or dependence problems; thus, it included overmedication and malicious poisoning.

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We also examined the use of alcohol and other drugs in combination with methylphenidate or dextroamphetamine-amphetamine.

Statistical Analyses

We restricted the samples from all 3 datasets to participants aged 12 years and older in order to have consistent age ranges for the 3 data sources. Treatment visits, nonmedical use, and ED visits involving methylphenidate and dextroamphetamine-amphetamine were examined quarterly from 2006 to 2011 for adults (aged 18 or above) and adolescents (aged 12–17). Ordinary linear squares (OLS) regression was used to assess the temporal trend in frequency of prescription, nonmedical use, and ED visits across quarters and their associations. Time (quarter) was the independent variable of interest in these models. We tested OLS models for autocorrelation across time using Durbin-Watson tests,²⁹ and we further reported results adjusting for autocorrelations using Newey-West standard errors if the Durbin-Watson test for autocorrelation produced inconclusive results.

Next, we examined the distribution in sources of methylphenidate and dextroamphetamine-amphetamine used in the past 30 days including primary and secondary sources. To examine whether time modifies the relationship between nonmedical prescription stimulant use and source of the misused drug, we divided these users into 3 mutually exclusive groups: (1) nonmedical dextroamphetamine-amphetamine users only, (2) nonmedical methylphenidate users only, and (3) nonmedical dextroamphetamine-amphetamine and methylphenidate users. Reasons for ER visits were analyzed separately for dextroamphetamine-amphetamine and methylphenidate among adolescents (age 12–17) and adults (aged 18 and above).

To obtain nationally representative quarterly frequency estimates, data were weighted to reflect the complex design of the NSDUH and DAWN samples and were analyzed by Stata 13.0 software.³⁰ We used Taylor series estimation methods as implemented in Stata svy commands to obtain proper standard error estimates for the cross-tabulations and logistic regressions.

RESULTS

Demographic Characteristics

On the basis of the NDTI data, stimulants were more commonly prescribed for males

Table 1. Characteristics of Participants in Samples Examining Trends in Prescriptions, Nonmedical Use, and Emergency Department Visits Involving Dextroamphetamine-Amphetamine and Methylphenidate Using Data From 2006 to 2011

Characteristics	Prescriptions in Treatment Visits ^b						Nonmedical Use						Emergency Department Visits					
	(National Disease and Therapeutic Index)						(National Survey on Drug Use and Health)						(Drug Abuse Warning Network)					
	Dextroamphetamine-Amphetamine (n = 15,125)		Methylphenidate (n = 8,654)		Dextroamphetamine-Amphetamine (n = 7,151)		Dextroamphetamine-Amphetamine (n = 3,197)		Dextroamphetamine-Amphetamine (n = 9,181)		Methylphenidate (n = 2,483)		Dextroamphetamine-Amphetamine (n = 9,181)		Methylphenidate (n = 2,483)		Dextroamphetamine-Amphetamine (n = 9,181)	
	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)
Gender																		
Male	8,846	58.5 (57.7–59.3)	4,649	53.7 (52.7–54.8)	3,855	55.6 (53.9–57.3)	1,654	53.7 (50.8–56.6)	4,229	45.1 (41.6–48.2)	1,246	50.0 (43.5–56.6)	4,948	54.9 (51.4–58.4)	1,237	50.0 (43.4–56.6)		
Female	6,102	40.3 (39.6–41.1)	3,889	44.9 (43.9–46.0)	3,296	44.4 (42.7–46.1)	1,543	46.3 (43.4–49.2)										
Age ^a																		
12–17 y	6,511	43.0 (42.3–43.8)	2,672	30.9 (29.9–31.9)	1,836	16.3 (15.3–17.4)	795	14.1 (12.7–15.7)	1,084	10.9 (8.6–13.8)	725	26.8 (22.1–31.1)						
18–25 y	3,319	21.9 (21.3–22.6)	1,113	12.9 (12.2–13.6)	4,771	59.7 (57.6–61.6)	2,030	50.8 (47.9–53.7)	1,881	19.4 (16.8–22.3)	497	19.7 (16.5–23.4)						
26–34 y	1,727	11.4 (10.9–11.9)	955	11.0 (10.4–11.7)	368	14.9 (13.1–16.8)	239	19.7 (16.5–23.3)	1,762	18.7 (16.1–21.6)	448	21.8 (10.1–17.0)						
35–49 y	2,340	15.5 (14.9–16.1)	1,661	19.2 (18.4–20.0)	154	7.2 (6.0–8.7)	114	10.4 (8.6–12.4)	2,598	26.4 (23.7–28.9)	626	26.5 (11.5–21.9)						
≥ 50 y	1,227	8.1 (7.7–8.6)	2,253	26.0 (25.1–27.0)	22	1.9 (1.1–3.4)	19	5.0 (2.7–9.0)	1,856	24.9 (21.0–29.2)	187	7.0 (16.0–23.6)						
Race																		
White	12,912	85.4 (84.8–85.9)	7,533	87.0 (86.3–87.7)	5,974	86.4 (84.8–87.8)	2,666	86.8 (84.2–89.1)	6,266	86.8 (82.7–89.9)	1,672	91.1 (86.9–94.1)						
Black	1,190	7.9 (7.4–8.3)	512	5.9 (5.4–6.4)	189	2.3 (1.9–2.8)	68	2.6 (1.5–4.3)	666	7.7 (5.4–10.9)	167	3.2 (2.0–5.0)						
Hispanic	584	3.9 (3.6–4.2)	271	3.1 (2.8–3.5)	502	6.8 (5.9–7.3)	226	6.6 (5.1–8.3)	473	4.7 (2.9–7.6)	146	4.8 (2.7–8.4)						
Others	439	2.9 (2.6–3.2)	337	3.9 (3.5–4.3)	486	4.6 (3.8–5.4)	237	4.1 (3.0–5.4)	125	0.8 (0.5–1.4)	40	0.9 (0.4–2.4)						
Year																		
2006	3,018	20.0 (19.3–20.6)	1,737	20.1 (19.2–20.9)	962	13.3 (12.1–14.5)	520	16.2 (14.4–18.3)	862	8.9 (5.8–13.5)	293	8.3 (4.8–13.9)						
2007	2,900	19.2 (18.5–19.8)	1,477	17.1 (16.3–17.9)	1,048	13.8 (12.6–15.1)	487	14.8 (12.7–17.3)	1,275	12.1 (7.3–19.2)	400	19.1 (12.0–29.1)						
2008	2,237	14.8 (14.3–15.4)	1,309	15.1 (14.4–15.9)	1,025	14.4 (13.2–15.7)	509	17.2 (15.0–19.6)	1,625	14.4 (9.4–21.6)	491	16.8 (10.3–26.3)						
2009	2,522	16.7 (16.1–17.3)	1,423	16.4 (15.7–17.2)	1,257	18.7 (17.2–20.3)	553	18.6 (16.3–21.1)	2,047	18.2 (12.0–26.8)	549	18.0 (12.1–26.0)						
2010	2,240	14.8 (14.2–15.4)	1,455	16.8 (16.0–17.6)	1,385	19.6 (18.3–21.1)	581	18.2 (16.0–20.7)	1,883	19.5 (13.0–28.1)	440	16.2 (10.1–25.0)						
2011	2,208	14.6 (14.0–15.2)	1,283	14.8 (14.1–15.6)	1,474	20.2 (18.5–21.9)	547	15.0 (13.2–16.9)	1,489	26.9 (16.5–40.8)	310	21.6 (12.6–34.3)						

^aThe age ranges for the public-access DAWN data are slightly different than those in other datasets. Participant ages in DAWN were categorized into ages 18–24, 25–34, 35–54, and ≥ 55 years.

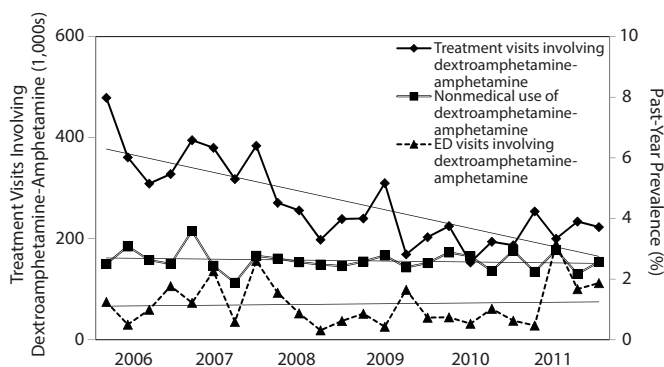
^bSource: IMS National Disease and Therapeutic Index, January 2006 to December 2012, IMS Health Incorporated. All Rights Reserved.

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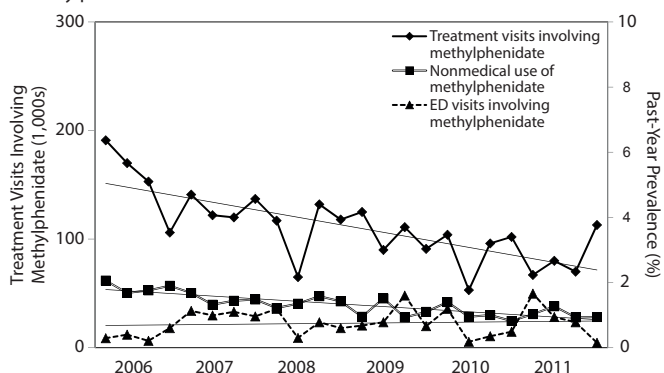
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Figure 1. Temporal Trends in Prescription, Nonmedical Use, and Emergency Department Visits Involving Dextroamphetamine-Amphetamine and Methylphenidate Among Adolescents (12–17 years)^a

A. Dextroamphetamine-Amphetamine



B. Methylphenidate



^aSource: IMS National Disease and Therapeutic Index, January 2006 to December 2012, IMS Health Incorporated. All Rights Reserved.
Abbreviation: ED = emergency department.

(dextroamphetamine-amphetamine: 58.5%, methylphenidate: 53.7%), non-Hispanic whites (dextroamphetamine-amphetamine: 85.4%, methylphenidate: 87.0%), and 12–17 year olds (dextroamphetamine-amphetamine: 43.0%, methylphenidate: 30.9%). Notably, while 26.0% of methylphenidate visits included adults 50 years and older, only 8.1% of dextroamphetamine-amphetamine visits fell in this age range.

On the basis of the NSDUH data, past-year nonmedical use of both dextroamphetamine-amphetamine and methylphenidate was commonly found in males (dextroamphetamine-amphetamine: 55.6%, methylphenidate: 53.7%), those in the age group of 18–25 years (dextroamphetamine-amphetamine: 59.7%, methylphenidate: 50.8%), and whites (dextroamphetamine-amphetamine: 86.4%, methylphenidate: 86.8%).

ED visits resulting from dextroamphetamine-amphetamine use, as reported in DAWN (Table 1), were more frequent among females (54.9%), those aged 35–54 years (26.4%), and whites (86.8%). ED visits involving methylphenidate use were equally common in both sexes (50.0%) and more frequent in those aged 12–17 years (26.8%) and in whites (91.1%). There was an increasing trend over 6 years for ED visits

involving dextroamphetamine-amphetamine and methylphenidate use.

Temporal Trends Among Adolescents

Dextroamphetamine-amphetamine treatment visits among adolescents decreased from 479,000 in the first quarter of 2006 to 223,000 visits in the last quarter of 2011. The Durbin-Watson test showed an inconclusive result, so an adjusted regression was performed (regression coefficient $[B] = -9.24$, standard error $[SE] = 1.57$, $P < .001$). Nonmedical dextroamphetamine-amphetamine use and ED visits, however, did not change appreciably during this period (Figure 1A). Methylphenidate treatment visits in adolescents also decreased from 191,000 in the first quarter of 2006 to 113,000 visits in the last quarter of 2011 ($B = -3.47$, $SE = 0.68$, $P < .001$). Nonmedical use of methylphenidate decreased significantly from 2.06% in the first quarter of 2006 to 0.94% in the last quarter of 2011 ($B = -0.04$, $SE = 0.01$, $P < .001$). The prevalence of ED visits involving methylphenidate in adolescents did not change significantly over time (Figure 1B). There was a statistically significant association between methylphenidate visits and nonmedical use of methylphenidate ($B = 0.01$, $SE = 0.002$, $P = .001$); other associations between the temporal trends were all nonsignificant.

Temporal Trends Among Adults

Dextroamphetamine-amphetamine treatment visits among adults changed little, from 379,000 in the first quarter of 2006 to 364,000 visits in the last quarter of 2011 (Figure 2A). However, the prevalence of nonmedical dextroamphetamine-amphetamine use increased from 0.73% in the first quarter of 2006 to 1.22% in the last quarter of 2011 ($B = 0.10$, $SE = 0.01$, $P < .001$). ED visits involving dextroamphetamine-amphetamine in adults similarly increased from 0.34% in the first quarter of 2006 to 0.87% in the last quarter of 2011 ($B = 0.02$, $SE = 0.003$, $P < .001$) (Figure 2B). A statistically significant association between nonmedical dextroamphetamine-amphetamine use and ED visits involving dextroamphetamine-amphetamine was found in adults ($B = 0.68$, $SE = 0.13$, $P < .001$). Treatment visits, nonmedical use, and ED visits involving methylphenidate did not change appreciably during the study period. We conducted a post hoc analysis among young adults aged 18–25 years, and results from this analysis were similar to those for the full adult population.

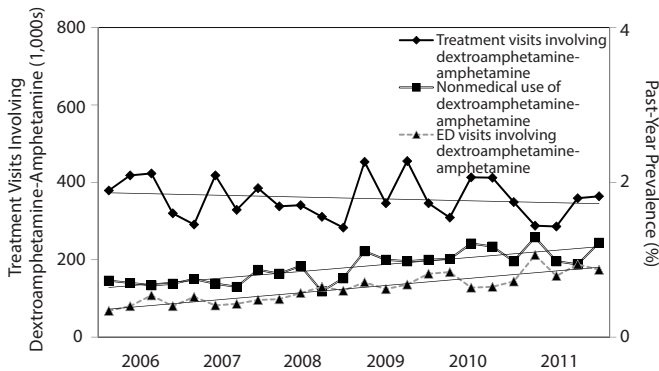
Reasons for ED Visits

In adolescents, 14.1% of ED visits involving dextroamphetamine-amphetamine and 16.4% of those involving methylphenidate were related to nonmedical use of these drugs, while, in adults, ED visits involving nonmedical use of these medications were slightly higher

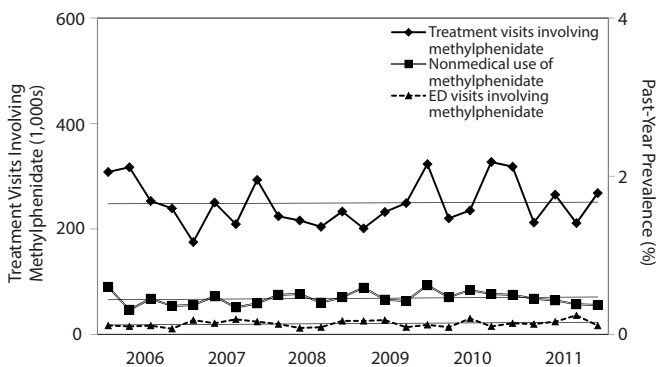
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Figure 2. Temporal Trends in Prescription, Nonmedical Use, and Emergency Department Visits Involving Dextroamphetamine-Amphetamine and Methylphenidate Among Adults (18 years or older)^a

A. Dextroamphetamine-Amphetamine



B. Methylphenidate



^aSource: IMS National Disease and Therapeutic Index, January 2006 to December 2012, IMS Health Incorporated. All Rights Reserved. Abbreviation: ED = emergency department.

(dextroamphetamine-amphetamine: 21.0%, methylphenidate: 18.2%) (Table 2). It is noteworthy that adverse reactions due to medical use of methylphenidate constituted about half of the ED visits among adolescents.

Only 45.1% of dextroamphetamine-amphetamine-related ED visits and 53.6% methylphenidate-related ED visits were single use. Alcohol was present in 16.1%, illicit drugs in 18.3%, and nonmedical use of other medications in 47.6% of dextroamphetamine-amphetamine-related ED visits. Alcohol was present in 13.1%, illicit drugs in 11.2%, and nonmedical use of other medications in 39.7% of methylphenidate-related ED visits.

Sources of Nonmedically Used Stimulants

Friends or relatives were the major primary source of nonmedically used stimulants, contributing 56.1%–68.3% of nonmedically used stimulants (Table 3). A physician's prescription was the main secondary source for both drugs across age groups, ranging from 69.3% to 83.2%. We created 3 mutually exclusive groups of nonmedical prescription stimulant users in order to examine the effect modification of time. The analyses showed that participants who used both dextroamphetamine-amphetamine

and methylphenidate nonmedically were more likely to obtain the drugs from physician sources (OR = 1.57; 95% CI, 1.11–2.21; $P = .009$) compared to those using dextroamphetamine-amphetamine alone. This effect did not change over time ($P = .087$).

DISCUSSION

This study had 3 principal findings. First, prescription visits did not show coincident changes with prevalence of nonmedical use. For instance, the prevalence of nonmedical use of dextroamphetamine-amphetamine in adults increased markedly while prescription trends for this drug remained stable. Second, nonmedical use of dextroamphetamine-amphetamine increased by 67% and associated ED visits went up by 156% in adults, while both trends remained unchanged in adolescents, suggesting different patterns for different age groups. Third, physicians were the major source for the misused stimulants regardless of types of stimulants or age group.

There was a sharp increase in the rate of ADHD treatment for children in the United States in the late 1990s,⁹ and this increase continued until recent years.^{31,32} Yet, our study showed that treatment visits for dextroamphetamine-amphetamine and methylphenidate among adolescents aged 12–17 years declined from 2006 to 2011. One explanation for this discrepancy is that the role of stimulants in ADHD treatment has changed in recent years. Stimulants were used in 96% of visits in 2000, but only 87% of visits in 2010.³³ Another explanation is the introduction of new stimulants such as lisdexamfetamine, which has supplanted use of dextroamphetamine-amphetamine and methylphenidate.

Our study further showed that the reduction in methylphenidate treatment visits for adolescents was associated with decreased nonmedical use (although a causal association cannot be inferred). In contrast, nonmedical use of dextroamphetamine-amphetamine in adults increased, while prescription visits did not grow. The former finding is consistent with the theory that decreased availability of these medications through physician prescriptions may reduce nonmedical use of the drug.³⁴ This conclusion, however, is not supported by the contrasting trends in dextroamphetamine-amphetamine prescriptions and nonmedical use in adults.

There are several potential explanations for the differences in the temporal trends of nonmedical use of dextroamphetamine-amphetamine and methylphenidate, including differences in pharmacologic properties and in social factors. The extended-release formulation of dextroamphetamine-amphetamine has a longer duration of action than methylphenidate, producing a more steady effect.³⁵ Furthermore, dextroamphetamine-amphetamine increases both dopamine and norepinephrine levels,

Table 2. Reasons for Past-Year Emergency Department Visits Involving Dextroamphetamine-Amphetamine or Methylphenidate Using the Drug Abuse Warning Network, 2006–2011

Reason	Adolescents				Adults			
	Dextroamphetamine-Amphetamine		Methylphenidate		Dextroamphetamine-Amphetamine		Methylphenidate	
	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)	n	Weighted % (95% CI)
Suicide	113	4.7 (2.8–7.9)	120	6.8 (4.3–10.4)	704	8.0 (6.8–10.3)	213	15.2 (10.8–20.9)
Adverse reaction	450	30.4 (23.3–38.6)	651	51.1 (44.0–58.2)	2,817	38.5 (34.2–42.9)	486	25.5 (19.2–33.0)
Nonmedical use	224	14.1 (9.5–20.3)	272	16.4 (11.7–22.6)	1,733	21.0 (17.8–24.5)	368	18.2 (13.1–24.7)
Accidental ingestion	284	27.4 (20.3–35.9)	147	14.1 (9.4–20.7)	84	1.0 (0.6–1.5)	29	2.5 (1.1–5.9)
Others	517	23.4 (18.0–30.0)	173	11.6 (8.2–16.0)	2,328	31.3 (27.9–34.8)	558	38.7 (31.5–46.4)

Table 3. Sources of Stimulants for Past-Month Nonmedical Use of Dextroamphetamine-Amphetamine and Methylphenidate Using Data From the National Survey on Drug Use and Health, 2006–2011

Source	Dextroamphetamine-Amphetamine		Methylphenidate	
	n	Weighted % (95% CI)	n	Weighted % (95% CI)
Adolescent (primary source)				
Friend or relative	166	60.2 (51.8–67.0)	144	56.1 (51.4–64.5)
Physicians	32	11.7 (7.7–17.3)	36	13.8 (9.6–19.5)
Illegal	30	13.0 (8.6–19.0)	33	14.9 (10.0–21.5)
Others	13	5.8 (3.1–10.8)	13	5.0 (2.3–10.6)
Multiple sources	31	9.4 (5.8–14.9)	31	10.2 (6.4–15.8)
Adolescent (secondary source) ^a				
Friend or relative	24	18.8 (12.0–28.0)	23	24.3 (15.7–35.6)
Physicians	68	76.4 (65.9–84.5)	54	69.3 (57.4–79.0)
Illegal	7	4.6 (1.7–11.9)	7	6.1 (2.4–14.6)
Adult (primary source)				
Friend or relative	681	68.3 (64.0–72.3)	540	64.9 (59.4–70.0)
Physicians	85	12.2 (9.3–15.9)	92	16.4 (12.8–20.7)
Illegal	84	7.7 (5.6–10.3)	80	8.8 (5.9–13.0)
Others	25	2.5 (1.4–4.4)	20	2.2 (1.1–4.2)
Multiple sources	82	9.4 (6.8–12.7)	67	7.8 (5.4–11.0)
Adult (secondary source) ^a				
Friend or relative	352	13.5 (8.0–21.8)	56	21.5 (12.9–33.8)
Physicians	51	83.2 (74.8–89.2)	283	75.2 (63.4–74.2)
Illegal	11	3.3 (1.3–7.9)	9	3.3 (1.2–8.5)

^aOther source and multiple sources were not shown in secondary source due to the limited number of reports.

which is associated with improved cognitive function.³⁶ Since cognitive enhancement is the most commonly reported reason for nonmedical use of prescription stimulants,^{6–8} differences between dextroamphetamine-amphetamine and methylphenidate with regard to cognitive enhancement properties could partially explain the increased popularity of dextroamphetamine-amphetamine, especially among college students.⁷

Social context in which the stimulant is used may provide an explanation for nonmedical use trends. A qualitative study of college students found that nonmedical stimulant users had limited knowledge of the side effects of the drugs.³⁷ Also, about 36% of the stimulant users believed that using dextroamphetamine-amphetamine could help them to be “smarter.” The reputation of dextroamphetamine-amphetamine on college campuses as “not harmful” and as a means of “getting smart” may contribute to the increased rate of nonmedical use among adults.

Our study also found that adult ED visits involving dextroamphetamine-amphetamine showed a strong correlation

with increased nonmedical use in adults, consistent with a previous DAWN report.³⁰ Our study further revealed that this trend is limited to dextroamphetamine-amphetamine use in the adult population. In addition, almost half of the ADHD medication-related ED visits involved use in combination with alcohol and other drugs, suggesting that the combination of other substance may heighten health risks.

Consistent with past research, our study found that a friend or relative was the major source for nonmedically used prescription stimulants.^{7,22,37–39} Our study further found that among those who obtained the drug from a friend or relative, more than 70% of them obtained their drug legitimately through a doctor's prescription. This finding suggests that drug diversion plays a crucial role in nonmedical prescription stimulant use. A study found that 61.7% of college students diagnosed with ADHD reported diverting their prescription stimulants.⁴⁰ Additionally, those who used both dextroamphetamine-amphetamine and methylphenidate nonmedically were more likely than those with nonmedical dextroamphetamine-amphetamine use only to report obtaining the drug from physician sources, implying a heavier role for doctor shopping among this population.

The limitations of this study should be considered. A major limitation was that the 3 datasets (NDTI, NSDUH, and DAWN) were not linked, which limited our capability to make further conclusions about the associations we found. For instance, we were not able to assess whether nonmedical use and ED visits happened among the same individuals who were prescribed these medications. Second, treatment visits for methylphenidate and dextroamphetamine-amphetamine are indirect measures of medication availability. Information on dosage or duration of treatment was not available in NDTI. Third, we examined only linear temporal trends. Stimulant prescriptions, nonmedical use, and ED visits may have followed nonlinear trends. Furthermore, we were unable to examine lagged associations between trends due to the short study period. Fourth, NSDUH used responses regarding the source of nonmedically used stimulants in general to ascertain the source of specific stimulants. Fifth, NSDUH relies on self-reports, which may be vulnerable to recall bias. Finally, effects of the

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shifts in drug market share may not be fully captured by these data (eg, entry of Vyvanse into the market—although we performed analyses for Vyvanse, and its nonmedical use is very limited).

In the context of these limitations, the findings highlight the urgent need for public health campaigns to target drug diversion from legitimately prescribed users. This

study showed that physician prescriptions constitute the main source of nonmedically used prescription stimulants and trends of nonmedical use of these stimulants did not correspond to their prescription trends. Future studies should focus on deeper understanding of the proportion of, risk factors for, and motivations for drug diversions for a more tailored preventive program for stimulant misuse.

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REFERENCES

- Einhorn C, Huang J, Lavalley M. In their own words: "study drugs." *The New York Times* Web site. http://www.nytimes.com/interactive/2012/06/10/education/stimulants-student-voices.html?_r=1&. Published June 13, 2012. Accessed December 1, 2014.
- Drug Enforcement Administration. *ARCOS 2: Report 1, Retail Drug Distribution*. Springfield, VA: Department of Justice, Drug Enforcement Administration; 2003.
- Arria AM, Caldeira KM, O'Grady KE, et al. Nonmedical use of prescription stimulants among college students: associations with attention-deficit-hyperactivity disorder and polydrug use. *Pharmacotherapy*. 2008;28(2):156–169.
- McCabe SE, Boyd CJ, Young A. Medical and nonmedical use of prescription drugs among secondary school students. *J Adolesc Health*. 2007;40(1):76–83.
- McCabe SE, Knight JR, Teter CJ, et al. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. *Addiction*. 2005;100(1):96–106.
- Teter CJ, McCabe SE, Cranford JA, et al. Prevalence and motives for illicit use of prescription stimulants in an undergraduate student sample. *J Am Coll Health*. 2005;53(6):253–262.
- Teter CJ, McCabe SE, LaGrange K, et al. Illicit use of specific prescription stimulants among college students: prevalence, motives, and routes of administration. *Pharmacotherapy*. 2006;26(10):1501–1510.
- McCabe SE, Teter CJ, Boyd CJ. The use, misuse and diversion of prescription stimulants among middle and high school students. *Subst Use Misuse*. 2004;39(7):1095–1116.
- Olfson M, Gameroff MJ, Marcus SC, et al. National trends in the treatment of attention deficit hyperactivity disorder. *Am J Psychiatry*. 2003;160(6):1071–1077.
- Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *The NSDUH Report: Nonmedical Use of Adderall Among Full-Time College Students*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2009.
- Substance Abuse and Mental Health Services Administration. *Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings*. NSDUH Series H-44, HHS Publication No (SMA) 12-4713. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2012.
- Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. *Treatment Episode Data Set (TEDS): 2002–2012. National Admissions to Substance Abuse Treatment Services*. BHSIS Series S-71, HHS Publication No (SMA) 14-4850. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.
- DrugFacts: stimulant ADHD medications: methylphenidate and amphetamines. National Institute on Drug Abuse Web site. <http://www.drugabuse.gov/publications/drugfacts/stimulant-adhd-medications-methylphenidate-amphetamines>. Updated January 2014. Accessed April 7, 2014.
- Gould MS, Walsh BT, Munfakh JL, et al. Sudden death and use of stimulant medications in youths. *Am J Psychiatry*. 2009;166(9):992–1001.
- Sichilima T, Rieder MJ. Adderall and cardiovascular risk: a therapeutic dilemma. *Paediatr Child Health (Oxford)*. 2009;14(3):193–195.
- Chen LY, Crum RM, Martins SS, et al. Patterns of concurrent substance use among nonmedical ADHD stimulant users: results from the National Survey on Drug Use and Health. *Drug Alcohol Depend*. 2014;142(142):86–90.
- Food and Drug Administration. Drug Safety and Risk Management Advisory Committee Meeting. February 9–10, 2006; Gathersburg, MD.
- Kornfield R, Watson S, Higashi AS, et al. Effects of FDA advisories on the pharmacologic treatment of ADHD, 2004–2008. *Psychiatr Serv*. 2013;64(4):339–346.
- Substance Abuse and Mental Health Services Administration. *The DAWN Report: Emergency Department Visits Involving Attention Deficit/Hyperactivity Disorder Stimulant Medications*. Rockville, MD: Center for Behavioral Health Statistics and Quality; 2013.
- Setlik J, Bond GR, Ho M. Adolescent prescription ADHD medication abuse is rising along with prescriptions for these medications. *Pediatrics*. 2009;124(3):875–880.
- McCabe SE, West BT, Wechsler H. Trends and college-level characteristics associated with the non-medical use of prescription drugs among US college students from 1993 to 2001. *Addiction*. 2007;102(3):455–465.
- White BP, Becker-Blease KA, Grace-Bishop K. Stimulant medication use, misuse, and abuse in an undergraduate and graduate student sample. *J Am Coll Health*. 2006;54(5):261–268.
- Substance Abuse and Mental Health Services Administration. *Results from the 2006 National Survey on Drug Use and Health: National Findings*. NSDUH Series H-32, DHHS Publication No SMA 07-4293. Rockville, MD: Office of Applied Studies, Substance Abuse and Mental Health Services; 2007.
- Substance Abuse and Mental Health Services Administration. *Results from the 2007 National Survey on Drug Use and Health: National Findings*. NSDUH Series H-34, DHHS Publication No SMA 08-4343. Rockville, MD: Office of Applied Studies, Substance Abuse and Mental Health Services Administration; 2008.
- Substance Abuse and Mental Health Services Administration. *Results from the 2008 National Survey on Drug Use and Health: National Findings*. NSDUH Series H-36, HHS Publication No SMA 09-4434. Rockville, MD: Office of Applied Studies, Substance Abuse and Mental Health Services Administration; 2009.
- Substance Abuse and Mental Health Services Administration. *Results from the 2009 National Survey on Drug Use and Health: Volume I*.

- Summary of National Findings. NSDUH Series H-38A, HHS Publication No SMA 10-4856. Rockville, MD: Office of Applied Studies, Substance Abuse and Mental Health Services Administration; 2010.
27. Substance Abuse and Mental Health Services Administration. *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*. NSDUH Series H-41, HHS Publication No SMA 11-4658. Rockville, MD; Substance Abuse and Mental Health Services Administration; 2011.
 28. Substance Abuse and Mental Health Services Administration. *Drug Abuse Warning Network, 2009: Methodology Report*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2011.
 29. Durbin J, Watson GS. Testing for serial correlation in least squares regression. I. *Biometrika*. 1950;37(3-4):409-428.
 30. Stata Statistical Software. Release 13 [computer program]. College Station, TX: StataCorp LP; 2013.
 31. Visser SN, Danielson ML, Bitsko RH, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *J Am Acad Child Adolesc Psychiatry*. 2014;53(1):34-46.e2.
 32. Zuvekas SH, Vitiello B. Stimulant medication use in children: a 12-year perspective. *Am J Psychiatry*. 2012;169(2):160-166.
 33. Garfield CF, Dorsey ER, Zhu S, et al. Trends in attention deficit hyperactivity disorder ambulatory diagnosis and medical treatment in the United States, 2000-2010. *Acad Pediatr*. 2012;12(2):110-116.
 34. Komro KA, Toomey TL. Strategies to prevent underage drinking. *Alcohol Res Health*. 2002;26(1):5-14.
 35. Markowitz JS, Straughn AB, Patrick KS. Advances in the pharmacotherapy of attention-deficit-hyperactivity disorder: focus on methylphenidate formulations. *Pharmacotherapy*. 2003;23(10):1281-1299.
 36. Pliszka SR, McCracken JT, Maas JW. Catecholamines in attention-deficit hyperactivity disorder: current perspectives. *J Am Acad Child Adolesc Psychiatry*. 1996;35(3):264-272.
 37. DeSantis AD, Hane AC. "Adderall is definitely not a drug": justifications for the illegal use of ADHD stimulants. *Subst Use Misuse*. 2010;45(1-2):31-46.
 38. Garnier-Dykstra LM, Caldeira KM, Vincent KB, et al. Nonmedical use of prescription stimulants during college: four-year trends in exposure opportunity, use, motives, and sources. *J Am Coll Health*. 2012;60(3):226-234.
 39. McCabe SE, Teter CJ, Boyd CJ. Medical use, illicit use and diversion of prescription stimulant medication. *J Psychoactive Drugs*. 2006;38(1):43-56.
 40. Garnier LM, Arria AM, Caldeira KM, et al. Sharing and selling of prescription medications in a college student sample. *J Clin Psychiatry*. 2010;71(3):262-269.