HHS Public Access

Author manuscript

Am J Prev Med. Author manuscript; available in PMC 2020 May 01.

Published in final edited form as:

Am J Prev Med. 2019 May ; 56(5): 639–647. doi:10.1016/j.amepre.2018.12.009.

U.S. Emergency Department Visits Resulting From Nonmedical Use of Pharmaceuticals, 2016

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Abstract

Introduction: National data on morbidity from nonmedical use of pharmaceuticals are limited. This study used nationally representative, public health surveillance data to characterize U.S. emergency department visits for acute harms from nonmedical use of pharmaceuticals and to guide prevention efforts.

Methods: Data collected in 2016 from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project were analyzed in 2018 to calculate national estimates of emergency department visits for harms from nonmedical use of pharmaceuticals.

Results: From review of 5,130 cases, there were an estimated 358,247 emergency department visits (95% CI=280,675, 435,819) in 2016 for harms from nonmedical use of pharmaceuticals and 41.1% resulted in hospitalization (95% CI=32.3%, 49.8%). One half (50.9%, 95% CI=46.6%, 55.3%) of estimated visits involved patients aged ≤34 years; more than one half of estimated visits also involved non-pharmaceutical substances (52.9%, 95% CI=49.7%, 56.1%), including illicit drugs in 34.1% (95% CI=30.9%, 37.2%) and alcohol in 21.8% (95% CI=19.8%, 23.9%). Overall, benzodiazepines were implicated in 46.9% (95% CI=42.5%, 51.2%) of estimated emergency department visits for nonmedical use of pharmaceuticals but were the only substance implicated in just 6.5% (95% CI=5.1%, 7.9%). Prescription opioids were implicated in 36.2% (95% CI=30.8%, 41.7%) of estimated emergency department visits and were the only substance implicated in 11.3% (95% CI=8.6%, 14.0%).

Conclusions: Although prescription opioids or benzodiazepines are frequently implicated in emergency department visits for nonmedical use, because other substances and additional

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Author contributions were as follows: Geller and Budnitz helped with study conception and design and drafting of the manuscript; all authors helped with acquisition of data, analysis and interpretation of data, critical revision for important intellectual content, and administrative, technical, or logistical support; Geller performed statistical analysis; and Budnitz supervised the study.

pharmaceuticals are most often involved, prescribing clinicians should consider implementing specific screening to address polysubstance use and, when warranted, treatment interventions.

INTRODUCTION

Nonmedical use of pharmaceuticals includes a spectrum of circumstances of use, from using a medication to manage a condition, but in a frequency, dose, or other manner that is not recommended, to using the medication to attain euphoria or other psychological or physiologic effect without medical justification.[1,2]

Nonmedical use of pharmaceuticals gained renewed attention in the last decade. The increase in deaths from prescription opioids has been called an epidemic[3] and overdoses from opioids (prescription and illicit) led HHS to declare a public health emergency in 2017.[4] Additionally, concerns have arisen about nonmedical use of pharmaceuticals other than opioids, such as benzodiazepines, non-benzodiazepine sleeping aids, stimulants, cough and cold products, and gabapentinoids.[5–10] To target interventions prior to fatal outcomes, data on morbidity from nonmedical use of pharmaceuticals can be helpful; however, since discontinuation of the Drug Abuse Warning Network after 2011, detailed national data describing morbidity from nonmedical use of pharmaceuticals are limited.[11] A newly expanded, nationally representative public health surveillance system is used to estimate numbers of emergency department (ED) visits for pharmaceutical harms by patient characteristics and intent of use, and identify clinical manifestations and specific implicated products.

METHODS

Study Sample

National estimates of ED visits for harms from pharmaceuticals were based on data from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project, a joint collaboration of the Centers for Disease Control and Prevention (CDC), the U.S. Consumer Product Safety Commission, and Food and Drug Administration. NEISS-CADES is an active public health surveillance system based on a nationally representative, stratified probability sample of 56 U.S hospitals with at ≥6 beds and a 24-hour ED.[12–14]

Trained data abstractors review clinical records of every ED visit to identify harms (adverse events) from therapeutic pharmaceutical use and, beginning in 2016, harms caused by pharmaceuticals used for any intent. Abstractors record up to four implicated pharmaceuticals, patient demographics, intent of pharmaceutical use, narrative descriptions of the event (including clinical manifestations, precipitating circumstances, and use of illicit drugs or alcohol in addition to pharmaceuticals), clinician diagnoses, laboratory testing, treatments administered, and discharge disposition. Clinical manifestations are coded by CDC using the Medical Dictionary for Regulatory Activities, version 9.1. Data collection from the NEISS-CADES project hospitals has been deemed a public health surveillance activity by the CDC human subject oversight bodies and did not require IRB approval.[15]

Measures

For this analysis (performed in 2018), cases included ED visits for pharmaceutical harms from January 1, 2016 to December 31, 2016. In some cases, pharmaceuticals were identified from toxicology testing (e.g., when patients were unable or unwilling to provide a drug use history). Cases involving unspecified drugs (e.g., diagnosis of opioid overdose but no indication if the opioid was a pharmaceutical product or heroin) were excluded. Cases involving inadequate therapy, drug withdrawal, detoxification treatment, medical clearance, occupational exposures, harms from ED treatment, and deaths are not included. Cases involving self-harm (administration of pharmaceuticals to injure or kill oneself) or unsupervised pediatric ingestions were excluded.

Intent of pharmaceutical use was classified as therapeutic (e.g., adverse effects, allergic reactions, medication errors) or nonmedical use. Nonmedical use includes abuse, therapeutic misuse, and overdoses without indication of intent. Abuse cases involve documented clinician diagnosis of abuse or documented recreational use (e.g., “to get high”); although concern has been raised that the term “abuse” may contribute to stigma,[16,17] it is employed here because the term remains commonly used by clinicians in their medical documentation. Therapeutic misuse cases involved documented therapeutic intent, but use was not as directed (e.g., taking someone else’s prescription medication for pain, intentionally taking larger doses than prescribed). Cases of overdoses without indication of intent lacked documentation of therapeutic intent, abuse, or self-harm (e.g., patients found unresponsive by paramedics and patients unable or unwilling to provide description of circumstances or intent).

Statistical Analysis

Each reported case is assigned a weight based on the inverse probability of selection, with adjustment for nonresponse, and post-stratified to adjust for changes in the total number of annual hospital ED visits.[13,14] National estimates of ED visits were calculated using these weights and corresponding 95% CIs were calculated to account for the sample design by using the SAS SURVEYMEANS procedure. Estimates based on <20 cases or total estimates <1,200 are considered statistically unstable and are not shown. Estimates with coefficient of variation >30% may be statistically unstable and are noted.

RESULTS

Case Characteristics

Based on 5,130 surveillance cases from 56 EDs, there were an estimated 358,247 (95% CI=280,675, 435,819) ED visits for harms from nonmedical use of pharmaceuticals in 2016 (hereafter nonmedical use visits), compared with 1,474,556 (95% CI=980,473, 1,968,639) ED visits for harms from therapeutic use of pharmaceuticals. More than four fifths (83.4%, 95% CI=80.9%, 85.8%) of nonmedical use visits involved abuse (39.7%) or overdoses without indication of therapeutic intent, abuse, or self-harm (43.7%); misuse for a therapeutic purpose was documented in 16.6% of estimated visits.

One half (50.9%, 95% CI=46.6%, 55.3%) of estimated nonmedical use visits involved patients aged ≤34 years (Table 1). Among patients aged 15–34 years, the estimated number of nonmedical use visits (175,107, 95% CI=133,910, 216,305) approached the number of visits involving therapeutic use (240,757, 95% CI=171,238, 310,277). Among patients aged ≥65 years, the estimated number of nonmedical use visits (17,303, 95% CI=11,303, 23,303) was 30-fold less than the number of visits involving therapeutic use (589,431, 95% CI=329,195, 849,668).

Patient demographics and disposition from the ED were similar for visits for abuse and for overdoses without indication of intent; patient demographics and disposition from the ED were similar for visits for therapeutic misuse and therapeutic use (Appendix Table 1). Overall, most (55.7%) estimated nonmedical use visits were made by males (Table 1); however, females made most of the nonmedical use visits involving therapeutic misuse (54.5%, 95% CI=50.7%, 58.2%), similar to the proportion of visits by females involving therapeutic use (55.7%).

Overall, an estimated 41.1% of nonmedical use visits resulted in hospitalization. Hospitalization was more common for nonmedical use visits involving abuse (36.3%, 95% CI=25.5%, 47.1%) or overdoses without indication of intent (50.5%, 95% CI=41.4%, 59.7%) than for therapeutic misuse visits (27.5%, 95% CI=21.4%, 33.7%), which resulted in hospitalization as frequently as visits for therapeutic use (27.2%).

Although a single pharmaceutical was implicated in 72.1% of estimated nonmedical use visits, most visits (52.9%) involved use of at least one non-pharmaceutical substance, most commonly alcohol (21.8%), marijuana (17.7%), and cocaine (10.5%). At least one illicit substance was documented in 44.1% (95% CI=40.5%, 47.8%) of estimated nonmedical use visits involving abuse compared with 9.4% (95% CI=7.0%, 11.7%) of nonmedical use ED visits involving therapeutic misuse. Use of illicit substances was rarely documented in ED visits involving therapeutic use of pharmaceuticals (0.6%).

Type of Pharmaceutical Involved

Overall, benzodiazepines and opioids were the most common pharmaceutical classes involved in ED visits for nonmedical use. Benzodiazepines were involved in 167,845 (46.9%) of estimated nonmedical use visits and prescription opioids were involved in 129,863 (36.2%) of nonmedical use visits (Table 2). Benzodiazepines or prescription opioids were involved in 71.0% (95% CI=67.2%, 74.8%) of nonmedical use ED visits. Benzodiazepines and prescription opioids were co-implicated in 12.1% (95% CI=9.4%, 14.8%) of nonmedical use visits. No other pharmaceutical category was involved in >10% of nonmedical use visits.

Although benzodiazepines were involved in more ED visits for nonmedical use than any other drug class, in 26.4% of estimated nonmedical use visits involving benzodiazepines (95% CI=19.7%, 33.1%), the benzodiazepine was identified from laboratory test results only; in 7.4% of visits involving opioids, the opioid was identified by laboratory testing only (95% CI=4.1%, 10.7%). In addition, benzodiazepines were implicated alone (without

involvement of other pharmaceutical or non-pharmaceutical substances) in far fewer estimated nonmedical use visits (23,335, 6.5%) than opioids alone (40,550, 11.3%; Table 2).

Therapeutic misuse was the most common type of nonmedical use for ED visits involving antibiotics (76.5%, 95% CI=63.4%, 89.7%) and nonopioid analgesics (48.1%, 95% CI=41.6%, 54.5%). One third of nonmedical use visits involving antihypertensives (36.7%, 95% CI=21.7%, 51.6%) and one quarter of visits involving muscle relaxants (28.5%, 95% CI=17.9%, 39.0%) were attributed to therapeutic misuse.

Patient Characteristics and Type of Pharmaceutical Involved

Males made most of the estimated nonmedical use visits involving stimulants (61.0%, 95% CI=50.9%, 71.0%), cough/cold products or antihistamines (59.8%, 95% CI=53.2%, 66.4%), prescription opioids (57.6%, 95% CI=54.8%, 60.4%), or benzodiazepines (57.2%, 95% CI=54.7%, 59.7%; Appendix Figure 1).

Patients aged <35 years made almost three quarters of estimated visits involving cough/cold or antihistamine-containing products (71.3%, 95% CI=65.2%, 77.4%) and stimulants (71.4%, 95% CI=61.9%, 81.0%); and approximately one half of estimated visits involving nonopioid analgesics (56.4%, 95% CI=49.6%, 63.1%), benzodiazepines (53.1%, 95% CI=50.6%, 55.7%), anticonvulsants (47.7%, 95% CI=32.8%, 62.6%), antidepressants (47.1%, 95% CI=40.4%, 53.9%), and antipsychotics (44.9%, 95% CI=37.1%, 52.7%; Appendix Figure 2). Adults aged ≥65 years made too few nonmedical use visits to calculate stable estimates of ED visits for categories other than benzodiazepines (4.1%, 95% CI=3.0%, 5.1%) and prescription opioids (6.2%, 95% CI=4.8%, 7.6%).

Involvement of Other Substances

Multiple pharmaceuticals or other substances were documented to be involved in at least two thirds of estimated nonmedical use visits involving gabapentinoids (88.8%, 95% CI=82.6%, 95.1%), benzodiazepines (86.1%, 95% CI=83.1%, 89.1%), non-benzodiazepine hypnotics (85.9%, 95% CI=79.7%, 92.2%), muscle relaxants (78.9%, 95% CI=71.1%, 86.6%), antidepressants (75.3%, 95% CI=69.3%, 81.3%), prescription opioids (68.8%, 95% CI=63.9%, 73.8%), and antipsychotics (68.5%, 95% CI=62.7%, 74.4%; Figure 1). Use of illicit drugs or alcohol was documented in an estimated 62.0% of nonmedical use visits involving benzodiazepines (95% CI=59.0%, 64.9%), but in less than one half of nonmedical use visits involving other categories: stimulants (46.5%, 95% CI=35.4%, 57.6%), non-benzodiazepine hypnotics (45.2%, 95% CI=37.3%, 53.1%), prescription opioids (43.8%, 95% CI=41.2%, 46.3%), antidepressants (42.3%, 95% CI=36.8%, 47.8%), and gabapentinoids (37.9%, 95% CI=26.6%, 49.3%). Concurrent use of illicit drugs was most commonly documented for nonmedical use visits involving benzodiazepines and prescription opioids, accounting for an estimated 44.5% and 33.1% of nonmedical use visits, respectively (95% CI=40.5%, 48.6%, and 95% CI=30.5%, 35.7%).

Clinical Manifestations

Nonmedical use visits frequently involved severe overdose. Overall, patients were unresponsive or experienced cardiorespiratory failure in 22.6% of estimated nonmedical use

visits and patients had altered mental status in an additional 35.4% of visits (Table 3). Unresponsiveness or cardiorespiratory failure was documented in more than one quarter of nonmedical use visits involving either a benzodiazepine (27.2%, 95% CI=19.6%, 34.7%) or a prescription opioid (29.6%, 95% CI=22.3%, 36.9%), but only one tenth (9.6%, 95% CI=6.6%, 12.6%) of nonmedical use visits not involving neither a benzodiazepine nor a prescription opioid. Excluding cases of co-implication with prescription opioids, unresponsiveness or cardiorespiratory failure was documented in 38.0% (95% CI=28.4%, 47.5%) of benzodiazepine nonmedical use visits involving an illicit drug (other than marijuana alone), compared with 18.5% (95% CI=8.5%, 28.5%) of visits involving no other substance. For visits involving co-implication of benzodiazepines and prescription opioids, unresponsiveness or cardiorespiratory failure was present in 28.9% (95% CI=19.5%, 38.2%) of the visits involving an illicit drug (other than marijuana alone), compared with 29.2% (95% CI=22.2%, 36.3%) of visits involving prescription opioids alone.

DISCUSSION

Harm from nonmedical use of pharmaceuticals led to an estimated 358,247 ED visits in the U.S. in 2016, with 23% involving unresponsiveness or cardiorespiratory failure and 40% resulting in hospitalization.

Despite indications of declining medical opioid prescribing,[18] nonmedical opioid use remains prevalent,[19] and ED visit morbidity data highlight opportunities for targeted prevention before patients suffer fatal overdoses from opioids. Two fifths of ED visits by patients treated for nonmedical use of opioids involved patients younger than 35 years, and 29% of patients treated for nonmedical use of opioids experienced unresponsiveness or cardiorespiratory failure. Although patients treated for nonfatal overdose have increased risk of another overdose,[20–22] and naloxone, which has shown efficacy in tertiary prevention of fatal opioid overdoses, naloxone is not routinely made available to overdose patients at ED discharge.[23] Thus, efforts to expand naloxone distribution could initially target patients who receive emergency care for serious overdose symptoms and their families and friends.[24,25] In addition, the ED can be a place to initiate secondary preventive interventions, such as brief motivational interviewing,[26,27] connecting patients to peer navigators for follow-up, and linking to or initiating medication-assisted treatment.[11,28–30] As 68.8% of the estimated 130,000 ED visits resulting from nonmedical use of opioids involved other pharmaceuticals, alcohol, or illicit substances, primary prevention efforts (in the ED or outpatient office) to reduce ED visits resulting from nonmedical use of opioids include screening for substance use before prescribing opioids, prescribing the lowest effective dose, and avoiding co-prescription with benzodiazepines when possible.[25,31,32]

Although the number of nonmedical use visits involving benzodiazepines was estimated to be higher than the number involving opioids in 2016, the degree to which benzodiazepines contributed to harms is less certain. First, in 26% of visits for nonmedical use involving benzodiazepines, the presence of benzodiazepines was based on laboratory findings in visits with a general diagnosis, such as drug overdose. Second, benzodiazepines were rarely the sole substance implicated in ED visits for nonmedical use. Use of benzodiazepines alone only accounted for one seventh of benzodiazepine nonmedical use visits. By comparison,

opioids alone accounted for one third of opioid nonmedical use visits. Third, additional substances appear to play a more prominent role in harms from nonmedical benzodiazepine use. Unlike opioid visits, benzodiazepine visits involved more severe effects (unresponsiveness or cardiorespiratory failure) when illicit substance use was also documented.

Should similar interventions be considered for benzodiazepines as for opioids? The benzodiazepine reversal agent flumazenil does not currently exist in auto-injector form, but even if it were developed, the frequency of co-implication with opioids (prescription and illicit) reduces the likelihood of benefit in these patients. Instead, screening to identify opioid use and recent opioid overdose history in patients prescribed benzodiazepines should prompt consideration of naloxone prescription. Screening patients prescribed benzodiazepines for use of other pharmaceuticals, alcohol, and illicit substances and addressing the use of these other substances may impact an even higher proportion of patients compared with screening those prescribed opioids, as a higher proportion of both ED visits and deaths involving benzodiazepines also involve such other substances. Although there currently is no Food and Drug Administration–approved medication to assist treatment for benzodiazepine dependence, behavioral interventions such as motivational interviewing could also apply to patients treated in EDs following nonmedical use of benzodiazepines.[33] Adoption of similar primary prevention approaches to those for opioids is warranted, such as judicious prescribing, and avoidance where possible of co-prescription of benzodiazepines with opioids.[25,34]

Reports of increased use of non-opioid pharmaceuticals (e.g., gabapentinoids,[35–37] loperamide,[38,39] and stimulants[40]) have prompted concerns for missing the next drug epidemic, but neither large numbers nor high severity of ED visits attributed to other pharmaceuticals were identified. Only 29% of estimated ED visits for nonmedical use did not involve opioids or benzodiazepines, and these visits were less likely than visits involving opioids or benzodiazepines to involve severe manifestations of unresponsiveness or cardiorespiratory failure (9.6%). Gabapentinoids, approved for seizure control and selected pain syndromes but increasingly prescribed for other pain indications, were involved in 3.3% of nonmedical use ED visits but most often involved other substances as well (88.8%). Thus, similar to benzodiazepines, the contribution of gabapentinoids to severe outcomes is not clear; yet, screening for other medication and substance use may also be appropriate for patients prescribed gabapentinoids. There were not enough ED visits involving nonmedical use of loperamide or kratom to calculate national estimates, although harms from these drugs may be less well-recognized in the ED setting. Most non-opioid, non-benzodiazepine nonmedical use visits involved pharmaceuticals known to be misused predominantly by certain age groups. Seven of ten ED visits for nonmedical use of cough/cold or antihistamine products and prescription stimulants involved patients aged younger than 35 years; six of ten ED visits for nonmedical use of muscle relaxants, gabapentinoids, and non-benzodiazepine hypnotics involved patients aged 35 years or older.

Limitations

Public health surveillance data used for this report have limitations. First, the overall burden of morbidity from nonmedical use of pharmaceuticals is underestimated, as only acute harms that are treated in EDs are included, with a maximum of four implicated products. Chronic conditions secondary to nonmedical use of pharmaceuticals that are not typically identified as such in EDs, such as certain infectious complications (e.g., HIV, hepatitis C virus), are not represented. Patients treated in other healthcare settings or non-healthcare settings (e.g., bystander naloxone administration), patients whose harms are not acute effects of active pharmaceutical use (e.g., withdrawal, seeking detoxification and substance use disorder treatment, and violence-related injuries), patients for whom a drug history could not be obtained, and deaths in or en route to the ED were not included. Second, because ED documentation is focused on recording the information deemed most relevant to clinical decision making, data helpful for public health surveillance may be incomplete. For example, 646 cases (representing nearly 46,000 estimated nonmedical use visits) were excluded because an unspecified drug (e.g., “opioid,” “amphetamine”) was the only product documented, as those cases could have involved prescription or illicit products (e.g., heroin, illicit methamphetamine). On the other hand, nonmedical use may be overestimated by including visits in which intent could not be determined (e.g., unresponsive patients) as some of these visits could have involved therapeutic use or self-harm attempts.[41–43] Third, some implicated pharmaceuticals and concomitant illicit drugs were identified based on laboratory testing alone, which could bias towards identification of drugs included on standard ED toxicology screens (e.g., benzodiazepine, methadone) and potentially against others (e.g., gabapentinoids). Similarly, there is the potential for cross-reactivity for laboratory tests, and some identified drugs may represent false positives. Finally, with a sample of less than 60 hospitals, state-level estimates are not possible and localized variations may not be reflected.

CONCLUSIONS

Nonmedical use of pharmaceuticals is a common cause of ED visits in the U.S. for medication-related harm, particularly among young adults, and represents an important opportunity for prevention. Although opioids and benzodiazepines account for most nonmedical use visits, additional substances (licit and illicit) are often involved. Thus, prescribing physicians should consider implementing specific screening to address polysubstance use and, when warranted, treatment interventions. Even though other pharmaceuticals are involved in far fewer ED visits for nonmedical use than opioids and benzodiazepines, ongoing surveillance remains important to identify emerging trends.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors thank Ms. Arati Baral and Mr. Alex Tocitu, from Northrop Grumman (contractor to Centers for Disease Control and Prevention [CDC]), for assistance with data coding and programming. The authors also thank Mr. Tom Schroeder, Ms. Elenore Sonski, Mr. Herman Burney, and data abstractors from the U.S. Consumer Product Safety

Commission, for their assistance with data acquisition. No individuals named herein received compensation for their contributions.

The findings in and conclusions of this study are those of the authors and do not necessarily represent the official position of CDC or Food and Drug Administration.

Funded solely by HHS, which had no role in study design; collection, analysis, and interpretation of data; writing the report; and decision to submit the report for publication.

No financial disclosures were reported by the authors of this paper.

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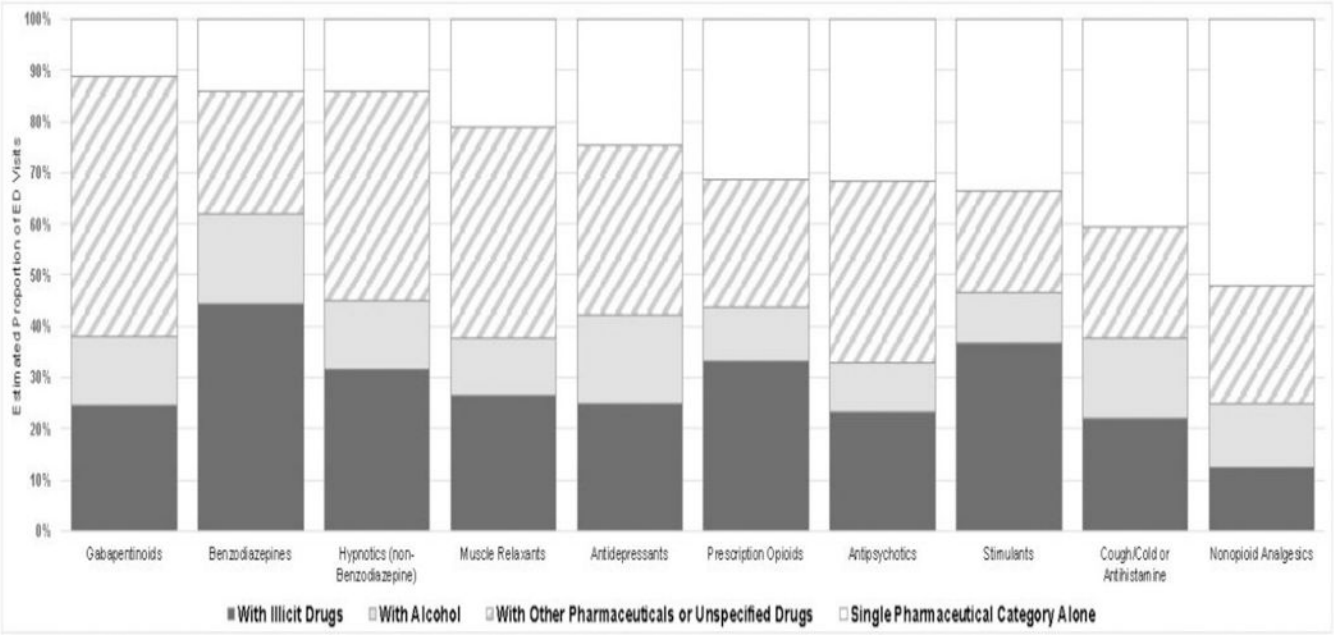

Figure 1.

Substances involved in emergency department visits due to nonmedical use of pharmaceuticals, 2016.

Table 1.

ED Visits Due to Nonmedical Use of Pharmaceuticals, 2016[a]

Case characteristics	Nonmedical use of pharmaceuticals[b]			Therapeutic use of pharmaceuticals[c]		
	Cases	Annual national estimate		Cases	Annual national estimate	
	n	*n*	% (95% CI)	*n*	*n*	% (95% CI)
Age, years[d]						
<15	159	7,333	2.0 (1.1, 3.0)	2,754	109,960	7.5 (5.6, 9.3)
5–24	1,208	81,928	22.9 (19.5, 26.2)	1,614	109,099	7.4 (6.0, 8.8)
25–34	1,305	93,179	26.0 (23.2, 28.8)	1,765	131,658	8.9 (7.6, 10.2)
35–44	852	61,437	17.1 (15.3, 19.0)	1,720	129,988	8.8 (7.7, 9.9)
45–54	790	54,905	15.3 (13.1, 17.5)	2,500	178,225	12.1 (10.6, 13.5)
55–64	587	42,161	11.8 (10.0, 13.6)	3,119	226,195	15.3 (14.4, 16.2)
65–74	186	13,455	3.8 (2.9, 4.6)	3,287	252,805	17.1 (14.7, 19.6)
>74	43	3,848[e]	1.1 (0.4, 1.7)	4,458	336,626	22.8 (19.1, 26.6)
Sex						
Female	2,195	158,673	44.3 (41.9, 46.7)	11,751	821,106	55.7 (53.1, 58.3)
Male	2,935	199,574	55.7 (53.3, 58.1)	9,466	653,450	44.3 (41.7, 46.9)
Discharge disposition[f]						
Hospitalized	2,085	147,091	41.1 (32.3, 49.8)	6,480	401,231	27.2 (21.6, 32.8)
Not hospitalized	3,045	211,156	58.9 (50.2, 67.7)	14,737	1,073,325	72.8 (67.2, 78.4)
Number of implicated pharmaceuticals						
1	3,689	258,343	72.1 (69.2, 75.0)	18,136	1,274,211	86.4 (84.7, 88.2)
2	1,033	68,784	19.2 (16.7, 21.7)	2,380	158,326	10.7 (9.1, 12.3)
3	296	22,215	6.2 (5.3, 7.1)	469	29,528	2.0 (1.7, 2.3)
4 or more	112	8,905	2.5 (1.8, 3.1)	232	12,491	0.8 (0.6, 1.1)
Additional substances documented						
Any substance	2,736	189,465	52.9 (49.7, 56.1)	350	23,174	1.6 (1.1, 2.0)
Alcohol	1,143	78,227	21.8 (19.8, 23.9)	235	15,280	1.0 (0.7, 1.3)

Case characteristics	Nonmedical use of pharmaceuticals[b]			Therapeutic use of pharmaceuticals[c]		
	Cases	Annual national estimate		Cases	Annual national estimate	
	n	*n*	% (95% CI)	*n*	*n*	% (95% CI)
Illicit substances	1,784	122,033	34.1 (30.9, 37.2)	133	8,896	0.6 (0.4, 0.8)
Marijuana	882	63,306	17.7 (15.1, 20.3)	83	6,463	0.4 (0.3, 0.6)
Cocaine	632	37,451	10.5 (7.8, 13.1)	47	2,174	0.1 (0.1, 0.2)
Heroin	413	28,285	7.9 (5.5, 10.3)	7	~	~
Methamphetamines	215	17,955	5.0 (2.9, 7.2)	8	~	~
Other illicit substances[g]	208	11,119	3.1 (2.1, 4.1)	5	~	~
Unspecified drugs[h]	513	38,083	10.6 (8.5, 12.7)	0	~	~
No additional substances	2,394	168,782	47.1 (43.9, 50.3)	20,867	1,451,382	98.4 (98.0, 98.9)
Total	5,130	358,247	100 (N/A)	21,217	1,474,556	100 (N/A)

[a]Case counts and estimates are from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project, CDC. Estimates based on <20 cases or total estimates <1,200 are considered statistically unstable and are not shown (~). Includes prescription and over-the-counter medications, dietary supplements, homeopathic products, and vaccines.

[b]Includes pharmaceutical abuse, therapeutic misuse, and overdoses without indication of intent.

[c]Includes therapeutic adverse drug events (e.g., adverse effects, allergic reactions, medication errors).

[d]Missing for 5 cases of nonmedical use, and 1 case of therapeutic use.

[e]Coefficient of variation >30%.

[f]*Hospitalized* includes inpatient admissions, observation admissions, and transfers to other hospitals. *Not hospitalized* includes treated-and-released and left against medical advice/without being seen.

[g]Includes illicit fentanyl, LSD, MDMA, phencyclidine, and other illicit drugs.

[h]Includes unspecified opioids and unspecified amphetamines. For these visits, there was not enough information to determine if the opioid was a prescription product or illicit substance (e.g., heroin) or if the amphetamine was a prescription amphetamine or illicit methamphetamine.

ED, emergency department; N/A, not applicable.

Table 2.

ED Visits Due to Nonmedical Use of Pharmaceuticals, by Category, 2016[a]

Category	Implicated alone or with other substances[b]		Implicated alone without other substances[c]		
	Annual national estimate[d]		Annual national estimate[e]		
	n	% total visits (95% CI)	*n*	% total visits (95% CI)	% category (95% CI)
Benzodiazepines	167,845	46.9 (42.5, 51.2)	23,335	6.5 (5.1, 7.9)	13.9 (10.9, 16.9)
Prescription opioids	129,863	36.2 (30.8, 41.7)	40,499	11.3 (8.6, 14.0)	31.2 (26.2, 36.1)
Antidepressants	24,350	6.8 (5.5, 8.1)	6,015	1.7 (1.1, 2.3)	24.7 (18.7, 30.7)
Cough/cold or antihistamines	23,966	6.7 (5.8, 7.6)	9,675	2.7 (2.0, 3.4)	40.4 (32.2, 48.5)
Nonopioid analgesics	23,758	6.6 (5.4, 7.9)	12,391	3.5 (2.6, 4.3)	52.2 (45.5, 58.8)
Hypnotics (non-benzodiazepine)	16,899	4.7 (3.8, 5.7)	2,374	0.7 (0.4, 1.0)	14.1 (7.8, 20.3)
Antipsychotics	15,874	4.4 (3.4, 5.5)	4,995	1.4 (1.0, 1.8)	31.5 (25.6, 37.3)
Muscle relaxants	14,731	4.1 (3.2, 5.0)	3,114	0.9 (0.5, 1.2)	21.1 (13.4, 28.9)
Gabapentinoids	11,669	3.3 (2.3, 4.2)	~	~	~
Stimulants	10,999	3.1 (1.8, 4.4)	3,677[f]	1.0 (0.4, 1.7)	33.4 (22.1, 44.8)
Antihypertensives	7,824	2.2 (1.6, 2.8)	2,958	0.8 (0.5, 1.1)	37.8 (25.6, 50.0)
Anticonvulsants	4,828	1.3 (0.9, 1.8)	1,966[f]	0.5 (0.2, 0.8)	40.7 (24.0, 57.4)
Antibiotics	4,278	1.2 (0.8, 1.6)	2,915	0.8 (0.5, 1.2)	68.1 (50.8, 85.5)
Other pharmaceuticals[g]	16,775	4.7 (3.9, 5.4)	6,978	1.9 (1.5, 2.4)	41.6 (33.1, 50.1)
Total	358,247	100 (N/A)	122,195	34.1 (30.5, 37.7)	N/A

[a] Estimates are from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project, CDC. Estimates based on <20 cases or total estimates <1,200 are considered statistically unstable and are not shown (~).

[b] Implicated alone or in combination with other pharmaceuticals, alcohol, unspecified drugs, or illicit substances.

[c] Implicated alone, without other categories of pharmaceuticals, and without alcohol, unspecified drugs, or illicit substances.

[d] Annual estimates and percentages total more than 100% because a single visit may involve multiple pharmaceuticals from different categories.

[e] Annual estimates and percentages total less than 100% because additional visits involve pharmaceuticals from different categories and additional visits involve alcohol or illicit substances.

[f] Coefficient of variation >30%.

[g] *Other pharmaceuticals* includes the following: vitamin and/or mineral supplements (n=32 cases), hypoglycemic agents (21 cases), neurologic agents (e.g., antiparkinsonian medications) (19 cases), gastrointestinal agents (e.g., laxatives, antispasmodics [e.g., loperamide], antacids) (14 cases), genitourinary agents (e.g., erectile dysfunction medications) (13 cases), endocrine/hormone agents (12 cases), anticoagulants/antiplatelets (9 cases), antirheumatics (8 cases), antivirals (4 cases), antigout agents (3 cases), analgesic supplement (e.g., kratom) (2 cases), and unspecified prescription or over-the-counter medications (117 cases).

ED, emergency department; N/A, not applicable.

Table 3.

ED Visits Due to Nonmedical Use of Pharmaceuticals, by Clinical Manifestation, 2016[a]

Clinical manifestation[b]	Annual estimate (2016)	
	n	% (95% CI)
Unresponsive or cardiorespiratory failure	81,057	22.6 (16.3, 29.0)
Severe allergic reaction	1,847	0.5 (0.2, 0.8)
Altered mental status	126,865	35.4 (30.8, 40.0)
Injection-related infection/reaction	7,889	2.2 (0.5, 3.9)
Fall/injury	8,727	2.4 (2.0, 2.9)
Presyncope/syncope/dyspnea	14,931	4.2 (3.2, 5.2)
Psychiatric or other central nervous system effect	20,380	5.7 (4.1, 7.3)
Cardiovascular effect	8,006	2.2 (1.6, 2.9)
Mild-to-moderate allergic reaction	2,430	0.7 (0.4, 1.0)
Gastrointestinal effect	9,498	2.7 (1.7, 3.6)
Other/unspecified effect	76,618	21.4 (16.5, 26.3)
Total	358,247	100 (N/A)

[a]Estimates are from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project, CDC.

[b]Clinical manifestations were categorized in a mutually exclusive and hierarchical manner (e.g., a case involving depressed consciousness and nausea would be classified as altered mental status based on the depressed consciousness).

ED, emergency department; N/A, not applicable.