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US Emergency Department Visits Attributed to Medication Harms, 2017-2019

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IMPORTANCE Assessing the scope of acute medication harms to patients should include both therapeutic and nontherapeutic medication use.

OBJECTIVE To describe the characteristics of emergency department (ED) visits for acute harms from both therapeutic and nontherapeutic medication use in the US.

DESIGN, SETTING, AND PARTICIPANTS Active, nationally representative, public health surveillance based on patient visits to 60 EDs in the US participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project from 2017 through 2019.

EXPOSURES Medications implicated in ED visits, with visits attributed to medication harms (adverse events) based on the clinicians' diagnoses and supporting data documented in the medical record.

MAIN OUTCOMES AND MEASURES Nationally weighted estimates of ED visits and subsequent hospitalizations for medication harms.

RESULTS Based on 96 925 cases (mean patient age, 49 years; 55% female), there were an estimated 6.1 (95% CI, 4.8-7.5) ED visits for medication harms per 1000 population annually and 38.6% (95% CI, 35.2%-41.9%) resulted in hospitalization. Population rates of ED visits for medication harms were higher for patients aged 65 years or older than for those younger than 65 years (12.1 vs 5.0 [95% CI, 7.4-16.8 vs 4.1-5.8] per 1000 population). Overall, an estimated 69.1% (95% CI, 63.6%-74.7%) of ED visits for medication harms involved therapeutic medication use, but among patients younger than 45 years, an estimated 52.5% (95% CI, 48.1%-56.8%) of visits for medication harms involved nontherapeutic use. The proportions of ED visits for medication harms involving therapeutic use were lowest for barbiturates (6.3%), benzodiazepines (11.1%), nonopioid analgesics (15.7%), and antihistamines (21.8%). By age group, the most frequent medication types and intents of use associated with ED visits for medication harms were therapeutic use of anticoagulants (4.5 [95% CI, 2.3-6.7] per 1000 population) and diabetes agents (1.8 [95% CI, 1.3-2.3] per 1000 population) for patients aged 65 years and older; therapeutic use of diabetes agents (0.8 [95% CI, 0.5-1.0] per 1000 population) for patients aged 45 to 64 years; nontherapeutic use of benzodiazepines (1.0 [95% CI, 0.7-1.3] per 1000 population) for patients aged 25 to 44 years; and unsupervised medication exposures (2.2 [95% CI, 1.8-2.7] per 1000 population) and therapeutic use of antibiotics (1.4 [95% CI, 1.0-1.8] per 1000 population) for children younger than 5 years.

CONCLUSIONS AND RELEVANCE According to data from 60 nationally representative US emergency departments, visits attributed to medication harms in 2017-2019 were frequent, with variation in products and intent of use by age.

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Supplemental content

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Efforts to assess and address medication harms typically categorize harmful events according to how patients intended to use the medications. When patients use their medications in recommended dosages and at recommended intervals for approved indications yet still experience harmful effects, these effects are considered adverse reactions from therapeutic use.[1] Clinicians and patients may unintentionally make medication errors that lead to harms; however, patients can also intentionally use medications in ways that are not recommended.[2,3] Some patients intentionally take their medications in amounts higher than recommended, take medications prescribed for others, or take medications for unapproved indications. The underlying reason for such nontherapeutic use may be categorized as misuse, substance use disorder, or self-harm, or in some cases may not be possible to determine by treating clinicians.[4] If harms from both therapeutic and nontherapeutic use are assessed concurrently, clinicians and policymakers can make more complete assessments of medication risks to patients.

The US Centers for Disease Control and Prevention (CDC) collaborates with the US Consumer Product Safety Commission (CPSC) and the US Food and Drug Administration (FDA) to conduct active, nationally representative public health surveillance for emergency department (ED) visits for harms attributed to medication use.[5,6] In this study, surveillance data from 2017-2019 were used to calculate national estimates of ED visits for acute harms related to therapeutic and nontherapeutic medication use.

Key Points

Question What were the most frequent medication types and intents of use associated with emergency department (ED) visits for medication harms in the US in 2017-2019?

Findings In this cross-sectional nationally representative sample that included 60 US EDs between 2017 and 2019, annual estimates of the most frequent medication types and intents of use associated with ED visits attributed to medication harms (adverse events) were therapeutic use of anticoagulants (4.5/1000 population) and diabetes agents (1.8/1000 population) for patients aged 65 years or older; therapeutic use of anticoagulants (0.6/1000 population) and diabetes agents (0.8/1000 population) for patients aged 45 to 64 years; nontherapeutic use of benzodiazepines (1.0/1000 population) and prescription opioids (0.7/1000 population) for patients aged 25 to 44 years; and unsupervised medication exposures (2.2/1000 population) and therapeutic use of antibiotics (1.4/1000 population) for children younger than 5 years.

Meaning Visits to US EDs attributed to medication harms in 2017-2019 were frequent and varied by medication type, intended use, and patient age.

Methods

Data Sources and Collection Methods

The National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance Project (NEISS-CADES) is a collaborative effort of CDC, CPSC, and FDA. This active public health surveillance system is based on a representative sample of hospitals in the United States and its territories, which includes 60 hospitals with at least 6 beds and a 24-hour ED.[7]

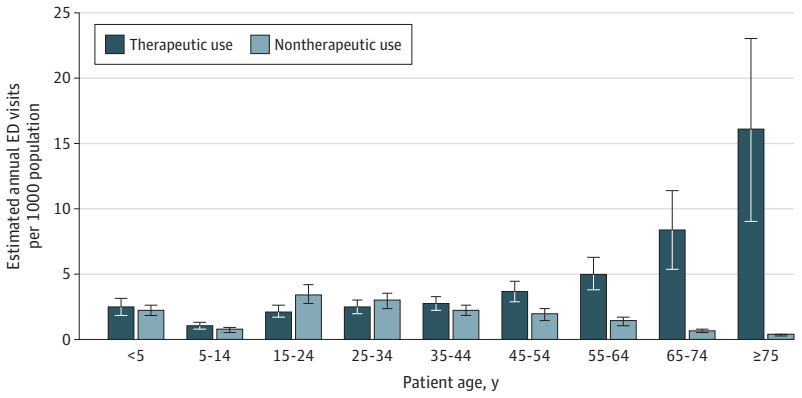
Trained CPSC abstractors at each hospital review medical records of ED visits to identify harms (adverse events) attributed to medications used for any reason. An adverse event case was defined as an incident ED visit for a condition or harm that the treating clinician explicitly attributed to the use of a drug or a drug-specific effect based on the clinicians' diagnoses and supporting data documented in the medical record (eg, documentation of supratherapeutic international normalized ratio in a patient taking warfarin, hypoglycemia in a patient taking insulin, oversedation in a patient taking prescription opioids).[5,8] Medication harms included adverse reactions to therapeutic doses, medication overdoses for any intent, medication errors, unsupervised exposures by children, and secondary injuries (eg, choking on a pill). CPSC abstractors record up to 4 implicated medications, intent of medication use, free-text narratives of the event (including clinical manifestations, documented medication errors, relevant preceding events, and concurrent illicit drug or alcohol use), clinician diagnoses, laboratory testing, treatments administered, and discharge disposition.

CDC codes reported clinical manifestations according to the Medical Dictionary for Regulatory Activities (MedDRA, version 9.1) and standardizes implicated medications by active ingredient according to pharmacologic classification. Data collection for the NEISS-CADES Project is considered a public health surveillance activity by federal human subjects oversight bodies and does not require human subjects review or institutional review board approval.[9]

Definitions

Cases included ED visits from January 1, 2017, through December 31, 2019, in which prescription or over-the-counter medications, dietary supplements (eg, herbals, vitamins, minerals), homeopathic products, or vaccines were implicated by the treating clinician or documented by toxicology testing. Patients' intent of medication use was classified as therapeutic or nontherapeutic use (eTable in the Supplement). Therapeutic use included use as directed or unintentional errors by adults or adolescents. Nontherapeutic use included (1) unsupervised exposures by children aged 10 years or younger; (2) misuse (trying to use medication for a salutary effect but not using it as directed [eg, taking someone else's prescription medication or taking additional doses for greater effect]); (3) abuse (clinician diagnosis of abuse or documentation of recreational use or use for euphoric or psychotropic effects); (4) self-harm (using medication to intentionally injure oneself); or (5) overdoses without documentation of therapeutic intent, misuse, abuse, or self-harm (eg, patients found unresponsive or unable or unwilling to provide description of circumstances or intent). Although concern has been raised that the term *abuse* may contribute

Figure 1. Estimated Annual Emergency Department (ED) Visits for Medication Harms per 1000 Population, by Therapeutic vs Nontherapeutic Medication Use—US, 2017-2019



Estimates and 2-sided 95% CIs (error bars) were calculated from statistical weighting of 96 925 cases from 60 nationally representative hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project for 2017-2019, Centers for Disease Control and Prevention. The population of each age group for 2017-2019 was calculated with intercensal estimates produced by the US Census Bureau. Patient age was missing for 13 cases (data not shown).

to stigma,[10,11] it is used here because the term remains commonly used by clinicians in medical documentation. ED visits for medication withdrawal, therapeutic failures, occupational exposures, and harms from medications received in the ED were excluded. Follow-up visits for previously diagnosed medication harm events and deaths in or en route to the ED were also excluded.

Statistical Analysis

Cases were weighted by CPSC according to the inverse probability of selection, adjusted for nonresponse and hospital nonparticipation, and poststratified to adjust for changes in the total number of hospital ED visits each year.[12] Based on these cases, national estimates (weighted percentages and weighted rates) of ED visits with corresponding 2-sided 95% CIs were calculated with the SURVEYMEANS procedure in SAS version 9.4 (SAS Institute) to account for the sample weights and complex sample design. The NEISS-CADES estimates for the 3-year period were divided by 3 to obtain the mean annual estimates. Estimates were considered statistically significantly different if their 2-sided 95% CIs were nonoverlapping. If 2 estimates had overlapping CIs, significance was determined by calculating 2-sided 95% CIs for the difference between estimates. To estimate age-specific population rates of ED visits, intercensal estimates from the US Census Bureau were used.[13] Estimates based on small numbers of cases (<20), or total (3-year) estimates less than 1200 were considered statistically unstable and are not shown. Estimates with coefficients of variation greater than 30% may be statistically unstable and are noted. Cases were not included in calculation of national estimates of a value when that value was missing. The numbers of cases with missing values for age (13 cases), sex (2 cases), and disposition (16 cases) out of 96 925 cases were trivial (≤0.03%), so imputation was not considered necessary.

Results

Between 2017 and 2019, based on 96 925 cases (mean patient age, 49 years; 55% female), there were an estimated 6.1 (95% CI, 4.8-7.5) ED visits for therapeutic and nontherapeutic medication harms combined per 1000 population annually. Population rates of ED visits for therapeutic and nontherapeutic medication harms combined among patients aged 5 to 14 years were lower (1.8 [95% CI, 1.4-2.2] per 1000 population) than the mean rate for the population overall (**Figure 1**). Population rates of ED visits for therapeutic and nontherapeutic medication harms combined were not significantly different for patients aged 15 to 24 years (5.6 per 1000 population) through 55 to 64 years (6.5 per 1000 population) (rate difference, −0.9 [95% CI, −2.7 to 0.9] per 1000 population). However, among patients aged 15 to 24 years, an estimated 61.8% (95% CI, 57.4%-66.1%) of ED visits for medication harms involved nontherapeutic use compared with an estimated 22.1% (95% CI, 17.8%-26.4%) of ED visits for medication harms among patients aged 55 to 64 years. Population rates of ED visits for therapeutic and nontherapeutic medication harms combined were higher for patients aged 65 years or older than for those younger than 65 years (12.1 vs 5.0 [95% CI, 7.4-16.8 vs 4.1-5.8] per 1000 population).

Overall, an estimated 38.6% of ED visits for medication harms required subsequent hospitalization, with hospitalization rates lowest for patients younger than 5 years (11.2%; 95% CI, 9.8%-12.5%) and highest for those aged 75 years or older (48.9%; 95% CI, 43.0%-54.8%) (**Table 1**). Overall, ED visits for medication harms involved more female patients (54.6%; 95% CI, 53.1%-56.2%) than male patients (45.4%; 95% CI, 43.8%-46.9%). Medication harm was attributed to effects of a single medication in an estimated 78.5% of ED visits; however, subsequent hospitalization was required more commonly when more than 1 medication was implicated (49.9% vs 35.5%; 95% CI, 46.3%-53.4% vs 31.7%-39.2%).

Overall, an estimated 69.1% of ED visits involved harms after therapeutic use of medications and an estimated 30.9% of them involved harms after nontherapeutic use; however, subsequent hospitalization was more common after nontherapeutic use (54.7% vs 31.3%; 95% CI, 49.7%-59.7% vs 26.2%-36.4%). Hospitalization rates varied by intent of use, ranging from 10.5% after allergic reactions to 80.1% after intentional self-harm.

Table 1. Cases and National Estimates of Emergency Department Visits for Medication Harms by Patient and Case Characteristics—US, 2017-2019[a,b]

Case characteristics	ED visits for medication harms overall (N = 96 925 cases)		ED visits for medication harms resulting in hospitalization (n = 39 628 cases)[c]	
	No. of cases	Nationally weighted, % (95% CI)[d]	No. of cases	Nationally weighted hospitalization rate (95% CI)[d,e]
Age, y[f]	96 912		39 621	
<5	7610	4.7 (3.6-5.7)	1276	11.2 (9.8-12.5)
5-14	6105	3.7 (2.8-4.5)	2476	29.7 (25.0-34.5)
15-24	12 448	12.0 (10.1-14.0)	5615	38.9 (35.7-42.1)
25-34	10 956	12.3 (10.7-13.9)	3800	33.4 (29.2-37.6)
35-44	9215	10.3 (9.1-11.5)	3280	33.6 (29.7-37.4)
45-54	10 462	11.6 (10.5-12.7)	4123	37.8 (34.3-41.3)
55-64	12 493	13.7 (13.0-14.4)	5456	41.5 (37.7-45.3)
65-74	11 899	13.7 (11.7-15.8)	5463	42.4 (38.3-46.6)
≥75	15 724	18.0 (13.7-22.4)	8132	48.9 (43.0-54.8)
Sex[g]	96 923		39 627	
Female patient	52 306	54.6 (53.1-56.2)	21 589	38.5 (35.7-41.3)
Male patient	44 617	45.4 (43.8-46.9)	18 038	38.6 (34.4-42.8)
No. of implicated medications	96 925		39 628	
1	76 723	78.5 (76.2-80.8)	28 981	35.5 (31.7-39.2)
>1	20 202	21.5 (19.2-23.8)	10 647	49.9 (46.3-53.4)
Intent of use	96 925		39 628	
Therapeutic	66 002	69.1 (63.6-74.7)	22 107	31.3 (26.2-36.4)
Adverse/secondary effect	31 830	32.5 (27.7-37.3)	11 585	33.0 (26.5-39.5)
Supratherapeutic effect	14 659	16.5 (14.1-19.0)	7568	48.7 (43.6-53.8)
Allergic reaction	14 161	14.4 (12.9-15.9)	1602	10.5 (8.3-12.7)
Medication error	5352	5.7 (4.8-6.6)	1352	24.3 (20.7-27.9)
Nontherapeutic	30 923	30.9 (25.3-36.4)	17 521	54.7 (49.7-59.7)
Self-harm	13 548	13.2 (10.8-15.6)	11 264	80.1 (74.9-85.4)
Abuse	6109	6.3 (5.1-7.6)	2057	33.4 (26.1-40.8)
Overdose without indication of intent	5380	6.2 (4.4-8.1)	2672	48.1 (40.0-56.2)
Misuse	2524	2.7 (2.2-3.1)	769	28.7 (24.9-32.6)
Unsupervised pediatric exposure	3362	2.4 (1.9-3.0)	759	17.4 (14.3-20.5)
Documented concurrent substance use	96 925		39 628	
Illicit or unspecified drugs	9901	10.4 (8.0-12.8)	5425	53.1 (46.8-59.4)
Alcohol	6181	7.0 (5.6-8.4)	3463	55.0 (48.9-61.0)
No. of substances documented[h]				
1	66 802	67.9 (63.8-72.0)	23 928	33.3 (28.9-37.6)
2	18 627	20.0 (18.0-22.0)	8933	45.5 (41.6-49.4)
3	6883	7.2 (6.0-8.4)	3859	53.5 (48.5-58.5)
4	3502	3.7 (2.9-4.4)	2160	59.7 (54.6-64.8)
≥5	1111	1.2 (0.9-1.6)	748	66.4 (57.6-75.1)
Total	96 925	100.0	39 628	38.6 (35.2-41.9)

Abbreviation: ED, emergency department.

[a] Medications include prescription or over-the-counter medications, dietary supplements, homeopathic products, and vaccines.

[b] Estimates and 2-sided 95% CIs were calculated from statistical weighting of 96 925 cases from 60 nationally representative hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project for 2017-2019, Centers for Disease Control and Prevention.

[c] Defined as hospital admission, observation status admission, or transfer to another facility. Discharge disposition missing for 16 cases.

[d] National estimates may vary for similar numbers of cases because of statistical weighting.

[e] Calculated as the estimated number of ED visits for medication harm resulting in hospitalization divided by the estimated number of ED visits for medication harm overall for each case characteristic.

[f] Patient age missing for 13 cases overall and 7 cases resulting in hospitalization.

[g] Patient sex missing for 2 cases overall and 1 case resulting in hospitalization.

[h] Includes medications, unspecified drugs, illicit substances, and alcohol.

Anticoagulants were implicated in an estimated 14.9% of ED visits for medication harms overall and in more visits involving therapeutic use of medications (21.5%; 95% CI, 16.5%-26.4%) than any other class of medications (**Table 2**). Analgesics were implicated in an estimated 13.9% of ED visits for medication harms overall, but only an estimated 33.0% of these visits involved therapeutic use. Similarly, sedative/hypnotic agents were implicated in an estimated 12.2% of ED visits for medication harms overall, but only an estimated 13.7% of these visits involved therapeutic use. Alcohol or illicit substances (eg, marijuana, heroin, cocaine, unspecified opioids) were frequently involved in ED visits for medication harms from nontherapeutic use of analgesics and sedative/hypnotic agents, including an estimated 49.1% (95% CI,

Table 2. Cases and National Estimates of Emergency Department Visits for Medication Harms by Drug Class—US, 2017-2019[a]

Drug class[b]	ED visits for medication harms overall		ED visits for medication harms from therapeutic use		Proportion of ED visits for medication harms attributed to therapeutic use, nationally weighted, % (95% CI)[c]
	No. of cases[a]	Nationally weighted, % (95% CI)[c]	No. of cases[a]	Nationally weighted, % (95% CI)[c]	
CNS agents					
Analgesics	13 135	13.9 (12.0-15.7)	4020	6.6 (5.7-7.5)	33.0 (27.9-38.0)
Prescription opioids	10 044	11.0 (9.4-12.5)	3532	5.8 (5.1-6.6)	36.7 (30.9-42.6)
Oxycodone-containing analgesics	3767	4.1 (3.4-4.8)	1268	2.1 (1.7-2.4)	34.8 (28.9-40.8)
Hydrocodone-containing analgesics	1463	1.8 (1.2-2.4)	631	1.2 (0.9-1.5)	45.7 (38.7-52.8)
Nonopioid-containing analgesics[d]	3083	2.9 (2.4-3.4)	417	0.7 (0.5-0.8)	15.7 (13.0-18.5)
Sedative/hypnotic agents	10 926	12.2 (9.9-14.5)	1431	2.4 (2.0-2.8)	13.7 (11.4-16.0)
Benzodiazepines	9655	10.8 (8.6-12.9)	1028	1.7 (1.4-2.0)	11.1 (9.0-13.2)
Nonbenzodiazepine hypnotics[e]	838	1.0 (0.8-1.2)	255	0.4 (0.3-0.6)	31.5 (26.8-36.2)
Barbiturates	309	0.4 (0.2-0.5)	22	0.0 (0.0-0.1)[f]	6.3 (3.0-9.6)
Other sedative/hypnotic agents	530	0.6 (0.5-0.7)	167	0.3 (0.2-0.4)	34.5 (27.8-41.1)
Antidepressants	5954	6.5 (5.4-7.5)	1731	3.0 (2.6-3.3)	31.9 (26.9-36.8)
Musculoskeletal agents	5128	5.2 (4.5-5.9)	1797	3.1 (2.6-3.6)	40.7 (35.9-45.5)
Nonsteroidal anti-inflammatory drugs[g]	3764	3.6 (3.0-4.2)	1225	2.1 (1.6-2.5)	39.9 (35.0-44.7)
Skeletal muscle relaxants	1403	1.7 (1.4-1.9)	557	1.0 (0.9-1.1)	40.4 (34.1-46.7)
Antipsychotics	4123	4.3 (3.4-5.2)	1874	2.9 (2.0-3.7)	45.9 (40.4-51.3)
Anticonvulsants	3175	3.4 (2.8-4.0)	1435	2.2 (1.8-2.5)	44.1 (38.6-49.7)
Stimulants	1324	1.3 (1.0-1.5)	394	0.6 (0.4-0.7)	30.0 (26.2-33.8)
Anesthetics (systemic)	338	0.3 (0.3-0.4)	269	0.4 (0.3-0.5)	81.4 (71.5-91.4)
Other CNS agents	874	1.0 (0.9-1.2)	561	1.0 (0.9-1.1)	67.0 (61.8-72.1)
Hematologic agents					
Anticoagulants	13 851	14.9 (10.7-19.1)	13 759	21.5 (16.5-26.4)	99.4 (99.1-99.7)
Vitamin K antagonists (warfarin)	7471	8.4 (6.4-10.4)	7427	12.1 (9.7-14.5)	99.4 (99.1-99.7)
Direct oral anticoagulants	5744	5.9 (3.7-8.1)	5697	8.5 (5.9-11.2)	99.4 (99.0-99.8)
Unfractionated and low-molecular-weight heparins	749	0.6 (0.4-0.9)	747	0.9 (0.6-1.3)	99.8 (99.7-100.0)
Antiplatelets	5324	5.8 (3.7-8.0)	4841	7.8 (5.1-10.5)	92.7 (88.3-97.1)
Platelet P2Y12 receptor antagonists[h]	4369	4.8 (2.6-7.0)	4350	6.9 (4.2-9.6)	99.6 (99.2-99.9)
Aspirin ± dipyridamole	1357	1.6 (0.8-2.3)	890	1.7 (0.6-2.8)[f]	73.8 (60.8-86.8)
Hormone-modifying agents					
Diabetes agents	9017	9.9 (8.7-11.1)	8554	13.7 (11.8-15.6)	96.0 (94.9-97.2)
Insulins	7107	7.8 (6.8-8.8)	6913	11.0 (9.3-12.6)	97.4 (96.7-98.2)
Oral diabetes agents	2727	3.1 (2.6-3.6)	2452	4.2 (3.6-4.8)	93.4 (90.9-95.9)
Other diabetes agents[i]	268	0.3 (0.2-0.4)	263	0.4 (0.3-0.6)	99.2 (98.2-100.0)
Adrenocortical steroids	994	1.1 (1.0-1.2)	923	1.5 (1.3-1.7)	94.4 (91.9-96.9)
Contraceptives	365	0.3 (0.3-0.4)	339	0.5 (0.3-0.6)	95.4 (92.4-98.5)
Other hormone-modifying agents	620	0.7 (0.5-0.8)	456	0.8 (0.6-1.0)	79.9 (73.3-86.5)
Systemic antimicrobial agents					
Antibiotics[j]	9513	9.2 (8.0-10.5)	9103	12.8 (10.8-14.9)	96.1 (95.3-96.9)
Amoxicillin-containing penicillins	3828	3.0 (2.5-3.5)	3680	4.1 (3.3-4.9)	95.7 (95.0-96.5)
Sulfonamide-containing agents	1344	1.6 (1.3-1.8)	1302	2.2 (1.8-2.5)	97.3 (96.3-98.3)
Cephalosporins	1245	1.2 (1.0-1.4)	1184	1.6 (1.3-2.0)	95.5 (93.8-97.1)
Quinolones	697	0.8 (0.7-1.0)	675	1.2 (1.0-1.4)	97.9 (96.8-99.0)
Lincosamides (clindamycin)	554	0.6 (0.5-0.7)	537	0.8 (0.7-1.0)	98.3 (96.8-99.7)
Erythromycins and macrolides	483	0.5 (0.4-0.6)	467	0.7 (0.6-0.9)	96.5 (95.0-98.0)
Tetracyclines	471	0.5 (0.5-0.6)	431	0.7 (0.6-0.8)	93.9 (90.8-97.1)
Metronidazole	348	0.4 (0.3-0.5)	315	0.5 (0.4-0.6)	93.2 (89.9-96.5)
Other penicillins	282	0.3 (0.2-0.4)	258	0.4 (0.3-0.5)	93.4 (90.4-96.5)
Nitrofurans	221	0.3 (0.2-0.3)	208	0.4 (0.3-0.5)	96.2 (92.9-99.6)
Other antibiotics	572	0.6 (0.5-0.8)	548	0.8 (0.6-1.1)	94.9 (92.5-97.3)
Antivirals and antiretrovirals	416	0.4 (0.4-0.5)	354	0.5 (0.4-0.7)	87.6 (82.6-92.5)
Other systemic antimicrobial agents	292	0.3 (0.2-0.3)	266	0.4 (0.3-0.5)	94.0 (91.0-97.0)

(continued)

Table 2. Cases and National Estimates of Emergency Department Visits for Medication Harms by Drug Class—US, 2017-2019[a] (continued)

Drug class[b]	ED visits for medication harms overall		ED visits for medication harms from therapeutic use		Proportion of ED visits for medication harms attributed to therapeutic use, nationally weighted, % (95% CI)[c]
	No. of cases[a]	Nationally weighted, % (95% CI)[c]	No. of cases[a]	Nationally weighted, % (95% CI)[c]	
Cardiovascular agents					
Renin-angiotensin system inhibitors[k]	2806	3.0 (2.4-3.6)	2407	3.8 (3.0-4.7)	87.1 (83.1-91.1)
β-Blockers	1274	1.5 (1.2-1.8)	857	1.6 (1.2-2.0)	72.7 (63.0-82.3)
Calcium-channel blockers	841	0.9 (0.7-1.0)	566	1.0 (0.7-1.2)	75.9 (70.3-81.5)
Centrally acting antiadrenergics	760	0.8 (0.5-1.0)	267	0.4 (0.3-0.5)	36.8 (27.8-45.8)
Diuretics	627	0.7 (0.5-0.9)	488	0.8 (0.6-1.1)	82.2 (77.5-86.9)
Lipid-lowering agents	371	0.4 (0.3-0.5)	264	0.4 (0.3-0.5)	75.9 (68.4-83.3)
Antianginals and antiarrhythmics	231	0.3 (0.2-0.3)	194	0.3 (0.3-0.4)	85.3 (77.6-93.0)
Other cardiovascular agents	837	1.0 (0.8-1.1)	530	1.0 (0.8-1.1)	69.1 (62.3-75.9)
Respiratory agents					
Single-ingredient antihistamines	2650	2.6 (2.1-3.1)	511	0.8 (0.7-1.0)	21.8 (18.5-25.2)
Cough and cold remedies[l]	1730	1.7 (1.5-1.9)	618	1.0 (0.9-1.2)	42.3 (36.4-48.3)
Other respiratory agents	433	0.4 (0.3-0.5)	270	0.5 (0.3-0.6)	73.2 (66.4-79.9)
Oncologic and immunologic agents					
Antineoplastic agents	5464	3.7 (2.1-5.3)	5442	5.4 (3.1-7.6)	99.5 (99.2-99.8)
Immune modulators[m]	463	0.4 (0.3-0.5)	447	0.6 (0.4-0.7)	98.0 (96.8-99.2)
Dietary supplements and related products					
Herbals (systemic and topical) and homeopathic agents	1357	1.4 (1.1-1.6)	687	1.1 (0.9-1.4)	58.4 (51.3-65.5)
Vitamins, minerals, trace elements, and combinations	1015	0.9 (0.8-1.0)	605	0.9 (0.8-1.0)	67.3 (60.0-74.5)
Gastrointestinal agents					
Antiulcer and antacid agents	503	0.5 (0.4-0.7)	318	0.6 (0.4-0.8)	69.9 (60.1-79.8)
Antidiarrheals, laxatives, and antiflatulents	454	0.4 (0.4-0.5)	302	0.5 (0.4-0.6)	73.0 (67.0-79.0)
Other gastrointestinal agents	511	0.6 (0.5-0.7)	371	0.7 (0.6-0.8)	79.3 (74.3-84.3)
Vaccines	1844	1.5 (1.2-1.7)	1844	2.1 (1.7-2.5)	100.0 (100.0-100.0)
Dermatologic agents[n]	688	0.7 (0.6-0.8)	588	0.9 (0.7-1.1)	89.4 (86.6-92.2)
Radiopharmaceuticals	429	0.5 (0.4-0.6)	428	0.7 (0.5-0.8)	99.9 (99.7-100.0)
Ophthalmic, otic, and nasal agents	382	0.4 (0.3-0.5)	344	0.5 (0.4-0.7)	91.7 (88.4-95.1)
Genitourinary agents	324	0.4 (0.3-0.4)	274	0.5 (0.4-0.6)	86.5 (81.4-91.6)
Other agents	473	0.5 (0.4-0.6)	423	0.6 (0.5-0.8)	88.8 (84.6-92.9)
Unspecified agents[o]	1888	2.1 (1.6-2.6)	891	1.6 (1.1-2.1)	52.9 (44.5-61.2)

Abbreviations: CNS, central nervous system; ED, emergency department.

[a] Estimates and 2-sided 95% CIs were calculated from statistical weighting of 96 925 cases from 60 nationally representative hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project for 2017-2019, CDC.

[b] Specific drug classes are shown if they were implicated in an estimated 0.3% or more of all ED visits for medication harms in 2017-2019. Drug classes are not mutually exclusive; for some ED visits, medications from >1 drug class were implicated in the medication harm; therefore, percentages may total more than 100%.

[c] National estimates may vary for similar numbers of cases because of statistical weighting.

[d] Excludes single-ingredient aspirin. Includes combination analgesic agents containing aspirin and combinations with antihistamines (eg, acetaminophen-diphenhydramine).

[e] Eszopiclone, zaleplon, and zolpidem.

[f] Coefficient of variation >30%.

[g] Includes nonsteroidal anti-inflammatory drugs in combination with antihistamines (eg, ibuprofen-diphenhydramine).

[h] Clopidogrel, prasugrel, ticagrelor, and ticlopidine.

[i] Includes injectable noninsulin diabetes agents (eg, injectable glucagon-like peptide 1 receptor agonists) and nonspecified diabetes agents.

[j] Antibiotics in combination with antiulcer agents (eg, amoxicillin clarithromycin-lansoprazole) are categorized as gastrointestinal agents.

[k] Single ingredient and in combination with diuretics (eg, hydrochlorothiazide-lisinopril) and calcium channel blockers (eg, amlodipine-benazepril).

[l] Single-ingredient antitussives, decongestants, and expectorants, as well as each of these in combination with antihistamines.

[m] Immunoglobulins, immune suppressants, interferons, and other immune modulators.

[n] Topically administered agents and acne agents (systemically or topically administered).

[o] Includes cases for which the specific medication or drug class was not documented (eg, a patient who reported being treated for a rash from a medication but did not recall the name of the product).

45.5%-52.8%) of ED visits for nontherapeutic use of prescription opioids and an estimated 66.3% (95% CI, 62.6%-69.9%) of visits for nontherapeutic use of benzodiazepines.

Considering only therapeutic use of medications, ED visits for medication harms involving diabetes agents (13.7%; 95% CI, 11.8%-15.6%) and antibiotics (12.8%; 95% CI,

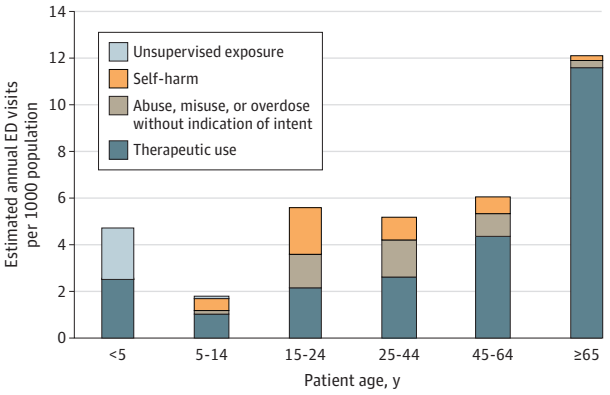
10.8%-14.9%) were more common than those involving analgesics (6.6%; 95% CI, 5.7%-7.5%). Among all classes of cardiovascular agents, centrally acting antiadrenergics (eg, clonidine) was the only class for which there were fewer ED visits for medication harms involving therapeutic use (36.8%; 95% CI, 27.8%-45.8%) compared with nontherapeutic use.

Medications commonly available over-the-counter (ie, nonsteroidal anti-inflammatory drugs, nonopioid analgesics, single-ingredient antihistamines, and cough and cold medications) were implicated in an estimated 10.0% (95% CI, 8.6%-11.4%) of visits overall, but only an estimated 30.8% (95% CI, 26.6%-35.1%) of these visits involved therapeutic use. The proportions of ED visits for medication harms involving therapeutic use were lowest for barbiturates (6.3% therapeutic use), benzodiazepines (11.1% therapeutic use), nonopioid analgesics (15.7% therapeutic use), and single-ingredient antihistamines (21.8% therapeutic use).

Among patients aged 65 years or older, an estimated 95.8% (95% CI, 94.6%-97.1%) of ED visits for medication harms involved therapeutic use, and the population rate of ED visits for medication harms owing to therapeutic use (11.6 [95% CI, 6.9-16.3] per 1000 population) was higher than that for all medication harms in any other age group (**Figure 2**). In contrast, among patients younger than 45 years an estimated 52.5% (95% CI, 48.1%-56.8%) of ED visits for medication harms involved nontherapeutic use. Among patients younger than 5 years, an estimated 47.1% (95% CI, 43.4%-50.8%) of ED visits for medication harms involved unsupervised medication exposures (2.2 [95% CI, 1.8-2.7] per 1000 population). The population rate of ED visits for medication harms involving self-harm was highest among patients aged 15 to 24 years (2.0 [95% CI, 1.6-2.4] per 1000 population). Medications commonly available over-the-counter (ie, nonsteroidal anti-inflammatory drugs, nonopioid analgesics, single-ingredient antihistamines, and cough and cold medications) were implicated in an estimated 45.2% (95% CI, 43.1%-47.2%) of self-harm visits, and an estimated 25.7% (95% CI, 23.9%-27.6%) of self-harm visits were attributed to antidepressants. The population rate of ED visits for medication harms involving abuse, misuse, or overdose without indication of intent was highest among patients aged 25 to 44 years (1.6 [95% CI, 1.2-2.0] per 1000 population). An estimated 44.9% of these visits (95% CI, 40.5%-49.2%) were attributed to benzodiazepines; an estimated 37.9% (95% CI, 32.3%-43.4%), to prescription opioids.

Among patients younger than 5 years, 4 of the 10 most frequently implicated drug products in ED visits for medication harms were antibiotics, with more than 95% of these ED visits attributed to therapeutic use (**Table 3**). The population rate of ED visits for medication harms from therapeutic use of all antibiotics was 1.4 (95% CI, 1.0-1.8) per 1000 population for children younger than 5 years. In contrast, therapeutic use was rarely involved in ED visits in which acetaminophen, ibuprofen, diphenhydramine, melatonin, or lisinopril were implicated. Among patients aged 5 to 14 years, 3 medications that can be used to treat attention-deficit/hyperactivity disorder (methylphenidate, clonidine, and guanfacine) were among the 10 most frequently implicated drug products in ED visits, but the population rates of ED visits for these medication harms (0.1 [95% CI, 0.07-0.14] per 1000 population) was lower than rates for the 10 most frequently implicated products for other age groups.

Figure 2. Estimated Annual Emergency Department (ED) Visits for Medication Harms per 1000 Population, by Age and Intent of Medication Use—US, 2017-2019



Estimates were calculated from statistical weighting of 96 925 cases from 60 nationally representative hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project for 2017-2019, Centers for Disease Control and Prevention. The population of each age group for 2017-2019 was calculated with intercensal estimates produced by the US Census Bureau. The estimate of ED visits for abuse, misuse, or overdose without indication of intent for children younger than 5 years is based on fewer than 20 cases and is considered statistically unstable. Patient age was missing for 13 cases (data not shown).

Among patients aged 15 to 24 years, 5 psychiatric medications (alprazolam, sertraline, trazadone, quetiapine, and fluoxetine) and 3 over-the-counter medications (ibuprofen, acetaminophen, and diphenhydramine) were among the 10 most frequently implicated products in ED visits for medication harms, with only an estimated 5.3% to 23.2% of visits involving therapeutic use.

Among patients aged 25 to 44 years, 6 of the 10 most frequently implicated products are used for treating pain (acetaminophen/oxycodone, oxycodone, gabapentin, and ibuprofen) or addiction to pain medications (methadone and buprenorphine/naloxone), with an estimated 59.8% to 89.8% of these visits involving nontherapeutic use. The population rate of ED visits for medication harms from nontherapeutic use of all prescription opioids was 0.7 (95% CI, 0.5-0.9) per 1000 population for patients aged 25 to 44 years.

Among patients aged 15 to 24 years and 25 to 44 years, alprazolam was the most frequently implicated drug product in ED visits for medication harms, and it was the third most frequently implicated drug product among patients aged 45 to 64 years, with an estimated 97.3%, 93.9%, and 87.0% of visits involving nontherapeutic use, respectively. The population rate of ED visits for medication harms from nontherapeutic use of all benzodiazepines was 0.9 (95% CI, 0.6-1.1) per 1000 population for patients aged 15 to 24 years and 1.0 (95% CI, 0.7-1.3) per 1000 population for patients aged 25 to 44 years. However, an estimated 61.3% (95% CI, 57.4%-65.3%) of ED visits involving alprazolam also involved alcohol or illicit substances.

Table 3. Cases and National Estimates of Emergency Department Visits for Medication Harms From the Most Commonly Implicated Drug Products by Patient Age Group and Intent of Medication Use—US, 2017-2019[a]

Drug product[b]	ED visits for medication harms overall		Proportion of ED visits for medication harms attributed to therapeutic use, nationally weighted, % (95% CI)[c,e]	ED visits for medication harms overall, estimated annual ED visits per 1000 individuals (95% CI)[c,f]
	No. of cases[a]	Nationally weighted, % (95% CI)[c,d]		
Patients aged <5 y				
Amoxicillin	1640	19.8 (17.2-22.3)	98.8 (97.8-99.7)	0.9 (0.7-1.2)
Acetaminophen	319	5.7 (4.5-6.8)	15.6 (9.5-21.6)	0.3 (0.2-0.3)
Ibuprofen	266	4.9 (3.7-6.0)	26.4 (19.8-33.0)	0.2 (0.2-0.3)
Diphenhydramine	168	2.8 (2.1-3.5)	NS	0.1 (0.1-0.2)
Cefdinir	247	2.7 (1.5-3.9)	100.0 (100.0-100.0)	0.1 (0.1-0.2)
Amoxicillin/clavulanate	248	2.3 (1.6-3.1)	96.8 (92.5-100.0)	0.1 (0.1-0.2)
Melatonin	111	1.8 (1.2-2.4)	NS	0.1 (0.1-0.1)
Lisinopril	83	1.6 (1.0-2.2)	0.0 (0.0-0.0)	0.1 (0.0-0.1)
Influenza vaccine	90	1.5 (0.8-2.1)	100.0 (100.0-100.0)	0.1 (0.0-0.1)
Azithromycin	65	1.3 (0.8-1.7)	99.3 (97.8-100.0)	0.1 (0.0-0.1)
Patients aged 5-14 y				
Amoxicillin	610	10.9 (8.7-13.1)	97.1 (95.4-98.7)	0.2 (0.1-0.2)
Ibuprofen	439	8.0 (6.8-9.2)	25.4 (15.7-35.0)	0.1 (0.1-0.2)
Acetaminophen	336	6.1 (4.8-7.4)	11.8 (5.8-17.8)	0.1 (0.1-0.1)
Diphenhydramine	151	2.9 (2.0-3.9)	NS	0.1 (0.0-0.1)
Fluoxetine	139	2.7 (1.8-3.6)	NS	0.05 (0.03-0.07)
Sulfamethoxazole/trimethoprim	103	2.4 (1.6-3.2)	99.1 (98.1-100.0)	0.04 (0.03-0.06)
Methylphenidate	128	2.4 (1.7-3.1)	58.8 (49.9-67.7)	0.04 (0.02-0.06)
Sertraline	143	2.3 (1.5-3.2)	24.9 (11.6-38.1)	0.04 (0.02-0.06)
Clonidine	109	2.2 (1.6-2.9)	43.4 (29.2-57.6)	0.04 (0.03-0.05)
Guanfacine	105	1.8 (1.1-2.5)	64.6 (53.9-75.3)	0.03 (0.02-0.05)
Patients aged 15-24 y				
Alprazolam	1013	9.2 (7.1-11.3)	2.7 (1.1-4.4)[g]	0.5 (0.3-0.7)
Ibuprofen	1007	7.2 (6.4-8.0)	17.0 (11.5-22.4)	0.4 (0.3-0.5)
Acetaminophen	887	6.5 (5.7-7.3)	5.3 (2.9-7.7)	0.4 (0.3-0.4)
Diphenhydramine	470	3.7 (3.1-4.2)	8.0 (4.6-11.3)	0.2 (0.2-0.3)
Sertraline	393	3.2 (2.7-3.7)	22.7 (15.7-29.8)	0.2 (0.1-0.2)
Acetaminophen/oxycodone	298	2.7 (1.9-3.5)	13.8 (8.7-19.0)	0.2 (0.1-0.2)
Trazodone	273	2.4 (1.9-2.8)	20.3 (14.0-26.6)	0.1 (0.1-0.2)
Quetiapine	302	2.4 (2.0-2.7)	23.2 (15.5-31.0)	0.1 (0.1-0.2)
Amoxicillin	273	2.3 (1.8-2.9)	86.3 (80.4-92.3)	0.1 (0.1-0.2)
Fluoxetine	295	2.3 (1.9-2.8)	13.9 (8.0-19.7)	0.1 (0.1-0.2)
Patients aged 25-44 y				
Alprazolam	1702	8.4 (6.1-10.6)	6.1 (4.8-7.3)	0.4 (0.3-0.6)
Insulin	1086	5.1 (4.2-6.0)	93.8 (92.0-95.6)	0.3 (0.2-0.3)
Acetaminophen/oxycodone	671	3.3 (2.4-4.2)	25.2 (19.4-31.0)	0.2 (0.1-0.2)
Clonazepam	676	3.3 (2.6-4.0)	11.9 (8.3-15.6)	0.2 (0.1-0.2)
Methadone	894	3.3 (1.2-5.4)[g]	17.7 (12.7-22.7)	0.2 (0.0-0.3)[g]
Quetiapine	634	3.2 (2.5-3.9)	17.4 (13.2-21.7)	0.2 (0.1-0.2)
Oxycodone	645	3.1 (2.4-3.8)	17.7 (12.8-22.7)	0.2 (0.1-0.2)
Buprenorphine/naloxone	429	2.7 (1.3-4.1)	10.2 (5.6-14.8)	0.1 (0.1-0.2)
Gabapentin	459	2.5 (1.8-3.2)	13.0 (9.0-16.9)	0.1 (0.1-0.2)
Ibuprofen	521	2.4 (2.0-2.9)	40.2 (33.6-46.8)	0.1 (0.1-0.2)

(continued)

Table 3. Cases and National Estimates of Emergency Department Visits for Medication Harms From the Most Commonly Implicated Drug Products by Patient Age Group and Intent of Medication Use—US, 2017-2019[a] (continued)

Drug product[b]	ED visits for medication harms overall		Proportion of ED visits for medication harms attributed to therapeutic use, nationally weighted, % (95% CI)[c,e]	ED visits for medication harms overall, estimated annual ED visits per 1000 individuals (95% CI)[c,f]
	No. of cases[a]	Nationally weighted, % (95% CI)[c,d]		
Patients aged 45-64 y				
Insulin	2553	11.1 (9.6-12.5)	97.6 (96.9-98.3)	0.7 (0.5-0.8)
Warfarin	1407	5.9 (4.4-7.3)	99.3 (98.8-99.9)	0.4 (0.2-0.5)
Alprazolam	871	3.8 (2.8-4.7)	13.0 (9.5-16.4)	0.2 (0.2-0.3)
Lisinopril	923	3.7 (2.9-4.5)	91.5 (88.4-94.6)	0.2 (0.2-0.3)
Oxycodone	801	3.4 (2.9-4.0)	35.8 (29.3-42.3)	0.2 (0.2-0.3)
Clopidogrel	803	3.2 (2.0-4.5)	99.5 (99.1-100.0)	0.2 (0.1-0.3)
Methadone	850	3.0 (0.2-5.8)[g]	24.2 (19.5-29.0)	0.2 (0.0-0.4)[g]
Metformin	528	2.4 (1.9-3.0)	94.2 (91.5-96.9)	0.1 (0.1-0.2)
Clonazepam	537	2.4 (1.8-2.9)	21 (14.6-27.3)	0.1 (0.1-0.2)
Quetiapine	467	2.1 (1.6-2.7)	31.3 (26.3-36.4)	0.1 (0.1-0.2)
Patients aged ≥65 y				
Warfarin	5706	20.7 (17.9-23.5)	99.8 (99.7-100.0)	2.5 (1.4-3.6)
Insulin	3146	11.1 (9.0-13.2)	99.3 (98.9-99.7)	1.3 (1.0-1.7)
Clopidogrel	3057	10.9 (7.8-14.0)	99.8 (99.6-100.0)	1.3 (0.5-2.2)[g]
Apixaban	2507	8 (6.0-10.1)	99.8 (99.6-100.0)	1.0 (0.4-1.6)
Rivaroxaban	1764	6.3 (5.0-7.5)	99.9 (99.8-100.0)	0.8 (0.4-1.2)
Metformin	729	3.0 (2.4-3.6)	98.8 (97.6-100.0)	0.4 (0.2-0.5)
Aspirin	621	2.6 (0.6-4.6)[g]	97.8 (96.4-99.2)	0.3 (0.1-0.5)[g]
Lisinopril	639	2.4 (1.8-3.1)	96.7 (94.9-98.6)	0.3 (0.2-0.4)
Glipizide	445	1.7 (1.3-2.1)	99.9 (99.7-100.0)	0.2 (0.1-0.3)
Oxycodone	370	1.4 (1.0-1.7)	69.2 (62.6-75.8)	0.2 (0.1-0.2)
All patients				
Warfarin	7471	8.4 (6.4-10.4)	99.4 (99.1-99.7)	0.5 (0.3-0.7)
Insulin	7107	7.8 (6.8-8.8)	97.4 (96.7-98.2)	0.5 (0.4-0.6)
Clopidogrel	3928	4.4 (2.4-6.3)	99.7 (99.4-100.0)[g]	0.3 (0.1-0.4)[g]
Alprazolam	3897	4.3 (3.2-5.4)	8.5 (6.6-10.4)	0.3 (0.2-0.3)
Apixaban	3055	3.0 (1.8-4.3)	99.4 (98.9-99.9)	0.2 (0.1-0.3)
Rivaroxaban	2376	2.5 (1.7-3.4)	99.2 (98.7-99.8)	0.2 (0.1-0.2)
Ibuprofen	2601	2.4 (1.9-2.8)	31.5 (25.9-37.1)	0.1 (0.1-0.2)
Amoxicillin	3133	2.3 (1.9-2.8)	95.5 (94.7-96.4)	0.1 (0.1-0.2)
Oxycodone	2119	2.3 (1.8-2.7)	34.2 (28.2-40.3)	0.1 (0.1-0.2)
Acetaminophen	2367	2.2 (1.7-2.6)	12.4 (9.9-14.9)	0.1 (0.1-0.2)

Abbreviations: ED, emergency department; NS, not shown.

[a] Estimates and 2-sided 95% CIs for each age group were calculated from statistical weighting of 96 925 cases from 60 nationally representative hospitals participating in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project for 2017-2019, CDC. Patient age was missing for 13 cases (not shown).

[b] Drug products are not mutually exclusive; for some ED visits, more than 1 drug was implicated in the medication harm. Drugs that were not identified at the active ingredient level (eg, unnamed antibiotic, cough medicine, unknown drug) are not shown.

[c] National estimates may vary for similar numbers of cases because of statistical weighting. Estimates based on <20 cases or total estimates of <1200 visits may be statistically unstable and are not shown.

[d] Refers to the percentage of ED visits for medication harm involving that drug product out of all ED visits for medication harm in the specified age group (column percentage).

[e] Refers to the percentage of ED visits for medication harm in the specified age group involving therapeutic use for that drug product (row percentage).

[f] The population of each age group for 2017-2019 was calculated with intercensal estimates produced by the US Census Bureau.

[g] Coefficient of variation >30%.

Among patients aged 45 years or older, insulin and warfarin were the 2 most frequently implicated drug products, with insulin implicated in an estimated 11.1% of ED visits for medication harm among patients aged 45 years or older and warfarin implicated in an estimated 20.7% of visits among those aged 65 years or older. The population rate of ED visits attributed to therapeutic use of all diabetes agents and all anticoagulants was 0.8 (95% CI, 0.5-1.0) and 0.6 (95% CI, 0.4-0.8) per 1000 population, respectively, for patients aged 45 to 64 years. Among patients aged 65 years or older, the population rate of ED visits attributed to therapeutic use of all diabetes agents and all anticoagulants and was 1.8 (95% CI, 1.3-2.3) and 4.5 (95% CI, 2.3-6.7) per 1000 population, respectively.

Discussion

ED visits attributed to medication harms were frequent in the US in 2017-2019 and varied by medication type, intended use, and patient age. Direct-acting oral anticoagulants (DOACs) require less rigorous management than warfarin because of more predictable pharmacologic profiles and lower rates of major bleeding[14,15]; however, with increased use, they are important contributors to medications associated with ED visits for medication harms. Nearly as many ED visits were attributed to DOACs (5.9%) as to warfarin (8.4%). There have been recent efforts to improve therapeutic use of anticoagulant

medications in outpatient settings, including improving the processes for periprocedural management and transitioning between agents and recognizing sentinel bleeding.[16] In 2019, the Joint Commission updated its national patient safety goals to specifically address DOACs, and their expert management, in addition to that of older anticoagulants, is being integrated into emerging anticoagulation stewardship efforts.[17,18] Consideration could also be given to incorporating measurement of anticoagulant adverse events into quality measures and improvement activities[19] while ensuring that anticoagulants continue to be prescribed when indicated.

Efforts to reduce unintended harms from diabetes medications have also increased recently, particularly for older adults. National treatment guidelines have been updated[20-23] and campaigns initiated[24] to balance risks and benefits of tight glycemic control in patients with high risk of hypoglycemia (eg, history of severe hypoglycemia, limited life expectancy, extensive comorbid conditions). New injectable diabetes agents with reduced risk of hypoglycemia have been introduced, but insulin remains the cornerstone of diabetes treatment.[25] Optimizing insulin prescribing, improving glucose monitoring and insulin delivery systems, and supporting patients' knowledge and actions in balancing their diabetes medication dosing, diet, and activities are approaches being used to reduce hypoglycemic events.[26-28]

The CDC guideline for prescribing opioids for chronic pain (2016)[29] and FDA's recent (2020) boxed warning for benzodiazepines[30] advise judicious prescribing of opioids and benzodiazepines for patients for whom these drugs are indicated and limiting excess supply available to others to reduce risk of adverse events, particularly among young and middle-aged adults. However, the finding that, overall, most visits involving nontherapeutic use of these medication classes also involved use of alcohol or illicit substances suggests opportunities for interventions that extend beyond judicious prescribing of prescription drugs.[31] Reducing ED visits for the most common medication harms among adolescents and young adults may also involve measures beyond improving clinician prescribing and that address underlying problems of mental health and substance use because an even higher proportion (>60%) of ED visits involved nontherapeutic medication use, and many involved over-the-counter or psychiatric medications.[32,33]

Reducing ED visits for the most common medication harms among young children could target inappropriate antibiotic prescribing, as well as unsupervised exposures. With intensive efforts, pediatric antibiotic overprescribing can be reduced,[34] and the addition of flow restrictors to bottles of liquid medications has been shown to decrease unsupervised ingestions and related ED visits.[35,36] Increasing use of outpatient antimicrobial stewardship, broader implementation of flow restrictors, and enhanced safety packaging for pills, such as unit-dose packaging and child-resistant pill organizers, have potential to further reduce ED visits.[37-39] Although older children (5-9 years) had the lowest rates of ED visits for medication harms, opportunities may exist for judicious prescribing of antibiotics and addressing nontherapeutic use of over-the-counter and attention-deficit/hyperactivity disorder medications.[40]

Limitations

This study has several limitations. First, it likely underestimated the prevalence of medication harms from therapeutic and nontherapeutic use of medications because it did not include medication harms diagnosed and treated outside of EDs or those not likely to be diagnosed in EDs (eg, low-severity or insidious events, those that did not contribute to the patient's chief concern, or those that required extensive evaluation to diagnose), or medication harms that resulted in deaths that occurred before the ED visit or in the ED (owing to variability in how such deaths were documented in ED medical record systems). Second, although the most common drug classes and products implicated in ED visits for medication harms were identified, appropriateness of prescribing could not be assessed. Third, population rates of ED visits for medication harms should be interpreted with caution because not every individual would have had medication exposure. Rates were not calculated by frequency of each specific medication exposure because data were not available for the range and specificity of products assessed and, although appropriate for comparisons within a class of medications, a single measure of exposure has limitations for comparing rates across medication classes, dose forms, and dosages. Fourth, for most visits involving nontherapeutic use, information to determine whether medications were prescribed to patients or obtained through other means was not available. Fifth, it is possible that intent of use was misclassified for some patients because they may have misreported intentionality or may have arrived to EDs unresponsive and unable to report intentionality, and clinicians may not have correctly identified or fully documented intentionality or details leading to the visit.

Conclusions

According to data from 60 nationally representative US emergency departments, visits attributed to medication harms in 2017-2019 were frequent, with variation in products and intent of use by age.

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