

STATISTICAL BRIEF #158

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Origin of Adverse Drug Events in U.S. Hospitals, 2011

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Introduction

Prescription medications are widely used to treat a variety of acute and chronic medical conditions, and their use has increased substantially in the United States over the past 20–25 years.¹ In the years 1988–1994, approximately 38 percent of the U.S. population reported that they had used a prescription drug in the past 30 days; this increased to nearly 48 percent of the population in the period from 2005 to 2008.² Prescription drug use has increased among all age groups, reaching 25 percent of children and 90 percent of the elderly in the years 2005–2008.³ Moreover, the number of medications per patient also has increased. For example, in the period from 1988–1994, just over one-third of the elderly used three or more prescription drugs in the past 30 days, compared to nearly two-thirds in the years 2005–2008.⁴

The intention of prescription medications is to help cure disease or alleviate symptoms; however, sometimes the drugs can cause patient injury, known as an *adverse drug event* (ADE). With the substantial rise in the use of medications, there has been a concomitant increase in the occurrence of ADEs reported to the FDA.⁵ However, the FDA's Adverse Event Reporting System only requires drug manufacturers to report ADEs while many ADEs are often reported in hospitals instead. Between 2004 and 2008, there was a 52 percent increase in the number of ADEs reported in U.S. hospitals.⁶ Adverse drug events increase the risk of death, the length of hospitalization, and the cost of care.^{7,8}

¹ National Center for Health Statistics. Health, United States, 2011: With Special Feature on Socioeconomic Status and Health. Hyattsville, MD: Centers for Disease Control and Prevention; 2012.

² Ibid.

³ Ibid.

⁴ Ibid.

⁵ Moore TJ, Cohen MR, Furberg CD. Serious adverse drug events reported to the Food and Drug Administration, 1998–2005. *Archives of Internal Medicine* 2007;167(15):1752–9.

⁶ Lucado J, Paez K, Elixhauser E. Medication-Related Adverse Outcomes in U.S. Hospitals and Emergency Departments, 2008. HCUP Statistical Brief #109. April 2011. Agency for Healthcare Research and Quality, Rockville, MD.

<http://www.hcup-us.ahrq.gov/reports/statbriefs/sb109.pdf>. Accessed June 24, 2013.

⁷ Classen DC, Jaser L, and Budnitz DS. Adverse Drug Events Among Hospitalized Medicare Patients: Epidemiology and National Estimates from a New Approach to Surveillance. *The Joint Comm.J. on Quality and Patient Safety*. 2010, 36:1, 12-21.

Highlights

- In 2011, adverse drug events (ADEs) in U.S. hospitals were three times more likely to be present on admission (388 per 10,000 discharges) than to originate during the hospital stay (129 per 10,000 discharges).
- The most common general causes of ADEs that were *present on admission* (POA) were antibiotics and anti-infectives (23.4 percent of all ADEs), systemic agents (13.6 percent), nonspecific ADE causes (12.9 percent), and hormones (11.9 percent).
- The most common general causes of ADEs that *originated during the stay* were antibiotics and anti-infectives (28.0 percent of all ADEs), nonspecific ADE causes (16.6 percent), hormones (16.1 percent), and analgesics (12.6 percent).
- Overall, the most common specific ADEs were related to *clostridium difficile* infection (95 per 10,000 discharges), antineoplastic drugs, and steroids (each at a rate of 57 per 10,000 discharges).
- Almost all ADEs were more likely to be POA than to originate during the stay. The largest differences were observed for antidepressants (17.6 times more likely to be POA) and central nervous system drugs (13.5 times more likely to be POA).
- ADEs due to CNS depressants and anesthetics were nearly two times more likely to originate during the stay than to be POA. Antibiotic-related ADEs were equally likely to be POA as to originate during the stay.

Hospital stays involving ADEs have been reported for a range of drugs, including hormones, analgesics, antibiotics, and cardiovascular drugs, among others.⁹ Adverse drug events may be a reason for admission to the hospital—that is, the ADE was present on admission (POA). Alternatively, ADEs may originate during the hospital stay because of medications administered during hospitalization. Adverse drug events are the most common nonsurgical adverse events in hospitals.¹⁰ In 2008, about 14 percent of Medicare patients experienced an adverse event originating during their hospital stay, costing an estimated \$3.8 billion a year, with about a third of the events being ADEs.¹¹ This Statistical Brief presents more recent data on national ADE rates over all payers in 2011.

In 32 of 46 States participating in the Healthcare Cost and Utilization Project (HCUP), the data indicate whether diagnoses are POA or originate during the hospital stay. In these States, inpatient data can be used to chart the frequency of in-hospital events and to report the frequency of community-occurring ADEs that are serious enough to require hospitalization and be observed at admission. This Statistical Brief presents data from these 32 States. The 2011 rates are reported for general classes as well as the specific types of drugs that cause ADEs.¹²

All numbers noted in the text and included in the tables are actual values, not estimates, because the data include a census of discharges rather than a sample of discharges. In other words, we count the actual number of hospital stays with ADEs in the 32 States. Because we analyze numbers for the actual population rather than a sample, there is no need to estimate how well the sample represents an underlying population. As a result, there is no sampling error associated with the calculated values presented, and significance testing is not necessary.¹³

⁸ Classen DC, Pestotnik SL, Evans RS, et al. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. *JAMA* 1997 Jan 22;277(4):301–6.

⁹ Lucado J, Paez K, Elixhauser E. Medication-Related Adverse Outcomes in U.S. Hospitals and Emergency Departments, 2008. HCUP Statistical Brief #109. April 2011. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.hcup-us.ahrq.gov/reports/statbriefs/sb109.pdf>. Accessed June 24, 2013.

¹⁰ de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. *Quality and Safety in Health Care*. 2008;17;216–23.

¹¹ Levinson DR. Adverse Events in Hospitals: National Incidence Among Medicare Beneficiaries. Office of Inspector General, Department of Health and Human Services, 2010. OEI-06-09-00090.

¹² 2010 HCUP ADE origination rates were presented in Encinosa WE and Bae J. Will Meaningful Use Hospital EMR Prevent Hospital-Acquired Drug Events? WHITE Conference, October, 2012. <http://www.rhsmith.umd.edu/chidswHITE/2012/program.aspx>. Accessed August 11, 2013.

¹³ Houchens, R. Inferences with HCUP State Databases Final Report. HCUP Methods Series Report # 2010-05. Online October 12, 2010. U.S. Agency for Healthcare Research and Quality. http://www.hcup-us.ahrq.gov/reports/methods/2010_05.pdf. Accessed June 24, 2013.

Findings

Frequency of adverse drug events, 2011

Across a total of 20,172,966 discharges in the 32 States included in our analysis, there were 782,757 ADEs that were present on admission and 259,662 ADEs that originated during the hospital stay. Table 1 presents the rate and percentage of ADEs for a range of causes. Overall, ADEs observed during hospitalization were more likely to be present on admission (388 per 10,000 discharges) than to originate during the hospital stay (129 per 10,000 discharges). Among ADEs present on admission, the most common general causes were antibiotics and anti-infectives (23.4 percent of all ADEs), systemic agents (13.6 percent), nonspecific ADE causes (12.9 percent), and hormones (11.9 percent). Among ADEs that originated during the stay, the most prevalent general causes were antibiotics and anti-infectives (28.0 percent of all ADEs), nonspecific ADE causes (16.6 percent), hormones (16.1 percent), and analgesics (12.6 percent).

Table 1. Adverse drug events (ADEs) in hospital inpatient settings, 32 states, 2011

Adverse drug event cause ^a	ADEs based on diagnoses present on admission		ADEs based on diagnoses that originated during the hospital stay	
	Number of ADEs per 10,000 discharges	Percent of ADEs ^b	Number of ADEs per 10,000 discharges	Percent of ADEs ^b
Any ADE cause	388.0	100.0	128.7	100.0
Antibiotics and anti-infectives	90.9	23.4	36.1	28.0
Antibiotics	12.5	3.2	12.9	10.0
<i>Clostridium difficile</i> infection ¹⁴	73.1	18.8	21.9	17.1
Other anti-infectives	6.3	1.6	1.7	1.3
Hormones	46.3	11.9	20.7	16.1
Steroids	37.3	9.6	19.7	15.3
Insulin and hypoglycemics	7.1	1.8	0.8	0.6
Other hormones	3.0	0.8	0.3	0.2
Systemic agents	52.8	13.6	8.5	6.6
Antineoplastic drugs	49.2	12.7	7.8	6.0
Antiallergy and antiemetic drugs	3.1	0.8	0.7	0.5
Other systemic agents	0.8	0.2	0.1	0.1
Agents affecting blood constituents	43.9	11.3	8.5	6.6
Anticoagulants	40.6	10.5	6.7	5.2
Other agents that affect blood constituents	3.9	1.0	1.9	1.5
Analgesics	45.5	11.7	16.2	12.6
Opiates/Narcotics	18.8	4.9	11.2	8.7
NSAIDs	28.3	7.3	5.1	4.0

¹⁴ *Clostridium difficile* infection (CDI) often occurs as a complication of antibiotic therapy; ampicillin, clindamycin, third-generation cephalosporins (such as cefotaxime and ceftazidime), and fluoroquinolones are commonly identified as high-risk drugs. From: Blondeau JM. What have we learned about antimicrobial use and the risks for *Clostridium difficile*-associated diarrhoea? Journal of Antimicrobial Chemotherapy 2009;63(2):230–7.

Table 1. Adverse drug events (ADEs) in hospital inpatient settings, 32 states, 2011 (continued)

Adverse drug event cause ^a	ADEs based on diagnoses present on admission		ADEs based on diagnoses that originated during the hospital stay	
	Number of ADEs per 10,000 discharges	Percent of ADEs ^b	Number of ADEs per 10,000 discharges	Percent of ADEs ^b
Anticonvulsants and anti-Parkinson drugs	11.0	2.8	1.5	1.2
Hydantoin	3.3	0.9	0.4	0.3
Other anticonvulsants	7.3	1.9	1.0	0.7
Anti-Parkinson drugs	0.8	0.2	0.1	0.1
Sedatives or hypnotics	11.0	2.8	5.7	4.4
CNS depressants and anesthetics	3.9	1.0	6.7	5.2
Psychotropic agents	34.8	9.0	4.2	3.2
Antidepressants	9.5	2.5	0.5	0.4
Antipsychotics	7.0	1.8	0.8	0.7
Benzodiazepine	18.1	4.7	2.2	1.7
Other psychotropic drugs	7.2	1.8	0.8	0.6
Central nervous system drugs	4.9	1.3	0.4	0.3
Autonomic nervous system drugs	2.6	0.7	0.7	0.5
Cardiovascular drugs	29.4	7.6	7.5	5.8
Digoxin	4.8	1.2	0.6	0.5
Antiadrenergics	4.2	1.1	1.1	0.9
Other cardiovascular drugs	21.6	5.6	5.9	4.6
GI system drugs	1.3	0.3	0.5	0.4
Water, mineral, and uric acid metabolism drugs	16.9	4.4	6.1	4.8
Saluretics	5.2	1.3	0.7	0.5
Other diuretics	10.7	2.8	4.6	3.6
Other drugs affecting mineral and uric acid metabolism	1.6	0.4	0.9	0.7
Smooth muscle and respiratory drugs	4.0	1.0	1.1	0.8
Skin, eye, mucous membrane drugs	1.0	0.3	0.3	0.3
Vaccines	0.3	0.1	0.1	0.1
Other specific drugs	0.2	0.1	0.0	0.0
Nonspecific ADE causes (drug type not specified)	49.9	12.9	21.4	16.6

Abbreviation: NSAIDS, nonsteroidal anti-inflammatory drugs

^aGeneral ADEs are in bold; specific ADEs are indented.

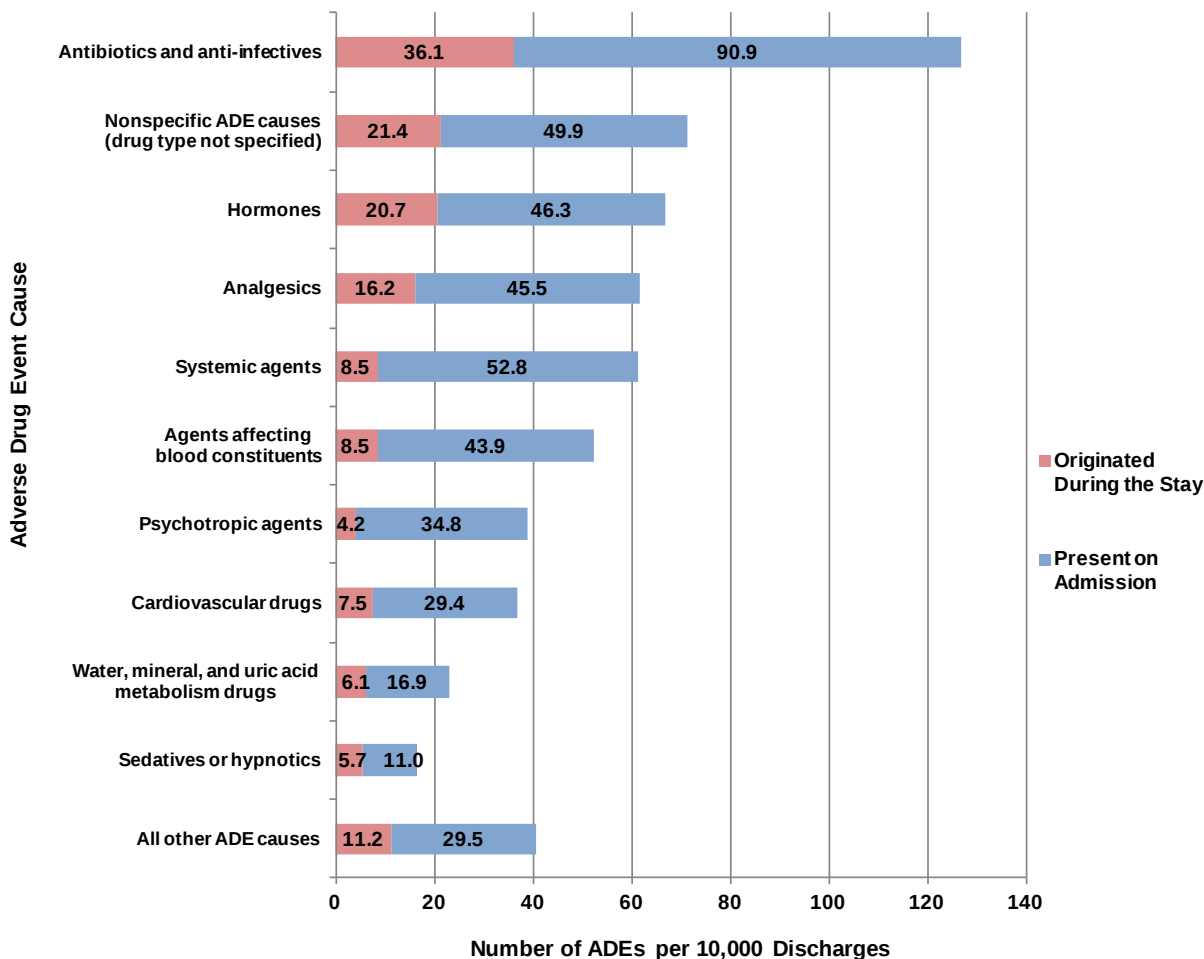
^b The sum may be greater than 100% because some hospital stays may involve more than one ADE.

Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) for 32 States, 2011

General causes of adverse drug events, 2011

The general causes of adverse drug events that were present on hospital admission and those that originated during the stay are provided in Figure 1. The order of the list is from the most to least frequently occurring cause overall. The most frequent general causes of ADEs were antibiotics and anti-infectives (127 events per 10,000 discharges), nonspecific ADE causes (71 events), hormones (67 events), and analgesics (62 events). Across all general causes, ADEs were substantially more likely to be present on admission than to originate during the stay.

Figure 1. General causes of adverse drug events (ADEs), 2011



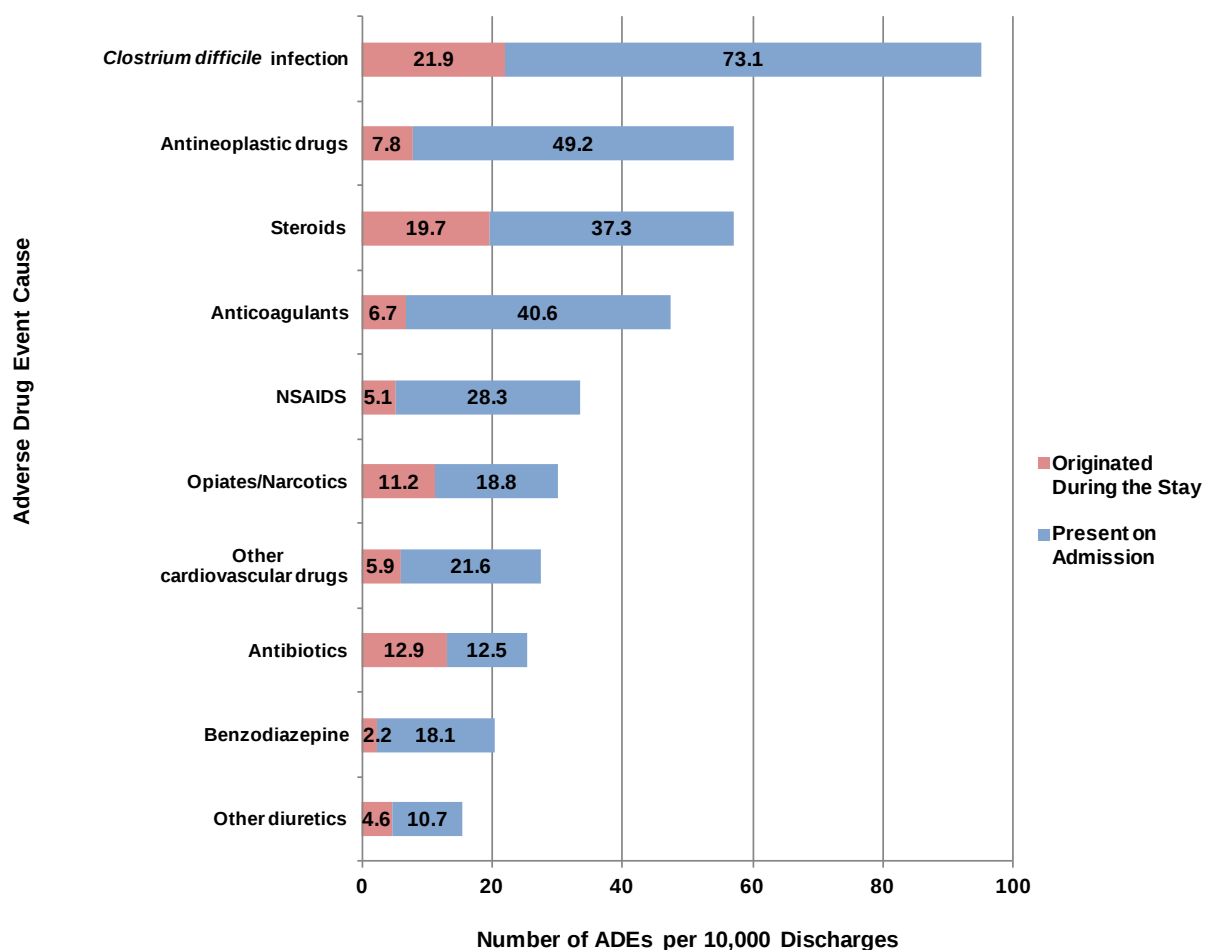
Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) for 32 States, 2011

Most common specific causes of adverse drug events, 2011

Figure 2 presents the 10 most common specific causes of adverse drug events. The data represent causes that occurred at a rate of more than 15 per 10,000 discharges. *Clostridium difficile* infection was the most common ADE cause, occurring at a rate of 95 per 10,000 discharges. The next two most frequently occurring ADE causes—antineoplastic drugs and steroids—each occurred at a rate of 57 per 10,000 discharges.

With the exception of antibiotics, all of the most common specific causes of ADEs were more likely to be present on admission than to originate during the hospital stay. For antibiotics, the number of events was nearly equal across the settings: 12.5 ADEs per 10,000 discharges were present on admission versus 12.9 ADEs that originated during the stay.

Figure 2. Ten most common specific causes of adverse drug events (ADEs), 2011



Abbreviation: NSAIDs, nonsteroidal anti-inflammatory drugs

Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) for 32 States, 2011

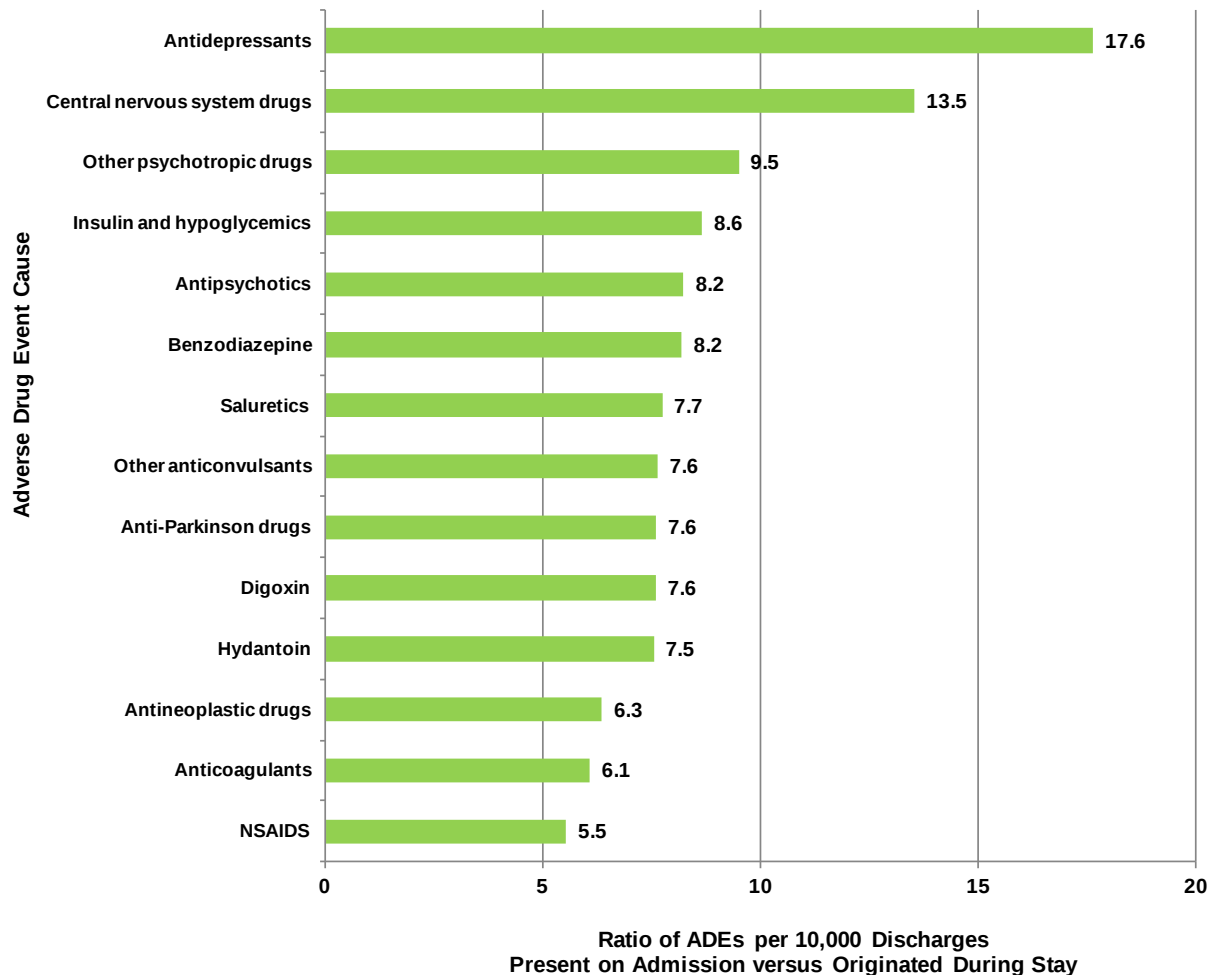
Most common causes of adverse drug events that were present on admission versus originated during the stay, 2011

Across all causes of adverse drug events, there were three times as many ADEs that were present on admission than originated during the stay. Most causes of adverse drug events were more likely to be present on admission.

Figure 3 presents the ratio of ADEs per 10,000 discharges that were present on admission versus those that originated during the stay for ADE causes that had at least a 5-fold difference (i.e., the ratio was at least 5.0). Most of the ADE causes had a ratio between 5.0 and 10.0. Only two ADE causes exceeded a ratio of 10.0: ADEs that were due to antidepressants (17.6 times more likely to be POA) and central nervous system drugs (13.5 times more likely to be POA).

Only one ADE cause—CNS depressants and anesthetics (data not shown)—was more likely to originate during the hospital stay (4 per 10,000 discharges were present on admission versus 7 per 10,000 discharges originated during the stay). ADEs caused by antibiotics were about equally likely to originate during the stay as to be present on admission (data not shown).

Figure 3. Most common causes of adverse drug events (ADEs) that were present on admission versus those that originated during the stay, 2011



Abbreviation: NSAIDS, nonsteroidal anti-inflammatory drugs

Source: Agency for Healthcare Research and Quality (AHRQ), Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) for 32 States, 2011

Data Source

The estimates in this Statistical Brief are based upon data from the Healthcare Cost and Utilization Project (HCUP) 2011 State Inpatient Databases (SID) from 32 States. These States included data elements that designated whether diagnoses were present on admission or originated during the stay: Arkansas, Arizona, California, Colorado, Florida, Georgia, Hawaii, Iowa, Illinois, Indiana, Kansas, Kentucky, Massachusetts, Maryland, Michigan, Minnesota, Montana, Nebraska, New Jersey, Nevada, New York, Oklahoma, Oregon, Pennsylvania, South Carolina, South Dakota, Tennessee, Texas, Virginia, Vermont, Washington, and Wisconsin.

Definitions

The specific causes of adverse drug events presented in this Statistical Brief were based on a review of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes and external cause of injury codes (E codes). The specific ICD-9-CM codes used for each ADE cause is provided in the separate appendix associated with this Statistical Brief on the HCUP-US website at: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb158_appendix.pdf.

Present on admission was determined for each discharge diagnosis based on two types of present-on-admission indicator flags in the SID: (1) a diagnosis-specific flag that indicates whether each diagnosis was present on admission, and (2) an E code flag that indicates whether each external cause of injury was present on admission.

A total of 4,554 hospitals and 30,149,145 discharges were in the original SID for the 32 States in this study. Hospitals and individual discharge records with missing or incomplete present-on-admission information were excluded from the analysis, as shown in Table 2.

Table 2. Exclusion criteria and the number of hospitals and discharges excluded

Exclusion Criteria	Hospitals Excluded ^a		Discharges Excluded ^a	
	Number	Percent	Number	Percent
Hospitals that reported all diagnoses and E codes as being present on admission	48	1.1	47,104	0.2
Hospitals with 20 percent or more discharges with a missing present on admission indicator for nonmissing diagnoses or E codes	1,768	38.8	8,619,776	28.6
Hospitals that only coded present on admission for Medicare patients	5	0.1	3,140	0.0
Discharges with missing present on admission information for nonmissing diagnoses or E codes	n/a	n/a	1,309,298	4.3

^aSome excluded hospitals and discharges are counted more than once, as a function of meeting more than one exclusion criteria.

The final analysis file for this Statistical Brief included 2,737 hospitals (60.1 percent) and 20,172,966 discharges (66.9 percent) across the 32 States.

Unit of analysis

The unit of analysis is the hospital discharge (i.e., the hospital stay), not a person or patient. This means that a person who is admitted to the hospital multiple times in one year will be counted each time as a separate "discharge" from the hospital.

About HCUP

HCUP is a family of powerful health care databases, software tools, and products for advancing research. Sponsored by the Agency for Healthcare Research and Quality (AHRQ), HCUP includes the largest all-payer encounter-level collection of longitudinal health care data (inpatient, ambulatory surgery, and emergency department) in the United States, beginning in 1988. HCUP is a Federal-State-Industry Partnership that brings together the data collection efforts of many organizations—such as State data organizations, hospital associations, private data organizations, and the Federal government—to create a national information resource.

HCUP would not be possible without the contributions of the following data collection Partners from across the United States:

Alaska State Hospital and Nursing Home Association
Arizona Department of Health Services
Arkansas Department of Health
California Office of Statewide Health Planning and Development
Colorado Hospital Association
Connecticut Hospital Association
Florida Agency for Health Care Administration
Georgia Hospital Association
Hawaii Health Information Corporation
Illinois Department of Public Health
Indiana Hospital Association
Iowa Hospital Association
Kansas Hospital Association
Kentucky Cabinet for Health and Family Services
Louisiana Department of Health and Hospitals
Maine Health Data Organization
Maryland Health Services Cost Review Commission
Massachusetts Center for Health Information and Analysis
Michigan Health & Hospital Association
Minnesota Hospital Association
Mississippi Department of Health
Missouri Hospital Industry Data Institute
Montana MHA - An Association of Montana Health Care Providers
Nebraska Hospital Association
Nevada Department of Health and Human Services
New Hampshire Department of Health & Human Services
New Jersey Department of Health
New Mexico Department of Health
New York State Department of Health
North Carolina Department of Health and Human Services
North Dakota (data provided by the Minnesota Hospital Association)
Ohio Hospital Association
Oklahoma State Department of Health
Oregon Association of Hospitals and Health Systems
Oregon Health Policy and Research
Pennsylvania Health Care Cost Containment Council
Rhode Island Department of Health
South Carolina Budget & Control Board
South Dakota Association of Healthcare Organizations
Tennessee Hospital Association
Texas Department of State Health Services
Utah Department of Health
Vermont Association of Hospitals and Health Systems
Virginia Health Information

Washington State Department of Health
West Virginia Health Care Authority
Wisconsin Department of Health Services
Wyoming Hospital Association

About the SID

The HCUP State Inpatient Databases (SID) are hospital inpatient databases from data organizations participating in HCUP. The SID contain the universe of the inpatient discharge abstracts in the participating HCUP States, translated into a uniform format to facilitate multistate comparisons and analyses. Together, the SID encompass more than 95 percent of all U.S. community hospital discharges in 2011. The SID can be used to investigate questions unique to one State, to compare data from two or more States, to conduct market area variation analyses, and to identify State-specific trends in inpatient care utilization, access, charges, and outcomes.

For More Information

For more information about HCUP, visit <http://www.hcup-us.ahrq.gov/>.

For additional HCUP statistics, visit HCUPnet, our interactive query system, at <http://hcupnet.ahrq.gov/>.

For information on other hospitalizations in the United States, download HCUP Facts and Figures: Statistics on Hospital-Based Care in the United States in 2009, located at <http://www.hcup-us.ahrq.gov/reports.jsp>.

For a detailed description of HCUP, more information on the design of the State Inpatient Databases (SID), please refer to the following publications:

Introduction to the HCUP State Inpatient Databases. Online. December 2012. U.S. Agency for Healthcare Research and Quality. http://hcup-us.ahrq.gov/db/state/siddist/Introduction_to_SID.pdf. Accessed June 24, 2013.

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AHRQ welcomes questions and comments from readers of this publication who are interested in obtaining more information about access, cost, use, financing, and quality of health care in the United States. We also invite you to tell us how you are using this Statistical Brief and other HCUP data and tools, and to share suggestions on how HCUP products might be enhanced to further meet your needs. Please e-mail us at hcup@ahrq.gov or send a letter to the address below:

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