

The CBHSQ Report

Short Report

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EMERGENCY DEPARTMENT VISITS FOR ADVERSE REACTIONS INVOLVING THE PAIN MEDICATION TRAMADOL

AUTHORS

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INTRODUCTION

Approximately 100 million adults in the United States experience pain that can affect performance on daily tasks, quality of life, and productivity in the workplace.¹ Management of chronic pain presents a great challenge for patients and their health care providers as they attempt to achieve adequate pain management with medication while avoiding major side effects or adverse reactions. Tramadol is a type of narcotic (i.e., opioid) pain medication approved by the U.S. Food and Drug Administration (FDA). Prescriptions for this drug have become increasingly common, up 88 percent from 23.3 million in 2008 to 43.8 million in 2013.^{2,3} Tramadol is typically used for the management of moderate to moderately severe acute or chronic pain in adults and is the active ingredient in the brand name drugs Ultram®, Ultram ER®, Ultracet®, ConZip®, Ryzolt®, and Rybix ODT®.^{4,5,6,7,8,9}

Among older patients, use of common over-the-counter pain relievers such as ibuprofen and naproxen (i.e., nonsteroidal anti-inflammatory drugs) carries a significant risk of gastrointestinal bleeding and kidney dysfunction. These side effects are generally not associated with use of tramadol, making it an option for older patients with chronic pain.¹⁰ However, as with all narcotic pain relievers, tramadol should be used cautiously in patients at risk for respiratory depression.^{4,5,6,7,8,9}

Harmful consequences, including seizures and a potentially fatal drug reaction known as serotonin syndrome, can occur even when tramadol is taken as prescribed by a physician.^{10,11} Additionally, when tramadol is combined with other drugs that depress the central nervous system—such as anti-anxiety medications (e.g., benzodiazepines), narcotic pain relievers, or alcohol—the sedative effects of tramadol can be enhanced.^{4,5,6,7,8,9} Tracking emergency department (ED) visits involving tramadol can provide data to help health professionals and patients understand the health consequences of adverse reactions associated with the use of this drug and to consider appropriate safeguards.



In Brief

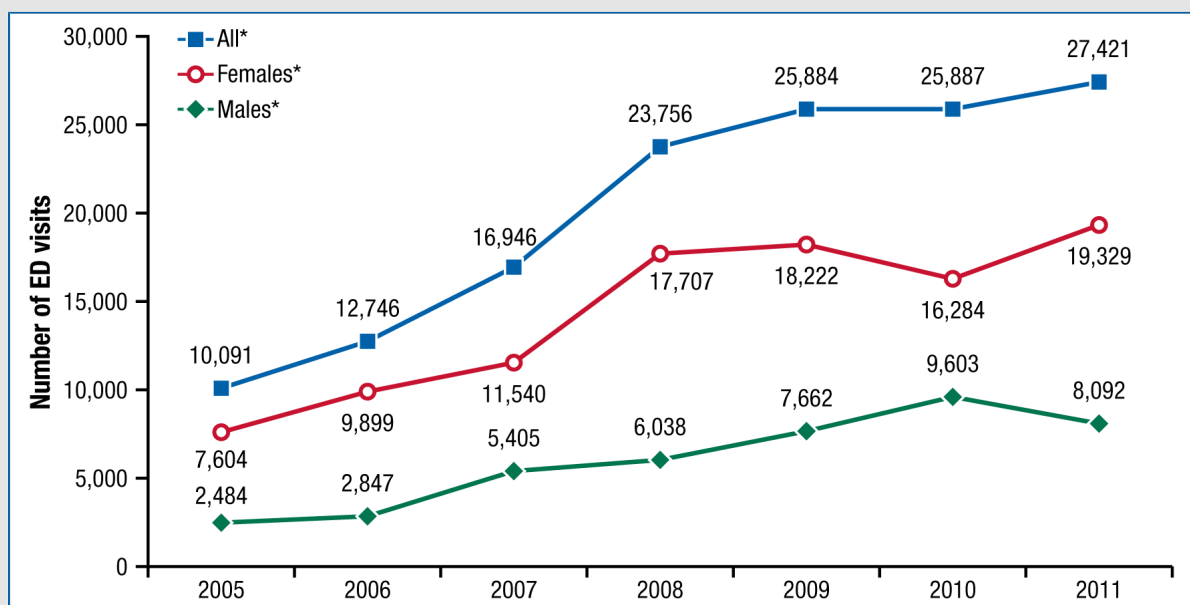
- The estimated number of tramadol-related emergency department (ED) visits involving adverse reactions increased 145 percent from 2005 to 2009, but then remained stable in 2010 and 2011.
- Females accounted for three-fourths (75 percent) of tramadol-related ED visits involving adverse reactions in 2005 and continued to account for the majority of visits through 2011.
- In 2011, visits made by patients aged 65 or older accounted for more than one-third (35 percent) of tramadol-related ED visits involving adverse reactions overall and accounted for half (52 percent) of such visits that resulted in admission to the hospital or transfer to another health care facility.

The Drug Abuse Warning Network (DAWN) was a public health surveillance system that monitored drug-related ED visits in the United States. To be a DAWN case, an ED visit must have involved a drug, either as the direct cause of the visit or as a contributing factor. Data were collected on numerous illicit drugs, including cocaine, marijuana, heroin, and stimulants (e.g., amphetamines and methamphetamines) as well as pharmaceutical products, such as prescription and over-the-counter medications. Data were also collected for visits involving alcohol combined with other drugs and for patients aged 20 or younger where alcohol was the only substance involved in the visit. Adverse reactions, as defined by DAWN, include ED visits in which a negative health consequence (e.g., side effects or an allergic reaction) occurred when taking prescription drugs as prescribed (and only if prescribed for the patient), or when taking over-the-counter medications or dietary supplements as recommended. A visit is not included in the adverse reaction analytic group if an illicit drug was involved. This issue of *The CBHSQ Report* focuses on tramadol-related ED visits involving adverse reactions in 2011 and trends between 2005 and 2011. More information on DAWN methodology can be found at <http://samhsa.gov/data/2k13/DAWN2k11ED/rpts/DAWN2k11-Methods-Report.htm>.

OVERVIEW AND TRENDS

In 2011, there were an estimated 54,397 ED visits involving tramadol, and 27,421 (50 percent) were attributed to adverse reactions. The number of tramadol-related ED visits involving adverse reactions increased 145 percent from 10,091 visits in 2005 to 25,884 visits in 2009, but then remained stable in 2010 (25,887 visits) and 2011 (27,421 visits) (Figure 1).

Figure 1. Trends in tramadol-related emergency department (ED) visits involving adverse reactions, by gender: 2005 to 2011



* The difference between 2005 and 2011 is statistically significant at the .05 level.

Note —The difference between males and females is statistically significant at the .05 level for each year from 2005 to 2011.

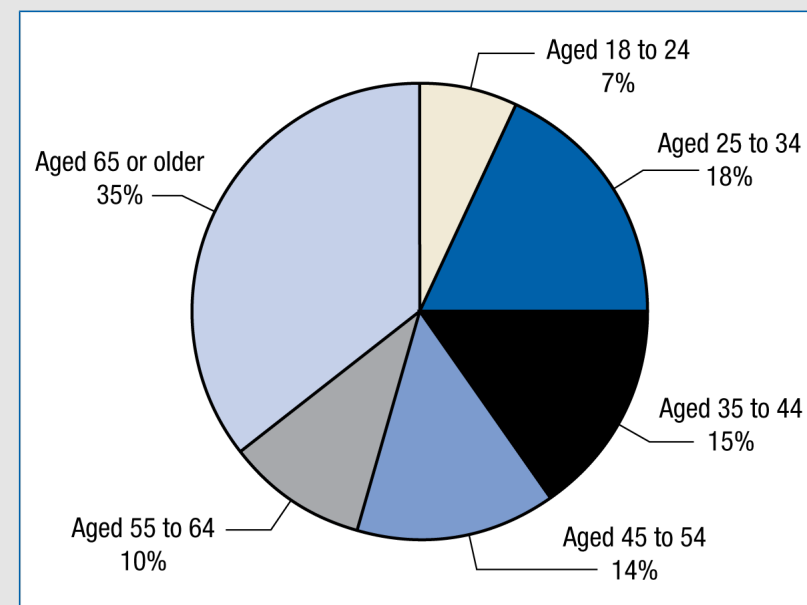
Source: 2005 to 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DEMOGRAPHIC CHARACTERISTICS

Tramadol-related ED visits involving adverse reactions increased for both males and females from 2005 to 2011; such visits rose overall by 226 percent for males (from 2,484 visits in 2005 to 8,092 visits in 2011) and by 154 percent for females (from 7,604 visits in 2005 to 19,329 visits in 2011) (Figure 1). Females accounted for three-fourths (75 percent) of such visits in 2005 and continued to account for the majority of visits through 2011. In each year from 2005 to 2011, visits for females were significantly higher than visits for males.

Visits made by patients aged 65 or older accounted for one-third (35 percent) of tramadol-related ED visits involving adverse reactions in 2011 (Figure 2). Patients aged 25 to 34 accounted for 18 percent of visits, followed by patients aged 35 to 44 (15 percent), aged 45 to 64 (14 percent), and aged 55 to 64 (10 percent). Patients aged 18 to 24 accounted for 7 percent of visits, and those younger than 18 accounted for less than 2 percent of visits.

Figure 2. Age distribution* among tramadol-related emergency department (ED) visits involving adverse reactions: 2011



* ED visits made by patients younger than age 18 accounted for less than 2 percent of visits.

Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DRUG COMBINATIONS INVOLVED IN ED VISITS

Among tramadol-related ED visits involving adverse reactions in 2011, 60 percent involved tramadol only (Table 1). Approximately 40 percent involved tramadol combined with other pharmaceuticals only; visits involving tramadol combined with alcohol were rare.

Nearly 1 in 5 visits involved tramadol combined with other pain relievers (5,007 visits, or 18 percent), with 2,586 visits (9 percent) involving tramadol combined with other narcotic pain relievers such as hydrocodone (1,424 visits, or 5 percent). In one-tenth of visits (2,606, or 10 percent), antidepressants were combined with tramadol, with 6 percent (1,726 visits) involving a class of antidepressants known as selective serotonin reuptake inhibitors (SSRIs; e.g., Celexa®, Lexapro®, Prozac®, Paxil®, Zoloft®).

Table 1. Selected drug combinations among tramadol-related emergency department (ED) visits involving adverse reactions: 2011

Drug category/combination	Number of ED visits*	Percentage of ED visits*
Total ED visits	27,421	100
Tramadol only	16,561	60
In combination with alcohol	**	**
In combination with other pharmaceuticals	10,833	40
Other pain relievers	5,007	18
Other narcotic pain relievers	2,586	9
Hydrocodone combinations	1,424	5
Cardiovascular medications	3,655	13
Antidepressants	2,606	10
SSRI*** antidepressants	1,726	6
Anticonvulsants	2,081	8
In combination with other pharmaceuticals only	10,782	39

* Because multiple drugs may be involved in each visit, estimates of visits by drug may add to more than the total, and percentages may add to more than 100 percent.

** Low precision; no estimate reported.

*** Selective serotonin reuptake inhibitors.

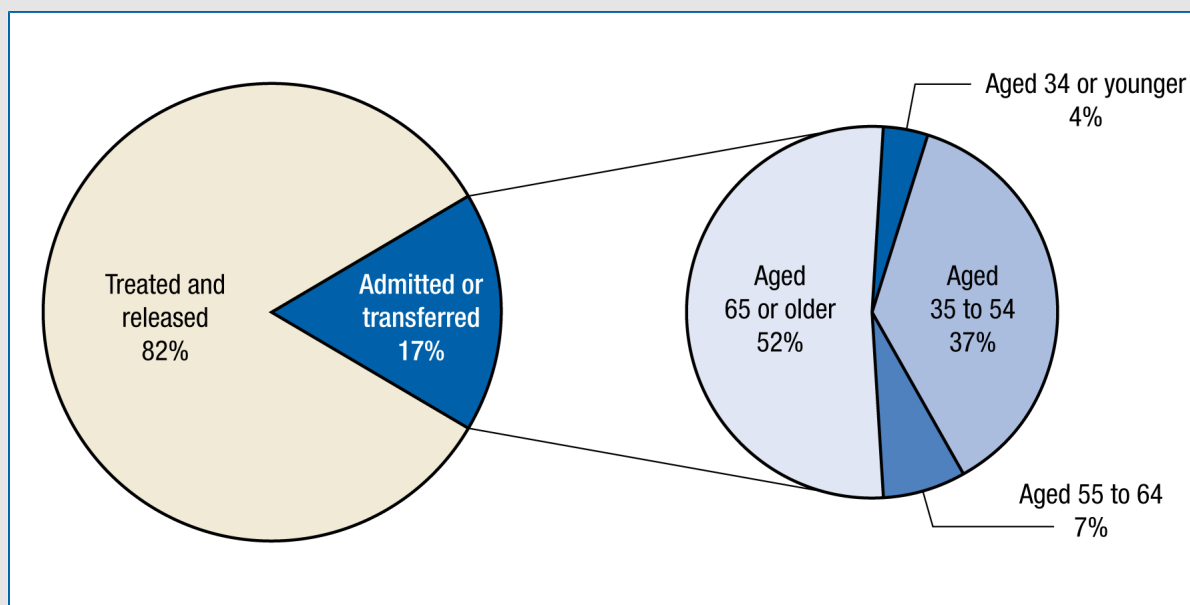
Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DISPOSITION OF ED VISITS

In 2011, the majority of tramadol-related ED visits resulted in the patient being treated and released (82 percent) (Figure 3). The remainder of patients were usually admitted to the hospital or transferred to another health care facility (17 percent); other dispositions (e.g., left against medical advice or died) were rare.

Among tramadol-related ED visits in which the patient was admitted to the hospital or transferred in 2011, about half were aged 65 or older (52 percent). Approximately 37 percent of tramadol-related ED visits involved patients aged 35 to 54, and the remainder involved those aged 55 to 64 (7 percent) or aged 34 or younger (4 percent).

Figure 3. Disposition* of tramadol-related emergency department (ED) visits involving adverse reactions, with age distribution of visits resulting in admission to the hospital or transfer to another health care facility: 2011



* Other dispositions not shown in the figure (e.g., left against medical advice or died) accounted for about 1 percent of visits.

Source: 2011 SAMHSA Drug Abuse Warning Network (DAWN).

DISCUSSION

Tramadol is now the second most commonly prescribed narcotic pain reliever in the United States, outranking oxycodone in 2012.³ Tramadol is often used safely with no severe health consequences, but visits to the ED for adverse reactions involving this drug do occur and sometimes result in admission to the hospital. These occurrences underscore the importance of careful clinical management of patients who are prescribed tramadol. The lowest dose of tramadol that is beneficial for each individual patient should be prescribed, and patients should be instructed not to use tramadol with alcohol, other opioid medications, or anti-anxiety or insomnia medications.^{4,5,6,7,8,9} This may be especially crucial for older adults, for whom acute or chronic pain is a common complaint and who often take other prescription medications that may interact with tramadol.¹⁰

When patients begin taking tramadol or increase the dose, they should be counseled to watch for symptoms of serotonin syndrome, which can be reversed if detected early.^{4,5,6,7,8,9} ED staff should be aware of this syndrome so they can promptly recognize the symptoms (e.g., fast heart rate, high blood pressure, dilated pupils, over-reactive reflexes, and/or elevated body temperature) and begin treatment immediately.¹¹ To further prevent this type of serious reaction, health care professionals should inquire about use of medications that elevate levels of serotonin, such as common antidepressant medications (i.e., SSRIs) before prescribing tramadol. Serotonin syndrome is most commonly caused by SSRIs. However, other drugs such as opioid analgesics, antibiotics, antimigraine agents, illicit drugs and over-the-counter drugs alone or in combination can also lead to serotonin syndrome. These drugs can interact with tramadol and can increase the risk of serotonin syndrome.¹¹

Data presented here underscore the critical importance of continued surveillance for adverse reactions to all drugs in order to evaluate drug safety. Enhancing drug safety is an important step toward improving public health and reducing health care costs. Pharmacists, nurses, mental health professionals, physicians, and specialists can work together with their patients to document all medications, supplements, and vitamins, including dosages. Sharing medical records with all providers can aid in this effort. Patients can also safeguard against adverse reactions by using one pharmacy for all prescriptions and by advising their pharmacy of previous adverse reactions to any medications.¹²

END NOTES

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SUGGESTED CITATION

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SUMMARY

Background: Approximately 100 million adults in the United States experience pain that can affect performance of daily tasks, quality of life, and productivity in the workplace. Tramadol is an opioid medication for the management of moderate to moderately severe pain in adults. Prescriptions for this drug increased 88% from 23.3 million in 2008 to 43.8 million in 2013. **Methods:** Data from the 2005 to 2011 Drug Abuse Warning Network (DAWN) were used to estimate the number of emergency department (ED) visits made for adverse reactions involving tramadol. We examined trends by age and gender, other drugs identified in these ED visits and the number of visits that resulted in admission to the hospital or transfer to another health care facility. **Results:** Data from 2011 DAWN shows an estimated 54,397 ED visits involving tramadol, 27,421 (50%) of which were attributed to adverse reactions. From 2005 to 2009, the number of estimated ED visits made for adverse reactions involving tramadol increased 145% (10,091 to 25,884 visits), and remained stable in 2010 and 2011 (25,887 and 27,421 visits, respectively). Females accounted for 75% of tramadol-related ED visits (7,604) involving adverse reactions in 2005 and continued to account for the majority of visits through 2011 (19,329). In 2011, although visits made by patients aged 65 or older accounted for 35% of tramadol-related ED visits involving adverse reactions (9,688), they accounted for 52% of the visits that resulted in admissions to the hospital or transferred to another health care facility. **Conclusion:** When tramadol is combined with other drugs that depress the central nervous system, such as anti-anxiety medications (e.g. benzodiazepines), narcotic pain relievers, or alcohol, the sedative effects of tramadol can be enhanced. This may be especially crucial for older adults, especially females, for whom acute or chronic pain is a common complaint and who often take other prescription medications that may interact with tramadol.

Key words: tramadol, adverse reactions, opioids, Drug Abuse Warning Network, DAWN

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KEYWORDS

Age Group, Short Report, Emergency Department Data, 2011, Men as Audience, Public Health Professionals, Women as Audience, Adverse Reaction, Females, Males, Older Adults as Population Group, Emergency Department Treatment, Multi-Year Trend, All US States Only, Tramadol

The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA's mission is to reduce the impact of substance abuse and mental illness on America's communities.

The Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related morbidity and mortality. DAWN uses a probability sample of hospitals to produce estimates of drug-related emergency department (ED) visits for the United States and selected metropolitan areas annually. DAWN also produces annual profiles of drug-related deaths reviewed by medical examiners or coroners in selected metropolitan areas and States.

Any ED visit related to recent drug use is included in DAWN. All types of drugs - licit and illicit - are covered. Alcohol involvement is documented for patients of all ages if it occurs with another drug. Alcohol is considered an illicit drug for minors and is documented even if no other drug is involved. The classification of drugs used in DAWN is derived from the Multum Lexicon, copyright 2012 Lexi-Comp, Inc., and/or Cerner Multum, Inc. The Multum Licensing Agreement governing use of the Lexicon can be found at <http://www.samhsa.gov/data/emergency-department-data-dawn>.

DAWN is one of three major surveys conducted by SAMHSA's Center for Behavioral Health Statistics and Quality (CBHSQ). For more information on other CBHSQ surveys, go to <http://www.samhsa.gov/data/>. SAMHSA has contracts with Westat (Rockville, MD) and RTI International (Research Triangle Park, NC) to operate the DAWN system and produce publications.

For publications and additional information about DAWN, go to <http://www.samhsa.gov/data/emergency-department-data-dawn>.



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