

# Recent Trends in Emergency Department Visits Resulting From Unintentional Overdose of Non-Opioid Analgesics, Antipyretics, and Antirheumatics in the United States

Ravi K. Goyal, Mayank R. Ajmera, Keith L. Davis

RTI Health Solutions, Research Triangle Park, NC, United States

## BACKGROUND

- Drug-related overdoses result in > 1 million emergency department (ED) visits in the United States (US) annually.<sup>1</sup>
- The US Food and Drug Administration (FDA) has taken significant steps in recent years to increase awareness about medication safety and reduce risks associated with overdosing of pain medications.<sup>2,4</sup> A few of these initiatives include:
  - Guidance for Industry: Labeling OTC Human Drug Products (2008)
  - Safe Use Initiative (2009)
  - Organ-Specific Warnings for Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use (2009)
  - Acetaminophen Drug Safety Communication (2010)
  - National Drug Abuse Prevention Plan (2011)
  - ER/LA Opioids REMS Program (2012)
  - Know Your Dose campaign (2013)
- It is imperative to follow up on the impact of these initiatives and to examine whether they have resulted in any demonstrable reduction in the rate of incidents related to unintentional overdoses with pain medications at the US population level.

## OBJECTIVE

- To assess changes over time in the incidence of ED visits resulting from unintentional drug overdoses, with a particular focus on non-opioid analgesic, antipyretic, and antirheumatic (NOAAA) drugs.

## METHODS

### Data Source

- Data from the National Hospital Ambulatory Medical Care Survey (NHAMCS), a nationally representative annual sample of visits in hospital outpatient and emergency departments and in ambulatory surgery centers in the US, were used.
- NHAMCS utilizes a multistage sampling procedure, which randomly selects physicians from primary sampling units composed of noninstitutional general and short-stay hospitals located in all states and Washington, DC (excluding federal, military, and Veteran's Administration hospitals).
- Visit-level data are collected on demographic characteristics, reasons for visit, diagnoses, diagnostic and screening services, procedures, types of health care professionals seen, and causes and intent of injury.

### Study Measures

#### ED Visits for Drug Overdose

- ED visits for overdose/poisoning with NOAAA drugs were identified based on evidence of any of the following:
  - An *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis code for poisoning by analgesics, antipyretics, and antirheumatics (excluding opioids): 965.1, 965.4-965.9
  - An ICD-9-CM cause-of-injury code for accidental poisoning by analgesics, antipyretics, and antirheumatics (excluding opioids): E850.3-E850.9
  - Use of acetylcysteine (antidote for treatment of acetaminophen poisoning)

#### Unintentional Overdose

- The unintentional nature of overdose related ED visit was determined using "intent" data collected in NHAMCS.
  - The patient record form in the NHAMCS survey specifically collects data on whether the injury/poisoning resulting in the ED visit was intentional (i.e., self-inflicted or an assault), unintentional, or unknown.

#### Data Analysis

- Three-year blocks of data were combined into four observation periods (2002-2004, 2005-2007, 2008-2010, and 2011-2013) to ensure adequate sample size.
- An inflation factor (i.e., visit weight) provided in the NHAMCS data was applied to produce nationally representative estimates for the total number of ED visits in each of the four year-groups; corresponding 95% confidence intervals (CIs) were derived.
- Rates of ED visits due to unintentional overdose of NOAAA drugs were assessed per 100,000 all-cause ED visits.
- All analyses were descriptive in nature and were performed using SAS statistical software, version 9.4 (SAS Institute Inc.; 2011).

## REFERENCES

1. Albert M, McCaig LF, Uddin S. Emergency department visits for drug poisoning: United States, 2008-2011. *NCHS Data Brief*. 2015 Apr;(196):1-8.
2. Taylor R Jr, Lemtouni S, Weiss K, Pergolizzi JV Jr. Pain Management in the Elderly: An FDA Safe Use Initiative Expert Panel's View on Preventable Harm Associated with NSAID Therapy. *Curr Gerontol Geriatr Res*. 2012;2012:196159.
3. Food And Drug Administration. Food and Drug Administration's Safe Use Initiative collaborating to reduce preventable harm from medications. *J Pain Palliat Care Pharmacother*. 2010 Mar;24(1):76-93.
4. Food And Drug Administration. Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse. 2014. Available at: <https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm338566.htm>. Accessed April 17, 2017.

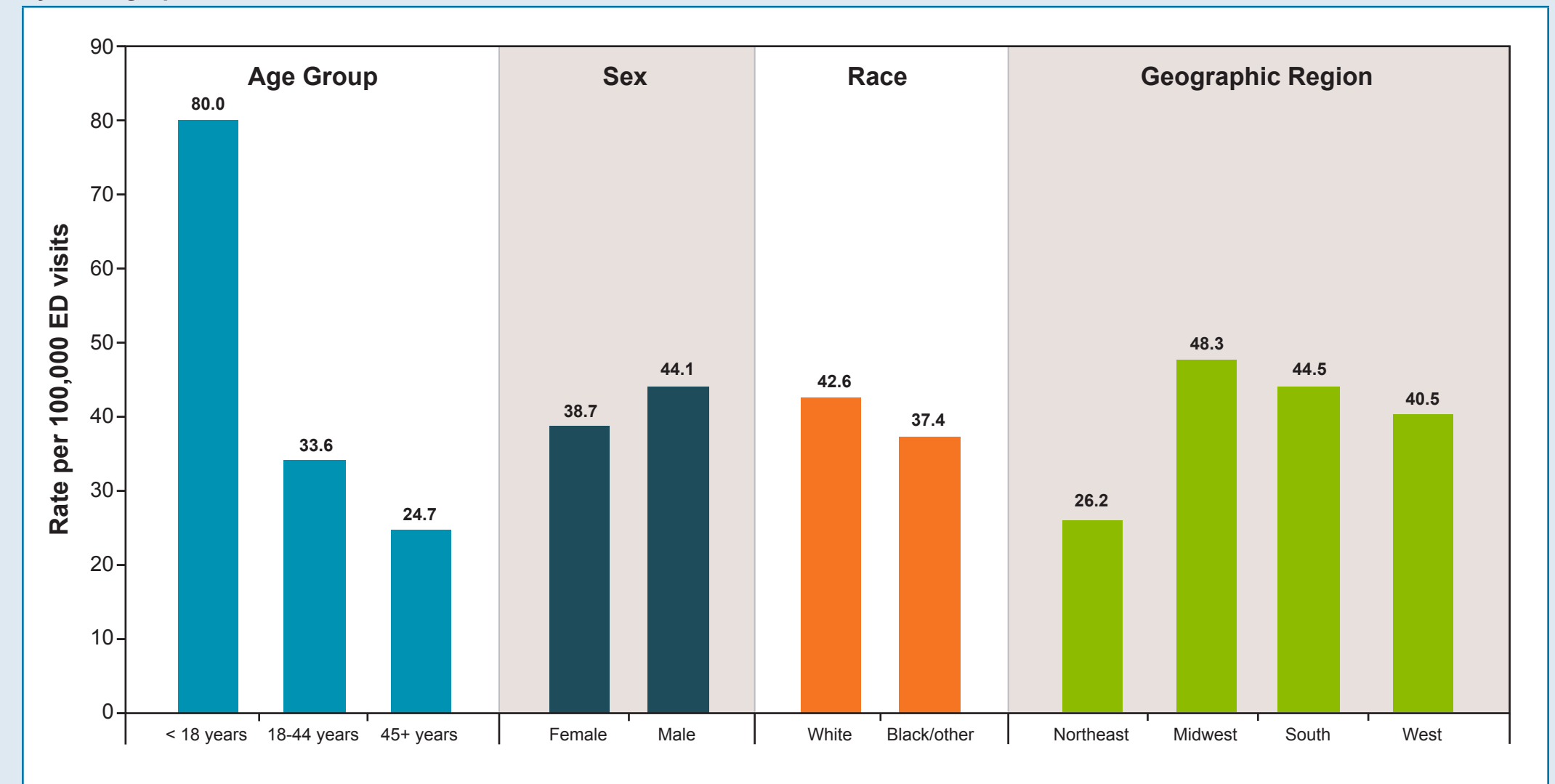
## RESULTS

- An estimated total of 1.5 billion unique ED visits took place in the US between 2002 and 2013.
- During the overall study period, unintentional overdose (associated with any drug) accounted for approximately 4.2 million visits. Of these, 14.4% (n = 606,595 [95% CI: 475,710-736,393]) were due to unintentional overdose of NOAAA drugs.
- The unweighted and estimated number of ED visits by demographic characteristics are presented in Table 1.
- The total numbers of ED visits resulting from unintentional overdose of NOAAA drugs during the four 3-year observation periods 2002-2004, 2005-2007, 2008-2010, and 2011-2013 were 144,946 (95% CI: 83,949-206,190), 146,730 (95% CI: 82,476-210,608), 170,559 (95% CI: 108,986-232,700), and 144,360 (95% CI: 72,167-216,500), respectively.

**Table 1. Characteristics of Patients With ED Visits for Unintentional Overdose of NOAAA Drugs, 2002-2013**

Characteristics	Unweighted Frequency	Weighted Frequency	95% CI	
<b>Total Patients</b>	<b>164</b>	<b>606,595</b>	<b>487,492</b>	<b>726,084</b>
<b>Age Group</b>				
< 18 years	69	273,692	192,935	354,942
18-44 years	56	202,305	125,187	279,829
45+ years	39	130,598	70,694	189,989
<b>Sex</b>				
Female	83	311,789	216,500	406,489
Male	81	294,806	207,663	381,452
<b>Race</b>				
White	127	459,845	351,996	567,023
Black/other	37	146,750	76,585	216,500
<b>Ethnicity</b>				
Hispanic	17	37,018	13,255	60,384
Not Hispanic	147	569,577	453,618	686,319
<b>Region</b>				
Northeast	29	71,629	38,292	104,568
Midwest	43	158,673	94,258	223,864
South	58	261,347	163,479	359,360
West	34	114,946	57,439	172,316

**Figure 2. Overall US ED Visit Rates for Unintentional Overdose of NOAAA Drugs Per 100,000 ED Visits, by Demographic Characteristics; 2002-2013**

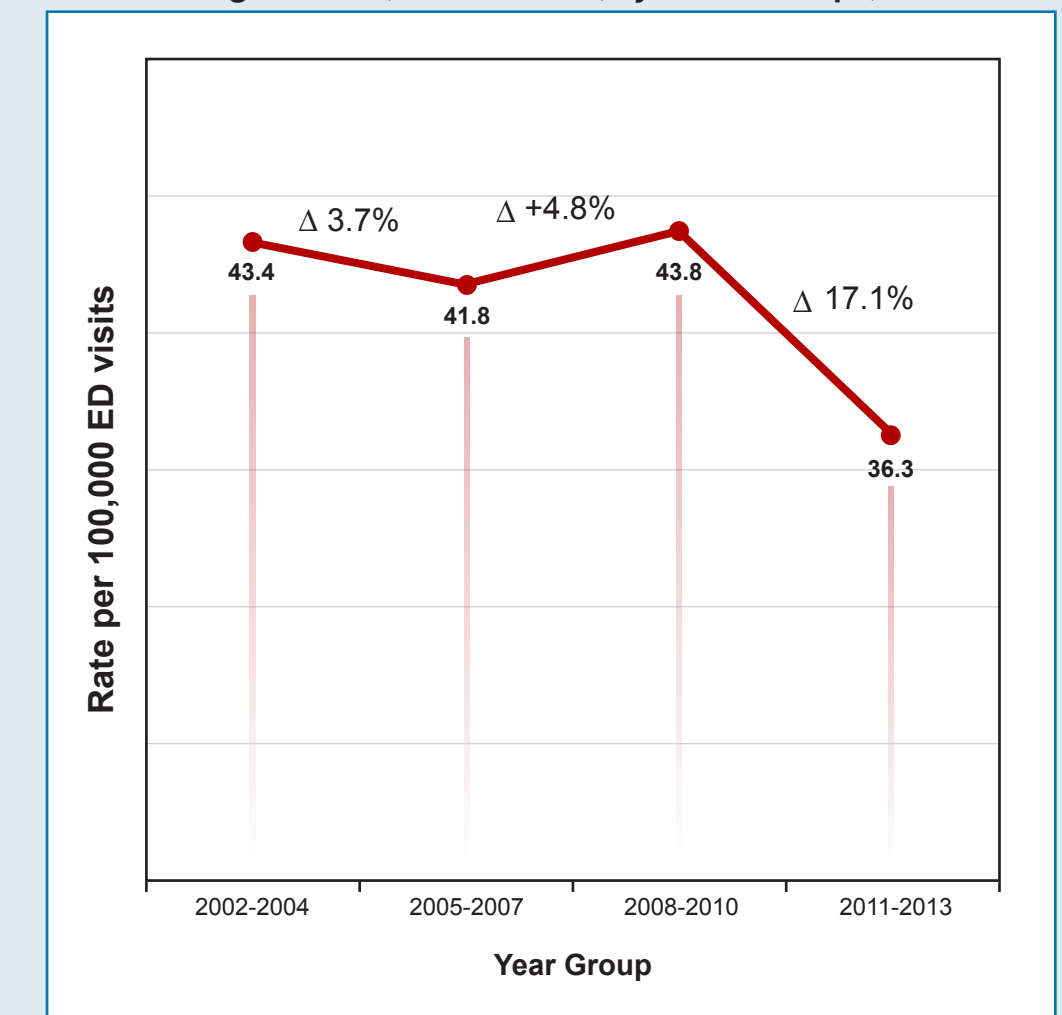


## DISCUSSION

- To our knowledge, this is the first study to analyze trends in ED visits associated with unintentional overdose of NOAAA drugs, particularly in the context of exploring the impact of FDA initiatives.
- The findings of this study indicate that unintentional NOAAA overdose declined by approximately 17% between the periods 2008-2010 and 2011-2013. The overlap in confidence intervals between the two year-groups suggests that this decline was not statistically significant.
  - Nonetheless, the direction of this trend is important evidence of potential success of recent FDA policies and initiatives toward reducing risks of injury from preventable medication misadventures.
- The findings of this study should be viewed in context of certain limitations.
  - ED visits for overdose/poisoning with NOAAA drugs were identified using ICD-9-CM diagnosis and cause-of-injury codes, and the use of an acetaminophen antidote medication was used as a proxy. Such an algorithm to identify NOAAA overdose has not been validated.
  - The data are incidental and were collected using a survey instrument, so inaccuracies and documentation bias may be present.

- The rate of ED visits for unintentional overdose of NOAAA drugs per 100,000 all-cause ED visits was 43.4 (95% CI: 31.8-57.8) during 2002-2004, which remained relatively constant through periods 2005-2007 (41.8 [95% CI: 30.5-55.9]) and 2008-2010 (43.8 [95% CI: 32.2-58.2]) but decreased to 36.3 per 100,000 ED visits (95% CI: 25.9-49.6) in the most recent period, 2011-2013, representing a relative decline of 17.1% (Figure 1).
- Stratified analysis of time trends in visit rates by various patient demographic characteristics were not performed due to limited sample sizes.
  - However, variation in the overall rates (2002-2013) across levels of patient characteristics were examined and are depicted in Figure 2.
  - Overall, the rate of ED visits for unintentional overdose of NOAAA drugs per 100,000 ED visits were highest among individuals aged < 18 years (80.0), males (44.1), and whites (42.6).

**Figure 1. Trend in US ED Visits for Unintentional Overdose of NOAAA Drugs Per 100,000 ED Visits, by 3-Year Groups; 2002-2013**



**Figure 2. Overall US ED Visit Rates for Unintentional Overdose of NOAAA Drugs Per 100,000 ED Visits, by Demographic Characteristics; 2002-2013**

## CONCLUSIONS

- This analysis of a nationally representative database of ED visits demonstrated a numerical decline in the rate of ED visits for unintentional NOAAA drug overdoses in recent years, suggesting that the FDA initiatives educating consumers about medication safety may be effective.
- Future research may be needed to validate the findings of this study and to examine whether the declining trend observed in this study is sustained over subsequent years.

## CONTACT INFORMATION

Ravi K. Goyal, MS, BPharm  
Senior Research Health Economist

RTI Health Solutions  
200 Park Offices Drive  
Research Triangle Park, NC 27709

Phone: +1.919.541.6019  
Fax: +1.919.541.7222  
E-mail: rgoyal@rti.org