




BMJ Open Amphetamine-related care in the USA, 2003–2014: cross-sectional analyses examining inpatient trends and factors associated with hospitalisation outcomes

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ABSTRACT

Objectives Although amphetamine use is a growing health problem in the USA, there are limited data on amphetamine-related hospitalisations. The primary objective of our study was to examine trends in amphetamine-related hospitalisations in the USA between 2003 and 2014, including by age and sex. Our secondary objectives were to examine whether demographic, clinical and care setting characteristics were associated with select outcomes of amphetamine-related hospitalisations, including in-hospital mortality, prolonged length of stay and leaving against medical advice.

Design, setting and participants Using the 2003–2014 National Inpatient Sample, we estimated the rate of amphetamine-related hospitalisations for each year in the USA among individuals 18+ years of age, stratified by age and sex. Subgroup analyses examined hospitalisations due to amphetamine causes. Unconditional logistic regression modelling was used to estimate the adjusted odds of admission outcomes for sociodemographic, clinical and hospital indicators.

Primary and secondary outcomes Our primary outcome was amphetamine-related hospitalisations between 2003 and 2014; secondary outcomes included in-hospital mortality, prolonged length of stay and leaving against medical advice.

Results Amphetamine-related hospitalisation rates increased from 27 to 69 per 100 000 population between 2003 and 2014. Annual rates were consistently greater among younger (18–44 years) individuals and men. Regional differences were observed, with admission to Western hospitals being associated with increased mortality (adjusted OR, AOR 5.07, 95% CI 1.22 to 21.04) and shorter (0–2 days) lengths of stay (AOR 0.70, 95% CI 0.58 to 0.83) compared with Northeast admissions. Males (AOR 1.26, 95% CI 1.15 to 1.38; compared with females) and self-pay (AOR 2.30, 95% CI 1.90 to 2.79; compared with private insurance) were associated with leaving against medical advice.

Conclusions Increasing rates of amphetamine-related hospitalisation risk being overshadowed by other public health crises. Regional amphetamine interventions may offer the greatest population health benefits. Future

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Data analysed originate from nationally representative datasets, which permitted us to compute precise estimates of amphetamine-related hospitalisation rates across the USA for more than 10 years.
- ⇒ Datasets used include in-depth socioeconomic, clinical and hospital data that permitted us to stratify our findings by age, sex and hospital location, as well as take factors, such as race, insurance status, comorbidities and hospital size, presumed to bias modelled associations into account in our regression analyses.
- ⇒ To our knowledge, our study is the first to highlight notable age and sex differences in amphetamine-related hospitalisations at a national level in the USA.
- ⇒ Due to the federally mandated adoption of International Classification of Diseases, 10th Revision (ICD-10) in 2015, newer diagnostic categorisation schemes for illicit substance use, abuse and poisoning are not directly comparable to established methods of classifying substance use via ICD-9-Clinical Modification codes and consequently we were unable to compute amphetamine-related trends for years 2015 onwards.
- ⇒ Our inability to adjust for behavioural factors, including health seeking behaviours and patterns of substance use, may bias our reported estimates.

studies should examine long-term outcomes among patients hospitalised for amphetamine-related causes.

INTRODUCTION

Use of recreational amphetamines has considerably increased in the USA since 2008.^{1–3} These include methamphetamines, which are by far the most common class of illicit amphetamines used in North America. Between 2008 and 2015, amphetamine-related hospitalisations also increased by almost 245%.²

Similarly, the proportion of admissions to USA-based substance use treatment centres for methamphetamine-related care increased by 8.5% between 2008 and 2017.¹ Population-adjusted mortality rates attributed to amphetamines have also increased sixfold between 2003 and 2017.³

Beyond the health consequences, amphetamine use poses a significant economic burden. Annual hospital costs related to amphetamines alone have increased from US\$436 million in 2003 to almost US\$2.2 billion by 2015.² In the USA, costs associated with morbidity and mortality, criminal justice and social welfare services, environmental clean-up from chemical production and lost productivity due to methamphetamine use reached US\$23.4 billion in 2005.⁴ A recent systematic review and meta-analysis also found that individuals who use illicit drugs, such as methamphetamines, use emergency department and inpatient services at a much greater rate than the general population.⁵

Prior studies of USA populations have found that individuals at higher risk of recreational amphetamine use include males, men who have sex with men and individuals with frequent encounters with law enforcement.⁶ Similarly, amphetamine treatment and health-seeking behaviours may differ by sex.^{7,8} Race and ethnicity are also important risk factors with American Indians and Alaska Natives exhibiting higher mortality rates compared with non-Hispanic whites.⁹ The Northwestern/Western region of the USA also shows the highest rates of psychostimulant-related deaths, whereas the Northeastern region has the lowest death rates.⁹

While evidence suggests that amphetamine use is a growing problem, current literature regarding the epidemiology of amphetamine use and related adverse outcomes is sparse. A small number of studies have explored this issue in the USA. However, these studies are often region-specific or survey based¹; few have looked at nationally representative hospital data. A study by Cox *et al*¹⁰ and more recently, by Winkelman *et al*² examined trends in hospitalisations with substance-related diagnoses using national inpatient data from the Healthcare Cost and Utilisation Project (HCUP). However, neither provided age-stratified and sex-stratified trends or examined risk factors for such amphetamine-related hospitalisations. These are important pieces of information required to effectively identify individuals who are most at risk of amphetamine misuse and associated health outcomes.

Given growing concerns surrounding amphetamine use and the paucity of research on this topic, the primary objective of our study was to examine trends in amphetamine-related hospitalisations in the USA between 2003 and 2014, including by age and sex. Our secondary objectives were to examine whether demographic, clinical and care setting characteristics were associated with select outcomes of amphetamine-related hospitalisations, including in-hospital mortality, prolonged length of stay and leaving against medical advice.

METHOD

Study design and setting

We conducted trend analyses that examined annual amphetamine-related hospitalisations among adults (18+ years of age) in the USA between 1 January 2003 and 31 December 2014. Additionally, for the year 2014, we also completed cross-sectional analyses that examined associations between sociodemographic, clinical and hospital characteristics with study outcomes of interest.

Data sources

We analysed National (formerly Nationwide) Inpatient Sample (NIS) datasets from 2003 to 2014 in our study. The NIS dates back to 1988 and is a large, annual, publicly available, all-payer inpatient database that is managed by the HCUP. Detailed demographic (such as age, sex, income quartile and health insurance information), clinical (including recorded diagnoses, length of stay and discharge disposition) and hospital (such as size, location and ownership) data are available for each calendar year. The NIS includes information for a sample of all inpatient hospitalisations for each calendar year that may be used to generate nationally representative estimates of hospital admission, outcomes and health service utilisation using HCUP-provided discharge weights and survey weighing methods. Prior to 2012, the NIS includes data from all discharges from approximately 20% HCUP-participating hospitals. From 2012 onwards, data within the NIS is an approximate 20% sample of discharges from all HCUP-participating hospitals. The change in sampling design is presumed to yield more precise estimates due to reductions in sampling error,¹¹ and HCUP has developed trend weights that may be used for trend analyses that span 2012 and earlier NIS data. For each year, the NIS contains data from more than seven million distinct hospital admissions, which when weighted, represents more than 35 million unique hospitalisations and 97% of the USA population.

Study participants

Hospitalisations between 2003 and 2014 where an International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) code for amphetamine dependence (304.40, 304.41, 304.42), abuse (305.70, 305.71, 305.72) or poisoning (969.72) was recorded as a primary (first diagnostic position; reason for admission) or secondary (all other diagnostic positions) diagnosis were eligible for inclusion in our analyses. Available diagnostic codes may not distinguish between methamphetamine use, other illicit amphetamine use, non-medical use of prescription amphetamines or adverse outcomes of medications that were prescribed to patients that were subsequently hospitalised. However, amphetamine-related diagnoses examined within our study were, based on previous literature, assumed to primarily be attributed to the use of methamphetamine and other non-prescription amphetamines or psychostimulants.^{2 12 13} To restrict our annual cross-sectional samples to current

users of amphetamines, we excluded all hospitalisations where an ICD-9-CM diagnosis for amphetamine dependence (304.43) or abuse (305.73) in remission were documented. We further excluded hospitalisations where patient age was missing, invalid, <18 years or >124 years, as well as hospitalisations where patient sex was missing or invalid. Due to ICD-9-CM to ICD-10-CM changes in 2015 and the inability to make inferences across different medical coding systems, we were limited to data ending in 2014.

Trend analyses

Using HCUP trend weights and survey weighting methods, we estimated the number of amphetamine-related hospitalisations for each calendar year among individuals 18+ years of age. We then used US Census Bureau data for individuals 18+ years of age from each calendar year to compute the annual rate of amphetamine-related hospitalisation per 100 000 persons from 2003 to 2014. Annual amphetamine hospitalisation rates were further stratified by age (18–44 years, 45–64 years and 65+ years of age) and sex. Age strata were chosen based on available census data from the US Census Bureau provided by HCUP.¹⁴ At the time of our analyses, census data were not readily available for our study population (18+) between 2003 and 2014 by geographical region (Northeast, Midwest, South and West).

All trend analyses were repeated for the subgroup of hospitalisations where the primary diagnostic code was specific to amphetamine use. For these analyses, trends were reported as the proportion of total amphetamine-related hospitalisations (defined as all hospitalisations for primary and secondary diagnoses of amphetamine dependence, abuse and poisoning) in each calendar year that had a primary diagnosis of amphetamine use (expressed as a percentage). Hospitalisation trends for amphetamine-related causes were stratified by age, sex and geographical region (Northeast, Midwest, South and West).

Outcome analyses: analytical cohort

We examined whether sociodemographic, clinical and hospital characteristics were associated with outcomes of amphetamine-related hospital admission, which included in-hospital mortality, prolonged length of stay and leaving against medical advice using all eligible 2014 NIS amphetamine-related hospitalisations. For these analyses, we further excluded hospitalisations where patient race, payer status and zip income quartile were missing or invalid, as well as hospitalisations with missing or invalid data for length of stay, discharge disposition and death variables.

Inpatient deaths were identified by examining the NIS 'died' variable ('died' or 'did not die') for each amphetamine-related hospitalisation. Prolonged lengths of stay were defined as those >2 days; the rationale for this threshold was based on clinical input (to generally distinguish patients according to their need for care

and/or account for weekend admissions) and the distribution of eligible hospitalisations. Discharge disposition was assessed according to NIS-defined categories (such as routine, against medical advice or transfer to another facility).

We used survey weighting methods that accounted for the NIS sampling design to generate nationally representative estimates of amphetamine-related hospitalisations, patient and hospital characteristics, and selected outcomes. Sociodemographic, clinical and hospital characteristics were reported using descriptive statistics.

Unconditional logistic regression modelling was used to quantify associations between sociodemographic, clinical and hospital characteristics of interest and each assessed outcome, with a single multivariable model being built for each outcome. Regression models accounted for the NIS survey design and incorporated the strata and clustering of patients and hospitals to generate accurate variance estimates. Model covariates were selected a priori based on clinical knowledge and were presumed to confound modelled relationships. The following covariates were included in each multivariable model: age, sex, race, primary expected payer, median household income, comorbidity score, hospital size, hospital ownership/control, hospital teaching status and hospital region. Comorbidities documented during hospitalisations were categorised according to enhanced ICD-9-CM coding algorithms for Elixhauser comorbidities.¹⁵ Individual Elixhauser comorbidities were then summed to create a single comorbidity score per admission.

Subgroup analyses were conducted to examine whether examined associations would be similar among hospitalisations with a primary diagnostic code specific to amphetamine use. For these analyses, the three multivariable models were re-run using the same parameters defined in our primary outcome analyses.

An alpha of 0.05 was set as the threshold for significance in all analyses, which were completed using SAS V.9.4 (SAS Institute). GraphPad V.8.3.1 (GraphPad Software, San Diego, California, USA) was used to graphically depict hospitalisation trends. Small cell counts (≤ 10) were suppressed in accordance with the HCUP Data Use Agreement.

Patient and public involvement

No patient involved.

RESULTS

Amphetamine-related hospitalisations trends

There were 1 083 932 distinct amphetamine-related hospitalisations between 1 January 2003 and 31 December 2014. Overall, there was a 151.8% increase in the rate of amphetamine-related hospitalisations between 2003 and 2014. Amphetamine-related hospitalisations increased from 27.4 to 37.6 per 100 000 population between 2003 and 2005, but then steadily declined to 24.1 per 100 000 population in 2008 (figure 1). Hospitalisations increased

Amphetamine-Related Hospitalisations, 2003-2014

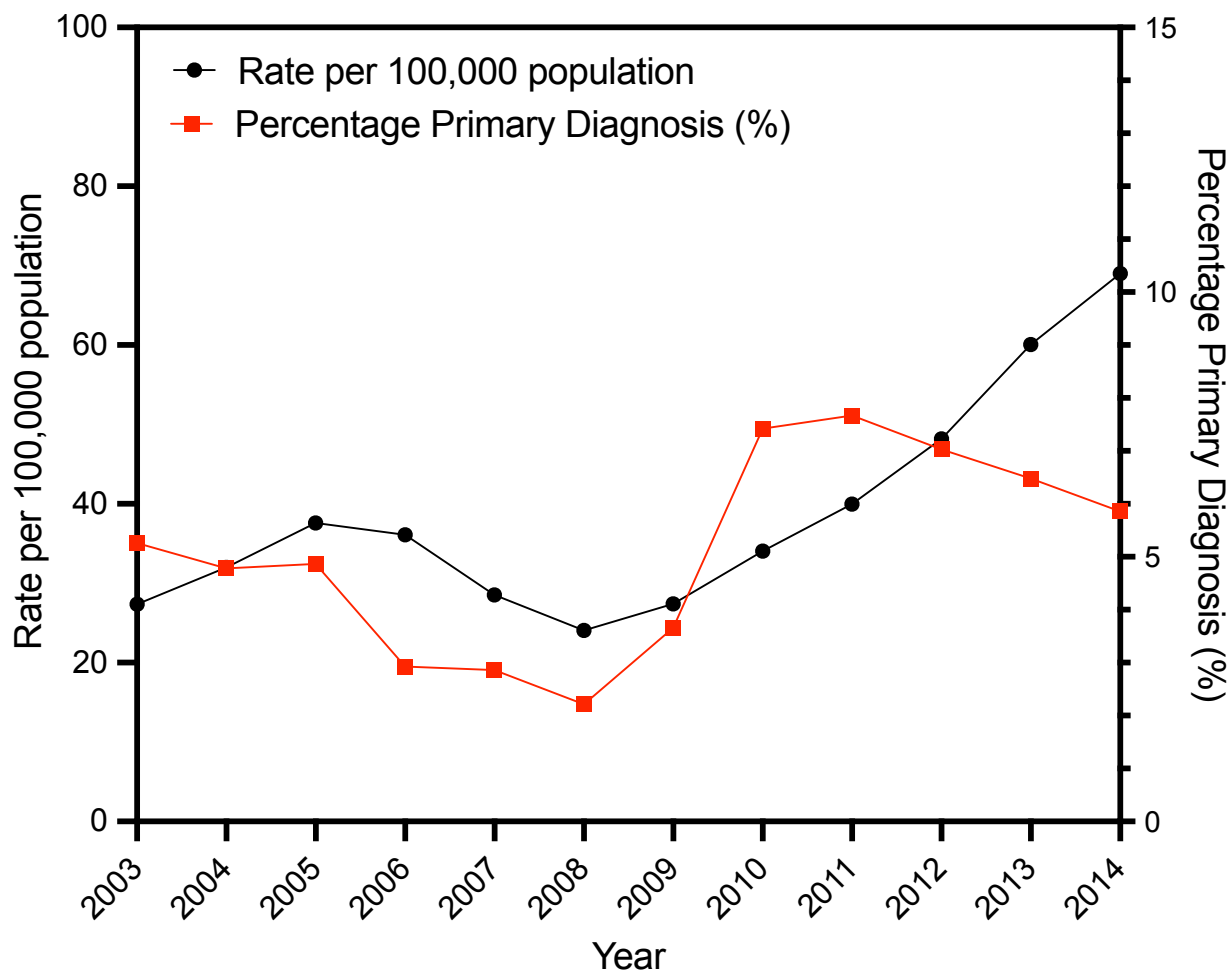


Figure 1 Rates of amphetamine-related hospitalisations in the USA over time, 2003–2014.

between 2008 and 2014, reaching a rate of 69.0 per 100 000 population in 2014. Similar trends were generally observed for the proportion of amphetamine-related hospitalisations with amphetamine causes as the primary reason for admission, with rates ranging from 2.2% (2008; 0.5 per 100 000 population) to 7.7% (2011; 3.1 per 100 000 population) during the study period (figure 1). A notable difference in trends was the decrease in proportion of amphetamine causes as primary reasons for hospitalisation between 2011 (7.7%; 3.1 per 100 000 population) and 2014 (5.9%; 4.1 per 100 000 population).

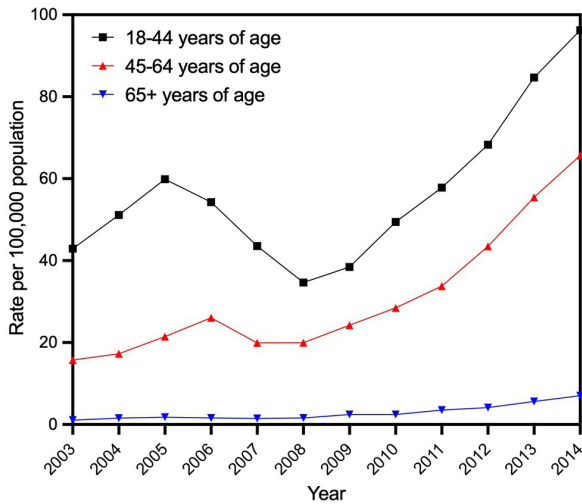
Stratified amphetamine-related hospitalisation trends are shown in figure 2. Annual hospitalisation rates were consistently greater among younger individuals (18–44 years) compared with older adult populations (figure 2A). Between 2003 and 2014, hospitalisation rates increased from 42.9 to 96.2 and from 15.7 to 65.6 per 100 000 population for groups 18–44 and 45–64 years of age, respectively. During the same period, hospitalisation rates among the oldest adults (65+ years of age) moderately increased from 1.1 to 7.0 per 100 000 population (figure 2A). Hospitalisation rates were higher

among males compared with females across all study years (figure 2B). Males exhibited a 177.8% (30.7–85.3 per 100 000 population) increase in hospitalisation rate between 2003 and 2014, whereas the increase in rate for females during the same period was 121.1% (24.2–53.5 per 100 000 population). Trends by age and sex in the proportion of amphetamine-related hospitalisations with amphetamine causes as the primary reason for admission were similar to those observed for the entire study population (figure 2C,D). Principal hospitalisations for amphetamine causes varied by geographical region, with Western hospitals having the lowest proportions of admissions attributed to amphetamine use, particularly after 2008 (figure 2E).

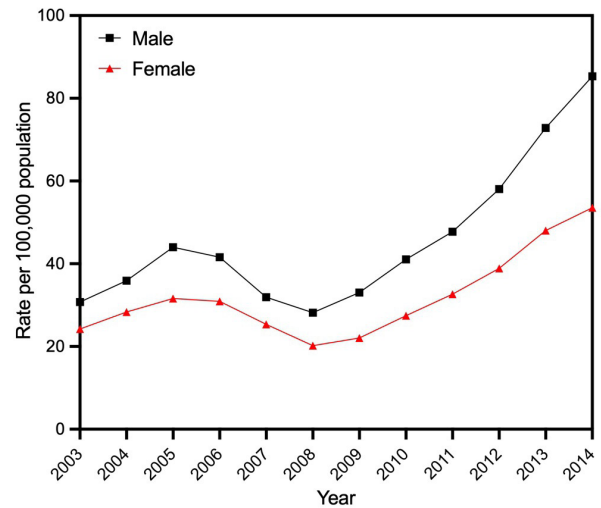
Analytical cohort, 2014: sociodemographic, clinical and hospital characteristics

There were 147 020 hospitalisations included in our 2014 analytical cohort, which represented 13.1% fewer admissions compared with the 2014 encounters in our trend analyses. The smaller cohort size resulted from missing or invalid sociodemographic data, especially for

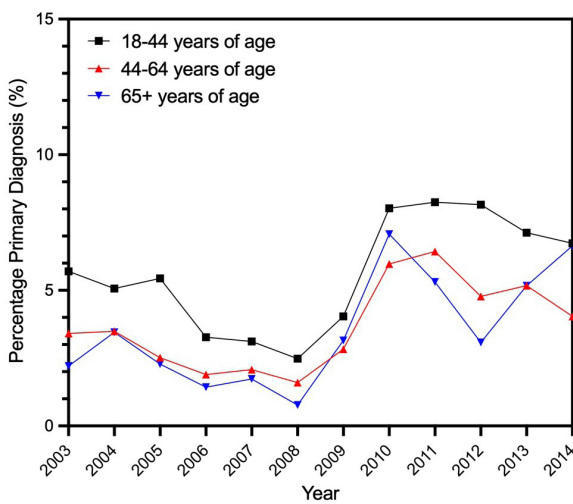
A. Amphetamine-Related Hospitalisations by Age, 2003-2014



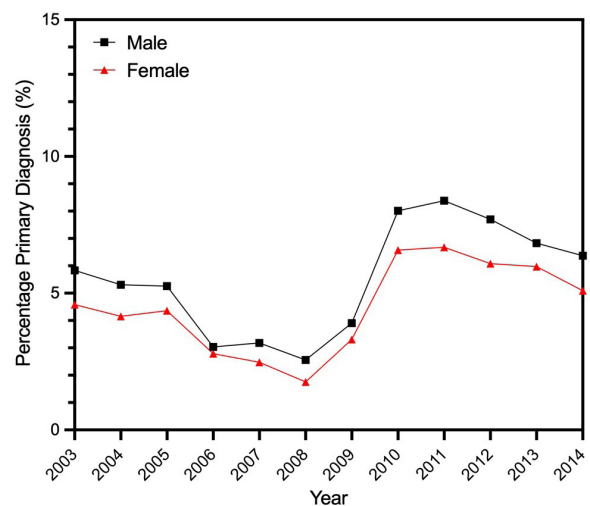
B. Amphetamine-Related Hospitalisations by Sex, 2003-2014



C. Amphetamine-Related Hospitalisations by Age, 2003-2014



D. Amphetamine-Related Hospitalisations by Sex, 2003-2014



E. Amphetamine-Related Hospitalisations by Region, 2003-2014

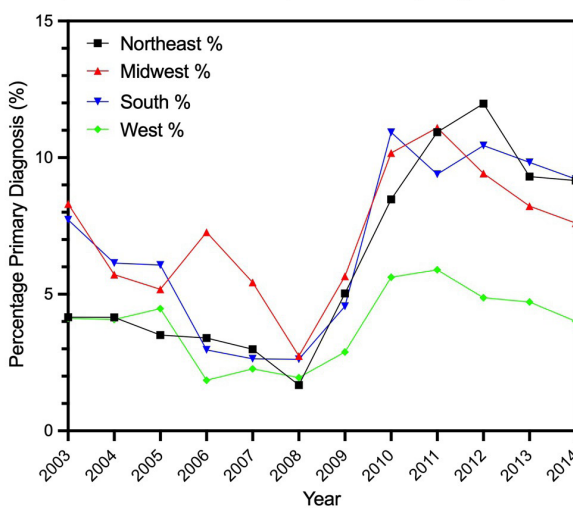


Figure 2 Stratified rates of amphetamine-related hospitalisations in the USA over time, 2003–2014. Hospitalisation rates per 100 000 population are shown stratified by age (A) and sex (B). Proportion of total amphetamine-related hospitalisations with a primary diagnosis of amphetamine use are shown stratified by age (C), sex (D), and geographical region (E).

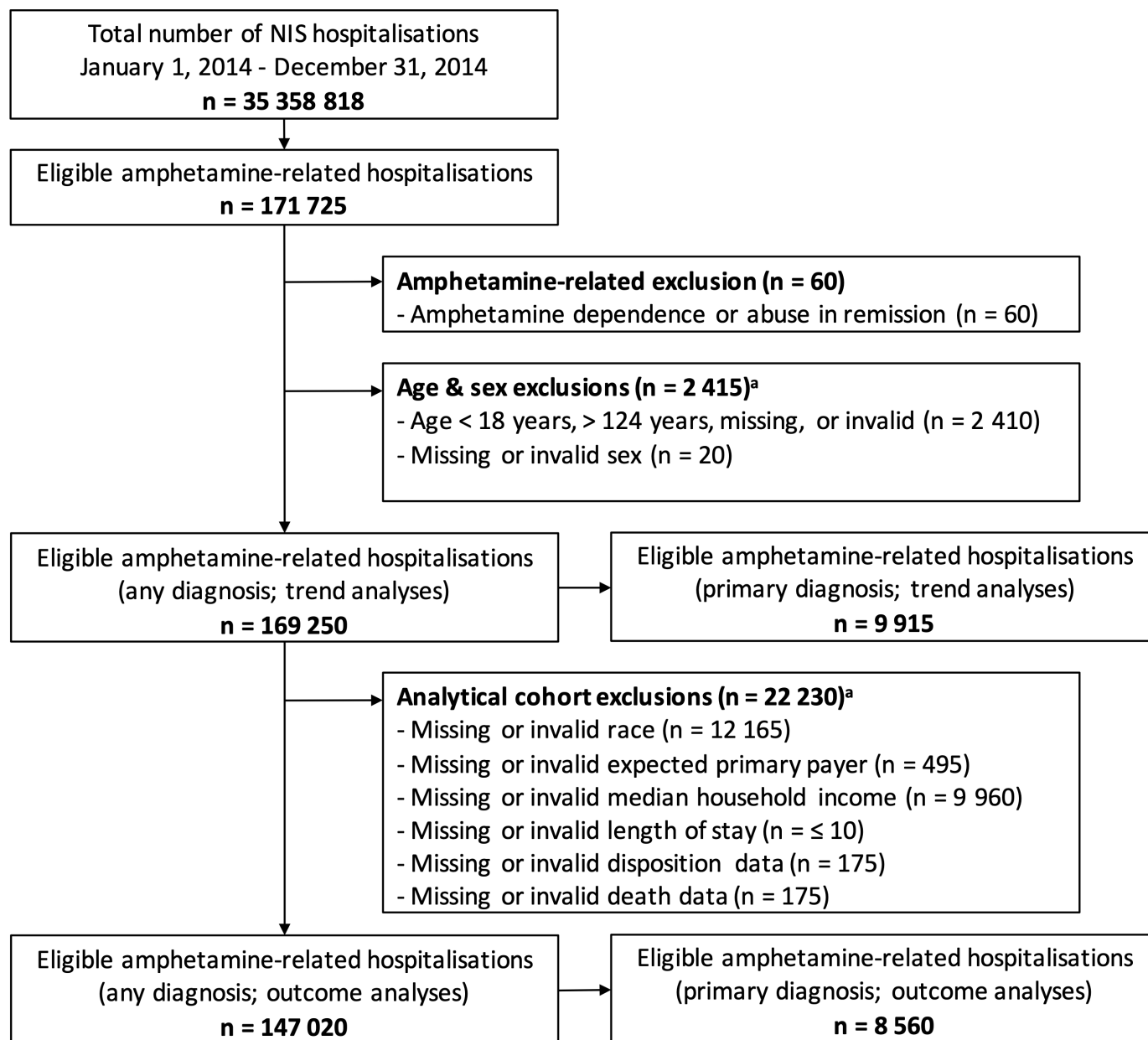


Figure 3 Selection of trend and cohort study samples, 2014. ^aDenotes exclusions that are not mutually exclusive. Individual patients/hospitalisations may be represented within multiple exclusion categories. NIS, national inpatient sample.

race and household income variables. Cohort assembly is described in [figure 3](#) and cohort characteristics are presented in [table 1](#). Most amphetamine-related hospitalisations were among younger (18–44 years; 64.7%), male (60.0%) and white (68.8%) populations, as well as recipients of Medicaid (50.0%) insurance. Over one-third of hospitalisations were by individuals in the lowest income quartile (US\$1–US\$39 999; 36.9%) and the majority resulted in inpatient stays greater than 2 days (63.5%) and routine discharges (76.8%). Hospitalisations most often occurred at private, non-profit hospitals (63.4%) and at urban teaching hospitals (61.4%). Only 3.4% of hospitalisations occurred at Northeastern hospitals, compared with 60.6% at Western hospitals. Similar patterns were observed for hospitalisations with a primary diagnosis related to amphetamine use. However, compared with all

amphetamine-related hospitalisations, a larger proportion of these admissions were by self-payers (25.6%) and resulted in shorter stays (0–2 days; 54.7%). Additionally, a greater proportion of these admissions were to Southern care facilities (38.4%).

Associated with study outcomes

Older age (65+ years relative to 18–44 years; adjusted OR, AOR 2.04, 95% CI 1.15 to 3.61) and self-pay (relative to private insurance; AOR 1.60; 95% CI 1.08 to 2.36) were positively associated with in-hospital mortality, while black race (relative to white; AOR 0.57, 95% CI 0.35 to 0.91) was negatively associated with inpatient death ([table 2](#)). Admission to both urban teaching (relative to rural; AOR 1.83, 95% CI 1.10 to 3.04) and Western (relative to

Table 1 Sociodemographic, clinical and hospital characteristics of amphetamine-related hospitalisations by diagnostic priority, 2014

Characteristic	Any diagnosis, n (%) n=1 47 020	Primary diagnosis, n (%) n=8560
Age		
18–44	95 095 (64.7)	6410 (74.9)
45–64	48 985 (33.3)	1950 (22.8)
65+	2940 (2.0)	200 (2.3)
Sex		
Male	88 145 (60.0)	5615 (65.6)
Female	58 875 (40.0)	2945 (34.4)
Race		
White	101 135 (68.8)	6435 (75.2)
Black	11 955 (8.1)	605 (7.1)
Hispanic	23 430 (15.9)	1085 (12.7)
Asian or Pacific Islander	4525 (3.1)	155 (1.8)
Native American	2725 (1.9)	80 (0.9)
Other	3250 (2.2)	200 (2.3)
Primary payer		
Medicare	21 290 (14.5)	1130 (13.2)
Medicaid	73 455 (50.0)	3080 (36.0)
Private insurance	19 895 (13.5)	1540 (18.0)
Self-pay	24 365 (16.6)	2190 (25.6)
No charge	1360 (0.9)	160 (1.9)
Other	6655 (4.5)	460 (5.4)
Median household income		
First quartile (US\$1–US\$39 999)	54 250 (36.9)	3300 (38.6)
Second quartile (US\$40 000–US\$50 999)	42 405 (28.8)	2325 (27.2)
Third quartile (US\$51 000–US\$65 999)	31 645 (21.5)	1795 (21.0)
Fourth quartile (US\$66 000+)	18 720 (12.7)	1140 (13.3)
Length of stay		
0–2 days	53 730 (36.5)	4685 (54.7)
>2 days	93 290 (63.5)	3875 (45.3)
Discharge disposition		
Routine	112 885 (76.8)	6205 (72.5)
Transfer to short-term Hospital	2885 (2.0)	150 (1.8)
Transfer other*	14 120 (9.6)	1110 (13.0)
Home healthcare	3840 (2.6)	†
Against medical advice	11 105 (7.6)	880 (10.3)
Died	2000 (1.4)	110 (1.3)
Discharge alive, destination unknown	185 (0.1)	†
Total Elixhauser groups per record		
0–2	55 785 (37.9)	3930 (45.9)
3–4	55 725 (37.9)	3285 (38.4)
5–6	25 000 (17.0)	1050 (12.3)
7+	10 510 (7.1)	295 (3.4)
Hospital bedsize‡		

Continued

Table 1 Continued

Characteristic	Any diagnosis, n (%) n=1 47 020	Primary diagnosis, n (%) n=8560
Small	23 880 (16.2)	1515 (17.7)
Medium	33 735 (22.9)	2415 (28.2)
Large	89 405 (60.8)	4630 (54.1)
Hospital ownership/control		
Government, non-federal	30 280 (20.6)	1475 (17.2)
Private, not-profit	93 145 (63.4)	5440 (63.6)
Private, invest-own	23 595 (16.0)	1645 (19.2)
Hospital location/teaching status		
Rural	11 960 (8.1)	985 (11.5)
Urban nonteaching	44 785 (30.5)	2615 (30.5)
Urban teaching	90 275 (61.4)	4960 (57.9)
Hospital region		
Northeast	4930 (3.4)	440 (5.1)
Midwest	16 800 (11.4)	1280 (15.0)
South	36 205 (24.6)	3290 (38.4)
West	89 085 (60.6)	3550 (41.5)

*Includes skilled nursing facility, intermediate care facility and other types of facilities.

†Data suppressed — 10 or fewer observations in some cells.

‡Hospital bedsize describes overall a hospital's size based on its number of short-term acute care beds, location and teaching status. There is no fixed threshold used to denote small, medium and large bedsize hospitals. Additional details on hospital bedsize are available on the HCUP website (www.hcup-us.ahrq.gov).

HCUP, Healthcare Cost and Utilisation Project.

Northeastern; AOR 5.07, 95% CI 1.22 to 21.04) hospitals was associated with increased in-hospital mortality.

Black (relative to White; AOR 0.88, 95% CI 0.79 to 0.98) and native American race (relative to white; AOR 0.82, 95% CI 0.68 to 0.98), self-pay (relative to private insurance; AOR 0.66, 95% CI 0.60 to 0.73) and care at Western (relative to Northeastern; AOR 0.70, 95% CI 0.58 to 0.83) hospitals were negatively associated with lengths of stay greater than 2 days. Conversely, Medicare insurance (relative to private insurance; AOR 1.14, 95% CI 1.02 to 1.27) and admission to urban (urban nonteaching relative to rural; AOR 1.47, 95% CI 1.27 to 1.71) hospitals were associated with longer inpatient stays.

A number of factors were negatively associated with being discharged against medical advice, including but not limited to older age (65+ years relative to 18–44 years; AOR 0.47, 95% CI 0.31 to 0.72), Hispanic race (relative to white; AOR 0.61, 95% CI 0.53 to 0.70) and being admitted to Midwestern (relative to Northeastern; AOR 0.55, 95% CI 0.41 to 0.75) hospitals. On the other hand, factors such as male sex (relative to female; AOR 1.26, 95% CI 1.15 to 1.38), self-pay (relative to private insurance; AOR 2.30, 95% CI 1.90 to 2.79), and admission to private, investor-owned hospitals (relative to government, non-federal; AOR 1.48, 95% CI 1.13 to 1.93) were positively associated with leaving against medical advice.

Subgroup analyses

A total of 8560 hospitalisations in 2014 had a primary diagnosis related to amphetamine use and were included in our subgroup analyses (table 3). The limited overall sample size of our subgroup and relatively few outcome events within examined strata resulted in a high level of imprecision in our reported associations.

DISCUSSION

We analysed nationally representative inpatient datasets from the USA between 2003 and 2014 to examine trends in amphetamine-related hospitalisations and associated outcomes, including in-hospital mortality, prolonged length of stay and leaving against medical advice. Our primary findings were that amphetamine-related hospitalisations increased by more than 150% between 2003 and 2014, and that hospitalisation rates varied according to both age and sex. Additionally, trends in admission for amphetamine-related conditions (primary diagnoses) were similar across examined factors and suggest possible differences in care or coding of amphetamine use by geographical region. Notable secondary findings from our study include: (1) significant associations between both race and insurance status with examined outcomes, (2) significant associations between geographical regions and all examined outcomes, and (3) compared with rural

Table 2 Associations between sociodemographic, clinical and hospital characteristics and study outcomes among amphetamine-related hospitalisations (any diagnostic position)

Characteristic	Died		Length of stay		Discharged against medical advice				
	No, n (%) n=145020	Yes, n (%) n=2000	AOR* (95% CI)	0–2 days, n (%) n=53730	>2 days, n (%) n=93290	AOR* (95% CI)	No, n (%) n=135915	Yes, n (%) n=11 105	AOR* (95% CI)
Age									
18–44	94320 (65.0)	775 (38.8)	Reference	36 325 (67.6)	58 770 (63.0)	Reference	87 595 (64.4)	7500 (67.5)	Reference
45–64	47 850 (33.0)	1135 (56.7)	1.54 (1.21 to 1.96)†	16 620 (30.9)	32 365 (34.7)	0.97 (0.91 to 1.02)	45 500 (33.5)	3485 (31.4)	0.84 (0.75 to 0.93)†
65+	2850 (2.0)	90 (4.5)	2.04 (1.15 to 3.61)‡	785 (1.5)	2155 (2.3)	1.06 (0.86 to 1.29)	2820 (2.1)	120 (1.1)	0.47 (0.31 to 0.72)‡
Sex									
Male	86 790 (59.8)	1355 (67.7)	1.16 (0.93 to 1.44)	32 045 (59.6)	56 100 (60.1)	0.99 (0.94 to 1.04)	81 040 (59.6)	7105 (64.0)	1.26 (1.15 to 1.38)§
Female	58 230 (40.2)	645 (32.2)	Reference	21 685 (40.4)	37 190 (39.9)	Reference	54 875 (40.4)	4000 (36.0)	Reference
Race									
White	99 785 (68.8)	1350 (67.5)	Reference	36 270 (67.5)	64 865 (69.5)	Reference	93 045 (68.5)	8090 (72.9)	Reference
Black	11 845 (8.2)	110 (5.5)	0.57 (0.35 to 0.91)‡	4455 (8.3)	7500 (8.0)	0.88 (0.79 to 0.98)‡	11 065 (8.1)	890 (8.0)	0.86 (0.72 to 1.04)
Hispanic	23 065 (15.9)	365 (18.3)	1.11 (0.83 to 1.48)	8965 (16.7)	14 465 (15.5)	0.95 (0.87 to 1.03)	22 025 (16.2)	1405 (12.7)	0.61 (0.53 to 0.70)§
Asian or Pacific Islander	4435 (3.1)	90 (4.5)	1.16 (0.76 to 1.78)	1725 (3.2)	2800 (3.0)	0.90 (0.76 to 1.06)	4275 (3.1)	250 (2.3)	0.60 (0.43 to 0.83)†
Native American	2690 (1.9)	35 (1.7)	0.89 (0.43 to 1.87)	1100 (2.0)	1625 (1.7)	0.82 (0.68 to 0.98)‡	2490 (1.8)	235 (2.1)	1.08 (0.71 to 1.64)
Other	3200 (2.2)	50 (2.5)	1.29 (0.67 to 2.50)	1215 (2.3)	2035 (2.2)	0.97 (0.81 to 1.16)	3015 (2.2)	235 (2.1)	0.83 (0.56 to 1.22)
Primary payer									
Medicare	20 970 (14.5)	320 (16.0)	0.66 (0.43 to 1.01)	6305 (11.7)	14 985 (16.1)	1.14 (1.02 to 1.27)†	19 760 (14.5)	1530 (13.8)	1.61 (1.31 to 1.98)§
Medicaid	72 445 (50.0)	1010 (50.5)	0.93 (0.64 to 1.35)	26 925 (50.1)	46 530 (49.9)	0.94 (0.86 to 1.03)	67 650 (49.8)	5805 (52.3)	1.63 (1.36 to 1.95)§
Private insurance	19 675 (13.6)	220 (11.0)	Reference	6910 (12.9)	12 985 (13.9)	Reference	18 930 (13.9)	965 (8.7)	Reference

Continued



Table 2 Continued

Characteristic	Died		Length of stay		Discharged against medical advice				
	No, n (%) n=145020	Yes, n (%) n=2000	AOR* (95% CI)	0–2 days, n (%) n=53730	>2 days, n (%) n=93290	AOR* (95% CI)	No, n (%) n=135915	Yes, n (%) n=11105	AOR* (95% CI)
Self-pay	24010 (16.6)	355 (17.8)	1.60 (1.08 to 2.36)†	10880 (20.2)	13485 (14.5)	0.66 (0.60 to 0.73)§	22015 (16.2)	2350 (21.2)	2.30 (1.90 to 2.79)§
No charge	¶	¶	0.95 (0.21 to 4.31)	550 (1.0)	810 (0.9)	0.74 (0.55 to 0.99)†	1265 (0.9)	95 (0.9)	1.71 (1.09 to 2.67)†
Other	¶	¶	1.13 (0.62 to 2.05)	2160 (4.0)	4495 (4.8)	1.17 (0.97 to 1.40)	6295 (4.6)	360 (3.2)	1.15 (0.81 to 1.65)
Median household income									
First quartile (US\$1–US\$39 999)	53545 (36.9)	705 (35.3)	1.10 (0.78 to 1.55)	19600 (36.5)	34650 (37.1)	0.96 (0.86 to 1.07)	50165 (36.9)	4085 (36.8)	1.05 (0.89 to 1.23)
Second quartile (US\$40 000–US\$50 999)	41780 (28.8)	625 (31.2)	1.29 (0.92 to 1.81)	15860 (29.5)	26545 (28.5)	0.91 (0.82 to 1.00)	39045 (28.7)	3360 (30.3)	1.10 (0.93 to 1.29)
Third quartile (US\$51000–US\$65 999)	31195 (21.5)	450 (22.5)	1.14 (0.80 to 1.63)	11700 (21.8)	19945 (21.4)	0.92 (0.84 to 1.01)	29375 (21.6)	2270 (20.4)	0.96 (0.82 to 1.12)
Fourth quartile (US\$66 000+)	18500 (12.8)	220 (11.0)	Reference	6570 (12.2)	12150 (13.0)	Reference	17330 (12.8)	1390 (12.5)	Reference
Total elixhauser groups per record									
0–2	55600 (38.3)	185 (9.2)	Reference	24070 (44.8)	31715 (34.0)	Reference	51240 (37.7)	4545 (40.9)	Reference
3–4	55140 (38.0)	585 (29.3)	3.03 (2.07 to 4.43)§	19625 (36.5)	36100 (38.7)	1.37 (1.30 to 1.46)§	51640 (38.0)	4085 (36.8)	0.91 (0.82 to 1.02)
5–6	24340 (16.8)	660 (33.0)	7.13 (4.71 to 10.79)§	7660 (14.3)	17340 (18.6)	1.68 (1.56 to 1.82)§	23180 (17.1)	1820 (16.4)	0.92 (0.79 to 1.06)
7+	9940 (6.9)	570 (28.5)	14.29 (9.08 to 22.48)§	2375 (4.4)	8135 (8.7)	2.56 (2.28 to 2.88)§	9855 (7.3)	655 (5.9)	0.78 (0.62 to 0.97)†
Hospital bedsize**									
Small	23620 (16.3)	260 (13.0)	Reference	9545 (17.8)	14335 (15.4)	Reference	21980 (16.2)	1900 (17.1)	Reference
Medium	33305 (23.0)	430 (21.5)	1.25 (0.86 to 1.81)	13045 (24.3)	20690 (22.2)	1.04 (0.92 to 1.19)	31005 (22.8)	2730 (24.6)	0.96 (0.80 to 1.16)
Large	88095 (60.7)	1310 (65.5)	1.37 (0.99 to 1.88)	31140 (58.0)	58265 (62.5)	1.29 (1.15 to 1.44)§	82930 (61.0)	6475 (58.3)	0.87 (0.73 to 1.03)
Hospital ownership/control									
Government, nonfederal	29900 (20.6)	380 (19.0)	Reference	11125 (20.7)	19155 (20.5)	Reference	28445 (20.9)	1835 (16.5)	Reference

Continued

Table 2 Continued

Characteristic	Died		Length of stay		Discharged against medical advice				
	No, n (%) n=145020	Yes, n (%) n=2000	AOR* (95% CI)	0–2 days, n (%) n=53730	>2 days, n (%) n=93290	AOR* (95% CI)	No, n (%) n=135915	Yes, n (%) n=11105	AOR* (95% CI)
Private, not-profit	91835 (63.3)	1310 (65.5)	1.12 (0.84 to 1.49)	33765 (62.8)	59380 (63.7)	0.97 (0.87 to 1.07)	85970 (63.3)	7175 (64.6)	1.29 (1.04 to 1.60)†
Private, invest-own	23285 (16.1)	310 (15.5)	1.26 (0.83 to 1.89)	8840 (16.5)	14755 (15.8)	0.96 (0.82 to 1.13)	21500 (15.8)	2095 (18.9)	1.48 (1.13 to 1.93)‡
Hospital location/teaching status									
Rural	11875 (8.2)	85 (4.2)	Reference	5165 (9.6)	6795 (7.3)	Reference	11080 (8.2)	880 (7.9)	Reference
Urban nonteaching	44285 (30.5)	500 (25.0)	1.21 (0.71 to 2.09)	16025 (29.8)	28760 (30.8)	1.47 (1.27 to 1.71)§	40880 (30.1)	3905 (35.2)	1.05 (0.81 to 1.36)
Urban teaching	88860 (61.3)	1415 (70.8)	1.83 (1.10 to 3.04)†	32540 (60.6)	57735 (61.9)	1.42 (1.25 to 1.63)§	83955 (61.8)	6320 (56.9)	0.90 (0.70 to 1.14)
Hospital region									
Northeast	†	†	Reference	1590 (3.0)	3340 (3.6)	Reference	4520 (3.3)	410 (3.7)	Reference
Midwest	†	†	3.40 (0.78 to 14.82)	5945 (11.1)	10855 (11.6)	0.87 (0.72 to 1.06)	15865 (11.7)	935 (8.4)	0.55 (0.41 to 0.75)†
South	35825 (24.7)	380 (19.0)	3.87 (0.92 to 16.26)	13155 (24.5)	23050 (24.7)	0.87 (0.73 to 1.05)	33855 (24.9)	2350 (21.2)	0.66 (0.50 to 0.87)†
West	87625 (60.4)	1460 (73.0)	5.07 (1.22 to 21.04)‡	33040 (61.5)	56045 (60.1)	0.70 (0.58 to 0.83)§	81675 (60.1)	7410 (66.7)	1.07 (0.82 to 1.40)

*Adjusted for all factors listed in table.

†p<0.01.

‡p<0.05.

§p<0.001.

¶Data suppressed — 10 or fewer observations in some cells.

**Hospital bedsize describes overall a hospital's size based on its number of short-term acute care beds, location and teaching status. There is no fixed threshold used to denote small, medium and large bedsize hospitals. Additional details on hospital bedsize are available on the HCUP website (www.hcup-us.ahrq.gov).

AOR, adjusted OR; HCUP, Healthcare Cost and Utilisation Project.



Table 3 Associations between sociodemographic, clinical and hospital characteristics and study outcomes among amphetamine-related hospitalisations (primary diagnostic position)

Characteristic	Died		Length of stay		Discharged against medical advice				
	No (%), n=8450	Yes (%), n=110	AOR* (95% CI)	0–2 days, n=4685	>2 days, n=3875	AOR* (95% CI)	No, n=7680	Yes, n=880	AOR* (95% CI)
Age									
18–44	6330 (74.9)	80 (72.7)	Reference	3715 (79.3)	2695 (69.5)	Reference	5740 (74.7)	670 (76.1)	Reference
45+	2120 (25.1)	30 (27.3)	0.50 (0.17 to 1.47)	970 (20.7)	1180 (30.5)	1.26 (0.99 to 1.62)	1940 (25.3)	210 (23.9)	1.09 (0.72 to 1.64)
Sex									
Male	5555 (65.7)	60 (54.5)	0.63 (0.25 to 1.58)	3135 (66.9)	2480 (64.0)	0.91 (0.73 to 1.14)	4930 (64.2)	685 (77.8)	2.05 (1.41 to 2.97)
Female	2895 (34.3)	50 (45.5)	Reference	1550 (33.1)	1395 (36.0)	Reference	2750 (35.8)	195 (22.2)	Reference
Race									
White	6345 (75.1)	90 (81.8)	Reference	3555 (75.9)	2880 (74.3)	Reference	5750 (74.9)	685 (77.8)	Reference
Black	†	†	0.47 (0.06 to 3.57)	295 (6.3)	310 (8.0)	1.37 (0.91 to 2.06)	530 (6.9)	75 (8.5)	1.15 (0.60 to 2.22)
Other†	†	†	0.45 (0.09 to 2.28)	835 (17.8)	685 (17.7)	1.09 (0.82 to 1.44)	1400 (18.2)	120 (13.6)	0.64 (0.38 to 1.06)
Primary payer									
Medicare	1115 (13.2)	15 (13.6)	0.90 (0.19 to 4.30)	465 (9.9)	665 (17.2)	1.40 (0.96 to 2.03)	1015 (13.2)	115 (13.1)	1.41 (0.72 to 2.75)
Medicaid	3030 (35.9)	50 (45.5)	1.04 (0.31 to 3.51)	1635 (34.9)	1445 (37.3)	1.01 (0.75 to 1.34)	2800 (36.5)	280 (31.8)	1.13 (0.66 to 1.93)
Private insurance	1520 (18.0)	20 (18.2)	Reference	835 (17.8)	705 (18.2)	Reference	1415 (18.4)	125 (14.2)	Reference
Self-pay	†	†	1.23 (0.30 to 5.05)	1395 (29.8)	795 (20.5)	0.66 (0.48 to 0.91)§	1885 (24.5)	305 (34.7)	2.17 (1.27 to 3.70)¶
Other	†	†	1.16 (0.16 to 8.59)	355 (7.6)	265 (6.8)	0.93 (0.57 to 1.50)	565 (7.4)	55 (6.3)	1.19 (0.53 to 2.66)
Median household income									
First quartile (US\$1–US\$39 999)	3265 (38.6)	35 (31.8)	1.01 (0.23 to 4.46)	1735 (37.0)	1565 (40.4)	0.92 (0.66 to 1.28)	2965 (38.6)	335 (38.1)	0.76 (0.46 to 1.27)
Second quartile (US\$40 000–US\$50 999)	2295 (27.2)	30 (27.3)	1.31 (0.30 to 5.65)	1355 (28.9)	970 (25.0)	0.75 (0.53 to 1.06)	2070 (27.0)	255 (29.0)	0.80 (0.46 to 1.38)
Third quartile (US\$51 000–US\$65 999)	1765 (20.9)	30 (27.3)	1.44 (0.34 to 6.12)	1000 (21.3)	795 (20.5)	0.87 (0.61 to 1.23)	1650 (21.5)	145 (16.5)	0.56 (0.32 to 0.99)¶
Fourth quartile (US\$66 000+)	1125 (13.3)	15 (13.6)	Reference	595 (12.7)	545 (14.1)	Reference	995 (13.0)	145 (16.5)	Reference
Total elixhauser groups per record									
0–2	3915 (46.3)	15 (13.6)	Reference	2450 (52.3)	1480 (38.2)	Reference	3465 (45.1)	465 (52.8)	Reference
3–4	3245 (38.4)	40 (36.4)	3.12 (0.89 to 10.87)	1715 (36.6)	1570 (40.5)	1.42 (1.14 to 1.78)¶	2975 (38.7)	310 (35.2)	0.78 (0.55 to 1.11)
5–6	1010 (12.0)	40 (36.4)	10.30 (2.08 to 50.98)¶	410 (8.8)	640 (16.5)	2.20 (1.59 to 3.05)**	960 (12.5)	90 (10.2)	0.71 (0.40 to 1.26)

Continued

Table 3 Continued

Characteristic	Died		Length of stay			Discharged against medical advice			
	No (%), n n=8450	Yes (%), n n=110	AOR* (95% CI)	0–2 days, n (%) n=4685	>2 days, n (%) n=3875	AOR* (95% CI)	No, n (%) n=7680	Yes, n (%) n=880	AOR* (95% CI)
7+	280 (3.3)	15 (13.6)	15.74 (2.02 to 122.47) ^{††}	110 (2.3)	185 (4.8)	2.24 (1.23 to 4.07) ^{††}	280 (3.6)	15 (1.7)	0.34 (0.10 to 1.11)
Hospital bedsize ^{††}									
Small	1490 (17.6)	25 (22.7)	Reference	865 (18.5)	650 (16.8)	Reference	1320 (17.2)	195 (22.2)	Reference
Medium	2390 (28.3)	25 (22.7)	0.65 (0.19 to 2.14)	1445 (30.8)	970 (25.0)	0.85 (0.61 to 1.17)	2145 (27.9)	270 (30.7)	0.86 (0.54 to 1.38)
Large	4570 (54.1)	60 (54.5)	0.72 (0.25 to 2.09)	2375 (50.7)	2255 (58.2)	1.24 (0.94 to 1.64)	4215 (54.9)	415 (47.2)	0.63 (0.42 to 0.95) [§]
Hospital ownership/ control									
Government, non-federal	1455 (17.2)	20 (18.2)	Reference	805 (17.2)	670 (17.3)	Reference	1395 (18.2)	80 (9.1)	Reference
Private, not-profit	5365 (63.5)	75 (68.2)	0.92 (0.32 to 2.64)	2945 (62.9)	2495 (64.4)	0.95 (0.71 to 1.28)	4810 (62.6)	630 (71.6)	2.71 (1.43 to 5.14) [¶]
Private, invest-own	1630 (19.3)	15 (13.6)	0.97 (0.25 to 3.82)	935 (20.0)	710 (18.3)	0.94 (0.65 to 1.35)	1475 (19.2)	170 (19.3)	2.08 (1.01 to 4.30) [§]
Hospital location/ teaching status									
Rural	†	†	Reference	605 (12.9)	380 (9.8)	Reference	855 (11.1)	130 (14.8)	Reference
Urban nonteaching	†	†	0.48 (0.05 to 4.98)	1440 (30.7)	1175 (30.3)	1.47 (0.98 to 2.20)	2335 (30.4)	280 (31.8)	0.56 (0.32 to 0.96) [§]
Urban teaching	4865 (57.6)	95 (86.4)	2.54 (0.36 to 18.06)	2640 (56.4)	2320 (59.9)	1.44 (0.99 to 2.09)	4490 (58.5)	470 (53.4)	0.53 (0.31 to 0.89) [§]
Hospital region									
Northeast and Midwest	1705 (20.2)	15 (13.6)	Reference	980 (20.9)	740 (19.1)	Reference	1540 (20.1)	180 (20.5)	Reference
South	3270 (38.7)	20 (18.2)	0.64 (0.15 to 2.78)	1800 (38.4)	1490 (38.5)	1.22 (0.92 to 1.63)	2975 (38.7)	315 (35.8)	0.85 (0.52 to 1.38)
West	3475 (41.1)	75 (68.2)	2.29 (0.58 to 9.01)	1905 (40.7)	1645 (42.5)	0.92 (0.68 to 1.26)	3165 (41.2)	385 (43.7)	1.43 (0.89 to 2.30)

*Adjusted for all factors listed in table.

[†]Data suppressed - 10 or fewer observations in some cells.

[‡]Includes Hispanic, Asian or Pacific Islander, Native American, and other races.

[§]p<0.05.

[¶]p<0.01.

^{**}p<0.001.

^{††}Hospital bedsize describes overall a hospital's size based on its number of short-term acute care beds, location and teaching status. There is no fixed threshold used to denote small, medium and large bedsize hospitals. Additional details on hospital bedsize are available on the HCUP website (www.hcup-us.ahrq.gov).

AOR, adjusted OR; HCUP, Healthcare Cost and Utilisation Project.

settings, positive associations between urban settings and the likelihood of in-hospital mortality and longer inpatients stays.

We observed that the amphetamine-related hospitalisation rate more than doubled over our study period, which coincides with reports of large population-based studies.^{2 16} Winkelman *et al*² found that the number of hospitalisations increased by 245% between 2008 and 2015, and Miller *et al*¹⁶ found a similar increase in the use of psychiatric emergency services between 2011 and 2015. Our study builds on prior findings by being the first to offer insight into national hospitalisation rates in the USA by age and sex. We found that younger adults (18–44 years) consistently had the highest amphetamine-related hospitalisation rate. Similarly, males experienced higher hospitalisation rates compared with females. Observed increases in amphetamine hospitalisations may be due to numerous factors. These include increases in the prevalence of methamphetamine use disorders¹ and polysubstance use (such as methamphetamine combined with alcohol, cannabis or opioids) throughout our study period.^{2 17} Decreasing methamphetamine price and increasing availability may have also contributed to our observed trends.¹⁸ Reports by the Drug Enforcement Agency highlight a supply of methamphetamine within the USA that is consistently high in purity and potency, with increasingly large amounts seized along the south-western border.^{19 20} We observed variability in the proportion of hospitalisations with an amphetamine-related primary diagnosis; however, annual rates remained within a narrow range (2%–8% of all amphetamine-related hospitalisations). Minor differences in observed primary diagnosis trends may reflect regional and hospital-specific variations in medical coding practices and not necessarily differences in patient care.

Our results support that it may be most advantageous to identify subpopulations that may experience poor health outcomes (such as in-hospital mortality, prolonged length of stay and discharge against medical advice) by examining amphetamine use and hospitalisations by age, sex, race and primary expected payer. Compared with younger populations (18–44 years), older age (65+ years) was associated with an increased likelihood of in-hospital mortality, but decreased likelihood of leaving against medical advice, whereas males were associated with leaving the hospital against medical advice. Observed differences in all examined outcomes by race and payer status may be, in part, reflections of differences in health-seeking behaviours and/or education between specific groups within these categories or downstream effects of structural racism and other barriers to care.^{21 22} For instance, black American men utilise fewer health services than other populations and often delay seeking care despite unmet healthcare needs; participants reported being fearful of seeking healthcare, having had negative interactions with physicians and having distrust in medical professionals.²³

In addition to observed relationships between examined sociodemographic factors and study outcomes, we

noted significant variations in outcomes of amphetamine-related hospitalisations by region. For example, relative to individuals admitted to Northeastern hospitals, patients admitted to Western hospitals were more likely to die in-hospital, even after adjusting for a number of factors presumed to bias modelled associations. Similarly, individuals hospitalised in the West experienced shorter lengths of stay. Our regional in-hospital mortality findings may be supported by analyses of overdose deaths in the USA using 2017 National Vital Statistics-Mortality data, which found that methamphetamine was the drug most frequently involved in overdose deaths in the Western USA.²⁴ Observed variations in mortality and length of stay in our study may therefore reflect regional differences in a number of factors, including but not limited to public health interventions; amphetamine availability, purity and potency; and patterns of polysubstance use.^{25 26} Alternatively, it is possible that our analyses do not account for all regional, sociodemographic, behavioural and/or environmental factors that may bias examined relationships. As such, future studies are necessary to elucidate the aforementioned pathways leading to these adverse outcomes.

We found that study outcomes differed between rural and urban hospitals, with the majority of patients being admitted to urban teaching hospitals. This coincides with other USA studies, where prolonged hospitalisations were increasingly observed at urban teaching centres.²⁷ We also observed an increased association between admission to urban hospitals and in-hospital mortality, as well as longer hospitalisations in urban settings. Our findings may be explained by time-consuming rural–urban transfers for specialty care, which may increase the likelihood of poorer health outcomes and contribute to longer hospital stays,^{28 29} as well as urban/rural differences in capacity to effectively treat substance use disorders.³⁰ Increased public health funding is required to support equitable access to healthcare for all populations and to mitigate amphetamine-related strain on existing health systems. Investment in broad upstream interventions (such as education) and/or harm reduction services may help to prevent avoidable downstream outcomes. Future research based on our findings will help to identify specific interventions that could be effective in reducing amphetamine-related hospitalisations.

Our study has a number of strengths. Data analysed originate from nationally representative datasets, which permitted us to compute precise estimates of amphetamine-related hospitalisation rates across the USA for more than ten years. Furthermore, datasets used include in-depth socioeconomic, clinical and hospital data that permitted us to stratify our findings by age, sex and hospital location, as well as take factors, such as race, insurance status, comorbidities and hospital size, presumed to bias modelled associations into account in our regression analyses. Selection of populations for inclusion in our cross-sectional analyses was based on previously reported ICD-9-CM

case definitions for amphetamine dependence, abuse and poisoning.² To our knowledge, our study is the first to highlight notable age and sex differences in amphetamine-related hospitalisations at a national level in the USA. Together, our reported findings are generalisable to the majority of USA adult populations, including rural populations and recipients of public health insurance. It, therefore, provides necessary benchmark data on amphetamine-related hospitalisations that may be used to assess the effectiveness of implemented health interventions.

Important limitations should be considered when interpreting our results. Amphetamine-related hospitalisations are presumed to be attributed to use of methamphetamine and other non-prescription amphetamines or psychostimulants; however, ICD-9-CM diagnostic codes do not permit documented use of illicit substances from being distinguished from use of prescribed and non-prescribed amphetamines. There is also no specific ICD-9-CM code for amphetamine-related withdrawal; though we suspect that available amphetamine dependence and/or abuse diagnostic codes may have been recorded for individuals admitted to hospital with amphetamine-related withdrawal symptoms. As a result, some individuals within our analyses may be patients with attention-deficit/hyperactivity disorder and/or narcolepsy who are prescribed amphetamines and subsequently hospitalised for adverse drug events. Our study may also omit hospitalisations solely related to amphetamine withdrawal. Furthermore, we are unable to ascertain whether individuals were hospitalised due to unintentional use of stimulants (such as from a contaminated drug supply). Due to the federally mandated adoption of ICD-10 in 2015, newer diagnostic categorisation schemes for illicit substance use, abuse and poisoning are not directly comparable to established methods of classifying substance use via ICD-9-CM codes. Therefore, we were unable to compute amphetamine-related trends for years 2015 onwards. Notwithstanding, the dramatic increase in amphetamine-related hospitalisation rates between 2003 and 2014, combined with anecdotal reports and findings from smaller studies, identify amphetamine use and care as an urgent population health priority.^{31–33} Although we employed the use of design and analytical approaches to minimise bias within our reported estimates of association, it is possible that residual bias exists. Specifically, due to study-specific exclusion criteria, reported values for our analytical cohort may underestimate the true number of amphetamine-related hospitalisations and examined outcome events. Moreover, our inability to adjust for behavioural factors, including health seeking behaviours and patterns of substance use, which could include polysubstance use, may bias our reported estimates. Finally, due to the exploratory nature of our study, we did not statistically account for multiple comparisons. Despite these limitations, our study

meaningfully adds to the limited data on amphetamine inpatient care and associated outcomes.

CONCLUSIONS

Overall, our study demonstrates that amphetamine-related hospitalisations have increased steadily between 2003 and 2014. Findings from our study also highlight notable differences in amphetamine-related hospitalisations by age and sex, and that select factors, including patient insurance status and hospital location, may serve as important variables in future risk-based algorithms to predict outcomes among patients admitted for amphetamine-related reasons.

Future research on amphetamine use and associated health outcomes is essential, especially among younger populations, by geographical region and from 2015 onwards using ICD-10-CM coding. Subsequent studies should also examine health outcomes among hospitalised patients diagnosed with amphetamine-related conditions who experience shorter lengths of stay, are discharged against medical advice and/or experience frequent readmission.

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Contributors JJC accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. All authors provided study design input. JAGC performed all data analyses and DPT provided guidance on statistical analyses. LJWL, JAGC, PB, DRA, AWW and JJC led the interpretation of results. LJWL and JAGC drafted the final manuscript. All authors contributed to manuscript revisions and approve the final manuscript.

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Patient consent for publication Not applicable.

Ethics approval This study was approved by the Behavioural Research Ethics Board at the University of British Columbia, Vancouver, British Columbia, Canada (H19-03040). Informed consent was not required from individuals included in this study, as all health records were anonymised and deidentified prior to our analyses.

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Data availability statement Data are available on reasonable request. Datasets analysed for this study are available from the HCUP (<https://www.hcup-us.ahrq.gov>).

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