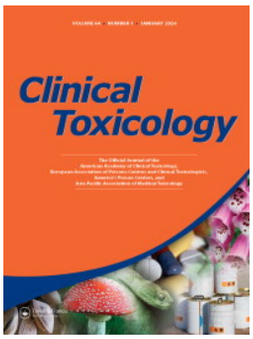

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POISON CENTRE RESEARCH

Gabapentin exposures in those aged 50 years and older reported to United States poison centers: reasons for exposure and medical outcomes

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ABSTRACT

Introduction: As off-label use of gabapentin has increased, safety concerns and misuse problems have emerged. Using United States poison center data on gabapentin-involved exposures in those aged 50 years and older, we examined correlates of reasons for exposure and medical outcomes.

Methods: Data were obtained from the United States National Poison Data System® from 2017 to 2024. Descriptive statistics and multinomial logistic regression models were used.

Results: Of 59,341 exposures, 30% involved gabapentin only, and the remainder involved gabapentin with a median of 2.0 other substances. In the gabapentin-only group, 60%, 12%, and 28% were unintentional exposures, intentional misuses, and suicide attempts, respectively; corresponding percentages in the multi-substance group were 40%, 8%, and 46%. Adults older than 50–59 years and females had a lower likelihood of intentional misuse and suicide attempt. Regarding medical outcomes, 81% of gabapentin-only and 56% of multi-substance exposures resulted in no/minor effects. Alcohol and psychotropic drugs were associated with a higher likelihood of intentional misuse and suicide attempt. A greater number of other substances was associated with a higher likelihood of moderate effects (relative risk ratio: 1.15; 95% CI: 1.12–1.18), major effects/death (relative risk ratio: 1.23; 95% CI: 1.20–1.26), and potentially toxic effects (relative risk ratio: 1.08; 95% CI: 1.01–1.15). Cardiovascular and psychotropic drugs were associated with a greater risk of serious outcomes.

Discussion: While gabapentin exposures in older adults in the United States commonly occur due to therapeutic errors, suicide attempts comprise nearly half of multi-substance cases. Polydrug use, particularly with psychotropic medications, contributes to more serious outcomes, underscoring the need for cautious prescribing and routine suicide risk assessment in older adults co-using gabapentin with these drugs.

Conclusion: Gabapentin exposures in older adults reported to United States poison centers most often result from unintentional therapeutic errors, though intentional exposures, including suspected suicide attempts, were also frequent, especially in multi-substance exposures.

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Drugs for cardiovascular disease; gabapentin; medical outcomes; older adults; psychotropics; suicide attempt

Introduction

Gabapentin is an anticonvulsant approved for treating neuralgia and frequently prescribed for off-label conditions such as fibromyalgia, neuropathic and various chronic pain, migraine, insomnia, aggression associated with dementia, anxiety disorder, diabetes, and alcohol and opioid withdrawal symptoms [1–7]. While opioid prescribing in the United States (US) has declined in response to the prescription opioid crisis over the past decade, gabapentin prescribing has risen steadily, placing it among the ten most commonly prescribed medications [8]. Use is especially common among older adults. The 2019–2021 Medical Expenditure Panel Survey [4] showed a prevalence of ~5% among those aged 50 years and ~9% among those aged more than 70 years.

Despite its therapeutic value, the increasing use of gabapentin has raised safety concerns. Side effects include blurred vision, drowsiness, impaired coordination, respiratory failure, myopathy, and hypoventilation, with heightened risks when combined with central nervous system depressants such as antipsychotics, benzodiazepines, anxiolytics, and opioids [9–12]. Gabapentin has been associated with psychiatric adverse events, including depression, anxiety, and suicidal ideation [13,14]. Gabapentin has also been misused to potentiate opioids, particularly among

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individuals with psychiatric or substance use disorders [15–17] and implicated in overdose deaths involving prescription and illicit opioids [15,18,19]. Increasing gabapentin use and associated problems have led several US states to implement gabapentin-specific policies in response to non-medical use, and a study found non-medical gabapentin use in those states to be significantly associated with recent pain, substance use treatment, and receipt of medication for opioid use disorder [20]. Research has also shown that gabapentin was associated with higher risks for falls or fractures, especially when concurrently used with opioids [21,22].

Older adults may be particularly vulnerable to these risks given their higher rates of comorbidities and polypharmacy. Gabapentin use has been linked to delirium, especially with high comorbidity, neurocognitive decline in those initially cognitively intact, and an increased fall risk among those with cognitive impairment or concurrent opioid use [23–26]. A Medicare cohort study further showed that concurrent high-dose gabapentin and opioid use was associated with higher all-cause mortality than high-dose opioids combined with duloxetine [27]. Concomitant prescription of opioids and/or benzodiazepines and gabapentin among US dialysis patients and kidney transplant patients was also associated with increased mortality and/or hospitalization [28,29].

Although these previous studies indicate polydrug use and associated problems among gabapentin users, important gaps remain in distinguishing therapeutic errors or drug reactions from intentional misuse or suicide attempt, as well as in understanding the role of co-involved substances in adverse outcomes among older gabapentin users. In the present study, we used the US National Poison Data System® (NPDS®) data on gabapentin-involved exposures occurring in those aged 50 years and older to examine the following:

1. Differences in demographic factors, exposure reasons (unintentional therapeutic errors or drug reactions, intentional misuse or abuse, and suicide attempts), level of care, and medical outcomes between the cases where gabapentin was the only substance involved (gabapentin-only exposures) and the cases where gabapentin was used with other substances (multi-substance cases);
2. Correlates of exposure reasons in these two groups of cases, including specific substances in the multi-substance group; and
3. Among intentional misuse and suicide attempts, the associations of medical outcomes (no/minor effect, moderate effect, major effect/death, and potentially toxic effect) with demographics, exposure reasons, and other substances involved.

Methods

Study design and setting

This observational study analyzed 8 years (January 1, 2017–December 31, 2024) of pooled NPDS® data from 55 US poison centers covering all 50 states, the District of Columbia, and Puerto Rico. The case volume across years was sufficient for subgroup analyses. Although reporting to poison centers is voluntary and not all exposures are captured, the NPDS® remains the most comprehensive source in the US for examining these research questions, encompassing human exposures to viral, bacterial, chemical, and drug agents. Detailed descriptions of the NPDS® are available on its website (https://poisoncenters.org/national-poison-data-system) and in Gummin et al. [30]. In accordance with the authors' institutional review board guidelines, this analysis of de-identified data was exempt from review.

Participants

We identified closed exposures aged 50 years and older involving gabapentin with or without concomitant exposure to other substances. The NPDS® lists all concomitantly used substances reported in each case using a sequence number. While the primary and secondary substances in the sequence of all involved substances tend to reflect the primary and secondary culprits, the sequence does not always reflect the order of importance. Although NPDS® lists cases, not individuals, the extent to which these cases include duplicate individuals is minimal, as poison center specialists are trained to detect duplication and correct it as soon as it is discovered.

Measures

Gabapentin-only group versus multi-substance group

The gabapentin-only group refers to exposures reported to involve no other substance than gabapentin, and the multi-substance group refers to the exposures that involved gabapentin and at least one other substance.

Exposure reasons

We used the following four categories: unintentional exposures, including primarily therapeutic errors and

misuses and adverse reactions; intentional misuses or abuses; suspected suicide attempts; and unknown exposure reasons. See Gummin et al. [30] for a detailed description/scenario of each exposure reason.

Medical outcomes

The NPDS® uses the following categories for human exposures: no effect, minor effect, moderate effect, major effect, directly reported death, indirectly reported death (that poison centers acquired information from medical examiners or media or state vital statistics but did not manage), and three expected outcomes for the cases that were not followed (judged to be nontoxic, minimally toxic, or potentially toxic).

In this study, we used the following four categories: (1) no or minor effect or judged to be nontoxic or minimally toxic (no/minor effects hereafter); (2) moderate effects; (3) major effect or death, directly or indirectly reported (major effects/death hereafter); and (4) judged to be potentially toxic (potentially toxic effects hereafter). While moderate effect refers to "signs or symptoms that were not life-threatening or had no residual disability or disfigurement," major effect refers to "signs or symptoms that were life-threatening or resulted in significant residual disability or disfigurement" [30]. A majority of cases of indirectly reported death (i.e., 104 out of 116) were from Arizona, as Arizona reports cases from its vital statistics [31]. The "potentially toxic" effects were retained as a separate category, based on preliminary analysis showing that cases in this category were similar to those with moderate or major effects when intentional misuse or abuse was the exposure reason, but similar to those with no/minor effects when suspected suicide attempts were the exposure reason.

Co-ingested substances

Among gabapentin-involved exposures classified as multi-substance exposures, our preliminary analysis identified the 11 most frequently co-ingested substances reported, in addition to the total number of other substances per case: alcohol; antidepressants (32 codes); antihistamines (12 codes); antipsychotics or anxiolytics other than benzodiazepines (7 codes); benzodiazepines; drugs for cardiovascular diseases (32 codes); hypoglycemics (10 codes); muscle relaxants (8 codes); non-steroidal anti-inflammatory drugs (18 codes); prescription opioids (32 codes); and other analgesics (17 codes).

Other covariates

These were year of exposure (2017–2018 [reference], 2019–2020, 2021–2022, and 2023–2024), age group (50–59 years [reference], 60–69 years, 70–79 years, and ≥80 years), sex (female versus male), and the census region of residence (Northeast [reference], Midwest, South, West, and Puerto Rico/other/unknown). We reported exposure and call sites, chronicity of event, and the level of care for descriptive purposes only.

Analysis

All analyses were conducted with Stata 19.5/MP (Stata Corp, College Station, TX). For descriptive analysis, we used Pearson's χ^2 and Cramer's V tests to compare demographic and exposure-related characteristics: (1) between the gabapentin-only and multi-substance groups; and (2) by exposure reason within the gabapentin group and the multi-substance group. Given the large sample size, Cramer's V test supplemented χ^2 tests to capture the practical importance of group differences, using the conventional cut-offs (very small or trivial effect: <0.1; small effect: 0.1–0.3; medium effect: 0.3–0.5; and large effect: >0.5 [32]).

Next, we fitted multinomial logistic regression models to examine the correlates of exposure reasons (intentional misuses or abuses and suspected suicide attempts versus unintentional exposures) in the gabapentin-only and multi-substance groups. In the multi-substance group, we examined both demographic factors and other substances. Finally, we focused on all cases (i.e., both gabapentin-only and multi-substance cases) where the exposure reasons were intentional misuse or suspected suicide attempts and fitted a multinomial logistic regression model to examine the correlates of medical outcomes, including other substances. We focused on these two exposure reasons as the majority of unintentional exposures had no/minor effects. The variance inflation factor, using a cut-off of 2.50 [33] from linear regression models, indicated no concerning multicollinearity among covariates. Multinomial logistic regression results are reported as relative risk ratios with 95% confidence intervals (95%CI).

Results

Of 61,540 gabapentin-involved exposures aged 50 and older reported to NPDS® from 2017 to 2024, 79 were confirmed non-exposure, and 2,120 were judged "probably not responsible for the effect(s)" per NPDS® exposure-reason codes. After these exclusions, 59,341 comprised the final analytic sample. Annual case counts increased from 6,736 in 2017 to 8,164 in 2024. Poisson regression indicated a significant upward linear trend (incidence rate ratio: 1.02; 95% CI: 1.02–1.03;

$P < 0.001$), corresponding to an average annual increase of approximately 2%.

Gabapentin-only versus multi-substance exposures

As shown in Table 1, 30.1% of cases involved gabapentin only, and 69.9% involved gabapentin with 1–37 additional substances. Additional analysis revealed that within the multi-substance group, gabapentin was identified as the primary, secondary, and tertiary substance in 28.0%, 31.8%, and 18.1% of cases, respectively.

Unintentional exposures accounted for approximately 60% of gabapentin-only and 40% of multi-substance cases; intentional misuses or abuses for

Table 1. Characteristics of gabapentin exposures.

	Gabapentin only exposures $n = 17,848$	Multi-substance exposures $n = 41,493$	P	Cramer's V
Year			0.381	0.007
2017–2018, *n* (%)	4,243 (23.8)	9,638 (23.2)		
2019–2020, *n* (%)	4,482 (25.1)	10,341 (24.9)		
2021–2022, *n* (%)	4,381 (24.5)	10,326 (24.9)		
2023–2024, *n* (%)	4,742 (26.6)	11,188 (27.0)		
Age group (years)			<0.001	0.068
50–59, *n* (%)	7,030 (39.4)	19,043 (45.9)		
60–69, *n* (%)	5,400 (30.3)	12,083 (29.1)		
70–79, *n* (%)	3,430 (19.2)	6,315 (15.2)		
80-89, *n* (%)	1,665 (9.3)	3,229 (8.0)		
≥90, *n* (%)	321 (1.8)	753 (1.8)		
Sex			<0.001	0.020
Male, *n* (%)	6,397 (35.8)	15,708 (37.9)		
Female, *n* (%)	11,443 (64.1)	25,758 (62.1)		
Unknown, *n* (%)	8	27		
US Census region			<0.001	0.043
Northeast, *n* (%)	2,647 (14.7)	6,036 (14.5)		
Midwest, *n* (%)	3,692 (20.7)	10.050 (24.2)		
South, *n* (%)	6,852 (38.4)	15,663 (37.7)		
West, *n* (%)	4,556 (25.5)	9,358 (23.0)		
Puerto Rico/other/refused, *n* (%)	121 (0.7)	206 (0.5)		
Exposure site			<0.001	0.046
Own residence, *n* (%)	17,037 (95.5)	38,782 (93.5)		
Others' residence, *n* (%)	190 (1.1)	554 (1.3)		
Healthcare facility, *n* (%)	119 (0.7)	214 (0.5)		
Other, *n* (%)	502 (2.8)	1,943 (4.7)		
Call site			<0.001	0.215
Own residence, *n* (%)	8,337 (46.7)	10,730 (25.9)		
Others' residence, *n* (%)	151 (0.8)	383 (0.9)		
Healthcare facility	7,539 (42.2)	26,607 (64.1)		
Other, *n* (%)	1,821 (10.2)	3,773 (9.1)		
Chronicity			<0.001	0.083
Acute, *n* (%)	8,019 (44.9)	18,347 (44.2)		
Acute-on-chronic, *n* (%)	8,409 (47.1)	19,693 (47.5)		
Chronic, *n* (%)	915 (5.1)	1,139 (2.7)		
Unknown, *n* (%)	505	2,314		
Exposure reason			<0.001	0.172
Unintentional exposure, including adverse reaction, *n* (%)	10,319 (57.8)	17,697 (42.7)		
Intentional misuse, *n* (%)	2,093 (11.7)	3,482 (8.4)		
Suicide attempt, *n* (%)	5,077 (28.4)	19,209 (46.3)		
Unknown, *n* (%)	359 (2.0)	1,105 (2.7)		
Number of substances other than gabapentin involved (range 1–37)				
Median (IQR)	Not applicable	2 (1–4)	Not applicable	
Level of care			<0.001	0.260
Managed on-site/other/unknown, *n* (%)	9,175 (51.4)	11,456 (27.6)		
Treated/evaluated and released from healthcare facility, *n* (%)	3,054 (17.1)	7,923 (19.1)		
Admitted to a noncritical care unit, *n* (%)	1,503 (8.4)	6,158 (14.8)		
Admitted to a critical care unit, *n* (%)	1,141 (6.4)	8,505 (20.5)		
Admitted to a psychiatric facility, *n* (%)	2,626 (11.4)	5,301 (12.8)		
Refused referral/no healthcare facility arrival, *n* (%)	264 (1.5)	534 (1.3)		
Lost to follow-up/left against medical advice, *n* (%)	685 (3.8)	1,616 (3.9)	<0.001	0.260
Medical outcomes			<0.001	0.283
No effect, *n* (%)	3,477 (19.5)	5,907 (14.2)		
Minor effect, *n* (%)	3,593 (20.1)	8,707 (21.0)		
Moderate effect, *n* (%)	2,209 (12.4)	12,103 (29.2)		
Major effect, *n* (%)	445 (2.5)	4,183 (10.1)		
Death, *n* (%)	24 (0.1)	304 (0.7)		
Indirectly reported death, *n* (%)	1 (0.0)	115 (0.3)		
Not followed, judged as nontoxic exposure, *n* (%)	596 (3.3)	480 (1.2)		
Not followed, minimal clinical effect possible, *n* (%)	6,803 (38.1)	8,122 (19.6)		
Unable to follow, judged as a potentially toxic effect, *n* (%)	700 (3.9)	1,572 (3.8)		

P values were calculated based on Pearson's χ^2 tests.

11.7% and 8.4%, respectively; and suspected suicide attempts for 28.4% and 46.3%, respectively. Although the distributions of demographic characteristics, exposure sites, and exposure chronicity differed significantly between groups, all effect sizes were minimal (Cramer's V<0.10).

A higher proportion of multi-substance cases required healthcare facility services. Medical outcomes indicated no/minor effects in 81.0% of gabapentin-only and 56.0% of multi-substance cases, moderate effects in 12.4% and 29.2%, respectively, and major effects/death in 2.6% and 11.1%, respectively; potentially toxic exposures were reported in 3.9% and 3.8%, respectively.

Characteristics by reasons for exposure

Table 2 shows that in the gabapentin-only group, exposure reasons did not vary significantly across years, but demographic characteristics, level of care, and outcomes differed by exposure reasons. Intentional misuses or abuses and suspected suicide attempts involved higher proportions of the 50–59 age group and males, and were more frequently managed in healthcare facilities. More than one-third of suspected suicide attempts resulted in psychiatric admission.

In the multi-substance group, unintentional exposures and suspected suicide attempts increased modestly between 2017 and 2018 and 2023–2024 (with a transient decline in 2021–2022). In contrast, intentional misuses or abuses decreased, yielding a small effect size (Cramer's $V = 0.04$). Patterns of age, sex, and clinical management were similar to those in the gabapentin-only group. Unintentional exposures involved a greater number of co-ingested substances than intentional misuses or abuses and suspected suicide attempts (Kruskal-Wallis ($H[2] = 838.57$, $P < 0.001$). Drugs for cardiovascular diseases were most common in unintentional exposures, alcohol and antidepressants were most common in suspected suicide attempts, and opioids were most common in intentional misuses or abuses. Antidepressant use was also common in unintentional exposures. Additional analysis showed that psychotropic medications (antidepressants, antipsychotics, or anxiolytics other than benzodiazepines, benzodiazepines, and prescription opioids) were involved in 61.7% of the multi-substance cases.

Across both groups, unintentional exposures most often resulted in no/minor effects, while intentional misuses or abuses and suspected suicide attempts produced more moderate or severe outcomes, particularly among multi-substance exposures.

Correlates of reasons for exposure: multinomial logistic regression results

As shown in Table 3, in the gabapentin-only group, the likelihood of suspected suicide attempts, compared to unintentional exposures, was higher in later years than in 2017 and 2018. Both intentional misuses or abuses and suspected suicide attempts were less likely among individuals aged 60 years and older, females, and residents outside the Northeast. In the multi-substance group, the relative likelihood of intentional misuses or abuses was lower from 2021 to 2024, and that of suspected suicide attempts was lower in 2021–2022 compared with 2017–2018. Associations with age, sex, and region mirrored those in the gabapentin-only group.

Within the multi-substance group, the likelihood of intentional misuse or abuse and suspected suicide attempts was negatively associated with the number of co-ingested substances. However, alcohol was associated with a significantly higher likelihood of intentional misuse or abuse (relative risk ratio: 11.07; 95% CI: 9.42–13.02) and suspected suicide attempts (relative risk ratio: 21.87; 95% CI: 19.05–25.12). Antipsychotics/anxiolytics, benzodiazepines, prescription opioids, and other analgesics were also associated with a higher likelihood of both intentional misuse or abuse and suspected suicide attempts. Antidepressants and antihistamines were associated with a higher likelihood of suspected suicide attempts, while drugs for cardiovascular diseases, hypoglycemics, and non-steroidal anti-inflammatory drugs were associated with a lower likelihood of intentional misuse or abuse and suspected suicide attempts.

Correlates of medical outcomes among intentional misuse and suicide attempts: multinomial logistic regression results

Table 4 shows that compared to no/minor effect, moderate effects and major effects/death were more likely from 2019 through 2024 and among females. Moderate effects were less likely among cases aged 70–79 years than among those aged 50–59 years, and major/fatal effects were less likely in regions outside the Northeast.

A greater number of co-ingested substances was positively associated with moderate effects (relative risk ratio: 1.15; 95% CI: 1.12–1.18), major effects/death (relative risk ratio: 1.23; 95% CI: 1.20–1.26), and potentially toxic effects (relative risk ratio: 1.08, 95% CI: 1.01–1.15). Antidepressants, antipsychotics/anxiolytics, benzodiazepines, drugs for cardiovascular diseases, and opioids were positively associated with moderate

Table 2. Characteristics of gabapentin exposures by exposure reason.

	Gabapentin-only exposure ($n = 17,489$)[a]					Multi-substance exposures ($n = 40,388$)[a]				
	Unintentional exposure	Intentional misuse	Suicide attempt			Unintentional exposure	Intentional misuse	Suicide attempt		
	10,319	2,093	5,077	*P*	Cramer's *V*	17,697	3,482	19,209	*P*	Cramer's *V*
Year				0.069	0.018				<0.001	0.039
2017–2018, *n* (%)	2,449 (23.7)	543 (25.9)	1,177 (23.2)			3,787 (21.4)	926 (26.6)	4,664 (24.3)		
2019–2020, *n* (%)	2,549 (24.7)	527 (25.2)	1,328 (26.2)			4,232 (23.9)	916 (26.3)	4,940 (25.7)		
2021–2022, *n* (%)	2,567 (24.9)	473 (22.6)	1,238 (24.4)			4,647 (26.3)	802 (23.0)	4,576 (23.8)		
2023–2024, *n* (%)	2,754 (26.7)	550 (26.3)	1,334 (26.3)			5,031 (28.4)	838 (24.1)	5,029 (26.2)		
Age Group (years)										
50–59, *n* (%)	2,713 (26.3)	988 (47.2)	3,181 (62.7)	<0.001	0.274	4,383 (24.8)	1,902 (54.6)	12,275 (63.9)	<0.001	0.335
60–69, *n* (%)	3,133 (30.4)	734 (35.1)	1,403 (27.6)			5,137 (29.0)	1,138 (32.7)	5,423 (28.2)		
70–79, *n* (%)	2,739 (26.5)	268 (12.8)	368 (7.2)			4,565 (25.8)	351 (10.1)	1,222 (6.4)		
≥80, *n* (%)	1,734 (16.8)	103 (4.9)	125 (2.5)			3,612 (20.4)	91 (2.6)	289 (1.5)		
Female, *n* (%)	7,172 (69.5)	1,075 (51.4)	2,967 (58.5)	<0.001	0.141	11,474 (64.9)	1,927 (55.4)	11,647 (60.7)	<0.001	0.059
US Census region				<0.001	0.077				<0.001	0.065
Northeast, *n* (%)	1,351 (13.1)	399 (19.1)	832 (16.4)			2,076 (11.7)	681 (19.6)	3,092 (16.1)		
Midwest, *n* (%)	2,101 (20.4)	450 (21.5)	1,072 (21.1)			4,506 (25.5)	805 (23.1)	4,494 (23.4)		
South, *n* (%)	3,768 (36.5)	808 (38.6)	2,094 (41.2)			6,476 (36.6)	1,366 (39.2)	7,363 (38.3)		
West, *n* (%)	3,014 (29.2)	429 (20.5)	1,053 (20.7)			4,531 (25.6)	627 (18.0)	4,170 (21.7)		
Puerto Rico/other/refused, *n* (%)	85 (0.8)	7 (0.3)	26 (0.50)			108 (0.6)	3 (0.1)	90 (0.5)		
Level of care				<0.001	0.599				<0.001	0.538
Managed on-site/other/ unknown, *n* (%)	8,735 (84.6)	376 (18.0)	35 (0.7)			11,082 (62.6)	285 (8.2)	48 (0.2)		
Treated/evaluated and released from healthcare facility, *n* (%)	849 (8.2)	754 (36.0)	1,368 (26.9)			3,306 (18.7)	1,030 (29.6)	3,395 (17.7)		
Admitted to a noncritical care unit, *n* (%)	232 (2.2)	358 (17.1)	809 (15.9)			1,294 (7.3)	773 (22.2)	3,805 (19.8)		
Admitted to a critical care unit, *n* (%)	101 (1.0)	266 (12.7)	690 (13.6)			808 (4.6)	889 (25.5)	6,346 (33.0)		
Admitted to a psychiatric facility, *n* (%)	46 (0.4)	119 (5.7)	1,847 (36.4)			98 (0.6)	225 (6.5)	4,933 (25.7)		
Refused referral/no healthcare facility arrival, *n* (%)	116 (1.1)	66 (3.2)	70 (1.4)			405 (2.3)	63 (1.8)	48 (0.2)		
Lost to follow-up/left against medical advice, *n* (%)	240 (2.3)	154 (7.4)	258 (5.1)			704 (4.0)	217 (6.2)	634 (3.30		
Medical outcomes				<0.001	0.260				<0.001	0.327
No, minor, or minimal effect, *n* (%)	9,637 (93.4)	1,328 (63.4)	3,384 (66.7)			14,353 (81.1)	1,266 (36.4)	7,373 (38.4)		
Moderate effect, *n* (%)	383 (3.7)	497 (23.7)	1,180 (23.2)			2,187 (12.4)	1,430 (41.1)	7,968 (41.5)		
Major effect/death, including indirectly reported, *n* (%)	33 (0.3)	124 (5.9)	273 (5.4)			313 (1.8)	610 (17.5)	3,390 (17.6)		
Unable to follow, judged as a potentially toxic effect, *n* (%)	266 (2.6)	144 (6.9)	240 (4.7)			844 (4.8)	176 (5.1)	478 (2.5)		
Number of other substances[a], median (IQR)						3.0 (2–5)	2.0 (1–3)	2.0 (1.3)	<0.001	Not available
Alcohol, *n* (%)						233 (1.3)	651 (18.7)	5,455 (28.4)	<0.001	0.356
Antidepressants, *n* (%)						5,518 (31.2)	770 (22.1)	6,692 (34.8)	<0.001	0.076
Antihistamines, *n* (%)						1,419 (8.1)	232 (6.6)	1,619 (8.4)	0.002	0.018
Antipsychotics or anxiolytics other than benzodiazepines, *n* (%)						2,950 (16.7)	578 (16.6)	4,371 (22.8)	<0.001	0.077
Benzodiazepines, *n* (%)						1,822 (10.3)	667 (19.2)	4,324 (22.5)	<0.001	0.157
Drugs for cardiovascular diseases[b] *n* (%)						8,811 (49.7)	419 (12.0)	4,339 (22.6)	<0.001	0.308
Hypoglycemics, *n* (%)						2,555 (14.4)	88 (2.5)	848 (4.4)	<0.001	0.183
Muscle relaxants, *n* (%)						1,541 (8.7)	270 (7.8)	1,606 (8.4)	0.138	0.010
Non-steroidal anti-inflammatory drugs, *n* (%)						2,997 (16.9)	281 (8.1)	1,950 (10.2)	<0.001	0.106
Opioids, *n* (%)						3,107 (17.6)	1,059 (30.4)	3,200 (16.7)	<0.001	0.097
Other analgesics[b], *n* (%)						1,066 (6.0)	238 (6.8)	1,286 (6.7)	0.018	0.014

Note: The numbers in both groups reflect the exclusion of those cases with unknown exposure reasons and unknown sex.

[a]The percentages of other substance involvement for all multi-substance exposures were drugs for cardiovascular diseases (33.4%) and antidepressants (32.3%), antipsychotics or anxiolytics other than benzodiazepines (19.8%), prescription opioids (18.6%), and benzodiazepines (17.0%), alcohol (15.5%), non-steroidal anti-inflammatory drugs (12.8%), hypoglycemics (8.6%), muscle relaxants (8.5%), antihistamines (8.1%), and other analgesics (6.4%).

[b]Including angiotensin converting enzyme inhibitors, angiotensin receptor blockers, antihyperlipidemics, antihypertensives, beta blockers, calcium antagonists, and other miscellaneous drugs for cardiovascular diseases.

[c]Including paracetamol, phenacetin, and phenazopyridine.

P-values were calculated based on Pearson's χ^2 tests for categorical variables and the Kruskal–Wallis test for the number of other substances.

Table 3. Correlates of exposure reasons: results from multinomial logistic regression models.

		Gabapentin-only exposures		Multi-substance exposures	
		Intentional misuse, relative risk ratio (95% CI)	Suicide attempts, relative risk ratio (95% CI)	Intentional misuse, relative risk ratio (95% CI)	Suicide attempts, relative risk ratio (95% CI)
		Versus unintentional exposure			
Year: versus 2017–2018					
	2019–2020	0.98 (0.85–1.12)	1.14 (1.03–1.27)*	0.94 (0.84–1.05)	1.01 (0.94–1.09)
	2021–2022	0.90 (0.78–1.04)	1.13 (1.02–1.25)*	0.80 (0.71–0.89)***	0.93 (0.86–0.99)*
	2023–2024	0.99 (0.86–1.13)	1.14 (1.03–1.27)*	0.79 (0.70–0.88)***	0.97 (0.91–1.05)
Age group: versus 50–59 years					
	60–69 years	0.66 (0.59–0.73)***	0.38 (0.35–0.42)***	0.59 (0.54–0.64)***	0.44 (0.42–0.47)***
	70–79 years	0.28 (0.24–0.32)***	0.12 (0.10–0.13)***	0.25 (0.22–0.29)***	0.14 (0.13–0.15)***
	≥80 years	0.17 (0.14–0.21)***	0.06 (0.05–0.08)***	0.09 (0.08–0.12)***	0.05 (0.04–0.06)***
Female versus male		0.47 (0.43–0.52)***	0.63 (0.58–0.68)***	0.61 (0.56–0.66)***	0.79 (0.75–0.83)***
Region: versus Northeast					
	Midwest	0.73 (0.62–0.85)***	0.83 (0.74–0.94)**	0.56 (0.50–0.64)***	0.69 (0.63–0.75)***
	South	0.75 (0.65–0.86)***	0.95 (0.85–1.06)	0.69 (0.62–0.78)***	0.89 (0.82–0.96)**
	West	0.52 (0.45–0.61)***	0.65 (0.57–0.73)***	0.46 (0.41–0.52)***	0.71 (0.65–0.77)***
	Puerto Rico/Other/Refused	0.28 (0.13–0.62)**	0.48 (0.30–0.78)**	0.12 (0.04–0.37)***	0.77 (0.55–1.09)
Number of other substances				0.92 (0.89–0.94)***	0.86 (0.85–0.87)***
Alcohol				11.07 (9.42–13.02)***	21.87 (19.05–25.12)***
Antidepressants				1.00 (0.90–1.11)	1.89 (1.77–2.00)***
Antihistamines				1.08 (0.92–1.26)	1.37 (1.25–1.50)***
Antipsychotics or anxiolytics other than benzodiazepines				1.25 (1.11–1.39)***	1.78 (1.66–1.90)***
Benzodiazepines				2.07 (1.86–2.31)***	2.99 (2.79–3.22)***
Drugs for cardiovascular diseases				0.31 (0.27–0.35)***	0.72 (0.67–0.77)***
Hypoglycemics				0.42 (0.33–0.52)***	0.64 (0.58–0.70)***
Muscle relaxants				0.87 (0.76–1.01)	0.92 (0.84–1.01)
Non-steroidal anti-inflammatory drugs				0.68 (0.59–0.78)***	0.90 (0.83–0.98)*
Prescription opioids				2.16 (1.97–2.38)***	1.29 (1.20–1.38)***
Other analgesics				1.87 (1.59–2.20)***	2.16 (1.95–2.40)***
Model statistics		$n = 17,481$; LR $\chi^2 = 3245.90$; $P < 0.001$		$n = 40,361$; LR $\chi^2 = 18060.45$; $P < 0.001$	

Note: Cases with unknown exposure reasons and unknown sex were excluded from the models.
*$P < 0.05$.
**$P < 0.01$.
***$P < 0.001$.

effects and major effects/death. Alcohol was positively associated with moderate effects but negatively associated with major effects/death and potentially toxic effects. Opioids were also positively associated with potentially toxic effects. Hypoglycemics were negatively associated with moderate effects and major effects/death, and non-steroidal anti-inflammatory agents were negatively associated with moderate effects, major effects/death, and potentially toxic effects.

Discussion

This 8-year observational study of gabapentin exposures among US adults aged 50 years and older revealed that almost one-third of cases involved gabapentin alone, while the remainder involved gabapentin in combination with other substances. Our findings offer insight into both distinct and similar profiles and risks associated with gabapentin-only and multi-substance cases in older adults. In the multi-substance cases, drugs for cardiovascular diseases and antidepressants were the most common co-ingestants, and psychotropic medications, including antidepressants, antipsychotics/anxiolytics, benzodiazepines, and prescription opioids, were implicated in nearly two-thirds of all multi-substance cases. In terms of the exposure reason, unintentional exposures were most common in gabapentin-only cases, whereas suspected suicide attempts predominated in multi-substance cases. Over time, unintentional exposures and suspected suicide attempts increased, with a dip in suspected suicide attempts during 2021–2022, consistent with pandemic-related fluctuations in suicide-related visits in US healthcare settings among the 50 and older age group [34]. The recent decline in intentional misuses or abuses may reflect heightened regulatory scrutiny as several states reclassified gabapentin as a controlled substance [7,35].

Demographic patterns were clear: younger-old adults were more likely to engage in intentional misuses or abuses or suspected suicide attempts, and women were consistently less likely than men to be involved in intentional exposures. These results align with previous studies showing that gabapentin prescription was high in late-middle-aged or younger-old individuals [36,37]. Although earlier prescribing data indicate higher gabapentin use among women than men, poison center-based studies have found that

Table 4. Correlates of medical outcomes among cases of intentional abuse/misuse and suicide attempt: Results from a multinomial logistic regression model.

	Moderate effect, relative risk ratio (95% CI)	Major effect/death, relative risk ratio (95% CI)	No follow-up: Potentially toxic effect, relative risk ratio (95% CI)
	Versus no/minimal effect		
Year: versus 2017–2018			
2019–2020	1.19 (1.11–1.28)***	1.63 (1.47–1.81)***	0.99 (0.82–1.18)
2021–2022	1.20 (1.12–1.29)***	1.66 (1.49–1.84)***	1.09 (0.90–1.30)
2023–2024	1.25 (1.16–1.34)***	1.62 (1.46–1.80)***	1.14 (0.96–1.36)
Age group: versus 50–59 years			
60–69 years	1.01 (0.95–1.07)	1.06 (0.98–1.15)	1.10 (0.96–1.27)
70–79 years	0.90 (0.81–0.99)*	0.94 (0.82–1.08)	0.90 (0.70–1.15)
≥80 years	0.84 (0.69–1.02)	0.92 (0.71–1.18)	1.29 (0.88–1.87)
Female versus male	1.17 (1.11–1.23)***	1.23 (1.15–1.33)***	1.05 (0.92–1.20)
Region: versus Northeast			
Midwest	1.06 (0.98–1.15)	0.87 (0.78–0.97)*	0.60 (0.47–0.76)***
South	1.03 (0.96–1.12)	0.94 (0.85–1.05)***	1.34 (1.11–1.62)**
West	0.80 (0.74–0.87)***	0.69 (0.61–0.78)***	1.23 (1.00–1.51)
Puerto Rico/other/refused [1]	0.55 (0.36–0.85)**	0.46 (0.25–0.85)*	1.41 (0.64–3.12)
Suicide attempt versus intentional misuse/abuse	0.96 (0.89–1.03)	1.02 (0.92–1.12)	0.56 (0.49–0.65)***
Number of other substances	1.15 (1.12–1.18)***	1.23 (1.20–1.26)***	1.08 (1.01–1.15)*
Alcohol	1.28 (1.20–1.37)***	0.87 (0.79–0.96)**	0.69 (0.57–0.84)**
Antidepressants	1.34 (1.25–1.45)***	1.52 (1.39–1.67)***	0.91 (0.74–1.12)
Antihistamines	1.11 (0.99–1.24)	0.90 (0.78–1.05)	0.95 (0.70–1.28)
Antipsychotics/anxiolytics	1.16 (1.07–1.25)***	1.20 (1.09–1.33)***	0.93 (0.75–1.16)
Benzodiazepines	1.16 (1.07–1.25)***	1.38 (1.25–1.52)***	0.88 (0.71–1.09)
Drugs for cardiovascular diseases	1.30 (1.18–1.42)***	1.27 (1.13–1.43)***	1.03 (0.80–1.32)
Hypoglycemics	0.81 (0.69–0.96)*	0.58 (0.47–0.72)***	0.78 (0.48–1.26)
Muscle relaxants	0.95 (0.87–1.05)	1.03 (0.90–1.17)	1.29 (1.05–1.59)*
Non-steroidal anti-inflammatory drugs	0.74 (0.66–0.83)***	0.68 (0.59–0.79)***	0.60 (0.43–0.83)**
Prescription opioids	1.71 (1.57–1.86)***	2.59 (2.34–2.87)***	1.39 (1.13–1.71)**
Other analgesics	0.97 (0.85–1.10)	1.14 (0.98–1.33)	0.83 (0.58–1.17)
Model statistics	$n = 29{,}847$; likelihood ratio $\chi^2 = 3273.87$; $P < 0.001$		

[1]Given the small number of cases in this category, caution is required when interpreting the relative risk ratios.
*$P < 0.05$.
**$P < 0.01$.
***<0.001.

men are more likely to engage in high-risk or intentional gabapentin use [38,39].

Regional variation, with a greater proportion of intentional cases in the Northeast, diverges from earlier reports showing smaller increases in gabapentin prescribing in that region. Pauly et al. [36] found that between 2009 and 2016, the largest prescription increases occurred in Kentucky and other states east of the Mississippi River and in the South, whereas the Northeast showed the smallest growth. Our findings also appear unrelated to regional differences in other substance use, as similar patterns were observed in both gabapentin-only and multi-substance groups. However, data from the 2014–2019 National Vital Statistics System indicate that while mortality from drug poisoning was higher in the Northeast, suicide rates were lower than in other US regions [40]. The higher proportion of intentional cases observed in the Northeast in our study may therefore reflect differences in poison center reporting practices, healthcare system characteristics, or case ascertainment. Further research linking poison center data with regional prescribing, toxicology, and mortality surveillance is needed to clarify these patterns.

Polypharmacy played a central role. A higher number of co-ingestants was paradoxically associated with fewer intentional misuses or abuses and suspected suicide attempts, likely reflecting therapeutic errors from drug interactions and unintentional mistakes in drug administrations. However, specific substances, including alcohol, psychotropics, and opioids, were strongly associated with intentional exposures. These findings are consistent with prior work linking gabapentin-opioid/benzodiazepine combinations to sedation, respiratory depression, and overdose [11,41]. Associations with antidepressants and antipsychotics also suggest that gabapentin may exacerbate psychiatric vulnerabilities, as others have reported [11,13,14].

Medical outcomes further underscore the dangers of concomitant use of gabapentin and psychotropics. While unintentional exposures were often managed on-site and resulted primarily in no/minor effects, intentional misuses or abuses and suspected suicide attempts carried significantly higher rates of hospitalization, critical care admission, and adverse outcomes. Each additional co-ingestant increased the risk of moderate effects, major effects/death, and

potentially toxic effects. The specific associations of drugs for cardiovascular diseases and psychotropic medications with poor outcomes align with prior studies documenting additive toxicity in polypharmacy, regardless of its varying definitions, in older adults, especially those with multimorbidity [42–44]. Alcohol was uniquely associated with moderate effects but not severe outcomes, consistent with poison center data showing high prevalence but variable severity of alcohol effects on other poison cases [45,46].

This study has several limitations. National Poison Data System® data are based on voluntary reporting, which likely underestimates true case counts. As with all poison center reports, exposures are self- or provider-reported, and there is no independent verification of substances ingested or agents responsible for observed effects. The NPDS® data also lacks detailed psychiatric histories, medication dosages, and information on intent validation. The cross-sectional design precludes causal inference regarding whether gabapentin contributes to suicidality or reflects underlying psychiatric vulnerability. In multi-substance cases, the relative contribution of each substance to medical outcomes could not be determined. Despite these limitations, the large, nationally representative dataset offers valuable real-world evidence on the characteristics and clinical consequences of gabapentin exposures in later life.

Conclusions

Gabapentin exposures in older adults most often result from unintentional therapeutic errors, though intentional exposures, including suspected suicide attempts, were also frequent, especially in multi-substance exposures. Co-exposures with psychotropics were strongly associated with intentional exposure and with more severe medical outcomes, underscoring the need to assess underlying psychiatric vulnerability alongside poor physical health among older adults co-using gabapentin with antidepressants, antipsychotics, sedatives, opioid analgesics, and/or cardiovascular agents. Since adverse outcomes in these cases likely reflect the cumulative pharmacologic burden rather than toxicity from gabapentin alone, cautious prescribing and close monitoring are warranted when gabapentin is used in combination with these medications. In sum, efforts to reduce unsafe polypharmacy, expand deprescribing initiatives, and strengthen poison center surveillance are essential to mitigating harms associated with multi-substance exposures in later life.

Author contributions

Each author certifies that their contribution to this work meets the standards of the International Committee of Medical Journal Editors.

Disclosure statement

America's Poison Centers® maintains the National Poison Data System® (NPDS®), which houses de-identified records of self-reported information from callers to the country's poison centers. National Poison Data System® data do not reflect the entire universe of US exposures and incidences related to any substance(s). Exposures do not necessarily represent a poisoning or overdose and America's Poison Centers® is not able to completely verify the accuracy of every report. National Poison Data System® data do not necessarily reflect the opinions of America's Poison Centers®.

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Data availability statement

NPDS® data are made available by the America's Poison Centers®.

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