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Gabapentinoid Dispensing to Children and Adolescents in the U.S.

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Abstract

Introduction: Gabapentin and pregabalin (gabapentinoids) are increasingly prescribed to children and adolescents off label for various conditions despite limited data and concerns for adverse outcomes including misuse and overdose. The extent of gabapentinoid use in children and adolescents is unknown.

Methods: Nationally representative retail pharmacy dispensing data from IQVIA was used to describe trends in gabapentinoid dispensing to children and adolescents aged ≤19 years from April 2017 through September 2023. The analysis was performed in 2024. Trends by patient age and sex and by prescriber specialty are presented along with median quarterly rates (MQR) and quarterly percentage changes (QPC).

Results: Over the study period, the gabapentinoid dispensing rate was 4534.9/100,000 individuals. The MQR was 168.9/100,000. Between Q2 2017 and Q2 2021, the QPC was not significant (QPC=0.08; 95% CI= -2.9, 0.8) but became significant between Q2 2021 and Q3 2023 (QPC=2.8; 95% CI=1.2, 8.4). Dispensing rates were highest for adolescents aged 10–19 years (MQR=267.3/100,000) and females (MQR=187.6/100,000). Nurse practitioners prescribed the highest percent of gabapentinoids dispensed (17.8%). The total number of gabapentinoids dispensed increased from 2018 to 2022 across all specialties except psychiatry (–14.8%) and internal medicine (–9.2%), with nurse practitioners (48.2%), surgical specialists (48.0%), and addiction medicine specialists (51.2%) representing the largest increases.

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CREDIT AUTHOR STATEMENT

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Conclusions: Gabapentinoid receipt among U.S. children and adolescents has increased. Future research can explore factors associated with prescribing including changing epidemiology of pain and psychiatric diagnoses in children and adolescents. Prescribing clinicians should carefully consider the potential risks and benefits of gabapentinoids in clinical practice.

INTRODUCTION

Gabapentin and pregabalin (gabapentinoids) are approved by the Food and Drug Administration (FDA) to treat partial onset seizures in children (gabapentin ages 3+ years, pregabalin ages 4+ years) and adults with epilepsy, and for postherpetic neuralgia in adults.^{1,2} Pregabalin is also approved for the treatment of fibromyalgia, spinal cord injury, and peripheral neuropathy in adults aged 18 years and older.¹ Gabapentinoids are increasingly prescribed off-label for various conditions including non-neuropathic acute and chronic pain and psychiatric disorders, despite limited data for these indications.^{3–5} There is also growing concern about potential adverse outcomes associated with gabapentinoids, including higher rates of unintentional overdose, suicidal behavior, and other injury.⁶ Gabapentinoids also have the potential for misuse, particularly in patients with co-occurring psychiatric and substance use disorders (SUDs).⁷

Evidence suggests off-label prescribing and use is increasing in pediatric populations as well.^{4,6,8,9} While there is some evidence for effectiveness in reducing opioid use in some postsurgical pediatric populations,^{9,10} overall data on safety and effectiveness in children and adolescents is limited. In one Finnish study of adolescents admitted to an inpatient psychiatric facility, gabapentinoid use was associated with early initiation of substance use, other drug use, and a SUD diagnoses.⁸ A better understanding of dispensing characteristics among children and adolescents could help inform guidance to reduce potential adverse outcomes including prescription drug misuse.

METHODS

IQVIA National Prescription Audit New to Brand data, which contains prescriptions dispensed from 48,900 retail pharmacies representing 93% of prescriptions dispensed in the U.S., was used to describe trends in gabapentinoid dispensing to children and adolescents aged ≤19 years from April 2017 through September 2023. Data are weighted to be nationally representative. Annual and quarterly dispensing rates are presented alongside annual specialty trends and 95% CIs. Rates were calculated per 100,000 persons aged ≤19 years by age group and sex using U.S. Census data.¹¹ Trends by patient age and sex, and by prescriber specialty are presented. Wilcoxon Rank Sum Tests examined the difference in median dispensing rates between males and females during the overall study period. Analysis was performed in SAS (9.4) and Joinpoint Trend Analysis Software (5.0.2) to calculate quarterly percent change (QPC) and 95% CI. Joinpoint models were fit with autocorrelated errors and models with the best fit using permutation tests were selected.¹² STROBE reporting guidelines were followed. Because records contained no identifying information, this study was exempt from review by the Centers for Disease Control and Prevention IRB.

RESULTS

Overall, 3,708,615 gabapentinoid prescriptions were dispensed to individuals aged ≤ 19 years from April 2017 –September 2023 (rate=4534.9/100,000 individuals aged ≤ 19 years; Table 1), median quarterly rate [(MQR)=168.9/100,000] (Figure 1a). Ninety-six percent of all gabapentinoid prescriptions dispensed were for gabapentin. Annual dispensing rates and percent change by age and sex are presented in Table 1. Quarterly dispensing rates were also calculated (data not shown). Between Q2 2017 and Q2 2021, the QPC was not significant (QPC=0.08; 95%CI= -2.9, 0.8) but became significant between Q2 2021 and Q3 2023 (QPC: 2.8; 95% CI=1.2,8.4) (data not shown). Dispensing rates were highest for adolescents aged 10–19 years (MQR=267.3/100,000) (Figure 1a). The MQR of gabapentinoids dispensed to females was significantly higher than for males (187.6/100,000 vs. 151.9/100,000; $p<0.0001$) (Figure 1b). Gabapentinoid dispensing by specialty is presented in Table 1. From April 2017 to September 2023, nurse practitioners prescribed the highest percent of gabapentinoids dispensed (17.8%) followed by neurology (15.0%). Pediatricians (including internal medicine-pediatric specialists) prescribed 7% of medications dispensed. Compared to 2018, the total number of gabapentinoids dispensed in 2022 increased across all specialties except psychiatry (-14.8%) and internal medicine (-9.2%), with nurse practitioners (48.2%), surgical specialists (48.0%), and addiction medicine specialists (51.2%) representing the largest increases (Table 1).

DISCUSSION

This study identified increasing rates of gabapentinoids dispensed to children and adolescents from 2017 to 2023, with dispensing rates significantly higher among females than males. These nationally representative trends are consistent with trends observed in smaller studies of both adults and children.^{3,4,13,14} While underlying diagnoses are not available, several factors may contribute to the observed changes. The observed trends could reflect efforts to offer nonopioid pain management options to youth in the setting of chronic and post-operative pain. Chronic pain prevalence among children and adolescents has been reported to be as high as 21%.¹⁵ Recent pediatric and adult guidelines on managing pain recommend non-opioid alternatives where appropriate.^{16–19} Studies in adults and youth have documented increases in gabapentinoid use in management of chronic pain.^{4,20} There has also been interest in reducing opioid prescribing for postoperative pain. Recently, opioid prescribing for postoperative pain in children has declined²¹ while gabapentin dispensing for pain postappendectomy pain has increased.⁹ Increasing rates of prescribing in neonates and infants may also reflect practices to control pain and agitation, including in the setting of neonatal opioid withdrawal syndrome.^{22,23}

Despite a paucity of evidence, gabapentin has frequently been used to treat a variety of mental health conditions.^{5,24} Patients with depression and anxiety are also more likely to experience chronic pain^{25,26} which may increase the likelihood of receiving gabapentinoid prescriptions, particularly as the COVID-19 pandemic further exacerbated the relationship between pain and mental health symptoms.²⁷ Coupled with an overall increase in mental health concerns among adolescents,²⁸ clinicians may be potentially seeking medications to address these comorbid conditions. Differing prevalence of pain¹⁵ and mental health

disorders²⁸ among girls relative to boys, as well as sex bias in diagnosis and treatment of pain²⁹ could also explain the differences in the observed trends by sex.

The increasing use of gabapentinoids is worrisome considering the limited data on efficacy and potential for harm including risk of overdose. A recent study of gabapentinoid exposures reported to poison control centers found increasing rates of exposure, with 22% of exposures associated with serious medical outcomes including fatalities, and nearly half of exposures associated with suspected suicide.³⁰ Studies of law-enforcement derived data and qualitative studies of individuals have found increasing rates of gabapentin diversion³¹ and high rates of self-reported misuse particularly among individuals with opioid use disorder.^{32,33} One study of retail pharmacy claims data reported high levels of concurrent prescribing with opioids³⁴ and gabapentin has been increasingly associated with opioid involved overdose deaths.³⁵

Limitations

This study has several limitations. IQVIA data captures only prescriptions dispensed through retail pharmacies. Gabapentinoids prescribed but not dispensed or dispensed through mail order, large health systems, or the Indian Health Service are not captured. True gabapentinoid prescribing rates might be higher. The data also have limited patient level information such as race and ethnicity and associated diagnoses, procedures, or comorbidities. Understanding the full landscape of gabapentinoid dispensing will require further exploration of these patient-level factors. Finally, the dataset does not include information on the specialty or practice settings of nurse practitioners and physician assistants, so the full extent of subspecialty practice variation in settings with large numbers of nurse practitioner and physician assistant prescribers is unknown.

CONCLUSIONS

These findings highlight a need for further research to better understand dispensing trends in children and adolescents. Understanding patient level factors associated with gabapentinoid receipt, including underlying diagnoses and psychiatric comorbidities, can inform efforts to ensure gabapentinoids are used safely. Prescribing clinicians should carefully consider the potential risks and benefits of gabapentinoids in clinical practice.

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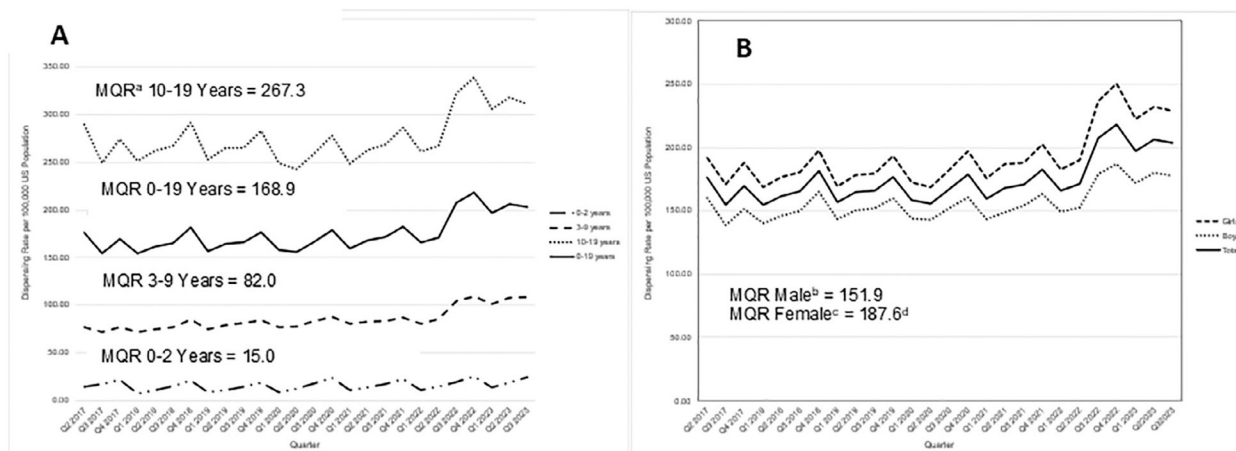


Figure 1.

Quarterly gabapentinoid dispensing rates to youth aged ≤ 19 years by age (A) and sex (B), U.S., 2017–2023 Data Source: IQVIA National Prescription Audit (NPA) New to Brand Data (2017–2023).

Note: Median quarterly rate, MQR.

^aPrescriptions per 100,000 persons ages 0–19 years.

^bPrescriptions per 100,000 persons ages 0–19 years and male.

^cPrescriptions per 100,000 persons ages 0–19 years and female.

^d $p < 0.00001$.

Table 1.
Annual gabapentinoids dispensing by age, sex and prescribing specialty, United States, 2017–2023

Demographic characteristics	2017 (Q2–Q4)			2018			2019			2020			2021			2022			2023 (Q1–3)			Total (2017–2023)			% Change (2018 vs 2022)
	N	Rate ^a	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	
Total	411,202	501.1	543,651	663.9	542,489	664.6	544,675	660.0	555,475	681.5	618,746	763.2	492,377	607.3	3,708,615	4,534.86									15.0%
Age (years)																									
0–2	6,383	53.7	6,438	55.0	6,142	53.2	7,117	63.6	7,174	65.4	7844	71.5	6,359	23.1	47,457	417.1089									30.1%
3–9	64,151	226.6	87,302	309.1	90,190	319.4	91,095	325.7	92,737	334.1	104,842	380.1	87,970	206.9	618,287	2,206.858									23.0%
10–19	340,672	813.8	449,915	1,072.9	446,155	1,066.0	446,466	1,029.6	455,568	1,065.2	506,061	1,190.0	398,049	1,005.6	3,042,886	7,179.345									10.9%
Sex																									
Females	221,127	550.9	289,998	724.0	287,494	720.0	290,367	720.4	300,153	754.1	340,154	859.4	270,753	652.6	2,000,046	5,003.932									18.7%
Males	188,538	449.7	251,263	600.7	252,603	605.8	253,165	599.7	254,096	609.4	277,210	668.1	219,724	271.0	1,696,599	4,058.012									11.2%
Specialty^b	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	N	%^c	% Change (2018–2022)
Family practice	25,450	6.2%	26,432	4.9%	24,531	4.5%	22,285	4.1%	19,419	3.5%	28,463	4.6%	25,728	5.2%	172,308	4.6%									7.7%
Psychiatry	62,876	15.3%	84,515	15.5%	79,753	14.7%	76,238	14.0%	76,093	13.7%	72,044	11.6%	48,318	9.8%	499,837	13.5%									–14.8%
General practice/ unspecified ^d	49,653	12.1%	75,444	13.9%	73,772	13.6%	75,535	13.9%	72,315	13.0%	77,431	12.5%	65,642	13.3%	489,792	13.2%									2.6%
Internal medicine ^e	16,369	4.0%	15,902	2.9%	13,367	2.5%	12,358	2.3%	9,653	1.7%	14,444	2.3%	14,326	2.9%	96,419	2.6%									–9.2%
Nurse practitioner	61,814	15.0%	82,748	15.2%	91,825	16.9%	95,738	17.6%	102,438	18.4%	122,614	19.8%	101,342	20.5%	658,519	17.8%									48.2%
Surgical specialties	15,912	3.9%	21,831	4.0%	24,837	4.6%	26,013	4.8%	28,999	5.2%	32,301	5.2%	25,515	5.2%	175,408	4.7%									48.0%
Anesthesia, pain, or PM&R ^f	26,461	6.4%	33,564	6.2%	32,178	5.9%	32,468	6.0%	34,401	6.2%	42,552	6.9%	35,922	7.3%	237,546	6.4%									26.8%
Emergency medicine	1,703	0.4%	1,989	0.4%	1,872	0.3%	1,781	0.3%	1,858	0.3%	2,480	0.4%	1,977	0.4%	13,660	0.4%									24.7%

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Other medical or pediatric subspecialties	27,274	6.6%	35,627	6.6%	35,351	6.5%	34,319	6.3%	34,182	6.2%	37,868	6.1%	29,454	6.0%	234,075	6.3%	6.3%
Physician assistant	18,940	4.6%	25,129	4.6%	26,753	4.9%	28,541	5.2%	30,620	5.5%	37,056	6.0%	30,510	6.2%	197,549	5.3%	47.5%
Addiction medicine	157	0.0%	125	0.0%	146	0.0%	148	0.0%	178	0.0%	189	0.0%	174	0.0%	1,117	0.0%	51.2%
Pediatrics ^g	29,566	7.2%	40,125	7.4%	37,907	7.0%	38,814	7.1%	41,451	7.5%	42,130	6.8%	31,463	6.4%	261,456	7.0%	5.0%
Other	11,446	2.8%	16,740	3.1%	15,800	2.9%	17,214	3.2%	18,155	3.3%	19,495	3.2%	14,797	3.0%	113,647	3.1%	16.5%
Neurology	63,573	15.5%	83,470	15.4%	84,406	15.6%	83,235	15.3%	85,718	15.4%	89,687	14.5%	68,206	13.8%	558,295	15.0%	7.4%

Data Source: IQVIA National Prescription Audit (NPA) New to Brand Data (2017–2023).

^aPrescriptions per 100,000 persons 0–19 years.^bSpecialties presented in no particular order.^cProportion of total prescriptions.^dIncludes general practice, general osteopathic medicine, and other unspecified specialty.^eDoes not include internal medicine-pediatrics.^fPhysical medicine and rehabilitation.^gIncluding internal medicine-pediatrics.