

High Prescribing and State-Level Variation in Z-Drug Use Among Medicare Patients

Authors

Kaitlin E. Anderson¹, Rachel I. Gifeisman¹, James L. Basting¹, Donovan J. Harris¹, Antonica R. Rajan¹, Kenneth L. McCall^{2, 3}, Brian J. Piper^{1, 4}

Affiliations

- 1 Department of Medical Education, Geisinger Commonwealth School of Medicine, Scranton, PA, USA
- 2 Department of Pharmacy Practice, University of New England, Portland, ME, USA
- 3 Department of Pharmacy Practice and School of Pharmacy and Pharmaceutical Sciences, Binghamton University, Johnson City, NY, USA
- 4 Center for Pharmacy Innovation & Outcomes, Danville, PA, USA

Key Words

elderly, older adult, zolpidem, zopiclone, zaleplon

received 26.01.2023

revised 17.04.2023

accepted 21.04.2023

published online 07.06.2023

Bibliography

Pharmacopsychiatry 2023; 56: 149–153

DOI 10.1055/a-2085-2299

ISSN 0176-3679

© 2023, Thieme. All rights reserved.

Georg Thieme Verlag, Rüdigerstraße 14,
70469 Stuttgart, Germany

Correspondence

Brian J. Piper

Geisinger Commonwealth School of Medicine
Medical Education, 2108 Medical Sciences Building
18503-1843 Scranton

United States

psy391@gmail.com,

bjpiper1@geisinger.edu



Supplementary Material is available under <https://doi.org/10.1055/a-2085-2299>

ABSTRACT

Background Z-drugs are nonbenzodiazepine hypnotics used for sleep initiation and maintenance; these drugs increase the risk of fall-related injuries in older adults. The American Geriatrics Society's Beers criteria classifies Z-drugs as high-risk and strongly recommends avoiding prescribing Z-drugs to older adults due to adverse effects. The study objectives were to determine the prevalence of Z-drug prescribing among Medicare Part D patients and identify state or specialty-dependent prescribing differences. This study also aimed to determine prescribing patterns of Z-drugs to Medicare patients.

Methods Z-drug prescription data was extracted from the Centers for Medicare and Medicaid Services State Drug Utilization Data for 2018. For all 50 states, the number of prescriptions per 100 Medicare enrollees and days-supply per prescription was determined. The percentage of total prescriptions prescribed by each specialty and the average number of prescriptions per provider within each specialty was also determined.

Results Zolpidem was the most prescribed Z-drug (95.0%). Prescriptions per 100 enrollees were significantly high in Utah (28.2) and Arkansas (26.7) and significantly low in Hawaii (9.3) relative to the national average (17.5). Family medicine (32.1%), internal medicine (31.4%), and psychiatry (11.7%) made up the largest percentages of total prescriptions. The number of prescriptions per provider was significantly high among psychiatrists.

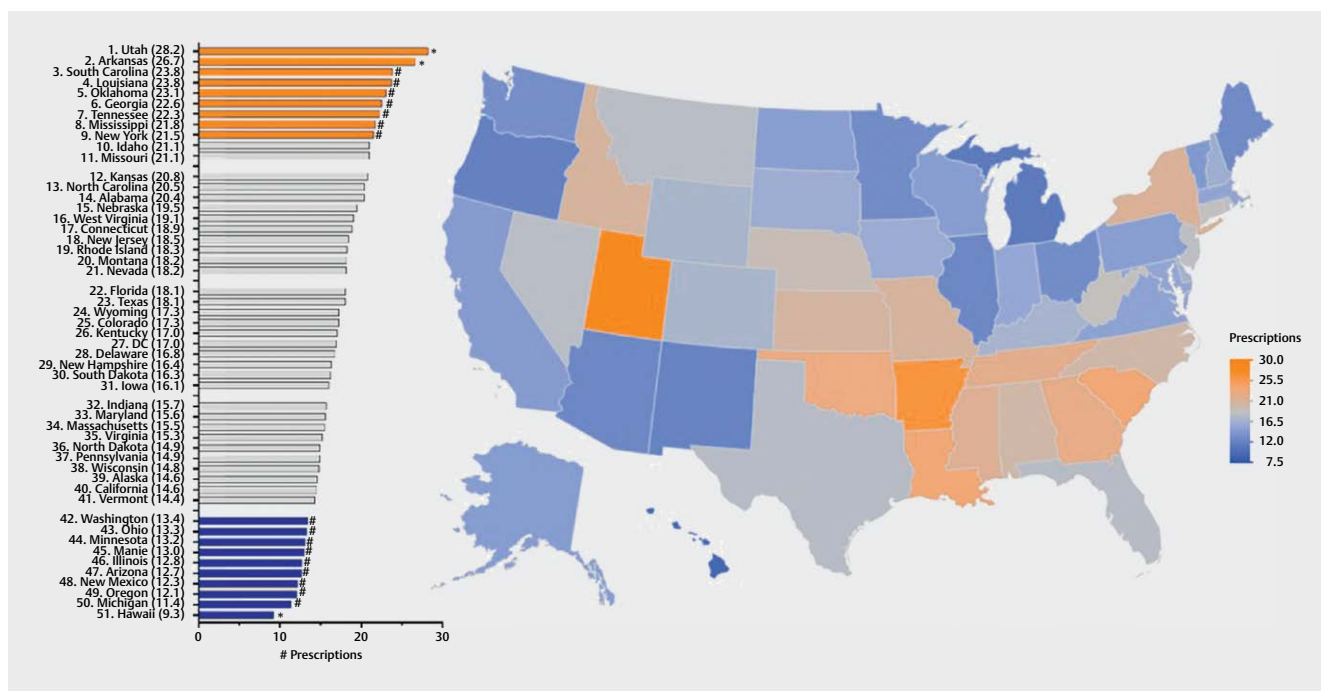
Discussion Contrary to the Beers criteria, Z-drugs are prescribed to older adults at high rates.

Introduction

Over one-third (35%) of the US population experiences short sleep, of less than 7 hours [1]. Nearly 50% of people over 60 years report sleep disorder symptoms, while 12–20% of older adults have been diagnosed with insomnia [1]. Symptoms include difficulty initiating and maintaining sleep, fatigue, mood disturbances, and impaired daytime performance [2]. Older adults are considered a “special population,” as they are at an increased risk for adverse drug effects

and frequently suffer from comorbidities such as heart disease, stroke, diabetes, depression, and cancer [3].

Nonbenzodiazepine hypnotics zolpidem, zaleplon, zopiclone, and eszopiclone, commonly referred to as ‘Z-drugs,’ are a class of sedatives approved by the US Food and Drug Administration for sleep initiation and maintenance. While most Z-drugs act as selective agonists at the GABA_A α₁ subunit, zopiclone and eszopiclone



► Fig. 1 Z-drug prescriptions per 100 Medicare enrollees ranked by state. States with a * were >1.96 SD and # were >1.50 SD.

are non-selective and bind to the α_1 , α_2 , α_3 , and α_5 subunits (i. e., the same mechanism as benzodiazepines) [4]. Z-drugs have been shown to increase the risk of fall-related injuries, such as fractures and traumatic brain injuries, in older adults [5]. A systematic review determined that zolpidem was associated with a 92 % increase in risk of fracture [6]. Among patients over age 65, the risk of zopiclone-associated fracture increased with age [7]. Additionally, withdrawal symptoms for these Schedule IV drugs include delirium, which can potentiate the risk of fall-related injuries. These adverse effects are reflected in the American Geriatrics Society (AGS) Beers criteria guidelines for these drugs, which, in 2015 and 2019, strongly recommended avoiding prescribing Z-drugs for patients 65 years and older [8]. The Fit for the Aged (FORTA) list also strongly recommends avoiding prescribing Z-drugs to older adults, listing them as class D – “avoid if at all possible, in the elderly, omit first, and use alternative substances” [9]. The AGS and FORTA list also report that Z-drugs provide only minimal improvement in sleep duration and latency in older adults [8, 9].

Therefore, it is important to track the prescription patterns of these drugs to patients aged 65 or older in the United States. This study provides a nationwide examination of Z-drug prescriptions to Medicare Part D patients.

Methods

Procedures

Medicare Part D data was acquired from the Centers for Medicare and Medicaid Services State Drug Utilization Data (CMS SDUD) for 2018 [10]. Both generic and name brand formulations of Z-drugs were considered for analysis (zolpidem, Ambien, Edluar, Intermezz-

zo, Zolpimist, eszopiclone, Lunesta, zopiclone, zaleplon, and Sonata, **Supplemental Table 1**).

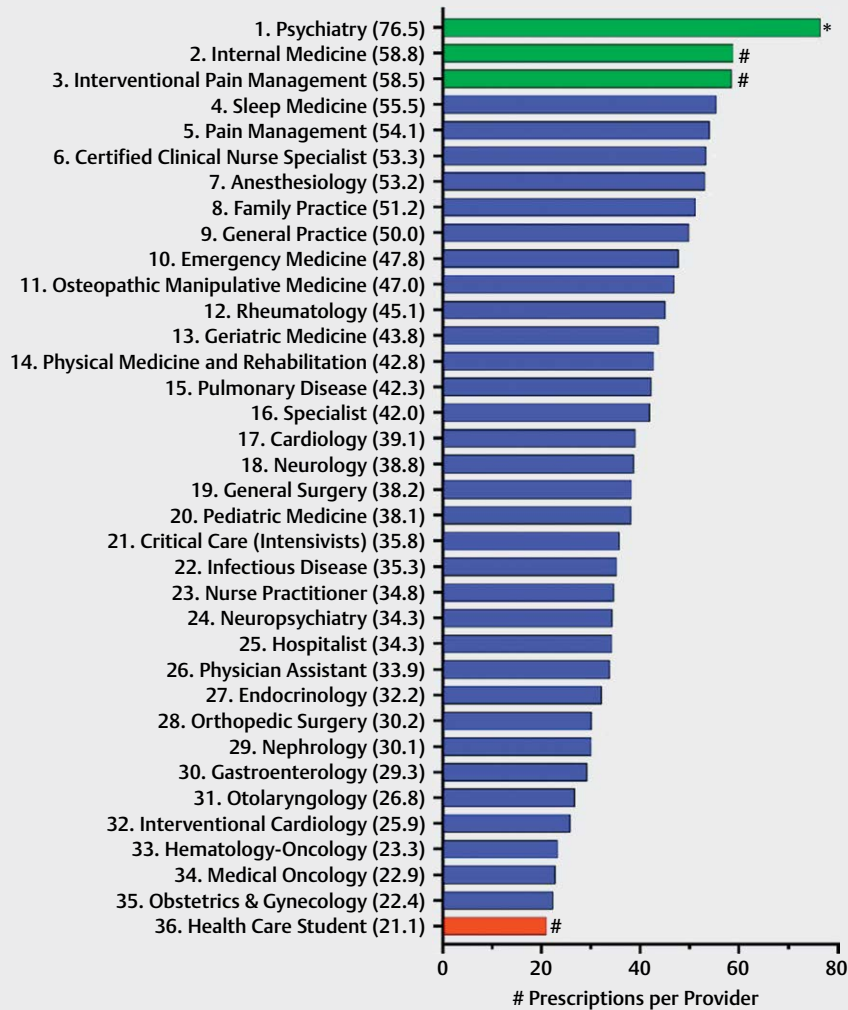
Data-analysis

Z-drug prescriptions were summed and divided by the number of Medicare enrollees in that state, as reported by the CMS, to find the number of prescriptions per enrollee for each state. These values were then multiplied by 100 and reported as the number of Z-drug prescriptions per 100 Medicare enrollees. States that were $\geq \pm 1.96$ standard deviations (SD) outside the mean were categorized as statistically significant ($p < 0.05$). Additionally, the supply for the total number of days was divided by the total number of prescriptions for each state and reported as days-supply per prescription. The providers prescribing Z-drugs were also analyzed. Prescriber data was obtained from the Medicare Part D Prescriber Dataset from CMS [10]. The sum of the total claim counts for each specialty was calculated Using a Python script (**Supplemental Appendix 2**) to determine the percentage of all Z-drug prescriptions prescribed by each specialty. Additionally, the total number of Z-drug prescriptions within each specialty with greater than 100 providers was divided by the number of providers within that specialty, as reported in CMS. Specialties with a prescriptions-per-provider value ≥ 1.96 SD outside the mean were identified as statistically significant ($p < .05$).

Results

Overall, zolpidem accounted for the vast preponderance (95.0 %) of Z-drug prescriptions in 2018. Additionally, generic formulations made up 99.7 % of prescriptions.

The average number of prescriptions per 100 Medicare enrollees was 17.5 ± 4.0 . There was a three-fold (3.04) difference between the highest and lowest states. The numbers of prescriptions per



► **Fig. 2** Z-drug prescriptions by specialty to Medicare patients in 2018. * were >1.96SD and # were >1.50SD.

100 Medicare enrollees for Utah (28.2) and Arkansas (26.7) were significantly elevated, and Hawai'i (9.3) was significantly lower relative to the state mean (► **Fig. 1**). The average days-supply per prescription was 34.9; it was significantly longer for Delaware (40.2) and significantly shorter for New York (29.3) than the national mean (**Supplemental Figure 1**). States with more prescriptions per enrollee tended to have shorter days' supply, but this was not significant ($r(51) = 0.26, p = 0.063$).

Three medical specialties comprised three-quarters (75.2%) of all Z-drug prescriptions. Family medicine (2,351,301; 32.1%) had the highest number of prescriptions, followed by internal medicine (2,298,487; 31.4%) and psychiatry (853,649; 11.7%). All other specialties combined comprised 24.8% (**Supplemental Figure 2**). The average number of Z-drug prescriptions per provider was 40.3 ± 12.1 . Psychiatry was significantly elevated relative to the average, with 76.5 prescriptions per provider in 2018 (► **Fig. 2**).

Discussion

Clearly, Medicare Part D patients are being prescribed Z-drugs, predominantly zolpidem, at high rates despite guidelines to avoid the use of these drugs in older adults due to the increased risk of adverse effects, including fractures from falls, stroke, and psychological distress [6–8]. While older adults are being prescribed these drugs nationwide, we also identified substantial state-level differences in Z-drug prescriptions. We are skeptical that the identified three-fold difference between states in prescribing rates is matched by a three-fold difference in the prevalence of sleep problems. While Utah and Arkansas had the highest Z-drug prescription rates, Hawaii had the lowest number of Z-drug prescriptions per 100 Medicare enrollees. This is consistent with other data showing that Hawaii also has the lowest rates of opioid and antibiotic prescriptions [12, 13]. This could be explained by both cultural differences and an overall healthier population (i. e., low rates of obesity and preventable hospitalizations and high rates of insurance coverage) in Hawaii [14, 15]. However, more research is necessary to understand the most significant influencing factors in keeping the number of

Z-drug prescriptions in Hawaii low and those in Arkansas and Utah high.

In the analysis of Z-drug prescriptions per specialty, family medicine, internal medicine, and psychiatry took the largest share of prescriptions. The predominance of family medicine and internal medicine over psychiatry may be explained by patients with sleep problems presenting more often to their primary care physician rather than a specialist provider [16]. This disparity may also be because only 23% of US psychiatrists are covered by Medicare [17]. However, it did not escape notice that 100% of the working group for the American Psychiatric Association's Diagnostic and Statistical Manual for Sleep/Wake Disorders had ties with the pharmaceutical industry which raises concerns about even further relaxation of the diagnostic criteria in the future revisions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) [18]. Other studies have documented mixed perspectives of general practitioners on Z-drug prescription, noting that many general practitioners experienced tension between their desire to help patients with insomnia and their fear of contributing to the over-prescription of drugs with such potentially severe adverse effects [19].

It is important to emphasize that the populations eligible for Medicare coverage include all adults aged 65 and over, patients with disabilities, and patients with end-stage renal disease. While not all Medicare beneficiaries are older adults, as of 2018, 91% of Medicare beneficiaries were age 65 and older, while only 9% were under age 65 [20]. In addition, less than 3% of Medicare enrollees received hospice care in 2018 [21]. Thus, while Beer's Criteria and FORTA list are not applicable to some Medicare recipients, the vast majority of beneficiaries are older adults who require these special prescribing considerations. Therefore, it is clear that in 2018 a significant number of Medicare enrollees received Z-drug prescriptions that were inconsistent with the Beers Criteria and FORTA List. Other research in Nordic countries has found that the use of Z-drugs was highest for those over the age of 80 [22]. As this report was limited to Medicare Part D patients in the US, further research with other databases, including electronic health records, will be necessary to identify additional subsets of Medicare patients where guidelines were not applicable, as well as determination of patient subgroups (e. g., nursing home residents and obese patients) at greatest risk of receiving potentially inappropriate Z-drug prescriptions.

Conclusion

Sleep disorders in older adults remain a significant problem and should not be ignored. Considering the guidelines in the US state of contraindication of Z-drug use in older adults due to the risk of adverse events, especially falls, it is important to implement changes in treatment practices. Alternative options that have proven successful include cognitive behavior therapy or the development of healthy sleeping habits. Pharmacotherapies may be appropriate if patients remain symptomatic; however, existing alternatives, such as melatonin receptor agonists (e. g., ramelteon), should still be used cautiously in older adults due to adverse effects [23]. Further research is needed to ascertain whether these alternative therapies are not being initiated, the reason for regional differences in the number of prescriptions of Z-drugs per individual prescribers, and compare Z-drug usage among different age groups.

Author contributions

All authors contributed to the study conception and design. Data collection and analysis were performed by Kaitlin E. Anderson, James L. Basting, Rachel I. Gifeisman, Donovan J. Harris, and Antonica R. Rajan. The first draft of the manuscript was written by Kaitlin E. Anderson. All authors commented on previous versions of the manuscript and read and approved the final manuscript.

Role of Sponsor: The sponsor played no role in this research.

Funding

National Institute of Environmental Health Sciences — <http://dx.doi.org/10.13039/100000066>; T32- ES007060-31A1

Acknowledgements

Thanks to Iris Johnston for technical support.

Conflict of Interest

BJP was part of an osteoarthritis research team from 2019–2021 supported by Pfizer and Eli Lilly. He receives research support from the Geisinger Academic Clinical Research Center. The other authors have no financial or personal disclosures.

References

- [1] Patel D, Steinberg J, Patel P. Insomnia in the elderly: A review. *J Clin Sleep Med* 2018; 14: 1017–1024
- [2] Sateia MJ. International classification of sleep disorders-third edition: Highlights and modifications. *Chest* 2014; 146: 1387–1394
- [3] Foley DJ, Monjan A, Simonsick EM et al. Incidence and remission of insomnia among elderly adults: An epidemiologic study of 6,800 persons over three years. *Sleep* 1999; 22: Suppl 2 S366–S372
- [4] Stahl SM. *Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications*. 5th ed. Cambridge, England: Cambridge University Press; 2021
- [5] Treves N, Perlman A, Kolenberg Geron L et al. Z-drugs and risk for falls and fractures in older adults—a systematic review and meta-analysis. *Age Ageing* 2018; 47: 201–208
- [6] Park SM, Ryu J, Lee DR et al. Zolpidem use and risk of fractures: A systematic review and meta-analysis. *Osteoporos Int* 2016; 27: 2935–2944
- [7] Nishtala PS, Chyou T. Zopiclone use and risk of fractures in older people: Population-based study. *JAMDA* 2017; 368: e1–e8
- [8] 2019 American Geriatrics Society Beers Criteria Update Expert Panel American Geriatrics Society 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2019; 67: 674–694
- [9] Pazan F, Gercke Y, Weiss C et al. The U.S.-FORTA (Fit for the Aged) list: Consensus validation of a clinical tool to improve drug therapy in older adults. *JAMDA* 2020; 21: 439e9–439e13
- [10] Medicare provider utilization and payment data: Part D Prescriber [Internet]. *Cms.gov*. [cited 2022 Mar 13] <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Part-D-Prescriber>

- [11] Centers for Disease Control and Prevention. 2018 BRFSS survey data and documentation. Cdc.gov. 2019 [cited 2022 May 1] https://www.cdc.gov/brfss/annual_data/annual_2018.html
- [12] Hawaii opioid summary. National Institute on Drug Abuse. 2019 [cited 2022 Mar 13] <https://nida.nih.gov/sites/default/files/21954-hawaii-opioid-summary.pdf>
- [13] Arizpe A, Reveles KR, Aitken SL. Regional variation in antibiotic prescribing among Medicare part D enrollees, 2013. *BMC Infect Dis* 2016; 16: 744
- [14] Explore health measures in Hawaii. America's Health Rankings. [cited 2022 Mar 13] <https://www.americashealthrankings.org/explore/annual/state/HI>
- [15] Jones RG. Live in Hawaii, and odds are you'll need fewer prescription meds. *NPR* 2017 Aug 31 [cited 2022 Mar 13] <https://www.npr.org/sections/health-shots/2017/08/31/547317533/ornstein-it-s-better-in-hawaii>
- [16] Abed Faghri NM, Boisvert CM, Faghri S. Understanding the expanding role of primary care physicians (PCPs) to primary psychiatric care physicians (PPCPs): Enhancing the assessment and treatment of psychiatric conditions. *Ment Health Fam Med* 2010; 7: 17–25
- [17] McGinty B. Medicare's mental health coverage: How COVID-19 highlights gaps and opportunities for improvement. *Commonwealth Fund* 2020 [cited 2022 Mar 13] <https://www.commonwealthfund.org/publications/issue-briefs/2020/jul/medicare-mental-health-coverage-covid-19-gaps-opportunities>
- [18] Cosgrove L, Krinsky S. A comparison of DSM-IV and DSM-5 panel members' financial associations with industry: A pernicious problem persists. *PLoS Med* 2012; 9: e1001190
- [19] Sirdifield C, Anthierens S, Creupelandt H et al. General practitioners' experiences and perceptions of benzodiazepine prescribing: Systematic review and meta-synthesis. *BMC Fam Pract* 2013; 14: 191
- [20] Data Analysis Brief: Medicare-Medicaid dual enrollment 2006 through 2018. CMS Medicare-Medicaid Coordination Office. 2019 [cited 2022 Mar 13] <https://www.cms.gov/Medicare-Medicaid-Coordination/Medicare-and-Medicaid-Coordination/Medicare-Medicaid-Coordination-Office/DataStatisticalResources/Downloads/MedicareMedicaidDualEnrollmentEverEnrolledTrendsDataBrief2006-2018.pdf>
- [21] NHPCO Facts and Figures. National Hospice and Palliative Care Organization. 2020 [cited 2022 Mar 13] <https://www.nhpco.org/hospice-facts-figures/>
- [22] Hojlund M, Gudmundsson LS, Anderson JH et al. Use of benzodiazepines and benzodiazepine-related drugs in the Nordic countries between 2000 and 2020. *Basic Clin Pharmacol Toxicol* 2022; 32: 60–70. DOI: <https://doi.org/10.1111/bcpt.13811>
- [23] Sateia MJ, Buysse DJ, Krystal AD et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: An American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med* 2017; 13: 307–349