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

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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 $GABA_A$ α_1 subunit, zopiclone and eszopiclone
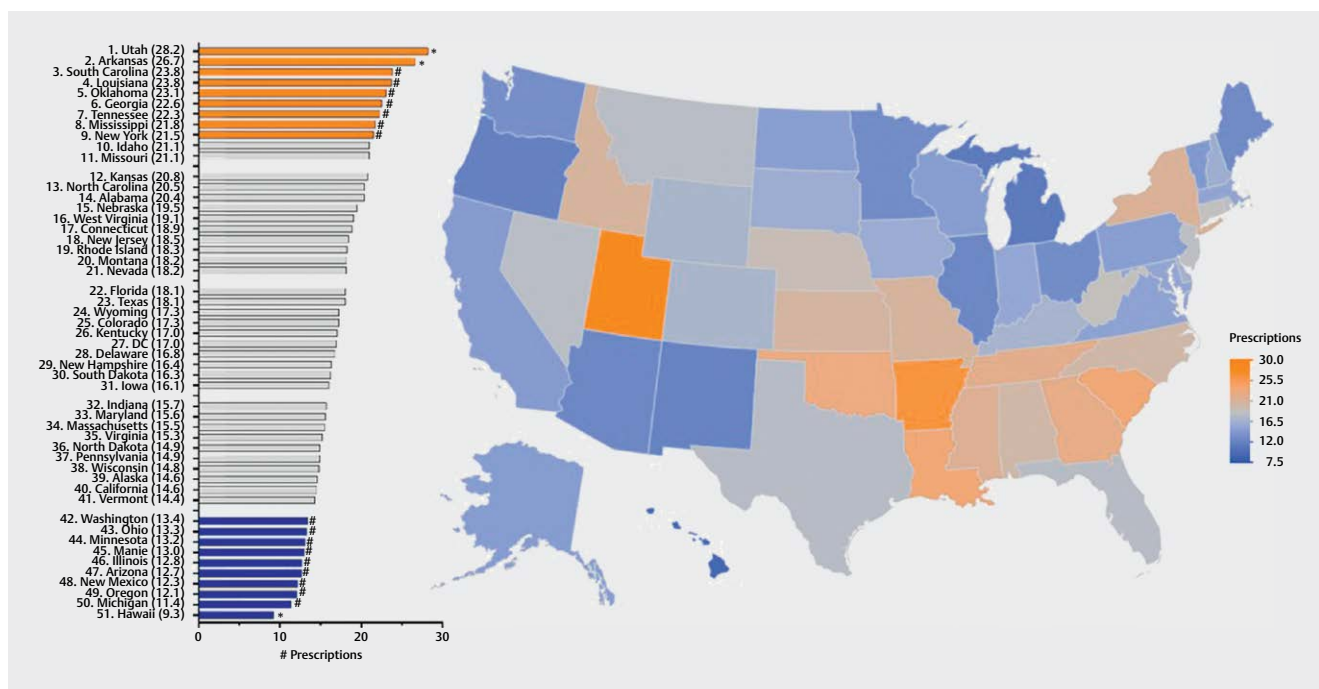
► **Fig. 1** Z-drug prescriptions per 100 Medicare enrollees ranked by state. States with a * were > 1.96 SD and # were > 1.50 SD.

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, Intermez-

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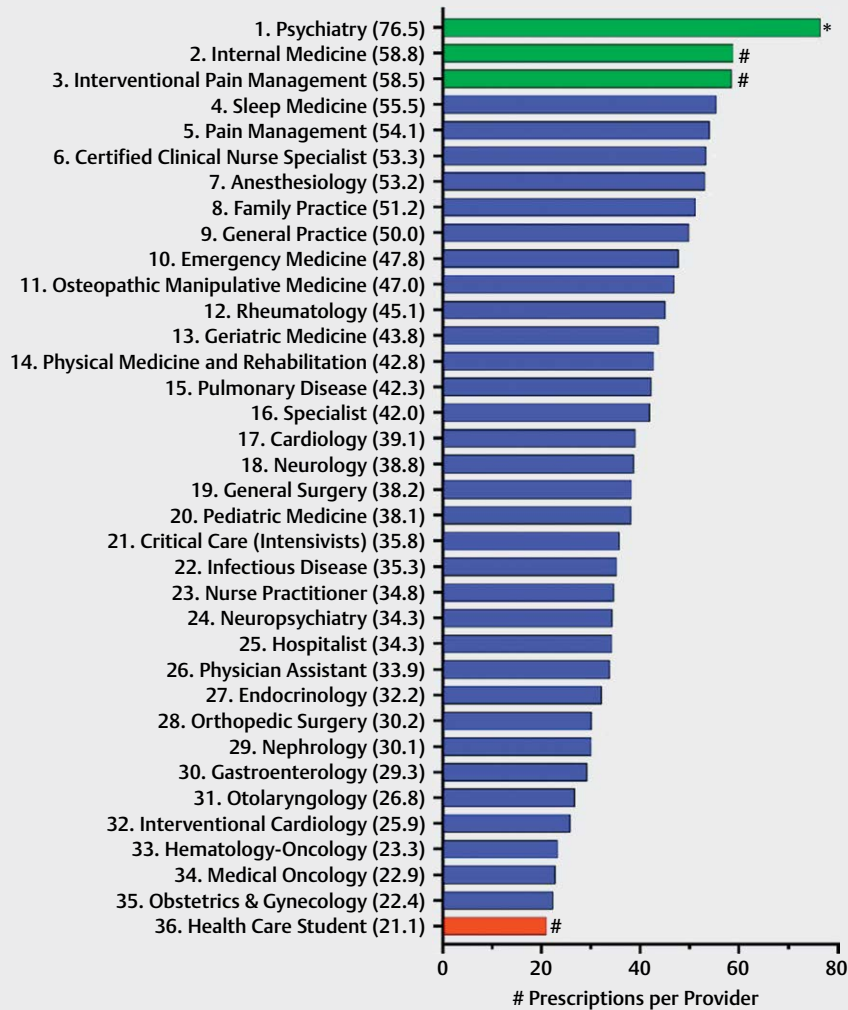
▶ **Fig. 2** Z-drug prescriptions by specialty to Medicare patients in 2018. * were > 1.96 SD and # were > 1.50 SD.

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.

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