

Original Investigation

Benzodiazepine Use in the United States

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IMPORTANCE Although concern exists regarding the rate of benzodiazepine use, especially long-term use by older adults, little information is available concerning patterns of benzodiazepine use in the United States.

OBJECTIVE To describe benzodiazepine prescription patterns in the United States focusing on patient age and duration of use.

DESIGN, SETTING, AND PARTICIPANTS A retrospective descriptive analysis of benzodiazepine prescriptions was performed with the 2008 LifeLink LRx Longitudinal Prescription database (IMS Health Inc), which includes approximately 60% of all retail pharmacies in the United States. Denominators were adjusted to generalize estimates to the US population.

MAIN OUTCOMES AND MEASURES The percentage of adults filling 1 or more benzodiazepine prescriptions during the study year by sex and age group (18-35 years, 36-50 years, 51-64 years, and 65-80 years) and among individuals receiving benzodiazepines, the corresponding percentages with long-term (≥ 120 days) benzodiazepine use, prescription of a long-acting benzodiazepine, and benzodiazepine prescriptions from a psychiatrist.

RESULTS In 2008, approximately 5.2% of US adults aged 18 to 80 years used benzodiazepines. The percentage who used benzodiazepines increased with age from 2.6% (18-35 years) to 5.4% (36-50 years) to 7.4% (51-64 years) to 8.7% (65-80 years). Benzodiazepine use was nearly twice as prevalent in women as men. The proportion of benzodiazepine use that was long term increased with age from 14.7% (18-35 years) to 31.4% (65-80 years), while the proportion that received a benzodiazepine prescription from a psychiatrist decreased with age from 15.0% (18-35 years) to 5.7% (65-80 years). In all age groups, roughly one-quarter of individuals receiving benzodiazepine involved long-acting benzodiazepine use.

CONCLUSIONS AND RELEVANCE Despite cautions concerning risks associated with long-term benzodiazepine use, especially in older patients, long-term benzodiazepine use remains common in this age group. More vigorous clinical interventions supporting judicious benzodiazepine use may be needed to decrease rates of long-term benzodiazepine use in older adults.

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Benzodiazepines are widely used in the treatment of anxiety and sleep problems.¹⁻³ The efficacy of benzodiazepines surpasses placebos in controlling a range of anxiety symptoms^{4,5} and reducing the onset of sleep latency.⁶ Although practice guidelines recommend newer antidepressants in place of benzodiazepines as first-line treatments for anxiety disorders,⁷ there is no evidence for the superior short-term efficacy of antidepressants for anxiety disorders.⁸ Moreover, practice guidelines recommend that initial approaches to the management of primary insomnia should include behavioral interventions,^{9,10} although behavioral interventions and benzodiazepines yield similar short-term sleep-related outcomes.¹¹

When benzodiazepines are used for extended periods of time, they may lead to problems associated with discontinuation and withdrawal symptoms^{12,13} and abuse.¹⁴ In 2008, there were approximately 272 000 emergency department visits in the United States involving nonmedical use of benzodiazepines, of which 40.0% also involved alcohol,¹⁵ which increased to approximately 426 000 visits in 2011, of which 24.2% also involved alcohol.¹⁶ Among older individuals, medical benzodiazepine use poses risks of serious adverse effects including impaired cognitive functioning,¹⁷ reduced mobility and driving skills,^{18,19} and increased risks of falls.²⁰ Research further indicates that the risks of falls is greater for benzodiazepines.

epines with a longer rather than shorter half-life,^{21,22} although results have been inconsistent.²³

In response to these risks, several guidelines and expert consensus statements have cautioned against benzodiazepine use for longer periods, especially in older populations.²⁴⁻²⁸ To evaluate the extent to which such cautions have been heeded in community practice, it is informative to examine benzodiazepine-prescribing patterns in the general population. A greater understanding of national benzodiazepine-prescribing patterns may help to focus the quality of care initiatives on groups at high risk of potentially inappropriate use.

Benzodiazepines are one of the most commonly prescribed classes of psychotropic medications in developed countries. In Europe and Canada, higher rates of benzodiazepine use have been reported for women compared with men and in older compared with younger adults.^{29,30} Several studies have further found that primary care physicians rather than psychiatrists write most of the benzodiazepine prescriptions^{31,32} and that a substantial proportion of benzodiazepine use is long term.^{2,33,34} In British Columbia, Canada, an estimated 8.4% of the population used a benzodiazepine in 2006 with 3.5% filling benzodiazepine prescriptions totaling in an excess of 100 days of supply.² Yet, surprisingly little is known about benzodiazepine-prescribing patterns in the United States. Prior research on benzodiazepine use in the United States has been largely limited to specific treatment settings,³⁵ payers,³⁶ age groups,³⁷ or crude prescription counts.^{38,39} For example, in 2007, there were approximately 85 million benzodiazepine prescriptions written in the United States to outpatients with mood and anxiety disorders,³⁸ which was not significantly changed from the 90 million written in 2001.³⁹

In the current report, we provide the first estimates, to our knowledge, of the annual prevalence of benzodiazepine use in the United States and examine variation in rates of benzodiazepine use by age. Within age groups, we further assess patterns of long-term benzodiazepine use, prescription of long-acting benzodiazepines, and the specialty of the prescribing physician.

Methods

We conducted a population-level retrospective observational study of benzodiazepine use in the United States with data from the LifeLink LRx Longitudinal Prescription database (IMS Health Inc) and the Medical Expenditure Panel Survey.⁴⁰ The LifeLink data contained deidentified individual prescriptions from approximately 33 000 retailers. The data covered approximately 60% of all retail prescriptions in the United States and are representative by sex, age, and insurance coverage. The LifeLink LRx Longitudinal Prescription database has been used extensively to examine patterns of prescription drug use.⁴¹⁻⁴³ These analyses, which relied exclusively on deidentified data, were exempt from consent by the institutional review board of the New York State Psychiatric Institute.

From IMS Health, we obtained all prescriptions written for benzodiazepines in 2008 by sex and age, as well as the total

population covered by the data set by sex and age. Only individuals filling a prescription at a retail outlet were captured in the LifeLink database. With data from IMS, we calculated rates of benzodiazepine use by age and sex among persons 18 to 80 years of age who filled at least 1 prescription for any medication between January 1, 2008, and December 31, 2008. To generalize our prevalence estimates to the entire population, including individuals who did not fill a prescription during the study, we adjusted the denominators using data from the Medical Expenditure Panel Survey. We used Medical Expenditure Panel Survey data on the percentage of the population by age and sex who reported that they did not fill a prescription medication in 2008 to adjust the population denominator to include persons who did not fill a prescription. This adjustment permitted estimation of benzodiazepine use by age and sex among all 18- to 80-year-olds in the United States. The demographic composition of the IMS population that filled at least 1 prescription of any kind closely resembled the composition of the corresponding population from the nationally representative Medical Expenditure Panel Survey.

In addition to the age and sex of the patient, the LifeLink data included the medication for which the prescription was written, days of supply, and specialty of the prescriber. Using this information, we calculated the total days of supply for each individual who filled 1 or more benzodiazepine prescriptions during the course of 2008 and examined the percentage of benzodiazepine users who filled prescriptions with a total of 120 days of supply or greater per year (long-term use).⁴⁴ We calculated the percentage of patients using long-acting benzodiazepines by classifying prescriptions into short- and long-acting formulations based on the Ashton Manual (eAppendix in the Supplement).⁴⁵ Nonbenzodiazepine hypnotics, such as zaleplon, zopiclone, eszopiclone, and zolpidem, were not included in the analysis. We then stratified these analyses by the specialty of the physician writing the prescription to assess whether patterns of benzodiazepine use differed among patients prescribed benzodiazepines by psychiatrists and all other providers.

Results

Overall Use of Benzodiazepines

Among adults 18 to 80 years of age, 5.2% (11 491 677 of 219 799 647) of the sample filled at least 1 prescription for a benzodiazepine in 2008. The IMS study population received approximately 46.9 million benzodiazepine prescriptions in 2008, which translates into roughly 75 million benzodiazepine prescriptions nationally. The rate of use was higher among women than men and increased steadily with age (Table 1). Among older adults aged 65 to 80 years, 6.1% of men and 10.8% of women used benzodiazepines. The highest rate of use (11.9%) was observed among 80-year-old women (Figure).

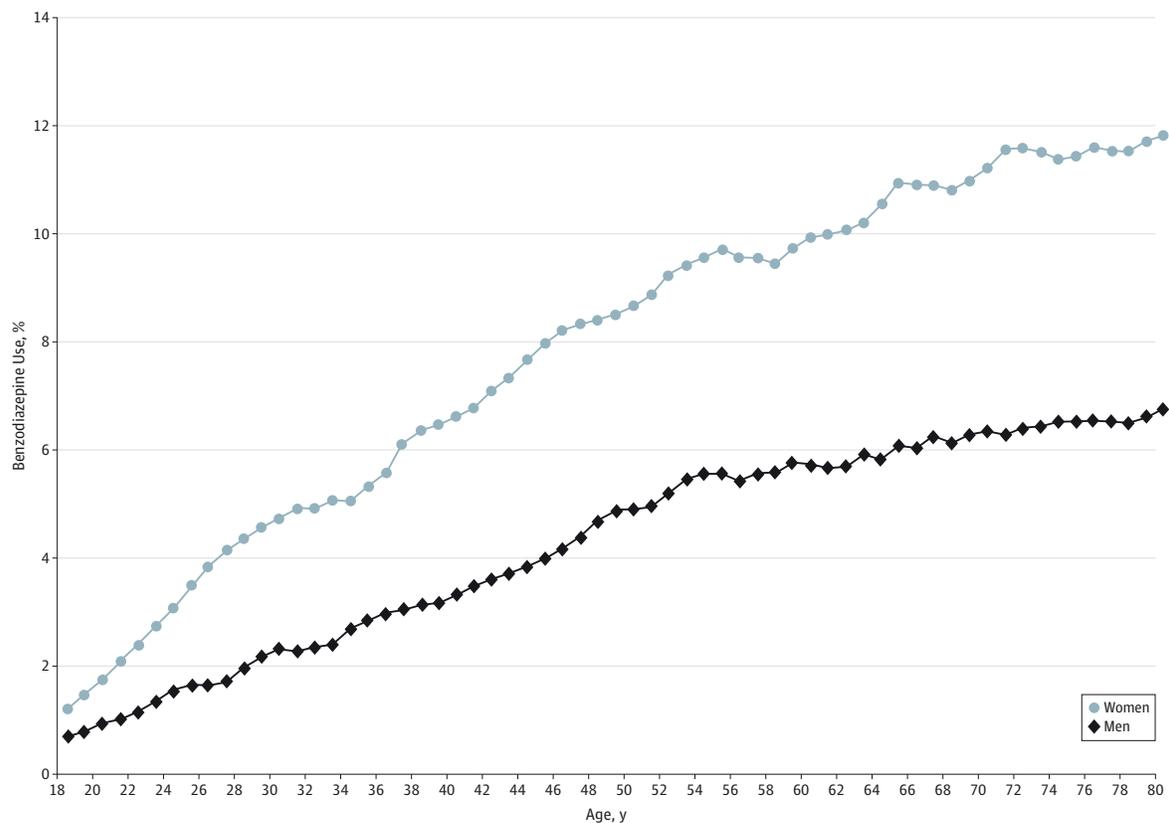
At all ages and across both sexes, a great majority of benzodiazepines were prescribed by nonpsychiatrist prescribers. The percentage of benzodiazepine users who received 1 or more prescriptions from a psychiatrist declined with age and was lowest among older adults aged 65 to 80 years (5.7%), with similar patterns for men (5.3%) and women (5.9%).

Table 1. Prevalence of Any Benzodiazepine Use, Long-term Benzodiazepine Use, and Use of Long-Acting Benzodiazepines by Sex and Age Group in the United States in 2008^a

Variable	Mean age, y, %			
	18-35	36-50	51-64	65-80
US Population				
With any benzodiazepine use, y	2.6	5.4	7.4	8.7
Among men	1.7	3.7	5.3	6.1
Among women	3.6	7.1	9.2	10.8
Among Persons With Any Benzodiazepine Use				
With long-term benzodiazepine use ^b	14.7	22.4	28.0	31.4
Among men	15.6	22.8	28.4	28.8
Among women	14.2	22.2	27.8	32.6
With any long-acting benzodiazepine use, y	24.1	25.4	25.4	23.8
Among men	26.9	29.5	29.4	27.1
Among women	22.7	23.3	23.4	22.4

^a The data source was 2008 LifeLink Information Assets-LRx Longitudinal Prescription Database, 2008 (IMS Health Inc).

^b Long-term use defined as 120 days' or more supply of benzodiazepine during 2008.

Figure. Percentage of Population in the United States in 2008 With Any Benzodiazepine Use by Sex and Age

The data source was 2008 IMS LifeLink Information Assets-LRx Longitudinal Prescription Database (IMS Health Inc).

Long-term Use of Benzodiazepines

Long-term use of benzodiazepines, defined as filling at least 120 days of supply during the study year, steadily increased with age. The percentage of persons in the United States with long-term benzodiazepine use increased from 0.4% (18-35 years of age) to 2.7% (65-80 years of age).

The age-related increase in long-term benzodiazepine use was driven by the joint effects of an aged-related increase in the rate of any benzodiazepine use and an age-related increase in the proportion of benzodiazepine use that was long term. Specifically, the percentage of benzodiazepine use that was long term steadily increased with age from 14.7% of young

Table 2. Prescriptions From Psychiatrists Among Persons With Any Benzodiazepine Use, Long-term Benzodiazepine Use, and Use of Long-Acting Benzodiazepines by Sex and Age Group in the United States in 2008^a

Variable	Mean age, y, %			
	18-35	36-50	51-64	65-80
Among Persons With Any Benzodiazepine Use				
With at least 1 prescription from psychiatrist	15.0	12.8	11.3	5.7
Among men	15.1	12.4	10.8	5.3
Among women	14.9	13.1	11.5	5.9
Among Persons With Long-term Benzodiazepine Use^b				
With at least 1 prescription from psychiatrist	32.6	25.0	20.4	9.8
Among men	31.9	23.5	19.0	9.4
Among women	33.0	25.8	21.1	10.0
Among Persons With Long-Acting Benzodiazepine Use				
With at least 1 prescription from psychiatrist	6.2	6.8	7.0	3.6
Among men	6.4	6.5	6.6	3.2
Among women	6.0	7.0	7.2	3.9
Among Persons With Long-Acting Benzodiazepine Use and at Least 1 Prescription From a Psychiatrist				
With long-term benzodiazepine use ^b	33.5	44.8	50.9	53.5
Among men	33.3	44.1	51.1	50.6
Among women	33.7	45.2	50.8	54.8

^a The data source was 2008 LifeLink Information Assets-LRx Longitudinal Prescription Database (IMS Health Inc).

^b Long-term use defined as 120 days' or more supply of benzodiazepines during 2008.

adult benzodiazepine users to 31.4% of older adult benzodiazepine users (Table 1). Similar trends were observed in men and women.

Most individuals with long-term benzodiazepine use received all of their benzodiazepine prescriptions from nonpsychiatrist prescribers. The percentage of long-term benzodiazepine users who received 1 or more prescriptions from psychiatrists declined with age from approximately one-third (32.6%) among young adults to 1 in 10 (9.8%) of older adults, with little variation between the sexes (Table 2).

In post hoc analyses, the mean (SD) duration of long-term benzodiazepine treatment episodes (≥ 120 days) within the study year was 224.9 (70.9) days for adults aged 18 to 35 years, 237.3 (73.5) for adults aged 36 to 50 years, 244.1 (74.4) for adults aged 51 to 64 years, and 245.4 (74.4) for adults aged 65 to 80 years.

Use of Long-Acting Benzodiazepines

A majority of patients filling benzodiazepine prescriptions received short-acting benzodiazepines. Among individuals who filled prescriptions for benzodiazepines, there was little variation in the percentage with use of long-acting benzodiazepines, ranging from 23.8% for adults aged 65 to 80 years to 25.4% for adults aged 36 to 64 years. Men were more likely than women to use long-acting formulations (Table 2).

In all age and sex groups, fewer than 1 in 10 individuals using long-acting benzodiazepines received a prescription from a psychiatrist. Older adult benzodiazepine users aged 65 to 80 years were especially unlikely to receive a prescription from a psychiatrist (3.6%). However, among those who used long-acting benzodiazepines who did receive a prescription from a psychiatrist, benzodiazepine use was commonly long term. In this group, the percentage with long-term use increased with age from 33.5% of younger adults to 53.5% of older adults (Table 2).

Discussion

Benzodiazepine use is common in the United States. Roughly 1 in 20 US adults filled a benzodiazepine prescription during the course of a year. Consistent with patterns observed in Canada and Europe, use of benzodiazepines in the United States is substantially higher among women than men and increases with age.^{1,30,33} Despite benzodiazepine-related risks of falls,⁴⁶ fractures,^{20,47} and motor vehicle crashes in older people, benzodiazepine use was approximately 3 times more prevalent in older than younger adults. Among benzodiazepine users, there is also an age-related increase in long-term use, which may pose added risks of fractures,^{20,49} subtle cognitive decline,⁵⁰ and benzodiazepine dependence.⁵¹ Although most nonmedical use of benzodiazepines and other anxiolytics occurs among people who have not received a prescription, individuals who receive anxiolytic prescriptions are, nevertheless, at increased risk of nonmedical anxiolytic use as well as lifetime drug abuse and dependence.⁵²

Among older adults who are treated with benzodiazepines, nearly one-third use benzodiazepines on a long-term basis. Roughly 9 of 10 older adults who use benzodiazepines on a long-term basis have their prescriptions written exclusively by primary care physicians or other nonpsychiatrists. Although we were unable to determine from the prescription data the clinical reasons why benzodiazepines are prescribed to older adults, previous research suggests that insomnia and anxiety play important roles. In 1 study of older adult primary care patients, insomnia (42%) and anxiety (36%) were the most common indications for new benzodiazepine prescriptions.⁵³ Insomnia and anxiety also predict initiation^{54,55} and continuation⁵⁶ of benzodiazepine use among older adults.

The prevalence of insomnia increases with age.⁵⁷ However, clinical guidelines recommend that benzodiazepines and

other hypnotics should only be used on a short-term basis for severe and impairing insomnia and only initiated following careful consideration of nonpharmacological options, such as sleep hygiene, stimulus control, and relaxation.⁵⁸ Yet, consistent with high rates of benzodiazepine use in older patients, most physicians do not view continuous use of benzodiazepines by older adults as a public health problem⁵⁹ and perceive these medications to be more effective than simple nonpharmacological approaches for insomnia.^{60,61}

Benzodiazepines are also often initiated for the treatment of anxiety.^{3,53} Unlike insomnia, which increases with age often related to poor health, depressed mood, and respiratory symptoms,⁵⁵ the prevalence of anxiety disorders tends to decline in later life.⁶² Therefore, age-related differences in rates of anxiety complaints are unlikely to explain the higher rate of benzodiazepine use in older adults compared with younger adults. In prior work, benzodiazepine use has been linked to older patient age after controlling for anxiety symptoms and several other health-related characteristics.⁵⁴ In practice, benzodiazepines are also commonly prescribed in combination with antidepressants to patients with sleep disturbances or anxiety related to depression.⁶³ Adding a benzodiazepine to an antidepressant tends to lower treatment dropout owing to adverse effects during the first few weeks of treatment of adult major depression.⁶⁴

Across age groups and sexes, approximately one-quarter of adults prescribed benzodiazepines in the United States receive long-acting agents. This proportion is consistent with a recent study of benzodiazepine use among older adults in Quebec, Canada, that reported 24.3% of benzodiazepine users received long-acting drugs.⁶⁵ Long-acting benzodiazepines may pose particular risks in older people, related to their extended period of action^{27,66} and age-related changes in their pharmacokinetics and pharmacodynamics.¹⁹

Research from Belgium⁶⁷ and the Netherlands⁶⁸ suggests that clinical differences exist in the reasons that benzodiazepines are prescribed to men and women. In the United States, men are proportionately more likely than women to receive long-acting agents that may be preferred for anxiety while the reverse is true of short-acting agents that may be preferred for insomnia.⁶⁹ Whether sex differences in the relative likelihood of receiving long- and short-acting agents reflect underlying sex differences in clinical targets of benzodiazepines awaits research on the clinical indications of community benzodiazepine-prescribing practices.

Several factors may contribute to the observed high rates of long-term benzodiazepine use in older adults. These factors may include treatment of persistent anxiety disorders; deficits in specialized knowledge concerning benzodiazepine prescribing risks in geriatric care⁷⁰; limited access to alternative effective evidence-based treatments, such as cognitive behavioral therapy for insomnia^{71,72}; an unwillingness of some older people to consider reducing or discontinuing benzodiazepines⁷³; and competing clinical demands on physician time related to the other physical health needs of their patients.

This analysis had several limitations. First, the IMS prescription data measured purchased medicines rather than medication use. Second, no data were available on the clinical indi-

cations of the benzodiazepines, the clinical characteristics of the benzodiazepine users, or the clinical appropriateness of benzodiazepine use. A greater understanding of the clinical reasons for benzodiazepine use in community practice, especially long-term use by older patients, would help to focus quality improvement initiatives. Third, although the population denominator was adjusted for the percentage of the population by age and sex who reported not filling a prescription medication in the study year, it was not possible to estimate the precision of the derived estimates. Fourth, because the data set was confined to a single year, we were unable to estimate the duration of benzodiazepine treatment episodes within the year that were initiated before or terminated after the study year. However, the long mean duration of long-term episodes suggested that many such episodes extended beyond 1 year. Finally, the data were based on 2008 dispensing patterns and since that time community benzodiazepine-prescribing practices may have changed in response to increasing use of zolpidem, which became generic in 2007, as well as the availability of other nonbenzodiazepine hypnotics, although no new benzodiazepines have been approved by the US Food and Drug Administration since the data were collected. The risk of fracture associated with zolpidem in the elderly population has been reported to exceed the risks associated with no hypnotic treatment⁷⁴ and the risks with either lorazepam or alprazolam.⁷⁵ In nonelderly adults, zolpidem has been linked to an increased risk of major injuries⁷⁶ while zolpidem and zopiclone have been reported to confer a risk of motor vehicle crashes that resembles the risk associated with some benzodiazepines.⁷⁷

Concerns about the potentially negative consequences of benzodiazepine use, particularly long-term use in the elderly population, have been highlighted in several consensus statements and guidelines. Given the divergence between clinical practice and expert opinion, guidelines urging cautious prescribing to older patients appear to be independently insufficient to reduce long-term use in older people to levels in younger adults. Although many primary care physicians are aware of practice guidelines that caution against long-term benzodiazepine use in the elderly population, few believe that this practice poses a serious clinical threat and many physicians feel unprepared to address the issue with their patients.⁷³ One means of reducing long-term benzodiazepine use in older patients involves investing in clinically effective strategies, such as multifaceted clinical interventions that combine clinical education and medication review.⁷⁸ Minimal strategies that involve consultation focused on clinical reassessment of benzodiazepine benefits and harms may also reduce long-term benzodiazepine use in primary care.⁷⁹

Conclusions

For withdrawing older individuals from benzodiazepines, an effective intervention involves gradual supervised benzodiazepine withdrawal combined with psychotherapy focused on coping with dependency symptoms and underlying psychiatric symptoms.⁷⁸ However, in many practice settings, pragmatic considerations may necessitate starting with less intensive interventions, such as letter or email communications to

patients or clinical consultations advising patients on how to gradually and safely reduce or stop benzodiazepine use.⁷⁹ Physicians should also be cognizant of the legal liability risks associated with inappropriate benzodiazepine prescription.⁸⁰ Un-

less greater clinical attention is devoted to reducing long-term use of benzodiazepines by older primary care patients in the United States, this practice and its attendant risks are likely to increase as the population ages during the coming years.

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