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OUTCOME OF NEW BENZODIAZEPINE PRESCRIPTIONS TO OLDER ADULTS IN PRIMARY CARE

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Abstract

Objective—Examine the indications, baseline characteristics, duration of use, and clinical outcomes for older primary care patients prescribed benzodiazepines.

Methods—Computerized records were used to identify outpatients (n=129) aged 60 or over receiving new benzodiazepine prescriptions from primary care physicians of a group-model managed care organization. A baseline telephone survey assessed indication for prescription, sleep quality (Pittsburgh Sleep Quality Index), depression (Symptom Checklist depression scale and Structured Clinical Interview for DSM-IV), alcohol use (CAGE), and functional status (SF-36). A two-month follow-up survey assessed benzodiazepine use, sleep quality, and depression.

Results—The most common indications for prescription were insomnia (42%) and anxiety (36%). At baseline, participants reported moderate sleep disturbance (mean Pittsburgh Sleep Index = 9.3, st. dev. 4.0), only 15% met criteria for current depressive episode, and only 3% reported at-risk alcohol use. After two months, 30% were using benzodiazepines at least daily. Both those continuing daily use and those not continuing reported significant improvements in sleep quality and depression, with no difference between groups in rate of improvement.

Conclusions—Initial benzodiazepine prescriptions to older adults are typically intended for treatment of anxiety or insomnia, with little evidence for occult depression or alcohol abuse. A significant minority develop a pattern of long term use, raising concerns about tolerance and dependence.

Keywords

benzodiazepine; sleep; anxiety; hypnotic; epidemiology

Prescription of benzodiazepines to elderly patients is one area in which common practice appears to diverge from expert opinion.

Expert guidelines and reviews typically urge caution when prescribing benzodiazepines to older adults^{1,2}, with greatest concerns regarding long-term use. Epidemiologic studies find that benzodiazepine use is associated with increased risk of falls and injuries^{3–5}, cognitive decline^{6,7}, and functional decline leading to institutionalization⁸. Concerns have also been raised regarding over-prescription of benzodiazepines to older adults with depressive disorders^{9,10}.

Despite these concerns, epidemiologic data^{11–13} indicate that benzodiazepines are among the drugs most commonly prescribed to older adults. Among community-dwelling older adults,

10–30% report using a benzodiazepine at any given time, with approximately half of those being long-term users.

This divergence between expert opinion and everyday practice raises questions regarding indications for benzodiazepine use, the clinical characteristics of users, and factors associated with progression to long-term use. Data regarding these questions are limited, as previous research has often relied on computerized pharmacy records or cross-sectional surveys.

Here we use data from a cohort of older primary care patients receiving a new prescription for a benzodiazepine to examine perceived indications for the initial prescription, clinical characteristics at time of prescription, and predictors of continued use two months later.

METHODS

The study was conducted between 2001 and 2002 at staff-model clinics of Group Health Cooperative, a prepaid health plan serving approximately 450,000 members in western Washington state. Most members are covered through employer-purchased plans, but the enrollment at the time of this study included approximately 45,000 Medicare members and 35,000 members covered by Medicaid or by Washington's Basic Health Plan (a state program for low-income residents). Group Health members are similar to Seattle area residents except for higher educational level and less representation of high-income residents¹⁴. Previous research in the Group Health population found that approximately 8% of members aged 65 and older used any benzodiazepine over a 6-month period and approximately 2.5% used a benzodiazepine daily for 60 days or more¹⁴.

During 2001, approximately 9% of Group Health members aged 60 and over filled any prescription for a benzodiazepine, and approximately 2.5% filled three or more prescriptions (suggesting long-term use). Of all benzodiazepine prescriptions, 77% were written by primary care physicians, 6% by psychiatrists, and 17% by physicians in other specialties. Newer hypnotic drugs (zolpidem and zaleplon) were not included in the Group Health formulary in 2001, and less than 0.4% of members aged 60 or over filled any prescription for these drugs. Older hypnotic drugs (chloral hydrate and barbiturates) were used by less than 0.1% of members over aged 60.

Each week, computerized pharmacy records were used to identify all health plan members aged 60 and older filling new prescriptions for benzodiazepines prescribed by primary care physicians (with new defined as no benzodiazepine prescription fill or refill in the prior 180 days). Primary care physicians were aware that a study of benzodiazepine use would occur, but they were not aware of the identities of specific participants or the specific dates of sampling.

An invitation letter was followed 5 days later by a telephone call to invite participation. Both the invitation letter and the telephone script included all elements of informed consent (description of study purpose and procedures, potential risks, voluntary nature of participation, procedures for confidentiality). All participants provided documented oral consent prior to enrollment. All procedures were reviewed and approved by the Group Health Cooperative Human Subjects Review Committee (Institutional Review Board).

Baseline assessments occurred a mean of 11 days after the index prescription (range 6 to 21 days). The interview included the following measures:

- The Pittsburgh Sleep Quality Index, a reliable and valid measure of sleep quality used in previous studies of general medical patients^{15 16}

- A 20-item depression severity scale extracted from the 90-item Hopkins Symptom Checklist ¹⁷
- The SF-36 functional status questionnaire ¹⁸
- The CAGE alcohol screening questionnaire and questions regarding frequency and quantity of alcohol use during the prior 3 months ¹⁹
- Additional questions regarding reasons or indications for the benzodiazepine prescription, benzodiazepine use since the index prescription, and past benzodiazepine use.

Participants were asked to rate the Sleep Quality Index and the SCL depression scale based on symptoms prior to the index prescription.

All participants were contacted for a follow-up assessment approximately two months after the initial prescription. This assessment included questions regarding benzodiazepine use as well as repeat assessments of the Pittsburgh Sleep Quality Index, Symptom Checklist depression scale, and SF-36.

Assessments were conducted by two experienced mental health interviewers, each of whom received a minimum of 12 hours of training and had at least two years experience with conduct of similar assessments ^{20,21}.

Unadjusted comparisons were made using chi-square statistics for dichotomous measures and t-tests for continuous measures. Characteristics of patients continuing and not continuing benzodiazepine use were made using logistic regression. Changes in symptoms scores over time were examined using repeated-measures analysis of variance including main effects of time, patient group (continuing daily benzodiazepine use vs. not continuing) and the interaction of group and time. All analyses were performed using SPSS statistical software (SPSS Inc., Chicago, IL).

RESULTS

Invitation letters were mailed to 200 potential participants. 17 could not be reached by telephone, and 10 were found ineligible (disenrolled from Group Health, index prescription was not a new prescription). 44 declined to participate, leaving a baseline sample of 129 (68% of those eligible).

Participants had a mean age of 73 (st. dev. 7.3) with a range of 61 to 95. 64% were female and 93% were Caucasian. Approximately half (47%, n=60) reported using a benzodiazepine at some time in the past (at least six months prior to the index prescription). Medications prescribed were temazepam in 33 cases (26%), oxazepam in 26 cases (20%), diazepam in 25 cases (19%), lorazepam in 20 cases (16%), alprazolam in 13 cases (10%), and clonazepam in 12 cases (9%).

Non-participants (those not reached and those declining to participate) did not differ from participants in mean age (74 vs. 73) or proportion female (60% vs. 64%).

Patients' reported reasons for the initial prescription are described in Table 1. Nearly 90% of participants reported either insomnia or anxiety as one of the reasons for prescription and nearly 80% reported insomnia or anxiety as the primary reason.

Table 2 displays baseline characteristics for the full sample and for subgroups with insomnia or anxiety as the primary reason for prescription. In the full sample, mean scores on the Pittsburgh Sleep Quality Index were similar to other samples of adults with moderate sleep

problems¹⁵, and mean¹⁶ SCL depression scores were in the mild range. The mean SF-36 Physical Component Summary score was approximately one standard deviation lower (i.e. poorer functioning) than the typical value for US adults, while the mean Mental Component Summary score was approximately the US population norm¹⁸. Compared to those reporting insomnia as the primary reason for prescription, those with anxiety as the primary reason were, on average, 4 years younger and reported less severe sleep disturbance.

At baseline, approximately 17% (n=22) reported that they had not used any of the index benzodiazepine prescription. More than half of those not using any medication (n=13) did so because medication didn't seem necessary. The remainder reported a variety of other reasons for not using medication. Approximately 16% of all participants (n=21) reported using medication less than daily, 52% (n=67) reported daily use, and the remaining 15% (n=19) reported benzodiazepine use more than once per day.

At baseline, approximately 15% (n=20) met criteria for current major depressive episode by SCID and an additional 16% (n=21) reported at least one past episode of major depression. Of the 20 participants who met criteria for current depressive disorder, 13 (65%) were currently using a prescribed antidepressant. No participants reported two or more positive items on the CAGE questionnaire and only 3% (n=3) reported drinking over 10 units of alcohol per week.

Of 129 participants interviewed at baseline, 124 (96%) completed the 2-month follow-up interview. Among those completing the follow-up interview, 59% (n=73) reported using no benzodiazepine during the last 2 weeks, 11% (n=14) reported use less than once per day, 25% (n=31) reported daily use, and 5% (n=6) reported use more than once per day. As an alternative measure of continued use, we used computerized refill data to identify those filling at least one prescription for a benzodiazepine between 60 and 120 days after the index prescription. This method identified 33 as ongoing users. Overall agreement between the two methods was 88% with a kappa statistic of 0.72.

Characteristics of the 37 participants reporting daily use at follow-up are compared to the remaining participants in Table 3. Those continuing daily use did not differ from remaining participants in any of the baseline demographic or clinical characteristics examined. In a logistic regression model predicting daily use at follow-up, none of the baseline characteristics listed in Table 3 were significant predictors ($p > .11$ for all).

Of the 37 participants continuing to use benzodiazepines daily, 18 (49%) reported discussing benzodiazepine use with the prescribing physician at some point between the initial prescription and the follow-up interview. Of the 87 participants not reporting daily use at follow-up, 33 (38%) reported discussing benzodiazepine use with the prescribing physician after the initial prescription.

Figures 1 and 2 compare sleep and depression scores at baseline and follow-up for participants who continued to use benzodiazepines daily and those who did not. For Pittsburgh Sleep Index scores, analysis of variance indicated significant decrease over time ($F=32.0$, $df=1$, $p<.001$) and no significant difference between groups in rate of decrease ($F=1.79$, $df=1$, $p=.18$). For SCL depression scores, analysis of variance indicated significant decrease over time ($F=3.91$, $df=1$, $p=.001$) and no significant difference between groups in rate of decrease ($F=0.12$, $df=1$, $p=.72$).

DISCUSSION

These findings provide some reassurance regarding initial prescription of benzodiazepines to older adults in primary care. First, the most common indications were insomnia and anxiety (where a benzodiazepine is potentially appropriate and efficacious) rather than depression.

Second, the proportion of patients with an alcohol use disorder or untreated depressive disorder (where a benzodiazepine prescription might be inappropriate or contraindicated) was small.

Limited data are available regarding the probability that an initial benzodiazepine prescription will lead to long-term use. Our previous research¹⁴ using pharmacy refill records estimated that 10% of adults receiving an initial prescription appeared to use benzodiazepines daily for at least 60 days. The strongest predictors of continued use were older age and a larger number of pills dispensed in the initial prescription. In this study, 30% of older adults receiving a new prescription reported daily use two months later. The higher rate of ongoing use in this study probably reflects both different patient populations (older adults vs. all adults) and measurement methods (patient report vs. refill records).

Those reporting daily benzodiazepine use described significant improvements in sleep quality over two months. We cannot determine whether this change represents benefits of benzodiazepine use or the natural history of insomnia complaints in older primary care patients. Those not continuing benzodiazepines reported a similar rate of improvement. After two months, approximately half of those continuing regular benzodiazepine use had Pittsburgh Sleep Index scores of 8 or more, suggesting clinically significant sleep disturbance.

We lack detailed data regarding patients' and physicians' decisions to continue or discontinue benzodiazepine use. Approximately half of those continuing benzodiazepine use reported some discussion with the prescribing physician. We cannot determine how often benzodiazepine refills were requested and how often those requests were approved or denied. Our data do suggest, however, that decisions regarding continuing or discontinuing benzodiazepine use are often made by patients absent any specific discussion with the prescribing physician.

By design, this study did not include patients who were already long-term users of benzodiazepines. We also cannot say what proportion of patients who reported daily use after 2 months would continue in a pattern of regular use. Our previous research suggests that approximately 7% of patients receiving an initial prescription continue regular use for 6 months or more¹⁴. Among those using medication daily at 60 days, the majority continued for 180 days or more. Long-term users were more often male and older than age 65.

These data were collected in a single prepaid health plan, and we cannot determine how these findings might generalize to other patient populations or health systems. Rates of benzodiazepine use in this health system may be somewhat lower than prevailing rates in the US or Western Europe¹⁴. Previous research in the Group Health population does suggest low rates of inappropriate benzodiazepine use (e.g. prescription of benzodiazepines as primary treatment of depression)²¹.

Interpretation of these findings should consider some additional limitations. Baseline assessments were conducted approximately two weeks following the index prescription. Assessments focused on depression, sleep disturbance and alcohol use disorders with no detailed assessment of anxiety disorder or personality disorder. One-third of those eligible did not participate, and non-participants may differ in clinical characteristics or probability of continued benzodiazepine use.

We observe an overall picture that includes some reassurance and some remaining causes for concern. Initial benzodiazepine prescriptions are typically intended for treatment of anxiety or insomnia, with little evidence for occult depression or alcohol abuse. For most older adults treated with benzodiazepines, use is episodic rather than chronic. Approximately 50% report prior use and only 30% continue regular use longer than two months. A significant minority, however, develop a pattern of long term use, raising concerns about tolerance and dependence.

Efforts to reduce inappropriate use of benzodiazepines might focus on decreasing the transition to long-term use rather than on preventing initial prescriptions.

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Figure 1.

Course of insomnia and depression symptoms in patients continuing and not continuing daily use of benzodiazepines

Table 1

Patient-reported reasons for initial benzodiazepine prescriptions.

	All Reported Reasons	Primary Reason
Insomnia	68 (53%)	54 (42%)
Anxiety	52 (40%)	46 (36%)
Depression	8 (6%)	2 (2%)
Pain	25 (19%)	14 (11%)
Other	18 (14%)	13 (10%)

Table 2

Baseline characteristics according to primary indication for prescription

	Total Sample(n=129)	Primary Indication of Insomnia(n=54)	Primary Indication of Anxiety(n=46)	Test Statistic(Insomnia Group vs. Anxiety Group)
Mean Age (st dev)	73 (7)	75 (7)	71 (7)	T=2.93, df=98, p=.004
% Female (number)	64% (83)	54% (20)	68% (59)	X ² =2.13, df=1, p=.14
Mean Pittsburgh Sleep Quality Index (st dev)	9.3 (4.0)	10.9 (4.0)	8.0 (3.5)	T=3.69, df=98, p<.001
Mean SCL Depression Score (st dev)	0.84 (0.60)	0.94 (0.64)	0.83 (0.60)	T=0.93, df=98, p=.35
Mean SF-36 Mental Component (st dev)	49 (12)	50 (13)	47 (11)	T=1.72, df=98, p=.09
Mean SF-36 Physical Component (st dev)	39 (13)	39 (14)	43 (13)	T=1.43, df=98, p=.16

Table 3

Baseline characteristics of participants who did and did not report daily use of a benzodiazepine at follow-up

	Daily Use(n=37)	Less Than Daily Use(n=87)	Test Statistic
Mean Age (st dev)	72 (7)	74 (7)	T=1.19, df=122, p=.23
% Female (number)	54% (20)	68% (59)	$X^2=2.13$, df=1, p=.14
Mean Pittsburgh Sleep Quality Index (st dev)	10.2 (3.9)	8.9 (4.0)	T=1.60, df=122, p=.11
Mean SCL Depression Score (st dev)	0.93 (0.70)	0.80 (0.56)	T=1.11, df=122, p=.27
Mean SF-36 Mental Component (st dev)	50 (12)	49 (12)	T=0.59, df=122, p=.56
Mean SF-36 Physical Component (st dev)	38 (14)	40 (13)	T=0.85, df=122, p=.40
% with Current Major Depression (number)	16% (6)	14% (12)	$X^2=0.12$, df=1, p=.73
% with Lifetime Major Depression (number)	32% (12)	31% (27)	$X^2=0.24$, df=1, p=.88
% with prior benzodiazepine use (number)	55% (20)	44% (38)	$X^2=1.44$, df=1, p=.23
% with insomnia as main indication (number)	51% (19)	40% (33)	$X^2=1.92$, df=1, p=.16