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## Design, Implementation, and Evaluation of a Pharmacist-Led Outpatient Benzodiazepine Tapering Clinic

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### Abstract

**Background**—Benzodiazepines are commonly used among older adults, despite well-known risks. Clinical pharmacists can lead tapering efforts, leveraging their clinical expertise and relieving time-pressured primary care providers.

**Objectives**—The objective is to describe the design, implementation, and evaluation of an outpatient pharmacist-led benzodiazepine tapering clinic.

**Practice Description**—The clinic is based within a community medical group associated with a large academic health system in Los Angeles, California.

**Practice Innovation**—The clinic is staffed by clinical pharmacists and supervised by a psychiatrist. The initial visit consists of patient education, design of patient-driven tapering schedule, and medical history review. Follow-up phone/video visits are used to monitor withdrawal symptoms and provide support.

**Evaluation Methods**—We used chart review to assess tapering status among those enrolled in the tapering clinic versus those who did not enroll. We compared outcomes across the two groups using bivariate statistics.

**Results**—From March 2017- May 2019, 176 patients were referred to the clinic; 17 were deemed ineligible. Of the 159 patients contacted, 62 patients enrolled in the clinic; 97 patients

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Author contributions

Conceptualization: Drs. Gregorian, Bradley, Campbell, Mashburn and Keller conceptualized the study.

Data curation: Drs. Gregorian, Bradley, and Beuttler curated the data.

Formal analysis: Drs. Beuttler and Keller analyzed the data.

Methodology: Drs. Gregorian, Bradley, Campbell, Mashburn, and Beuttler, and Keller conceptualized the methodology.

Roles/Writing - original draft: Drs. Gregorian, Bradley, Campbell, Mashburn and Keller all contributed to the original draft.

Writing - review & editing: Drs. Gregorian, Bradley, Campbell, Mashburn and Keller edited and revised the paper.

**Conflicts of interest:** Dr. Gregorian was employed at the Cedars-Sinai Medical Care Foundation at the time of the study and is now employed at AstraZeneca.

did not enroll. Among patients in the clinic, 13 (27%) of patients were tapered down, 29 (60%) completely tapered off, 6 (13%) were unable to taper, and 14 (23%) were in the process of tapering. In contrast, among patients who did not enroll, 3 (4%) of patients were tapered down, 15 (20%) completely tapered off, 57 (76%) were unable to taper, and 22 (22%) were in the process of tapering. 90% of patients had at least some benzodiazepine tapering when enrolled in the clinic compared to 41% among not enrolled in the clinic ( $p<0.001$ ).

**Conclusion**—A pharmacist-led benzodiazepine tapering clinic can be an effective way to engage patients motivated to taper down. Lessons learned include the importance of ensuring referring providers adequately counsel patients prior to referral.

### Keywords

Benzodiazepines; tapering; deprescribing; quality improvement

## BACKGROUND

Benzodiazepines comprise a widely prescribed class of medications for insomnia, anxiety, seizure disorders, sleep-related movement disorders/parasomnias, tic disorders, and chronic back pain. More than 5% of U.S. adults are prescribed benzodiazepines, with use among 50–64-year-olds (12.9%) now exceeding that of older adults 65 years old (8.6%).<sup>[1, 2]</sup> Among older adults treated with benzodiazepines, almost one-third are long-term users.<sup>[3]</sup> The majority of long-term benzodiazepines prescriptions are from non-psychiatrists, accounting for 90% of older adults taking BZDs.<sup>[3]</sup> Misuse, defined as taking benzodiazepines differently than prescribed or taking non-prescribed benzodiazepines, accounts for nearly 20% of use overall, with benzodiazepine misuse as prevalent as use-as-prescribed among 18–25-year-olds.<sup>[2]</sup>

While effective for short-term use, benzodiazepines have no clear evidence-based indication or benefit for long-term use while serious risks are well understood.<sup>[4]</sup> These risks include sedation and risk of overdose; drowsiness and lethargy contributing to falls; impairment of psychomotor skills, judgment and coordination increasing risk of accidents; cognitive and memory impairment; depression and emotional blunting; physiologic dependence and abuse potential; interactions with other medications; and the potential for withdrawal.<sup>[5, 6]</sup> Guidelines for benzodiazepines detail optimal use of 2–4 weeks (two weeks for a hypnotic, four weeks for an anxiolytic),<sup>[7]</sup> but prescriptions are often prolonged because of the development of dependence and prescription inertia. The American Geriatrics Society and other physician societies regards benzodiazepines as medications that should be avoided in older adults or for long-term use.<sup>[8–10]</sup>

For providers who wish to taper benzodiazepines, little evidence exists about the optimal approach.<sup>[5]</sup> Accepted general taper principles exist for long-term use and include gradual dose reduction rather than abrupt discontinuation, monitoring for withdrawal symptoms (which can manifest both physically and psychologically), and adjusting the taper rate based on individual patient response and experience.<sup>[11, 12]</sup> Tapering requires careful attention, frequent patient education and reassurance, and regular follow-up to monitor for withdrawal and to make appropriate adjustments. Supportive interventions such as providing

anticipatory guidance about potential withdrawal symptoms, giving encouragement, and reinforcing alternative strategies for stress management and sleep are helpful both before and during tapering.<sup>[6, 12]</sup> This approach can be time-consuming and may stretch beyond the comfort zone of some primary care providers. Indeed, many providers may be reluctant to taper based on perceived and actual patient resistance, time, and effort to taper, and a lack of knowledge about how to treat withdrawal symptoms and the reappearance of the very symptoms initially leading to the benzodiazepine prescription.<sup>[13]</sup>

## OBJECTIVE

With this background, in 2017, leadership at the Cedars Sinai Medical Care Foundation (CSMCF), the outpatient arm of the Cedars-Sinai Health System (CSHS) in Los Angeles, California, implemented an outpatient, pharmacist-led benzodiazepine tapering clinic. The work was driven by a recognition that while the system had begun to address opioid prescribing, there had been less attention paid to benzodiazepine prescribing. We published a study focused on opioid prescribing in primary care at CSHS from 2012–2017 finding that, among patients with chronic opioid use, the predicted probability of an opioid prescribed along with a benzodiazepine in the same primary care visit for patients with low back pain was 24%.<sup>[14]</sup> Thus, the objective of the tapering clinic was to (a) increase benzodiazepine deprescribing in the health system, and (b) relieve the pressure of deprescribing from time-pressured primary care physicians. The objective of this paper is to detail the design, implementation, and evaluation of the clinic, with a focus on lessons learned.

## PRACTICE DESCRIPTION

CSMCF contains multiple medical groups. The largest is a multi-specialty group, Cedars-Sinai Medical Group, which has more than 250 physicians, including approximately 90 primary care providers. The benzodiazepine taper clinic is housed in the same suite as the pain management and mental health services teams. Patients are predominantly insured through Medicare (37%) and commercial insurance (40%).

## PRACTICE INNOVATION

The pharmacist-led benzodiazepine tapering clinic is a referral-based clinic and operates under a Collaborative Practice Agreement (CPA). As defined by the Centers for Disease Control and Prevention, a CPA is a “formal agreement in which a licensed provider makes a diagnosis, supervises patient care, and refers patients to a pharmacist under a protocol that allows the pharmacist to perform specific patient care functions.”<sup>[15]</sup> The clinical pharmacists staffing the benzodiazepine tapering clinic completed advanced post-graduate residency training, had backgrounds in pain management and/or mental health, and completed motivational interviewing training. The benzodiazepine clinic was initially staffed by one clinical pharmacist for a total of .25 full-time equivalents (FTEs) and supervised by a board-certified psychiatrist. The number of clinical pharmacists has since increased to two for a total of 1 FTE.

The majority of referrals to the clinic were made from primary care physicians, outpatient pain management physicians, or geriatricians; referrals were reviewed by clinic pharmacists for appropriateness and eligibility before scheduling. Patient service representatives scheduled the patient's first appointment and clinical pharmacists scheduled subsequent appointments. Patient service representatives attempted to reach patients three times by phone. A letter was sent to the patient's recorded home address before deeming the patient uninterested in the clinic. Pharmacists bill incident to the supervising physician's license (CPT code 99211).

### Patient Eligibility Criteria

Patients were eligible for referral to the clinic if they were prescribed benzodiazepines long-term (e.g., in excess of 2–4 weeks) (Figure 1). There were no dose or medication exclusions. For example, patients on very low doses or taking medications on an “as needed” basis were welcome to enroll in the clinic. There were also no exclusions based on the length of long-term use, i.e., patients who had been on these medications for months or years were welcome to enroll. Patients were deemed ineligible for the clinic for the following reasons: <18 years of age, active substance use disorder, active pregnancy, history of seizures, and history of moderate-to-severe benzodiazepine withdrawal (including hypertension, moderate/severe anxiety and insomnia, delirium, seizures). Patients with opioid prescriptions  $\geq 80$  morphine milligram equivalent daily dose were reviewed and deemed eligible for the pharmacist clinic by the mental health medical director (a supervising psychiatrist overseeing the clinic) or the chronic pain medical director (supervising anesthesiologist).

### Intervention

During the initial 60-minute visit, clinical pharmacists reviewed the patient's reason for benzodiazepine use (i.e., the indication) and the patient's past medical history, specifically regarding anxiety, panic disorders, depression, seizure disorders, and substance use disorders. The clinical pharmacist also conducted a thorough medication history focusing on the history of benzodiazepine use, including the types of benzodiazepines used, the dose, and the duration of use. The clinical pharmacist also reviewed the patient's history of using alternative treatment options for the indication (pharmacologic and nonpharmacologic).

Activities during the initial visit included:

- reviewing the risks of benzodiazepines and potential withdrawal symptoms associated with sudden discontinuation of benzodiazepines;
- highlighting the rationale for tapering benzodiazepines;
- developing and discussing a tapering schedule for reducing benzodiazepines; checking baseline vital signs; conducting a urine drug screen;
- reviewing the California prescription drug monitoring program database; discussing the risks associated with concurrent benzodiazepine use with alcohol, marijuana, other substances, and opioids;
- providing a prescription and education for naloxone if the patient has a concurrent opioid; and establishing follow-up visit timelines.

Patients were also asked to sign a Controlled Substances Agreement (see Appendix 1), which outlined responsibilities for patients and their clinicians.

During follow-up 30-minute visits, which typically occurred over the phone or via videoconferencing, clinical pharmacists completed the following activities:

- assessed adherence to the benzodiazepine tapering schedule;
- reviewed any changes to the patient's medications or medical history/condition pertinent to the therapy;
- assessed for withdrawal symptoms associated with tapering of benzodiazepine using the Benzodiazepine Withdrawal Symptom Questionnaire;
- discussed and initiated adjunct medication(s) for insomnia or anxiety (e.g., gabapentin, mirtazapine, selective serotonin reuptake inhibitors) to aid with withdrawal symptoms as appropriate based on indication for benzodiazepine;
- and discussed current alcohol, marijuana, opioids, and other substance use.

In-person visits took place in a private exam room, part of a physician practice including clinical support staff available to perform urine drug testing and vitals. Pharmacists also had access to a private room for telephone visits.

### Tapering protocol

The overarching goal was to set a patient-driven tapering schedule. Tapering schedules were aimed to taper no faster than a 10%–25% dose reduction every 1–2 weeks, or at the pharmacists' discretion. When one-quarter to one-half of the daily dose was reached, pharmacists could slow the taper to a 5% dose decrease every 2–4 weeks. If patients encountered a difficult life event or experienced any withdrawal symptoms, tapering was slowed or stopped temporarily until the patient was ready to start again. Per the protocol, pharmacists had Drug Enforcement Administration and prescribing privileges for benzodiazepines and other medications (e.g., adjunctive pharmacotherapy for anxiety and insomnia).

If patients were on short-acting benzodiazepines (e.g., alprazolam, lorazepam), pharmacists could switch to long-acting benzodiazepines (e.g., clonazepam, diazepam) by reducing 25% for metabolic variance. Other adjuvant medications were introduced as needed (Table 1). Adjunctive treatments recommended included referrals to a psychologist or psychiatrist, grieving resources, sleep hygiene, and recommendations on managing anxiety. The process was designed to be very patient focused and patient centered with tapering schedule, adjuvants medications and treatment decisions made in conjunction with the patient. Although pharmacists made a concerted effort to completely taper patients off benzodiazepines, an important goal was to view any tapering as a success. Some patients were tapered down to the lowest possible dose, and when stabilized, were discharged from the program back to their primary care physician.

## EVALUATION METHODS

We collected baseline by chart review at the point of referral and captured the following information for all referred patients: age, sex, indication for benzodiazepine prescription, diazepam equivalent daily dose (DEDD), specialty of the referring provider, and concurrent opioid use. We used chart review in May 2019 to evaluate the effectiveness of the clinic. To compare outcomes, we used a comparison group of patients who were referred to the clinic but who were not seen in the clinic. We used the following definitions for tapering outcomes:

- Tapering complete: The patient stopped benzodiazepine use for at least four weeks
- Tapered down: The patient saw a reduction in DEDD 16 weeks post-referral to the clinic
- Unable to taper: The patient did not see changes in benzodiazepine use 16 weeks post-referral to the clinic
- Currently tapering: The patient was currently in the clinic at the time of data analysis

We used t-tests to compare the age of the patients across the two groups (enrolled and not enrolled in the tapering clinic). We used chi-square or Fisher's Exact tests to compare categorical variables across the two groups, including the sex of the patients, the indications for which the benzodiazepines were prescribed, whether patients had concurrently prescribed opioids, and the referral source. We calculated z-scores across the two groups for each individual categorical tapering outcome. We compared all patients with any tapering versus no tapering across the two groups. We calculated medians and the interquartile range for each group's final DEDD and used a Wilcoxon Mann-Whitney test to examine differences between the groups' DEDD.

The study was granted an exemption from the institution's Institutional Review Board. We used the revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) to report the results of this paper.

## RESULTS

From March 2017-May 2019, 176 patients were referred to the clinic; 17 were deemed ineligible. Of the 159 patients contacted, 62 patients agreed to be seen in the benzodiazepine tapering clinic and 97 patients did not respond to an invitation. Patient characteristics of patients enrolled and non-enrolled in the clinic are in Table 2.

Outcomes of patients enrolled and not enrolled in the pharmacist-led benzodiazepine tapering clinic are in Table 3. Among those seen in the benzodiazepine tapering clinic, 13 (27%) of patients were tapered down, 29 (60%) completely tapered off, 6 (13%) were unable to taper, and 14 (23%) were in the process of tapering. In contrast, among patients who did not enroll, 3 (4%) of patients were tapered down, 15 (20%) completely tapered off, 57 (76%) were unable to taper, and 22 (22%) were in the process of tapering. The



differences in proportions across three out of the four outcomes (completely tapered off benzodiazepines, tapered down benzodiazepines, unable to taper) using individual one-tailed z-tests were also statistically significant. We compared the proportions of any tapering versus no tapering across the two groups, finding that 90% of patients had at least some benzodiazepine tapering when enrolled in the clinic compared to 41% among those invited but not enrolled in the clinic ( $p < 0.001$ ).

The median DEDD of enrolled patients was 11.25 (interquartile range: 5–20) versus 10.00 among patients not enrolled (interquartile range: 5–20). The differences between the groups in final DEDD was calculated with a Wilcoxon Mann-Whitney test and found to be not statistically significant ( $p = 0.40$ ). The average time to taper down or off benzodiazepines in the clinic was 15 weeks (SD: 11.8). Only 1 adverse event (1 seizure) was reported among the 62 patients enrolled in the clinic.

## PRACTICE IMPLICATIONS

We encountered a variety of operational challenges. First, some primary care providers did not adequately explain the referral for the tapering clinic or the recommendation for tapering, which led to a range of responses, including patient no-shows, confusion about the purpose of the clinic, or hostility towards the pharmacists. Second, some patients with active substance use disorders or other significant mental health issues were inappropriately referred to the clinic. These patients were referred to other resources, including behavioral health providers when possible. Third, when patients would call the pharmacy for refills, the community pharmacy would call the doctor a refill for the higher pre-tapering benzodiazepine dose, which was subsequently refilled, slowing progress on the tapering. This required pharmacists at the clinic to call community pharmacies to ensure that refills were filled at the appropriate dose. Fourth, the national shortage of mental health providers taking insurance made it challenging for pharmacists to find mental health partners.

The implementation of this clinic demonstrates the ability of pharmacists to partner with primary care providers to support both providers and patients in tapering patients off benzodiazepines utilizing an established protocol. The success of the pharmacist-led clinic outlined in this paper can be attributed to multiple factors, including (1) physician-pharmacist communication with the patient prior to referral to the clinic, (2) the focused nature of the tapering clinic appointments, and (3) the patient-centered focus of the clinic.

The clinic gave pharmacists the ability to focus entirely on this aspect of the patient's care. During the benzodiazepine clinic appointments, pharmacists were able to focus solely on the benzodiazepines, including reasons for use of the benzodiazepines, concerns about tapering, and benzodiazepine education. The patient-centered nature of the clinic included telephone appointments to increase access, frequent follow-up visits, and patient-centered tapering schedules. An important contextual factor was the health system's existing use of pharmacists in a variety of contexts, which may have allowed patients to feel more comfortable seeing a pharmacist. The health system currently employs pharmacists for post-discharge medication management phone calls;<sup>[16]</sup> diabetes, hypertension, and statins management; a travel clinic; and specialty clinic medication management (e.g., neurology).

Existing working relationships with pharmacists may also enable physicians to feel more comfortable referring patients to a pharmacist-led clinic.

Our findings are similar to the few studies which have examined the effectiveness of pharmacist-led sedative-hypnotic deprescribing in the primary care setting. Lui *et al* describes an intervention where family physicians referred patients to a pharmacist for sedative-hypnotic deprescribing, finding that 32% achieved complete deprescribing and 32% reduced their dose by  $\geq 50\%$ .<sup>[17]</sup> To our knowledge, while stand-alone benzodiazepine tapering clinics are relatively rare, health systems have instituted deprescribing clinics for other medications. For example, Kuntz *et al* describes the establishment of an stand-alone pharmacist tapering clinic in an integrated health system for opioids.<sup>[18]</sup> Whitman *et al* describes the implementation of a pharmacist-led deprescribing intervention for older adults with cancer at a geriatric oncology clinic.<sup>[19]</sup> These interventions, in addition to our findings, underscore the potential for pharmacist-led clinics to improve medication management in a variety of settings.

Our study has some limitations. This was not a randomized controlled study, so our comparison group consists of individuals who opted not to participate in the clinic. This group of patients may have had substantial concerns about withdrawal or fears of returning symptoms and thus may have been less amenable to tapering. It is also possible that this group of patients preferred to have their medications managed by their primary care provider. Additionally, the clinic operated out of a single health system in Southern California with a predominantly insured population; other settings may see different results based on different populations.

## CONCLUSION

In conclusion, a pharmacist-led tapering clinic can help providers and patients alike achieve their goals in deprescribing benzodiazepines, and potentially reduce morbidity, mortality, and healthcare costs. Future research on such tapering clinics could include: identifying reasons why patients declined referrals, examining physician and patient satisfaction with the benzodiazepine taper clinic, identifying the most successful approaches to tapering (e.g., frequency of appointments, tapering schedules), examining the cost-effectiveness of this type of tapering clinic, and analyzing the effect of the clinic on clinical and patient-centered outcomes (e.g., falls, hospitalizations, quality of life).

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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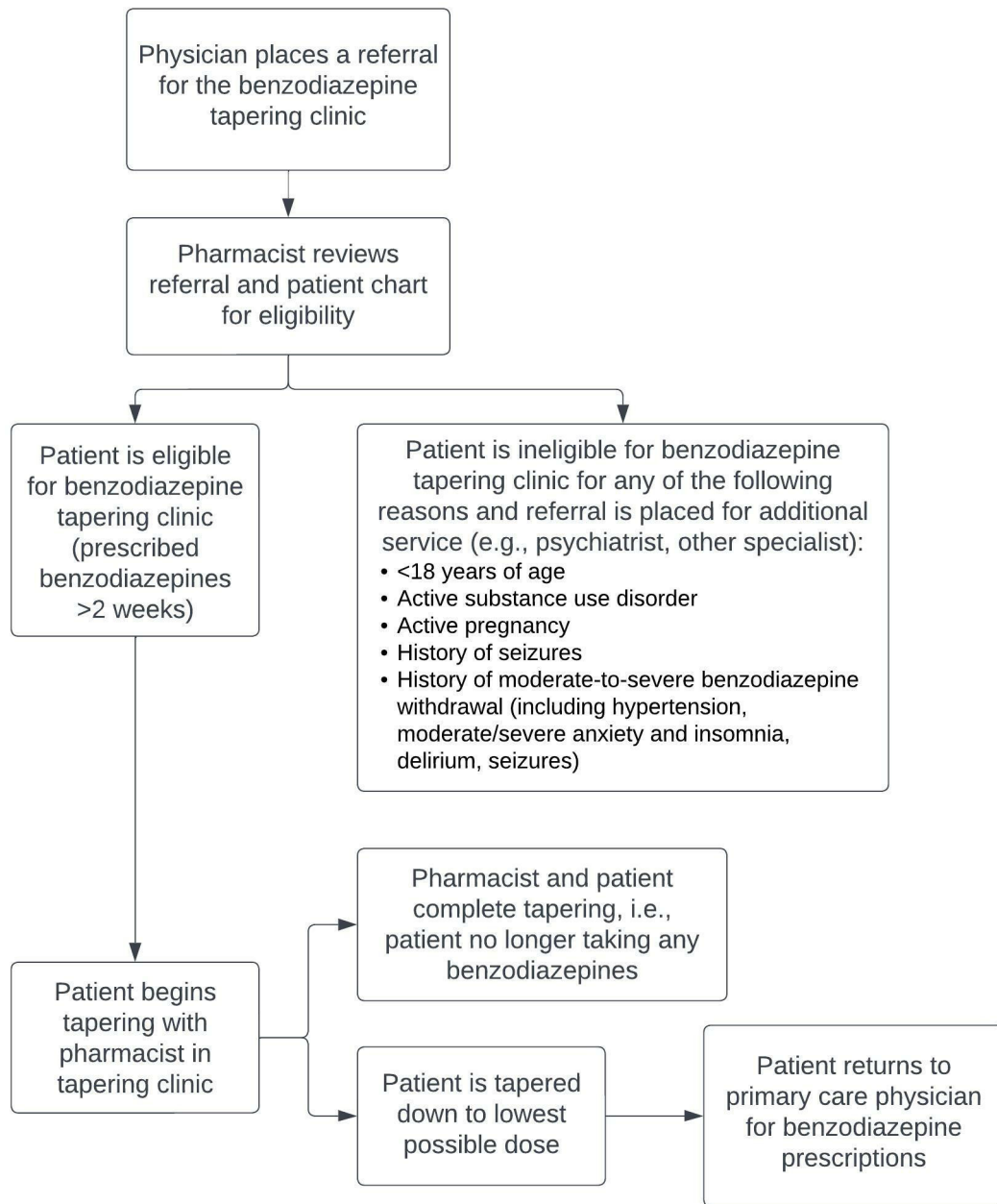
### Key points

**What was already known:**

- Tapering benzodiazepines in the primary care setting can be time-consuming and challenging
- Pharmacists can play critical roles in deprescribing benzodiazepines

**What this study adds:**

- This study highlights the structure of a pharmacist-led clinic focused on deprescribing benzodiazepines, relieving time-pressured primary care physicians
- Engaging primary care physicians in appropriate referrals is critical to the success of deprescribing benzodiazepines in a pharmacist-led clinic setting
- Among patients in the benzodiazepine tapering clinic, 27% of patients had a dose reduction, 60% completely tapered off, 13% were unable to taper, and 23% were in the process of tapering.



**Figure 1.**  
Benzodiazepine clinic referral workflow.

**Table 1.**

Adjunctive medications employed in the benzodiazepine tapering clinic

Indication for benzodiazepine prescription	Adjunctive medications to consider
Insomnia	Trazodone Doxepin Ramelteon Mirtazapine Tricyclic antidepressants Gabapentin/Pregabalin
Anxiety	SSRI/SNRI or other antidepressants with evidence of effectiveness for anxiety at usual doses Gabapentin /Pregabalin Hydroxyzine Buspirone

Note: SSRI: Selective serotonin reuptake inhibitor; SNRI: Selective norepinephrine reuptake inhibitor

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**Table 2.**

Patient characteristics of patients enrolled and not enrolled in the outpatient pharmacist-led benzodiazepine tapering clinic

Patient characteristic	Enrolled in the benzodiazepine tapering clinic, N=62	Invited but not enrolled in the benzodiazepine tapering clinic, N=97	P-value
Age, mean (SD)	61 (17.5)	61 (18.1)	0.80
Female, n (%)	38 (61%)	68 (71%)	0.23
<b>Indication, n (%)</b>			<0.001
Anxiety only	23 (37%)	41 (42%)	
Insomnia only	20 (32%)	22 (23%)	
Anxiety and insomnia	18 (29%)	3 (3%)	
Other/unknown	1 (2%)	31 (32%)	
<b>Concurrent opioid use</b>			0.11
Yes	15 (24%)	32 (33%)	
No	47 (76%)	55 (57%)	
<b>Referral source</b>			0.30
Primary care physician	54 (87%)	90 (93%)	
Pain specialist	1 (2%)	0 (0%)	
Geriatrician	7 (11%)	7 (7%)	

Notes: SD: standard deviation. We used a t-test to compare the mean age across the two groups and chi-square/Fisher's Exact tests to compare sex, indication, concurrent opioid use, and referral source.

**Table 3.**

Outcomes of patients enrolled and not enrolled in the outpatient pharmacist-led benzodiazepine tapering clinic

<b>Benzodiazepine outcomes</b>	<b>Enrolled in the benzodiazepine tapering clinic, N=62</b>	<b>Invited but not enrolled in the benzodiazepine tapering clinic, N=97</b>	<b>P-value</b>
<b>Benzodiazepine tapering status</b>			
Completely tapered off benzodiazepines	13 (27%)	3 (4%)	<0.001
Tapered down benzodiazepines	29 (60%)	15 (20%)	<0.001
Unable to taper	6 (13%)	57 (76%)	<0.001
Currently tapering	14 (23%)	22 (23%)	0.50
Any tapering	56 (90%)	40 (41%)	<0.001
<b>Final DEDD, Median (Interquartile range)</b>	11.25 (5.00–20.00)	10.00 (5.00–20.00)	0.40

Note: DEDD: diazepam equivalent daily dose. SD: standard deviation. Tapering complete: The patient stopped benzodiazepine use for at least four weeks. Tapered down: The patient saw a reduction in DEDD 16 weeks post-referral to the clinic. Unable to taper: The patient did not see changes in benzodiazepine use 16 weeks post-referral to the clinic. Currently tapering: The patient was currently in the clinic at the time of data analysis. We used a Wilcoxon Mann-Whitney test to compare final DEDD. We used one-tailed z-tests to compare the benzodiazepine tapering outcomes across the two groups.