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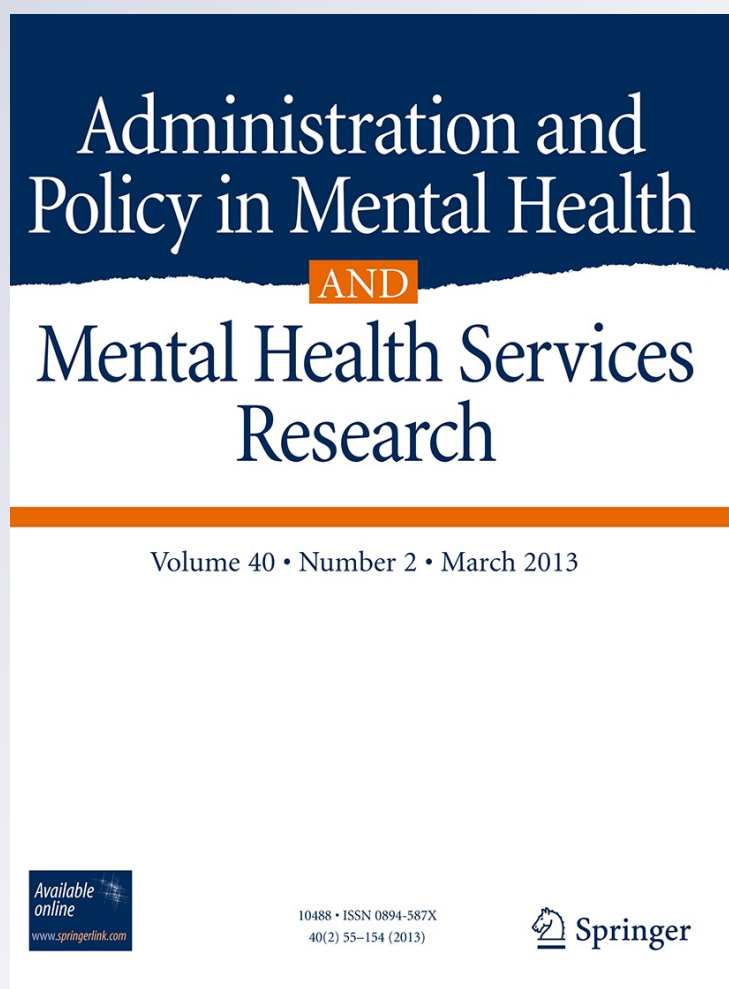
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# Patients' and Physicians' Characteristics Associated with the Purchase of Benzodiazepines by Older Primary Care Patients in Israel

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**Abstract** This study evaluated patients' and physicians' characteristics associated with the purchase of benzodiazepines by older primary care patients in Israel. The analytic sample consists of those 6,421 patients age 65 and older. We used multi-level analysis with whether or not benzodiazepines were purchased at least once between June 2005 and 2007 as an outcome. We also evaluated patients' and physicians' characteristics associated with the purchase of benzodiazepines for 6 months or longer. Almost half the sample (41.5%) purchased benzodiazepines at least once during the study period and more than half (54.5%) of those purchasing benzodiazepines had a continued purchase for 6 months or longer. Physicians' characteristics explained only a small portion of the variance associated with purchasing, whereas patients'

demographic and clinical characteristics were associated with purchasing. Any intervention to improve the use of benzodiazepines should be directed at both patients and physicians.

**Keywords** Epidemiology · Older adults · Geriatrics · Depression · Anxiety · Mental illness · Primary care

## Introduction

Benzodiazepines are among the most commonly used psychotropic medications prescribed in primary care (Benitez et al. 2008; Pinsker and Suljaga-Petchel 1984). The use of benzodiazepines is particularly common in older adults and may be partially attributed to the high prevalence of sleep problems in old age (Glass et al. 2005). This is despite ample evidence to link benzodiazepines with increased risk for falls (Ray et al. 2000), impaired sleep (Béland et al. 2011), cognitive deterioration (Curran et al. 2003; Pinsker and Suljaga-Petchel 1984), and even car accidents (Hemmelgarn et al. 1997). Long-term use is particularly counter indicated because of the risk for dependency and tolerance (Gregory and Evette 2006).

The majority of research, to date, has focused on patient-level variables associated with the use of benzodiazepines, with the most consistent variables being female gender (Alvarenga et al. 2008) and older age (Benitez et al. 2008). Researchers found that older adults in particular tend to report psychological dependence, to overestimate the benefits associated with these drugs, and to undermine physical dependence (Cook et al. 2007).

To date, little attention has been given to physician-level characteristics that may be associated with the prescription and use of benzodiazepines. The few studies conducted

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have focused on physicians' attitudes and beliefs concerning benzodiazepines. These studies found that similar to patients, physicians overestimate the advantages of these drugs and undermine potential side-effects (Cook et al. 2007). Other studies have shown that physicians who have graduated many years ago, general practitioners, and those practicing in long term care settings are more likely to prescribe long-acting benzodiazepines (Monette et al. 1997). Others found that psychiatrists and female physicians are less inclined to prescribe benzodiazepines (Järbrink et al. 1999).

In contrast to past research, the present study evaluates simultaneously both patients' and physicians' characteristics that are potentially associated with the purchase of benzodiazepines in older primary care patients in Israel. We rely on a comprehensive computerized medical registry of the Clalit Health Services, the largest health care fund in Israel that insures 53% of the Israeli population. Under the Israeli system, the primary care provider is considered responsible for all patient health care needs. The provider is responsible for the care of a defined number of patients and refers patients for consultants as needed. Based on expert recommendations, the primary care provider determines patients' treatment. The database includes purchasing data and, thus, enables a distinctive analysis of the actual purchasing of patients instead of relying on self-reports, which have known limitations in particular regarding sensitive issues (Sallis and Saelens 2000). Important to note that Israel employs a universal health care system, providing a comprehensive uniform basket of services, which includes psychotropic medications, but not psychotherapy (Shirom and Gross 2002). Hence, we evaluate purchasing patterns in a way that is independent of financial considerations at the patient-level, but not at the managed care organization-level. Based on past research, we expected gender and age to be associated with increased purchase of benzodiazepines as well as with continued purchase for 6 months or longer. We also expected patients of physicians with a specialty and patients of younger physicians to be less likely to purchase benzodiazepines.

## Methods

We randomly sampled 30,000 primary care patients over the age of 22 as of January, 2006 from Clalit Health Services' computerized medical registry. This study is based on a secondary analysis of those 6,421 patients 65 and over. These patients were listed with 1,261 physicians, working in 707 clinics all over the country. The sample consisted of primarily women (58%). The average age of the sample was 73.6 (SD = 6.6). Physicians were primarily female (53%), born in Russia or East Europe (52%), with a specialty in family medicine (50%). See Table 1.

## Measures

The Clalit Health Services employs a computerized medical registry that contains both patient and physician data. All physician visits are recorded in this registry and are matched with pharmacy data using patients' and physicians' unique IDs, available to all Israelis.

*Purchase of Benzodiazepines.* We extracted data regarding whether or not benzodiazepines (e.g., clonazepam, diazepam, lorazepam, oxazepam) were purchased for at least once between 2005 and 2007. If benzodiazepines were purchased by a patient at least once during this period, we also checked whether they were purchased for 6 months or longer.

### Patient-level Predictors

*Demographic Information* Date of birth, gender, birth country, and number of years in Israel are listed in the registry based on patients' reports during their first visit.

*The Charlson Comorbidity Index (CCI)* This comorbidity score reflects both the number and seriousness of medical conditions in order to predict mortality (Charlson et al. 1987). This score is calculated by Clalit Health Services' medical division for all primary care patients adjusted for their age.

*Sleep Diagnosis* Having a medical record diagnosis of insomnia or fatigue was classified as sleep diagnosis.

*Psychiatric Diagnosis* Mood disorders, anxiety disorders, adjustment disorders, and somatoform disorders were included under this category, using the International Classification of Disease (ICD-10) codes. We excluded post-traumatic stress disorder, obsessive compulsive disorder, bipolar disorder, and body dysmorphic disorder as our aim was to focus on psychiatric conditions that are within the mandate of Clalit's primary care physicians (Goldfracht et al. 2006), rather than psychiatrists.

*Socioeconomic Status (SES)* SES (low, medium, high) was based on the Israeli Central Bureau of Statistics (CBS) classification (Central Bureau of Statistics 2003). Although these data are available at the primary care clinic level and not at the patient-level, data are considered a good proxy of patients' SES (Gross et al. 2009). The vast majority of patients are registered in neighborhood clinics and, thus, the SES of clinics reflects that of the patients' place of residence.

*Population Group* Individuals were classified as Arabs or Jews based on the Clalit Health Services' classification of primary care clinics into locations that serve at least 70%

**Table 1** Sample characteristics by whether or not benzodiazepines were purchased at least once

	Total (6,421)	No benzodiazepines (3,753)	Benzodiazepines (2,668)	Chi-square/ <i>t</i> -test	<i>P</i>
<i>Patient characteristics</i>					
Gender				98.9	<0.001
Female	3,716 (57.9%)	1,978 (52.7%)	1,738 (65.1%)		
Age	73.6 (6.6)	71.8 (5.4)	76.1 (6.9)	−14.4	<0.001
				278.4	<0.001
<i>Population group</i>					
Jews born in Israel	747 (11.6%)	495 (13.5%)	252 (9.7%)		
Arabs	406 (6.3%)	341 (9.3%)	65 (2.5%)		
Jews born in Russia, East Europe	2,371 (36.9%)	1,128 (30.7%)	1,243 (47.9%)		
Jews born in Europe or America	442 (6.9%)	235 (6.4%)	207 (8.0%)		
Jews born in Asia or Africa	2,301 (35.8%)	1,474 (40.1%)	827 (31.9%)		
Years in Israel				0.11	0.06
≤ 10	249 (3.9%)	158 (4.2%)	91 (3.4%)		
Charlson	4.9 (2.2)	4.5 (2.1)	5.4 (2.3)	−16.8	<0.001
Sleep diagnosis	865 (13.5%)	365 (9.7%)	500 (18.7%)	108.7	<0.001
Psychiatric diagnosis	341 (5.3%)	74 (2.0%)	267 (10.0%)	200.2	<0.001
Socioeconomic status				20.5	<0.001
Low	2,267 (35.3%)	1403 (37.1%)	864 (32.6%)		
Medium	2,768 (43.1%)	1,588 (42.7%)	1,180 (44.5%)		
High	1,341 (20.9%)	732 (19.7%)	609 (23.9%)		
<i>Physician characteristics (1,262)</i>					
Gender					
Female	673 (53.3%)				
Age	49.6 (7.3)				
<i>Birth country</i>					
Israel	447 (35.4%)				
Russia, East Europe	651 (52.1%)				
Europe or the U.S.	115 (9.2%)				
Number of years in Israel	31.9 (15.7)				
Number of years of experience	16.0 (7.8)				
<i>Specialty</i>					
None	446 (43.3%)				
Family	636 (50.4%)				
Other	79 (6.3%)				

Israeli Jews vs. Israeli Arabs. Although these data are available at the primary care clinic level, they are considered a good proxy of patient's ethnicity, given Israel's highly segregated nature (Falah 1996).

*Physician-level Predictors*

Physicians' age, gender, place of birth, number of years in the country, number of years of experience, and expertise (none, family, other) were available from employee records.

*Analysis* We first conducted univariate and bivariate analyses. Next, we conducted multilevel analysis, with

patient-level data representing the first level of predictors (e.g., patients' age, gender, SES) and physician-level data (e.g., physicians' age, gender, number of years in the country) representing the second level of predictors. The outcome variables were: (a) whether or not a patient purchased benzodiazepines at least once between June 2005 and 2007; and (b) if purchased at least once, whether purchased for 6 months or longer.

The first step of a multi-level analysis employs an empty model with physician random effect. This model estimates the outcome per physician, rather than per patient. Such an analysis yields an Intraclass Correlation (ICC) score. ICC reflects the degree to which patients of the same physician

are more similar to one another than patients of other physicians. Thus, it reflects the proportion of the total variance that is due to differences between physicians. ICC ranges between 0 and 1. If the ICC is relatively large, a multi-level analysis is justified. On the other hand, if the ICC is relatively low, a multi-level analysis is unjustified, and analysis should take into consideration only patient level variables (i.e., level 1). As a rule of thumb, ICC of 0.05, 0.10, and 0.15 represent small, medium, and large effect sizes, respectively (Hox 2002). This analysis was conducted using HLM 6.08.

Given the binary nature of the outcome, we used the linear threshold model to calculate ICC (Snijders and Bosker 1999). Following the calculation of ICC (which was 3.9%), logistic analysis was conducted with the purchase of benzodiazepines, as an outcome. Only significant ( $P < 0.05$ ) patient-level predictors identified in bivariate analyses were entered into the model.

In an additional analysis, we conducted multi-level analysis to evaluate patient- and physician-level predictors associated with the purchase of benzodiazepines for 6 months or longer. The ICC was less than 1%. Hence, we conducted a logistic analysis with significant patient-level variables identified in bivariate analyses ( $P < 0.05$ ) as potential predictors. These analyses were conducted using STATA Intercooled 8.

## Results

Almost half the sample (2,668; 41.5%) purchased benzodiazepines at least once between June 2005 and 2007. Because physician characteristics explained only a minor percentage of the variations associated with benzodiazepine purchase (3.9%), they were not included in further analyses. In bivariate analyses, those purchasing benzodiazepines were more likely to be older, female, and to be born in Russia, Europe or America and less likely to be Arabs or Jews born in Israel, Asia or Africa. They had a higher Charlson score and were more likely to have a sleep or psychiatric diagnosis, and to be of higher socioeconomic status. See Table 1.

Multivariate logistic regression revealed that females, older adults, and those with a higher Charlson score were more likely to purchase benzodiazepines at least once within the study period. Those with a psychiatric or sleep diagnosis were also more likely to purchase benzodiazepines at least once. Relative to Israeli Jews, Israeli Arabs were less likely to purchase benzodiazepines and Jews born in Russia, Europe or America were more likely to purchase benzodiazepines. Finally, those of high socioeconomic status also were more likely to purchase benzodiazepines. See Table 2.

**Table 2** Logistic regression with patient-level variables as predictors and whether or not patient purchased benzodiazepines as an outcome

	OR	95%CI
<i>Patient characteristics</i>		
Gender		
Female	1.65	1.48–1.85
Age	1.02	1.01–1.02
Population group		
Jews born in Israel	–	–
Arabs	0.38	0.27–0.53
Jews born in Russia, East Europe	1.70	1.41–2.06
Jews born in Europe or America	1.32	1.02–1.71
Jews born in Asia or Africa	0.92	0.76–1.11
Charlson	1.17	1.14–1.21
Sleep diagnosis	1.77	1.51–2.08
Psychiatric diagnosis	4.29	3.25–5.67
Socioeconomic status		
Low	–	–
Medium	1.09	0.96–1.23
High	1.20	1.02–1.41

LRchi<sup>2</sup>[11] = 861.5,  $P < 0.001$

In an additional analysis, we evaluated the characteristics of those who purchased benzodiazepines for 6 months or longer vs. those who purchased benzodiazepines for less than 6 months. Of the 2,668 patients over the age of 65, who purchased benzodiazepines at least once within the study period, 1,455 (54.5%) purchased the medications for 6 months or longer. Because physician characteristics explained only a minor percentage of the variations associated with benzodiazepine purchase for 6 months or longer (1%), they were not included in the analysis. In bivariate analyses, those purchasing the medications for 6 months or longer were more likely to be female, older, have a higher Charlson score and a psychiatric diagnosis. In addition, they were more likely to be Jews born in Russia, Europe or America and less likely to be Jews born in Israel, Asia or Africa or Israeli Arabs. See Table 3.

Table 4 summarizes results of multivariate logistic analysis. Those purchasing benzodiazepines for 6 months or longer were more likely to be female, older, and to have a psychiatric diagnosis. Relative to Jews born in Israel, Israeli Arabs were less likely to purchase benzodiazepines and Jews born in Russia, Europe or America were more likely to purchase benzodiazepines.

## Discussion

Clinical guidelines are cautious about the use of benzodiazepines with older adults and recommend a brief course of

**Table 3** Sample characteristics of those purchasing benzodiazepines for less than 6 months vs. those purchasing benzodiazepines for 6 months or longer

	Purchase <6 (1,213)	Purchase >=6(1,455)	Chi-square/ t-test	P
<i>Patient characteristics</i>				
Gender			10.2	<0.01
Female	751 (61.9%)	987 (67.8%)	–	–
Age	75.1 (6.8)	77.0 (6.9)	–7.0	<0.001
Population group			75.1	<0.001
Jews born in Israel	143 (12.1%)	109 (7.7%)		
Arabs	46 (3.9%)	19 (1.3%)		
Jews born in Russia, East Europe	488 (41.1%)	755 (53.6%)		
Jews born in Europe or America	73 (6.2%)	134 (9.5%)		
Jews born in Asia or Africa	436 (36.8%)	391 (27.8%)		
Years in Israel			2.6	0.06
<= 10	49 (4.1%)	42 (2.9%)	–	–
Charlson	5.3 (2.4)	5.5 (2.2)	–2.7	<0.01
Sleep diagnosis	222 (18.3%)	278 (19.1%)	0.28	0.31
Psychiatric diagnosis	84 (6.9%)	183 (12.6%)	23.4	<0.001
Socioeconomic status			1.4	0.47
Low	406 (33.7%)	458 (31.6%)		
Medium	523 (43.5%)	657 (45.3%)		
High	274 (22.8%)	335 (23.1%)		

**Table 4** Logistic regression with patient-level variables as predictors and whether or not patient purchased benzodiazepines for 6 months or longer as an outcome

	OR	95%CI
<i>Patient characteristics</i>		
Gender		
Female	1.25	1.06–1.48
Age	1.03	1.01–1.04
Population group		
Jews born in Israel	–	–
Arabs	0.55	0.30–0.99
Jews born in Russia, East Europe	1.69	1.28–2.25
Jews born in Europe or America	2.08	1.41–3.06
Jews born in Asia or Africa	1.08	0.81–1.44
Charlson	1.00	0.96–1.04
Psychiatric diagnosis	1.82	1.38–2.41

LRchi<sup>2</sup>(8) = 132.1, P < 0.001

treatment, limited to acute situations. Nevertheless, we found that almost half the sample of older adults over the age of 65 purchased benzodiazepines at least once within the study period and over 50% of those who purchased benzodiazepines did so for an extended period of 6 months or longer. One notable finding of this study concerns the potentially inappropriate purchase of benzodiazepines by older primary care patients in Israel. Other notable findings concern the lack of association between physician

characteristics and the purchase of benzodiazepines in contrast to the association of various clinical and demographic patient characteristics with the purchase of benzodiazepines.

Although there is a tendency toward over-use of benzodiazepines worldwide, the prevalence rate found in the present study is higher than previous reports (Manthey et al. 2011). This finding may be partially attributed to the high levels of stress and anxiety experienced by Israelis in general, given the multiple wars and acts of terror in the country. Yet, other factors such as patients' and physicians' beliefs or preferences may also play a role.

An important finding of this study is that physicians' characteristics explained only a small percentage of the variance associated with the purchase of benzodiazepines or with continued purchase. Because some patients may not purchase their medication, despite having a prescription, purchasing patterns are not synonymous with prescription patterns. Hence, it is possible that physicians' characteristics play a greater role with regard to prescription patterns. In addition, several patients' characteristics that have shown to play a role in the purchase of benzodiazepines, such as the documentation of a psychiatric or sleep diagnosis are actually determined by the physician, suggesting that physicians' characteristics may still play an important role in patients' purchasing patterns. Finally, lack of variance between physicians may be accounted for by the organizational setting—all work in a managed care organization that employs specific guidelines for the management of mental illness.

As in previous studies, advanced age and female gender were consistently associated with a greater likelihood of purchasing benzodiazepines at least once and once purchased, with a greater likelihood of purchasing benzodiazepines for 6 months or longer. These variations may reflect the preferences of different groups in the population. For instance, past research has shown that older adults tend to favor the use of benzodiazepines and disregard potential side-effects (Cook et al. 2007). In addition, research has shown that females are more receptive towards mental health treatment in general (Anita and Cynthia 2006). In addition, those of high socioeconomic status were more likely to purchase benzodiazepine at least once. This is somewhat surprising given the universal healthcare system employed in Israel and may suggest that even in a country that employs a universal health care system, variations by socioeconomic status exist.

There were also notable differences between different groups in the population. Relative to Israeli Jews, Israeli Arabs were less likely and Jews born in Russia, Europe or America were more likely to purchase benzodiazepines and once purchased, to purchase the medications for 6 months or longer. The fact that Jews born in Russia, Europe or America were more likely to purchase benzodiazepines might be attributed to past traumatic experiences during the Holocaust. The lower purchase of benzodiazepines by Israeli Arabs, on the other hand, might be explained by the tendency of this group to rely on informal support and by the stigma towards mental illness, which might be more prevalent in this group (al-Krenawi and Graham 2000).

In addition to demographic variables, the presence of a sleep or a psychiatric diagnosis was indicative of a greater likelihood of purchasing benzodiazepines at least once over the study period. Whereas almost 20% of those who purchased benzodiazepines at least once had a documented diagnosis of sleep problems, only 10% had a documented psychiatric diagnosis. Nevertheless, the odds of those carrying a psychiatric diagnosis were 4.3 times higher to purchase benzodiazepines, whereas the odds of those with a sleep diagnosis were only 1.7 times higher. This finding is only partially in line with past research that has attributed the use of benzodiazepines to sleep disturbance (Gregory and Evette 2006). This finding may suggest a tendency to under-document or under-diagnose mental illness in primary care. Possibly, both physicians and patients are more comfortable with the documentation of a sleep diagnosis, rather than a psychiatric condition. This may be due to stigma of patients and/or physicians or due to inadequate training in the diagnosis of mental illness. Nevertheless, only the presence of a psychiatric diagnosis was associated with continued purchase of benzodiazepines for 6 months or longer, suggesting that those with a documented psychiatric diagnosis may constitute a distinguished group with

greater mental health needs. However, taking benzodiazepines for such a long period of time is counter indicated also in this case. Moreover, we found that those with a higher Charlson score were more likely to purchase benzodiazepines at least once within the study period. This may be particularly counter-indicated given the side-effect profile of benzodiazepines.

This study has several limitations that should be addressed. First, the focus on a cross-sectional analysis does not allow for inferences about cause and effect. In addition, as already noted, this study is focused on purchasing patterns rather than prescription patterns or actual use. Although our method is likely more reliable than solely relying on self-report, purchasing data may still represent an underestimation of prescription as our data do not include patients who may have been prescribed medication but never filled the prescription. Data may also not be synonymous with use as some patients who purchased medication may have failed to take it as prescribed. It is, however, important to note that the purchase of benzodiazepines does indicate an active decision on the part of the patient and involves a financial investment. In addition, once benzodiazepines have been purchased for 3 months or longer, they are considered a chronic medication. As such, they are listed in all patient related correspondence. Discontinuation of a chronic medication is not automatic, but instead requires a discussion between patient and provider. Finally, the present study leaves several important questions unanswered. For instance, both patients' demographic and clinical characteristics have shown to correlate with the purchase of benzodiazepines. Hence, either a clinical need or patients' greater persuasiveness and persistence are responsible for inappropriate purchase of benzodiazepine. By specifically examining the interactions between patients and physicians at the physician's office as well as patients' and physicians' beliefs about depression, anxiety and their management, one may be able to tease out potential non-clinical contributors to the purchase on benzodiazepines. Such analysis may also assist in teasing out whether the purchase of benzodiazepines is primarily guided by physicians' erroneous beliefs about their efficacy, despite clinical guidelines to the contrary or whether this is primarily due to patients' direct requests and preferences.

Nevertheless, our findings are important as we simultaneously evaluate the role of both patients and providers in the purchase of benzodiazepines in primary care. The present study found that older primary care patients in Israel tend to purchase benzodiazepines in a way that is inconsistent with current clinical guidelines. Our findings are notable as we demonstrate the relative importance of patients' characteristics. Therefore, any intervention to improve the use of benzodiazepines should be directed at both patients and providers. The present study identified



certain patients' characteristics (some demographic and some clinical) that may put patients at a greater risk for inappropriate purchase of benzodiazepines. Hence, these groups should be specifically targeted. Although further education of both patients and physicians may eliminate or reduce the practice of inappropriate benzodiazepine prescription, about 25% of the old adults in this sample had continued use of benzodiazepine. This group likely presents with both physiological and psychological symptoms of dependence and may require assistance in withdrawing from current medication practices.

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