

PRESCRIBING OF BENZODIAZEPINES AMONG SLOVENIAN FAMILY PHYSICIANS

PREDPISOVANJE BENZODIAZEPINOV MED SLOVENSKIMI ZDRAVNIKI DRUŽINSKE MEDICINE

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Abstract

Background: In spite of their side effects, benzodiazepines are the most frequently prescribed psychotropic drugs in family medicine. The objective of this study was to investigate the possible association between physician characteristics, practice structure and practice population size with the pattern of prescribing benzodiazepines among Slovenian family physicians.

Methods: We studied a representative sample of 100 family physicians using a combination of self-administered questionnaire, demographic data and data on prescribing provided by the Institute of Public Health of the Republic of Slovenia. The characteristics potentially influencing frequent prescribing were investigated by multiple linear regression analysis.

Results: The estimated annual benzodiazepine consumption in Slovenia is nearly 3-fold lower than in the United Kingdom. Benzodiazepines were found to be less frequently prescribed by physicians with lower numbers of registered patients, as well as by female physicians, younger physicians, physicians following the specialist training, those with short length of service, and by physicians working in large towns of the central healthcare region. The physicians' age and access to computerised decision-making support for drug management at the workplace were found to be significantly associated with increased prescription of benzodiazepines compared to the volume of prescribed psychotropic drugs.

Conclusions: The results indicate that family physicians in Slovenia prescribe appropriate amounts of benzodiazepines. Benzodiazepines are less frequently prescribed in practices with less workload, by younger and female family physicians, in practices located in central Slovenia and by family physicians with online access to information at their workplace.

Key words: family physicians, drug prescriptions, benzodiazepines

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Izvleček

Izhodišča: Kljub stranskim učinkom so benzodiazepini najpogostejše predpisani psihofarmaki v družinski medicini. Z raziskavo smo ocenjevali povezanost značilnosti zdravnikov, značilnosti ambulantnega dela in velikosti populacije bolnikov s predpisovanjem benzodiazepinov pri slovenskih zdravnikih družinske medicine.

Metode: Na reprezentativnem vzorcu stotih zdravnikov družinske medicine smo z multiplo linearno regresijo ocenili, kateri dejavniki vplivajo na pogosto predpisovanje benzodiazepinov.

Rezultati: Zdravniki družinske medicine v Sloveniji predpišejo v povprečju skoraj trikrat manj benzodiazepinov kot v Veliki Britaniji. Manj pogosto so benzodiazepine predpisovali zdravniki z manjšim številom opredeljenih bolnikov, zdravnice, mlajši zdravniki, specializanti, zdravniki s krajšo delovno dobo in zdravniki v večjih krajih v osrednjem delu države. Delež benzodiazepinov med vsemi recepti za psihofarmake je bil večji pri starejših zdravnikih in zdravnikih,

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ki na delovnem mestu niso imeli dostopa do spletne informacijske podpore pri predpisovanju zdravil.

Zaključek: *Zdravniki družinske medicine v Sloveniji zmerno predpisujejo benzodiazepine. Manjše predpisovanje je povezano z manjšimi delovnimi obremenitvami, ženskim spolom, nižjo starostjo, umeščenostjo ambulate v centralnih delih Slovenije in dostopom do spletne informacijske podpore pri predpisovanju zdravil na delovnem mestu.*

Ključne besede: zdravniki družinske medicine, predpisovanje zdravil, benzodiazepini

1 Introduction

Benzodiazepines (BZD) are among the most commonly prescribed psychotropic drugs, even though family physicians regard prescribing these drugs as one of the most demanding and uncomfortable tasks in their clinical work (1). BZD have strong anti-anxiety effects (2), yet they also induce physical and psychological addiction and withdrawal symptoms upon treatment discontinuation (3). In the elderly, they cause cognitive impairment, and are responsible for falls and consecutive hip fractures (4). In a Spanish study, addiction was identified in 47% of the patients prescribed BZD for over one month (5).

On the basis of their structure BZD are divided into three subclasses: 2-keto, 3-hydroxy and triazolo BZD. They differ in their pharmacokinetic properties, i.e. plasma half-lives, and may therefore be further grouped into long-acting (plasma half-life of > 20 hours), intermediate-acting (plasma half-life of 6 - 20 hours) and short-acting BZD (plasma half-life of < 6 hours) (6). The advantages of long-half-life drugs over short-half-life drugs are: less frequent dosing, less variation in plasma concentration, and less severe withdrawal phenomena. The disadvantages include: drug accumulation, increased risk of daytime psychomotor impairment, and increased daytime sedation. Rebound insomnia and anterograde amnesia are more severe with the short-half-life drugs (6, 7). In our study, BZD classes were not subdivided—despite the different levels of severity—because all groups presented with considerable addiction problems, as well as with sedation and psychomotor impairment. Anxiety is also controlled by antidepressant agents, mainly by selective serotonin reuptake inhibitors (SSRIs) (8). These drugs show other drug-related problems (DRP), such as sexual dysfunction, risk of bleeding, hyponatremia, discontinuation symptoms, and increased body weight (9, 10). Modern treatment guidelines advocate short term use and combining BZD with antidepressants, or using only antidepressants for anxiety control (11).

General practices vary in practice population parameters, such as the practice list size and age-

gender structure; in their organization, such as practice location and the quantity and type of resources available; and in family physicians' characteristics, such as age and training level (12, 13). A Danish study, which used the defined daily dose (DDD) as a measure of prescribing psychotropic drugs, reported larger prescribing rates in rural areas and in small towns compared to cities, but found no differences in prescribing rates in relation to the size and type of practice, or to the age and gender of the physician (14). In their studies, Rosser and Pimlott proved that educational programmes on psychotropic drug prescribing for family physicians reduced the rates of prescribing BZD to patients over 65 years of age (15, 16). The Danish restriction of BZD prescribing to one month at a time and only following consultation reduced prescribing of BZD hypnotics to 46.5% and the use of BZD anxiolytics to 41.7% (17). Computer-based access to drug profiles and alerts about potential prescribing problems significantly reduced the rate of potentially inappropriate prescribing, but only selectively effected discontinuation of this prescribing (18). To our knowledge, there have been no studies exploring the connection between general practitioners' workload and the rate of prescribing BZD.

The goal of the study was to analyze the factors that influence frequent prescribing of BZD in a representative sample of Slovenian family physicians.

2 Materials and methods

2.1 Sampling and research procedure

Data were obtained from the national database of all prescriptions, which is maintained by the Institute of Public Health (IPH). A representative sample of 160 family physicians was selected by means of stratified random sampling. The sample was well-matched to the total population in terms of regional representation, age distribution, gender ratio and percentage of public and private practitioners. The study did not include physicians who worked part time, those who were absent from work for over three months during the year

under study, and/or those who were retired or worked at emergency departments.

The questionnaire described below was sent to the selected family practitioners. A letter explaining the aims and procedures of the survey was attached to ensure their collaboration. A coding system was used to facilitate follow-up, and two reminders were added in order to increase response rate while keeping the family physician's identity confidential.

The questionnaire was completed by 100 family physicians, yielding a 62.5% response rate. Further analyses were performed on the respondent sample because the non-respondents did not consent to the use of their data from the IPH prescription database.

2.2 Family physician characteristics and practice structure variables

A questionnaire was used to obtain demographic data on the physicians' gender and age; workload data (practice list size, number of extra duty hours per week, number of house calls per day, number of standby hours per week, emergency treatment during regular practice hours, number of telephone consultations per day, mentorship); data on physicians' training (specialist training in family medicine, further training in psychopharmacology, recognition and treatment of anxiety and depression); data on practice organization (population area covered, distance from the nearest general hospital, employment in a public institution versus private practice, implementation of the appointment system, duration of employment in family practice and in the current surgery in years); and data on the access to information (computerised decision-making support for drug management) at the workplace.

2.3 Prescribing data

Data on the prescribed medications for the year 2005 were obtained from the national database. In total, 52 115 prescriptions for psychotropic drugs were taken into consideration. Drugs were coded according to the Anatomical Therapeutic and Chemical Classification System (ATC).

2.4 Statistical analysis

For each physician, we calculated the proportion of patients who were prescribed a monotherapy with BZD more than six times in the year under study (considered as frequent prescribing) (11). For BZD and antidepressants, the annual defined daily dose (DDD) per 1000 practice population was calculated.

The first step of the study was to calculate descriptive statistics for all the variables studied; and to analyze univariately their relationship with frequent prescribing of BZD using the Student's t-test for numeric variables and the Fisher's exact test for binary variables.

The second step consisted of excluding physicians who did not prescribe BZD more than six times in a given year to the same patient. Frequent prescribing of BZD per patient, and frequent prescribing of BZD per patient with at least one psychotropic drug prescribed were analyzed using multiple linear regression.

The third step of the study was to apply multiple linear regression analysis to the entire sample to determine the ratio of BZD prescriptions to the total number of psychotropic drug prescriptions, and the ratio of BZD annual DDD to the total annual DDD of antidepressants

Variables for all the multiple regression models were selected on the basis of univariate analyses and mutual correlation in order to avoid overfit and collinearity.

Data were analysed using the SPSS for Windows 14.0.2 software (SPSS Inc., Chicago, IL, 2003). Two-sided statistical tests were used with the significance level of $p < 0.05$.

3 Results

Annual DDD of BZD per 1000 practice population ranged from less than 1 to 5.2, with a mean of 1.8 (standard deviation 1.2) and a median of 1.7, which shows a large variation in prescribing BZD between Slovenian physicians (Figure 1).

Table 1 presents univariate comparisons of demographic and work characteristics between family physicians who, by the Muijters et al. definition (11), could be labeled as frequent prescribers of BZD and the remaining respondents.

Multiple regression on the sample of 93 physicians who prescribed BZD more than six times per year to at least one patient indicated that physicians with a larger number of patients on their list ($p = 0.001$) and those working in healthcare regions other than the central part of the country ($p = 0.006$) had more patients to whom BZD were frequently prescribed (Table 2). In the same sample, the rate of frequent BZD prescribing among patients prescribed at least one psychotropic drug also proved to be higher among physicians located in the peripheral healthcare regions ($p = 0.002$) (Table 3).

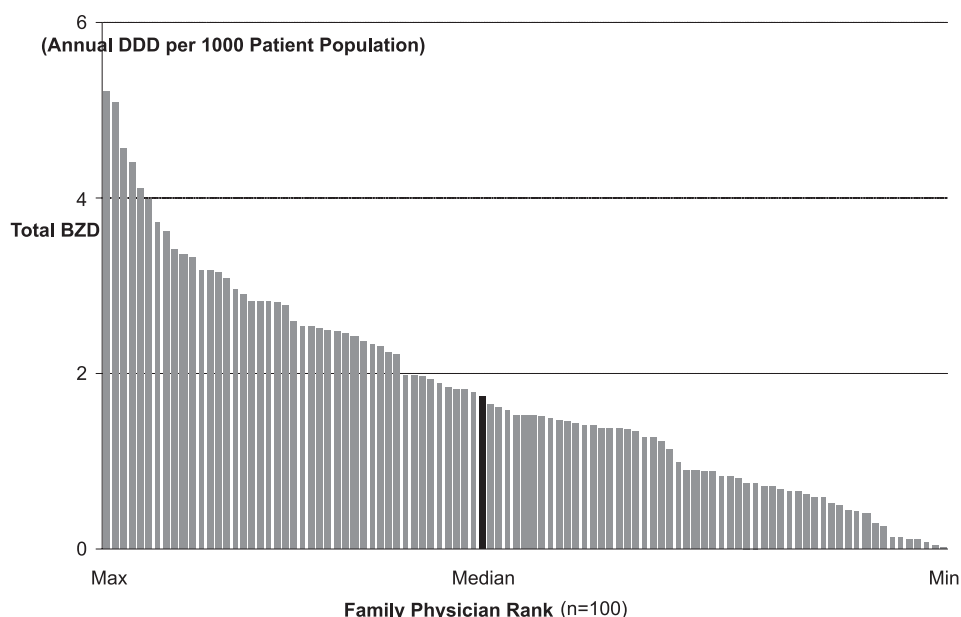


Figure 1. Distribution of annual DDD of BZD per 1000 practice population.

Slika 1. Porazdeljenost DDD BZD na 100 bolnikov splošne prakse na leto.

Table 1. Comparison of demographic and work characteristics between family physicians who frequently prescribed a BZD drug and those who did not.

Tabela 1. Primerjava demografskih in delovnih značilnosti pri zdravnikih družinske medicine, ki pogosto predpisujejo BZD in pri tistih, ki jih ne predpisujejo pogosto.

Physician/practice characteristic		BZD prescribed to the same patient > 6 times in the studied year				
		No (N=7)		Yes (N=93)		
Binary variables		Category counts		Category counts		p (FET)
Gender		0 male	7 female	37 male	56 female	0.044
Specialisation		5 ongoing	2 done/none	20 ongoing	73 done/none	0.030
CDS at work		5 yes	2 no	54 yes	39 no	0.697
Town size (number of inhabitants)	of	7 >10,000 inh.	0 <10,000 inh.	52 >10,000 inh.	41 <10,000 inh.	0.032
Practice type		7 public	0 private	72 public	21 private	0.340
Appointment system		4 yes	3 no	54 yes	39 no	0.748
Emergency duty		6 yes	1 no	72 yes	21 no	1.000
Healthcare region		1 peripheral	6 central	35 peripheral	53 central	0.647

Numeric variables	Mean (SD)		Mean (SD)		p (t)
Age (years)	36.9	(6.4)	46.5	(8.9)	0.006
Employment in family practice (years)	8.1	(7.5)	17.9	(10.1)	0.013
Employment in present surgery (years)	3.5	(2.3)	12.4	(8.9)	<0.001
Training (days per year)	9.4	(1.2)	10.5	(6.1)	0.174
Telephone calls (number per day)	4.9	(4.1)	12.0	(10.1)	0.066
Home visits (number per day)	1.1	(1.8)	0.9	(1.0)	0.601
Extra duty (hours per week)	10.6	(16.4)	8.6	(8.3)	0.762
Number of designated patients	1478.3	(423.9)	1821.2	(409.5)	0.036
Distance from nearest general hospital (km)	29.4	(25.5)	20.6	(18.3)	0.235

Legend: SD=standard deviation, p=statistical significance (FET=Fisher's exact test, t=independent-samples t-test); CDS=computerised decision-making support for drug management.

Table 2. *Summary of multiple linear regression model for predicting the proportion of patients who were often prescribed BZD per designated patients.*

Tabela 2. *Povzetek multiple linearne regresije za napoved deleža bolnikov, ki so jim pogosto predpisali BZD, na opredeljenega bolnika.*

Independent variable	b	SE	β	p
Gender (male vs. female)	0,0017	0,0019	0,095	0,358
Age (years)	0,0001	0,0001	0,049	0,715
Employment in present practice (years)	0,0001	0,0001	0,008	0,948
Specialisation (ongoing vs. completed or none)	-0,0044	0,0025	-0,205	0,077
Number of designated patients	0,0001	0,0001	0,329	0,001
Healthcare region (peripheral vs. central)	0,0053	0,0019	0,275	0,006

Legend: n=93 GPs, model $p < 0.001$, adjusted $R^2 = 0.209$, b=regression coefficient, SE=standard error, β=standardized regression coefficient, p=statistical significance.

The analysis of BZD prescriptions compared to the total number of psychotropic prescriptions in the year studied, performed on the entire sample, showed that higher proportion of BZD was prescribed by older practitioners ($p = 0.028$) and by those who had no access to a computerised decision-making support

for drug management at their workplace ($p = 0.022$) (Table 4). The analysis of the ratio of BZD to the total annual DDD of antidepressants, performed on the total sample, confirmed the association of older age with higher share of BZD ($p = 0.008$) (Table 5).

Table 3. *Summary of multiple linear regression model for predicting the proportion of patients who were often prescribed BZD per patient with prescribed at least one psychotropic drug in the studied year.*

Tabela 3. *Povzetek multiple linearne regresije za napoved deleža bolnikov, ki so jim pogosto predpisali BZD, na bolnika s predpisanim najmanj enim psihotropnim zdravilom na leto.*

Independent variable	b	SE	β	p
Gender (male vs. female)	-0,0114	0,0252	-0,048	0,653
Age (years)	0,0004	0,0018	0,031	0,823
Employment in present practice (years)	0,0012	0,0016	0,096	0,438
Specialisation (ongoing vs. completed or none)	-0,0609	0,0334	-0,218	0,072
Number of designated patients	0,0001	0,0001	0,050	0,610
Healthcare region (peripheral vs. central)	0,0799	0,0253	0,322	0,002

Legend: n=93 GPs, model p=0.003, adjusted R²=0.146, b=regression coefficient, SE=standard error, β=standardized regression coefficient, p=statistical significance.

Table 4. *Summary of multiple linear regression model for predicting the ratio between the number of BZD prescriptions and total number of psychotropic prescriptions.*

Tabela 4. *Povzetek multiple linearne regresije za napoved razmerja med številom receptov za BZD in celotnim številom receptov za psihotropna zdravila.*

Independent variable	b	SE	β	p
Gender (male vs. female)	0,0063	0,0188	0.037	0.740
Age (years)	0,0030	0,0013	0.319	0.028
Employment in present practice (years)	0,0004	0,0012	0.042	0.736
Home visits (number per day)	-0,0059	0,0078	-0.074	0.453
Specialisation (ongoing vs. completed or none)	0,0310	0,0233	0.161	0.186
Number of designated patients	0,0001	0,0001	0.025	0.800
Distance from nearest general hospital (km)	0,0006	0,0004	0.147	0.145
CDS at work (yes vs. no)	-0,0386	0,0165	-0.229	0.022
Healthcare region (peripheral vs. central)	0,0104	0,0186	0.058	0.579

Legend: n=100, model p=0.021, adjusted R²=0.109; b=regression coefficient, SE=standard error, β=standardized regression coefficient, p=statistical significance; CDS=computerised decision-making support for drug management.

4 Discussion

The estimated annual DDD for BZD in Slovenia is on average 2.7-fold lower than in the United Kingdom, a finding indicating a reasonable and appropriate prescribing practice among Slovenian family physicians

(19). Nevertheless, the study demonstrated large variation in BZD prescribing patterns between the family physicians studied.

Univariate comparisons of demographic and work characteristics of family physicians labeled as frequent prescribers of BZD according to the

Table 5. *Summary of multiple linear regression model for predicting the ratio of the BZD annual DDD to the total annual DDD of antidepressants.*

Tabela 5. *Povzetek multiple linearne regresije za napoved razmerja med letno DDD za BZD in celotno etno DDD za antidepressive.*

Independent variable	b	SE	β	p
Gender (male vs. female)	0,0594	0,1606	0,041	0,713
Age (years)	0,0309	0,0113	0,389	0,008
Employment in present practice (years)	-0,0063	0,0100	-0,078	0,533
Home visits (number per day)	-0,0479	0,0669	-0,070	0,476
Specialisation (ongoing vs. completed or none)	0,0445	0,1988	0,027	0,823
Number of designated patients	0,0001	0,0002	0,079	0,425
Distance from nearest general hospital (km)	0,0043	0,0037	0,114	0,257
CDS at work (yes vs. no)	-0,2096	0,1409	-0,146	0,140
Healthcare region (peripheral vs. central)	0,1266	0,1588	0,082	0,428

Legend: n=100, model p=0.019, adjusted R²=0.111; b=regression coefficient, SE=standard error, β =standardized regression coefficient, p=statistical significance; CDS=computerised decision-making support for drug management.

Muijers et al. definition (11), and of the remaining respondents revealed the following physician and practice characteristics associated with increased BZD prescribing: male gender, no or completed specialist training, older age, longer employment in family practice and longer employment in the present surgery as physician characteristics, and smaller town size and larger number of registered patients. However, because of the very small number of family physicians who did not prescribe BZD on a frequent basis, and because of the inflated alpha error due to multiple statistical tests, these analyses should be interpreted with caution, and may serve merely as indicators of potential BZD prescribing issues. The criterion of prescribing BZD to the same patient more than six times in a given year labels over 90% of the family physicians studied as frequent prescribers of BZD even though the estimated total BZD consumption appears to be low, which renders the usefulness of this criterion questionable.

Hence, multiple linear regression analysis was performed in order to determine which factors had greatest influence on prescribing BZD, and to what extent. The analysis of registered patients suggested that frequent prescribing may be due to short consultation time assigned to patients because of their high number, an observation applying mostly to smaller

and more remote regions with a presumably limited access to specialists. The difference between regions was confirmed by the analysis of patients prescribed at least one psychotropic drug.

The analysis of the total number of psychotropic prescriptions showed that younger age of family physicians predicted lower BZD prescribing rates. This finding was confirmed by the total annual DDD. Older physicians with longer service periods who had had good results with BZD in terms of controlling anxiety in their patients may have insufficient experience with the anxiolytic effects of newer antidepressants. As a rule, they care for older patients, many of whom are likely to be already addicted to BZD and are therefore unlikely candidates for drug change or dosage reduction (2). Access to computerised decision-making support for drug management at the workplace was also predictive of lower BZD prescribing, a finding stressing the need for information support in the medical work environment in the Slovenian primary care setting.

4.1 Study limitations

Other factors, which are not addressed in this study, but undoubtedly affect BZD prescribing include diagnosis and other patient characteristics, the physician's attitude towards psychiatric disorders, expectations

about therapeutic outcomes and diagnostic skills, and advertising by pharmaceutical companies (20). Individual prescribing was not studied, because a nation-wide system of computerized patient records has not yet been established in the Slovenian primary care. Excessive doses, duration of therapy and use of different BZD derivatives were not examined because of limitations of the data source.

Considering the available (i.e., aggregated) data, the meta-regression approach would be a possible alternative to the multivariate models used (21). Yet, as the parameter estimates would probably not differ substantially from the ordinary least-squares models (22), we opted for the simpler and more easily interpretable approach.

5 Conclusions

The data collected in the representative sample of Slovenian family physicians indicate that they prescribe appropriate volumes of BZD. In order to further decrease the rate of BZD prescribing, it would be advisable to reduce the family physicians' work overload, especially in the peripheral healthcare regions. Older physicians with older patient population would probably need specialist advice on how to change their prescribing practice and start prescribing antidepressants instead of BZD. Also, access to information should be improved by implementing a better computerized information-support system in family practice environments.

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