



# Outpatient benzodiazepine utilization in Croatia: drug use or misuse

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## Abstract

**Background** Benzodiazepines are commonly prescribed medications, especially among elderly, despite known risks and guidelines focused on short term usage. There is an increased trend of benzodiazepine consumption in Croatia. Consumption of anxiolytics in 2015 and 2016 in Croatia can almost entirely be ascribed to benzodiazepines, with diazepam being the most commonly prescribed drug, followed by alprazolam. **Objective** The aim of this study was to examine benzodiazepine utilization habits among the Croatian population. **Setting** This study was conducted on the national level, based on digital prescribing data. **Method** Data regarding the prescription of anxiolytics in Croatia was sourced and analyzed from the Croatian Health Insurance Fund database for the years 2015 and 2016. Drugs included in the study were classified according to The Anatomical and Therapeutic Classification of Medicines System, and consist of several chemical therapeutic subgroups (N05BA, N05BC, N05CD, N05CF). **Main outcome measures** The prescribing frequency of the most often prescribed benzodiazepines in Croatia. **Results** The total number of benzodiazepine prescriptions was 5,085,695 in 2015, and 5,294,075 in 2016; this represents a 208,380 increase in prescriptions, or 4.1% more than the previous year. The number of patients who utilized benzodiazepines showed an increase from 860,664 (8.67%) in 2015 to 876,046 (8.76%) in 2016. In relation to gender, benzodiazepine consumption was higher among female patients in all age groups, with the number of utilized benzodiazepine prescriptions per patient being highest in the oldest age group (80+), comprising 7 prescriptions per patient in a 12 months period. **Conclusion** Increased utilization and long-term treatment with benzodiazepines remains a serious challenge for the health care system in Croatia. National prescription guidelines, improved control of benzodiazepine usage and prescriptions, along with restricted release drug lists, should all be considered as potential measures to rationalize benzodiazepine prescription, control unnecessary expenditure in the country and improve the well-being of the patients.

**Keywords** Benzodiazepine · Croatia · Drug utilization · Inappropriate medication · Prescription

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## Impacts on practice

- Despite the recommendations for short-term utilization because of potentially serious adverse reactions, benzodiazepines are commonly prescribed drugs in Croatia.
- Women are more likely to use benzodiazepines than men in all age groups, except in the age group 0–19 years.
- In Croatia, there is a need for continuous monitoring and evaluation of benzodiazepine prescription habits among healthcare professionals, since this group of drugs is known for their risk of dependence, the lack of long-term effectiveness, tolerance and withdrawal syndromes.

## Introduction

According to the World Health Organization (WHO), mental health is an integral part of overall health and well-being. In the past decades mental disorders have become highly prevalent globally, affecting people across all regions of the world [1]. A comparative analysis across EU countries has shown that more than one in six people had had some sort of a mental health issue in 2016 [2], while 4% of all deaths in the EU in 2015 was a result of mental and behavioral disorders [3].

Benzodiazepines (BZDs), having been available on the market since 1960, are among the most commonly utilized psychopharmacs by the adult population [4–8].

BZDs are effective pharmacological treatments that are indicated for several conditions including sleeping disorders, anxiety, general mood disorders and chronic back pain [9–11], but are contraindicated for chronic use [12, 13]. The indication for prolonged BZD use is only when disorder is severe, disabling or subjecting the individual to extreme distress [14]. BZDs have significant adverse effects, especially in long-term use. BZDs utilization has been associated with side effects such as memory loss, increased risk of falls and fractures, increased risk of Alzheimer's disease, and dependency incidence [15–19].

During the years, BZDs have been over-prescribed in many countries [20–24], and discontinuing BZDs is widely advised but seems difficult to implement [25–27]. There is no consensus on the optimal prescription strategy [25, 28], however, long-term use of BZDs is discouraged in guidelines [29–31] due to the lack of its effectiveness after 4 weeks [32, 33].

The Croatian population is covered by a basic health insurance carried out only by the Croatian Health Insurance Fund (CHIF). In 2006, CHIF introduced two drug lists: the main list, containing all essential drugs covered by compulsory health insurance, and a supplementary list of drugs covered in part from the compulsory health insurance and in part by the patients [34]. Although CHIF is continuously updating both main and supplementary list of drugs, there are no limitations for the duration of specific drug utilization or its dosage. The majority of outpatient prescriptions are financially covered by CHIF (87%). BZDs are a drug group included in the Croatian main drug list, meaning patients do not financially participate in the cost. Additionally, there is a possibility of obtaining a private prescription for any drug group in Croatia, including BZDs. The estimate of an outpatient drug utilization through private prescription in Croatia is 4% out of the total number of drugs utilized in 2015 and 2016.

As a compulsory health insurance in Croatia, CHIF does not have any limitations regarding the drug prescription

policy, except the permission to prescribe the drug in one turn for the maximum duration of 30 days, and maximum 2 packages of the same drug per prescription [35].

In 2015 and 2016 there were 64 registered BZDs in Croatia, including: 17 diazepam, 24 alprazolam, 8 bromazepam, 4 oxazepam, 2 lorazepam, 6 midazolam, 2 flurazepam, 1 nitrazepam. The total number of 39 BZDs were available on the main drug list (completely covered by CHIF) in 2015, while 34 different BZDs were available in 2016, with the price range from 0.07EUR (diazepam) to 1.74EUR (midazolam) expressed as Defined Daily Dose with tax (DDD). The supplementary list of drugs included 23 BZDs both in 2015 and 2016. The highest additional charge (partially covered by CHIF) was 0.46EUR (bromazepam), while the lowest supplementary payment was 0.07EUR (alprazolam), expressed as DDD with tax [36].

There are no existing national guidelines regarding BZD prescription, and even the official literature used in daily healthcare routine does not offer unambiguous answer. Jakovljević et al. [37] offer different recommendations regarding the length of utilization of BZDs, depending on the dosage, type of anxiolytic, and diagnosis. These recommendations vary from 4 weeks to 4 months, and in certain cases up to 1 year. However, Jakovljević et al. [37] claim that, in principle, it can be said that BZDs should be used only for a few weeks. Francetić et al. [38] have similar recommendations, stating that the duration of BZD utilization should not exceed 2 or 4 weeks, with maximum duration of 4 months. Regarding specific diagnoses, if patient is suffering from anxiety, the average BZD utilization is 6 months, while for generalized anxiety disorder the therapy should last between 4 and 8 weeks [39].

## Aim of the study

The present study is aimed to examine the benzodiazepine utilization pattern in the Croatian population.

## Ethics approval

The study was approved by the Ethics Committee of the Faculty of Medicine, University of Zagreb, under Numbers 380-59-10106-19-111/184, 641-01/19-02/01.

## Method

The Anatomical and Therapeutic Classification of Medicines (ATC) system is an internationally accepted classification system, which divides all medical products into 14 anatomical main groups, each with 2 therapeutic

subgroups and 2 chemical subgroups [40]. We have processed the data at the levels of the chemical therapeutic subgroup (N05BA, N05BC, N05CD, N05CF).

The data used in this study were sourced from the state-owned CHIF database. Number of insured persons, together with all outpatient prescriptions can be approximated to the entire Croatian population because of the universal health insurance coverage from the CHIF. The insured persons will, therefore, be considered simply as Croatian inhabitants.

CHIF collects prescription records directly from the pharmacies. This population-based database is up to date and provides information about prescribed drugs (using the ATC classification [40], diagnosis (using ICD-10 classification [41], date of prescription, physician identification number, and a patient identification number. In Croatia, only primary-care physicians can prescribe drugs that will be reimbursed. For this study, only the outpatient prescriptions were used, and for the purposes of our analyses, we assumed that the patients took the number of pills as prescribed.

Similar as in France, prescription drugs in Croatia are dispensed for a maximum of 30 days whatever the actual prescription is [35, 42].

For the analyses, we used SPSS FOR WINDOWS ver. 14.0 (SPSS, Chicago, IL, USA). Differences between the groups were studied using Student's *T* test and The Wilcoxon signed-rank test. Levels of significance were set to  $p < 0.05$ ,  $p < 0.01$  or  $p < 0.001$ .

## Results

Outpatient utilization of BZDs in Croatia for the period 2015–2016 is presented in Table 1. The total number of issued prescriptions was 5,085,695 in 2015, and 5,294,075 in 2016; There is a 208,380 increase in prescriptions in 2016, which is 4.1% more than the previous year. The number of patients who utilized BZDs showed an increasing pattern from 860,664 (8.67%) in 2015 to 876,046 (8.76%) in 2016, as shown in Table 1.

According to the Census of Population, Households and Dwellings, issued by the Croatian Bureau of Statistics, the number of inhabitants in Croatia in the latest data report from 2011 was about 4,284,889, with an average age of 41.7 years old [43].

The data published by the Croatian Bureau of Statistics showed that the average number of insured persons in 2016 (obligatory health insurance) was 4,325,852. In the same year, the total number of drug prescriptions was 3,116,165,185 [44].

For the purpose of this analysis, BZDs were placed into the chemical therapeutic subgroup (N05BA, N05BC, N05CD, N05CF) (Table 1). The BZDs utilized during the years 2015 and 2016 are shown as an absolute number of prescriptions, and as an average number of prescriptions for the total number of insured people in Croatia.

The drugs showing an increase in consumption were diazepam, lorazepam, alprazolam, zolpidem and bromazepam, while oxazepam, nitrazepam and zaleplon showed a

**Table 1** Outpatient utilization of BZDs in Croatia during the years 2015 and 2016 expressed as total number of prescriptions per patient, as an amount and average

ATC5 code	ATC7 code	Generic name	2015			2016		
			Total number of BZD prescriptions	% of BZD prescriptions	Average number of BZD prescriptions per patient	Total number of BZD prescriptions	% of BZD prescriptions	Average number of BZD prescriptions per patient
N05BA	N05BA01	Diazepam	2,129,830	41.88	4.18	2,216,570	41.87	4.22
N05BA	N05BA04	Oxazepam	589,263	11.59	5.53	581,769	10.99	5.70
N05BA	N05BA06	Lorazepam	230,312	4.53	8.23	234,270	4.43	8.45
N05BA	N05BA08	Bromazepam	22,216	0.44	2.48	56,698	1.07	3.50
N05BA	N05BA12	Alprazolam	1,457,074	28.65	5.62	1,481,148	27.98	5.76
N05BC	N05BC01	Meprobamate	1	0.00	1.00	1	0.00	1.00
N05CD	N05CD02	Nitrazepam	199,002	3.91	4.39	186,261	3.52	4.82
N05CF	N05CF02	Zolpidem	454,184	8.93	4.00	535,762	10.12	4.44
N05CF	N05CF03	Zaleplon	3813	0.07	2.96	1596	0.03	2.40
Total number of BZD prescriptions			5,085,695	100	5.51	5,294,075	100	6.04
Number of patients who utilized BZDs			860,664	/		876,046	/	
Total number of prescriptions in Croatia			58,658,535	/		60,434,646	/	
Amount of BZDs in total number of prescriptions (%)			8.67	/		8.76	/	

decrease (Table 1). The greatest increase was shown in the consumption of diazepam, which was the most prescribed drug in the analyzed period (41.9% of all BZDs in both years), followed by alprazolam (28.7% in 2015 and 27.9% in 2016).

The average annual number of BZD prescriptions per capita among the Croatian population was 5.51 in 2015 and 6.04 in 2016. Lorazepam was the most frequently prescribed BZD in a year, with more than 8 prescriptions in 12 months (Table 1).

The data on distribution of BZD prescriptions to patients with the 10 most frequent diagnoses is given in Table 2. It is evident that these drugs were mainly prescribed to patients with psychiatric diseases, but also for cardiovascular diseases, particularly hypertension (Table 2). The highest incline in BZDs prescription, according to the diagnosis, was noticed for I10 (essential hypertension), which might be associated with other comorbidities, such as anxiety and/or insomnia.

Outpatient BZD utilization according to age and gender for years 2015 and 2016 is shown in Table 3. In relation to gender, BZD consumption was higher among female patients in all age groups (in total 64.19% females utilized BZDs in 2015, and 64.32% females in 2016), except in the age group 0–19 years. However, statistical significance was not reached (Table 3).

Older age groups had higher prevalence of BZD use than younger age groups, with the highest prevalence being found in the age group of 60–69 (Table 3). In relation to age, the observed differences were not statistically significant.

The number of utilized BZD prescriptions per patient was highest in the oldest age group (80+), respectively 7 prescriptions per patient in 12 months (Table 3).

## Discussion

There has been an increasing trend of BZD utilization among Croatian population for the years 2015 and 2016, in both males and females. Extended life expectancy and other (direct and indirect) consequences of a lifestyle nowadays have resulted in growing cost of healthcare worldwide, due to rapid increase in pharmaceutical expenses [45]. It is estimated that the global medicine utilization in 2020 will go up 24%, compared to 2015 [46]. The recent data published by the Agency for Medicinal Products and Medical Devices of Croatia showed that N group of drugs were the second most prescribed drugs in Croatia in 2016, according to ATC classification, with an expenditure of 849 million kuna (approximately 115 million EUR) [47].

Although their per-unit price is low, BZDs play a significant role in profit made by companies that manufacture and distribute them. The drugs from this group are sold in high volumes, are inexpensive to manufacture, and have little or no research and development costs [48]. The largest BZD manufacturers in the past decade were located in Italy, India, China and Brazil. Diazepam, midazolam, clonazepam, alprazolam and lorazepam were the most manufactured psychotropic substances in 2017, in terms of S-DDD [49].

The decision-making process for BZD prescription should be a result of successful communication between the health care professional and the patient, with appropriate monitoring throughout tapering and after drug usage has been discontinued. These steps have been confirmed as effective at minimizing adverse drug withdrawal reactions [50]. According to WHO, in most European countries general practitioners are health care providers that identify, diagnose and regularly treat people with mental health issues [51].

**Table 2** BZD prescription in 10 most frequent diagnoses in the population of patients in general practice in Croatia, expressed as total number of BZD prescriptions per patient and in the amounts (out of total number of diagnoses)

ICD-10 code	Diagnosis	2015		2016	
		Total number of BZD prescriptions	% of BZD prescriptions	Total number of BZD prescriptions	% of BZD prescriptions
F41	Other anxiety disorders	872,484	17.16	895,297	16.91
F32	Depressive episode	419,782	8.25	414,093	7.82
F48	Other neurotic disorders	409,508	8.05	406,430	7.68
F41.2	Mixed anxiety and depressive disorder	375,764	7.39	394,223	7.45
F51	Nonorganic sleep disorders	286,517	5.63	321,166	6.07
F43.1	Post-traumatic stress disorder	162,980	3.20	160,345	3.03
I10	Essential (primary) hypertension	101,177	1.99	164,665	3.11
F40	Phobic anxiety disorders	93,490	1.84	99,638	1.88
F20	Schizophrenia	91,443	1.80	92,918	1.76
F43	Reaction to severe stress, and adjustment disorders	80,406	1.58	90,926	1.72

**Table 3** Prevalence of BZD utilization stratified according to age and gender for the years 2015 and 2016, expressed as total number of BZD prescriptions per patient and in the amounts

Age	2015				2016			
	Males	Females	Total number of BZD prescriptions (males + females)	Average of total number of BZD prescriptions	Males	Females	Total number of BZD prescriptions (males + females)	Average of total number of BZD prescriptions
0–19	8461	8360	16,821	2.34	8658	8366	17,024	2.32
%	0.46	0.26	0.33	X	0.46	0.25	0.32	X
20–29	45,811	50,102	95,913	3.62	45,625	49,848	95,473	3.60
%	2.52	1.53	1.89	X	2.42	1.46	1.80	X
30–39	163,760	172,745	336,505	4.96	164,312	175,358	339,670	4.98
%	8.99	5.29	6.62	X	8.70	5.15	6.42	X
40–49	305,581	346,195	651,776	5.54	303,574	353,186	656,760	5.60
%	16.78	10.61	12.82	X	16.07	10.37	12.41	X
50–59	428,235	627,518	1,055,753	5.84	439,890	640,330	1,080,220	5.96
%	23.51	19.22	20.76	X	23.29	18.80	20.40	X
60–69	418,653	728,243	1,146,896	5.99	449,663	780,405	1,230,068	6.15
%	22.99	22.31	22.55	X	23.81	22.92	23.23	X
70–79	279,629	717,197	996,826	6.38	291,586	737,214	1,028,800	6.51
%	15.35	21.97	19.60	X	15.44	21.65	19.43	X
80+	171,275	613,930	785,205	6.96	185,456	660,604	846,060	7.20
%	9.40	18.81	15.44	X	9.82	19.40	15.98	X
Total number of BZD prescriptions	1,821,405	3,264,290	5,085,695	5.91	1,888,764	3,405,311	5,294,075	6.04
%	100		X		100		X	

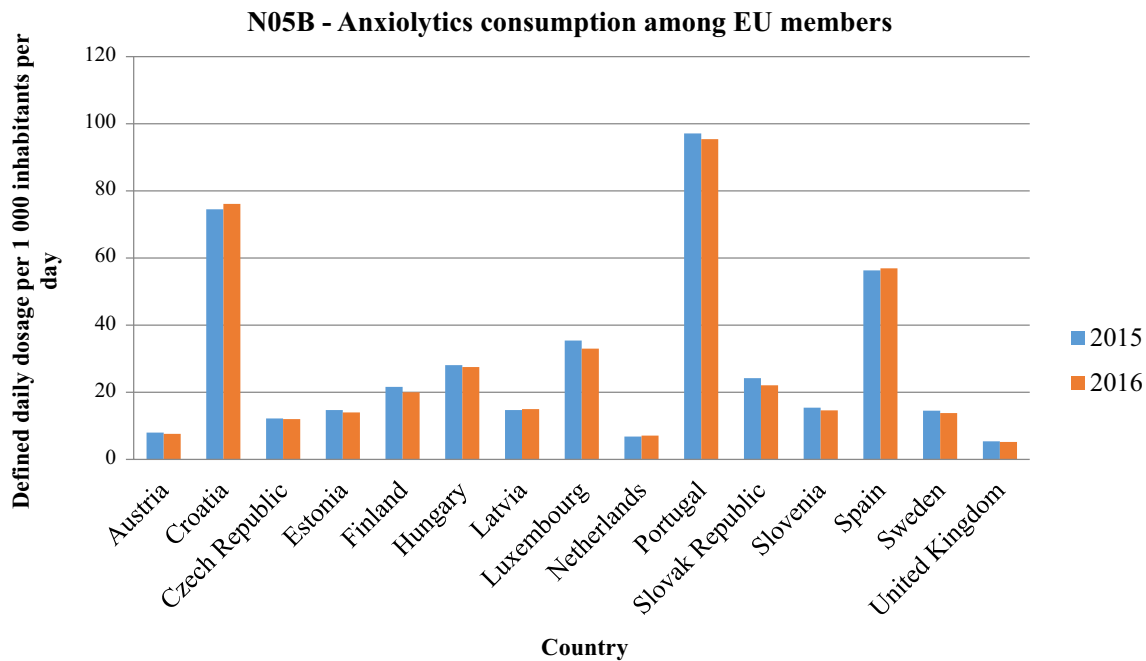
BZDs are widely prescribed drugs. To our knowledge, no systematic review of the literature on BZD prescriptions in the EU has been published till this date. Nevertheless, the database for some EU members provided by the Organisation for Economic Cooperation and Development (OECD) enables a health status determinants follow-up (including anxiolytic utilization) throughout the years (Fig. 1).

Despite a methodological difference (DDD/1,000 inhabitants per day), the data provided by the OECD places Portugal, Spain and Croatia in the group of countries with highest BZD consumption in Europe [52]. Only Latvia, the Netherlands, Spain and Croatia had an increase in anxiolytic consumption during the analyzed period, while other countries had a decline in the same period (Fig. 1). Although these countries have national recommendations concerning drug reconciliation, there are no official guidelines on how general practitioners should prescribe BZDs [53, 54]. According to the data of The Agency for Medicinal Products and Medical Devices (HALMED) that monitors the consumption of medicinal products in Croatia, DDD/1 000 inhabitants per day for anxiolytics in Croatia is increasing, placing Croatia in the second place in comparison to the available data of other European countries [55, 56].

Recent research conducted in France and Italy showed the prevalence of BZD use, now estimated to be 13.8% [57, 58], similar as in the Netherlands, where prevalence varied between 10 and 25% [59], and in the United Kingdom, where 26.1% of the respondents reported having taken a BZD or Z-drug [60], while BZDs in Pakistan were the most recognized category of medication (75.3%) used for all mental health conditions [61]. Similar variations were found in the United States of America, Canada and the Netherlands, where BZDs were most often prescribed by primary care physicians [62–64]. Previous studies conducted in the City of Zagreb, the capital of Croatia, showed that BZDs accounted for more than 50% of the outpatient utilization of psychopharmaceuticals throughout the study period [8]. On the other hand, the prevalence of long-term BZD use among Finnish adults showed a declining trend (from 5.3 to 3.6%), from the year 2006 to 2014 [65].

The similar prescription pattern is recognized in Croatia and confirmed by the results in this study, with an average of 8.7% in the analyzed period. Croatian primary care physicians prefer BZDs because of good effectiveness and fast response with a small number of initial side effects [66].

There is no internationally agreed-on consensus on the duration of BZD usage [67]. Some treatment guidelines



**Fig. 1** Anxiolytics utilization among EU members for the period 2015–2016 (DDD/1 000 inhabitants per day). *Source:* Organisation for Economic Co-operation and Development (OECD), available at: [https://stats.oecd.org/index.aspx?DataSetCode=HEALTH\\_STAT#](https://stats.oecd.org/index.aspx?DataSetCode=HEALTH_STAT#) and The Agency for Medicinal Products and Medical Devices (HAL-

MED, Croatia), available at: [http://halmed.hr/fdsak3jnFsk1Kfa/ostale\\_stranice/Tablica\\_16-Ukupna\\_potrosnja\\_lijekova\\_u\\_2016\\_godini.pdf](http://halmed.hr/fdsak3jnFsk1Kfa/ostale_stranice/Tablica_16-Ukupna_potrosnja_lijekova_u_2016_godini.pdf) and [http://halmed.hr/fdsak3jnFsk1Kfa/ostale\\_stranice/Tablica\\_16-Ukupna\\_potrosnja\\_lijekova\\_u\\_2015\\_godini.pdf](http://halmed.hr/fdsak3jnFsk1Kfa/ostale_stranice/Tablica_16-Ukupna_potrosnja_lijekova_u_2015_godini.pdf)

recommend that BZDs should be used intermittently for less than 2 weeks in the treatment of insomnia and should not be used for more than 6 weeks (including tapering before withdrawal) for anxiety treatment [68–70]. BZD dependence is a frequent complication of a regular prescription for 4 weeks or longer, occurring in almost one-third of patients [71]. Long-term use individuals are at a higher risk for the development of tolerance reaction [59, 66, 72].

Previous studies have shown that caution should be taken when prescribing BZDs to older people [73], since long-term use individuals are at a higher risk of dependence, as well as other side effects including falls, dizziness, psychomotor side effects, fatigue, cognitive dysfunction, and Alzheimer's disease [22]. The results of this study have shown that BZD users were more likely to be older females, which confirms previously published data [4, 74].

In terms of medical indications, Croatian primary care physicians prescribed BZDs under the diagnoses of anxiety disorders, depressive episodes and other neurotic disorders. However, the interpretation of these results should be approached with caution, because the reliability of data could be questioned, because only the first diagnosis is noted on the prescription when the primary care physician prescribes the drug, and it is commonly known that patients usually have several comorbidities.

Kapil et al. [62] conducted an internet-based questionnaire in the UK, results of which showed that the main reasons for the use of BZD and Z-drugs were to help with sleep (66.4%), to cope with stress (37.1%) and/or to get high (31.0%). Paradoxically, in a study conducted in Quebec, Canada long-term BZD users were more likely to report poor sleep quality [33].

According to our results, the female population utilizes more BZDs in comparison to the male population, except in the age group 0–19. Results presented here are similar to recent European data. Tournier et al. [75] confirmed that the use of BZDs increases with age and is more frequent in women than in men. Čulig et al. [76] emphasized the fact that 33.9% of pregnant women in the City of Zagreb utilized diazepam during the pregnancy. All BZDs have the same mechanism of action, but widely differ depending on their pharmacokinetic properties. That is the reason why BZDs are classified in terms of their elimination half-life. Short-acting BZDs have a median elimination half-life of 1–12 h (i.e. alprazolam, lorazepam, clonazepam, midazolam), intermediate-acting BZDs have an average elimination half-life of 12–40 h, while long-acting BZDs have an average elimination half-life of 40–250 h (i.e. diazepam) [77].

In terms of prescriptions of BZDs by primary care physicians in the analyzed period (years 2015 and 2016), the most prescribed drug from the group of BZDs was diazepam,

followed by alprazolam. This finding is in line with previous study conducted in Croatia, where the most common inappropriate prescription drug was diazepam (56% of all inappropriate prescription drugs, with an overall prevalence of 1.2%) [78]. European data confirms this prescription habit, where Ireland, Serbia, Portugal and Croatia had the highest rates of calculated consumption [49, 79, 80].

A remarkably high number of patients who utilize BZDs indicates the need for recognition and implementation of the international and national guidelines. Many countries noticed a similar problem, but only a few managed to make progress in resolving this issue [81]. For example, utilization of BZDs among the New Zealand population remained relatively low between 2005 and 2013, with a decrease from 7.0 to 5.4%. However, the utilization of psychotropic medicine in older people increased by one fifth in the same period [82]. The reason for this growing BZD prescription problem might be the fact that for many clinicians, experience with BZDs is positive as drugs with little chance of fatal overdose and mostly manageable side effects compared to other alternatives. From the patient's perspective, the reason for continuous BZD utilization is fast drug response, physiological dependence (even for lower doses of BZDs), and fear of discontinuation [66].

Not only have BZDs shown an increase in utilization trend, but Rapić et al. [83] recently concluded that there is an existing over-utilization of psychotropic drugs trend in existence Croatia, and that the interventions that are being implemented to control the drug utilization have not brought about any changes. Total utilization of psychotropic drugs continuously increased, confirmed by other smaller study [8]. Additionally, Štimac et al. [84] previously showed that in Croatia, BZDs accounted for 86.9% of psychopharmaceutical utilization.

Unfortunately, clinical recommendations on the national and international levels are often time not in harmony, and sometimes even influenced by negative propaganda which has been confirmed in the recent Opinion published by The International Task Force on Benzodiazepines [85]. In 2013, representatives drawn from the Psychopharmacology Special Interest Group of the Royal College of Psychiatrists and the British Association for Psychopharmacology organized a working group that produced a joint statement regarding BZD utilization in clinical practice. They recommend that whenever BZDs are prescribed, the potential for dependence or other harmful effects must be considered as well. This group of authors also believes that the risks of dependence associated with the long-term use (longer than 1 month) increases and health professionals should be conscious of this when considering the relative benefits and risks of treatment [86]. Additionally, by encouraging stakeholders to recognize the need to reduce the harms associated with the abuse of drug prescriptions by implementing stronger

legislative measures based on current (and updated) guidelines and clinical recommendations might change prescription habits among health care providers [87].

The monitoring of drug consumption requires a multidisciplinary approach of clinicians, primary care providers, clinical pharmacologists, pharmacists and epidemiologists [17, 88]. The development of a national health dataset that includes inpatient and outpatient utilization prescription data presents a good measure for the improvement of current services towards better results for health care users [89].

In terms of discontinuing long-term BZD use, Voshaar et al. [90] conducted the meta-analysis and evidence was found for the efficacy of an intervention such as advice provided by letter or by organizing a meeting of a larger group, followed by systematic discontinuation alone led by a physician or psychologist [28].

### Strengths and limitations

This was a retrospective, observational study, using nationally representative data available from the official source, CHIF - a national agency for health insurance in Croatia. The findings of this study are based on a real number of prescriptions collected from all working pharmacies in Croatia for the years 2015 and 2016. To the best of our knowledge, this is the first time that both utilization habits, and diagnoses related to the usage of BZD, were included in this and similar studies.

The limitation of this study is the lack of data regarding the trend of BZD utilization throughout the years, since only years 2015 and 2016 were included in the study. In addition, we could only assume that patients are utilizing prescribed drugs according the doctor's recommendations.

### Conclusion

The aim of this study was to analyze the prevalence of BZD use in the Croatia. The obtained results clearly indicate a high prevalence of BZD use, with a variation observed in gender and age. Patients aged  $\geq 80$  years have been responsible for the greatest use of BZDs, with presumption of some of the usage being inappropriate. The most prescribed BZD was diazepam, followed by alprazolam. These results indicate the need for rationalization in BZD prescriptions. Established expert guidelines and stricter national regulations will assist in achieving this goal.

The data presented in this study suggests considering the use of drugs from the other group with similar effect, but less potential side effects.

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