Family Medicine and Community Health

Challenge of long-term benzodiazepine use in primary care: insights from a real-world cohort study in Catalonia

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ABSTRACT

Introduction Long-term use of benzodiazepines (BZD) triggers health problems. Although Spain leads European use of BZD, the number of long-term users (LTUs) remains unknown.

Objective The aim of the study is to estimate the proportion of primary care (PC) patients who initiate a BDZ prescription that subsequently become LTU and to identify its associated factors.

Design Retrospective real-world data cohort.

Setting and participant It included the population over 15 years with a new prescription of BZD in PC in Catalonia. Users were considered LTU if they had been dispensed at least three prescriptions within 3 months. Sociodemographic characteristics of patients and prescribers, pathologies, previous BZD use, number and type of visits, and prescription quality standard were considered. We estimated the proportion of LTU among patients with a new prescription, stratified by age and sex, and estimated risk factors by multivariate generalised linear models.

Result 100 638 users with a new BZD prescription were included. 27.1% were LTU at 3 months and 14.5% at 6 months. LTU increases with age and is higher in women. Predictors of LTU are Spanish nationality, living in rural areas, having a mental illness, having used BZD, having virtual visits or not meeting pharmacy-therapeutic quality standards.

Conclusion The number of patients who develop LTU is high, especially in the elderly. Exploring the causes of this phenomenon could contribute to the development of future interventions.

WHAT IT IS ALREADY KNOWN ON THIS TOPIC

⇒ The use of benzodiazepines (BZD) has become a public health problem due to its widespread usage and gradual increase.

⇒ There is a lack of knowledge about the risk of becoming a long-term user (LTU) of BZD in primary care (PC) after receiving a new prescription.

WHAT THIS STUDY ADDS

⇒ One in four new users becomes an LTU at 3 months.

⇒ Advanced patient age is an important risk factor for becoming LTU and the quality of the physician's prescription is a protective factor for LTU.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The development of an intervention for physicians and patients in PC to decrease the rates of LTU of BZD in PC will be aided by this result.

INTRODUCTION

Benzodiazepines (BZD) are mainly used to treat insomnia, anxiety and muscular problems. Globally, the annual prevalence of BZD use varies between 2% and 18%.[1–3] The prevalence in Spain is 16%, making it one of the countries with the highest use in Europe, while in countries such as Germany and the UK, it is around 6%.[4]

An increase in the prevalence of BZD use has been observed worldwide in recent years.

In the USA, annual BZD use rose from 5% in 2008 to 12% in 2016,[5 6] and, in Spain, figures also show a rise in both prevalence and quantity used.[7–9 1] Use increases with age, reaching 30% in people older than 65 years,[10] and this is notably higher in women, which can be double that of men.[1 4] The presence of comorbidities,[9 11–13] and having a lower educational and/or socioeconomic level, is also associated with a greater prevalence of BZD use.[1 14]

According to the recommendations of the European Medicines Agency on the patient information leaflet, the use of BZD should not exceed 12 weeks, while clinical practice guidelines limit use to 4 weeks,[15–17] advice which is not complied with in many countries.[18] Despite these recommendations, approximately 3% of the general population

worldwide engages in prolonged use (defined as greater than 12 weeks), although this can vary between 0.6% and 3.5%, depending on the studies' observation periods.[13 19–21] Prolonged BZD use can cause cognitive impairment,[20] increased risk of falls and fractures,[22] accidents,[23] heightened drug tolerance and dependence[24 25] and increased all-cause mortality.[26]

In health contexts where primary care (PC) is the gateway to healthcare, this is where the majority of BZD prescriptions are initiated.[27] Studies carried out at this care level identify factors associated with long-term BZD use as being female, being of advanced age, having a low socioeconomic and/or educational level, having previously been prescribed BZD, or having high prescribed doses.[4 11 28] However, these studies are performed with a prevalent sample and, as such, we do not know which factors (related to patient, prescribing physician or the system) influence long-term use following a new prescription.

The only study worldwide that analysed the prevalence of new prescriptions and percentage of long-term use was conducted in Japan and determined that advanced age, prescription by a psychiatrist, high doses and concomitant prescription with other psychotropics are associated with long-term use.[29] However, this study was carried out in a non-European context and did not assess which characteristics associated with professionals and/or the system itself might influence long-term use.

Despite the widespread use of BZD, there is a lack of studies, particularly in Spain and other European countries that examine the factors contributing to long-term use among individuals who initiate a new BZD's prescription. Identifying these factors is essential for designing effective interventions aimed at reducing inappropriate prescriptions and their associated harms.

The present study aims to fill this gap by determining the proportion of long-term users (LTUs) among those who receive a new prescription for BZD in PC, and by identifying user-level, professional-level and system-level factors that increase the probability of long-term use. These findings can provide a critical evidence base for improving prescribing practices and informing public health strategies to minimise the negative impact of long-term BZD use.

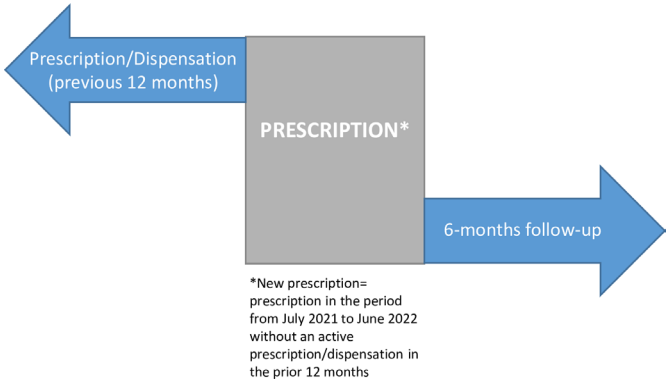


Figure 1 Graphic description of the study.

METHODS

Study design

Information was used from a retrospective real-world cohort with data consisting of users who had received a BZD prescription between July 2021 and June 2022 in a PC setting in Catalonia, Spain. Data were obtained from the Information System for the Development of Research in Primary Care (SIDIAP)[30] database which collects information generated in the public PC system in Catalonia. This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology statement.

Context

Health coverage provided by the Spanish public healthcare system is universal. Health services are free at the point of use, except for medications, for which a copayment system operates according to users' income bracket and employment status. Online supplemental file 1 contains a more detailed description of the health system in Catalonia.

Database of the SIDIAP

The SIDIAP database was created in 2010 and contains all information from the medical records of users treated in 80% of the PC system in Catalonia (sociodemographic data and indicators, clinical variables, service use, drug prescription and dispensing, geohealth variables, etc).[31] Regarding information on drugs, the prescription register is an accurate daily record, while the dispensing register is monthly. It is an encrypted, anonymised database that meets all current legal requirements. The present study includes the population aged over 15 years that received a BZD prescription during the study period at a Catalan Health Institute (ICS) PC centre. Drugs included are N05BA, N05CD and N05CF, according to the Anatomical Therapeutic and Chemical classification, which is detailed in online supplemental table 1.

Users

Users' cohort inclusion criteria: all users who received a BZD prescription between July 2021 and June 2022 were initially selected.

New users' cohort inclusion criteria: being prescribed with a new BZD prescription, that is, not having an active prescription or dispensing record of another BZD in the previous 12 months. New users' cohort exclusion criteria: not having a minimal follow-up (3 or 6 months based on the outcome) in the database (figure 1).

Variables

Dependent variable: LTU defined as a user with at least three consecutive monthly records of BZD dispensed following a new prescription. This definition has been chosen to follow strictly the clinical practice guidelines,

which recommend not to exceed over 3 months the prescription of BZD in order to avoid the risk of dependency.[15–17] As a time sensitivity analysis, these three records over 3 months were extended to six records over 6 months (figure 1).

Independent variables:

1. Sociodemographic variables: sex, age (years), nationality (categorical, see online supplemental table 2), rurality (indicates whether the user resides in an urban or rural area).
2. Clinical variables: active comorbidities in the clinical history at the time of the BZD prescription (according to the International Classification-10-Clinical Modification, grouped in detailed categories in online supplemental table 3); history of previous BZD prescription (any prescription between commencement of data registration (March 2019) and the 12 months prior to what was considered a new prescription) (figure 1).
3. Use of service variables: number and type of PC visit (virtual or face to face). Virtual visits are healthcare services provided remotely through communication technology. Visits were grouped (0, 1–3 and more than 3) into those made 6 months prior to and 3 and 6 months after the prescription. Those that took place 6 months subsequently were only taken into account in the 6-month time sensitivity analysis. Visits where the user was present were considered face to face whether they were in the PC centre or at home (figure 1).
4. Prescription variables: duration (in months) indicated by the professional prescriber in the first prescription.
5. Dispensing and use variables: dispensing month and defined daily dose (DDD) dispensed in each filled prescription.
6. Variables related to the PC physician (PCP) prescriber: sex and age (categorised as: 18–29, 30–44, 45–55, >55 years). The global pharmaco-therapeutic prescription quality standard (EQPF) for each physician, along with the specific one for anxiolytics-hypnotics (EQPF-ANSH), was included.[32] The EQPF is an annual indicator that takes into account compliance with prescription quality indicators for different therapeutic groups and where higher scores on a range from 1 to 100 show better compliance. Cut-off points determined by the ICS were selected (online supplemental file 1).
7. PC centre variables: teaching centre (those where physicians and/or specialist nurses are trained) or non-teaching.

Analysis

BZD use

Based on the population assigned to the SIDIAP database, the prevalence of people who were dispensed or prescribed at least one BZD during the study period and the proportion of people who received a new prescription were calculated. Average six-monthly use per new user was calculated by dividing the total quantity of active ingredient dispensed (measured in DDD) by the total number of new users of the drug.

Long-term BZD user

The proportion of LTUs compared with the total number of users who received a new BZD prescription during the study period was calculated.

All analyses were stratified by sex and age groups.

Factors associated with long-term BZD use

The factors associated with being an LTU among users with new prescriptions were estimated through calculation of risk ratio (RR) with multivariate generalised linear models with a Poisson distribution with standard errors and a log link. These models were used in light of the proportion of LTUs; however, alternative models using multivariate logistic regression were also performed (data will be shared on request). Associated factors include user, system and professional variables (age, sex, EQPF). This analysis was stratified by sex and the effect size of sex was assessed in a model using all data.

The following variables showed missing data: nationality, rurality and professional variables. The proportion of missing data ranged from 4% to 24% according to the variable. These data were imputed using multiple imputation with chained equations.

Analyses were carried out using STATA V.17.0 software.

Patient and public involvement

No patient involved.

RESULTS

Figure 2 illustrates the flowchart of data extracted from the database. Furthermore, it shows the flowchart for the subgroup of users examined in this study and their respective prevalence of BZD prescription.

Prescription and dispensing prevalence of BZD in the population treated in PC

The analysed population of 5 650 755 PC users showed an annual BZD prescription prevalence of 11% (table 1). Differences were observed by sex with prescription prevalence among women (13.78%) being nearly double that among men (7.29%). Differences were also observed by age group. Prescription prevalence increased with age in both sexes, reaching a maximum prescription prevalence of 20.74% in women aged 65–74 years and 9.79% in men aged 55–64 years.

The number of users with new prescriptions was 371 226 (238,623 women (8.31%) and 132 603 men (4.77%)). This implies a prevalence of 6.57% of new BZD prescriptions among the total number of people treated in PC (62.04% of the total number of people receiving BZD) (table 1). The proportion of new prescriptions increased progressively with age, except for the age groups over 74 years in women and over 64 in men.

Six-monthly quantification of BZD dispensing among users with a new prescription

Average six-monthly dispensing measured in DDD for new users was higher among women (77.05) than men

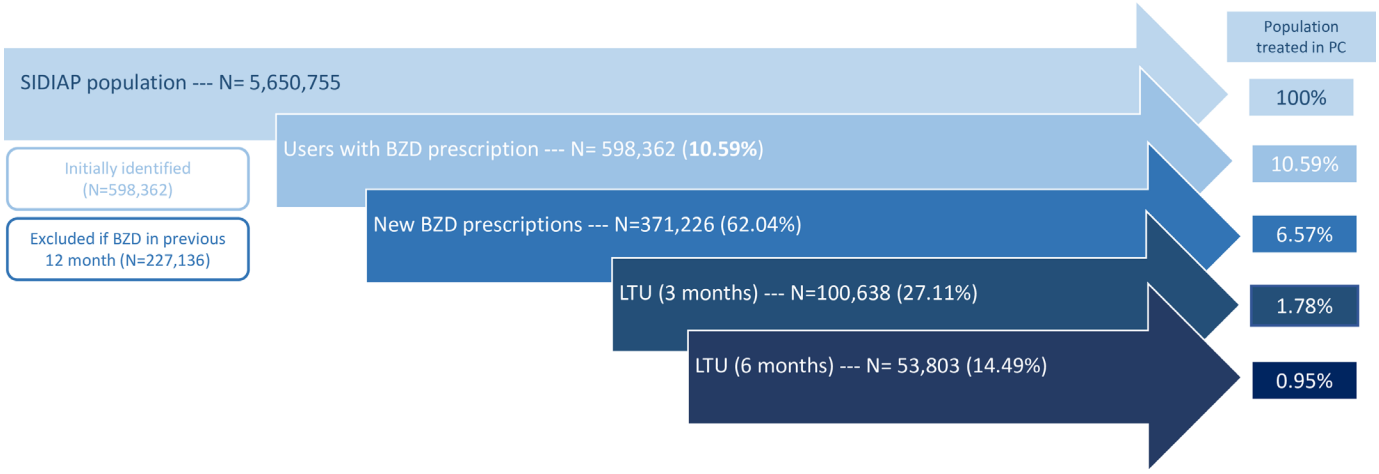


Figure 2 Flow chart of subgroup users analysed in the study and their respective prevalences of BZD prescription. BZD, benzodiazepines; LTU, long-term user; PC, primary care; SIDIAP, Information System for the Development of Research in Primary Care.

(69.77) (Table 1). However, when stratifying by age, this pattern was not observed in all age groups. Among those under 55 years, semiannual DDD per new user was higher in men than in women, while among those over 55 years, the relationship was inverted and was higher in women. In both sexes, six-monthly DDD per new user increased progressively. In women, it ranged from 26.66 in the population under 25 years to 117.81 in those over 74 years and in men from 29.36 to 103.24, respectively.

Proportion of LTUs

The overall proportion of users who receive a first prescription and become LTU at 3 months is 27.11%, while, at 6 months, the figure is 14.49% (figure 2). Differences were observed by sex. In women, the proportion of LTU at 3 months was 28.94% and in men it was 23.81%, and at 6 months, the percentages for women and men were 15.71% and 12.30%, respectively. A clear increase in the percentage of LTU at 3 months can be seen as age advances, proportions that exceed 44% in both sexes in those older than 74 years. Long-term use in this population at 6 months is over 22% (figure 3).

Factors associated with LTU

Factors that influence prolonged BZD use can be divided into those related to the user (table 2) and those associated with the health system (table 3).

Among user-related factors, analysis of the overall sample showed that women have a slightly greater risk of being LTU at 3 months, although with a small effect size (RR=1.01; p=0.04). When stratifying by sex, it can be observed in both men and women that being older, being of Spanish nationality, living in rural areas, having a history of pathology and having received previous BZD prescriptions (prior to the 12-month period preceding the new BZD prescription) are risk factors for becoming LTU. Having psychiatric comorbidity, apart from organic mental disorders, raises the risk of becoming LTU in both sexes. The RR of risk ranges, in women, from 1.13 to 1.66 between that observed in personality disorders and developmental disorders, respectively, and in men from 1.10 to 1.58 also observed in personality disorders and developmental disorders, respectively. In contrast, osteoarthritis, other joint pathologies and muscle and soft-tissue disorders demonstrate a protective effect in both sexes, while organic mental disorders show a protective effect in women but not in men. It was observed that the presence of neurological disorders increases the risk of LTU in men.

Among factors related to the health system, having virtual visits with the PCP at 3 and 6 months following a new prescription is associated with a higher risk of becoming LTU in both men and women. Similarly, other risk factors were observed, including having a longer duration of a new prescription scheduled, the PCP not complying to an excellent degree with the specific EQPF-ANSH, and the prescribing PCP being under 30 years old.

Conversely, in-person visits prior to the new BZD prescription and at 3 months are protective factors for both sexes.

Some differences by sex were observed. Women have a lower probability of being LTU at 3 months if the PCP is female, although the effect is small. On the other hand, although both sexes showed a greater risk of being LTU if their visits to the PCP were virtual prior to the BZD prescription, the effect observed in men is larger.

No notable differences were observed regarding the sensitivity analysis of the factors associated with becoming LTU carried out at 6 months (online supplemental table4). Although slightly smaller effect sizes were observed in generalised linear models with Poisson distribution, results were similar in logistic regression models.

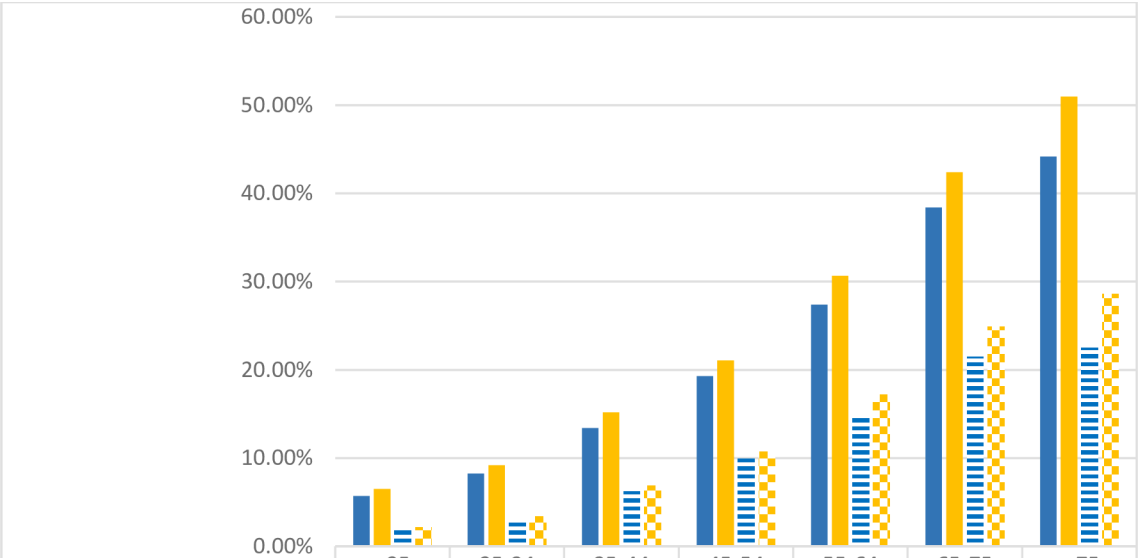
DISCUSSION

A quarter of users who receive a new prescription become LTU at 3 months and almost 15% at 6 months,

Table 1 Prevalence of prescription and new prescription of benzodiazepines during the period July 2021 to June 2022 and six-monthly use among new users, stratified by sex and age

	Population treated in PC		Prescriptions		New prescriptions		Average (SD) six-monthly use in new users (DDD)	
	N=5 650 755		N=598 362 (10.59%)		N=371 226 (6.57%)			
Sex, N (%)	Woman	Man	Woman	Man	Woman	Man	Woman	Man
	2 871 328 (50.81%)	2 779 427 (49.19%)	395 703 (13.78%)	202 659 (7.29%)	238 623 (8.31%)	132 603 (4.77%)	77.05 (115.12)	69.77 (114.27)
Age group, N (%)								
<25	290 061 (10.10%)	312 395 (11.24%)	12 319 (4.25%)	6820 (2.18%)	9758 (3.36%)	5569 (1.78%)	26.66 (36.67)	29.36 (53.29)
25–34	334 951 (11.67%)	341 635 (12.29%)	30 253 (9.03%)	19 241 (5.63%)	22 421 (6.69%)	15 055 (4.41%)	32.24 (52.46)	37.63 (75.69)
35–44	438 537 (15.27%)	455 607 (16.39%)	55 009 (12.54%)	33 705 (7.40%)	36 615 (8.35%)	23 922 (5.25%)	45.27 (79.94)	48.89 (99.36)
45–54	465 644 (16.22%)	494 016 (17.77%)	75 389 (16.19%)	43 139 (8.73%)	46 753 (10.04%)	28 615 (5.79%)	59.87 (102.57)	62.72 (121.79)
55–64	387 605 (13.50%)	386 516 (13.91%)	72 486 (18.70%)	37 842 (9.79%)	42 552 (10.98%)	23 597 (6.11%)	83.07 (127.38)	76.50 (123.86)
65–74	317 914 (11.07%)	301 658 (10.85%)	65 944 (20.74%)	29 409 (9.75%)	36 584 (11.51%)	17 548 (5.82%)	104.28 (133.70)	93.11 (119.35)
≥75	636 616 (22.17%)	487 600 (17.54%)	84 303 (13.24%)	32 503 (6.67%)	43 940 (6.90%)	18 297 (3.75%)	117.81 (127.50)	103.24 (117.76)

DDD, defined daily dose; N, absolute number; PC, primary care.



	<25	25-34	35-44	45-54	55-64	65-75	> 75
Men 3 months (23.81%)	5.69%	8.24%	13.43%	19.31%	27.38%	38.39%	44.19%
Women 3 months (28.94%)	6.52%	9.19%	15.18%	21.07%	30.66%	42.41%	50.97%
Men 6 months (12.30%)	1.94%	3.01%	6.25%	9.91%	14.94%	21.46%	22.54%
Women 6 months (15.71%)	2.14%	3.37%	6.90%	10.75%	17.20%	24.89%	28.58%

Figure 3 Proportion of long-term user at 3 and 6 months among the population with a new benzodiazepines' prescription stratified by sex and age.

with higher proportions seen in women. Factors associated with becoming an LTU are similar in both sexes, with age, history of mental disorders and/or previous BZD prescriptions, and virtual follow-up visits to the PCP, among others, of particular note.

Differences identified with respect to sex in the prevalence of prescription are well documented. A higher prescription ratio is observed among women, with a rate of 2:1.[19 28] This may be explained by the higher reported prevalence of mood and anxiety disorders in women.[33 34] Women tend to have more frequent contact with health services and be more willing to disclose these symptoms compared with men.[35] Additionally, there is a greater tendency among physicians to prescribe psychotropic drugs to women.[36] Despite health recommendations discouraging the use of BZD among individuals over 65 years of age,[13 37] and advocating for non-pharmacological approaches to manage anxiety or insomnia, prescription rates in this group remain high.

Long-term use of BZD should be a matter of considerable importance for health authorities due to the heightened risk of complications. Clinical practice guidelines recommend not exceeding 4 weeks use[15–17] for insomnia and 12 weeks use for anxiety. Our study showed proportions of LTU at 3 and 6 months to be 27.11% and 14.49% of new prescriptions; 1.78% and 0.95% of the total population treated in PC. These data are somewhat lower than those reported in the systematic review by Kurko *et al*.[13] This review included studies carried out in Europe, Asia, Australia and Canada, where the proportion of LTU in the general population ranges from 2% to 3.5%. Another study conducted in the Netherlands recorded similar figures, with 2.9% at 3-month and 2.0% at 6-month follow-up.[19] The differences observed are likely due to our use of a stricter definition of long-term use, which aligns with local clinical practice guidelines by using 3 months but also considers a minimum number of prescriptions to be filled in that period. Both studies considered an individual to be LTU if they received at least one prescription during the follow-up period, while in our study BZD needed to be dispensed at least three times in the 3 months after the initial prescription to meet criteria for LTU. This definition was taken trying to be consistent with the Clinical Practical Guidelines and adopting a conservative point of view, keeping in mind that figures shown in this paper are highlighting a major public health issue. On the other hand, our findings with regard to the high proportion of LTU among elderly people are in line with other studies. In these studies, despite the use of BZD not being recommended in older adults, rates reach almost half of new users.[13] Women showed a greater likelihood of becoming LTU than men at both 3 and 6 months, although the effect was small. This differs from the Japanese study, where being male was associated with a higher risk of continuing to use BZD 3 months after a new prescription.[29]

The factors associated with becoming an LTU of BZD observed in this study are similar for both sexes. These findings are consistent with other studies where factors such as older age,[4 11] having a history of mental and/or neurological pathology,[29] having received previous BZD prescriptions and inadequate follow-up after the

Table 2 User-related risk factors for becoming long-term user of BZD at 3 months, stratified by sex

	Women				Men			
	N (%)	RR	95% CI		N (%)	RR	95% CI	
Age (mean, years (SD))	56.49 (18.34)	1.02	1.02	1.02	53.72 (17.50)	1.01	1.02	1.02
Nationality (Ref value: Spanish)	154 635 (85.39)				83 319 (83.15)			
America (except North America)	10 980 (6.06)	0.80	0.76	0.84	4482 (4.47)	0.69	0.63	0.75
Eastern Europe	4924 (2.72)	0.89	0.84	0.95	2022 (2.02)	0.82	0.73	0.91
North Africa	4246 (2.34)	0.80	0.73	0.87	3999 (3.99)	0.85	0.78	0.92
Rest of nationalities	6303 (3.48)	0.77	0.72	0.81	6383 (6.37)	0.76	0.72	0.81
Enrolment in rural area (Ref value: urban)	35 354 (16.85)	1.04	1.02	1.06	20 809 (18.11)	1.04	1.01	1.06
Pathological history (Ref value: no record of)								
Osteoarthritis and other joint pathologies	147 991 (62.02)	0.88	0.87	0.89	74 796 (56.41)	0.81	0.80	0.82
Muscle and soft-tissue disorders	49 240 (20.64)	0.99	0.98	1.01	18 069 (13.63)	0.91	0.88	0.93
Neurological disorders	13 031 (5.46)	1.00	0.98	1.02	5899 (4.45)	1.07	1.03	1.10
Schizophrenia	810 (0.34)	1.25	1.16	1.34	1026 (0.77)	1.49	1.38	1.59
Behavioural syndromes	56 156 (23.53)	1.26	1.25	1.28	27 478 (20.72)	1.33	1.31	1.36
Mood disorders	50 918 (21.34)	1.23	1.21	1.24	16 791 (12.66)	1.25	1.22	1.29
Anxiety disorders	136 639 (57.26)	1.19	1.18	1.21	60 554 (45.67)	1.27	1.24	1.29
Developmental disorders	91 (0.04)	1.66	1.24	2.23	187 (0.14)	1.58	1.24	2.02
Mental disorders of organic origin	2893 (1.21)	0.91	0.88	0.95	1249 (0.94)	0.93	0.87	1.00
Mental disorders due to substance abuse	39 188 (16.42)	1.22	1.20	1.24	34 880 (26.30)	1.19	1.17	1.22
Adult personality and behavioural disorders	4706 (1.97)	1.13	1.20	1.24	4649 (3.51)	1.10	1.04	1.15
History of BZD description (Ref value: no history)	132 344 (55.46)	2.05	2.01	2.08	57 329 (43.23)	1.99	1.94	2.04

Analysis: generalised linear multivariable models with a Poisson distribution and log link function.
BZD, benzodiazepines; N, absolute number; Ref, reference; RR, risk ratio.

prescription have been shown to be associated with prolonged use.[13] The relationship between multimorbidity and the consumption of certain drugs, such as BZDs, has been confirmed. Moreover, the risk of dependence and side effects may increase when BZDs are prescribed to patients with polypharmacy.[9]

Nonetheless, to date, it is unknown whether factors associated with the quality or duration of the prescription affect the risk of becoming an LTU. Availability of these types of indicators could help improve the use of BZD. According to the findings of qualitative studies, PC professionals suggest that workload, users' demands and the lack of alternatives contribute to elevated rates of BZD prescription and its consequent extended use.[38 39] However, the quality of the prescription and the duration set by the physician are not mentioned. Our study shows that conducting follow-up through face-to-face visits reduces the risk of LTU. So far, this factor has not been analysed and could be confirmation of the results of a systematic review of qualitative studies, where users referred to a lack of follow-up by PC professionals once the BZD prescription was received, along with insufficient health education on the risks of BZD.[25] It is clear that interventions that consider these factors are needed. Furthermore, as shown in a Spanish study, such interventions should target general practitioners, given the lack of awareness about the risk of patients with newly prescribed BZD becoming LTUs.[40]

The main strengths of this study are the representativeness of the sample and the availability of information. As far as we are aware, this is the first study focussing on long-term BZD use among individuals receiving a new prescription in Spain and the first, internationally, to consider variables related to the quality of the prescriber's pharmaco-therapeutic prescription and type of visit.

Among the study limitations, we calculated BZD use through analysis of dispensing data, and it is possible that some users fill the prescription but do not take the drug. The prevalence of BZD use could also have been underestimated by not considering prescriptions from services outside the public health system in Catalonia, frequently used by private insurance. In addition, dispensing databases provide information monthly rather than daily, which could affect the accuracy of the data. Some variables, such as those that depend on manual registration by professionals, could be under-recorded. This could have occurred with some potential confounders, such as alcohol use, which could not be included in the multivariate generalised linear models due to a high proportion of missing data. Another potential confounder is opioid coprescription; however, we did not have access to this data for analysis. Finally, some patients who received

Table 3 Health system-related risk factors for becoming long-term user of BZD at 3 months, stratified by sex

	Women				Men			
	N (%)	RR	95% CI		N (%)	RR	95% CI	
Professional prescriber characteristics								
Gender female (Ref value: male)	160 118 (70.71)	0.98	0.96	0.99	83 711 (67.37)	1.00	0.98	1.02
Age (Ref value: >55 years)	73 938 (32.65)				41 058 (33.04)			
18–29	2038 (0.90)	1.10	1.04	1.17	1081 (0.87)	1.14	1.04	1.25
30–44	74 628 (32.96)	1.02	1.01	1.04	41 488 (33.39)	1.00	0.98	1.02
45–55	75 834 (33.49)	0.99	0.98	1.01	40 635 (32.70)	0.98	0.96	1.01
Prescription quality standards								
Global (EQPF) (Ref value: excellent result)	42 069 (18.42)				22 852 (18.23)			
Satisfactory	92 933 (40.69)	1.00	0.98	1.02	50 942 (40.63)	1.00	0.98	1.03
Not satisfactory	93 386 (40.89)	1.00	0.98	1.02	51 592 (41.15)	0.98	0.96	1.01
BZD specific (EQPF-ANSH) (Ref value: excellent result)	93 597 (43.54)				51 482 (43.72)			
Satisfactory	56 656 (26.35)	1.08	1.06	1.10	30 772 (26.13)	1.05	1.02	1.07
Not satisfactory	64 727 (30.11)	1.15	1.14	1.17	35 508 (30.15)	1.13	1.11	1.16
Initial duration of BZD prescription (mean, months (SD))	4.92 (6.46)	1.03	1.03	1.03	4.12 (6.02)	1.04	1.04	1.04
Teaching centre (Ref value: non-teaching centre)	80 162 (33.59)	1.01	0.99	1.02	44 559 (33.60)	1.01	0.99	1.03
Characteristics of primary care visits								
6 months prior to prescription								
Face to face and home (Ref value: no visits)	14 559 (6.10)				8617 (6.50)			
1–3 visits	99 325 (41.62)	0.92	0.90	0.95	61 937 (46.71)	0.92	0.89	0.96
>3 visits	124 739 (52.27)	0.88	0.86	0.90	62 049 (46.79)	0.88	0.85	0.92
Virtual (Ref value: no visits)	33 358 (13.98)				26 585 (20.05)			
1–3 visits	97 870 (41.01)	1.04	1.02	1.06	56 073 (42.29)	1.09	1.06	1.13
>3 visits	107 395 (45.01)	1.03	1.00	1.05	49 945 (37.67)	1.11	1.07	1.14
3 months after prescription								
Face to face and home (Ref value: no visits)	26 103 (10.94)				14 029 (10.58)			
1–3 visits	117 531 (49.25)	0.96	0.94	0.97	68 278 (51.49)	0.95	0.92	0.97
>3 visits	94 989 (39.81)	1.10	1.07	1.11	50 296 (37.93)	1.12	1.20	1.33
Virtual (Ref value: no visits)	42 961 (18.00)				28 690 (21.64)			
1–3 visits	116 453 (48.80)	1.23	1.21	1.26	62 872 (47.41)	1.29	1.26	1.33
>3 visits	79 209 (33.19)	1.39	1.36	1.42	41 041 (30.95)	1.45	1.41	1.50

Analysis: generalised linear multivariable models with a Poisson distribution and log link function.
BZD, benzodiazepines; EQPF, pharmaco-therapeutic prescription quality standard; EQPF-ANSH, BZD-specific pharmacological prescription quality standard; Ref, Reference; RR, risk ratio.

a new prescription died or were transferred to another health provider during the follow-up period. This could have underestimated the proportion of LTU; however, the proportion of these cases was 0.7% and 1.5%, respectively, for the 3-month and 6-month follow-up periods, and they have a minimal impact.

It would be highly valuable to complement the results obtained in this study with a qualitative study that explores the motives that lead to long-term BZD use from the perspectives of both users and PC professionals. Contrasting qualitative and quantitative results would help to examine the phenomenon in greater depth and aid the design of future interventions to improve BZD use in PC.

To sum up, this study demonstrates that a high proportion of users who receive a new BZD prescription become LTU. This risk worsens, owing to factors related to the user profile such as age, having comorbidity with mental and/or neurological illnesses or having previous BZD prescriptions. Also, there are risk factors influenced by the health system, including failure to comply with prescription quality standards or carrying out follow-up through virtual visits. The increase in risk is similar for both sexes, although women have a higher

baseline risk than men. In conclusion, the results of this study provide health planners and health institutions with information for the design of strategies addressed to both users and professionals that can reduce BZD use.

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