

## BRIEF REPORT

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# Role of private prescriptions in the long-term use of benzodiazepines and Z-drugs: A patient-related follow-up study

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**Abstract**

**Purpose:** To analyse (1) how often patients insured under the statutory health insurance (SHI) scheme received repeated prescriptions for benzodiazepines or Z-drugs as private prescriptions and (2) how often doctors switched from SHI prescriptions to private prescriptions and vice versa when issuing repeat prescriptions.

**Methods:** On basis of anonymized prescriptions from 874 ambulatory practices in Germany, we analysed the percentage of private prescriptions for Z-drugs, benzodiazepines/anxiolytics, and benzodiazepines/hypnotics and sedatives over 6 years (2014 to 2020).

**Results:** Of 2 200 446 prescriptions for a benzodiazepine or Z-drug, 38% were private prescriptions. In case of Z-drugs, the rate of private prescriptions was 44.1% for single prescriptions and 48.9% for refills. The difference was smaller for anxiolytics (23.3% vs. 26.0%) and, for benzodiazepine/hypnotics and sedatives, the proportion of private prescriptions for refills was even lower than for single prescriptions. In case of Z-drugs, the proportion of private prescriptions was, on average, 42.7% for the first prescription of a series of repeat prescriptions and 49.6% for the tenth prescription. The increase was smaller for anxiolytics and negligible for benzodiazepine/hypnotics and sedatives. Doctors stayed with their initial decision in more than three quarters of repeat prescriptions, be it a SHI or private prescription.

**Conclusion:** While we observed a large number of private prescriptions for benzodiazepines and Z-drugs, the proportion was only slightly higher for refills than for single prescriptions. Doctors do not seem to issue private prescriptions as a strategy to mask especially long-term use of these substances.

**KEYWORDS**

ambulatory care, cohort studies, drug prescriptions, hypnotics and sedatives, physicians' practice patterns

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### Key Points

- Previous studies have reported that ambulatory physicians in Germany prescribe a large part of benzodiazepines and Z-drugs as so-called private prescriptions, also for patients insured under the statutory health insurance (SHI) scheme.
- According to one hypothesis, this could be a strategy to mask the long-term use of benzodiazepines and, thus, to comply with the guidelines that recommend only short-term use.
- Our study confirmed that a high proportion of prescriptions for these drugs was issued privately for SHI patients.
- However, the difference between single and repeat prescription in the proportion of private prescriptions was only moderate.
- Doctors do not seem to use private prescriptions to mask especially the long-term use of benzodiazepines and Z-drugs.

## 1 | INTRODUCTION

Benzodiazepines and Z-drugs are often used for the treatment of insomnia.<sup>1</sup> They have demonstrated benefits for short-term use,<sup>2</sup> but there are difficulties in preventing from extending indefinitely with the risk of tolerance, dependence, and other adverse effects, including falls and hip fractures.<sup>1</sup> According to national guidelines<sup>3</sup> and international guidelines,<sup>4</sup> hypnotics and tranquilizers should not be prescribed for more than 4 weeks. However, many individuals still receive repeated prescriptions of benzodiazepines and Z substances over a longer period of time.<sup>5</sup> Among other things, this may increase the risk of interactions as patients with concurrent opioid use have a significantly increased mortality risk, compared to those without a concurrent benzodiazepine–opioid exposure.<sup>6</sup>

Usually, the cost of prescriptions for patients insured under the statutory health insurance (SHI patients) in Germany are covered, either at no costs to the patient or requiring a small co-pay, mostly not more than 5 Euro for the drugs under study. Approximately 11% of the German population is privately insured.<sup>7</sup> These individuals receive so-called private prescriptions or out-of-pocket prescriptions from their physicians and have to bear the cost of medicine at pharmacies but are subsequently reimbursed by their private insurance. While nearly all prescriptions for SHI patients are covered by the SHI, physicians can also issue private prescriptions to SHI-insured individuals who have to pay for these out of pocket without reimbursement. Private prescriptions cannot be monitored by the SHI so that it is difficult to recognize if prescribing practices violate guidelines.

Previous studies have reported that office-based physicians prescribe  $\geq 40\%$  of benzodiazepines and Z-drugs as private prescriptions, also for SHI-insured patients.<sup>8–10</sup> The question arises why. According to a survey of general practitioners and community pharmacist in Germany, switching to private prescriptions could be a strategy to mask long-term use of benzodiazepines and, thus, to comply with the respective guidelines and directives that recommend only short-term use.<sup>11</sup> However, it is to date unknown whether private prescriptions are especially used for long-term prescriptions of benzodiazepines and Z-drugs and, if so, to what extent.<sup>12</sup>

Based on a representative database of prescriptions in German ambulatory care practices, the aim of this study was to analyse (1) how often SHI patients received repeated prescriptions for benzodiazepines or Z-drugs in form of private prescriptions and (2) how often doctors switched from SHI prescriptions to private prescriptions and vice versa when issuing repeat prescriptions.

## 2 | METHODS

This observational study involved a secondary analysis of anonymized data, provided by the IMS<sup>®</sup> Disease Analyzer. Currently, the database includes anonymised aggregate data from approximately 2500 practices with nearly 8 million patients.<sup>13</sup>

All patients who received a benzodiazepine or Z-drug prescription for the first time or as a follow-up prescription between 1 January 2014 and 31 August 2020 were included. For these patients we had access to prescription data also for previous years. Privately insured patients were excluded. The drugs under study were divided into benzodiazepines, classified as anxiolytics (ATC code N05BA) or hypnotics and sedatives (N05CD), and Z-drugs (N05CF).<sup>14</sup> Prescriptions were classified as ‘private prescriptions’, which were paid for by the patient, or ‘SHI prescriptions’, which were issued at the expense of SHI.

The first benzodiazepine or Z-drug prescription of a patient, starting from 1 January 2014, was considered an initial prescription. If it was not followed by a further prescription, issued either as a private or SHI prescription within 90 days, it was defined as a ‘single prescription’. If there was a previous prescription within 90 days or if it was followed by a further prescription within 90 days, it was defined as a ‘repeat prescription’. A patient could be included several times if she or he started a new prescription episode after a gap of more than 90 days.

We compared benzodiazepine and Z-drug prescriptions issued as SHI prescriptions versus private prescriptions, both for single prescriptions and repeat prescriptions. We additionally calculated the survival curves of repeat prescriptions, that is, how often a SHI prescription was repeated until it changed to a private prescription and vice versa, displayed as Kaplan–Meier curves.

### 3 | RESULTS

#### 3.1 | Practices and patients

We included patient data from 874 practices, run by general practitioners, community neurologists and psychiatrists as the most important doctors for the prescription of hypnotic/sedative drugs. A total of 267 260 SHI patients received at least one prescription for a benzodiazepine or Z-drug in 2014 or later; their average age was  $65.2 \pm 19.0$  (median 66) years; 64.0% were women. Most of these patients (160 243) received benzodiazepine anxiolytics, 17 302 received benzodiazepine hypnotics and 122 884 Z-drugs.

#### 3.2 | Private prescriptions

Between January 2014 and August 2020, the 267 260 patients received 2 200 446 prescriptions. Nearly half of them (1 071 047/2 200 446) were Z-drug prescriptions, 41.8% were benzodiazepine anxiolytics while only 9.5% were issued for benzodiazepine hypnotics and sedatives.

Nearly 61% (1 337 696/2 200 446) of all prescriptions were issued as SHI prescriptions, 38.2% (841 591/2 200 446) as private prescriptions, and a few could not be classified. Z-drugs were most often issued as private prescriptions (48.1%), followed by benzodiazepine hypnotics (45.0%) and anxiolytics (25.2%).

Few practices ( $n = 14$ ) issued only SHI prescriptions and 1 practice only private prescriptions. The remainder ( $n = 859$ ;  $\pm 98.3\%$ ) issued both types of prescriptions.

#### 3.3 | Repeat prescriptions

The rate of private prescriptions for Z-drugs was 44.1% for single prescriptions and 48.9% for repeat prescriptions, a difference of 4.8% points (Table 1). The difference was smaller for anxiolytics (23.3% vs. 26.0%). For benzodiazepine/hypnotics and sedatives, the proportion of private prescriptions for repeat prescriptions was even lower than for single prescriptions (see also Table A1, Appendix for a comparison between some of the most often prescribed substances).

The Table 1 also shows how the proportion of private prescriptions changed with the rising number of repeat prescriptions per patient. In case of Z-drugs, the proportion of private prescriptions was 42.7% for the first prescription of a series of repeat prescriptions; it increased to 49.6% for the 10th prescription of patients with at least 10 prescriptions without a prescription gap. The increase was a bit smaller for anxiolytic and negligible for benzodiazepine/hypnotics and sedatives (see also Table A1, Appendix for single substances).

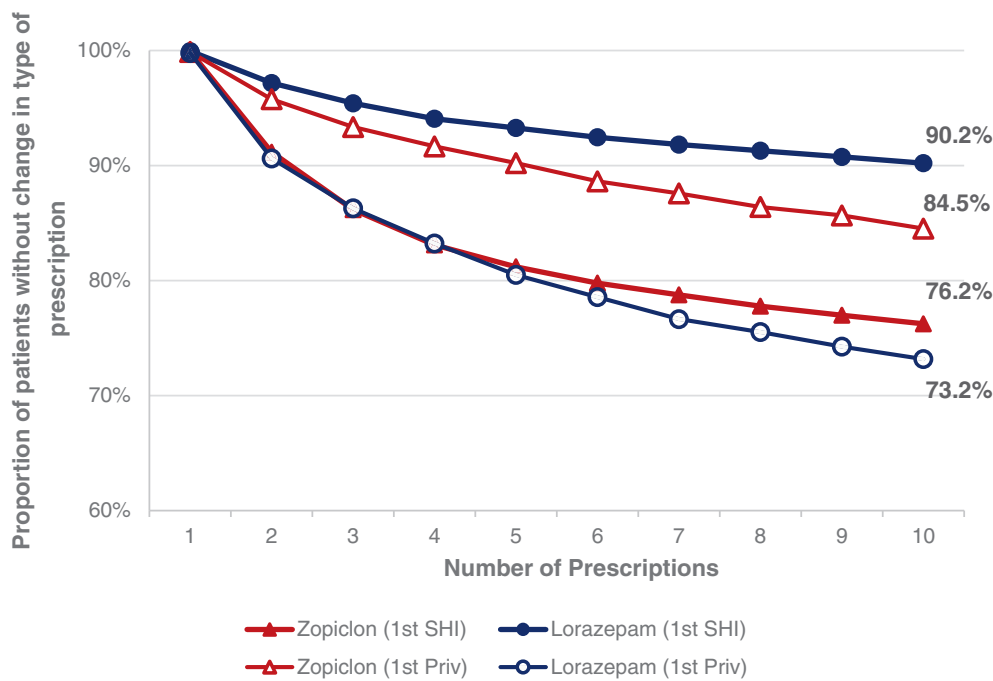
This moderate trend of anxiolytics and Z-drugs towards private prescriptions in case of refills can be cleared up more deeply if we investigate the drug switches from SHI prescriptions to private prescriptions and vice versa. If doctors started an anxiolytic as a SHI prescription, the next refills up to the tenth prescription were also SHI prescriptions in 87.4% of cases; after a first prescription as a private prescription, the next refills were also private prescriptions in 75.0% of cases. We observed a reverse trend in case of Z-drugs where the next refills up to the 10th prescription were SHI prescriptions in 75.3% of cases after an initial SHI prescription, and were private prescriptions in 84.1% of cases after an initial private prescription.

**TABLE 1** Single and repeat prescriptions of benzodiazepines and Z-drugs, 2014 to 2020

No. of prescriptions <sup>a</sup>	All		Benzodiazepine/Anxiolytics		Benzodiazepine/Hypnotics and sedatives		Z-drugs	
	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions
1 (Single <sup>a</sup> )	418 448	32.7%	250 147	23.3%	23 750	47.2%	173 469	44.1%
1 (Repeat <sup>b</sup> )	171 004	32.7%	84 989	21.9%	11 988	44.0%	77 739	42.7%
2	173 706	34.5%	86 661	22.9%	12 392	45.3%	79 738	46.0%
3	100 769	36.5%	46 551	23.5%	7863	45.2%	48 710	47.7%
4	72 259	37.3%	32 270	23.7%	5918	44.1%	36 020	48.6%
5	57 835	37.5%	25 065	23.9%	4908	44.3%	29 290	48.6%
6	48 634	38.4%	20 544	24.5%	4196	44.9%	25 094	49.1%
7	42 339	39.0%	17 558	24.8%	3739	44.0%	21 983	49.5%
8	37 632	39.2%	15 215	25.1%	3383	43.5%	19 839	49.5%
9	34 087	39.7%	13 530	25.8%	3100	43.8%	18 090	49.7%
10	31 229	39.7%	12 257	25.8%	2848	44.0%	16 660	49.6%
>10	1 012 504	42.2%	315 856	28.9%	124 671	44.8%	524 415	50.3%
All repeat	1 781 998	39.5%	670 496	26.0%	185 006	44.7%	897 578	48.9%
All	2 200 446	38.2%	920 643	25.2%	208 756	45.0%	1 071 047	48.1%

<sup>a</sup>One or more single prescriptions with a distance of more than 90 days.

<sup>b</sup>1 to 10 = number of prescriptions, issued in an interval of 90 days or less (=repeat prescriptions).



**FIGURE 1** Maintenance of SHI prescriptions for repeat prescriptions; zopiclone and lorazepam

The Figure 1 exemplarily shows the switches for lorazepam and zopiclone as the two most often prescribed anxiolytics and Z-drugs. Patients starting with zopiclone on a private prescription had a higher chance to stay on a private prescription for the next 10 refills, compared to the chance of patients who started with a SHI prescription to stay on a SHI prescription. The opposite was true for lorazepam.

## 4 | DISCUSSION

The proportion of prescriptions that were issued privately for SHI patients was high, both for single prescriptions and repeat prescriptions. If doctors issued repeat prescriptions for the most relevant groups of Z-drugs or anxiolytics, the proportion of private prescriptions increased compared to single prescriptions, but only moderately by less than 5% points. Even so, the percentage of private prescriptions only moderately increased with a rising number of repeat prescriptions. Overall, doctors stayed to a high degree with their initial decision in the case of repeat prescriptions, no matter whether it was a SHI or private prescription.

### 4.1 | Comparison with literature

Some studies have investigated the proportion of private prescriptions of benzodiazepines and Z-drugs in Germany and found high rates of private prescriptions for Z-drugs and benzodiazepines,<sup>8,9</sup> with an even upward trend in the last years.<sup>10</sup> But none of these studies investigated whether the long-term use of these substances dramatically increased the proportion of private prescriptions. Only in a survey about 10 years ago, 62% of the participating German general

practitioners thought that patients with long-term use receive more often private prescriptions.<sup>11</sup>

Doctors' real prescribing behaviour seems to be in some contrast to this survey result—in three respects. First, repeat prescriptions were only moderately more often issued as private prescriptions than single prescriptions. Second, an increase in private prescriptions with the number of repeat prescriptions could be observed at least in Z-drug prescriptions and anxiolytics, but also only to a limited degree. Third, doctors who start issuing an SHI prescription tend to maintain this prescribing behaviour in approximately more than three quarters of cases, even after many repeat prescriptions.

Therefore, we would reject the hypothesis that private prescriptions serve as a strategy to mask the long-term use of benzodiazepines. We can only suggest some not necessarily contradicting explanations for doctors' prescribing behaviour: They seem to anticipate which type of prescription appeared to be most adequate for a patient, or vice versa, patients indicated the type of prescription they expected, may it be for a single prescription or long-term prescriptions. Alternatively, doctors use private prescriptions to mask on principle all their benzodiazepine and Z-drug prescriptions, not only long-term prescriptions, since they are probably familiar with the often heard accusation they prescribe these substances contrary to current evidence.<sup>15</sup> Perhaps they issue private prescriptions with the associated costs to make their patients aware of their own responsibility,<sup>16</sup> for single prescriptions as well as for refills.

### 4.2 | Limitations

Patients could not be followed up if they had changed the practice they attended. Therefore, we likely underestimated the rate of repeat

prescriptions in patients who changed their doctor to obtain additional prescription for a benzodiazepine or Z-drug.

The available data did not allow to evaluate whether a long-term prescription was justified and, if so, whether such prescriptions were more frequently issued as SHI prescriptions. This could be an interesting question for further research.

### 4.3 | Conclusions

Our findings may contribute to more transparency as a basis for the future assessment of the appropriateness of hypnotic/sedative prescriptions. While we observed an extremely large number of private prescriptions for benzodiazepines and Z-drugs, the proportion was only slightly higher for repeat prescriptions than for single prescriptions. Doctors do not seem to issue private prescriptions for SHI patients as a strategy to mask especially long-term use of these substances. The reasons and motives for the high use of private prescriptions, especially for Z-drugs, are still waiting to be clarified.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### ETHICS STATEMENT

Ethical approval was obtained from the local ethics committee of the University Medical Center Göttingen (No. 25/5/21). The study complies with the principles of the Declaration of Helsinki.

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## APPENDIX

**TABLE A1** Single and repeat prescriptions of benzodiazepines and Z-drugs; single substances, 2014 to 2020

No. of prescriptions <sup>a</sup>	Zopiclon		Zolpidem		Lorazepam		Diazepam	
	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions	<i>n</i>	% Private prescriptions
1 (Single <sup>a</sup> )	109 627	41.3%	67 156	48.7%	108 145	15.1%	59 695	24.5%
1 (Repeat <sup>b</sup> )	48 239	39.0%	30 426	48.8%	33 440	13.1%	17 898	23.9%
2	49 422	42.5%	31 285	51.6%	33 993	14.3%	18 303	24.6%
3	30 375	43.9%	18 978	53.7%	18 326	14.7%	9435	26.4%
4	22 584	45.2%	13 926	54.3%	12 801	15.1%	6331	26.9%
5	18 523	45.1%	11 167	54.2%	9982	15.1%	4841	27.2%
6	15 828	45.7%	9592	54.8%	8246	15.3%	3945	28.6%
7	13 844	45.7%	8436	55.5%	6995	15.5%	3360	28.7%
8	12 483	46.0%	7590	55.3%	6050	15.6%	2837	29.5%
9	11 400	46.0%	6890	55.5%	5401	15.8%	2484	30.2%
10	10 451	46.1%	6349	55.7%	4855	15.9%	2255	29.9%
>10	307 621	46.5%	208 667	55.9%	115 580	19.1%	61 742	33.6%
All repeat	540 770	45.2%	353 306	54.6%	255 669	16.6%	133 431	29.5%
All	650 397	44.5%	420 462	53.7%	363 814	16.1%	193 126	28.0%

<sup>a</sup>One or more single prescriptions with a distance of more than 90 days.

<sup>b</sup>1 to 10 = number of prescriptions, issued in an interval of 90 days or less (=repeat prescriptions).