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Posted Date: 27 November 2024

doi: 10.20944/preprints202411.2155.v1

Keywords: sedative psychotropics; insomnia; benzodiazepines; Z-drugs; sedative antidepressants; melatonin; regional variations; South Tyrol; Daily Defined Dose



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Article

Distinct Regional Pattern of Sedative Psychotropic Drug Use in South Tyrol: A Comparison with National Trends in Italy

Christian J. Wiedermann ^{1,*}, Katja Sangermano ², Pasqualina Marino ¹, Dietmar Ausserhofer ¹, Adolf Engl ¹ and Giuliano Piccoliori ¹

- Institute of General Practice and Public Health, College of Healthcare Professions Claudiana, 39100 Bolzano–Bozen, Italy; pasqualina.marino@am-mg; dietmar.ausserhofer@claudiana.bz.it; adolf.engl@am-mg.claudiana.bz.it; giuliano.piccoliori@am-mg.claudiana.bz.it
- Medical Directorate, South Tyrolean Medical Service (SABES-ASDAA), 39100 Bolzano-Bozen, Italy; katja.sangermano@sabes.it
- * Correspondence: christian.wiedermann@am-mg.claudiana.bz.it

Abstract: This study investigated regional variations in the use of sedative psychotropic medications, often prescribed for insomnia, by comparing Italy and the culturally distinct Autonomous Province of Bolzano, South Tyrol. Using daily defined dose (DDD) data per 1,000 inhabitants per day, benzodiazepines, Z-drugs, sedative antidepressants, and melatonin consumption from 2019 to 2023 were examined. The findings indicate significantly lower benzodiazepine use in South Tyrol compared to the national Italian average, with a trend toward increased sedative antidepressant use, especially mirtazapine, likely reflecting regional prescription preferences. Z-drug use was similar across both regions, whereas melatonin exhibited a gradual increase, albeit lower, in South Tyrol. Distinctive patterns in sedative psychotropic use in South Tyrol may be influenced by its unique cultural and linguistic composition, notably its significant German-speaking population. This demographic factor may contribute to different health behaviours and treatment preferences. Additionally, local healthcare policies and availability of non-pharmacological treatments may play a role in shaping prescription practices. This study underscores the importance of developing region-specific strategies to optimise insomnia management, considering cultural influences and the potential benefits of non-pharmacological interventions.

Keywords: sedative psychotropics; insomnia; benzodiazepines; Z-drugs; sedative antidepressants; melatonin; regional variations; South Tyrol; Daily Defined Dose

1. Introduction

Insomnia, a growing global public health issue, is associated with cardiovascular disease, depression, and cognitive impairment [1,2]. Effective management, particularly Cognitive Behavioural Therapy for Insomnia (CBT-I), is becoming increasingly important and recommended as the primary treatment because of its effectiveness and safety [3]. Nevertheless, pharmacological treatments remain prevalent owing to patient preference, accessibility, and limited psychotherapeutic resources [4,5]. Commonly prescribed sedative psychotropic medications include benzodiazepines, non-benzodiazepine hypnotics (Z-drugs), melatonin, and off-label sedative antidepressants [6].

South Tyrol, an autonomous province in northern Italy with a bilingual (German- and Italian-speaking) population, offers a unique setting for studying regional variations in insomnia treatment. Health professionals in both Italian and German countries receive training and continuing education, leading to diverse clinical practices [7,8]. Previous studies have also identified regional differences in health behaviours and healthcare access within Italy, including distinct attitudes toward vaccination and preventive health measures in South Tyrol [9,10]. German-speaking residents in South Tyrol show a notably higher inclination toward complementary and alternative medicine (CAM),

indicating potential cultural influences on healthcare choices and preferences [10]. These cultural and systemic factors make South Tyrol a compelling case for exploring regional patterns of psychotropic drug use, particularly sedatives for insomnia.

Despite the growth of sleep medicine in Italy and promotion of evidence-based insomnia treatments such as CBT-I, pharmacological approaches remain common [11–13]. Digital CBT-I (dCBT-I) can improve access to non-pharmacological treatments, yet sedative psychotropic medication still significantly influences insomnia management, particularly in primary care [11]. However, there are limited data on how sedative psychotropic medication use in South Tyrol aligns with national trends in Italy, especially given the region's bilingual and culturally unique healthcare system.

This study examined whether South Tyrol's context affects sedative psychotropic medication use compared to national Italian patterns. By analysing the Daily Defined Dose (DDD) levels [14] for benzodiazepines, Z-drugs, melatonin, and sedative antidepressants from 2019 to 2023, we investigated whether drug dispensation in South Tyrol aligns with or differs from national trends. The findings aim to enhance the understanding of region-specific healthcare, cultural influences on medication use, and opportunities to improve guideline-based, non-pharmacological insomnia treatments.

2. Results

Sedative psychotropic medication utilisation in Italy and South Tyrol from 2019 to 2023 was expressed as DDD per 1,000 inhabitants per day across four drug classes: benzodiazepines, Z-drugs, sedative antidepressants, and melatonin. These data provide an annual representation of consumption patterns (Table 1).

Table 1. Provision patterns of sedative psychotropic drugs in Italy and South Tyrol in Daily Defined Dose (DDD) per 1,000 inhabitants with correlation analysis and regional comparison from 2019 to 2023.

ъ :	Sedative Psychotropic			DI	OD per	1000 In	habitan	ts per D	ay		
Region	Drug ²	Mean ³	SD ³	p-value 4	2019	2020	2021	2022	2023	r s ⁵	p-value 6
	Benzodiazepines	17.04	0.454	0.0079	16.94	17.66	17.12	17.07	16.39	0.4000	n.s.
	Z-Drugs	2.55	0.495	n.s.	1.94	2.08	2.82	2.92	2.97	1.0000	0.0200
Italy	Sedative Antidepressants	1.29	0.020	0.0079	1.25	1.28	1.29	1.30	1.31	1.0000	0.0200
	Melatonin	0.22	0.063	n.s.	0.16	0.18	0.2	0.24	0.32	1.0000	0.0200
	Total	21.09	0.493	0.0079	20.29	21.20	21.43	21.53	20.99	0.4000	n.s.
	Benzodiazepines	9.50	0.455		9.84	10.01	9.58	9.25	8.88	-0.9000	0.0374
6 4	Z-Drugs	2.09	0.080		2.05	2.09	1.98	2.11	022 2023 rs 5 7.07 16.39 0.4000 .92 2.97 1.0000 .30 1.31 1.0000 .24 0.32 1.0000 1.53 20.99 0.4000 2.25 8.88 -0.9000 .11 2.20 0.7000 .66 2.69 0.8198 .13 0.21 0.9750	n.s.	
South Tyrol	Sedative Antidepressants	2.62	0.322		1.92	2.53	2.63	2.66	2.69	0.8198	0.05
1 9101	Melatonin	0.13	0.049		0.09	0.09	0.12	0.13	0.21	0.9750	0.0048
	Total	14.34	0.325		13.9	14.72	14.31	14.15	13.98	0.0000	n.s

¹ Rank by mean DDD per 1000 inhabitants per day in Italy from 2019 to 2024. ² Benzodiazepines (Alprazolam, Benzodiazepine derivatives, Bromazepam, Brotizolam, Clotiazepam, Clorazepate, Diazepam, Etizolam, Flunitrazepam, Flurazepam, Ketazolam, Lorazepam, Lormetazepam, Nitrazepam, Nordazepam, Oxazepam, Pinazepam, Prazepam, Triazolam); Z-Drugs (Zopiclone, Zolpidem, Eszopiclone); Sedative Antidepressants (Mirtazapine, Amitriptyline, Amitriptiline combinations with antipsychotics, Clomipramine, Trimipramine). ³ Mean and standard deviation of DDD per 1000 inhabitants per day from 2019 to 2024. ⁴ Mann Whitney U-Test of DDD values Italy against South Tyrol. ⁵ Spearman's rank correlation coefficient beween year and DDD per 1000 inhabitants per day. ⁶ Spearman's rank correlation. Abbreviations: DDD, defined daily dose; n.s., not significant (P ≥ 0.05).

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Table 1 shows that Italy's overall consumption of sedative psychotropic drugs exceeded that of South Tyrol, with both regions displaying stable trends. Italy consistently used more benzodiazepines, whereas South Tyrol showed a notable decline in their use over time, possibly indicating changes in prescribing practices or a preference for alternative therapies in the region. Z-drug usage was similar in Italy and South Tyrol, with a rising trend in Italy, indicating increased reliance on these medications instead of benzodiazepines. Sedative antidepressants are more frequently used in South Tyrol, showing a gradual increase, possibly due to regional prescription preferences or a preference for these over traditional anxiolytics. Melatonin usage increased in both regions, although it was marginally lower in South Tyrol than in Italy. This trend suggests a growing preference for non-benzodiazepines and non-sedative sleep support options. Overall, these differences indicate distinct healthcare practices and cultural attitudes toward sedative medications for sleep issues.

In Italy, the seven most frequently used sedative psychotropic drugs account for 80.2% of the total consumption, representing 17.6 of the 21.9 DDD per 1,000 inhabitants per day across 28 psychotropics. As shown in Table 2, the results reveal distinct regional differences in consumption patterns and trends over the observation period from 2019 to 2023.

- 1. Lormetazepam ranks as the top sedative psychotropic in both areas, with its use in Italy nearly twice that of South Tyrol. Italy's usage remains steady, whereas South Tyrol shows a marked decline, indicating a regional shift from this benzodiazepine.
- 2. Alprazolam ranks second, with Italy showing a higher usage than South Tyrol. In Italy, alprazolam use is relatively steady, whereas South Tyrol exhibits a modest, stable pattern with consistently lower DDD values, likely indicating a more conservative prescription approach.
- 3. Lorazepam is the third most used drug, with higher usage in Italy than in South Tyrol. Italy exhibited a slight decline, whereas South Tyrol showed a significant decrease, indicating a shift in prescribing practices favouring alternatives.
- 4. Zolpidem, a Z-drug, exhibits similar usage in Italy and South Tyrol, with a slight increase in both areas. Italy's use trends were marginally higher, showing a comparable acceptance of this non-benzodiazepine hypnotic in both regions.
- 5. Triazolam usage was slightly higher in Italy than in South Tyrol, where a mild decrease contrasts with Italy's stable pattern, possibly reflecting a preference for other short-acting hypnotics in South Tyrol.
- 6. Mirtazapine, a sedative antidepressant, was used at significantly higher levels in South Tyrol than in Italy, with increasing trends in both regions. This indicates that South Tyrol may favour sedative antidepressants over benzodiazepines as alternatives for managing sleep disturbances.
- 7. Benzodiazepine derivatives (unspecified, including infrequently used drugs) exhibit moderate and stable usage in Italy. In contrast, South Tyrol demonstrated significantly lower and declining usage, indicating reduced dependence on these agents.

These top quarter drugs highlight Italy's greater reliance on benzodiazepines than South Tyrol.

Table 2. Provision patterns of sedative psychotropic drugs in Italy and South Tyrol in Daily Defined Dose (DDD) per 1,000 inhabitants with correlation analysis and regional comparison from 2019 to 2023.

Ra	Sedative	DDD per 1000 Inhabitants per Day										
nk 1	Psychotropic Drug ²	Region		S D³	p- valu e ⁴	20 19	20 20	20 21	20 22	20 23	r s ⁵	p- valu e ⁶
1	Lormetazepam	Italy	5.05	0.0 91	0.011 9	4.9 8	5.1 4	5.0 6	5.1 4	4.9 4	- 0.20 52	n.s.

		South Tyrol	2.67	0.1 67		2.8	2.8	2.7	2.5	2.4	-1.0	< 0.000 1
		Italy	3.79	0.1	0.007	3.6 0	3.9 0	3.8	3.8 7	3.7 5	0.1	n.s.
2	Alprazolam	South Tyrol	1.2	0.0 62	9	1.1 0	1.2 5	1.2 4	1.2 2	1.1 7		< 0.000 1
	_	Italy	3.73	0.1 84	0.011	3.8	3.9 6	3.7 4	3.6	3.4 8	-0.9	0.037 4
3	Lorazepam	South Tyrol	2.44	0.1 43	9	2.5 8	2.5 8	2.4 4	2.3 6	2.2 5	0.1 0 -0.9 - 0.97 47 1.0 0.7 - 0.35 91 -0.9 1.0 1.0 0.05 13 - 0.35 36 - 0.94 87 -1.0 - 0.97 47 - 0.97	0.004 8
4	Zoldipem	Italy	2.05	0.1 33	n.s.	1.8 6	2.0	2.0 5	2.1 5	2.2	0.1 0 -0.9 -0.97 47 1.0 0.7 -0.35 91 -0.9 1.0 1.0 0.05 13 - 0.35 36 - 0.94 87 -1.0 -1.0 -1.0	< 0.000 1
-	Zompen	South Tyrol	2.06	0.0 81	11.0.	2.0	2.0 6	1.9 5	2.0 8	2.1 7	0.7	n.s.
5	Triazolam	Italy	1.35	0.0 29	0.015 7	1.4 0	1.4 0	1.3 5	1.3 5	1.3 2		n.s.
		South Tyrol	1.22	0.0 72	7	1.2 6	1.3 2	1.2 1	1.1 7	1.1 4	0.1 0 -0.9 -0.97 47 1.0 0.7 -0.35 91 -0.9 1.0 1.0 0.05 13 -0.35 36 -0.35 36 -0.94 87 -1.0 -1.0 -1.0	0.037 4
6	Mirtazapin	Italy	0.67	0.0 26	0.007	0.6 4	0.6 6	0.6 7	0.6 8	0.7 1	1.0	< 0.000 1
O	Mintazapin	South Tyrol	1.9	0.0 76	9	1.1 8	1.8 4	1.9 1	1.9 4	2.0	1.0	< 0.000 1
5	Benzodiazepine	Italy	0.93	0.0 25	0,009	0.8 9	0.9 5	0.9 4	0.9 4	0.9 1		n.s.
7	(Derivatives)	South Tyrol	0.54	0.0 22	5	0.5	0.5 8	0.5	0.5	0.5	0.35	n.s.
		Italy	0.53	0.0 12		0.5 4	0.5 4	0.5	0.5	0.5 1		0.013 8
8	Brotizolam	South Tyrol	0.51	0.0 35	n.s.	0.5 7	0.5	0.5	0.4 9	0.4	0.1 0 -0.9 -0.97 47 1.0 0.7 -0.35 91 -0.9 1.0 1.0 0.05 13 -0.94 87 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0 -1.0	< 0.000 1
9	Bromazepam	Italy	0.52	0.0 38	0.011	0.5 5	0.5 5	0.5	0.5	0.4 6		0.004 8
,	Бтошагераш	South Tyrol	0.21	0.0 13	7	0.2	0.2	0.2	0.2	0.1 9		0.004

0.3 74

n.s.

0.49

Italy

10

Zopiclone

8

0.0 0.0

8

0.7

0.7

0.7

5

n.s.

47

0.63

25

4

		South Tyrol	0.03	0		0.0 3	0.0	0.0	0.0 3	0.0	n.a.	n.a.
11	Diazepam	Italy	0.48	0.0 18	0.010	0.4 8	0.5 1	0.4 9	0.4 8	0.4 6	- 0.56 43	n.s.
	1	South Tyrol	0.14	0.0 11	9	0.1 4	0.1 4	0.1	0.1 5	0.1 4	0.22 36	n.s.
		Italy	0.31	0.0 05	0.010	0.3 1	0.3	0.3	0.3 1	0.3 1	0.28 87	n.s.
12	Amitryptiline	South Tyrol	0.52	0.0 11	7	0.5	0.5	0.5 1	0.5	0.5	- 0.05 13	n.s.
13	Flurazepam	Italy	0.25	0.0 04	0.008	0.2 5	0.2 5	0.2 5	0.2 5	0.2 4	- 0.70 71	n.s.
		South Tyrol	0.21	0.0 09	0	0.2	0.2	0.2	0.2	0.2 1	2 0.22	n.s.
14	Melatonin	Italy	0.22	0.0 63	n.s.	0.1 6	0.1 8	0.2	0.2 4	0.3	1.0	< 0.000 1
		South Tyrol	0.13	0.0 49		0.0 9	0.0 9	0.1 2	0.1 3	0.2 1	0.97 47	0.004 8
		Italy	0.21	0.0 05	0.009	0.2	0.2	0.2	0.2 1	0.2	0	n.s.
15	Clomipramine	South Tyrol	0.17	0.0 14	9	0.1 8	0.1 6	0.1 8	0.1 8	0.1 5	- 0.44 72	n.s.
16	Prazepam	Italy	0.11	0.0 38	0.010	0.1 4	0.1 4	0.1	0.1	0.0 5	- 0.97 47	0.004 8
10	Tuzepuin	South Tyrol	0.03	0.0 11	7	0.0 4	0.0 4	0.0 4	0.0	0.0	- 0.56 43 0.22 36 0.28 87 - 0.05 13 - 0.70 71 0.22 36 1.0 0.97 47 0 - 0.44 72 - 0.97	n.s.
		Italy	0.12	0	0.006	0.1	0.1	0.1	0.1 2	0.1	n.a.	n.a.
17	Etizolam	South Tyrol	0.07	0.0 05	5	0.0 8		0.0 7	0.0 7		n.s.	
18	Amitrypline (Combination with	Italy	0.1	0.0 04	0.008	0.1	0.1	0.1	0.1	0.0 9		n.s.
10	Antipsychotic Agent)	South Tyrol	0.03	0.0 05	6	0.0	0.0	0.0	0.0	0.0		n.s.
19	Clotiazepam	Italy	0.06	0.0 18	0.008	0.0	0.0 7	0.0 5	0.0 5	0.0 5		0.040 5

		South Tyrol	0.02	0.0 04		0.0	0.0	0.0	0.0	0.0	- 0.70 71	n.s.
20	Flunitrazepam	Italy	0.03	0.0 08	0.010	0.0 4	0.0 4	0.0	0.0	0.0	- 0.94 87	0.013 8
		South Tyrol	0.06	0.0 07	7	0.0 7	0.0 6	0.0 6	0.0 6	0.0 5	- 0.89 44	0.040 5
01		Italy	0.03	0	0.004	0.0 3	0.0	0.0	0.0	0.0	n.a.	n.a.
21	Oxazepam	South Tyrol	0.13	0	0.004	0.1 3	0.1	0.1	0.1 3	0.1	n.a.	n.a.
22	V-11	Italy	0.02	0	0.004	0.0 2	0.0 2	0.0	0.0 2	0.0 2	n.a.	n.a.
22	Ketazolam	South Tyrol	0	0	0.004	0	0	0	0	0	n.a.	n.a.
		Italy	0.02	0	0.005 6	0.0	0.0	0.0	0.0	0.0	n.a.	n.a.
23	Nitrazepam	South Tyrol	0.03	0.0 04		0.0 4	0.0	0.0	0.0	0.0	- 0.70 71	n.s.
		Italy	0.01	0		0.0 1	0.0 1	0.0	0.0	0.0 1	n.a.	n.s.
24	Clorazepate	South Tyrol	0.01	0.0 05	0.177	0.0	0.0	0.0	0.0	0.0	0.89 44 1	n.a.
25	Trimipramine	Italy	0	0.0 05	n.s.	0	0.0	0.0	0	0		n.s.
		South Tyrol	0	0		0	0	0	0	0	1 n.a. n.s0 0.86 1 60 n.a 0 0.28 n.s. 87	
		Italy	0	0		0	0	0	0	0	n.a.	n.a.
26	Nordazepam	South Tyrol	0	0	n.s.	0	0	0	0	0	n.a.	n.a.
		Italy	0	0		0	0	0	0	0	n.a.	n.a.
27	Pinazepam	South Tyrol	0.01	0.0 04	0.02	0.0 1	0.0	0.0	0.0	0		n.s.
26	Eczonialono	Italy	0	0.0 09		0	0	0	0	0.0 2	0.70 71	n.s.
28	Eszopiclone	South Tyrol	0	0	n.s.	0	0	0	0	0	n.a.	n.a.

 1 Rank by mean DDD per 1000 inhabitants per day in Italy from 2019 to 2024. 2 Mean and standard deviation of DDD per 1000 inhabitants per day in Italy from 2019 to 2024. 3 Mann Whitney U-Test of DDD values Italy against South Tyrol. 4 Spearman's rank correlation coefficient between year and DDD per 1000 inhabitants per day. 6 Spearman's rank correlation. Abbreviations: DDD, defined daily dose; n.a., not analysed; n.s., not significant ($P \ge 0.05$). The results indicated significant regional differences in sedative psychotropic drug use between Italy and South Tyrol. Italy showed higher

benzodiazepines, with stable trends, reflecting consistent prescribing practices. Conversely, South Tyrol exhibited a marked decrease in benzodiazepine use, indicating a regional shift toward reducing reliance on these medications. The increased use of sedative antidepressants, particularly Mirtazapine, in South Tyrol suggests a preference for alternatives to benzodiazepines, aligning with the cautious approach of prescribing anxiolytics and hypnotics. Z-drug class utilisation is comparable, with zoldipem showing increased use in Italy but not in South Tyrol. The rising trend in melatonin use in both regions reflects the growing acceptance of non-habit-forming sleep aids, although at a lower level in the South Tyrol.

3. Discussion

Based on a 2023 consensus update on the management of insomnia in clinical practice in Italy [13], current recommendations emphasise that CBT-I should be the first-line treatment owing to its effectiveness and safety profile, particularly for chronic insomnia. Pharmacological treatments, including sedative psychotropic agents, are generally advised only when CBT-I is unavailable or rapid symptom relief is necessary for transient insomnia. Specifically, benzodiazepines and Z-drugs are recommended only for short-term use (up to four weeks), while the newer Z-drug eszopiclone may be considered for extended use up to six months, particularly in elderly patients. Melatonin and the novel dual orexin receptor antagonist daridorexant have been suggested as options for long-term insomnia management, with specific indications based on patient age and insomnia severity [13].

The results presented here elucidate significant regional disparities in sedative psychotropic drug utilisation, with Italy exhibiting higher overall levels compared to South Tyrol, particularly in the use of benzodiazepines (Table 1). The consistent utilisation of benzodiazepines in Italy likely reflects a sustained reliance on traditional anxiolytics and hypnotics, whereas South Tyrol demonstrates a notable reduction in this class, indicating a regional shift that may prioritise minimising benzodiazepine use because of concerns regarding dependency, especially among elderly populations. This trend in South Tyrol aligns with the observed increase in sedative antidepressant use, specifically mirtazapine, a drug off-label for insomnia in Italy [13]. The increased use of antidepressants with sedative properties in South Tyrol may indicate a deliberate choice of medications that offers additional benefits for treating comorbid depression. Nevertheless, the general agreement highlights the lack of substantial evidence supporting the prolonged use of antidepressants to address sleep disorders [13].

Z-drugs, such as zolpidem, demonstrate relatively comparable utilisation across both regions, although Italy exhibits a slight upward trend. This comparable usage may indicate a shared acceptance of Z-drugs as a benzodiazepine alternative for short-term insomnia treatment. Eszopiclone, which was recently introduced to the Italian market, attained a DDD of 0.02 per 1,000 inhabitants in Italy in 2023. However, it has not yet been introduced in the South Tyrol. This disparity likely reflects the varying local prescribing practices.

Melatonin usage, while low, increased across both Italy and South Tyrol, indicating a growing acceptance of non-prescription, non-benzodiazepine options for sleep regulation, particularly in cases of mild insomnia or circadian rhythm disturbances. The relatively lower level in South Tyrol might indicate either limited acceptance or more cautious adoption compared to Italy.

A recent study conducted by the Statistics Institute of the Autonomous Province of Bolzano (ASTAT) and the Institute of General Practice and Public Health Bolzano found that most adults in South Tyrol rate their sleep quality positively. Using the Pittsburgh Sleep Quality Index (short version), the study revealed that 82% of the participants perceived their sleep as fairly or very good, while 18% reported poor sleep quality. The prevalence of sleep difficulties in South Tyrol is influenced by factors such as gender, age, and chronic health conditions, with women, older adults, and those with chronic conditions experiencing more sleep issues [15].

A key finding is the lower prevalence of reported sleep disturbances among the Germanspeaking majority in South Tyrol compared to the Italian-speaking minority, with German speakers experiencing less frequent sleep quality issues and more consistent adherence to sufficient sleep habits [15]. This observation may partially explain the lower overall use of sedative psychotropics in South Tyrol than in Italy, as a larger portion of South Tyrol's German-speaking population may experience fewer sleep disruptions, reducing the demand for sedative medications.

This research had several constraints, including the use of DDD as a measurement tool. Although DDD offers an approximation of the average daily medication usage per 1,000 people, it fails to capture data at the individual level or specific patient characteristics. This metric provides a standardised, albeit not entirely accurate, measure of the actual doses prescribed or consumed, particularly because it may not account for dosage variations based on age or specific medical conditions. The chosen data type, specifically the DDD metric, imposes inherent constraints on statistical analysis. This constraint hinders the ability to perform more sophisticated statistical evaluations such as examining how comorbidities or demographic factors influence drug usage patterns. Moreover, while other studies have noted an increase in the use of sedative psychotropic medications during the COVID-19 pandemic, the DDD data utilised in this research only allowed for the identification of indicative trends, rather than providing definitive evidence of pandemic-related increases. Although some medications exhibited peak DDD levels within the observation period, the quantitative estimates were inherently approximate. More comprehensive, individual-level data are necessary to confirm any changes in prescribing practices attributable to the pandemic. Furthermore, the lack of data on specific indications hinders the understanding of the clinical rationale behind prescription patterns, particularly in distinguishing between treatments for insomnia and other conditions.

The strength of this study is its focus on South Tyrol, a unique cross-cultural region influenced by Italian and German-speaking healthcare practices, enabling a comparison of sedative psychotropic drug use in a single system that serves two linguistic and cultural communities. Using DDD as a standardised metric allows the systematic analysis of drug utilisation trends over time, facilitating robust comparisons at the national and regional levels. The multi-year observation period provides insights into longitudinal trends, capturing shifts in prescribing practices and the impact of cultural and regulatory differences on medication choice, offering a better understanding of regional variations in insomnia management and highlighting opportunities for evidence-based, non-pharmacological treatments.

4. Methods

4.1. Study Design and Data Source

This descriptive study is a pharmacoepidemiological analysis of sedative psychotropic medication use in Italy and the Autonomous Province of Bolzano (South Tyrol). A retrospective analysis was conducted on sedative psychotropic medication use (ATC N05 and N06 [16]) for the period 2019-2023. The IQVIA database was used as a data source, which collects the databases of drugs dispensed in the National Health Service (SSN) and purchased privately by the population. Data provide information on prescriptions dispensed in Daily Defined Doses (DDDs) per 1,000 inhabitants per day [14], offering a standardised measure of medication use. This approach enables the estimation of the average daily treatment proportion of the population for each drug or drug group. For instance, 10 DDDs per 1,000 inhabitants per day suggest that on average, 1% of the population receives this medication daily.

4.2. Medication Grouping

To facilitate targeted analysis, sedative psychotropic medications were categorised based on pharmacological class and typical indications for sleep disturbances, following established classifications such as the WHO Anatomical Therapeutic Chemical (ATC) system [16]. The groups analysed included benzodiazepines, Z-drugs (non-benzodiazepine hypnotics), sedative antidepressants, and melatonin [17].

4.2.1. Benzodiazepines

This group comprises sedative-anxiolytic medications commonly prescribed for anxiety-related and chronic sleep disturbances, although their use is often limited owing to risk [4]. Benzodiazepines

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included in this study were alprazolam, bromazepam, brotizolam, clotiazepam, clorazepate, diazepam, etizolam, flunitrazepam, flurazepam, ketazolam, lorazepam, lormetazepam, nitrazepam, nordazepam, oxazepam, pinazepam, prazepam, and triazolam.

4.2.2. Z-Drugs (Non-Benzodiazepine Hypnotics)

Known for their selective action on GABA-A receptors, Z-drugs are typically first-line agents for short-term sleep initiation disorders and are associated with fewer residual daytime effects than traditional benzodiazepines [18]. This group included patients treated with zopiclone, zolpidem, and eszopiclone.

4.2.3. Sedative Antidepressants

Sedative antidepressants are mostly used off-label to treat sleep disturbances, particularly in cases where insomnia co-occurs with depressive symptoms [19]. Medications in this category include mirtazapine, amitriptyline (in combination with antipsychotics), clomipramine, and trimipramine.

4.2.4. Melatonin

As an over-the-counter and prescription supplement, prolonged-release melatonin is used to manage circadian rhythm disorders and mild sleep disturbances, providing a non-habit-forming alternative that is especially suitable for patients with circadian-related sleep issues [20].

This structured categorisation, grounded in recognised pharmacological classifications and clinical guidelines, supported the consistency and validity of the analysis.

4.3. Data Analysis

For each medication group, we calculated the DDD per 1,000 residents per day for each year between 2019 and 2023. Comparisons were made between South Tyrol and the broader national averages for Italy, with a focus on identifying regional differences in utilisation trends over time. Spearman's rank correlation analysis was applied to assess trends within each medication group over time (n = 5 years). Sedative psychotropics were ranked by national DDD values to identify differences in the most frequently prescribed compounds between regions.

5. Conclusions

This study revealed significant regional differences in sedative psychotropic drug use, with Italy demonstrating higher overall levels, particularly in benzodiazepine use, than South Tyrol. The reduced benzodiazepine use and increased utilisation of sedative antidepressants, notably mirtazapine, in South Tyrol suggests a shift towards alternatives considered more appropriate for long-term use. Z-drug use was comparable in both regions. Rising melatonin use reflects an increased acceptance of non-prescription options for mild sleep disturbances, although melatonin uptake remains lower in South Tyrol. The limitations of DDD data, including the absence of individual-level and indication-specific insights, restrict more detailed conclusions. Nonetheless, this study underscores the cultural and regulatory impact of sedative drug use in South Tyrol. Future research should incorporate individual-level data to better elucidate prescribing motivations and assess the role of nonpharmacological treatments in reducing sedative psychotropic use.

Author Contributions: Conceptualization, C.J.W. and G.P.; methodology, C.J.W. and K.S.; software, C.S.; formal analysis, C.J.W.; investigation, P.M. and K.S.; writing—original draft preparation, C.J.W.; writing—review and editing, G.P., A.E., P.M. and K.S.; supervision, A.E. All the authors have read and agreed to the published version of the manuscript.

Funding: This study received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Restrictions apply to the availability of these data. The datasets, sourced from a commercial database, include detailed sales figures by ATC substance class across Italy, including South Tyrol. Due to the commercial sensitivity and potential for misuse, access will be provided only upon request and after review of the intended use. Requests should be directed to the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

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