

Trends in outpatient prescribing of anxiolytics, hypnotics, and antidepressants in North Macedonia before and after the COVID-19 pandemic

Abstract

The COVID-19 pandemic has been associated with substantial adverse effects on mental health worldwide, contributing to increased prevalence of anxiety, depression, and sleep disturbances. These changes have influenced psychopharmacological treatment practices and psychotropic medication utilization across healthcare systems.

Objective: To evaluate trends in outpatient prescribing of anxiolytics, hypnotics, and antidepressants in North Macedonia before, during, and after the COVID-19 pandemic and to explore psychotropic medication use and mental health-related behaviors among adults during the pandemic period.

Methods: A mixed-methods study was conducted comprising a retrospective pharmaco-epidemiological analysis of national outpatient prescription data from 2018–2024 and a cross-sectional survey conducted in 2022. Prescription data were obtained from the national electronic prescription system and Health Insurance Fund reports. Temporal prescribing trends were assessed using Spearman's rank correlation and Mann–Whitney U tests. The survey included 340 adults and assessed psychotropic medication use, reasons for use, prescribing practices, and perceptions of the pandemic's impact on mental health.

Results: Significant upward prescribing trends were observed for alprazolam ($p=0.964$, $p<0.001$), zolpidem ($p=1.000$, $p<0.001$), venlafaxine ($p=1.000$, $p<0.001$), and sertraline ($p=0.964$, $p<0.001$). Zolpidem showed the largest relative increase (+64.8%), followed by venlafaxine (+36.4%) and alprazolam (+28.2%). Diazepam remained the most frequently prescribed psychotropic medication throughout the study period. Survey findings showed that 71.2% of respondents initiated psychotropic medication use during the pandemic. Anxiety (52.7%), tension (31.2%), and insomnia (25.0%) were the most commonly reported reasons for use. Approximately one-third of participants reported dose escalation, while many reported feelings of reassurance when medication was available and discomfort when access was limited.

Conclusion: Psychotropic medication prescribing increased substantially in North Macedonia following the onset of the COVID-19 pandemic. The findings highlight the need for continued monitoring of psychotropic medication utilization, rational prescribing practices, and strengthened mental health services to address the long-term consequences of public health crises.

Keywords: COVID-19, mental health, anxiolytics, hypnotics, antidepressants, psychotropic medications, prescription trends, pharmaco-epidemiology, outpatient prescribing

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Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, world health organization; ATC, anatomical therapeutic chemical classification system; HIF, health insurance fund

Introduction

The SARS-CoV-2 disease (COVID-19) pandemic, declared by the World Health Organization (WHO) in March 2020, rapidly evolved into an unprecedented global health crisis with profound medical, social, and economic consequences. Beyond the direct morbidity and mortality associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pandemic substantially affected mental health worldwide. Public health measures implemented to contain viral transmission, including lockdowns, social distancing, quarantine, and restrictions on movement, significantly altered daily life and contributed to increased psychological distress across

populations. Numerous studies have demonstrated that the pandemic was associated with elevated levels of anxiety, depression, stress-related disorders, loneliness, and sleep disturbances, creating an additional burden on healthcare systems already challenged by the management of COVID-19 cases.^{1–4}

North Macedonia was not exempt from these challenges. The first confirmed COVID-19 case was reported on 26 February 2020, while the first COVID-19-related death was registered less than a month later. By the end of July 2020, more than 450 deaths had been attributed to COVID-19 in the country. The rapid spread of the virus, together with prolonged periods of uncertainty, social isolation, and economic instability, raised concerns regarding the psychological impact of the pandemic on the Macedonian population. As highlighted by Batic and Krsteska,⁵ the country lacked a comprehensive psychosocial support system capable of adequately addressing mental health needs during public health emergencies, emphasizing the necessity for structured psychological support interventions and crisis-response mechanisms.

The psychological consequences of the pandemic have been extensively documented in the scientific literature. Meta-analyses and longitudinal studies consistently report a substantial increase in the prevalence of anxiety and depressive disorders during the pandemic period. Lear-Claveras et al., observed significant worsening of anxiety and depression symptoms during the first six months of the pandemic, while other studies described increased rates of reactive psychoses and other psychiatric manifestations associated with COVID-19-related stressors.^{2,3} Furthermore, Santomauro et al.,⁶ estimated that the global prevalence of anxiety disorders and major depressive disorder increased by more than 25% during the first year of the pandemic, highlighting the magnitude of its impact on mental health worldwide.

The growing burden of mental health disorders was accompanied by important changes in psychopharmacological treatment patterns. Increased demand for mental health services, reduced availability of face-to-face consultations, expansion of telemedicine, and heightened psychological distress collectively influenced prescribing practices across healthcare systems. Consequently, anxiolytics, hypnotics, sedatives, and antidepressants emerged among the most frequently utilized therapeutic classes during the pandemic period. Several studies reported increased prescribing and utilization of these medications, reflecting both the rising prevalence of mental health conditions and attempts to manage pandemic-related psychological symptoms pharmacologically.^{7–9}

A nationwide interrupted time-series analysis conducted in Portugal demonstrated significant changes in outpatient prescribing patterns of anxiolytics, sedatives, hypnotics, and antidepressants during the COVID-19 pandemic, emphasizing the importance of monitoring psychotropic medicine utilization as an indicator of population mental health needs.⁷ Similar findings have been reported across Europe and other regions, although the magnitude and persistence of these changes varied according to healthcare system characteristics, public health measures, and population-specific factors. Recent systematic reviews have confirmed that antidepressant utilization increased consistently across multiple countries during and after the pandemic, while prescribing trends for anxiolytics and hypnotics showed greater heterogeneity.^{10,11}

Evidence from Southeast Europe also indicates increased consumption of psychotropic medications during the pandemic period. A Croatian longitudinal study covering the period 2012–2021 demonstrated a continuous rise in the utilization of antidepressants, anxiolytics, hypnotics, and antipsychotics, with anxiolytics accounting for the largest proportion of total psychotropic drug consumption.¹² Given the similarities in healthcare organization, prescribing practices, and sociocultural determinants within the region, these findings may provide important context for evaluating psychotropic medicine utilization in North Macedonia.

Despite growing international evidence regarding the effects of the COVID-19 pandemic on psychotropic prescribing, data from North Macedonia remain limited. To date, few pharmaco-epidemiological studies have examined national trends in the outpatient use of anxiolytics, hypnotics, and antidepressants before, during, and after the pandemic. Understanding such trends is essential not only for evaluating the indirect consequences of the pandemic on mental health but also for identifying potential risks associated with long-term psychotropic medication use, including dependence, inappropriate prescribing, polypharmacy, and increased healthcare utilization.

Aim

To evaluate the impact of the COVID-19 pandemic on outpatient prescribing patterns of psychotropic medications in North Macedonia

and to explore psychotropic medication use and mental health-related behaviors among adults during the pandemic period.

Objectives

- I. To analyze national trends in outpatient prescribing of anxiolytics, hypnotics, and antidepressants in North Macedonia between 2018 and 2024.
- II. To compare prescribing patterns observed during the pre-pandemic period (2018–2019) with those recorded during the pandemic and post-pandemic period (2020–2024).
- III. To identify the most frequently prescribed psychotropic medications and quantify changes in their utilization over time.
- IV. To assess self-reported psychotropic medication use, prescribing practices, and reasons for use among adults during the COVID-19 pandemic through a cross-sectional survey conducted in 2022.
- V. To explore potential indicators of inappropriate psychotropic medication use, including dose escalation, self-medication, and medication-related dependence behaviors.
- VI. To provide evidence that may support rational prescribing practices, mental health service planning, and public health policy development in future health emergencies.

Materials and methods

Study design

This study employed a mixed-methods analytical design consisting of two complementary but independent components. The first component involved a retrospective pharmaco-epidemiological analysis of national outpatient prescription data to evaluate trends in psychotropic medication prescribing before, during, and after the COVID-19 pandemic. The second component consisted of a cross-sectional survey conducted during the pandemic period to assess psychotropic medication use, prescribing practices, and self-reported mental health experiences among adults in North Macedonia.

The two components were analyzed separately and were intended to provide complementary perspectives: population-level prescribing trends and individual-level medication use and perceptions.

Part I: Retrospective analysis of psychotropic drug prescribing trends

A retrospective analysis of outpatient prescription data was conducted for the period January 2018–December 2024. Data were obtained from official national healthcare sources, including the electronic prescription system “My Appointment” (Moj Termin) maintained by the Ministry of Health and annual reports published by the Health Insurance Fund of North Macedonia.

The analysis focused on psychotropic medicines commonly prescribed in outpatient settings, including anxiolytics (diazepam, alprazolam, bromazepam), hypnotics (zolpidem), and antidepressants (venlafaxine, sertraline, and paroxetine).

Annual prescription volumes were extracted and analyzed across three predefined periods:

- i. Pre-pandemic period (2018–2019)
- ii. Pandemic period (2020–2022)
- iii. Post-pandemic period (2023–2024)

The primary outcome measure was the annual number of issued outpatient prescriptions in the total population for each investigated medicine.

Part II: Cross-sectional survey

A cross-sectional online survey was conducted between June and August 2022 using the Google Forms platform.

A total of 360 adults were invited to participate, of whom 340 completed the questionnaire, yielding a response rate of 94.4%.

Eligibility criteria included:

- i. Age ≥ 18 years;
- ii. Residence in North Macedonia;
- iii. Voluntary participation and informed consent.

The survey represented a cross-sectional assessment of psychotropic medication use and perceptions during the COVID-19 pandemic and was not designed to evaluate longitudinal changes over time.

The questionnaire consisted of two sections.

The first section collected demographic information, including age, sex, educational attainment, marital status, employment status, and place of residence.

The second section assessed psychotropic medication use and mental health-related experiences during the pandemic. Participants were asked about:

- I. Previous psychiatric diagnoses;
- II. Use of anxiolytics, hypnotics, and antidepressants;
- III. Reasons for medication use;
- IV. Source of prescription or recommendation;
- V. Dosage patterns;
- VI. Perceived effectiveness;
- VII. Medication-related behaviors;
- VIII. Perceived impact of the COVID-19 pandemic on mental health.

For questions addressing reasons for medication use, respondents were allowed to select more than one answer. Therefore, percentages for these variables may exceed 100%.

This demographic skew limits the generalizability of the survey findings, as it does not accurately reflect the behaviors and access to healthcare of rural or less-educated populations in North Macedonia.

Statistical analysis

Descriptive statistics were used to summarize prescription data and survey responses. Continuous variables were presented as annual counts, while categorical survey variables were expressed as frequencies and percentages.

Because the prescription dataset consisted of a limited number of annual observations (2018–2024), non-parametric statistical methods were applied.

Temporal trends in psychotropic prescribing were evaluated using Spearman's rank correlation coefficient (ρ), assessing the association between calendar year and annual prescription volume for each investigated medicine.

To explore the potential impact of the COVID-19 pandemic on prescribing patterns, annual prescription volumes during the pre-pandemic period (2018–2019) were compared with those observed during the combined pandemic and post-pandemic period (2020–2024) using the Mann–Whitney U test.

Survey data were analyzed descriptively using frequencies and percentages.

Statistical significance was defined as $p < 0.05$.

All analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA).

Ethical Considerations

Participation in the survey was voluntary and anonymous. Prior to completing the questionnaire, participants were informed about the study objectives and provided electronic informed consent.

No personally identifiable information was collected or processed.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable national regulations governing research involving human participants.

Methodological considerations

Several methodological considerations should be acknowledged. First, the prescribing trend analysis was based on aggregated annual prescription data, limiting the number of observations available for statistical testing. Consequently, the study may have limited statistical power to detect differences between the pre-pandemic and pandemic/post-pandemic periods.

Second, the survey component was conducted at a single time point during 2022 and therefore reflects respondents' experiences during the pandemic period rather than longitudinal changes over time.

Finally, self-reported survey responses may be subject to recall bias and reporting bias, particularly regarding medication use and perceived mental health changes during the pandemic.

Results

A retrospective analysis of national prescription data demonstrated an overall increase in the prescribing of anxiolytics, hypnotics, and antidepressants between 2018 and 2024. Positive correlations were observed between calendar year and annual prescription volume for all investigated medicines, indicating sustained growth in psychotropic medication utilization during the study period.

Official data from the Ministry of Health (electronic prescriptions "Moj termin") and reports from the Health Insurance Fund are presented in Table 1.

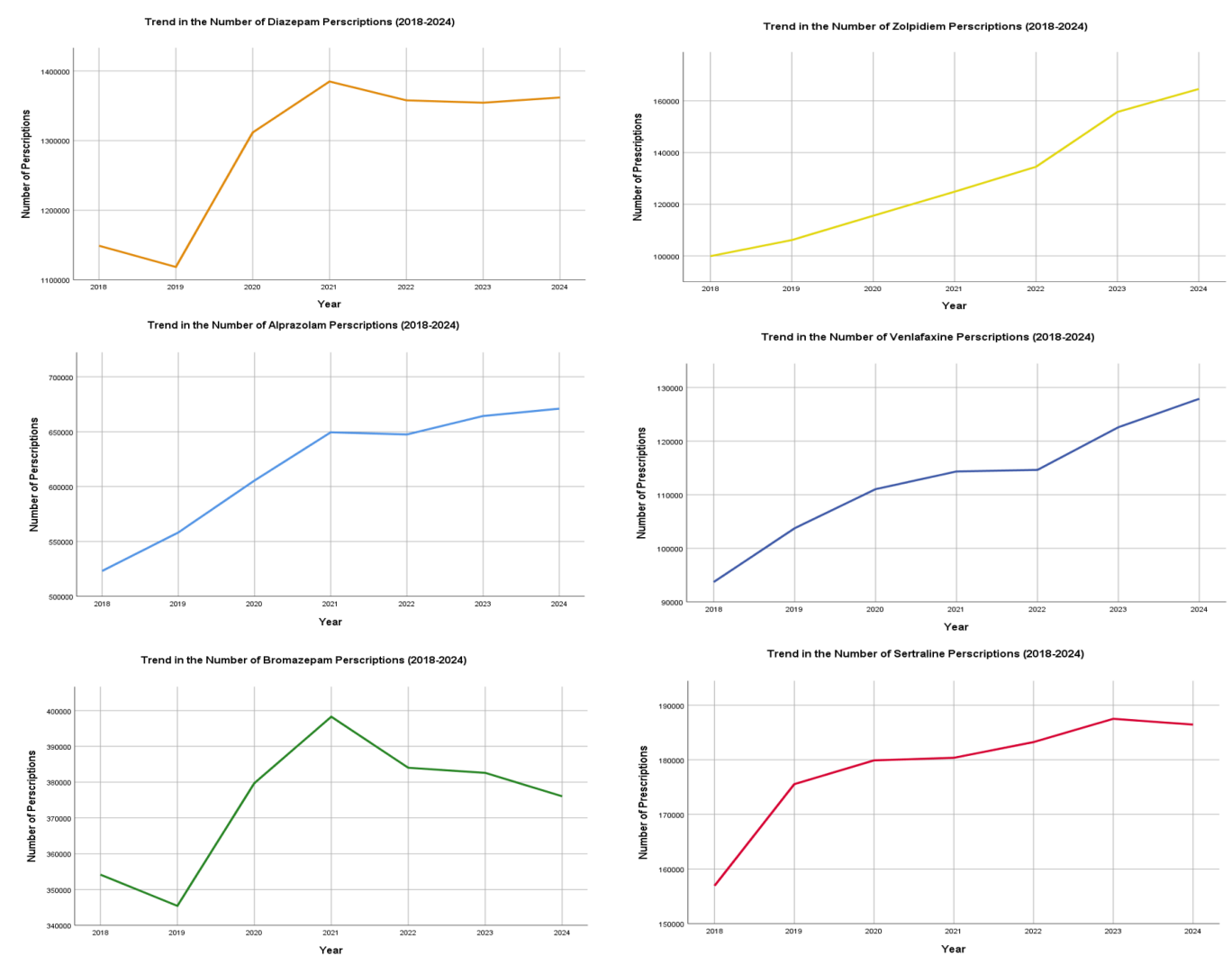
Table 1 Overview of issued prescriptions for psychotropic drugs (2018–2024)

Year	Diazepam	Alprazolam	Bromazepam	Zolpidem	Venlafaxine	Sertraline	Paroxetine
2018	1148983	523166	354162	99903	93727	156933	166039
2019	1118501	558202	345437	106136	103753	175537	174337
2020	1311615	605532	379725	115537	111041	179888	177848
2021	1384878	649403	398278	124854	114338	180361	176267
2022	1357857	647453	384020	134496	114627	183233	170668
2023	1354411	664255	382602	155704	122586	187494	160264
2024	1361912	670909	376048	164615	127886	186435	157021

Overall, statistically significant upward prescribing trends were identified for Alprazolam, Zolpidem, Venlafaxine, and Sertraline.

Table 2 Summary of drug's usage trends

Drug	Spearman's ρ	p-value	Trend	% Change (2018–2024)
Diazepam	0.714	0.071	Positive, non-significant	+18.5%
Alprazolam	0.964	<0.001	Significant increase	+28.2%
Bromazepam	0.464	0.294	Positive, non-significant	+6.2%
Zolpidem	1.000	<0.001	Significant increase	+64.8%
Venlafaxine	1.000	<0.001	Significant increase	+36.4%
Sertraline	0.964	<0.001	Significant increase	+18.8%
Paroxetine	-0.536	0.215	Negative, non-significant	-5.4%



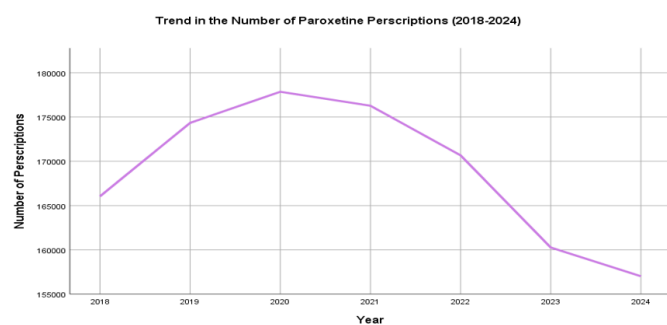


Figure 1 Correlation graphs of psychotropic drug prescriptions.

Although prescription rates for diazepam, alprazolam, bromazepam, zolpidem, venlafaxine, and sertraline were consistently higher during the pandemic period, none of the observed differences reached statistical significance. For all six medications, the Mann–Whitney U statistic was 0.000, with $Z = -1.936$ and an exact p-value of 0.095. Paroxetine showed no difference between the pre-pandemic and pandemic periods ($U = 5.000$, $Z = 0.000$, $p = 1.000$). Overall, these findings suggest a tendency toward increased prescribing of several psychotropic medications following the onset of the COVID-19 pandemic. However, statistical significance was not achieved, likely due to the limited number of annual observations available before the pandemic (Table 3).

Table 3 Mann–Whitney U test analysis of psychotropic drug prescribing rates during the pre-pandemic (2018–2019) and pandemic / post-pandemic period (2020–2024)

Drug	Mann-Whitney U	Z	Exact p-value
Diazepam	0.000	-1.936	0.095
Alprazolam	0.000	-1.936	0.095
Bromazepam	0.000	-1.936	0.095
Zolpidem	0.000	-1.936	0.095
Venlafaxine	0.000	-1.936	0.095
Sertraline	0.000	-1.936	0.095
Paroxetine	5.000	0.000	1.000

A total of 340 individuals adults ($n = 340$) participated in this study (Table 4), females (58.8%). Responders were of all age groups, mostly 50 to 59 age (39.1%), and the smallest group of over 18 and under 30 years (9.4%), primarily with high (faculty) education (58.82%), married (47%) and employed (48.8%). The majority of participants lived in urban areas (83%). Multiple responses were permitted; therefore, percentages do not total 100%.

Table 4 Overview of the demographic characteristics of the study groups

Gender	N=340	%
Male	140	41.18
Female	200	58.82
Age		
<30	32	9.41
30-39	48	12.94
40-49	60	17.65
50-59	129	39.12
>59	71	20.88
Education		
Primary	44	12.94
High	79	23.24

Table 4 Continued..

Faculty	200	58.82
Masters	17	5
Marital status		
Married	160	47
Cohabiting	16	5
Divorced	24	7
Widow	24	7
In a relationship	51	15
Single	65	19
Employment status		
Employee	166	48.8
Unemployed	39	11.5
Students	58	17.1
Academia	9	2.6
Working and studying	4	1.2
Pensioners	64	18.8
Place of residence		
Urban	280	83
Rural	56	17

To further understand the habits of using psychotropic drugs and their impact on mental health, data from a survey questionnaire were used, which is included in the second part of the study (Table 5). A total of 340 respondents ($N = 340$) participated.

Table 5 Overview of the answers from a survey questionnaire

question/Q	N=340	%
Q.1 Have you ever been diagnosed with a mental (psychiatric) disorder?		
Yes	79	23.2
No	261	76.8
Q.2 Timing of psychotropic medication initiation in relation to the COVID-19 pandemic -How many psychotropic drugs do you use before (2018-2019) and during COVID-19 crisis (2020-2024)?		
Before	98	28.8
During	242	71.2
Q.3 What did you use?		
Diazepam	154	45.3
Alprazolam	56	16.5
Bromazepam	39	11.5
Paroxetine	26	7.6
Sertraline	31	9.1
Venlafaxine	8	2.4
Zolpidem	26	7.6
Q.4 What were the reasons to use the above medicines?		
Anxiety	179	52.65
Tension	106	31.18
Insomnia	85	25
High pressure	74	21.76
Other reasons	69	20.29
Fear	100	12.94
Restlessness	99	12.06
Q.5 Who recommended the above medicines?		
Family doctor	159	46.8
Psychiatrist	88	25.9
Internal medicine specialist	26	7.6
Self-initiated	18	5.3

Table 5 Continued..

Pharmacist	10	2.9
Friend/Relative	39	11.5
Q.6 How do you use the medicine		
As prescribed	207	60.9
I tried to stop on myself	6	2
I used higher dose	110	32
I arbitrarily determined the dose	17	5
Q.7 Evaluate the statement "The COVID-19 crisis has had a major impact on determining my dosage"		
Completely true	200	59
Partially true	124	36
I am not sure	5	1
Completely incorrect	2	1
Partially incorrect	9	3
Q.8 Evaluate the statement "I took a higher dose, otherwise I didn't feel well"		
Completely true	68	20
Partially true	77	22.65
Completely incorrect	125	36.76
Partially incorrect	70	20.59
Q.9 Evaluate the statement "I felt nervous when the medicines were not available to me"		
Completely true	77	23
Partially true	137	40
I am not sure	12	4
Completely incorrect	83	24
Partially incorrect	31	9
Q.10 Evaluate the statement "I took more than prescribed"		
Completely true	44	12.94
Partially true	56	16.47
Completely incorrect	150	44.12
Partially incorrect	90	26.47
Q.11 Evaluate the statement "I was told to take lower doses"		
Completely true	43	12.65
Partially true	58	17.06
Completely incorrect	187	55
Partially incorrect	52	15.29
Q.12 Evaluate the statement "I feel/felt safe when they are/were next to me"		
Completely true	84	25
Partially true	140	41
Completely incorrect	8	2
Partially incorrect	57	17
I am not sure	51	15
Q.13 Evaluate the statement "The effect of the drug is now weaker compared to the beginning of use"		
Completely true	44	12.94
Partially true	55	16.18
Completely incorrect	50	14.71
Partially incorrect	64	18.82
I am not sure	127	37.35

A total of 76.8% of the participants were not using psychotropic drugs permanently and 71.2% of them started during the pandemic crisis (Q.1 and Q.2), mostly with diazepam (45.3%) and alprazolam (16.5%) (Q.3), because of combination of reasons, mostly anxiety (52.65%), tension (31.18%) and insomnia (25%) (Q.4). Over two thirds

of the participants (Q.5) used the above medicines in consultation with family doctors (46.8%) and psychiatrist (25.9%). It is notable that self-medication (5.3%) and pharmacist recommendation (2.9%) were rare.

Most of the participants use the drugs as prescribed (60%), but almost one third of them used higher dose (32%) (Q.6). COVID-19 crisis has had a major impact on the medicines use in almost all of the responders (Q.7 - answered "completely true" - 59% and "partially true" - 36%). More than a half of the participants were not increasing the doses to have better well-feeling (Q.8 - "completely incorrect" - 36.76% and "partially incorrect" - 20.59%). Addicted to the availability of the medicines (Q.9) were more than a half of them ("completely true" - 23% and "partially true" - 40%) and feel safe when they have medicines near them (Q.12) ("completely true" - 25% and "partially true" - 41%). Half of the responders were aware to use the prescribed doses, and they didn't take more than prescribed (Q.10 - "completely" - 44.12% and "partially" - 26.47%) and do not use lower doses as well (Q.11 - "completely" - 55% and "partially" - 15.29%). One third of all participants were not sure is the effect of the medicine now weaker than at the beginning of use (Q.13) (37.35%).

Discussion

The present study evaluated outpatient prescribing trends of anxiolytics, hypnotics, and antidepressants in North Macedonia between 2018 and 2024 and explored psychotropic medication use and mental health-related experiences among adults during the COVID-19 pandemic. The findings demonstrate a sustained increase in psychotropic medication prescribing throughout the study period, accompanied by substantial self-reported use of these medicines during the pandemic, particularly for anxiety, tension, and sleep-related problems.

The observed increase in prescribing of anxiolytics, hypnotics, and antidepressants is consistent with growing international evidence indicating that the COVID-19 pandemic significantly affected mental health and psychopharmacological treatment practices. The pandemic introduced multiple stressors, including social isolation, fear of infection, economic insecurity, uncertainty, and disruption of daily routines, all of which have been associated with increased prevalence of anxiety, depression, and sleep disturbances. Similar increases in psychotropic medication utilization have been reported in several European countries, including Portugal, Croatia, France, and the United Kingdom, suggesting that North Macedonia followed a broader international trend in response to the mental health consequences of the pandemic.^{7,8,12,13}

Among the investigated medicines, diazepam remained the most frequently prescribed psychotropic medication throughout the study period. This finding is not unexpected, considering the long-standing role of benzodiazepines in the management of anxiety disorders and acute stress-related symptoms. However, the persistent predominance of benzodiazepine prescribing warrants attention, particularly given concerns regarding tolerance, dependence, cognitive impairment, and prolonged use associated with this therapeutic class. Similar prescribing patterns have been reported in other countries in Southeast Europe, where benzodiazepines continue to account for a substantial proportion of psychotropic drug consumption.^{12,13}

The marked increase observed for zolpidem and venlafaxine may reflect growing recognition and treatment of sleep disturbances and depressive disorders during and after the pandemic. Sleep problems emerged as one of the most frequently reported psychological consequences of COVID-19-related restrictions, while increasing

rates of depression and anxiety likely contributed to greater utilization of antidepressants. These findings are consistent with international studies reporting sustained increases in antidepressant prescribing following the acute phase of the pandemic, even after the relaxation of public health restrictions.^{1,4,9,10}

Although positive correlations between calendar year and prescription volume were observed for all investigated medicines, comparisons between the pre-pandemic and pandemic/post-pandemic periods did not reach statistical significance. This finding should be interpreted cautiously. The analysis was based on aggregated annual prescription data and included a limited number of annual observations, reducing statistical power to detect differences between periods. Consequently, the absence of statistical significance should not necessarily be interpreted as evidence of a lack of pandemic-related impact but rather as a limitation of the available data structure and analytical approach.

The survey findings provide additional insight into psychotropic medication use during the pandemic period. Seven out of ten respondents reported initiating psychotropic medication use during the COVID-19 period, suggesting that the pandemic may have acted as an important trigger for treatment seeking or medication initiation. Anxiety, psychological tension, and insomnia were identified as the most common reasons for medication use, corresponding closely with symptoms most frequently reported in studies examining the psychological impact of the pandemic. These findings support previous research demonstrating that anxiety-related symptoms and sleep disturbances represented some of the earliest and most persistent mental health consequences of COVID-19.^{1,6}

An important finding of the present study relates to medication-related behaviors among respondents. Approximately one-third reported increasing medication doses, while many participants indicated feelings of reassurance when medication was available and discomfort or nervousness when access to medication was limited. Although the study was not designed to assess clinical dependence, these findings may indicate increased psychological reliance on psychotropic medication among some users. This observation is particularly relevant for benzodiazepines and hypnotics, which are associated with tolerance and dependence when used for prolonged periods. The results underscore the importance of regular treatment review, patient education, and adherence to prescribing guidelines aimed at minimizing inappropriate long-term use.

The findings should also be interpreted within the broader context of mental health service provision in North Macedonia. WHO reports have highlighted persistent limitations in mental health service capacity, including shortages of trained professionals, insufficient funding, and restricted availability of community-based psychosocial services. In settings where psychological and psychiatric support services are insufficiently accessible, psychotropic medications may represent one of the few readily available therapeutic options, thereby contributing to increased utilization. Strengthening community mental health services and improving access to non-pharmacological interventions may therefore represent important components of future public health preparedness strategies.¹⁴

Several limitations of this study should be acknowledged. First, the prescribing analysis relied on aggregated annual prescription data and did not include patient-level information, preventing assessment of treatment duration, prescribing indications, or individual medication trajectories. Second, the survey component was cross-sectional and conducted at a single time point during 2022; therefore, causal relationships between pandemic and psychotropic medication use

cannot be established. Third, survey responses were self-reported and may be subject to recall bias and reporting bias. Finally, the limited number of annual observations available for trend analysis may have reduced the statistical power of comparative analyses.

Despite these limitations, this study provides one of the first comprehensive assessments of psychotropic medication prescribing trends in North Macedonia spanning the pre-pandemic, pandemic, and post-pandemic periods. By combining national prescription data with survey-based evidence, the study offers valuable insight into changing psychopharmacological treatment patterns and their potential public health implications. Continued monitoring of psychotropic medication utilization, together with strengthening mental health services and promoting rational prescribing practices, will be essential for addressing the long-term mental health consequences of the COVID-19 pandemic and future public health emergencies.

The observed dose escalation and reported discomfort when medication was unavailable may indicate patterns of medication use that warrant further investigation, particularly for benzodiazepines and related agents, which are known to be associated with tolerance, dependence, and prolonged use when prescribed over extended periods.

Conclusion

This study demonstrated a sustained increase in outpatient prescribing of anxiolytics, hypnotics, and antidepressants in North Macedonia during the pre-pandemic, pandemic, and post-pandemic periods. The observed trends indicate that the COVID-19 pandemic was associated with long-lasting changes in psychotropic medication use and prescribing practices.

However, the prescribing patterns observed during the pre-pandemic period (2018–2019) with those recorded during the pandemic and post-pandemic period (2020–2024) was explicitly not statistically significant.

Diazepam remained the most frequently prescribed psychotropic medicine throughout the study period, while the most pronounced increases were observed for zolpidem, venlafaxine, alprazolam, and sertraline. These findings suggest an expanding burden of anxiety, sleep, and mood-related symptoms in the population, with a corresponding rise in pharmacological management.

Survey data further showed that most respondents initiated psychotropic medication use primarily because of anxiety, tension, and insomnia. Reported dose escalation, nervousness when medication was unavailable, and feelings of safety when medicines were available may indicate patterns of prolonged use and possible psychological reliance, particularly for benzodiazepines and hypnotics.

Overall, the findings emphasize the need for continued monitoring of psychotropic medication utilization, promotion of rational prescribing, and strengthening of mental health services in North Macedonia. Future research based on patient-level data is needed to better assess prescribing appropriateness, treatment duration, and long-term outcomes associated with psychotropic medication use.

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None.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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