The impact of the COVID-19 pandemic in the use of psychoactive substances.

[Eric Vleeshouwers, Katholieke Universiteit Leuven]

[Ben Verbeke, Katholieke Universiteit Leuven]

Promotor: [Prof. Dr. Bert Vaes, Katholieke Universiteit Leuven, ACHG]

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2. ABSTRACT

Background:
Exposure to disasters and critical events has been associated with various mental health issues. Research suggested that these critical events may be associated with a higher rate of psychotropic drug use, but literature is scarce and contradictory. During the COVID-19 pandemic, a high number of mental health problems was observed. This study investigated the correlation between the use of psychoactive substances and the COVID-19 pandemic. Therefore, we conducted a literature review and a retrospective cohort study.

Methods:
Literature review: The MEDLINE database was screened for relevant articles using a strict search algorithm. Major components were "COVID-19 pandemic", "psychotropic drug use". Besides this, we used other critical events such as "disasters", "terrorism", "war" and "economic recession" as control group. Articles were systematically selected based on inclusion/exclusion criteria. Data were extracted using a standardized data extraction table.
Retrospective cohort study: The Intego database, a general practice morbidity register in Flanders, was used to conduct our retrospective cohort study from 01-02-2018 to 31-01-2022. Our study population consisted of all patients aged 18 years and older and fluctuated annually between 15297 and 183851 patients. Psychotropic drug prescriptions were measured and divided into antidepressants (AD), antipsychotics (AP), benzodiazepines (BZP) and Z-drugs. We monitored absolute prescriptions, prescription rates and demographics, i.e., gender and age. To compare these findings, we divided our time frame into two periods of two years each.
Data was visualized into a linear model to evaluate time trends and gender differences. Possible variations in age are displayed in a bar graph.

Results:
Literature review: A sufficient amount of articles was evaluated, but their methods and results presented a high level of heterogeneity for "critical events" and the COVID-19 pandemic.
Retrospective cohort study: An increase in the absolute amount of prescriptions was observed since the start of the COVID-19 pandemic (AD +14.36% F, +16.73% M; AP: +16.45% F, +23.63% M; BZP: +10.63% F, +9.24% M; Z-drugs: +16.79% F, +15.48% M), but not in prescription rates.
Prescription rates in females were twice as high for antidepressants and Z-drugs, 1.75 times as high for benzodiazepines and slightly higher in antipsychotics compared to male subjects. These findings were similar before the onset of the pandemic.
Age groups 58 and older showed the highest increase in absolute prescriptions for both genders and all selected medication types, except for antipsychotics in males.

Conclusion:
In this retrospective cohort study, we observed an increase in the absolute amount of prescriptions in the investigated psychotropic drugs since the onset of the COVID-19 pandemic. No significant differences were discovered in the prescription rates. Sex category differences remained stable during our full study period with overall higher prescription rates in female subjects. Patients of 58 years and older showed the highest increase in absolute prescriptions.

3. NEDERLANDSTALIGE SAMENVATTING

Achtergrond:
Rampen en kritische events werden in verband gebracht met verschillende gevolgen voor de mentale gezondheid. Onderzoek suggereerde dat deze kritische events mogelijks geassocieerd kunnen zijn met een toename in psychoactief medicatie gebruik. Huidige gegevens uit de literatuur zijn echter beperkt en contradictorisch. Tijdens de COVID-19 pandemie werd er een hoge graad van mentale gezondheidsproblemen geobserveerd. In deze studie hebben we aldus de correlatie tussen het gebruik van psychoactieve middelen en de COVID-19 pandemie trachten te onderzoeken. Hiervoor hebben we een literatuurstudie en een retrospectieve cohortstudie uitgevoerd.

Methoden:
Literatuuronderzoek: De MEDLINE databank werd gescreend voor relevante artikels middels een strikt zoekalgoritme. Hoofdcomponenten betroffen “COVID-19 pandemic”, “psychotropic drug use”. Daarnaast hebben we kritische events, zoals “disasters”, “terrorism”, “war” and “economic recession” gebruikt als controle. Artikels werden systematisch geselecteerd op basis van inclusie/exclusie criteria. De data werden verwerkt middels een gestandaardiseerde extractietabel.
Retrospectieve cohortstudie: De Intego databank, een Vlaams huisartsenregistratienetwerk, werd gebruikt voor onze cohortstudie van 01-02-2018 tot 31-01-2022. De studiepopulatie bestond uit alle patiënten van 18 jaar en ouder en fluctueerde jaarlijks tussen 15297 en 183851 patiënten. Voorschriften van psychoactieve medicatie werden gemeten en onderverdeeld in antidepressiva (AD), antipsychotica (AP), benzodiazepines (BZP) en Z-drugs. Vervolgens hebben we absolute aantallen en ratio’s van voorschriften berekend, rekening houdende met demografische factoren, i.e. leeftijd en geslacht. Om onze bevindingen te vergelijken werd de tijdsperiode onderverdeeld in twee termijnen van twee jaar. De data werden gevisualiseerd middels een lineair model, om tijds- en geslachtsverschillen te evalueren. Leeftijdsverschillen werden weergegeven in een staafdiagram.

Resultaten:
Literatuurstudie: De geselecteerde artikels toonden een hoge mate van heterogeniteit in hun methodologie en resultaten, zowel voor kritische events als voor de COVID-19 pandemie.
Retrospectieve cohortstudie: Er werd een stijging in absolute aantallen van de voorschriften geobserveerd sinds het begin van de COVID-19 pandemie (AD +14.36% V, +16.73% M; AP: +16.45% V, +23.63% M; BZP: +10.63% V, +9.24% M; Z-drugs: +16.79% V, +15.48% M), maar niet in de ratio’s.
De ratio’s van voorschriften in de vrouwelijke studiepopulatie waren twee keer zo hoog voor antidepressiva en Z-drugs, 1.75 keer zo hoog voor benzodiazepines en discreet verhoogd voor antipsychotica in vergelijking met mannen. Deze bevindingen werden ook voor de COVID-19 pandemie geobserveerd. Leeftijdsgroepen van 58 jaar en ouder toonden de grootste stijging in absolute aantallen van de voorschriften voor beide geslachten en alle medicatietypes, behalve bij antipsychotica in de mannelijke populatie.

Conclusie:
In deze retrospectieve cohortstudie zagen we sinds het begin van de COVID-19-pandemie een toename van het absolute aantal voorschriften voor de onderzochte psychofarmaca. Er werden geen significante verschillen ontdekt in de ratio’s van voorschriften. Verschillen tussen geslachtscategorieën bleven stabiel tijdens onze volledige onderzoeksperiode met over het algemeen hogere ratio’s van voorschriften bij vrouwelijke patiënten. Patiënten van 58 jaar en ouder vertoonden de grootste toename in absolute voorschriften.

4. INTRODUCTION

Exposure to disasters has been associated with various mental health issues including posttraumatic stress disorder, major depressive disorder, substance use disorder and other psychological symptoms[1]. Historically, we can identify numerous natural disasters and critical events such as economic recession, terrorist attacks and war, which can have an influence on mental health and the use of psychoactive substances. Specifically for previous pandemics, there was evidence of increased anxiety and depression symptoms as well as an increase in first-time admissions in psychiatric units[2]. Prior research suggested that these critical events could be associated with short-term and/or long-term mental health effects[3–8]. However, this proved to be a topic of discussion. Deteriorating mental health could lead to increased use of psychotropic agents, although the literature seemed limited and contradictory.

For COVID-19 specifically, Torales et al. (2020) described an increase in health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger and fear due to the COVID-19 outbreak[9]. According to Prati et al (2021), the deterioration of mental health was linked to several factors, most notably the lockdown restrictions and its associate effects such as reduction in income and physical activity[10]. However, they also noticed that the psychological impact of the lockdown only affected a small minority, suggesting that most people were resilient. The people affected tended to be those with prior psychiatric disorders. Moreover, Robillard et al (2021) also reported a rise in new mental disorders[11]. Risk factors for developing psychiatric symptoms included female sex, lower income, decreased physical health, younger age and several others. Overall, the existing literature on the use of psychoactive medication during the COVID-19 pandemic showed a high level of heterogeneity. Differences on multiple levels were observed including setting, medication types, time intervals and measurement methods. Subsequently, the results were contradictory[12–15].

Prior research pointed to a possible link between disasters in general and the deterioration of mental health. However, few studies have examined whether this decline effectively leads to increased use of psychoactive medication. The available studies reported contradictory results. The COVID-19 pandemic was a relatively new disaster of which the long-term effects need further investigation. Due to a high level of heterogeneity in the available articles, the link between the pandemic and the use of psychoactive medication remained unclear.

Therefore, we synthesized the current evidence and investigated the correlation between the use of psychoactive substances and the COVID-19 pandemic. More specifically, we conducted a literature review on this subject. Furthermore, we zoomed in on different disasters and critical events as a control group, in order to evaluate the possibility of a trend. Additionally, we performed a retrospective epidemiological research in the Intego database. Hereby focusing on absolute amounts of prescriptions and prescription rates of psychoactive agents during the COVID-19 pandemic and compared these to the period before the pandemic.

5. METHODS

5.1 Literature Review

5.1.1 Search strategy

This literature review was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[16]. We performed an extensive literature search in May 2022 using the MEDLINE database. To investigate the influence of the COVID-19 pandemic, but also disasters in general, on the use of psychoactive substances, our search strategy was based on 3 major components using MESH terms. We manually fine-tuned our search using several specific terms for title and abstract, cfr. Supplementary file 1.

The first major component consisted of (1) "Covid-19"[MESH] OR (2) "Sars-cov-2"[MESH].
The second major component consisted of (1) "Pandemics"[MESH] OR (2) "Emergencies"[MESH] OR (3) "Economic Recession"[MESH] OR (4) "Disasters"[MESH] OR "Natural disasters"[MESH] OR (5) "Terrorism"[MESH] OR (6) "Mass casualty incidents"[MESH] OR (7) "September 11 terrorist attacks"[MESH] OR (8) "armed conflicts"[MESH].
The last component was linked with an AND to the previous 2 major elements and consisted of (1) "Psychotropic drugs"[MESH] OR (2) "Antidepressive agents" OR (3) "Benzodiazepines"[MESH] OR (4) "Drug prescriptions"[MESH].
Detailed search terms are presented in supplementary file 1.

5.1.2 Study selection

First, we searched for any duplicates using the duplicate finder software on Rayyan and excluded these articles. Second, we added two extra filters to narrow down our study selection. The first filter we used was the date of publication, i.e. from the year 2000 until the date of our PUBMED search. The second filter was based on language, i.e. only articles written in the English or Dutch language. Third, we evaluated the articles by title. In the fourth phase, we reviewed the remaining articles by abstract. Finally, the full text of the remaining articles was analyzed and divided into four subcategories, i.e. COVID-19, economics, disasters and terrorism-related articles. In the last three phases we have taken our in- and exclusion criteria into account.
Publications were found suitable for inclusion in this review if they met all of the following criteria: (1) COVID-19, disaster, terrorism or economics related articles (2) which investigated the psychotropic drug use (i.e. antidepressants, antipsychotics, benzodiazepines, z-drugs) (3) and compared it to other time periods. (Figure 1).

Articles not related to the subject or to the defined outcomes of interest were excluded.
Other exclusion criteria were articles that focused on other types of medication; articles where the full text was not available; articles in any other language than English and Dutch; articles with a wrong study design. This last exclusion criterium included articles with a population aged below 18 years; in vitro studies or non-human studies; case reports; commentaries; editorials; conference abstracts; letters; guidelines.

5.1.3 Data extraction

Data were extracted from 55 included publications using a standardized data extraction table (supplementary tables 2, 3, 4 and 5).

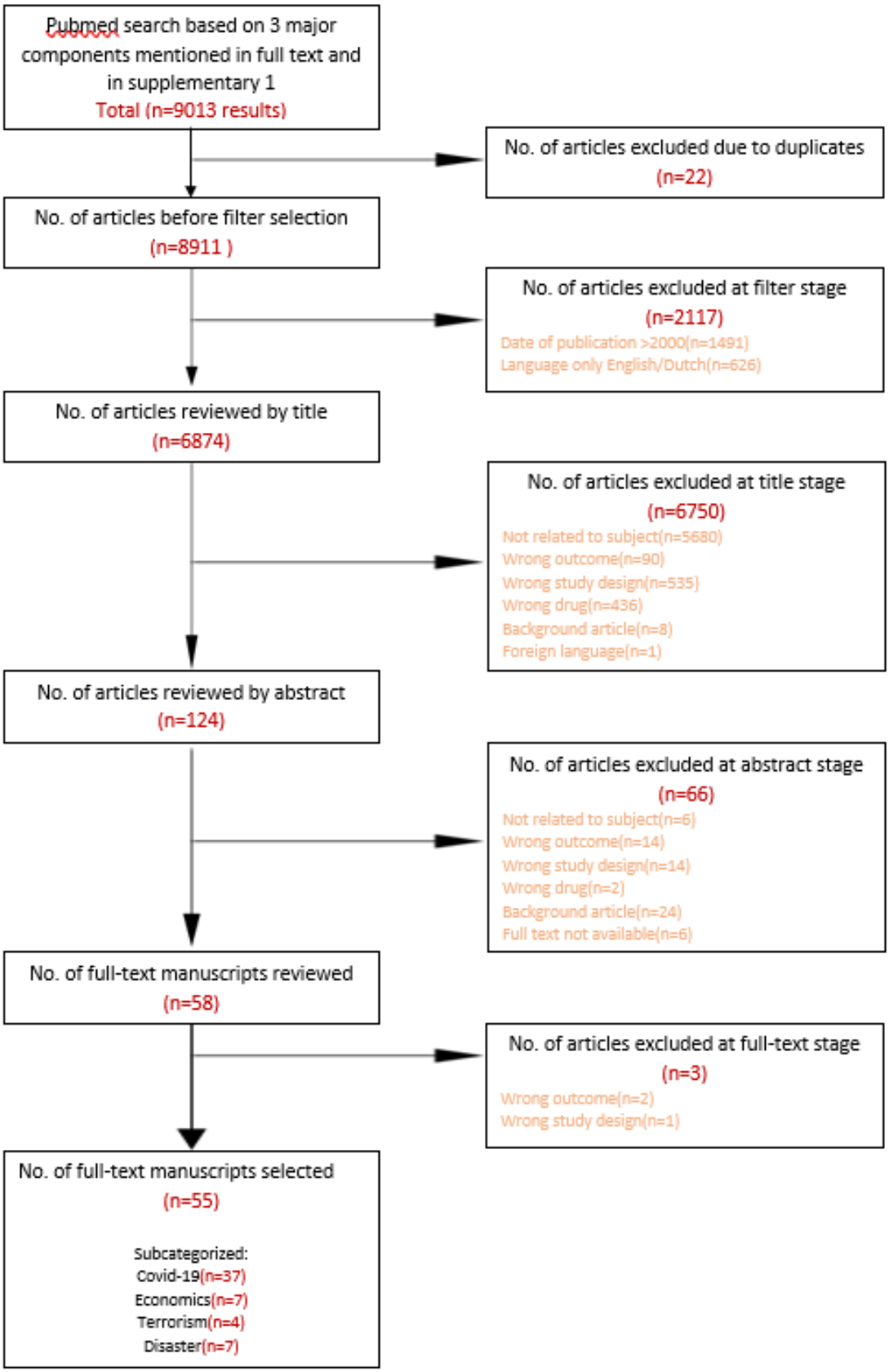


Figure 1. Flow diagram showing the study selection process and criteria of the included studies.

5.2 Intego Database

5.2.1 Intego

The Intego database was used to conduct a retrospective cohort study. The main goal of this research was to detect a possible quantifiable difference in prescription rates and/or absolute prescription numbers of psychotropic drugs in times of COVID-19 compared to a time period beforehand.

The database itself is a general practice morbidity register in Flanders, the Dutch-speaking region of Belgium[17]. Data was extracted from the electronic health records of the 105 Intego practices. In our case, data included the absolute amount of prescriptions, calculated prescription rates of psychotropic drugs and demographic characteristics, i.e. gender and age at that moment in time.
Our study population was defined as all patients aged 18 years and older, who visited one of the Intego practices between 01-02-2018 and 31-01-2022. The total number of visiting patients was measured for each calendar year and consisted of 140602, 164800, 181271, 183851 and 15297 patients for respectively 2018, 2019, 2020, 2021 and 2022. Within this study population, absolute numbers of patients receiving a psychotropic drug prescription were measured and extracted using the WHO anatomical therapeutic chemical (ATC) classification[18]. Based on our data, we calculated prescription rates for the given psychotropic medication types to correct for the fluctuant study population size.

5.2.2 Medication classification

As mentioned above, the Intego Database registers prescriptions of medication via the WHO anatomical therapeutic chemical (ATC) classification[18].
To monitor and evaluate our prescriptions, we selected the ATC codes of the most common psychotropic drugs prescribed in a general practice. We then further divided them into four subcategories: anti-depressive agents, antipsychotic agents, benzodiazepines and Z-drugs. Further specifications can be found in figure 2.

Group	ATC code	Specifics
Antidepressants	**N06A**	
	N06AA	Non-selective monoamine reuptake inhibitors
	N06AB	Selective serotonin reuptake inhibitors
	N06AG	Monoamine oxidase A inhibitors
	N06AX	Other antidepressants
Antipsychotics	**N05A**	
Benzodiazepines	**N03AE**	Benzodiazepine derivatives
	N05BA	Benzodiazepine derivatives
	N05CD	Benzodiazepine derivatives
Z-drugs	**N05CF**	Benzodiazepine-related drugs

Figure 2. Groups of psychoactive drugs based on their ATC classification.

5.2.3 Data collection and selected time periods

To investigate the potential difference in absolute prescriptions and prescription rates during the COVID-19 pandemic, we tried to select a time period before the pandemic which was free of any other disaster or critical events to prevent any bias. Eventually, we decided to compare the two years before the pandemic (i.e. from 01-02-2018 to 31-01-2020) with the first two years since the onset of the pandemic (i.e. from 01-02-2020 to 31-01-2022).

We measured the monthly absolute amount of patients receiving a psychotropic drug prescription and calculated prescription rates for our study population over the given time periods. Prescription rates were automatically calculated in the data collection phase and described as the monthly absolute amount of prescriptions per psychotropic medication type divided by the annual study population. We hereby took the demographics of the selected patients into account. Further details on the data collection can be found in supplementary table 8.

5.2.4 Data extraction/Statistical analysis

Prescription rates were extracted from the database following the above-mentioned methods. Prescription rates were divided into the four subcategories and split into monthly time periods.
To compare and visualize the first two years of the COVID-19 pandemic to the two years prior to the pandemic, we used a linear graph. The x-axis represented the time period over 24 months, divided into one month each. The y-axis represented the prescription rates per 1000 patients. In order to account for our demographic characteristics, we chose to visualize female and male graphics separately. In addition to these findings, we also processed the absolute amounts of psychotropic prescriptions following the same data extraction method.
In order to observe any differences between age groups, we used a bar graph. We divided our study population into subgroups with a range of ten years starting from the age of eighteen. We then compared the total amount of prescriptions during the pre-COVID-19 period to the total amount of prescriptions during the COVID-19 pandemic for the different subgroups. We hereby took the subcategories of psychotropic drugs and gender differences into account. The analysis was conducted using Microsoft Excel.

5.2.5 Ethical approval

K.U. Leuven Ethics Committee (nr. ML1723) and the National Privacy Commission's Sectoral Committee (decision nr. 13.026 of March 19, 2013, last modified on April 17, 2018) approved the Intego Databank methods.

6. RESULTS

6.1 Literature review

6.1.1 General

In this chapter, we will discuss the included articles of our literature review in four major segments, which are based on the four subcategories of psychotropic drugs mentioned in our methods section. Within each segment, we will also make a distinction between the main subjects of our literature review, namely COVID-19, terrorism, economic crisis and disasters.
Supplementary tables 2, 3, 4 and 5 display the characteristics of the selected articles.

6.1.2 Antidepressants

Forty-two articles evaluated the use of antidepressants.

COVID-19

Twenty-seven articles handled COVID-19 specifically.
Thirteen articles observed an increase in antidepressant use during the COVID-19 pandemic[12,15,19–29].
Campitelli et al (2021) reported an increase in weekly dispensation of psychotropic drugs, including antidepressants, in 630 nursing homes in Ontario, Canada[15]. Antibiotics, ACE-inhibitors and angiotensin receptor blockers were used as a control and showed no change. The other articles observed a similar trend in different settings and for different time periods. Interestingly, Pazzagli et al (2022) noticed an overall increase in the prescription of antidepressants, particularly in men and age group 30-59[27]. Other articles however, observed a similar trend in women and higher age groups.

On the other hand, four articles noticed a decrease in the prescription rates of antidepressants[30–33].
Five articles witnessed no change in antidepressant prescription rates[13,34–37].
Jones et al (2021) researched the monthly prescription rates between 2019 and May 2020. They noticed an increase in antidepressant prescriptions in March 2020 above the forecasted estimates. However, control medication (statins and angiotensin receptor blockers) followed the same trend[37].
Uthayakumar et al (2022) examined the monthly prescription rates of antidepressants and benzodiazepines in Canadian community pharmacies between 2017 and 2020. They noted a temporary decrease in the antidepressant rates in April 2020. However, there was no overall change compared to the period before the COVID-19 pandemic[35].

The remaining articles followed a specific trend, which will be discussed below.
Antonazzo et al (2022) and Farina et al (2021) reached compatible conclusions. Both studies were executed in Italy respectively Tuscany region and Rome. They observed an initial reduction in antidepressant prescribing during the first lockdown, followed by an increase afterwards till the end of 2020, the end of the observation period[14,38]. Stephenson et al (2022) noted the same reduction at the beginning of the COVID-19 pandemic. However, they observed no significant change in the prescribing trend during the second half of 2020[39].

Leong et al revised the quarterly incidence and prevalence rates of antidepressants in Manitoba, Canada from 2015 till the end of 2020. They reported a decrease in the incidence of antidepressants three months after the start of the lockdown. Furthermore, they observed an increase in incidence in the fourth quarter of 2020 for females, patients >40y, but the biggest increase was seen in patients >80y[40].

Zhang et al (2022) reported an increase in weekly prescriptions for antidepressants between March and May 2020. However, they also noticed a decline in incidence rates of antidepressants for the same period[41].

Terrorism

One article reported about the use of psychotropic drugs related to terrorism[42].

Druss et al (2004) performed a retrospective study on the prescription rates and dose adjustments of psychotropic drugs comparing the three months before 9/11 to the three months afterwards. They investigated three different levels: nationally, Washington DC and New York. They noticed no difference in the total of new prescriptions. However, they observed two events. On the national and Washington DC level, they noticed an overall small decline in dose increase. On the New York level, they observed an overall small dose increase, particularly for antidepressants[42].

Economic crisis

Seven articles have reviewed the use of antidepressants during times of economic crisis[43–49].

Four articles have reported an increase in antidepressant prescription rates[44,45,47,49].

Cherrie et al (2021) investigated the effects of the Great Recession of 2008 on the use of antidepressants in a sample of the Scottish population. The conclusion was that living in a region characterized by low and declining fulltime employment during the recession was associated with an increased likelihood of consuming antidepressants[49].

Three articles observed no change in antidepressant use[43,46,48].

Arroyo et al (2018) examined the psychotropic drug use in Spain before and during the financial crisis of 2008. No significant change was observed in the probability of consuming antidepressants[43].

Disasters

Finally, seven articles investigated the prescription rates of antidepressants after disasters[50–56]. Five articles reported a temporary or persistent rise in the prescription rates[51–53,55,56]. Two articles noted no difference[50,54].

Han et al (2017) reported on the monthly prescription rate of psychotropic drugs in Ansan, South Korea, after the Sewol Ferry disaster. They observed a 5,6% increase in antidepressant use compared to a control city[52].

6.1.3 Antipsychotics

Our search yielded nineteen relevant articles examining antipsychotics.

COVID-19

Twelve of those eighteen articles focused on COVID-19.

Four articles noted an increase in the prescription rate of antipsychotics[12,13,15,40].

Stall et al (2021) investigated the use of antipsychotics among nursing home residents in Ontario, Canada. They used statins and metformin as the control group. They noted a rise in the monthly proportion of residents receiving antipsychotics[12].

Nevertheless, two articles reported a decrease in prescription rates[21,57].

Kisely et al (2022) investigated the impact of COVID-19 on the prescription rate of new and repeat antipsychotics for patients with schizophrenia in Australia. They observed a reduction in new and repeated prescriptions. However, after the analysis, the results were deemed not significant[57].

Four articles reported no change in the prescription of antipsychotics[29,34,58,59].
McKee et al (2021) analyzed the monthly incidence rate of long-acting injectable antipsychotics in Cananda. They observed no significant change. However, they noticed a switch from one-month injectables to three-month injectables. This is probably due to a reduction of doctor visitations[58].

The two remaining articles could not be categorized.
Another study performed on not institutionalized dementia patients (Moretti et al 2021)) presented an increase in antipsychotic prescribing during the first lockdown followed by a slight reduction afterwards[60].
Zhang et al (2022) have been mentioned in the previous section on antidepressants. For antipsychotics, they reached a similar conclusion: an overall increase in prescriptions but a decrease in incidence rate[41].

Terrorism
One article focused on antipsychotic use during times of terrorism[42].
Druss et al (2004), already discussed in the section of antidepressants, observed a dose increase for patients already on antipsychotics, particularly for the national and Washington DC level[42].

Economic crisis
Three articles were found which investigated the use of antipsychotics during economic crisis[45,46,48].
Kozman et al (2012) investigated the association between unemployment rates and antipsychotic drug use. They observed a small increase in antipsychotic use with an increased unemployment rate[46].
Cornaggia et al (2016) also noted an increase[45] , while Vittadini et al (2014) reported a gradual increase but not statistically significant compared to before the COVID-19 pandemic[48].

Disasters
Three articles reported on the use of antipsychotics after disasters[50,54,55].
Rossi et al (2011) analyzed the prescription rate of antidepressants and antipsychotics after an earthquake in Italy. They used statins and diabetic medication as the control group. They noted a 129,5% increase in antipsychotic use. The controls have increased with 37% and 51,4%, respectively[54].
Trifiro et al (2013) examined the effect of the L'Aquila earthquake on the prescription rate of psychotropic drugs. They observed a temporary (two months) increase in antipsychotics. This was mostly observed in older women[55]. Beaglehole et al (2019) reported no change in the prescription rate[50].

6.1.4 Benzodiazepines
A total of thirty-three articles discussed the use of benzodiazepines.

COVID-19
Twenty-four articles dealt with the COVID-19 pandemic specifically.

Twelve articles reported an increase in the prescription rate of benzodiazepines[15,19,23,25,26,29,32,33,61–64].
Estrela et al (2021) analyzed the monthly prescription rate of anxiolytics on a national level in Portugal between January 2018 and March 2021. Anxiolytics had an initial reduction followed by an increasing trend over the given time period[32].
Gonzalez-Lopez et al (2022) researched the consumption of antidepressants, anxiolytics and sedatives/hypnotics in the primary health district of Almeria, Spain. They found a 6.1% overall increase in psychotropic drugs[23]. The most pronounced increase was observed in the anxiolytics group.

Four articles witnessed a decrease in the prescription rate[13,21,30,40].
Carr et al (2021) researched the incidence rates of benzodiazepines in a primary care database in the UK compared to the expected values based on previous data. For benzodiazepines, they observed a similar 16.5% decrease. For May and June 2020, they noted an increase in the incidence rate and by September 2020, the observed rate was similar to the expected rate[30].

Four articles observed no change in the prescription rate[12,34–36].
Sizoo et al (2022) researched the prescription rates of benzodiazepines in Dutch nursing home residents. They observed no significant change in the prescription rate[34].

The remaining articles will be discussed below.
We already discussed the article by Farina et al (2021) in the section of antidepressants. They also investigated the prescription rate of benzodiazepines during the three lockdown periods. With the benzodiazepines, they noticed a wave pattern: a decrease during the first period, followed by an increase during the second period and finally another decrease during the third period[14].
Although Jones et al (2021) noticed an overall increase in the prescription rate, the control medication followed a similar increase[37]. Therefore, it is not significant.
Moretti et al (2021) have been discussed in the previous section. They noticed an increase in benzodiazepine use during the first lockdown period followed by a slight decrease afterwards[60].
Zhang et al (2021) reported an increase of the overall prescription rate but a decrease in incidence rate[41].

Terrorism
Two articles reported on the use of benzodiazepine during terrorism-related events[42,65].
Gouraud et al (2021) performed an interrupted time series analysis on the use of benzodiazepines in the French population after the November 2015 terrorist attacks. They witnessed an increase in the weekly number of individuals with a benzodiazepine prescription and elevated weekly defined daily doses[65]. Druss et al (2004) also reported an increase[42].

Economic crisis
Two articles have investigated the prescription rate of benzodiazepines during times of economic struggle[44,47]. Both reported an increase in benzodiazepine prescription rates.
Barcelo et al (2016) examined the use of antidepressants and benzodiazepines in a cohort study in Catalonia, Spain, during the financial crisis of 2008. They reported an increase in benzodiazepine use, particularly for patients already on psychotropic drugs and for those most likely to be unemployed[44].

Disasters
Six articles have investigated the prescription rate of benzodiazepines after disasters[50–53,56,66]. Three of those reported an increase[50,53,66] , while three noted no change[51,52,56].
Okazaki et al (2022) performed a cohort study on the effect of the Japan Floods of 2018 on benzodiazepine use. They observed an increase in the mean prescription rate in the group of the victims. They also noted a significant increase in use immediately after the floods and after 1 year in the victim group[66]

6.1.5 Hypnotics/Z-drugs

Seventeen articles were identified which reported on the use of hypnotics.

COVID-19

Ten articles evaluated the prescription rate of hypnotics during the COVID-19 pandemic.

Five articles have reported an increase in hypnotics use[19,23,25,26,32].

Levaillant et al (2021) performed a retrospective cohort study in different age groups in France, examining the consumption of anxiolytics, hypnotics and antidepressants. They reported a significant increase in consumption for all investigated drugs in all age groups[25].

Two articles observed a decrease in the prescription rate[13,31].

Kowall et al (2022) carried out a study of the quarterly incidence rate of antidepressants and hypnotics in the diabetes type 2 population. They reported a reduced incidence rate in all quarters of 2020 and the first quarter of 2021[31].

Three articles witnessed no change in the prescription rate[33,36,40].

Lear-Claveria et al (2022) conducted an observational study in patients treated with anxiety or depression. They analyzed the use of antidepressants and anxiolytics 6 months before the lockdown and compared it to the 6 months following the end of the lockdown. They noted no change in hypnotics use[33].

Terrorism

Druss et al (2004) reported no change in new or total prescriptions for hypnotics after the 9/11 attacks[42].

Economic crisis

Two studies have investigated the use of hypnotics during the Great Recession of 2008[43,47]. One observed an increase in hypnotic use[47] , while the other reported no change[43].

Silva et al (2020) performed a cross-sectional survey study in Portugal comparing the time period from 2008 to 2009 with the time period from 2015 to 2016. They noted a 6,74% increase in psychotropic drug use, particularly for hypnotics[47].

Disasters

Four studies have examined the effect of disasters on the use of hypnotics[50–53]. Three articles noted an increase[50,51,53] , while one article observed no change[52].

Beaglehole et al (2019) observed the impact of the Canterbury earthquakes on the prescription rate of psychotropic drugs. They reported a short-term increase for benzodiazepines and hypnotics (one month). No long-term effect was observed[50].

Lastly, we would like to discuss three remaining articles[67–69]. These articles did not specify which medication type they investigated.

Boscarino et al (2003 + 2004) performed two survey studies on the use of psychotropic drugs following the 9/11 terrorist attacks. The first study observed a slight increase in psychotropic drug use six months after the attacks[67]. The second one reported a slight increase in usage 30 days after the attacks. This increase was mostly observed in patients with panic attacks or PTSD[68].

De Bocanegra et al (2006) conducted interviews with Chinese workers who were affected by the 9/11 terrorist attacks. Of these workers, 60% reported that they received a prescription for psychotropic drugs[69].

6.2 Intego database

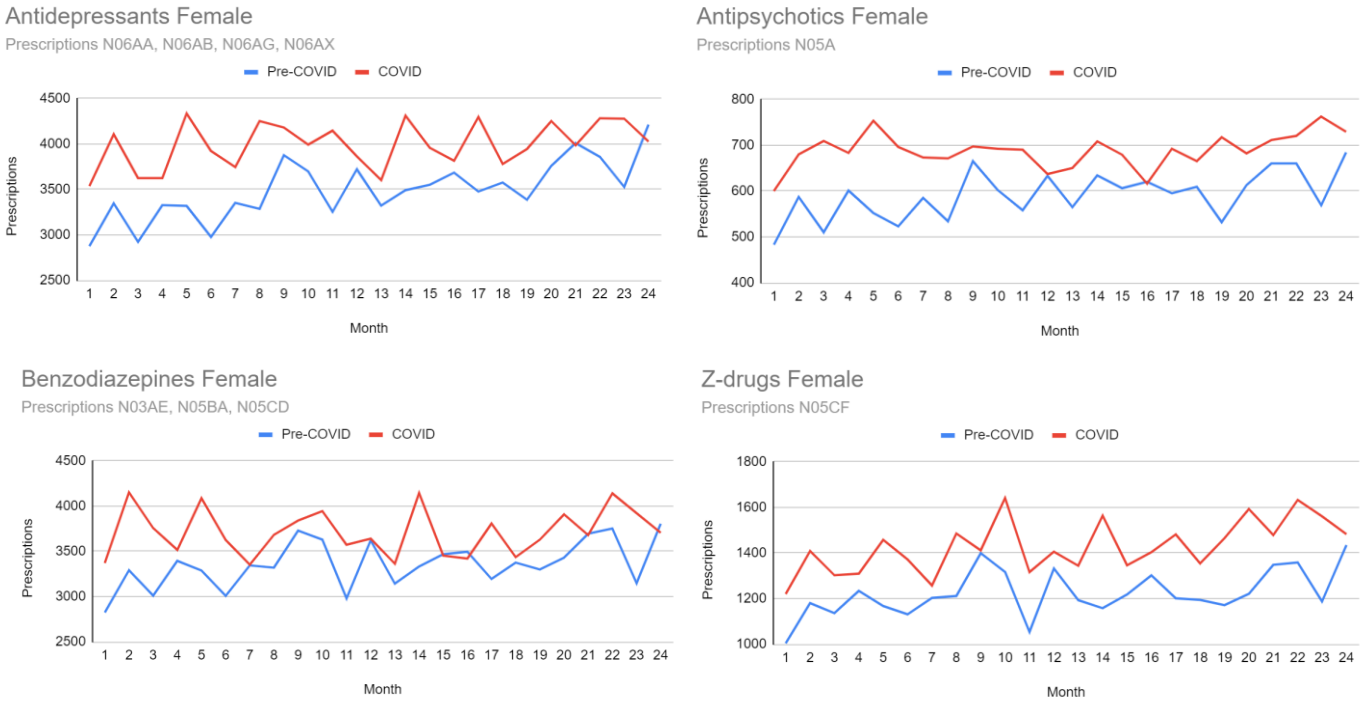


Figure 3. Absolute amount of prescriptions of psychotropic drugs based on time period in females.

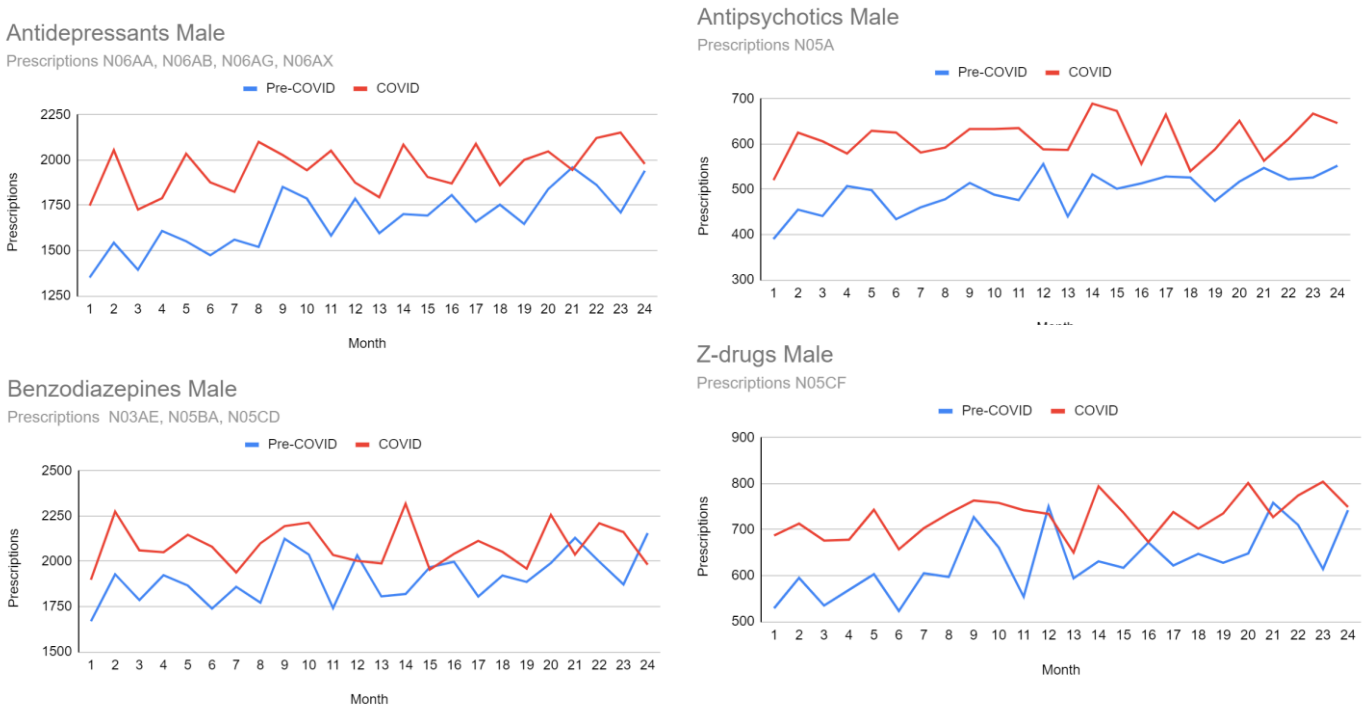


Figure 4. Absolute amount of prescriptions of psychotropic drugs based on time period in males.

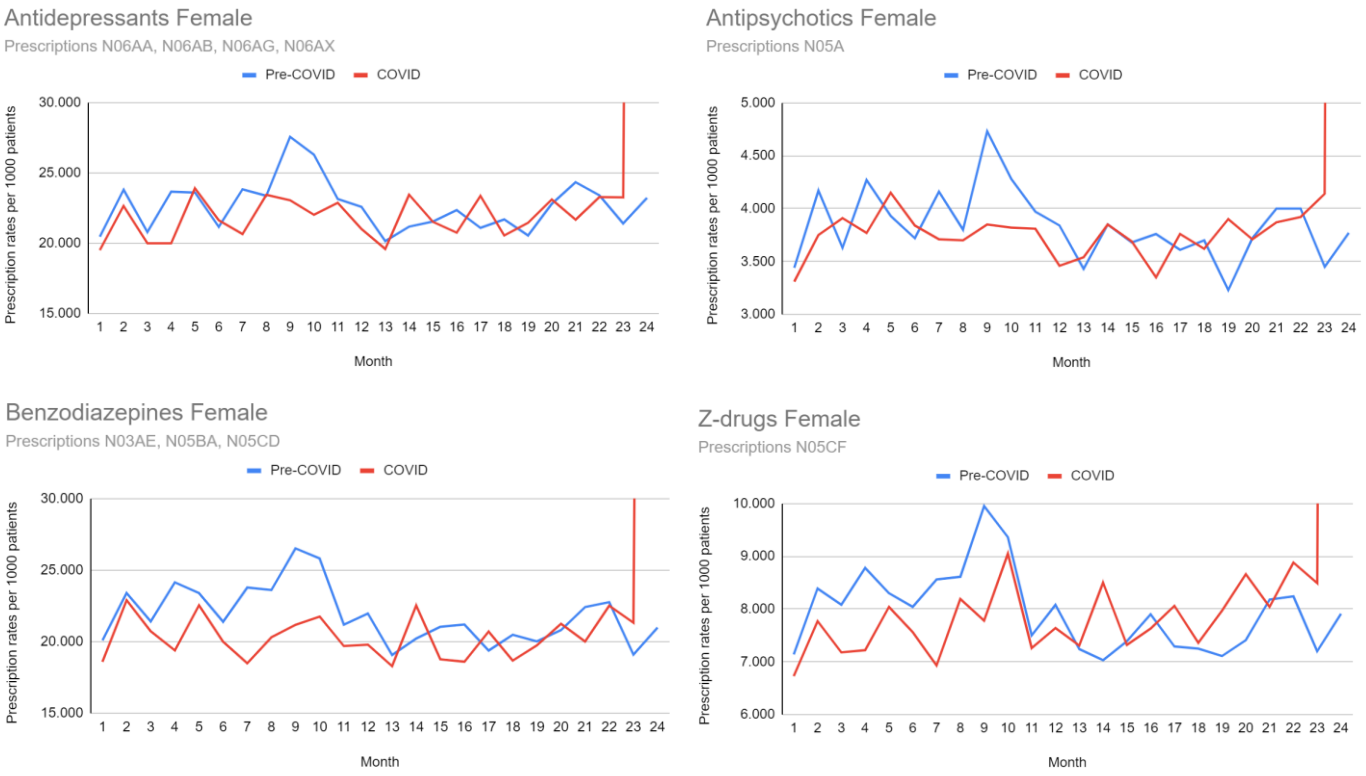


Figure 5. Prescriptions rates per 1000 patients of psychotropic drugs based on time period in females.

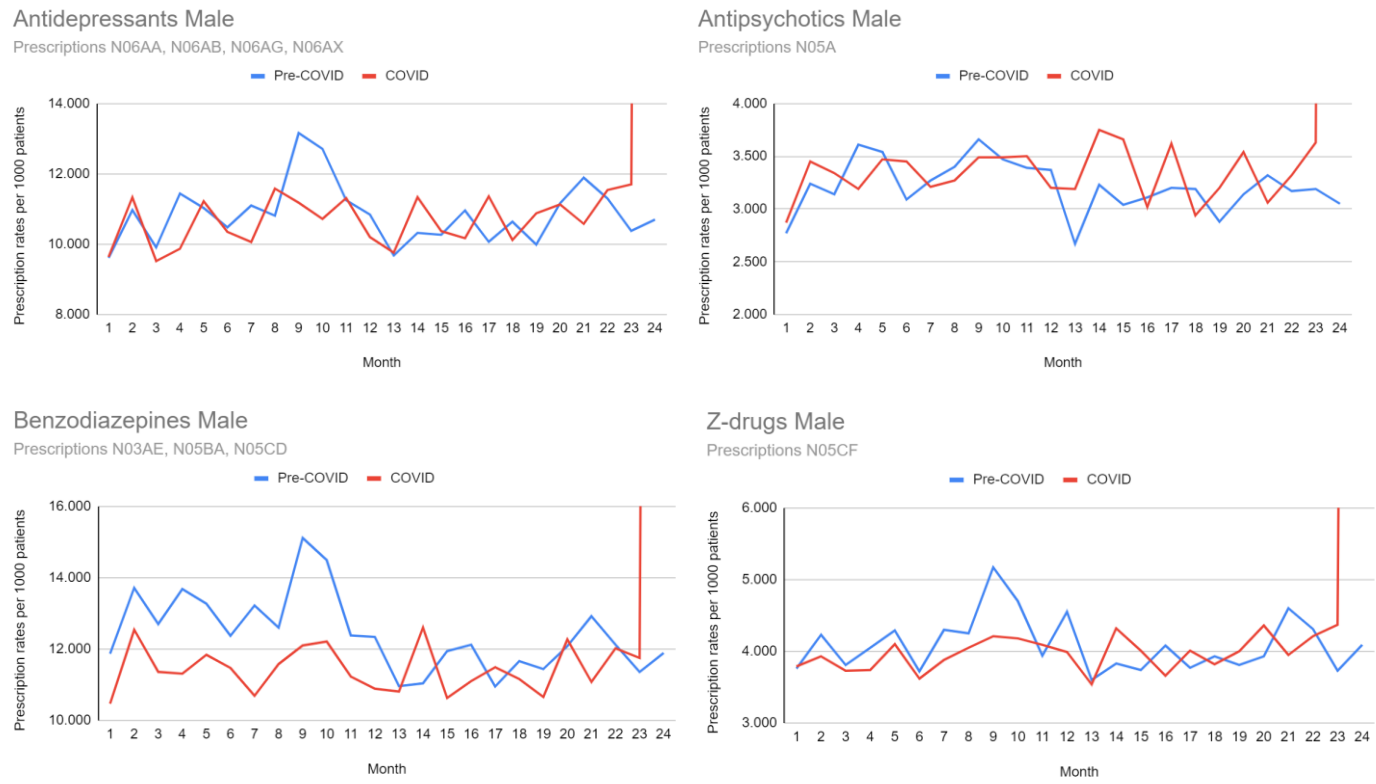


Figure 6. Prescriptions rates per 1000 patients of psychotropic drugs based on time period in males.

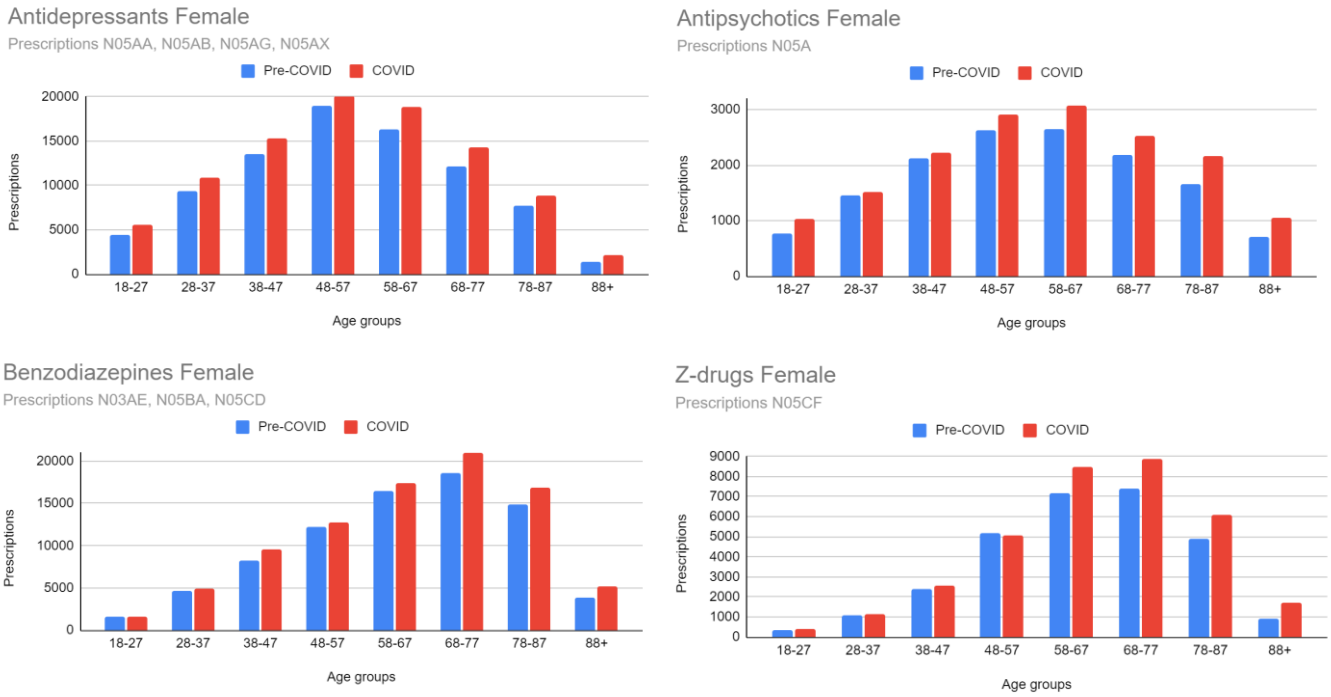


Figure 7. Absolute amount of psychotropic drug prescriptions based on age groups in females.

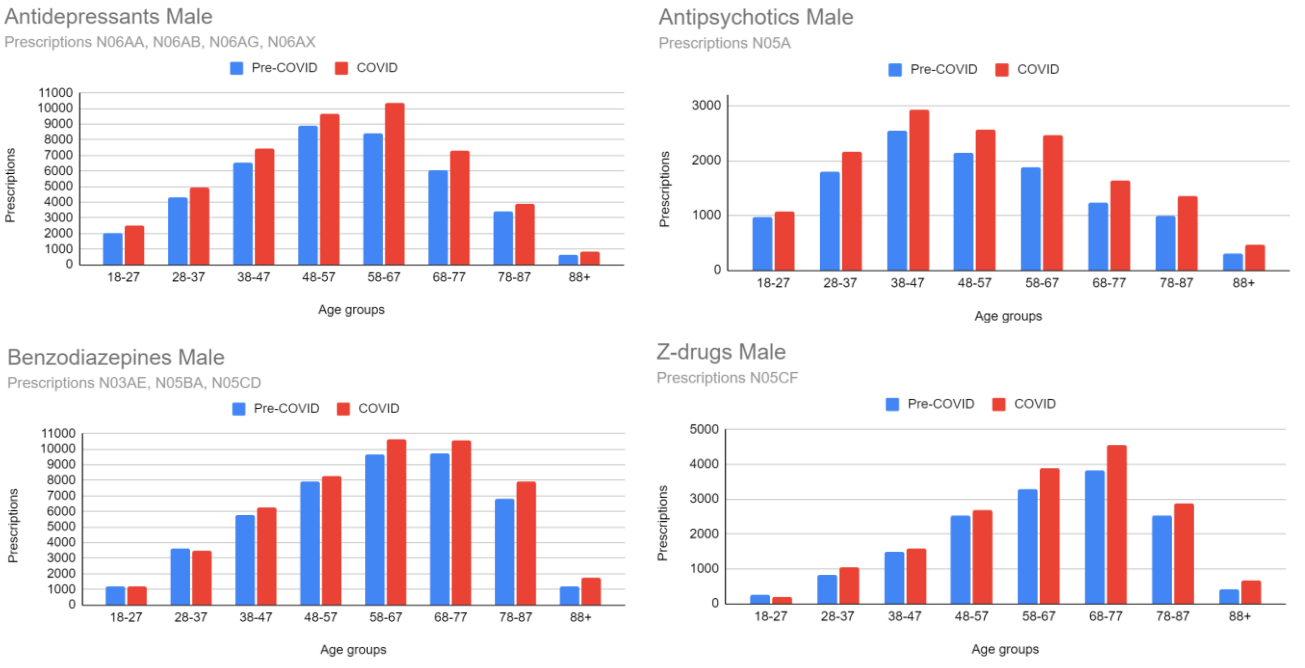


Figure 8. Absolute amount of psychotropic drug prescriptions based on age groups in males.

6.2.1 General

As mentioned in our methods, we visualized our results in a linear and a bar graph. In figures 3 and 4, we can find the results on absolute amounts of prescriptions, in figures 5 and 6 we can find the results on prescription rates. Both graphs are based on monthly time periods for female and male subjects, respectively. The blue line shows the information pre COVID-19 where the first month is February 2018. The red line displays the information since the onset of the COVID-19 pandemic, i.e. February 2020. We distributed both lines in the same graph to visualize any differences within the two time periods. For a closer look at the absolute amounts and prescription rates of the different types of antidepressants, we refer to supplementary tables 6 and 7.

In figures 7 and 8, our results based on age groups for respectively female and male subjects are shown. Further information can be found in our methods chapter. For specifics on absolute amounts and prescription rates, we refer to our supplementary table 8.

To discuss our observations of psychotropic drug use, we zoom in on each of our four selected subcategories. Per subcategory, we describe our findings consecutively. First, we present our general findings on absolute amounts of prescriptions. Afterwards, we take a closer look at prescription rates and their specific time trends. Finally, we discuss any gender and age differences.

Worth to mention beforehand are some general findings. All medication types present a decrease in prescription rates in the first month of the COVID-19 pandemic compared to the month prior. In the period prior to the COVID-19 pandemic, we observed a peak in prescription rates in October 2018 and November 2018 for all medication types and both genders. Overall prescription rates were slightly higher in 2018 compared to the following years and most pronounced in benzodiazepines and Z-drugs. Noticeable by interpreting our results is the exponential rise in the final month of the COVID-19 curve for all medication types and both sex categories. This month corresponds with January 2022. Unfortunately, we only received the population number for this first month and not for the whole year of 2022. As a consequence, corresponding calculated prescription rates are significantly higher and thus unrepresentative for our results.

6.2.2 Antidepressants

Generally, there was an increase in both female and male absolute prescriptions (14.36% F; 16.73% M), but not in prescription rates comparing the two time periods. The overall trend in prescription rates was more or less the same when you compare the periods before and since the onset of the COVID-19 pandemic for both genders.

When we watch our prescription rate data in depth, we obtained several interesting findings. The small dip since the onset of the COVID-19 pandemic was followed by a small peak in March 2020 with afterwards a decline in prescription rates for two months (April 2020, May 2020) and for both sex categories. Note a small peak in June 2020. Afterwards, we saw a sawtooth pattern with drops in February 2021, and to a lesser extent in April 2021, May 2021 and July 2021. Mentionable peak prescription rates were described in March, June, November and December of the year 2021.

We found no significant differences in the prescription patterns between male and female subjects. Note that the overall prescription rates were more than twice as high in females compared to males, as well before as during the COVID-19 pandemic.

When taking a closer look at figures 7 and 8, we saw that for each age group, there was a higher number of prescriptions after the start of the pandemic for both genders. However, the biggest difference in absolute prescriptions was found in the age groups of 58-67 and 68-77 years of age.

6.2.3 Antipsychotics

As well as the antidepressants, there was an increase in female and male absolute prescriptions of antipsychotics comparing the two given time periods. In females, there was an increase of 16.45% and in males, an even higher increase of 23.63%.

When we take a closer look at our prescription rates, the female curve was a little bit higher in 2018 but for the other years more or less equal. In male subjects, there was a slightly higher prescription rate in 2021.

When zooming in on the prescription rate data itself, we found a small dip in the first month of the COVID-19 period in females and males compared to the month prior. When we watch our female curve, there was also a small peak in June 2020 followed by a stable period from July 2020 to December 2020. Afterwards, we observed a saw tooth pattern with dips in January 2021, February 2021 and May 2021 and a slightly higher prescription rate in December 2021. In male subjects, we can mention the same stable period from July 2020 until December 2020. Afterwards, we observed the same sawtooth pattern but with higher peak prescription rates in March, April, June, September and December of the year 2021 and dips in January, February, May, July and October 2021.

When looking at the prescription rates by sex category, we observed that the overall prescription rate was slightly higher in females.

Age differences visualized in figures 7 and 8 showed an overall higher absolute amount of prescriptions for all age groups in males. The increase was less pronounced for the group of 18-27 years old compared to the other age groups. In females the pattern was a little bit different: overall there was also a higher absolute amount of prescriptions in all age groups, but most noticeable in age groups 48-57 years of age and older.

6.2.4 Benzodiazepines

For our third subcategory, we noted an increase in absolute prescriptions since the start of the COVID-19 pandemic (+10.63% F; +9.24% M). Benzodiazepines had the lowest percentual rise in absolute prescriptions.

Prescription rates, however, were slightly higher in 2018, but were more or less equal the following years.

More specifically, there was a small dip in prescription rates the first month of the COVID-19 pandemic, followed by a peak in March 2020 for both genders. Interestingly, several peak moments of prescription rates were noted. For male subjects, we observed a peak in March 2021 and September 2021. For female subjects, there was a peak in June 2020, March 2021 and November 2021. An important dip was observed for both sexes in January and February 2021.

The prescription rates in this subcategory were 1,75-1.78 times higher for female subjects compared to male subjects, respectively pre COVID-19 and during the COVID-19 time period.

When watching our age groups, we saw the biggest increase for females 68 years of age and older, males 58 years of age and older. In the younger population, the difference was less distinct. In the age groups of 18-27 years of age, absolute prescriptions were more or less equal. In male subjects age 28-37 years of age, there was even a higher absolute amount of prescriptions in the pre COVID-19 time period.

6.2.5 Z-drugs

In our last subcategory, we found an increase in absolute prescriptions as well. We observed an increase of 16.79% and 15.48% for female and male subjects, respectively.

When we watch our prescription rates in general, we observed a higher prescription rate in 2018 for both genders and in the fourth quarter of 2021 for female subjects more than for male subjects.

Also, in this category, we took a closer look at our linear graph. In our female subjects, there was a slight dip in prescription rates the first month of COVID-19, followed by a small increase the month afterwards and a dip during April 2020 and May 2020. Afterwards, we saw a few peak periods, i.e. November 2020, March 2021 and a higher prescription rate at the end of 2021. Note the period of December 2020 to February 2021, were there was a slight decrease after the peak period in November 2020.
In our male curve, the pattern is different. There was no peak at the beginning of the COVID-19 period and prescription rates stayed more or less at the same level for the first year of the COVID-19 pandemic. During the second year, there was a peak period in March 2021 followed by a slightly higher prescription rate at the end of 2021.
The prescription rates were more or less twice as high in female subjects compared to our male subjects, with no significant differences between our two time periods.
Comparing our different age groups, we observed the highest increase in females and males age 58 and older. In females, the absolute prescription count in the younger age groups were more or less equal to each other, with a slightly higher absolute number of prescriptions pre COVID-19 in the age group of 48-57. In our male bar graph, we could see a slightly higher absolute amount of prescriptions pre COVID-19 in the age group of 18-27. The age groups between 28-57 had a slightly higher count of prescriptions since the COVID-19 pandemic but not as distinct as the older population.

7. DISCUSSION

7.1 General

The purpose of this literature review and retrospective cohort study was to identify possible trends in the psychotropic drug use since the COVID-19 pandemic. We tried summarizing our literature findings and used other critical events as a control group. To zoom in on a national level, i.e. Belgium, we conducted our Intego database study. Furthermore, we compared our literature review with our epidemiologic study, where we concentrate on general findings, specific trends, age and gender differences. Finally, we discuss our strengths, limitations and future directions.

7.2 Comparison of literature review and Intego database

7.2.1 Comparison with other critical events

Due to the limited articles found on the use of psychoactive drugs related to other events besides COVID-19, it is difficult to make a comparison. Overall, the articles on other critical events can be categorized into two sections: increased prescription rate or no change in prescription rate.
For terrorism, only two articles were useful. Druss et al (2004) observed no change of the total or new prescriptions[42]. This was supported by a minority of the articles on COVID-19 that also observed no change. Gouraud et al (2021) reported an increase in benzodiazepine use after a terrorist attack[65]. This was supported by twelve of twenty-four articles on benzodiazepine use during COVID-19, which also reported an increase.
For economic crisis and disasters, a slight majority of the articles reported an increased prescription rate. Due to the limited prior research and the limited number of withheld articles, it was difficult to draw conclusions.
Compared to COVID-19, we noticed that certain articles could not be categorized because they reported a specific trend. Therefore, statistical analysis was not possible. Overall, we observed that around half of the articles reported an increase in the prescription rate.

7.2.2 General trends

As described in paragraph 6.2, our Intego database study showed an overall increase in absolute prescriptions but not necessarily in prescription rates since the start of the COVID-19 pandemic. The elevation in absolute prescriptions was seen in all the psychoactive medication types included in this thesis. Specifically, the lowest increase was seen in benzodiazepines (female 10.63%, male 9.24%) and the highest increase in antipsychotics but only in the male population (+23.63%). For antipsychotics in female subjects, antidepressants and Z-drugs elevation levels were more or less similar and between 14.36% and 16.79%. However, absolute prescriptions do not take our fluctuant study population into account. Therefore, we focused mainly on prescription rates to correct for this factor.

Overall prescription rates did not differ significantly comparing the two given time periods, but as mentioned above, there are some interesting findings evaluating the specific time trends of our data. This will be discussed in the next paragraph.

When we compared these general findings to our literature study, we noticed a discrepancy. Only a minority of the articles reported no change in the prescription rate. Compared to this, more articles reported a rise in the prescription rate, but a high level of heterogeneity was observed among the available articles. This made it difficult to make a comparison.

Important to mention is that we did not have the opportunity to conduct a statistical analysis on the data. Therefore, these data should be interpreted with great care.

7.2.3 Specific trends

To observe if there was a possible influence of COVID-19 waves and lockdown periods, we consulted the website of Sciensano, the scientific institute of public health in Belgium, to identify correct time frames[70,71]. Specific dates can be found in supplementary table 9. When we compared our COVID-19 waves and lockdown periods with our epidemiologic and literature study, there were some mentionable observations.

During the first wave/first lockdown period, we saw a small dip in prescription rates since the start of the pandemic for all medication types and all genders(i.e. February 2020). In antidepressants for both genders and in Z-drugs for only females, there was a decrease in April and May 2020. Rather interesting were the peak prescription rates for benzodiazepines in March 2020 and June 2020 for both genders. There was also a small peak in Antipsychotic usage in June 2020, but only in woman.

This trend has also been reported in certain articles. Farina et al (2021) and Antonazzo et al (2022) noticed an initial reduction in antidepressant prescription rates during the first lockdown period[14,38]. This trend was also observed by Stephenson et al (2022)[39]. The authors assigned this trend to the enforcement of the lockdown, which decreased the circulation of people and made certain health services unavailable. The worry of being infected also played a part in this. On the contrary, Moretti et al (2021) observed an increase in benzodiazepine and antipsychotic use in 221 not institutionalized dementia patients during the lockdown period[60]. They hypothesized that social isolation led to an increased feeling of loneliness, which in turn caused increased anxiety and depression. This was supported by the slight decrease in the prescription rate after the end of the lockdown.

During the second wave/second lockdown period, prescription rates for all medication types showed a small dip between January 2021 and February 2021 in our data. For benzodiazepines in both genders and Z-drugs only in females, we observed this decrease a little bit earlier, starting in December 2020.

Compared to the literature, Krupa et al (2022) observed the same dip in these months for antidepressants[24]. This could possibly be caused by the fact that this period is an interwave period.

In COVID-19 wave three, our data showed an increase in prescription rates for all medication types and both sex categories in March 2021. As to antipsychotic usage in male subjects, there were also peak prescription rates worth to mention in April 2021 and June 2021. For antidepressants, also peak prescription rates were noticed for both genders in June 2021.

Again, Krupa et al (2022) observed this increase for antidepressants[24]. A rise in the monthly COVID-19 incidence could have been the cause of this trend. Estrela et al (2022) reported an increased prescription rate for anxiolytics and hypnotics in this time period[32]. Contrary to this, they reported a decreasing trend in antidepressants.
Finally, for waves 4 and 5 our data showed an overall higher prescription rate in the fourth quarter of 2021 in Z-drugs and to a lesser extent in benzodiazepines (i.e. peak in females November 2021, peak in males September 2021). Antidepressants and antipsychotics seemed to follow this pattern with an increasing prescription rate specifically for December 2021. Further data are necessary to observe this possible trend.
In the literature, there were no articles with a follow-up period as long as the one in our cohort study. Krupa et al (2022) had an observation period until October 2021. Between June and September 2021, they reported a decrease in the prescription rate for antidepressants. In October 2021, they noticed an increase in the prescription rate[24]. This could possibly be the result of the rise in COVID-19 incidence.

7.2.4 Differences in sex category

Another interesting finding was the difference in prescription rates between female and male subjects. Several previous studies have described the same differences in sex category[72–74]. Clara Maestre-Miquel et al (2021) conducted a cross-sectional study in Spain. They reported that women experience more psychological stress, mental disorders and significantly consume more psychotropic drugs than men. Possible reasons could be intrinsic biological traits, emotional processing differences and a lower threshold to visit a doctor with these symptoms. Kovess-Masfety et al (2014) also described that women use mental health care and visited general practitioners more often[75].
The results of our cohort study were very similar to these general findings. In antidepressants and Z-drugs, we monitored twice as many prescriptions for females compared to males. For benzodiazepines, the difference was slightly lower compared to antidepressants and Z-drugs (+/- 1.75 times higher in females), but still significantly higher for the female population. The lowest difference was found in the medication group of the antipsychotics (+/- 1.12-1.19 times higher in females, pre-COVID-19 versus during the COVID-19 pandemic).
Almost every article investigated the difference in prescription rates for males and females. Overall, there was a clear trend. The increase in the prescription rate in females was significantly higher compared to the males. The range varied differently depending on the article.
Pazzagli et al (2022) observed an interesting trend in the Friuli Venezia Giulia region. They noticed a similar increase in the prescription rate for antidepressants in both genders. However, for men, the monthly mean of the observed defined daily doses was higher than predicted[27]. The authors hypothesized that men were more affected by the pandemic. This is contrary to other studies conducted in Italy, where women on average consumed more antidepressants. Perhaps some regional socioeconomical differences could be the cause of this trend.

7.2.5 Age differences

Furthermore, we took a closer look at our age groups and potential differences. In antidepressants, we could see a higher prescription rate in the COVID-19 pandemic period, in all age groups and for both genders. However, the highest rise was seen in the age groups of 58-67 and 68-77 years old. In antipsychotics, there was also an overall higher prescription rate for all age groups and genders. Note that in females, the highest elevation was seen in age group 48 and older and in males all age groups except for 18-27 years of age.
In benzodiazepines and Z-drugs, prescription rates before and during the COVID-19 pandemic were more or less equal for the age groups between 18 and 57 years old for both male and female subjects.

For these two psychoactive drug types, we saw an increase in our COVID-19 pandemic time in age groups 58 and older for both genders, but the least pronounced in the age group 58-67 in females.
To summarize these findings: in general, the highest increase in prescription rates of psychoactive drugs was seen in the middle-aged and older population, for both genders and for all selected medication types, except for antipsychotics in males.
Compared to the literature, most articles supported this observation. However, there were a few exceptions. De Oliveira et al (2022) reported an increase in prevalence and incidence for antidepressants, inversely proportionate to higher age[20]. The highest rise in incidence was observed for age group 10-17y. This was probably due to the higher impact of disruptions in daily routines and social interactions in adolescents. Levaillant et al (2021) reached a similar conclusion[25]. They noticed an increase in the prescription rate for antidepressants, anxiolytics and hypnotics for all age groups. However, the most pronounced increase was observed in age group the 12-25 years of age. Hirschritt et al (2021) observed decreased fills for hypnotics and antidepressants in older patients (>65y) compared to younger (18-44y) and middle-aged (45-64y) patients[13]. According to the authors, possible explanations could have been a less severe mental health impact, a more cautious prescribing behavior in the context of comorbidities and/or less familiarity with telemedicine.

7.3 Strengths and limitations of the study

Our study has several strengths and limitations, which we should consider while interpreting the results.
One of the strengths of this study is the combination of a literature review and a retrospective cohort study. An extensive literature review gave us extra information on psychotropic drug use worldwide. It also provides us with a baseline of comparison for our database investigation in the Flemish population.
Another strength of our literature review is the use of critical events in our history, i.e. disasters, economical recession and terrorism attacks, as a control for our further investigation about the COVID-19 pandemic.
Finally, we used data from a large primary care registry database, i.e. Intego. This provided us information on a substantial sample of the Flemish population.

However, there are also some limitations to the study.
Related to our database investigation, there were several shortcomings worth to mention.
Our first limitation concerns our data analysis. We measured absolute amounts of prescriptions for our time analysis but also for our analysis of age groups. In order to correct for our study population, we calculated prescription rates for our time analysis and gender differences. Unfortunately, with the given data (i.e. only data on total study population but not on the total amounts of the different age groups) it was impossible to calculate prescription rates for our different age groups. Therefore, these data should be interpreted with great care.
Our second limitation involves our study design. In our database investigation, we could only measure absolute amounts of prescriptions and prescription rates. Therefore, we did not have any information on incidence rates. This limited our study because we could not take into account the influence of the COVID-19 pandemic on new psychotropic drug prescriptions for possible new patients with a (psychiatric) diagnosis.
Third, we only had information on the absolute amount of prescriptions and prescription rates, and thus no data on actual consumption and adherence by the study population. Although, Grymonpre et al (2006) showed a concordance of +/- 80% between dispensing and consumption[76].

Fourth, our database only contained information on prescriptions from the Flemish general practitioners. No data on prescription rates in hospitals, psychiatric wards and/or the private sector were available.
Furthermore, we did not manage to compute a statistical regression model. This model would have been necessary to calculate the expected prescription rates when the COVID-19 pandemic did not occur. Afterwards, we could have compared these calculated values with our prescription rates from the database. This brings us to our fifth limitation: with no regression model available and a fluctuant study population, it was impossible to conduct a statistical analysis. As a consequence, we could not present any statistical significance to our database research.
The sixth shortcoming concerns our limited information about patient characteristics. In our research, we only evaluated data on age and gender. No further information about medical history, socioeconomic status, ethnicity, residency, etc. was available, thus not investigated. Additionally, we did not have any data on the patients clinical diagnosis.
The final limitation is related to our literature review.
In the process of the article selection, we only used PUBMED and excluded other medical databases. Therefore, a possible selection bias could be present.

7.4 Future directions

Hopefully, our retrospective cohort study initiates further investigation in this epidemiologic domain. We observed some interesting findings, but as mentioned above, there are also several limitations to the study. These limitations are at the same time new challenges for the future. The comparison of our data with other time periods of critical events (disasters, terrorism, economic crisis), an even longer follow-up period after the start of the COVID-19 pandemic, an additional prospective cohort study, data analysis on incidence rates and more extensive research of patient demographics are some interesting opportunities. However, in our opinion, one of the main future goals would be the comparison between a computed regression model (linear or multivariate) based on the years before the COVID-19 pandemic and our original data. This could provide us with more details and possibly statistically significant findings about the influence of the pandemic on psychotropic drug use.

8. CONCLUSION

In this retrospective cohort study, we observed an increase in the absolute amount of prescriptions in the investigated psychotropic drugs since the onset of the COVID-19 pandemic. However, no significant differences in prescription rates were discovered compared to the two years prior to the pandemic. Sex category differences maintained stable during our full study period with overall higher prescription rates in female subjects compared to males. These observations were the most pronounced in antidepressants and Z-drugs followed by benzodiazepines and antipsychotics. Generally, age groups 58 and older showed the highest increase in absolute prescriptions for both genders and practically all selected medication types.
Furthermore, our literature review presented a high level of heterogeneity in methods and results for “critical events” as well as the COVID-19 pandemic. Therefore, it was difficult to compare these results to our retrospective cohort study.
Due to these heterogeneous findings and the limitations of the study, further investigation on the subject is necessary. Specifically, to examine the possible effect of the COVID-19 pandemic on the use of psychoactive substances.

9. CONFLICTS OF INTEREST

None.

10. FUNDING

None.

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13. PERSOONLIJKE REFLECTIE

13.1 Eric Vleeshouwers

Groepsproces en persoonlijk aandeel

Op de eerste plaats zou ik graag nog mijn beide praktijkopleiders(Dr. Nicole de Becker, Dr. Valerie Lebon) en Ben Verbeke, mede HAIO, willen bedanken voor de prettige samenwerking en steun gedurende het traject van de Masterproef. Daarnaast wil ik ook zeker onze promotor, Prof. Dr. Bert Vaes , bedanken voor de fijne samenwerking en nuttige tips tijdens het proces.

Wat betreft de Masterproef zelf is het een traject met ups en downs geweest. Ik ben van mening dat Ben en ik er tijdens de start van ons eerste jaar als HAIO enorm naar uit keken om aan de slag te gaan met deze thesis. Het vinden van een definitief onderwerp bleek echter lastiger dan gedacht. Uit onze ervaringen vanuit het stagejaar en de periode als co-assistent hebben we beide veel patiënten gezien met psychologische problematiek, die zeker ten tijde van de COVID-19 pandemie extra benadrukt zijn geweest. Dit leek ons dan ook een interessant onderwerp, echter hoe we dit concreet zouden aanpakken was nog onduidelijk. Onze voorkeur ging initieel uit naar een systematisch literatuuronderzoek, maar hier kwam al snel verandering in. Na adviezen van Prof. Dr. Vaes zijn we tot ons definitieve onderwerp gekomen: De impact van COVID-19 op het gebruik van psychoactieve substanties. Hierbij kwam er de extra mogelijkheid om een epidemiologische studie uit te voeren vanuit de Intego databank. Een interessante optie voor ons beiden.

Gedurende de eerste maanden van de MaNaMa Huisartsgeneeskunde kwam ik er persoonlijk echter achter dat het combineren van voltijds werk met het schrijven van de Masterproef zwaarder bleek dan gedacht. Hierdoor hebben we het eerste en tweede jaar van de opleiding minder werk kunnen steken in de Masterproef, waardoor we uiteindelijk het laatste jaar een inhaalslag hebben moeten maken.

Wat betreft de samenwerking binnen de masterpaper verliep dit naar mijn mening initieel vlot. Als groep zijnde zaten we op dezelfde golflengte en probeerden we er evenveel werk in te steken. Gedurende de eerste aanzet en het literatuuronderzoek zijn de taken adequaat verdeeld geweest. We hebben dan ook beiden het volledige literatuuronderzoek uitgevoerd om van daaruit samen tot een consensus te komen. Geïncludeerde artikels en twijfelgevallen werden uitvoerig besproken en overlopen, inclusie en exclusie criteria werden te samen bepaald en zelf gestelde deadlines kwamen we beiden na. Verwerking van de literatuurstudie in de systematische tabel is eveneens netjes verdeeld, waarbij we beiden de helft van de artikels hebben verwerkt.
Het protocol voor de databank studie hebben we tevens in overleg opgesteld.

Van hieruit komen we natuurlijk naar het daadwerkelijk schrijven van de masterpaper. Hier hebben we geprobeerd om een eerlijke verdeling te maken in het schrijven van de paper, die achteraf gezien toch niet helemaal overeenkwam. De inleiding hebben we gedeeltelijk te samen geschreven, de

methodologie is door mij geschreven. Resultaten werden onderverdeeld in de literatuurstudie(Ben) en de databankstudie(Eric). Achteraf bleek de analyse en extractie van de databankgegevens, de verwerking hiervan en het maken van de grafieken en tabellen toch meer werk dan gedacht. Hier zit er dan ook een kleine mismatch in ieders persoonlijke aandeel. Iets wat we op voorhand niet hadden zien aankomen. De discussie hebben we uiteindelijk samen proberen te schrijven, waarbij mijn aandeel naar mijn mening iets groter is geweest. Dit heeft Ben uiteraard kunnen compenseren door zich bezig te houden met het overzicht van de paper, correcte verwijzingen en lay-out.
Alles te samen gevat hebben we naar mijn mening een aangename en vlotte samenwerking gehad, waarbij er enige discrepantie is geweest in de werkverdeling. Een identieke werkverdeling bij een project als de Masterproef is echter bijna onmogelijk.
Afsluitend wil ik nog terugkoppelen op de samenwerking met onze promotor. Van onze kant uit had er gedurende het traject wat meer initiatief mogen komen om bepaalde zaken te overleggen. De samenwerking zelf verliep verder zeer goed, waarbij we altijd op de input van de professor konden rekenen en hij ons fantastisch heeft ondersteund.

Persoonlijke visie
Wat betreft de impact van deze studie op het werkveld zijn er een aantal interessante zaken om mee te nemen. Deze studie toont aan dat “critical events”(pandemieën, terreur, oorlog, disasters, economische crisis, …) een wezenlijke invloed hebben op het gebruik van psychoactieve geneesmiddelen. Met name vanuit de literatuurstudie zijn er enkele significante stijgingen in medicatiegebruik gezien en tevens voor een langdurige periode. Dit geeft mogelijks een onrechtstreeks verband met een toename in psychische problematiek, ten tijde van deze “critical events”, maar ook in de jaren nadien. Wat betreft de klinische praktijkvoering ben ik van mening dat wij als eerstelijns arts waakzaam en proactief moeten zijn voor mentale gezondheidsproblemen. Zowel in het algemeen, evenals tijdens deze periodes kunnen we een belangrijke spil zijn voor onze patiënt. Op de eerste plaats om de patiënt te ondersteunen, maar zeker ook om vroege symptomen op te sporen en eventueel medicatiegebruik te kunnen beperken. Een multidisciplinaire aanpak heeft immers de voorkeur.
Helaas heeft onze epidemiologische studie op heden nog geen significante verschillen kunnen aantonen in onze Vlaamse studie populatie. Uitvoerigere epidemiologische investigatie, zowel retro- als prospectief, zou in de toekomst kunnen helpen om een beter beeld te krijgen op nationaal niveau.

13.2 Ben Verbeke

Groepsproces en persoonlijk aandeel
Over het algemeen is deze paper relatief vlot verlopen. Het onderwerp hadden we samen vastgelegd met prof. dr. Matheï. Dit onderwerp leek ons wel interessant, want tijdens onze specialisatie voor huisarts zijn we allebei in aanraking gekomen met patiënten met psychologische problemen ten gevolge van de Covid pandemie. In het begin was er wat onduidelijkheid over het type studie en de verwachtingen van prof. dr. Matheï. Dit vond ik wel stresserend omdat we de deadline van de definitieve aanmelding aan het naderen waren. Uiteindelijk hadden we beslist om samen te werken met prof. dr. Vaes aan een epidemiologische studie in de Intego databank gekoppeld aan een literatuuronderzoek.
Origineel wilde ik liever een systematic review maken. De reden hiervan was dat ik al een soort systematic review had gemaakt in de master geneeskunde. Ik was hier meer vertrouwd mee. Ik dacht een review maken vlotter ging verlopen in vergelijking met een praktijkverbeterend project.

Het eerste jaar hadden we weinig vooruitgang geboekt. Na een orienterende zoektocht in de bestaande literatuur werd het duidelijk dat er weinig literatuur bestond over ons onderwerp. Dit hadden we dan opnieuw besproken met prof. dr. Vaes. Toen werd er beslist om ons onderwerp wat meer open te trekken en andere kritische events zoals economische crisis, etc. toe te voegen aan ons literatuuronderzoek. Vervolgens hadden we ons literatuuronderzoek voorlopig on hold gezet in de hoop om wat meer artikels te kunnen weerhouden op een later tijdstip.
Achteraf bekeken hadden we wat meer moeten doen in het eerste jaar. Echter, ik heb gemerkt dat de combinatie van studeren en werken nogal moeilijk was. Zeker omdat ik ook voor de eerste keer vader was geworden op het einde van 2020. Ik was wel tevreden over de samenwerking met Eric. We hadden allebei dezelfde visie over de paper. Er was open communicatie tussen ons.
Helaas hadden we dan vernomen dat prof. dr. Matheï overleden was op het einde van dit academiejaar. Dit vond ik wel jammer gezien zij de eerste aanzet heeft gegeven voor onze paper.

Het tweede jaar hadden we ons gefocust op onze literatuurstudie en de algemene opbouw van onze paper. We hadden gezocht in de Medline databank en onze artikels opgeladen op de Rayyan website. We hadden dan allebei apart alle artikels bekeken en hadden de relevante artikels geselecteerd.
Opnieuw verliep de samenwerking vlot. We voerden het werk samen uit en hadden constructief overleg. Onze methoden hadden we samen geschreven. Wederom hadden we misschien meer moeten doen. Er was nog redelijk veel werk om uit te voeren. Tijdstekort en werkdruk waren de voornaamste redenen.

Het derde jaar waren we dan een versnelling hoger geschakeld. We voelden allebei de druk om onze paper af te werken. Tot dit punt hadden we alles vrijwel samen gemaakt. Nu moesten we echter alles verdelen omdat samen schrijven niet vlot zou verlopen. Ik had mezelf meer gefocust op het literatuuronderzoek en het schrijven van deze resultaten, terwijl Eric zich meer bezig hield met het databankonderzoek. Vanaf dit punt was er ook een duidelijke imbalans te merken in ons groepswerk. Eric had relatief meer geschreven en uitgewerkt ten opzichte van mezelf. We hadden deze imbalans ook benoemd en besproken. We hadden dit dan wel proberen te corrigeren. Ik heb mij meer bezig gehouden met de verwijzingen correct weer te geven, de lay-out aan te passen/corrigeren en overzicht van de paper. Je kan het werk nooit 100% eerlijk verdelen, maar toch vond ik dit wel vervelend.
Het is misschien een zwak excuus, maar ik was ook vader geworden van twee kinderen over het hele verloop van deze paper en mijn specialisatie. Dit was op bepaalde momenten wel een uitdaging. Daarnaast is statistiek niet mijn sterkste kant. Ik ervaarde dat ik hier veel moeite mee had.

Over het algemeen ben ik tevreden over het verloop. De samenwerking met Eric is altijd vlot verlopen. We hadden van in het begin dezelfde mindset. Er waren nooit conflictsituaties. Als er problemen waren, is dit altijd besproken geweest en werd er gezocht naar een oplossing. Persoonlijk vind ik de werkverdeling aanvaardbaar. Hoewel er een imbalans was op het einde, hebben we deze proberen te corrigeren. Ik heb het gevoel dat we allebei hard hebben gewerkt aan deze paper en dat het resultaat er wel mag zijn.

Persoonlijke visie
Door deze paper te schrijven, ben ik mij meer bewust geworden van de psychologische problemen bij patiënten. Persoonlijk heb ik ook de indruk dat meer patiënten hiervoor langskomen ten opzichte van drie jaar geleden. Vooral bij ouderen en adolescenten heb ik dit gevoel. Hoewel corona grotendeels voorbij is, merk ik dat deze pandemie wel zijn gevolgen heeft gehad. Ouderen die hun partner of familie zijn verloren waardoor deze meer angst en/of depressieklachten hebben. Dit zorgt dan voor het opstarten van medicatie en een verwijzing naar de psycholoog. Daarover heb ik de indruk dat de

wachtlijsten van psychologen langer en langer geworden zijn de voorbije drie jaren. Daarnaast is het tegenwoordig een ramp om een psychiater vinden in de Kempen. Uit ons onderzoek was ook duidelijk dat dit mogelijks lange termijn gevolgen zijn waardoor deze situatie niet snel zal verbeteren.

14. APPENDIX

Supplementary 1

(((“COVID-19”[Mesh] OR COVID-19*[tiab] OR “SARS-CoV-2”[Mesh] OR SARS-CoV-2*[tiab] OR infection,-SARS-CoV-2*[tiab] OR 2019-novel-coronavirus*[tiab] OR 2019-ncov*[tiab] OR disease,-2019-ncov*[tiab] OR infection,-covid-19-virus*[tiab] OR virus-infection,-covid-19*[tiab] OR coronavirus*[tiab] OR severe-acute-respiratory-syndrome-coronavirus*[tiab] OR sars-coronavirus-2*[tiab] OR disease,-covid-19-virus*[tiab] OR virus-disease,-covid-19*[tiab] OR infection,-2019-ncov*[tiab] OR covid19*[tiab] OR pandemic,-covid*[tiab] OR coronavirus-2,-SARS*[tiab] OR coronavirus,-2019-novel*[tiab] OR novel-coronavirus*[tiab] OR wuhan-seafood-market-pneumonia-virus*[tiab] OR virus,-SARS-cov-2*[tiab] OR virus,-covid*[tiab] OR wuhan-coronavirus*[tiab]) OR (“Pandemics”[Mesh] OR pandemic*[tiab] OR “Emergencies”[Mesh] OR emergenc*[tiab] OR “Economic Recession”[Mesh] OR economic-recession*[tiab] OR recession,-economic[tiab] OR recessions,-economic[tiab] OR economic-depression*[tiab] OR depression,-economic[tiab] OR depressions,-economic[tiab] OR “Disasters”[Mesh] OR disaster*[tiab] OR “Natural Disasters”[Mesh] OR natural-disaster*[tiab] OR disaster,-natural[tiab] OR disasters,-natural[tiab] OR “Terrorism”[Mesh] OR terrorism[tiab] OR radioactive-terrorism[tiab] OR terrorism,-radioactive[tiab] OR “Mass Casualty Incidents”[Mesh] OR mass-casualty-incident*[tiab] OR casualty-incident,-mass[tiab] OR casualty-incidents,-mass[tiab] OR incident,-mass-casualty[tiab] OR incidents,-mass-casualty[tiab] OR mass-casualt*[tiab] OR casualty,-mass[tiab] OR casualties,-mass[tiab] OR “September 11 Terrorist Attacks”[Mesh] OR september-11-terrorist-attack*[tiab] OR 9-11-2001-attack*[tiab] OR attack,-9-11-2001[tiab] OR attacks,-9-11-2001[tiab] OR world-trade-center-attack,-2001[tiab] OR “Armed Conflicts”[Mesh] OR armed-conflict*[tiab] OR war[tiab] OR conflict,-armed[tiab] OR conflicts,-armed[tiab])) AND (“Psychotropic Drugs”[Mesh] OR psychotropic-drug*[tiab] OR “Antidepressive Agents”[Mesh] OR antidepressive-agent*[tiab] OR “Benzodiazepines”[Mesh] OR benzodiazepine*[tiab] OR drug,-psychotropic[tiab] OR drugs,-psychotropic[tiab] OR psychoactive-agent*[tiab] OR agent,-psychoactive[tiab] OR OR agents,-psychoactive[tiab] OR psychopharmaceutical*[tiab] OR antidepressant-drug*[tiab] OR drug,-antidepressant[tiab] OR drugs,-antidepressant[tiab] OR antidepressant*[tiab] OR medication,-antidepressant[tiab] OR agent,-antidepressive[tiab] OR thymoanaleptic*[tiab] OR thymoleptic*[tiab] OR “Drug Prescriptions”[Mesh] OR drug-prescri*[tiab] OR prescribing,-drug[tiab] OR prescribings,-drug[tiab]))

Supplementary 1. Definitive search strategy Pubmed

Supplementary table 2. Covid 19 related articles

Article	Author(Year)	Study Type	Methods	Study Population	Medication Type	Outcome variables	Limitations
COVID-19 lockdown impact on mental health in a large representative sample of Italian adults	Amerio A. et al (06-2021)	Cross-sectional study	Self- administered online questionnaire Reported usage 4 weeks prior to the COVID-19 lockdown versus in the last 4 weeks prior to the questionnaire	6003 Italian adults aged 18-74 years recruited from 27-04-2020 to 03-05-2020	Benzodiazepines/Anxiolytics, Mood Stabilizers, Antidepressants, Hypnotics	Use of at least one psychotropic drug increased by 20% compared to pre-lockdown BZP 32% increase MS 20% increase AD 14% increase Hypnotics 8% increase	• Cross sectional study design • Selection bias • Information bias • No clinical evaluation
Antidepressant Drug Use during COVID-19 Waves in the Tuscan General Population: An Interrupted Time-Series Analysis	Antonazzo I.C. et al (01-2022)	Population-based study Observational retrospective study	Prevalence and incidence on a weekly basis: pre-lockdown(01-01-2018 to 08-03-2020); first lockdown(09-03-2020 to 15-06-2021); post first lockdown(16-06-2020 to 15-11-2020) and second lockdown(16-11-2020 to 27-12-2020)	+/- 3 500 000 people based on healthcare administrative database of Tuscany Dynamic cohort with at least one AD dispensing from 01-01-2018 to 27-12-2020	Antidepressants	Reduction of AD incidence and a slight weekly decrease of prevalence during the first lockdown Increase in AD incidence after the first lockdown(rebound effect?)	• Only AD fully reimbursed but not anxiolytics • No information on indications • Only six datapoints on second lockdown, cautious with results Not able to ensure a causal correlation between COVID-19 waves and studied outcomes
Comparison of Medication Prescribing Before and After the COVID-19 Pandemic Among Nursing Home Residents in Ontario, Canada	Campitelli M. et al (06-2021)	Population-based cohort study with an interrupted time-series analysis	Prescription rate analysis with comparison between observed and projected use Weekly observation from 05/05/2017 till 26/09/2020	630 nursing homes in Ontario, Canada. 75 850 to 76 549 residents	Antipsychotics, benzodiazepines, antidepressants, anticonvulsants, opioids, antibiotics, angiotensin receptor blockers (ARBs), and angiotensin-converting enzyme (ACE) inhibitors.	Increase in weekly dispensation of antipsychotics, antidepressants, benzodiazepines, opoids and anticonvulsants. No increase observed for ARBs, antibiotics and ACE inhibitors.	• Limited timeframe (Mar 2019 till sept 2020) • No indications for prescriptions

Effects of the COVID-19 pandemic on primary care-recorded mental illness and self-harm episodes in the UK: a population-based cohort study	Carr M.J. et al (01-2021)	Population based cohort study	Prescription rate analysis using the UK Clinical Practice Research Datalink Based on Incidence rates and compared to the expected values based on previous data, i.e. 01-01-2010 to 29-02-2020.	14210507 patients from 1697 UK general practices between 01-01-2010 and 10-09-2020.	Antidepressants, Benzodiazepines	First Antidepressant prescribing decreased by 36.4% from 01-04-2020 until 01-05-2020	• Insufficient information about ethnicity • No information on mental health referrals • Population bias • Inaccuracies in coding in the EMD No data on indication for the prescription
Prescription fill patterns for benzodiazepine and opioid drugs during the COVID-19 pandemic in the United States	De Dios C. et al (11-2021)	Retrospective study	Prescription rate analysis Weekly comparison in pandemic period (27/01 till 24/05/2020) and pre-pandemic period (28/01 till 26/05/2019)	Database of prescription monitoring in 38 states and the military health system	Benzodiazepines and opoids	2% increase in benzodiazepines	• Comparison with controlled substances
Changes in antidepressant use in Australia: A nationwide analysis(2015-2021)	De Oliveira Costa J. et al (02-2022)	Retrospective cohort study	Prescription rate analysis Based on annual prevalence and incidence comparing two time periods: 2015-2019 versus 03-2020 until 02-2021(COVID-19 period) using time series analysis to quantify changes	Two national PBS(Pharmaceutil Benefits Scheme) dispensing datasets Using PBS10% - i.e. a random 10% of the databases in which patients needed to be >10 years of age	Antidepressants	Higher overall prevalence in AD dispensing in the first year of COVID-19 No significant overall change in incidence rates in the first year of COVID-19 Among adolescent(10-17y) females there is a significant increase in prevalence and incidence	• No clinical data on prescriptions • No information on private and inpatient prescriptions • Limited insight into the course of treatment at an individual rather than population level • Data only generalizable to other countries where the circulation rate of COVID-19 was low

Consumption and ocurrence of antidepressants (SSRIs) in pre- and post-COVID-19 pandemic, their environmental impact and innovative removal methods: A review.	Diaz-Camal et al (07-2022)	Review	/	/	/	/	/
Prescription of anxiolytics, sedatives, hypnotics and antidepressants in outpatient, universal care during the COVID-19 pandemic in Portugal: a nationwide, interrupted time-series approach.	Estrela M et al (04-2022)	Interrupted time-series analysis	Prescription rate analysis Monthly prescription rate between 01/2018 till 03/2021	NHS monitoring prescriptions in Portugal	Antidepressants, anxiolytics and hypnotics/sedatives	Anxiolytics, sedatives and hypnotics: initial reduction at the start followed by an increasing trend over the time period Antidepressants: Decreasing trend	• No data on private practices
Psychotropic medications sales during COVID-19 outbreak in Italy changed according to the pandemic phases and related lockdowns	Farina B. et al. (10-2021)	Retrospective and observational study	Prescription rate analysis Comparison of 3 lockdown periods (T1: 03 till 05/2020, T2: 06 till 09/2020 and T3: 10/2020 till 02/2021) to the same time periods in the previous year	5 pharmacies in Rome – approximately 150000 patients	Benzodiazepines, Mood stabilizers, SSRI's	T1: decrease BZP, MS, SSRI. T2: Increase BZP, MS, SSRI sales. T3: Increase MS, SSRI, decrease BZP	• Small sample population • Strong relation prescription and consumption, but not one on one. • Only 3 classes of psychotropic medication • Only medication rate sales
Psychotropic Drug Prescription in Nursing Homes During	Ferro Uriguen T. et al (06-2022)	Cross-sectional study	Prescription rate analysis	511 residents in geriatric units (GU) and 163 residents in	Antidepressant, benzodiazepines, antipsychotics and antiepileptics	GU: antipsychotics stable (−0.41, 95% CI −1.41, −0.60; p = 0.416)	Increased death due to covid reduce the total participants could lead to changed

the COVID-19 Pandemic.			Comparison between pre-pandemic period (04/2018 till 03/2020) and pandemic period (04/2020 till 03/2021)	psychogeriatric units (PSU) in seven nursing homes in Gipuzkoa, Spain.		Benzodiazepines decrease (−2.00; 95% CI −3.00, −1.00; $p < 0.001$) Antidepressants stable (0.02; 95% CI −0.97, 1.01; $p = 0.962$) Antiepileptics increase (2.93; 95% CI 2.27, 3.60; $p < 0.001$) PSU: antipsychotics decrease (−2.31; 95% CI −3.63, − 0.93; $p < 0.001$) Benzodiazepines stable (−0.28; 95% CI −2.40, 2.34; $p = 0.981$) Antidepressants increase (8.57; 95% CI 6.89, 10.24; $p < 0.001$) Antiepileptics increase (6.10; 95% CI 3.20, 9.00; $p < 0.001$)	sociosanitary variables in these residents
Increased incident rates of antidepressants use during the COVID-19 pandemic: interrupted time-series analysis of a nationally representative sample	Frangou S. et al (06-2022)	Interrupted time series analysis (Retrospective)	Prescription rate analysis Based on incidence rates per month from 01-01-2013 until 01-02-2021 and compared to a counterfactual to distinguish between rates during COVID-19 and expected rates without COVID-19	852233 patients from the EMD of the Israeli population	Antidepressants	Significant increase in the slope of incidence rates of antidepressant fills and a 2% increase compared to the counterfactual	• No link between prescription and diagnosis • No info on severity of mental health problems • Potentially missed diagnosis during consultation • No control group • Residual confounding
Analysis of primary care prescription trends in England during the COVID-19 pandemic compared against a predictive model.	Frazer J. et al (08-2021)	Retrospective study	Prescription rate analysis Comparison between pre-pandemic period (01/2014 till 10/2019) and pandemic period (11/2019 till 11/2020)	All residents of England who received a prescription from primary care facilities in 2014-2020.	1654 individual drugs including benzodiazepines	Increase in lorazepam, other benzodiazepines unchanged	• Too many drugs • No patient information or medication indication

Consumption of Psychiatric Drugs in Primary Care during the COVID-19 Pandemic.	González-López M. et al (04-2022)	Cross-sectional observational study	Prescription rate analysis Comparison between pre-pandemic period (03/2019 till 02/2020) and pandemic period (03/2020 till 02/2021)	Primary Health District of Almeria, in the country of Spain, with a population of 304,182 inhabitants	Antidepressants, anxiolytics and sedatives/hypnotics	6.1% increase in all psychiatric drugs with most effect in anxiolytics subgroup	• Prescriptions from private practices not included
Psychotropic medication prescribing during the COVID-19 pandemic	Hirschtritt M. et al (10-2021)	Cohort study Retrospective study	Prescription rate analysis Comparison between pandemic period (03/12/2019 till 02/06/2020) and pre-pandemic period (04/12/2018 till 02/06/2019)	2,405,824 patients	Antidepressants, benzodiazepines, non-benzodiazepine hypnotics, trazodone, mood stabilizers, antipsychotics and stimulants. Statins as a non-psychotropic comparator.	Increased fills for trazodone (RRR = 1.03, 95% CI = 1.02, 1.04) Decreased fills for benzodiazepines (RRR = 0.95, 95% CI = 0.94, 0.96) and hypnotics (RRR = 0.97, 95% CI = 0.96, 0.99) Stable fills for antidepressants (RRR = 1.00, 95% CI = 0.99, 1.00) Slightly increased fills for mood stabilizers and antipsychotics (RRR = 1.01, 95% CI = 1.00, 1.02) Stable fills for stimulants (RRR = 1.02, 95% CI = 0.98, 1.06) Slightly increased fills for statins (RRR = 1.01, 95% CI = 1.00, 1.01)	• Limited timeframe (13 weeks prior compared to first 13 weeks)
Comparing actual and forecasted numbers of unique patients dispensed select medications for opioid use disorder, opioid over	Jones C. et al (02-2021)	Retrospective study	Prescription rate analysis Monthly dispensation from 01/2019 till 05/2020	IQVIA Total Patient Tracker database, which captures 92 % of prescriptions dispensed from	Antidepressants and benzodiazepines Statins and ARB for comparison	Increase in dispensed antidepressants and benzodiazepines in 03/2020 above forecasted estimates Control medication following similar patterns	• Limited time frame (March till May 2020) • No individual health information

dose reversal, and mental health, during the COVID-19 pandemic, United States, January 2019 to May 2020.				U.S. retail pharmacies			
The impact of COVID-19 on antipsychotic prescriptions for patients with schizophrenia in Australia	Kisely S. et al (2022)	Retrospective database study	Prescription rate analysis Primary: volumes of new antipsychotic prescriptions that required a medical consultation and were dispensed between 01-04 and 31-05 for the years 2016-2019 compared to 2020. Secondary: Same as primary but for new and repeat prescriptions	10% random sample of the full database All patients age >18 years with 3 or more supplies of antipsychotics for the treatment of schizophrenia between 01-06-2015 and 31-05-2020	Antipsychotics	Primary: reduction of 5.7% Secondary: reduction of 3.5%	• Possibility not only prescribed for patients with schizophrenia • No data on usage • No data on long-term effects • Low level of COVID-19 infections in Australia compared to the rest of the world
Effects of the COVID-19 pandemic on clinically diagnosed psychiatric disorders in persons with type 2 diabetes.	Kowall B. et al (08-2022)	Retrospective study	Prescription rate analysis Quarterly new psychotropic drugs prescriptions	95,765 persons with type 2 diabetes in 2018 or earlier, at least one visit to a physician practice in 2019 or 2020 with no diagnosis of anxiety, depression or stress disorder by 2018	Antidepressants and hypnotics	Reduced prescription rate in all quarters of 2020 and first quarter of 2021	• Incomplete data • No comparison to control group without diabetes

Impact of COVID-19 Pandemic on the Use of Antidepressant and Antianxiety Pharmaceuticals as Well as Sick Leave in Poland.	Krupa D.et al (02-2022)	Retrospective study	Prescription rate analysis Monthly prescription rate from 01/2018 till 10/2021	National-level database containing information on all products purchased in community pharmacies across Poland	SSRI, SNRI, other antidepressants and Buspirone	Linear increase in psychoactive drugs consumption with a peak around March 2020	• Limited time frame
Analysis of Drug and Health Resource Use Before and After COVID-19 Lockdown in a Population Undergoing Treatment for Depression or Anxiety	Lear-Claveria A. et al (04-2022)	Observational study	Prescription rate analysis Based on DDD 6 months prior to lockdown(14-09-2019 to 15-03-2020) compared to the 6 months following its end(03-05-2020 to 04-11-2020)	110694 patients aged >16y suffering from active or undergoing treatment for depression or anxiety	Antidepressants, Anxiolytics, Sedatives/hypnotics	Increase in anxiolytic drug use Decrease in antidepressant drug use	• Database study, no clinical information • Population bias • Duration of the study •
Psychotropic Medication Use Before and During COVID-19: A Population-Wide study	Leong C. et al (04-2022)	Longitudinal observational study	Prescription rate analysis Based on quarterly incidence rates and prevalence using data from Manitoba Population Research Data Repository from 01-01-2015 until 31-12-2020. Due to public health restrictions from 03-2020 a indicator	Ranged between 1331188 patients in 2015 to 1394885 patients in 2020 in Manitoba Canada (Center of Health)	Antidepressants, Antipsychotics, Anxiolytics/sedative-hypnotics	Decrease in incidence for AD and anxiolytics 3 months after covid restrictions Increase in the 4th quarter of 2020 in incidence in AD and AP in females, people age >40y and the highest in the >80y	

			variable was used to determine if there was a significant difference.				
Impact of COVID-19 pandemic lockdowns on the consumption of anxiolytics, hypnotics and antidepressants according to age groups: a French nationwide study	Levaillant M. et al (11-2021)	Retrospective Cohort study	Prescription rate analysis Based on the French health insurance database between 01-01-2015 and 28-02-2021 Measurement of reimbursed prescriptions per week and ratio between average number of new drug consumers per week over the total number of drug consumers	+/- 65 000 000 inhabitants of France Divided into 5 age classes, i.e. 12-18y, 19-25y, 26-50y, 51-75y, >75y.	Anxiolytics, Hypnotics or Sedatives, Antidepressants	Increase in all 3 medication groups for all age classes since onset of COVID-19 restrictive policies	• Non optimal statistical model • Lack of confounders • Medication groups may mask trends in individual groups • No information on consumption • No information on diagnosis •
Long-acting injectable antipsychotic (LAI) prescribing tren ds during COVID-19 restrictions in Canada: a retrospective observational study.	McKee K. et al (12-2021)	Retrospective observational study	Prescription rate analysis Monthly comparison between specific time periods: pre-pandemic (03-05/2019), covid awareness (12/2019 till 02/2020), primary covid escalation (03 till 05/2020), covid maintenance (06 till 08/2020) and second covid escalation (09 till 11/2020)	72% of national pharmacy prescriptions in Canada	Second-generation long-acting injectable antipsychotics	The proportion of discontinuations and new starts were not significantly different over any of the epochs examined Increase in three-month injectabels	

Trends in the Use of Benzodiazepines, Z-Hypnotics, and Serotonergic Drugs Among US Women and Men Before and During the COVID-19 Pandemic	Milani S.A. et al (10-2021)	Cohort study	Prescription rate analysis - Changes in prescription rates during Covid-19(2020 – 2021) compared to prior period(2018 – 2019) in men and women	Records of commercial health insurance database of adult patient(18+) 2018 – 17255033 pt 2019 – 17340731 pt 2020 – 16916910 pt 2021 – 15135998 pt	Benzodiazepines, Z-hypnotics, SSRI's, SNRI's	Increase in Z-hypnotics, SSRI, SNRI prescriptions in both male and female. Increase in benzodiazepine prescriptions in females.	• Study population not representative for US population(commercial insurance programs) • Prescription rate, not representative for use and treatment adherence • No information about race, ethnicity, socioeconomic status • Only individuals with private insurance
COVID-19 Lockdown Effect on Not Institutionalized Patients with Dementia and Caregivers	Moretti R. et al (07-2021)	Longitudinal study	General behavior assessment and prescription rate analysis From 10-03-2020 until 18-07-2020 with three peakpoints: start of the lockdown, end of the lockdown(i.e 18-05-2020) and two months afterwards	221 patients with subcortical vascular dementia, not institutionalized divided into 2 groups(low/medium and severe group)	Benzodiazepines, Antipsychotics	Increase of BZP and AP prescriptions during lockdown period, followed by a slight decrease afterwards	• Limited number of patients • Based on video-calls
Impact of the COVID-19 pandemic on remote mental healthcare and prescribing in psychiatry: an electronic health record study	Patel R. et al (02-2021)	Retrospective databank analysis(cohort ?)	Mentions of Antipsychotics and Mood Stabilisers within the EHR From 07-01-2019 till 20-09-2020	Electronic Health Record from SlaM NHS foundation trust(secondary mental health care) 37563 patients	Antipsychotics, Mood Stabilisers	No significant difference in prescribing rates of Antipsychotics and Mood Stabilisers	• Mentions not necessarily equals prescription rates, dispensed prescriptions or usage • Secondary mental health care records. No information about prescriptions in first line(GP)

Increased antidepressant use during the COVID-19 pandemic: Findings from the Friuli Venezia Giulia region, Italy, 2015-2020	Pazzagli L. et al (09-2022)	Population based study	Prescription rate analysis Based on DDD per 1000 inhabitants per day comparing two time periods: 2015-2019 followed by a linear trend model to predict AD use in 2020 versus actual DDD in 2020	75725552 DDDs over 2015-2019, 17766301 DDDs in 2020 Data from the Social and Health Informations System of Friuli Venezia Giulia region	Antidepressants	Average increase of 20% in each month of 2020 compared to 2015-2019, with even more then 30% in the first four and last two months of 2020 More particular in men and in age group 30-59y	• No information on diagnosis • No data on the individual level • Only data from GP, psychiatrist and other public physicians • No assessment of adherence • No information on socio-economic status •
Surging trends in prescriptions and costs of antidepressants in England amid COVID-19	Rabeesa S. et al (06-2021)	Retrospective study	Prescription rate analysis and economic impact Comparison of pandemic period (01 till 08/2020) to non-pandemic period (2016 till 2019)	England	Antidepressants with subgroups	Overall prescription rate was elevated with peak in March 2020	• Limited timeframe (jan till aug 2020) • Overall prescription rate without subgroups • No patient characteristics • Poor and limited analysis
Trends in the Use of Anxiolytics in Castile and Leon, Spain, between 2015-2020: Evaluating the Impact of COVID-19.	Sanchez Diaz M. et al (06-2021)	Retrospective study	Prescription rate analysis Monthly prescription rate from 2015 till 2020	Pharmacies in Castile and Leon, Spain, from 2015 to 2020	Anxiolytics	14,41% increase in anxiolytics in time period with 6,63% increase in 2020 compared to 2019 Elevation of benzodiazepines in 2020 compared to previous 5 years with significant elevation in March 2020 No correlation between new covid cases and anxiolytics consumption	• No correlation between number of Covid cases and consumption of anxiolytics • Limited time frame (until December 2020)

Benzodiazepine misuse: An Epidemic within a Pandemic	Sarangi A. et al (06-2021)	Review	/	/	/	/	/
The course of neuropsychiatric symptoms and psychotropic drug use in Dutch nursing home patients with dementia during the first wave of COVID-19: A longitudinal cohort study	Sizoo E.M. et al (02-2022)	Longitudinal cohort study	Prescription rate analysis Data from the electronic health record: retrospectively for 02/03/04-2020 and prospectively for 05/06/07/08-2020 Neuropsychiatric symptom measured by NPI-Q scores	252 residents with dementia in 19 Dutch nursing homes	Antipsychotics, Antidepressants, Benzodiazepines, Anti-dementia drugs	No significant change in prescription drug use	• No NPI-Q scores from before the lockdown • NPI-Q cannot distinguish clinically relevant symptoms • Doctor and nurses more aware of symptoms(Hawthorne effect) • Not possible to analyze different effects of particular restrictions
Assessment of Psychotropic Drug Prescribing Among Nursing Home Residents in Ontario, Canada, During the COVID-19 Pandemic	Stall N.M. et al (06-2021)	Cross-sectional study	Prescription rate analysis Monthly proportion of residents who were prescribed psychotropic drugs as a proportion of the monthly number of residents receiving a prescription of any drug(controls statins and metformin) Interval: March to September 2020 compared to January and February 2020	77291 residents in 623 licensed nursing homes	Antipsychotics, Antidepressants, SNRIs, benzodiazepines and trazodone	Absolute increase in mean monthly proportion of nursing home residents receiving antipsychotics, antidepressants and trazodone. No significant difference in benzodiazepine prescriptions	• Lack of data on prescribing indications •
Effects of COVID-19 pandemic on anxiety and depression in	Stephenson E. et al (02-2022)	Retrospective cohort study	Prescription rate analysis based on incidence rates.	322920 patients from electronic medical records	Antidepressants	Early pandemic phase(March – June 2020): Incidence rates were lower than expected	• Small time window, no data on third wave and further)

primary care: A retrospective cohort study			Timeline: precovid(01-2018 until 02-2020) versus covid (03-2020 until 12-2020), where precovid period will be baseline	from the University of Toronto(UTOPIAN physicians)		Late pandemic phase(July – December 2020): No significant change in prescribing trends compared to baseline	• Incidence only, no data on patients with preexisting mental illness • Only based on EMD from UTOPIAN physicians
The effects of COVID-19 on the dispensing rates of antidepressants and benzodiazepines in Canada.	Uthayakumar S. et al (02-2022)	Population-based, cross-sectional time-series analysis	Prescription rate analysis Monthly prescription rate between 01/2017 and 12/2020	Canadian community pharmacies between January 2017 and December 2020	Antidepressants and benzodiazepines	Temporary decrease in antidepressants rate in April 2020 due to lockdown. No overall change compared to before covid. No significant change in benzodiazepines rate.	• Limited time frame (till december 2020)
Impact of the COVID-19 Pandemic on the General Mental Health in Sweden: No Observed Changes in the Dispensed Amount of Common Psychotropic Medications in the Region of Scania	Wolfschlag M. et al (12-2021)		Prescription rate analysis, interrupted time series analysis Based on DDD per month From 01-01-2018 to 01-2021, with 03-2020 as a reference point for COVID-19	+/-1 380 000 people in the region of Scania	Antidepressants, Benzodiazepine related drugs, Psychostimulants, other hypnotics and sedatives, Anxiolytic benzodiazepines, mood stabilizers	No general trend changes were observed	• Different epidemical approach compared to other countries • Late onset of infection rates in the region of Scania
Dispensing patterns of mental health medications before and during the COVID-19 pandemic in Alberta, Canada: an interrupted time series analysis	Ying L.T.L et al (05-2022)	Interrupted time series analysis	Dispensing rate analysis Based on Dispensing data/Dispensing slope from Alberta Health's Pharmaceutical Information Network 13 months before versus 13 months after the first case of COVID-19 in Alberta	Not further specified	Antidepressants, Antipsychotics, Benzodiazepines/Anxiolytics, Mood Stabilizers, Stimulants	Significant increase in dispensing rate for: Amytriptyline, Escitalopram, Fluoxetine, Paroxetine, Bupropion, Desvenlafaxine, Venlafaxine and Oxazepam.	• No info on in-hospital dispensing rates • Dispensing rates are not equivalent to medication consumption rates • Not able to determine the origin of prescription • Only data on first and second COVID-19 wave • No clinical information on diagnosis

The impact of COVID-19 on benzodiazepine usage in psychiatric inpatient units.	Zaki N. et al (06-2022)	Retrospective study	Prescription rate analysis Monthly prescription rate from 01/2019 till 12/2020	Two 33-bed acute adult psychiatric units in a major psychiatric hospital in Sydney, Australia.	Benzodiazepines: diazepam, lorazepam and midazolam Atorvastatin as control	38% increase in benzodiazepine consumption Decrease in atorvastatin	• Only 1 class of medication and within this class, only 3 different medications • Limited time frame (till December 2020) • Limited population
Mental Health Treatment and the Role of Tele-Mental Health at the Veterans Health Administration During the COVID-19 Pandemic	Zhang J. et al (04-2021)	Longitudinal observational study	Prescription rate analysis Weekly prescription fills, number of patients with new prescription fills on-hand, patients with new prescription fills Percent change between the expected and actual deliveries from 18-03-2020 until 05-05-2020	Approximately 1800000 veterans receiving health treatment at a VHA facility located in the contiguous United States.	Antidepressants, Antipsychotics, Benzodiazepines, Opioids, Mood Stabilizers	Weekly prescription fills: - AD 2% increase - AP 2% increase - MS 2% increase - Opioid 4% decline - BZP 4% increase Prescription fills on hand: - AD 2% decline - AP 1% decline - MS 3% decline - Opioid 1% decline - BZP 2% increase New patient prescribing: - AD 27% decline - AP 21% decline - MS 26% decline - Opioid 50% decline - BZP 33% decline	• Study population not representative for general population

Supplementary table 3. Terrorism related articles

Article	Author(Year)	Study Type	Methods	Study Population	Medication Type	Outcome variables	Limitations
Changes in benzodiazepine use in the French general population after November 2015 terrorist attacks in Paris: an interrupted time series analysis of the national CONSTANCES cohort	Gouraud C. et al (08-2021)	Interrupted time series analysis	Prescription rate analysis Based on weekly number of individuals with a benzodiazepine delivered prescription(BDP) and weekly number of defined daily dose(DDD)	90258 patients included in the population based CONSTANCES cohort from 2012-2017, age 18-69 years.	Benzodiazepines	Benzodiazepine use was elevated weekly number of individuals with a benzodiazepine delivered prescription(BDP) and also elevated by weekly number of defined daily dose(DDD)	• Participants may not be representative for the general population • Based on prescription and not on usage • No data on over the counter consumption • Results are from exploratory analyses • No examination of individual usage
Mental Health Service and Medication Use in New York After the September 11, 2001, Terrorist Attack	Boscarina J.A. et al (03-2004)	Survey study	Telephone survey using random digits Standardized Questionnaire interviewing the use of mental health services and psychotropic medication usage in New York City 1 month before and 4-5 months after the 9/11 attacks	2001 responders, English or Spanish speaking and age >17 years	Psychotropic medication usage – not further specified	A slight increase in psychotropic medication usage: 6.8% in the month before versus 7.7% 4 to 5 months after the 9/11 attacks	• Heightened state of alert after the attacks, which may affect usage • Self-reported data • Sample selection bias • Short time frame
Psychiatric Medication Use Among Manhattan Residents Following the World Trade Center Disaster	Boscarina J.A. et al (06-2003)	Survey study	Telephone survey sing random digits Standardized Questionnaire interviewing the use of psychotropic medication	1008 responders, English or Spanish speaking and age >17 years	Psychotropic medication usage – not further specified	92% of the responders used psychotropic medication before and after the 9/11 attacks 3.3% used psychotropic medication only 30 days after the 9/11 attacks	• Heightened state of alert after the attacks, which may affect usage • Self-reported data • Sample selection bias • Short time frame

			30 days before and 30 days after the 9/11 attacks			New users tended to be those with panic attacks(44.1%) and/or PTSD(69.2%)	
PTSD, Depression, Prescription Drug Use, and Health Care Utilizitation of Chinese Workers Affected by the WTC Attacks	de Bocanegra H. et al (07-2006)	Survey study	Interviews conducted in march 2003 Semistructured interviews with two scales to measure PTSD(PTSD checklist) and depression(Beck Depression Scale), demographics, mental health service utilization and prescription drug use	148 chinese workers who lost their jobs due to the WTC attacks and had received 9/11 emergency service from Safe Horizon	Non specific	60% said they received a prescription from their GP	• Survey study • No information on actual prescription rates • Small study population • Not representative for general population •
Use of psychotropic medi cations before and after Sept. 11, 2001.	Druss B. et al (08-2004)	Retrospective study	Presription rate analysis Comparison of pre-disaster period (09 till 12/2000) to post-disaster period (09 till 12/2001)	USA nationally and also specifically New York City and Washington DC	Antidepressants, antipsychotics, anxiolytics and hypnotics	No effect on total or new prescriptions Nationally/Washington DC: Small significant decline in dose increase overall Dose increase for patients already on anipsychotics New York: Overall increase in dose increase, specifically for antidepressants	• Limited time frame (12 weeks before and after) • No patient characteristics

Supplementary table 4. Economical crisis related articles

Article	Author(Year)	Study Type	Methods	Study Population	Medication Type	Outcome variables	Limitations
Did psychotropic drug consumption increase during the 2008 financial crisis? A cross-sectional population-based study in Spain	Arroyo E. et al (11-2018)	Cross-sectional population based study	Survey/Questionnaires Comparing psychotropic drug use before financial crisis(2006-2007) versus during financial crisis(2011-2012)	Individuals >15 years, i.e.: 2006-2007: 28954 patients 2011-2012: 20509 patients	Antidepressant and Sedatives	No significant change in the probability of taking antidepressants or sedatives(based on OR) Quid: differences between specific groups(cfr. Full article)	• Cross sectional data, which does not conclude direct relationships between the financial crisis and psychotropic drugs use. • Reporting bias • Reluctance to respond to sensitive questions in interviews
Effects of the financial crisis in psychotropic drug consumption in a cohort from a Semi-urban region in catalonia, Spain	Barcelo M.A. et al (02-2016)	Retrospective cohort study	Prescription rate analysis - number of drugs prescribed per individual per month AND DDD per individual per month Comparison between pre(2005-2008) and during/post(2009-2012) economic recession	Records of "basic area of health(ABS)" in Catalonia aged 15 years and older 42267 patients	Anxiolytics, Antidepressants	Increase in consumption of psychotropic drug use, significantly higher increase in patients who already where using psychotropic drugs. Increase of greater significance in number of drugs being taken, than by DDD, with peak in 2011. Increase occurred in those most likely to be unemployed	• No direct measure of the socio-economic status • Not able to measure exposure of the crisis on the individual level • No family level information • No information on suicides, self-harm, violence
A data linkage study of the effects of the Great Recession and austerity on antidepressant pr escription usage.	Cherrie M. et al (04-2021)	Individual level longitudinal study	Prescription rate analysis	Sample (n=86500) of Scottisch Longitudinal study	Antidepressants	Living in a region characterized by low and declining FT employment following the Great Recession was associated with increased likelihood of antidepressant use.	• No data on diagnosis of depression (overshooting)

Psychotropic Drug Consumption and Employment Status in Time of Economic Crisis(2007-2011)	Cornaggia C.M. et al (07-2016)	Case-Control study	Prescription rate analysis Based on incidence rates, likelihood and probability to receive a prescription based on propensity score matching model	Information from regional database Cases: people with a permanent contract on 01-01-2008 but terminated between 2008-2010, who did not find a new job within 12 months, and not previously described psychotropic drugs(n=208061) Controls: cfr. Cases but without losing their jobs(n=547985)	Antidepressants, Antipsychotics, Mood stabilizers	• Similar incidence rates • Case 17% more likely to receive one or more drug prescriptions then control group, but only significant for male subjects	• No information on drug consumption • Not only psychiatric indications for the medicine • No data on psychiatric history of the patient • No data on self-employed individuals, i.e. population bias
Association between unemployment rates and prescription drug utilization in the United States, 2007-2010	Kozman D. et al (11-2012)	Retrospective mixed ecological design	Prescription Rate analysis Based on database of pharmaceutical retail Drug utilization per 100000 people from 07-2007 until 07-2010 for new and refilled prescriptions	Not specified	Antidepressants, Antipsychotics	No statistically associations between unemployment and SSRI/SNRI use Inverse relationship with unemployment for atypical antipsychotics(i.e. decrease)	• ecological analysis preclude an analysis of important patient, provider and health system characteristics • No data on usage • No information on all drug classes

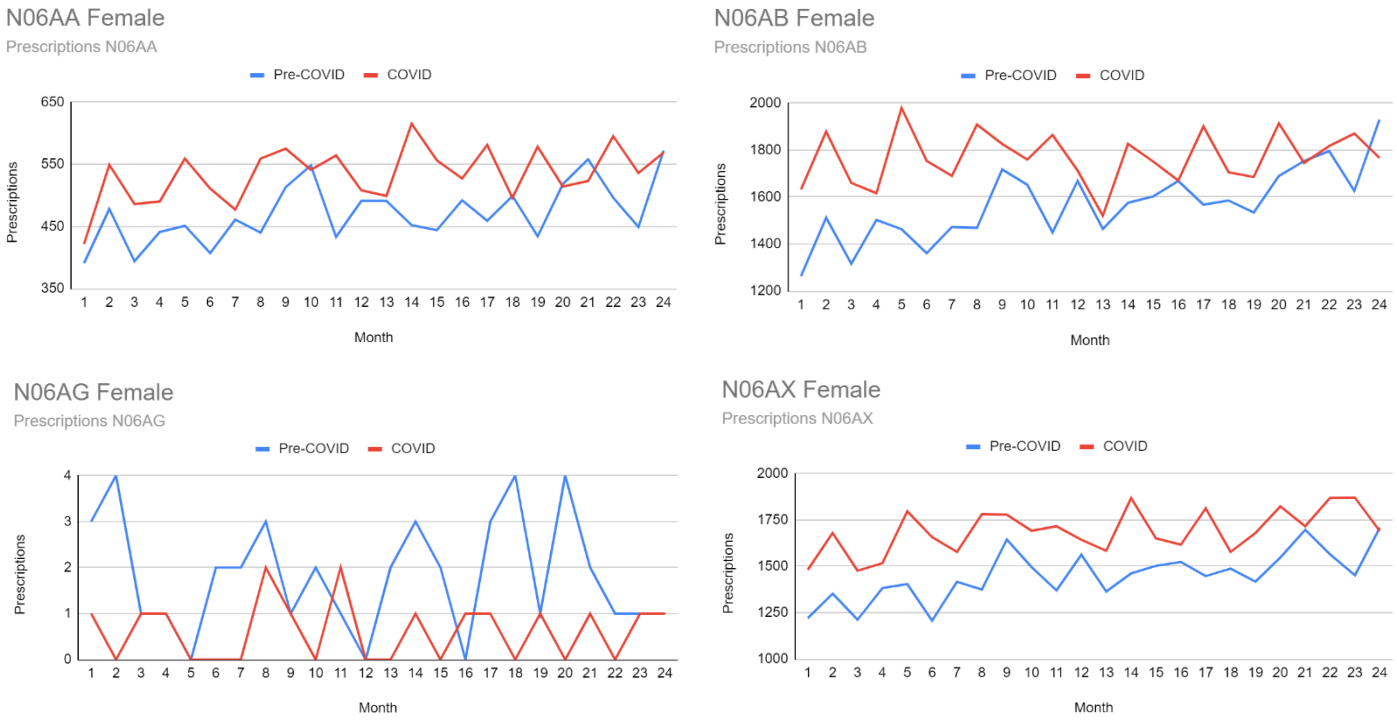
The 2008 Financial Crisis and Changes in Lifestyle-Related Behaviors in Italy, Greece, Spain, and Portugal: A Systematic Review.	Sane Schepisi M. et al (08-2021)	Review	/	/	/	/	/
How did the use of psychotropic drugs change during the great recession in Portugal? A follow-up to the National Mental Health Survey	Silva M. et al (05-2020)	Cross-sectionql survey study	Survey/Questionnaires Comparing psychotropic drug use in 2008-2009 versus 2015-2016	911 patients who completed both surveys	Antidepressants, Anxiolytics, Hypnotics/Sedatives	Increase of 6.74% in consumption of psychotropic drugs. Population odds of consuming psychotropic drugs in 2015-2016 1.5 times higher, particularly for hypnotics/sedatives	• Self-reported use of psychotropic drugs(recall bias) • No information of clinical diagnosis • assessment of age through a dichotomous variable • analysis did not include terms to account for time trends in drug prescriptions
Use of psychotropic drugs in Lombardy in time of economic crisis (2007-2011): a population-based study of adult employees	Vittadini G. et al (12-2014)	Retrospective survey	Prescription rate analysis Time period of 5 years	All adult employees in Lombardy, Northern Italy, aged >18 years in the period 2007-2011	Antidepressants, antiepileptics, mood stabilizers and antipsychotics	Gradual increase in psychotropic drugs consumption, no significant increase compared to before economic crisis	• Demographic changes could influence the results (more elderly and less youth) • No control group • Self-employed workers not represented

Supplementary table 5. Disaster related articles

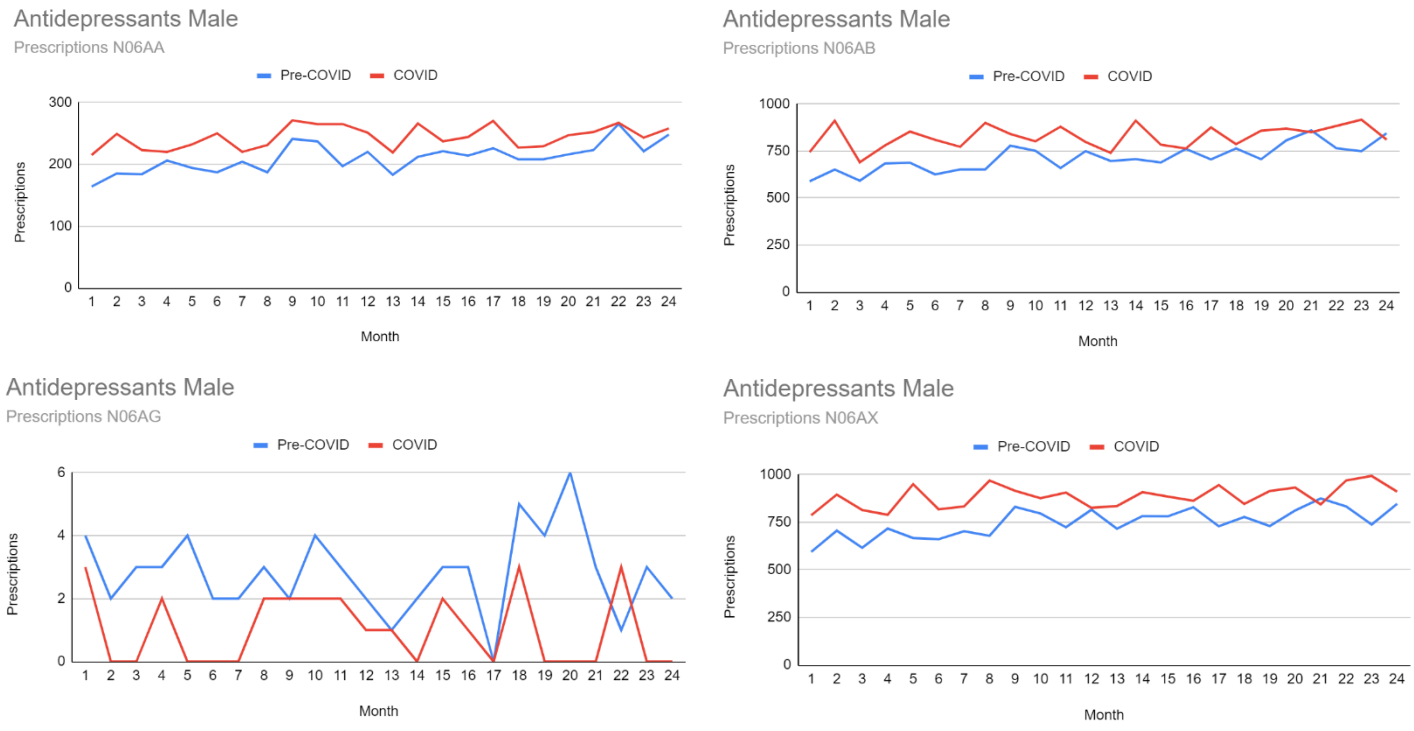
Article	Author(Year)	Study Type	Methods	Study Population	Medication Type	Outcome variables	Limitations
The impact of the Canterbury earthquakes on dispensing for older person's mental health.	Beaglehole B. et al (11-2019)	Retrospective study	Prescription rate analysis Observation period from 01/2008 till 03/2018	Data of inhabitants of Canterbury regio (n=67760) compared to the rest of New Zealand (n=469055)	Antidepressants, antipsychotics, anxiolytics and sedative/hypnotics	No effect of antipsychotic, antidepressant prescripton rate long term and short term Short term increase in anxiolytics and sedative/hypnotics (1 month), no long term effect	•
Psychotropic drug us e in a cohort of workers 4 years after an industrial disaster in France.	Diène E. et al (08-2014)	Cohort study Cross-sectional survey	Prescription rate analysis 5 year follow-up	50000 initial participants 13,129 surveys 3,006 final participants	Neuroleptics, anxiolytics, antidepressants, stimulants and hypnotics	Increased rates of antidepressants and hypnotics, correlated with personal distance to epicenter	• Small cohort sample compared to initial participants
Increase in the prescription rate of antidepressants after the Sewol Ferry disaster in Ansan, South Korea.	Han K. et al (09-2017)	Case control study	Prescription rate analysis Monthly prescription rate between 01/2013 and 06/2016	Danwon district of Ansan city compared to Cheonan city before and after the Sewol Ferry disaster on April 16, 2014.	Antidepressants, anxiolytics and sedatives/hypnotics	5.6% increase in prescription rate of antidepressants compared to control city	• Other explanations not excluded • Compared cities less compatible
Increase in Psychotropic Drug Deliveries after the Xynthia Storm, France, 2010	Motreff Y. et al (06-2013)	Retrospective cohort study	Prescription rate analysis Number of new psychotropic treatments in relative risks from 1-9-2009 until 24-12-2010 ass baseline, compared to 3 weeks after the storm(1-3-2010 until 21-3-2010)	48842 people living in 15 municipalities	Tranquilizers, Hypnotics, Antidepressants	Increase in relative risk of 1.53 in all psychotropic drug prescriptions during three weeks following the storm. Tranquilizers RR 1.78 Hypnotics RR 1.53 Antidepressants RR 1.26	• Underestimating the number of psychotropic treatments(second homes, hospital treatment not taken into account, only new prescriptions) • Other treatments not taken into account(psychotherapy) • No clinical information

Impact of the 2018 Japan Floods on benzodiazepine use: a longitudinal analysis based on the National Database of Health Insurance Claims.	Okazaki Y. et al (04-2022)	Retrospective Cohort study	Prescription rate analysis Difference in difference analysis to compare the occurrence of benzodiazepine use before and after the floods	5000129 people from which 31235 were victims Divided into victims and non-victims and afterwards into non user, occasional user and continuous user	Benzodiazepines	Increase in mean prescription rate in the victims group(11.3% before vs 11.8% after) Difference in difference analysis revealed a significant increase immediately after the disaster and after 1 year in the victims group	• No information on diagnosis • No information on victims whom did not seek any medical care • No information on people who moved to another city/country • No information on clusters, only individuals No information on other psychoactive medication
A quantitative analysis of antidepressant and antipsychotic prescriptions following an earthquake in Italy.	Rossi A. et al (02-2011)	Quantitative study	Prescription rate analysis Comparison of new prescriptions between 12 months before disaster and 6 months after disaster	103,788 patients	Antidepressant and antipsychotics Statins and diabetic medication as control	Antidepressants: 36.6% increase Antipsychotics: 129.5% increase Statins: 37% increase Diabetic medication: 51.4%	• Multiple prescriptions
Effects of L'Aquila earthquake on the prescribing pattern of antidepressant and antipsychotic drugs	Trifiro G. et al (12-2013)	Retrospective, drug utilization study	Prescription rate analysis Observed monthly prescriptions 1 year before disaster compared to 1 year after disaster	General population of L'Aquila and Caserta provinces from Southern Italy	Antidepressants and antipsychotics	Temporary (2 months) increase in antipsychotics and to lesser extent antidepressant in L'Aquila. The increase was mostly seen in older women.	• No evidence of incidence
Rate of prescription of anti depressant and anxiolytic drugs after Cyclone Yasi in North Queensland.	Usher K. et al (12-2012)	Cohort study Correlation study	Prescription rate analysis Comparison of pre-disaster period (02 till 08/2010) to post-disaster period (02 till 08/2011)	A number of communities along the North Queensland coast of Australia	Antidepressant and anxiolytics Oral anti-diabetic and statin as control	Increase in antidepressant use No effect on anxiolytics	• Limited time frame • Limited study population • No comparison with national level

Supplementary table 6

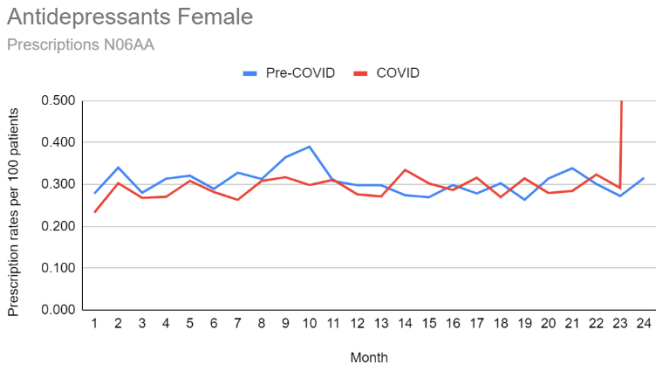


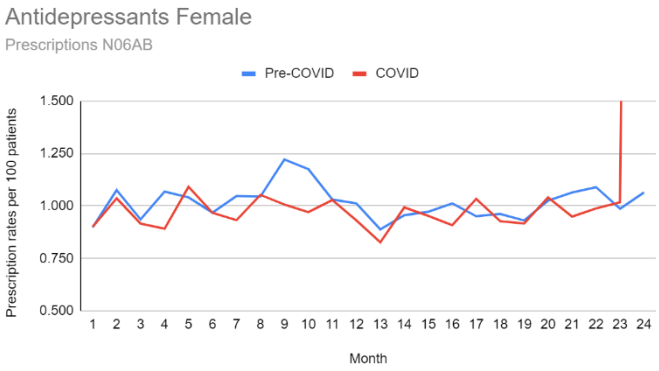
Supplementary 6.1 Absolute amount of prescriptions per type of Antidepressant based on time period in females.

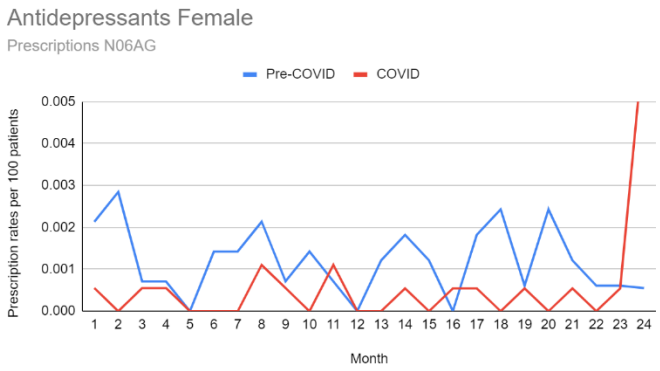


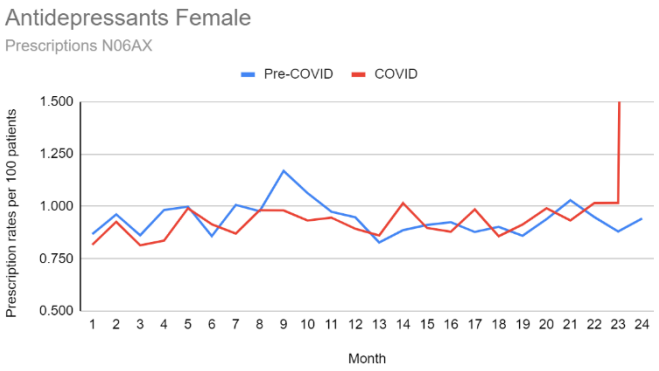
Supplementary table 6.2. Absolute amount of prescriptions per type of Antidepressant based on time period in females.

Supplementary table 7

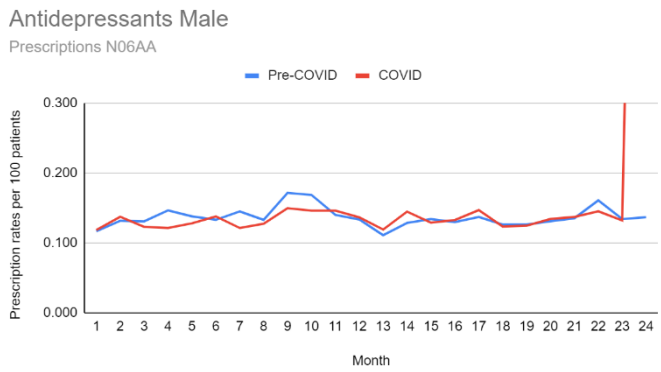


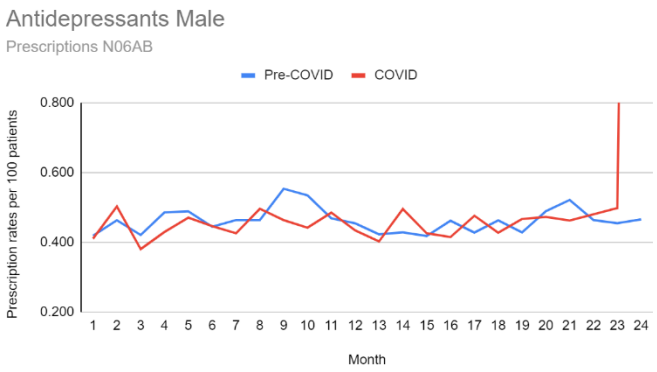


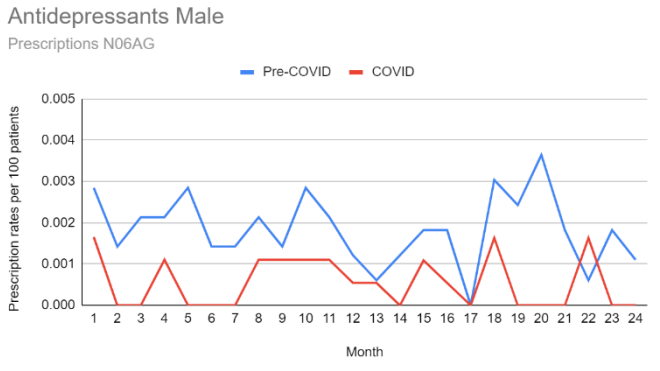


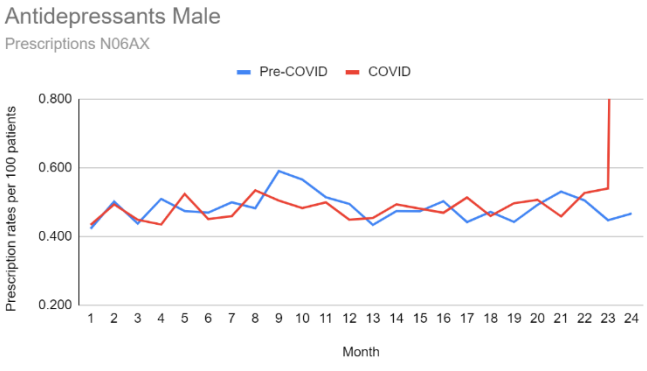


Supplementary table 7.1. Prescriptions rates per 100 patients per type of Antidepressant based on time period in females.









Supplementary table 7.2. Prescriptions rates per 100 patients per type of Antidepressant based on time period in males.

Supplementary table 8. Data extraction Intego Database

Supplementary table 8.1. Female absolute amount of prescriptions classified per medication type, time period and age groups. Calculate absolute differences can be found at the bottom of the table.

| Dataset | Gender: F | | |

Dataset **Gender: F**

	Pre-COVID																								COVID																							
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressiva	**2877**	**3346**	**2923**	**3326**	**3318**	**2977**	**3361**	**3286**	**3876**	**3897**	**3263**	**3721**	**3321**	**3481**	**3660**	**3883**	**3476**	**3575**	**3386**	**3768**	**4009**	**3866**	**3527**	**4210**	**3636**	**4106**	**3823**	**3823**	**4333**	**3921**	**3744**	**4249**	**4179**	**3981**	**4145**	**3862**	**3802**	**4309**	**3957**	**3814**	**4294**	**3778**	**3943**	**4249**	**3984**	**4280**	**4276**	**4025**
N06AA	391	478	394	441	451	407	461	440	513	548	433	491	491	452	444	492	459	499	434	518	558	496	449	572	422	549	486	490	559	511	477	559	575	541	564	508	499	615	556	527	581	496	578	514	523	595	536	569
N06AB	1263	1512	1316	1502	1463	1361	1472	1469	1717	1652	1449	1668	1464	1575	1602	1668	1567	1585	1534	1689	1753	1795	1626	1929	1632	1878	1660	1616	1978	1753	1690	1908	1825	1759	1864	1712	1520	1826	1751	1670	1900	1705	1685	1913	1745	1817	1870	1766
N06AG	3	4	1	1	0	2	2	3	1	2	1	0	2	3	2	0	3	4	1	4	2	1	1	1	1	0	1	1	0	0	0	2	1	0	2	0	0	1	0	1	1	0	1	0	1	0	1	1
N06AX	1220	1352	1212	1382	1404	1207	1416	1374	1644	1495	1370	1562	1364	1461	1502	1523	1447	1487	1417	1547	1696	1564	1451	1708	1481	1679	1476	1516	1796	1657	1577	1780	1778	1691	1715	1642	1583	1867	1650	1616	1812	1577	1679	1822	1715	1868	1869	1689
Antipsychotica	**483**	**587**	**510**	**601**	**562**	**523**	**586**	**534**	**686**	**602**	**558**	**633**	**586**	**634**	**606**	**620**	**586**	**609**	**532**	**613**	**660**	**660**	**569**	**684**	**600**	**680**	**709**	**683**	**753**	**698**	**673**	**671**	**697**	**692**	**690**	**637**	**650**	**708**	**679**	**616**	**692**	**665**	**717**	**682**	**711**	**720**	**782**	**729**
N05A	483	587	510	601	552	523	585	534	665	602	558	633	565	634	606	620	595	609	532	613	660	660	569	684	600	680	709	683	753	696	673	671	697	692	690	637	650	708	679	616	692	665	717	682	711	720	762	729
Benzodiazepines	**2826**	**3290**	**3010**	**3384**	**3288**	**3008**	**3343**	**3319**	**3728**	**3829**	**2978**	**3820**	**3142**	**3332**	**3467**	**3484**	**3184**	**3375**	**3299**	**3429**	**3884**	**3761**	**3147**	**3803**	**3370**	**4160**	**3767**	**3614**	**4086**	**3825**	**3362**	**3881**	**3840**	**3843**	**3671**	**3838**	**3382**	**4142**	**3451**	**3419**	**3806**	**3435**	**3829**	**3807**	**3879**	**4138**	**3921**	**3704**
N03AE	257	242	243	258	241	231	273	281	291	298	279	289	249	265	274	265	230	271	270	293	298	298	253	307	246	347	284	291	357	334	276	326	324	306	304	277	304	354	296	278	353	288	293	309	331	370	318	268
N05BA	1841	2149	1940	2191	2144	1934	2158	2158	2421	2287	1865	2310	1996	2151	2229	2290	2050	2180	2112	2231	2371	2432	2041	2465	2226	2698	2412	2283	2604	2351	2155	2432	2517	2569	2326	2396	2168	2740	2276	2268	2460	2266	2375	2562	2368	2638	2561	2394
N05CD	727	899	827	945	903	843	912	880	1016	1044	835	1021	897	916	964	939	914	924	917	905	1025	1021	853	1031	898	1105	1061	940	1124	940	921	923	999	1068	941	966	890	1048	879	873	993	881	961	1036	980	1131	1042	1042
Z-drugs	**1004**	**1180**	**1138**	**1234**	**1167**	**1131**	**1203**	**1211**	**1399**	**1318**	**1064**	**1332**	**1193**	**1158**	**1218**	**1302**	**1201**	**1194**	**1171**	**1221**	**1348**	**1358**	**1187**	**1434**	**1220**	**1408**	**1302**	**1309**	**1457**	**1371**	**1257**	**1485**	**1411**	**1640**	**1316**	**1405**	**1344**	**1563**	**1346**	**1403**	**1481**	**1354**	**1465**	**1592**	**1478**	**1632**	**1560**	**1482**
N05CF	1004	1180	1136	1234	1167	1131	1203	1211	1399	1316	1054	1332	1193	1158	1218	1302	1201	1194	1171	1221	1348	1358	1187	1434	1220	1408	1302	1309	1457	1371	1257	1485	1411	1640	1316	1405	1344	1563	1346	1403	1481	1354	1465	1592	1478	1632	1560	1482
Group 58-67																																																
Antidepressiva	**548**	**642**	**582**	**668**	**626**	**580**	**661**	**582**	**768**	**727**	**584**	**783**	**637**	**713**	**686**	**718**	**686**	**686**	**663**	**713**	**783**	**820**	**664**	**790**	**709**	**884**	**687**	**748**	**878**	**788**	**770**	**825**	**820**	**847**	**836**	**699**	**731**	**862**	**777**	**678**	**861**	**751**	**782**	**801**	**781**	**787**	**864**	**738**
N06AA	83	95	79	82	108	87	95	86	93	97	69	103	89	79	86	104	85	103	88	96	111	120	90	107	82	129	96	110	114	126	106	126	121	120	134	96	114	144	108	92	139	99	126	103	111	111	106	101
N06AB	234	260	265	299	261	237	262	346	317	321	256	303	259	309	281	320	294	263	275	301	332	341	294	340	323	367	295	314	378	320	324	337	328	360	323	293	265	317	318	283	325	312	252	338	316	314	339	278
N06AG	0	1	0	1	0	0	1	1	0	2	0	0	1	1	0	0	1	2	1	3	1	1	0	1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
N06AX	232	286	238	286	256	266	293	259	349	307	269	357	288	324	319	294	306	328	299	313	339	358	280	342	304	388	295	325	386	342	340	360	371	367	378	310	352	401	351	301	387	340	354	360	334	372	409	359
Antipsychotica																																															
N05A	92	98	98	97	100	86	109	103	115	115	93	134	110	123	119	121	111	128	112	108	133	116	99	122	111	129	147	128	141	133	114	139	144	120	138	102	123	113	128	116	113	124	146	114	133	134	143	145
Benzodiazepines	570	701	597	706	702	586	686	711	786	781	582	762	618	688	748	736	676	691	676	698	688	746	667	747	676	805	699	687	821	729	693	714	760	766	697	705	642	782	709	672	768	686	707	768	723	784	746	664
N03AE	49	48	42	45	45	42	59	53	44	54	44	64	50	52	65	54	49	56	54	63	65	57	51	70	55	76	52	60	65	72	56	69	64	59	54	60	68	70	59	57	78	60	56	70	73	72	61	48
N05BA	356	456	386	440	456	382	435	460	475	489	349	472	396	421	451	484	425	439	439	444	428	472	426	483	442	520	450	442	540	461	444	481	480	492	436	458	395	542	470	439	490	453	473	498	477	519	489	425
N05CD	165	197	169	221	201	171	191	198	246	238	189	216	172	196	232	198	201	196	182	191	205	216	190	194	178	209	197	185	216	196	193	164	216	204	207	187	179	180	180	176	188	172	178	188	173	203	195	181
Z-drugs																																															
N05CF	259	286	266	296	285	302	288	307	324	332	265	339	258	293	310	316	300	302	278	278	328	330	276	334	297	381	301	331	345	334	331	390	351	420	339	340	312	374	325	341	370	338	360	396	358	386	391	341
Group 68-77																																															
Antidepressiva	**382**	**481**	**437**	**444**	**481**	**467**	**476**	**467**	**587**	**579**	**401**	**483**	**487**	**521**	**520**	**533**	**481**	**537**	**503**	**544**	**574**	**638**	**483**	**586**	**613**	**611**	**549**	**667**	**679**	**682**	**629**	**868**	**628**	**608**	**682**	**667**	**485**	**623**	**603**	**683**	**667**	**687**	**810**	**618**	**681**	**710**	**810**	**684**
N06AA	74	82	77	74	86	86	80	89	103	104	69	93	95	81	86	83	84	96	80	100	110	111	80	112	80	107	92	105	119	96	84	120	102	99	109	94	78	113	102	104	121	84	114	99	90	127	96	94
N06AB	159	216	162	197	200	196	215	198	242	247	171	203	202	256	217	219	220	230	209	231	234	294	190	259	223	235	252	235	289	238	218	277	276	261	252	228	198	237	245	247	267	249	249	264	237	267	254	239
N06AG	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
N06AX	159	163	198	173	205	175	180	169	222	228	161	197	190	184	217	231	186	211	214	213	230	234	223	224	210	269	205	227	271	258	227	271	248	248	221	235	219	273	256	231	269	234	246	255	254	316	260	251
Antipsychotica																																															
N05A	66	83	89	95	76	98	86	69	114	87	94	99	84	99	105	96	83	95	85	99	95	91	93	108	90	97	112	110	110	103	102	104	111	125	105	93	98	111	102	101	108	107	92	108	114	117	110	105
Benzodiazepines	621	703	697	814	748	718	776	744	878	874	663	833	707	781	811	778	731	806	736	767	887	933	728	834	768	881	872	777	1022	861	786	922	833	1003	782	838	781	840	820	779	853	812	888	882	848	1017	816	829
N03AE	28	47	39	41	33	35	37	49	44	50	36	48	37	46	39	37	31	45	45	41	49	57	46	39	41	54	46	40	67	50	48	50	55	69	51	46	49	50	53	48	66	51	51	46	56	68	55	43
N05BA	400	439	431	528	475	453	490	472	555	546	418	534	460	475	525	513	464	499	432	477	556	591	446	529	505	595	554	494	624	532	501	579	589	629	482	530	488	594	514	490	570	499	549	571	512	613	591	537
N05CD	193	217	227	245	238	230	249	223	280	278	209	251	220	260	247	229	236	261	258	239	282	285	236	266	220	332	272	243	331	269	236	293	289	305	249	263	224	296	253	241	297	262	286	265	280	336	269	249
Z-drugs																																															
N05CF	230	294	259	310	294	268	288	302	368	361	267	291	327	288	306	322	301	301	287	335	333	374	301	359	311	367	326	342	403	350	305	395	364	444	328	349	359	413	354	361	392	346	378	414	403	452	370	371
Group 78-87																																															
Antidepressiva	**280**	**296**	**287**	**313**	**282**	**282**	**304**	**303**	**347**	**340**	**276**	**318**	**320**	**316**	**327**	**338**	**336**	**386**	**317**	**380**	**388**	**364**	**306**	**384**	**307**	**377**	**389**	**342**	**404**	**380**	**365**	**382**	**368**	**388**	**316**	**334**	**329**	**348**	**334**	**340**	**378**	**368**	**362**	**374**	**379**	**425**	**430**	**422**
N06AA	46	57	56	57	44	51	68	51	62	62	59	49	64	65	53	48	68	71	63	61	58	50	51	69	48	56	74	66	71	67	61	69	68	68	56	59	51	53	67	68	58	62	64	57	65	71	72	82
N06AB	107	132	120	133	120	131	134	117	161	143	109	143	142	133	143	159	131	151	146	147	160	157	140	183	133	178	169	137	190	169	160	171	151	158	152	149	135	151	135	131	174	150	154	173	166	176	178	174
N06AG	0	1	1	0	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N06AX	107	105	90	123	118	100	101	135	124	135	107	124	114	116	130	132	137	142	108	152	148	147	113	132	126	143	145	139	143	144	134	152	137	162	107	126	143	144	132	141	146	154	134	144	148	178	180	166
Antipsychotica																																															
N05A	56	78	52	73	64	54	75	73	72	71	61	69	62	69	69	69	72	74	65	68	89	85	66	77	75	92	105	98	103	86	101	78	76	82	69	94	91	108	82	73	97	80	95	92	86	101	112	89
Benzodiazepines	611	824	681	606	606	579	826	686	879	865	504	834	624	587	838	663	680	666	662	818	688	726	631	721	643	784	768	702	784	674	612	868	688	777	826	842	615	768	687	826	867	642	874	778	866	868	786	800
N03AE	34	28	38	30	33	32	42	29	46	33	39	30	32	28	45	36	33	38	40	34	35	41	22	52	44	41	38	52	54	47	35	51	43	38	42	25	37	38	40	37	41	34	33	41	42	62	44	35
N05BA	308	372	330	353	348	340	367	334	389	398	274	354	363	359	353	382	329	388	390	361	398	438	329	418	374	485	445	425	456	408	345	401	406	473	361	370	361	454	351	376	381	384	395	450	402	493	430	475
N05CD	169	224	213	223	224	207	216	222	244	264	191	250	229	210	240	245	228	240	222	223	256	246	180	251	225	258	273	225	284	219	232	217	239	266	223	247	217	264	196	213	245	224	246	285	252	301	292	290
Z-drugs																																															
N05CF	174	195	207	216	175	168	218	179	233	201	155	236	189	203	229	228	190	190	212	194	228	248	171	252	217	259	261	233	264	242	214	227	252	289	190	249	229	278	218	262	266	236	271	262	243	337	294	294
Group 88_plus																																															
Antidepressiva	**38**	**43**	**61**	**68**	**62**	**47**	**66**	**48**	**88**	**64**	**64**	**68**	**78**	**81**	**88**	**78**	**82**	**74**	**71**	**68**	**81**	**84**	**67**	**80**	**84**	**104**	**105**	**87**	**111**	**86**	**79**	**70**	**80**	**83**	**76**	**88**	**82**	**92**	**88**	**79**	**76**	**83**	**81**	**91**	**81**	**100**	**111**	**128**
N06AA	6	5	10	8	9	4	11	8	10	9	9	9	16	9	13	9	10	13	8	8	9	9	11	13	3	13	13	16	12	8	11	9	14	15	10	17	12	13	13	11	5	12	14	14	20	16	16	31
N06AB	17	22	25	25	26	28	21	20	30	21	29	22	29	30	25	32	25	35	35	21	22	27	25	34	37	48	44	37	49	42	31	37	34	31	34	26	27	43	33	30	28	34	37	36	30	52	51	44
N06AG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N06AX	16	16	26	25	17	15	23	21	28	24	16	27	34	22	28	37	27	26	28	27	29	28	21	33	24	43	48	34	50	35	37	24	32	37	31	46	43	36	42	38	42	47	30	41	31	32	44	53
Antipsychotica																																															
N05A	21	29	22	23	27	29	24	24	27	27	22	35	35	37	43	28	22	34	24	41	41	38	32	32	33	30	53	37	46	43	46	38	41	35	42	57	42	49	36	34	50	37	44	44	42	50	63	51
Benzodiazepines	117	138	131	161	146	148	140	162	166	178	120	188	170	168	179	174	167	174	163	184	197	186	143	225	202	268	288	215	218	206	181	186	184	189	189	208	189	238	185	201	221	180	189	248	222	267	247	308
N03AE	10	3	5	7	4	8	3	14	5	7	6	9	3	3	9	9	5	6	10	4	13	5	5	9	5	15	11	9	12	7	8	6	6	6	4	7	10	5	8	5	8	11	3	10	4	9	5	6
N05BA	56	73	79	88	82	78	76	63	82	100	62	92	79	84	102	97	87	97	76	85	100	104	80	129	115	131	137	121	115	117	93	111	98	96	94	121	100	136	110	114	124	111	114	136	135	137	139	158
N05CD	51	62	47	66	59	62	61	75	68	69	52	87	88	69	68	68	65	71	67	75	84	77	58	87	82	110	121	85	91	81	80	68	80	87	71	80	79	95	77	82	89	68	82	100	83	121	103	142
Z-drugs																																															
N05CF	35	44	36	39	35	28	40	36	29	36	29	38	38	36	36	50	29	43	41	34	51	42	36	55	49	60	70	57	75	71	59	57	64	67	54	75	62	87	74	72	71	61	80	85	82	80	92	98

Total absolute prescriptions count per age group, Pre-COVID versus COVID

Age groups	18-27	28-37	38-47	48-57	58-67	68-77	78-87	88+
Antipsychotics precovid	764	1448	2127	2630	2642	2189	1663	717
Antipsychotics postcovid	1023	1520	2226	2921	3078	2536	2165	1043
Z-drugs precovid	355	1077	2399	5196	7152	7366	4891	916
Z-drugs postcovid	375	1130	2556	5082	8452	8897	6087	1702
Antidepressants precovid	4431	9360	13525	18955	16311	12091	7672	1447
Antidepressants postcovid	5531	10897	15239	20062	18823	14322	8816	2133
Benzo precovid	1612	4658	8226	12233	16514	18556	14912	3849
Benzo postcovid	1642	4869	9507	12735	17375	20965	16828	5200

Calculated differences in absolute prescriptions, Pre-COVID versus COVID

Som AD pre covid	83792	Percentage verschil	14,36%	((95823 - 83792) / 83792) x 100%
Som AD post covid	95823			
Som AP pre covid	14180	Percentage verschil	16,45%	
Som AP post covid	16512			
Som benzo pre covid	80560	Percentage verschil	10,63%	
Som benzo post covid	89121			
Som Z-drugs pre covid	29352	Percentage verschil	16,79%	
Som Z-drugs post covid	34281			

Supplementary table 8.2. Female prescription rates classified per medication type, time period and age groups. Calculate prescription rates per 1000 patients can be found at the bottom 4 lines of the table.

Dataset: **Gender:** **F**

	Pre-COVID																								COVID																								
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**	**46**	**47**	**48**
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	**2.046**	**2.380**	**2.079**	**2.386**	**2.360**	**2.117**	**2.383**	**2.337**	**2.756**	**2.629**	**2.314**	**2.258**	**2.015**	**2.118**	**2.154**	**2.235**	**2.109**	**2.169**	**2.055**	**2.280**	**2.433**	**2.340**	**2.140**	**2.322**	**1.951**	**2.265**	**1.999**	**1.999**	**2.390**	**2.163**	**2.065**	**2.344**	**2.305**	**2.202**	**2.287**	**2.101**	**1.959**	**2.344**	**2.152**	**2.075**	**2.336**	**2.055**	**2.145**	**2.311**	**2.167**	**2.328**	**2.326**	**28.312**
N06AA	0.278	0.340	0.280	0.314	0.321	0.289	0.328	0.313	0.365	0.390	0.308	0.298	0.298	0.274	0.269	0.299	0.279	0.303	0.263	0.314	0.339	0.301	0.272	0.316	0.233	0.303	0.268	0.270	0.308	0.282	0.263	0.308	0.317	0.298	0.311	0.276	0.271	0.335	0.302	0.267	0.316	0.270	0.314	0.280	0.284	0.324	0.292	3.720
N06AB	0.898	1.075	0.998	1.068	1.041	0.988	1.047	1.045	1.221	1.175	1.031	1.012	0.888	0.956	0.972	1.012	0.951	0.962	0.931	1.025	1.064	1.089	0.987	1.064	0.900	1.036	0.916	0.891	1.091	0.967	0.932	1.053	1.007	0.970	1.029	0.931	0.827	0.993	0.952	0.908	1.033	0.927	0.917	1.041	0.949	0.988	1.017	11.545
N06AG	0.002	0.003	0.001	0.001	0.000	0.001	0.001	0.002	0.001	0.001	0.001	0.000	0.001	0.002	0.001	0.000	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.007
N06AX	0.868	0.962	0.862	0.983	0.999	0.858	1.007	0.977	1.169	1.063	0.974	0.948	0.828	0.887	0.911	0.924	0.878	0.902	0.860	0.939	1.029	0.949	0.880	0.942	0.817	0.926	0.814	0.836	0.991	0.914	0.870	0.982	0.981	0.933	0.946	0.893	0.861	1.015	0.897	0.879	0.986	0.858	0.913	0.991	0.933	1.016	1.017	11.041
Antipsychotics	**0.344**	**0.417**	**0.363**	**0.427**	**0.393**	**0.372**	**0.416**	**0.380**	**0.473**	**0.428**	**0.397**	**0.384**	**0.343**	**0.385**	**0.368**	**0.376**	**0.361**	**0.370**	**0.323**	**0.372**	**0.400**	**0.400**	**0.345**	**0.377**	**0.331**	**0.375**	**0.391**	**0.377**	**0.415**	**0.384**	**0.371**	**0.370**	**0.385**	**0.382**	**0.381**	**0.346**	**0.354**	**0.385**	**0.369**	**0.335**	**0.376**	**0.362**	**0.390**	**0.371**	**0.387**	**0.392**	**0.414**	**4.766**
N05A	0.344	0.417	0.363	0.427	0.393	0.372	0.416	0.380	0.473	0.428	0.397	0.384	0.343	0.385	0.368	0.376	0.361	0.370	0.323	0.372	0.400	0.400	0.345	0.377	0.331	0.375	0.391	0.377	0.415	0.384	0.371	0.370	0.385	0.382	0.381	0.346	0.354	0.385	0.369	0.335	0.376	0.362	0.390	0.371	0.387	0.392	0.414	4.766
Benzodiazepines	**2.009**	**2.340**	**2.141**	**2.414**	**2.339**	**2.139**	**2.378**	**2.361**	**2.651**	**2.581**	**2.119**	**2.197**	**1.907**	**2.022**	**2.104**	**2.120**	**1.938**	**2.048**	**2.002**	**2.081**	**2.242**	**2.276**	**1.910**	**2.098**	**1.859**	**2.289**	**2.073**	**1.939**	**2.254**	**2.000**	**1.849**	**2.031**	**2.118**	**2.175**	**1.970**	**1.979**	**1.829**	**2.253**	**1.877**	**1.860**	**2.070**	**1.868**	**1.974**	**2.125**	**2.001**	**2.251**	**2.133**	**24.214**
N03AE	0.183	0.172	0.173	0.183	0.171	0.164	0.194	0.200	0.207	0.212	0.198	0.175	0.151	0.161	0.166	0.161	0.140	0.164	0.164	0.178	0.181	0.181	0.154	0.169	0.136	0.191	0.157	0.161	0.197	0.184	0.152	0.180	0.179	0.169	0.168	0.151	0.165	0.193	0.161	0.151	0.192	0.157	0.159	0.168	0.180	0.201	0.173	1.752
N03BA	1.309	1.528	1.380	1.558	1.525	1.376	1.535	1.535	1.722	1.627	1.326	1.402	1.211	1.305	1.353	1.390	1.244	1.323	1.282	1.354	1.439	1.476	1.236	1.360	1.228	1.488	1.331	1.259	1.437	1.297	1.189	1.342	1.389	1.417	1.283	1.303	1.179	1.490	1.238	1.234	1.338	1.233	1.292	1.394	1.288	1.435	1.393	15.650
N05CD	0.517	0.639	0.588	0.672	0.642	0.600	0.649	0.626	0.723	0.743	0.594	0.620	0.544	0.556	0.585	0.570	0.555	0.561	0.556	0.549	0.622	0.620	0.518	0.569	0.495	0.610	0.585	0.519	0.620	0.519	0.508	0.509	0.551	0.589	0.519	0.525	0.484	0.570	0.478	0.475	0.540	0.479	0.523	0.563	0.533	0.615	0.567	6.812
Z-drugs	**0.714**	**0.839**	**0.808**	**0.878**	**0.830**	**0.804**	**0.856**	**0.861**	**0.995**	**0.936**	**0.750**	**0.808**	**0.724**	**0.703**	**0.739**	**0.790**	**0.729**	**0.725**	**0.711**	**0.741**	**0.818**	**0.824**	**0.720**	**0.791**	**0.673**	**0.777**	**0.718**	**0.722**	**0.804**	**0.756**	**0.693**	**0.819**	**0.778**	**0.905**	**0.726**	**0.764**	**0.731**	**0.850**	**0.732**	**0.763**	**0.808**	**0.736**	**0.797**	**0.866**	**0.804**	**0.888**	**0.849**	**9.688**
N05CF	0.714	0.839	0.808	0.878	0.830	0.804	0.856	0.861	0.995	0.936	0.750	0.808	0.724	0.703	0.739	0.790	0.729	0.725	0.711	0.741	0.818	0.824	0.720	0.791	0.673	0.777	0.718	0.722	0.804	0.756	0.693	0.819	0.778	0.905	0.726	0.764	0.731	0.850	0.732	0.763	0.808	0.736	0.797	0.866	0.804	0.888	0.849	9.688
Group 18-27																																																	
Antidepressive	**0.105**	**0.115**	**0.098**	**0.115**	**0.115**	**0.107**	**0.140**	**0.137**	**0.135**	**0.150**	**0.137**	**0.106**	**0.105**	**0.110**	**0.107**	**0.113**	**0.111**	**0.122**	**0.114**	**0.126**	**0.132**	**0.122**	**0.132**	**0.122**	**0.115**	**0.111**	**0.102**	**0.111**	**0.109**	**0.109**	**0.114**	**0.118**	**0.119**	**0.119**	**0.151**	**0.128**	**0.115**	**0.148**	**0.118**	**0.136**	**0.135**	**0.123**	**0.133**	**0.146**	**0.145**	**0.154**	**0.137**	**1.569**
N06AA	0.009	0.011	0.010	0.011	0.016	0.009	0.018	0.013	0.014	0.014	0.011	0.010	0.009	0.007	0.010	0.016	0.012	0.009	0.010	0.011	0.016	0.009	0.012	0.009	0.017	0.012	0.009	0.009	0.006	0.008	0.008	0.011	0.009	0.012	0.010	0.013	0.012	0.010	0.011	0.013	0.010	0.010	0.013	0.008	0.010	0.016	0.008	0.131
N06AB	0.061	0.071	0.063	0.060	0.065	0.063	0.078	0.084	0.084	0.085	0.085	0.066	0.065	0.064	0.063	0.063	0.061	0.073	0.064	0.075	0.072	0.076	0.078	0.075	0.071	0.069	0.060	0.073	0.074	0.065	0.070	0.071	0.071	0.069	0.092	0.075	0.071	0.097	0.073	0.060	0.083	0.067	0.080	0.101	0.097	0.090	0.080	0.961
N06AG	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000
N06AX	0.033	0.032	0.026	0.043	0.034	0.034	0.044	0.041	0.038	0.052	0.041	0.030	0.031	0.039	0.035	0.035	0.038	0.039	0.040	0.041	0.045	0.037	0.042	0.038	0.026	0.030	0.033	0.029	0.030	0.036	0.036	0.036	0.039	0.038	0.049	0.040	0.032	0.042	0.033	0.042	0.041	0.026	0.040	0.038	0.038	0.048	0.049	0.477
Antipsychotics																																																
N05A	0.022	0.024	0.014	0.031	0.029	0.019	0.021	0.016	0.031	0.030	0.021	0.021	0.020	0.022	0.017	0.018	0.014	0.017	0.017	0.019	0.019	0.025	0.015	0.017	0.018	0.020	0.021	0.009	0.028	0.025	0.023	0.024	0.019	0.019	0.026	0.021	0.027	0.026	0.025	0.027	0.026	0.022	0.027	0.026	0.026	0.022	0.026	0.294
Benzodiazepines	**0.041**	**0.045**	**0.041**	**0.046**	**0.048**	**0.039**	**0.054**	**0.046**	**0.055**	**0.055**	**0.044**	**0.049**	**0.033**	**0.036**	**0.036**	**0.038**	**0.042**	**0.038**	**0.047**	**0.048**	**0.047**	**0.049**	**0.031**	**0.042**	**0.031**	**0.040**	**0.032**	**0.035**	**0.040**	**0.042**	**0.034**	**0.038**	**0.039**	**0.040**	**0.045**	**0.043**	**0.029**	**0.034**	**0.034**	**0.031**	**0.030**	**0.039**	**0.043**	**0.039**	**0.032**	**0.032**	**0.040**	**0.562**
N03AE	0.009	0.002	0.003	0.002	0.005	0.004	0.006	0.006	0.004	0.010	0.004	0.005	0.004	0.002	0.004	0.001	0.003	0.004	0.002	0.005	0.004	0.004	0.003	0.003	0.004	0.002	0.002	0.003	0.006	0.004	0.002	0.006	0.003	0.003	0.003	0.003	0.003	0.001	0.005	0.004	0.002	0.003	0.005	0.006	0.003	0.002	0.003	0.039
N03BA	0.030	0.041	0.036	0.041	0.041	0.029	0.048	0.037	0.048	0.043	0.034	0.038	0.024	0.030	0.029	0.033	0.036	0.030	0.039	0.037	0.038	0.036	0.023	0.033	0.024	0.035	0.028	0.029	0.040	0.035	0.030	0.028	0.034	0.032	0.038	0.034	0.024	0.030	0.028	0.025	0.028	0.035	0.035	0.032	0.027	0.028	0.034	0.484
N05CD	0.003	0.002	0.002	0.002	0.002	0.006	0.002	0.003	0.003	0.002	0.006	0.007	0.005	0.005	0.004	0.004	0.004	0.003	0.005	0.005	0.007	0.008	0.005	0.006	0.003	0.003	0.002	0.003	0.003	0.003	0.002	0.004	0.002	0.004	0.004	0.005	0.002	0.003	0.001	0.002	0.001	0.001	0.003	0.001	0.002	0.002	0.003	0.039
Z-drugs																																																
N05CF	0.007	0.014	0.014	0.008	0.010	0.011	0.016	0.010	0.013	0.014	0.011	0.012	0.010	0.005	0.008	0.010	0.008	0.007	0.010	0.006	0.008	0.010	0.007	0.007	0.006	0.007	0.007	0.008	0.009	0.008	0.010	0.007	0.008	0.009	0.014	0.010	0.009	0.009	0.011	0.007	0.009	0.005	0.010	0.006	0.005	0.011	0.010	0.124
Group 28-37																																																
Antidepressive	**0.263**	**0.289**	**0.253**	**0.292**	**0.262**	**0.231**	**0.272**	**0.277**	**0.280**	**0.293**	**0.264**	**0.264**	**0.204**	**0.228**	**0.240**	**0.243**	**0.226**	**0.231**	**0.224**	**0.251**	**0.263**	**0.256**	**0.248**	**0.266**	**0.225**	**0.238**	**0.206**	**0.212**	**0.254**	**0.216**	**0.236**	**0.241**	**0.273**	**0.233**	**0.270**	**0.259**	**0.228**	**0.276**	**0.272**	**0.236**	**0.277**	**0.231**	**0.248**	**0.269**	**0.255**	**0.266**	**0.278**	**3.171**
N06AA	0.025	0.026	0.026	0.028	0.021	0.025	0.021	0.022	0.026	0.031	0.033	0.021	0.021	0.024	0.018	0.026	0.019	0.021	0.019	0.025	0.027	0.021	0.024	0.027	0.022	0.022	0.020	0.017	0.023	0.021	0.021	0.023	0.028	0.022	0.026	0.027	0.026	0.032	0.030	0.023	0.026	0.025	0.028	0.026	0.027	0.029	0.030	0.301
N06AB	0.131	0.151	0.145	0.141	0.140	0.126	0.139	0.139	0.142	0.147	0.131	0.140	0.110	0.114	0.127	0.129	0.128	0.130	0.125	0.144	0.141	0.142	0.140	0.140	0.125	0.130	0.112	0.119	0.132	0.116	0.134	0.125	0.147	0.125	0.147	0.143	0.119	0.135	0.147	0.132	0.148	0.119	0.129	0.140	0.134	0.140	0.148	1.713
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.107	0.111	0.083	0.092	0.100	0.080	0.112	0.116	0.112	0.115	0.100	0.104	0.072	0.090	0.095	0.087	0.079	0.079	0.079	0.083	0.095	0.093	0.082	0.099	0.079	0.086	0.074	0.077	0.099	0.079	0.081	0.093	0.098	0.087	0.097	0.090	0.083	0.109	0.094	0.081	0.101	0.086	0.091	0.104	0.094	0.097	0.100	1.157
Antipsychotics																																																
N05A	0.031	0.047	0.036	0.048	0.041	0.040	0.048	0.041	0.048	0.049	0.045	0.033	0.030	0.034	0.037	0.044	0.042	0.039	0.031	0.042	0.036	0.032	0.034	0.039	0.031	0.032	0.026	0.035	0.039	0.031	0.031	0.027	0.036	0.044	0.036	0.029	0.031	0.033	0.038	0.035	0.036	0.033	0.037	0.035	0.036	0.039	0.040	0.516
Benzodiazepines	**0.127**	**0.151**	**0.117**	**0.132**	**0.134**	**0.116**	**0.151**	**0.148**	**0.164**	**0.135**	**0.140**	**0.132**	**0.100**	**0.120**	**0.120**	**0.116**	**0.113**	**0.104**	**0.114**	**0.131**	**0.126**	**0.124**	**0.109**	**0.114**	**0.099**	**0.105**	**0.097**	**0.102**	**0.108**	**0.109**	**0.102**	**0.113**	**0.119**	**0.118**	**0.118**	**0.119**	**0.110**	**0.131**	**0.112**	**0.110**	**0.118**	**0.113**	**0.114**	**0.120**	**0.106**	**0.109**	**0.110**	**1.137**
N03AE	0.018	0.018	0.018	0.018	0.016	0.012	0.017	0.018	0.031	0.021	0.021	0.013	0.013	0.016	0.011	0.015	0.012	0.011	0.016	0.018	0.013	0.020	0.015	0.013	0.007	0.014	0.012	0.010	0.015	0.018	0.010	0.012	0.013	0.010	0.013	0.011	0.011	0.016	0.014	0.007	0.014	0.014	0.014	0.006	0.011	0.015	0.015	0.124
N03BA	0.095	0.115	0.085	0.099	0.097	0.091	0.117	0.112	0.119	0.100	0.064	0.101	0.073	0.090	0.094	0.087	0.084	0.083	0.081	0.103	0.102	0.086	0.079	0.088	0.078	0.090	0.072	0.078	0.078	0.082	0.080	0.083	0.096	0.094	0.097	0.091	0.085	0.102	0.086	0.094	0.092	0.089	0.090	0.101	0.084	0.085	0.085	0.922
N05CD	0.015	0.018	0.014	0.017	0.021	0.013	0.017	0.018	0.015	0.014	0.025	0.018	0.013	0.015	0.015	0.013	0.017	0.011	0.016	0.010	0.010	0.018	0.015	0.013	0.014	0.013	0.014	0.014	0.014	0.009	0.012	0.018	0.010	0.014	0.008	0.017	0.014	0.013	0.011	0.009	0.011	0.010	0.010	0.013	0.011	0.009	0.010	0.092
Z-drugs																																																
N05CF	0.019	0.032	0.034	0.028	0.035	0.028	0.038	0.027	0.041	0.029	0.023	0.032	0.022	0.032	0.021	0.024	0.031	0.025	0.033	0.031	0.033	0.021	0.031	0.031	0.025	0.025	0.019	0.019	0.023	0.028	0.024	0.026	0.020	0.025	0.029	0.028	0.029	0.030	0.029	0.026	0.028	0.024	0.021	0.032	0.029	0.029	0.022	0.333
Group 38-47																																																
Antidepressive	**0.329**	**0.405**	**0.309**	**0.383**	**0.404**	**0.332**	**0.393**	**0.416**	**0.445**	**0.441**	**0.390**	**0.359**	**0.331**	**0.333**	**0.338**	**0.355**	**0.344**	**0.322**	**0.308**	**0.381**	**0.391**	**0.360**	**0.337**	**0.386**	**0.300**	**0.339**	**0.312**	**0.304**	**0.357**	**0.340**	**0.322**	**0.397**	**0.378**	**0.325**	**0.376**	**0.358**	**0.319**	**0.376**	**0.342**	**0.349**	**0.367**	**0.324**	**0.340**	**0.383**	**0.349**	**0.353**	**0.358**	**4.458**
N06AA	0.044	0.047	0.031	0.049	0.038	0.037	0.048	0.051	0.044	0.070	0.048	0.037	0.048	0.039	0.029	0.039	0.047	0.041	0.030	0.047	0.049	0.044	0.033	0.039	0.031	0.039	0.036	0.034	0.038	0.029	0.033	0.035	0.047	0.042	0.040	0.038	0.038	0.047	0.042	0.039	0.037	0.040	0.037	0.033	0.037	0.048	0.042	0.634
N06AB	0.145	0.187	0.129	0.176	0.190	0.162	0.184	0.198	0.203	0.197	0.180	0.171	0.150	0.147	0.159	0.166	0.158	0.147	0.146	0.170	0.181	0.164	0.167	0.181	0.131	0.168	0.148	0.136	0.169	0.157	0.143	0.190	0.167	0.143	0.167	0.171	0.140	0.160	0.158	0.158	0.170	0.152	0.150	0.176	0.142	0.154	0.157	2.013
N06AG	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000
N06AX	0.139	0.171	0.149	0.159	0.176	0.133	0.181	0.166	0.198	0.174	0.165	0.150	0.135	0.145	0.150	0.150	0.139	0.134	0.133	0.164	0.162	0.151	0.137	0.166	0.138	0.133	0.129	0.134	0.151	0.154	0.146	0.172	0.164	0.140	0.169	0.150	0.141	0.169	0.142	0.153	0.159	0.133	0.154	0.174	0.170	0.151	0.159	1.811
Antipsychotics																																																
N05A	0.055	0.058	0.061	0.075	0.060	0.062	0.063	0.058	0.073	0.058	0.064	0.055	0.055	0.053	0.048	0.056	0.055	0.050	0.044	0.052	0.052	0.065	0.058	0.060	0.050	0.061	0.050	0.057	0.058	0.054	0.047	0.045	0.057	0.049	0.053	0.047	0.039	0.054	0.048	0.040	0.055	0.047	0.057	0.055	0.049	0.045	0.049	0.641
Benzodiazepines	**0.216**	**0.239**	**0.225**	**0.221**	**0.236**	**0.196**	**0.215**	**0.243**	**0.274**	**0.224**	**0.247**	**0.220**	**0.216**	**0.224**	**0.211**	**0.213**	**0.198**	**0.205**	**0.218**	**0.220**	**0.218**	**0.214**	**0.220**	**0.229**	**0.190**	**0.242**	**0.217**	**0.204**	**0.225**	**0.204**	**0.186**	**0.222**	**0.241**	**0.215**	**0.230**	**0.219**	**0.211**	**0.268**	**0.212**	**0.208**	**0.223**	**0.199**	**0.198**	**0.221**	**0.221**	**0.207**	**0.234**	**2.504**
N03AE	0.033	0.023	0.027	0.026	0.031	0.020	0.027	0.034	0.031	0.027	0.035	0.026	0.027	0.026	0.022	0.029	0.020	0.024	0.021	0.024	0.026	0.020	0.029	0.030	0.017	0.030	0.023	0.020	0.029	0.026	0.021	0.030	0.026	0.023	0.029	0.021	0.028	0.038	0.024	0.027	0.028	0.021	0.026	0.027	0.031	0.025	0.024	0.333
N03BA	0.158	0.172	0.166	0.166	0.174	0.150	0.156	0.189	0.206	0.161	0.161	0.157	0.155	0.165	0.161	0.155	0.149	0.148	0.171	0.169	0.158	0.164	0.163	0.165	0.145	0.185	0.163	0.155	0.165	0.149	0.140	0.167	0.183	0.165	0.170	0.175	0.152	0.191	0.162	0.158	0.171	0.152	0.148	0.162	0.162	0.154	0.176	1.791
N05CD	0.025	0.044	0.031	0.028	0.032	0.026	0.032	0.020	0.037	0.036	0.031	0.036	0.033	0.033	0.027	0.029	0.029	0.033	0.027	0.028	0.034	0.030	0.028	0.034	0.029	0.027	0.031	0.029	0.030	0.029	0.026	0.025	0.031	0.027	0.032	0.023	0.031	0.040	0.026	0.023	0.024	0.026	0.027	0.033	0.026	0.027	0.033	0.379
Z-drugs																																																
N05CF	0.065	0.063	0.075	0.083	0.069	0.079	0.071	0.080	0.085	0.070	0.062	0.067	0.056	0.043	0.049	0.063	0.052	0.055	0.050	0.066	0.059	0.058	0.073	0.073	0.051	0.055	0.058	0.049	0.050	0.053	0.054	0.060	0.063	0.064	0.056	0.061	0.059	0.063	0.055	0.057	0.057	0.058	0.054	0.068	0.065	0.057	0.070	0.752
Group 48-57																																																
Antidepressive	**0.468**	**0.547**	**0.460**	**0.551**	**0.548**	**0.469**	**0.522**	**0.510**	**0.659**	**0.536**	**0.580**	**0.541**	**0.451**	**0.471**	**0.499**	**0.512**	**0.473**	**0.480**	**0.465**	**0.507**	**0.564**	**0.463**	**0.504**	**0.528**	**0.432**	**0.487**	**0.424**	**0.409**	**0.526**	**0.480**	**0.439**	**0.510**	**0.497**	**0.462**	**0.492**	**0.441**	**0.407**	**0.496**	**0.440**	**0.441**	**0.491**	**0.411**	**0.457**	**0.488**	**0.437**	**0.449**	**0.462**	**4.870**
N06AA	0.051	0.085	0.055	0.068	0.070	0.056	0.061	0.060	0.091	0.081	0.072	0.076	0.062	0.082	0.068	0.069	0.052	0.059	0.059	0.071	0.073	0.051	0.063	0.074	0.046	0.063	0.052	0.047	0.068	0.061	0.056	0.060	0.064	0.056	0.065	0.054	0.057	0.070	0.061	0.062	0.065	0.055	0.063	0.065	0.055	0.053	0.054	0.641
N06AB	0.193	0.218	0.192	0.226	0.214	0.196	0.216	0.210	0.260	0.225	0.233	0.229	0.179	0.189	0.220	0.211	0.197	0.199	0.192	0.212	0.217	0.210	0.208	0.218	0.178	0.212	0.176	0.165	0.216	0.205	0.181	0.213	0.187	0.187	0.202	0.184	0.157	0.195	0.176	0.163	0.200	0.164	0.181	0.183	0.168	0.164	0.184	2.053
N06AG	0.001	0.001	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Dataset: **Gender:** **F**

	Pre-COVID																								COVID																									
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	**2.046**	**2.380**	**2.079**	**2.386**	**2.360**	**2.117**	**2.383**	**2.337**	**2.756**	**2.629**	**2.314**	**2.258**	**2.015**	**2.118**	**2.154**	**2.235**	**2.109**	**2.169**	**2.055**	**2.280**	**2.433**	**2.340**	**2.140**	**2.322**	**1.951**	**2.285**	**1.999**	**1.999**	**2.390**	**2.163**	**2.065**	**2.344**	**2.305**	**2.202**	**2.287**	**2.101**	**1.959**	**2.344**	**2.152**	**2.075**	**2.336**	**2.055**	**2.145**	**2.311**	**2.167**	**2.328**	**2.326**	**26.312**
N06AA	0.278	0.340	0.280	0.314	0.321	0.289	0.328	0.313	0.365	0.390	0.308	0.298	0.298	0.274	0.269	0.299	0.279	0.303	0.283	0.314	0.339	0.301	0.272	0.316	0.293	0.303	0.268	0.270	0.308	0.282	0.263	0.308	0.317	0.298	0.311	0.276	0.271	0.335	0.302	0.287	0.316	0.270	0.314	0.280	0.284	0.324	0.292	3.720
N06AB	0.898	1.075	0.936	1.068	1.041	0.958	1.047	1.045	1.221	1.175	1.031	1.012	0.888	0.956	0.972	1.012	0.951	0.962	0.931	1.025	1.064	1.089	0.987	1.064	0.900	1.036	0.916	0.891	1.091	0.967	0.932	1.053	1.007	0.970	1.028	0.931	0.827	0.993	0.952	0.908	1.033	0.927	0.917	1.041	0.949	0.988	1.017	11.545
N06AG	0.002	0.003	0.001	0.001	0.000	0.000	0.001	0.002	0.001	0.001	0.001	0.000	0.001	0.002	0.001	0.000	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.007
N06AX	0.868	0.962	0.862	0.983	0.999	0.858	1.007	0.977	1.169	1.063	0.974	0.948	0.828	0.887	0.911	0.924	0.878	0.902	0.860	0.939	1.029	0.949	0.880	0.942	0.817	0.926	0.814	0.836	0.991	0.914	0.870	0.982	0.981	0.933	0.946	0.893	0.861	1.015	0.897	0.879	0.986	0.858	0.913	0.991	0.933	1.016	1.017	11.041
Antipsychotics	**0.344**	**0.417**	**0.363**	**0.427**	**0.393**	**0.372**	**0.416**	**0.380**	**0.473**	**0.428**	**0.397**	**0.384**	**0.343**	**0.385**	**0.368**	**0.376**	**0.361**	**0.370**	**0.323**	**0.372**	**0.400**	**0.400**	**0.345**	**0.377**	**0.331**	**0.375**	**0.391**	**0.377**	**0.415**	**0.384**	**0.371**	**0.370**	**0.385**	**0.382**	**0.381**	**0.346**	**0.354**	**0.385**	**0.369**	**0.335**	**0.376**	**0.362**	**0.390**	**0.371**	**0.387**	**0.392**	**0.414**	**4.766**
N05A	0.344	0.417	0.363	0.427	0.393	0.372	0.416	0.380	0.473	0.428	0.397	0.384	0.343	0.385	0.368	0.376	0.361	0.370	0.323	0.372	0.400	0.400	0.345	0.377	0.331	0.375	0.391	0.377	0.415	0.384	0.371	0.370	0.385	0.382	0.381	0.346	0.354	0.385	0.369	0.335	0.376	0.362	0.390	0.371	0.387	0.392	0.414	4.766
Benzodiazepines	**2.009**	**2.340**	**2.141**	**2.414**	**2.339**	**2.139**	**2.378**	**2.361**	**2.651**	**2.581**	**2.119**	**2.197**	**1.907**	**2.022**	**2.104**	**2.120**	**1.938**	**2.048**	**2.002**	**2.081**	**2.242**	**2.276**	**1.910**	**2.098**	**1.859**	**2.289**	**2.073**	**1.939**	**2.254**	**2.000**	**1.849**	**2.031**	**2.118**	**2.175**	**1.970**	**1.979**	**1.829**	**2.253**	**1.877**	**1.860**	**2.070**	**1.868**	**1.974**	**2.125**	**2.001**	**2.251**	**2.133**	**24.214**
N03AE	0.183	0.172	0.173	0.183	0.171	0.164	0.194	0.200	0.207	0.212	0.198	0.175	0.151	0.161	0.166	0.161	0.140	0.164	0.164	0.178	0.181	0.161	0.154	0.169	0.136	0.191	0.157	0.161	0.197	0.164	0.152	0.160	0.179	0.169	0.168	0.151	0.165	0.193	0.161	0.151	0.192	0.157	0.159	0.168	0.160	0.201	0.173	1.752
N03BA	1.309	1.528	1.380	1.558	1.525	1.376	1.535	1.535	1.722	1.627	1.326	1.402	1.211	1.305	1.353	1.390	1.244	1.323	1.282	1.354	1.439	1.476	1.238	1.360	1.228	1.488	1.331	1.259	1.437	1.297	1.189	1.342	1.389	1.417	1.283	1.303	1.179	1.490	1.238	1.234	1.338	1.233	1.202	1.394	1.288	1.435	1.393	15.650
N05CD	0.517	0.639	0.588	0.672	0.642	0.600	0.649	0.626	0.723	0.743	0.594	0.620	0.544	0.556	0.585	0.570	0.555	0.561	0.556	0.549	0.622	0.620	0.518	0.569	0.495	0.610	0.585	0.519	0.620	0.519	0.508	0.509	0.551	0.589	0.519	0.525	0.484	0.570	0.478	0.475	0.540	0.479	0.523	0.563	0.533	0.615	0.567	6.812
Z-drugs	**0.714**	**0.839**	**0.808**	**0.878**	**0.830**	**0.804**	**0.856**	**0.861**	**0.995**	**0.936**	**0.750**	**0.808**	**0.724**	**0.703**	**0.739**	**0.790**	**0.729**	**0.725**	**0.711**	**0.741**	**0.818**	**0.824**	**0.720**	**0.791**	**0.673**	**0.777**	**0.718**	**0.722**	**0.804**	**0.756**	**0.693**	**0.819**	**0.778**	**0.905**	**0.726**	**0.764**	**0.731**	**0.850**	**0.732**	**0.763**	**0.806**	**0.736**	**0.797**	**0.866**	**0.804**	**0.888**	**0.849**	**9.888**
N05CF	0.714	0.839	0.808	0.878	0.830	0.804	0.856	0.861	0.995	0.936	0.750	0.808	0.724	0.703	0.739	0.790	0.729	0.725	0.711	0.741	0.818	0.824	0.720	0.791	0.673	0.777	0.718	0.722	0.804	0.756	0.693	0.819	0.778	0.905	0.726	0.764	0.731	0.850	0.732	0.763	0.806	0.736	0.797	0.866	0.804	0.888	0.849	9.688
N06AB	0.166	0.185	0.188	0.213	0.186	0.169	0.186	0.175	0.225	0.228	0.182	0.184	0.157	0.188	0.171	0.194	0.178	0.160	0.167	0.183	0.201	0.207	0.178	0.188	0.178	0.202	0.163	0.173	0.209	0.177	0.179	0.186	0.181	0.199	0.178	0.159	0.144	0.172	0.173	0.154	0.177	0.170	0.137	0.184	0.172	0.171	0.184	1.817
N06AG	0.000	0.001	0.000	0.001	0.000	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.002	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.007
N06AX	0.165	0.203	0.169	0.203	0.182	0.169	0.208	0.184	0.248	0.218	0.191	0.217	0.175	0.197	0.194	0.178	0.186	0.199	0.181	0.199	0.206	0.217	0.170	0.189	0.168	0.214	0.163	0.179	0.213	0.189	0.188	0.199	0.205	0.202	0.209	0.169	0.191	0.218	0.191	0.164	0.210	0.185	0.193	0.196	0.182	0.202	0.222	2.347
Antipsychotics																																																	
N05A	0.065	0.070	0.070	0.069	0.071	0.061	0.078	0.073	0.082	0.082	0.066	0.081	0.067	0.075	0.072	0.073	0.067	0.078	0.068	0.066	0.081	0.070	0.060	0.067	0.061	0.071	0.081	0.071	0.078	0.073	0.063	0.077	0.079	0.066	0.076	0.055	0.067	0.061	0.070	0.063	0.061	0.067	0.079	0.062	0.072	0.073	0.078	0.948
Benzodiazepines	**0.405**	**0.499**	**0.425**	**0.502**	**0.499**	**0.423**	**0.487**	**0.506**	**0.544**	**0.555**	**0.414**	**0.456**	**0.375**	**0.406**	**0.454**	**0.447**	**0.410**	**0.419**	**0.410**	**0.424**	**0.424**	**0.452**	**0.405**	**0.412**	**0.372**	**0.444**	**0.386**	**0.379**	**0.453**	**0.402**	**0.382**	**0.394**	**0.419**	**0.417**	**0.385**	**0.383**	**0.349**	**0.431**	**0.386**	**0.366**	**0.411**	**0.373**	**0.385**	**0.411**	**0.393**	**0.432**	**0.405**	**4.275**
N03AE	0.035	0.034	0.030	0.032	0.032	0.030	0.042	0.038	0.031	0.038	0.031	0.039	0.030	0.032	0.039	0.033	0.030	0.034	0.033	0.038	0.039	0.035	0.031	0.039	0.030	0.042	0.029	0.033	0.036	0.040	0.031	0.038	0.035	0.033	0.030	0.033	0.037	0.038	0.032	0.031	0.042	0.033	0.030	0.038	0.040	0.039	0.033	0.314
N03BA	0.253	0.324	0.275	0.313	0.324	0.272	0.309	0.327	0.338	0.348	0.286	0.240	0.255	0.274	0.294	0.258	0.266	0.266	0.269	0.260	0.286	0.258	0.266	0.244	0.244	0.287	0.248	0.244	0.298	0.254	0.245	0.265	0.265	0.271	0.241	0.249	0.215	0.295	0.256	0.239	0.267	0.248	0.257	0.271	0.259	0.282	0.266	2.778
N05CD	0.117	0.140	0.120	0.157	0.143	0.122	0.136	0.141	0.175	0.169	0.134	0.131	0.104	0.119	0.141	0.120	0.122	0.119	0.110	0.116	0.124	0.131	0.115	0.107	0.098	0.115	0.109	0.102	0.119	0.108	0.106	0.090	0.119	0.113	0.114	0.102	0.097	0.098	0.098	0.096	0.102	0.094	0.097	0.102	0.094	0.110	0.106	1.183
Z-drugs																																																
N05CF	0.184	0.203	0.189	0.211	0.203	0.215	0.205	0.218	0.230	0.236	0.188	0.206	0.157	0.178	0.188	0.192	0.182	0.183	0.169	0.169	0.199	0.200	0.167	0.184	0.164	0.210	0.166	0.183	0.190	0.184	0.183	0.215	0.194	0.232	0.187	0.185	0.170	0.203	0.177	0.185	0.201	0.184	0.196	0.215	0.195	0.210	0.213	2.229
Group 55-77																																																
Antidepressive	**0.279**	**0.328**	**0.311**	**0.316**	**0.349**	**0.325**	**0.338**	**0.325**	**0.403**	**0.412**	**0.285**	**0.299**	**0.296**	**0.316**	**0.316**	**0.323**	**0.298**	**0.326**	**0.305**	**0.330**	**0.348**	**0.388**	**0.299**	**0.328**	**0.283**	**0.337**	**0.303**	**0.313**	**0.375**	**0.327**	**0.292**	**0.360**	**0.345**	**0.335**	**0.321**	**0.303**	**0.260**	**0.339**	**0.328**	**0.317**	**0.357**	**0.308**	**0.332**	**0.336**	**0.316**	**0.386**	**0.332**	**3.818**
N06AA	0.053	0.058	0.055	0.053	0.061	0.061	0.057	0.063	0.073	0.074	0.049	0.056	0.058	0.049	0.052	0.050	0.051	0.058	0.049	0.061	0.067	0.067	0.049	0.062	0.044	0.059	0.051	0.058	0.066	0.053	0.046	0.066	0.056	0.055	0.060	0.051	0.042	0.061	0.055	0.057	0.066	0.048	0.062	0.054	0.049	0.069	0.052	0.614
N06AB	0.113	0.154	0.115	0.140	0.142	0.139	0.153	0.141	0.172	0.176	0.122	0.123	0.123	0.155	0.132	0.133	0.133	0.140	0.127	0.140	0.142	0.178	0.115	0.143	0.123	0.130	0.139	0.130	0.159	0.131	0.120	0.153	0.152	0.144	0.139	0.124	0.108	0.129	0.133	0.134	0.145	0.135	0.135	0.144	0.129	0.145	0.138	1.562
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000
N06AX	0.113	0.116	0.141	0.123	0.146	0.124	0.128	0.120	0.158	0.162	0.115	0.120	0.115	0.112	0.132	0.140	0.113	0.128	0.130	0.129	0.140	0.142	0.135	0.124	0.116	0.148	0.113	0.125	0.149	0.142	0.125	0.149	0.137	0.137	0.122	0.128	0.119	0.148	0.139	0.126	0.146	0.127	0.134	0.139	0.138	0.172	0.141	1.641
Antipsychotics																																																
N05A	0.047	0.059	0.063	0.068	0.054	0.070	0.061	0.049	0.061	0.062	0.067	0.060	0.051	0.060	0.064	0.058	0.050	0.058	0.052	0.060	0.058	0.055	0.056	0.060	0.050	0.054	0.062	0.061	0.061	0.057	0.056	0.057	0.061	0.069	0.058	0.051	0.053	0.060	0.055	0.055	0.059	0.058	0.050	0.059	0.062	0.064	0.060	0.693
Benzodiazepines	**0.442**	**0.500**	**0.498**	**0.579**	**0.531**	**0.511**	**0.552**	**0.529**	**0.625**	**0.622**	**0.472**	**0.505**	**0.429**	**0.474**	**0.492**	**0.473**	**0.444**	**0.488**	**0.446**	**0.459**	**0.538**	**0.586**	**0.442**	**0.460**	**0.423**	**0.541**	**0.481**	**0.429**	**0.564**	**0.469**	**0.433**	**0.509**	**0.515**	**0.553**	**0.437**	**0.456**	**0.414**	**0.511**	**0.446**	**0.424**	**0.507**	**0.442**	**0.482**	**0.480**	**0.461**	**0.553**	**0.498**	**5.419**
N03AE	0.020	0.033	0.028	0.029	0.023	0.025	0.026	0.035	0.031	0.036	0.026	0.029	0.022	0.028	0.024	0.022	0.019	0.027	0.027	0.025	0.030	0.035	0.028	0.022	0.023	0.030	0.025	0.022	0.037	0.028	0.026	0.028	0.030	0.038	0.028	0.025	0.027	0.027	0.029	0.026	0.036	0.028	0.028	0.025	0.030	0.037	0.030	0.281
N03BA	0.284	0.312	0.307	0.376	0.338	0.322	0.349	0.336	0.395	0.388	0.297	0.324	0.273	0.288	0.319	0.311	0.282	0.303	0.282	0.289	0.337	0.359	0.271	0.292	0.279	0.328	0.306	0.273	0.344	0.293	0.276	0.319	0.325	0.347	0.271	0.288	0.265	0.323	0.280	0.267	0.310	0.271	0.299	0.311	0.278	0.333	0.321	3.510
N05CD	0.137	0.154	0.161	0.174	0.169	0.164	0.177	0.159	0.199	0.198	0.149	0.152	0.133	0.158	0.150	0.139	0.143	0.158	0.157	0.145	0.171	0.173	0.143	0.147	0.121	0.183	0.150	0.134	0.183	0.148	0.130	0.162	0.159	0.168	0.137	0.143	0.122	0.161	0.138	0.131	0.162	0.143	0.156	0.144	0.152	0.183	0.146	1.628
Z-drugs																																																
N05CF	0.164	0.209	0.184	0.220	0.209	0.191	0.205	0.215	0.262	0.257	0.190	0.177	0.198	0.175	0.186	0.195	0.183	0.183	0.174	0.203	0.202	0.227	0.183	0.198	0.172	0.202	0.180	0.189	0.222	0.193	0.168	0.218	0.201	0.245	0.181	0.190	0.195	0.225	0.193	0.196	0.213	0.188	0.206	0.225	0.219	0.246	0.201	2.425
Group 78-87																																																
Antidepressive	**0.185**	**0.210**	**0.190**	**0.223**	**0.201**	**0.201**	**0.216**	**0.216**	**0.247**	**0.242**	**0.196**	**0.192**	**0.194**	**0.191**	**0.198**	**0.206**	**0.204**	**0.221**	**0.192**	**0.218**	**0.222**	**0.215**	**0.185**	**0.212**	**0.169**	**0.208**	**0.215**	**0.189**	**0.223**	**0.210**	**0.196**	**0.216**	**0.196**	**0.214**	**0.174**	**0.182**	**0.179**	**0.189**	**0.182**	**0.185**	**0.206**	**0.190**	**0.191**	**0.203**	**0.206**	**0.231**	**0.234**	**2.759**
N06AA	0.033	0.041	0.040	0.041	0.031	0.036	0.048	0.036	0.044	0.044	0.042	0.030	0.039	0.039	0.032	0.029	0.041	0.043	0.038	0.037	0.035	0.030	0.031	0.038	0.026	0.031	0.041	0.036	0.039	0.037	0.034	0.038	0.038	0.038	0.031	0.032	0.028	0.029	0.036	0.037	0.032	0.034	0.035	0.031	0.035	0.039	0.039	0.536
N06AB	0.076	0.094	0.085	0.095	0.085	0.093	0.095	0.083	0.115	0.102	0.078	0.087	0.086	0.081	0.087	0.096	0.079	0.092	0.089	0.089	0.097	0.095	0.085	0.101	0.073	0.098	0.093	0.076	0.105	0.093	0.088	0.094	0.083	0.087	0.084	0.081	0.073	0.082	0.073	0.071	0.095	0.082	0.084	0.094	0.090	0.096	0.097	1.137
N06AG	0.000	0.001	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.076	0.075	0.064	0.087	0.084	0.071	0.072	0.096	0.088	0.096	0.076	0.075	0.069	0.070	0.079	0.080	0.083	0.086	0.086	0.092	0.090	0.089	0.089	0.073	0.070	0.079	0.080	0.077	0.079	0.079	0.074	0.084	0.076	0.089	0.059	0.069	0.078	0.078	0.072	0.077	0.079	0.084	0.073	0.078	0.080	0.097	0.098	1.085
Antipsychotics																																																
N05A	0.040	0.055	0.037	0.052	0.046	0.038	0.053	0.052	0.051	0.050	0.043	0.042	0.038	0.042	0.042	0.042	0.044	0.045	0.039	0.041	0.054	0.052	0.040	0.042	0.041	0.051	0.058	0.054	0.057	0.047	0.056	0.043	0.042	0.045	0.038	0.051	0.049	0.059	0.045	0.040	0.053	0.044	0.052	0.050	0.047	0.055	0.061	0.582
Benzodiazepines	**0.383**	**0.444**	**0.413**	**0.431**	**0.430**	**0.412**	**0.445**	**0.416**	**0.483**	**0.473**	**0.358**	**0.385**	**0.379**	**0.362**	**0.387**	**0.402**	**0.358**	**0.404**	**0.396**	**0.375**	**0.418**	**0.440**	**0.322**	**0.398**	**0.355**	**0.433**	**0.417**	**0.387**	**0.438**	**0.372**	**0.338**	**0.360**	**0.380**	**0.429**	**0.345**	**0.349**	**0.335**	**0.411**	**0.319**	**0.340**	**0.363**	**0.349**	**0.367**	**0.422**	**0.379**	**0.466**	**0.417**	**5.230**
N03AE	0.024	0.020	0.027	0.021	0.023	0.023	0.030	0.021	0.033	0.023	0.028	0.018	0.019	0.017	0.027	0.022	0.020	0.023	0.024	0.021	0.021	0.025	0.013	0.029	0.024	0.023	0.021	0.029	0.030	0.028	0.019	0.028	0.024	0.021	0.023	0.014	0.020	0.021	0.022	0.020	0.022	0.018	0.018	0.022	0.023	0.034	0.024	0.229
N03BA	0.219	0.265	0.235	0.251	0.248	0.242	0.261	0.238	0.277	0.262	0.195	0.215	0.220	0.218	0.214	0.232	0.200	0.235	0.237	0.219	0.242	0.266	0.200	0.231	0.206	0.268	0.245	0.234	0.252	0.225	0.190	0.221	0.224	0.261	0.199	0.201	0.196	0.247	0.191	0.205	0.207	0.209	0.215	0.245	0.219	0.268	0.234	3.105
N05CD	0.120	0.159	0.151	0.159	0.159	0.147	0.154	0.158	0.174	0.188	0.136	0.152	0.139	0.127	0.146	0.149	0.138	0.146	0.135	0.135	0.155	0.149	0.109	0.138	0.124	0.142	0.151	0.124	0.157	0.121	0.128	0.120	0.132	0.147	0.123	0.134	0.118	0.144	0.107	0.116	0.133	0.122	0.134	0.155	0.137	0.164	0.159	1.696
Z-drugs																																																
N05CF	0.124	0.139	0.147	0.154	0.124	0.119	0.155	0.127	0.166	0.143	0.110	0.143	0.115	0.123	0.139	0.138	0.115	0.115	0.129	0.118	0.138	0.150	0.104	0.139	0.120	0.143	0.144	0.129	0.146	0.134	0.118	0.125	0.139	0.159	0.105	0.135	0.125	0.151	0.119	0.143	0.145	0.128	0.147	0.143	0.132	0.183	0.160	1.922
Group 88_plus																																																
Antidepressive	**0.025**	**0.031**	**0.043**	**0.041**	**0.037**	**0.033**	**0.039**	**0.035**	**0.048**	**0.038**	**0.038**	**0.035**	**0.048**	**0.037**	**0.040**	**0.047**	**0.038**	**0.045**	**0.043**	**0.034**	**0.037**	**0.039**	**0.035**	**0.044**	**0.035**	**0.057**	**0.058**	**0.048**	**0.061**	**0.047**	**0.044**	**0.039**	**0.044**	**0.046**	**0.041**	**0.048**	**0.045**	**0.050**	**0.048**	**0.043**	**0.041**	**0.051**	**0.044**	**0.049**	**0.044**	**0.054**	**0.060**	**0.837**
N06AA	0.004	0.004	0.007	0.006	0.006	0.003	0.008	0.006	0.007	0.006	0.006	0.005	0.010	0.005	0.008	0.005	0.006	0.008	0.005	0.005	0.005	0.005	0.007	0.007	0.007	0.007	0.007	0.009	0.007	0.004	0.006	0.005	0.008	0.008	0.006	0.009	0.007	0.007	0.007	0.006	0.003	0.007	0.008	0.008	0.011	0.009	0.009	0.203
N06AB	0.012	0.016	0.018	0.018	0.018	0.020	0.015	0.014	0.021	0.015	0.021	0.013	0.018	0.018	0.015	0.019	0.015	0.021	0.021	0.013	0.013	0.018	0.015	0.019	0.020	0.026	0.024	0.020	0.027	0.023	0.017	0.020	0.019	0.017	0.019	0.014	0.015	0.023	0.018	0.016	0.015	0.018	0.020	0.020	0.016	0.028	0.028	0.288
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.011	0.011	0.018	0.018	0.012	0.011	0.016	0.015	0.020	0.017	0.011	0.016	0.021	0.013	0.017	0.022	0.016	0.016	0.017	0.016	0.018	0.017	0.013	0.018	0.013	0.024	0.026	0.019	0.028	0.019	0.020	0.013	0.018	0.020	0.017	0.025	0.023	0.020	0.023	0.021	0.023	0.026	0.016	0.022	0.017	0.017	0.024	0.346
Antipsychotics																																																
N05A	0.015	0.021	0.016	0.016	0.019	0.021	0.017	0.017	0.019	0.019	0.016	0.021	0.021	0.022	0.026	0.017	0.013	0.021	0.015	0.025	0.025	0.023	0.019	0.018	0.018	0.017	0.029	0.020	0.025	0.024	0.025	0.021	0.023	0.019	0.023	0.031	0.023	0.027	0.020	0.018	0.027	0.020	0.024	0.024	0.023	0.027	0.034	0.333
Benzodiazepines	**0.083**	**0.

Dataset: **Gender:** **F**

	Pre-COVID																								COVID																								
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	2.046	2.380	2.079	2.366	2.360	2.117	2.383	2.337	2.756	2.629	2.314	2.258	2.015	2.118	2.154	2.235	2.109	2.169	2.055	2.280	2.433	2.340	2.140	2.322	1.951	2.265	1.999	1.999	2.390	2.163	2.065	2.344	2.305	2.202	2.287	2.101	1.959	2.344	2.152	2.075	2.336	2.055	2.145	2.311	2.167	2.328	2.326	26.312
N06AA	0.278	0.340	0.280	0.314	0.321	0.289	0.328	0.313	0.385	0.390	0.308	0.298	0.298	0.274	0.289	0.299	0.279	0.303	0.283	0.314	0.339	0.301	0.272	0.316	0.293	0.303	0.268	0.270	0.308	0.282	0.263	0.308	0.317	0.298	0.311	0.276	0.271	0.335	0.302	0.287	0.316	0.270	0.314	0.280	0.264	0.324	0.292	3.720
N06AB	0.898	1.075	0.936	1.068	1.041	0.968	1.047	1.045	1.221	1.175	1.031	1.012	0.888	0.956	0.972	1.012	0.951	0.962	0.931	1.025	1.064	1.089	0.987	1.064	0.900	1.036	0.916	0.891	1.091	0.967	0.932	1.053	1.007	0.970	1.028	0.931	0.827	0.993	0.952	0.908	1.033	0.927	0.917	1.041	0.949	0.988	1.017	11.545
N06AG	0.002	0.003	0.001	0.001	0.000	0.001	0.001	0.002	0.001	0.001	0.001	0.000	0.001	0.002	0.001	0.000	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.001	0.000	0.001	0.000	0.001	0.007
N06AX	0.868	0.962	0.862	0.983	0.999	0.858	1.007	0.977	1.169	1.083	0.974	0.948	0.828	0.887	0.911	0.924	0.878	0.902	0.860	0.939	1.029	0.949	0.880	0.942	0.817	0.926	0.814	0.838	0.991	0.914	0.870	0.982	0.981	0.933	0.946	0.893	0.861	1.015	0.897	0.879	0.986	0.858	0.913	0.991	0.933	1.016	1.017	11.041
Antipsychotics	0.344	0.417	0.363	0.427	0.393	0.372	0.416	0.380	0.473	0.428	0.397	0.384	0.343	0.385	0.368	0.376	0.381	0.370	0.323	0.372	0.400	0.400	0.345	0.377	0.331	0.375	0.391	0.377	0.415	0.384	0.371	0.370	0.385	0.382	0.381	0.346	0.354	0.385	0.369	0.335	0.376	0.362	0.390	0.371	0.387	0.392	0.414	4.766
N05A	0.344	0.417	0.363	0.427	0.393	0.372	0.416	0.380	0.473	0.428	0.397	0.384	0.343	0.385	0.368	0.376	0.381	0.370	0.323	0.372	0.400	0.400	0.345	0.377	0.331	0.375	0.391	0.377	0.415	0.384	0.371	0.370	0.385	0.382	0.381	0.346	0.354	0.385	0.369	0.335	0.376	0.362	0.390	0.371	0.387	0.392	0.414	4.766
Benzodiazepines	2.009	2.340	2.141	2.414	2.339	2.139	2.378	2.361	2.651	2.581	2.119	2.197	1.907	2.022	2.104	2.120	1.938	2.048	2.002	2.081	2.242	2.276	1.910	2.098	1.859	2.289	2.073	1.939	2.254	2.000	1.849	2.031	2.118	2.175	1.970	1.979	1.829	2.253	1.877	1.860	2.070	1.868	1.974	2.125	2.001	2.251	2.133	24.214
N05AE	0.183	0.172	0.173	0.183	0.171	0.164	0.194	0.200	0.207	0.212	0.198	0.175	0.151	0.161	0.166	0.161	0.140	0.164	0.164	0.178	0.181	0.181	0.154	0.169	0.136	0.191	0.157	0.161	0.197	0.164	0.152	0.180	0.179	0.169	0.168	0.151	0.165	0.193	0.161	0.151	0.192	0.157	0.159	0.168	0.160	0.201	0.173	1.782
N05BA	1.309	1.528	1.380	1.558	1.525	1.376	1.535	1.535	1.722	1.627	1.326	1.402	1.211	1.305	1.353	1.390	1.244	1.323	1.282	1.354	1.439	1.478	1.238	1.360	1.228	1.488	1.331	1.259	1.437	1.297	1.189	1.342	1.389	1.417	1.263	1.305	1.179	1.490	1.238	1.234	1.338	1.233	1.292	1.394	1.268	1.435	1.393	15.050
N05CD	0.517	0.639	0.588	0.672	0.642	0.600	0.649	0.626	0.723	0.743	0.594	0.620	0.544	0.556	0.585	0.570	0.555	0.561	0.556	0.549	0.622	0.620	0.518	0.569	0.495	0.610	0.585	0.519	0.620	0.519	0.508	0.509	0.551	0.589	0.519	0.525	0.484	0.570	0.478	0.475	0.540	0.479	0.523	0.563	0.533	0.615	0.567	6.812
Z-drugs	0.714	0.839	0.808	0.878	0.830	0.804	0.856	0.861	0.995	0.938	0.750	0.808	0.724	0.703	0.739	0.790	0.729	0.725	0.711	0.741	0.818	0.824	0.720	0.791	0.673	0.777	0.718	0.722	0.804	0.756	0.693	0.819	0.778	0.905	0.726	0.764	0.731	0.850	0.732	0.763	0.806	0.736	0.797	0.866	0.804	0.888	0.849	9.588
N05CF	0.714	0.839	0.808	0.878	0.830	0.804	0.856	0.861	0.995	0.938	0.750	0.808	0.724	0.703	0.739	0.790	0.729	0.725	0.711	0.741	0.818	0.824	0.720	0.791	0.673	0.777	0.718	0.722	0.804	0.756	0.693	0.819	0.778	0.905	0.726	0.764	0.731	0.850	0.732	0.763	0.806	0.736	0.797	0.866	0.804	0.888	0.849	9.588
Z-drugs	7.140	8.390	8.080	8.780	8.300	8.040	8.560	8.610	9.950	9.380	7.500	8.080	7.240	7.030	7.390	7.900	7.290	7.250	7.110	7.410	8.180	8.240	7.200	7.910	6.730	7.770	7.180	7.220	8.040	7.560	6.930	8.190	7.780	9.050	7.260	7.640	7.310	8.500	7.320	7.630	8.060	7.360	7.970	8.660	8.040	8.880	8.490	96.880
Antidepressive	20.460	23.800	20.790	23.660	23.600	21.170	23.830	23.370	27.560	26.290	23.140	22.580	20.150	21.180	21.540	22.350	21.090	21.690	20.550	22.800	24.330	23.400	21.400	23.220	19.510	22.650	19.990	19.990	23.900	21.630	20.650	23.440	23.050	22.020	22.870	21.010	19.590	23.440	21.520	20.750	23.360	20.550	21.450	23.110	21.870	23.280	23.260	283.12
Antipsychotics	3.440	4.170	3.630	4.270	3.930	3.720	4.160	3.800	4.730	4.280	3.970	3.840	3.430	3.850	3.680	3.760	3.810	3.700	3.230	3.720	4.000	4.000	3.450	3.770	3.310	3.750	3.910	3.770	4.150	3.840	3.710	3.700	3.850	3.820	3.810	3.460	3.540	3.850	3.690	3.350	3.760	3.620	3.900	3.710	3.870	3.920	4.140	47.660
Benzodiazepines	20.090	23.400	21.410	24.140	23.390	21.390	23.780	23.610	26.510	25.810	21.190	21.970	19.070	20.220	21.040	21.200	19.380	20.480	20.020	20.810	22.420	22.760	19.100	20.980	18.590	22.890	20.730	19.390	22.540	20.000	18.490	20.310	21.180	21.750	19.700	19.790	18.290	22.530	18.770	18.800	20.700	18.680	19.740	21.250	20.010	22.510	21.330	242.14

Supplementary table 8.3. Male absolute amount of prescriptions classified per medication type, time period and age groups. Calculate absolute differences can be found at the bottom of the table.

Dataset **Gender: M**

	Pre-COVID																								COVID																							
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	1361	1543	1384	1608	1551	1474	1580	1520	1861	1787	1582	1788	1696	1701	1883	1806	1868	1763	1847	1838	1968	1882	1710	1840	1748	2064	1728	1788	2034	1878	1824	2100	2027	1843	2061	1875	1794	2084	1908	1870	2088	1881	2000	2047	1945	2121	2161	1878
N06AA	164	185	184	206	194	187	204	187	241	237	197	220	183	212	221	214	226	208	208	216	223	265	221	248	215	249	223	220	232	250	220	231	271	265	265	251	219	266	237	244	270	227	229	247	252	267	243	258
N06AB	589	651	592	683	687	625	652	652	778	751	659	749	697	706	689	761	705	763	706	806	869	764	749	844	744	911	690	779	853	809	772	899	840	801	879	798	740	911	783	763	875	786	858	869	850	883	916	810
N06AG	4	2	3	3	4	2	2	3	2	4	3	2	1	2	3	3	0	5	4	6	3	1	3	2	3	0	0	2	0	0	0	2	2	2	2	1	1	0	2	1	0	3	0	0	0	3	0	0
N06AX	594	705	615	716	666	660	702	678	830	795	723	815	715	781	780	828	728	777	729	811	874	832	737	846	786	894	813	788	949	817	832	968	914	875	905	825	834	907	884	862	944	845	913	931	843	968	992	910
Antipsychotics																																																
N05A	390	455	441	507	498	434	460	478	514	488	476	566	440	533	501	513	528	526	474	517	547	522	526	552	520	625	606	579	629	625	581	592	633	633	635	588	587	689	673	556	665	540	588	651	563	611	667	646
Benzodiazepines	1889	1928	1788	1923	1888	1739	1868	1771	2124	2037	1741	2033	1806	1818	1967	1997	1805	1921	1888	1990	2129	1998	1872	2166	1888	2274	2060	2060	2148	2080	1938	2099	2184	2213	2035	2002	1868	2317	1864	2041	2112	2062	1868	2268	2037	2210	2181	1981
N03AE	122	147	139	151	150	134	148	127	156	173	134	156	135	139	163	160	157	136	142	165	168	173	153	180	140	161	151	154	169	177	162	180	174	199	179	159	175	199	176	169	185	188	160	202	192	207	202	165
N05BA	1113	1289	1203	1297	1274	1170	1227	1200	1389	1334	1140	1346	1163	1217	1290	1321	1195	1298	1247	1324	1441	1287	1232	1407	1279	1511	1352	1360	1420	1358	1278	1411	1460	1464	1337	1335	1339	1536	1320	1377	1379	1353	1300	1482	1335	1455	1406	1261
N05CD	434	492	444	475	442	435	484	444	579	530	467	531	508	463	514	516	453	487	497	501	520	538	487	568	479	602	557	536	557	545	498	508	560	550	519	508	474	582	458	495	548	511	499	572	510	548	553	555
Z-drugs																																																
N05CF	529	595	535	569	603	523	605	597	727	661	554	750	594	631	617	672	622	647	628	648	758	710	614	742	687	713	676	678	743	657	703	735	763	758	742	734	650	794	737	673	738	702	735	801	727	774	804	749
Group 18-27																																																
Antidepressive	86	74	80	84	81	88	98	75	102	88	88	103	94	83	68	88	87	82	82	80	91	86	95	114	73	90	88	82	112	99	103	115	124	93	134	95	107	102	103	120	113	99	113	112	109	104	123	116
N06AA	4	3	7	4	7	6	8	1	11	5	10	12	6	12	4	3	6	5	3	4	7	10	9	12	9	9	5	10	8	6	8	8	14	7	15	8	5	11	9	5	12	13	12	10	6	7	12	8
N06AB	40	41	31	58	34	40	49	43	52	55	40	54	50	40	35	41	46	57	54	41	59	45	47	64	40	49	52	38	58	46	48	65	60	47	62	51	56	53	54	76	57	57	59	56	59	57	59	52
N06AG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	0
N06AX	21	30	22	22	20	23	41	31	39	38	38	37	38	31	29	44	35	30	25	35	25	31	39	38	24	32	31	34	46	47	47	42	50	39	57	36	46	38	40	38	44	29	42	46	44	38	52	55
Antipsychotics																																																
N05A	25	42	30	36	41	42	32	41	45	48	37	56	42	43	38	43	36	50	34	36	51	45	41	33	34	36	40	39	47	46	49	51	54	49	51	48	44	51	40	46	51	42	30	53	43	36	43	41
Benzodiazepines	37	61	48	66	61	35	42	50	48	68	47	51	40	42	48	60	52	47	48	48	68	68	50	42	36	63	42	38	40	40	55	60	53	64	48	47	53	62	38	42	68	42	41	68	63	58	58	42
N03AE	3	3	5	7	1	3	5	4	0	7	6	2	5	6	4	4	8	2	3	5	6	7	5	2	3	3	2	4	2	3	4	8	5	2	3	2	3	4	2	2	5	3	3	3	3	9	2	3
N05BA	31	55	39	44	46	32	34	42	41	47	37	46	33	34	39	38	39	41	39	39	47	46	43	31	26	39	37	30	32	33	48	38	44	48	43	42	46	46	32	36	50	38	37	52	53	47	52	37
N05CD	3	3	4	5	4	0	3	4	7	5	4	3	2	2	3	8	5	4	4	2	5	6	2	9	6	11	3	5	6	4	3	4	4	4	3	3	4	2	4	4	1	1	1	4	7	3	5	2
Z-drugs																																																
N05CF	5	13	14	10	13	8	10	15	14	11	9	14	10	11	8	12	10	7	5	13	6	15	11	11	8	9	5	7	4	4	11	11	9	5	10	10	7	7	9	9	7	7	9	11	4	8	11	12
Group 28-37																																																
Antidepressive	183	162	150	180	184	188	169	183	208	189	188	183	176	177	176	189	183	211	173	217	206	183	197	189	189	202	148	167	200	189	181	211	180	203	244	217	177	253	217	209	216	214	228	217	187	240	238	184
N06AA	17	12	13	18	20	17	14	18	25	14	18	21	15	15	22	19	20	19	9	15	10	22	16	16	21	28	14	15	17	19	15	21	23	13	25	19	21	26	16	20	12	18	16	22	19	16	18	16
N06AB	80	75	81	83	97	79	81	71	101	86	91	89	103	94	89	93	75	107	95	120	104	99	98	98	89	106	72	95	99	96	96	111	97	117	126	122	91	134	123	101	116	99	120	118	104	137	132	105
N06AG	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
N06AX	66	65	56	59	67	70	64	74	82	68	79	73	58	68	65	87	68	85	69	82	92	62	83	75	79	68	60	57	84	74	70	79	70	73	93	76	65	93	78	88	88	96	92	77	64	87	89	73
Antipsychotics																																																
N05A	69	59	67	85	70	63	65	77	80	79	86	92	52	80	71	70	78	77	64	80	80	79	81	98	70	94	73	79	84	80	96	85	91	86	107	88	97	98	139	85	100	80	94	92	72	96	97	87
Benzodiazepines	143	163	163	176	168	134	169	148	182	166	99	173	118	128	182	141	143	142	147	165	187	148	129	180	128	164	145	142	157	149	134	168	151	168	138	135	161	187	148	143	168	142	138	161	134	133	138	123
N03AE	13	12	15	16	14	10	8	14	13	21	10	16	11	12	15	11	5	16	18	13	17	13	13	18	8	11	3	7	14	17	10	19	10	19	15	10	20	14	17	18	16	16	9	14	13	12	14	14
N05BA	116	127	130	146	126	113	131	118	137	133	84	148	97	105	134	120	126	116	116	124	141	121	101	142	110	127	131	121	136	119	114	115	132	130	113	106	118	142	126	112	128	114	112	128	111	108	113	90
N05CD	14	14	18	13	16	11	20	17	12	11	5	9	8	9	13	10	12	10	13	18	9	15	15	20	10	16	11	14	7	13	10	14	9	7	10	19	13	11	5	13	14	12	17	19	10	13	11	19
Z-drugs																																																
N05CF	31	26	22	26	33	36	36	41	51	33	33	41	32	31	28	37	41	39	35	34	39	37	25	34	43	39	42	35	35	37	51	51	44	38	47	47	42	53	50	46	40	45	45	45	41	47	47	41
Group 38-47																																																
Antidepressive	222	278	229	260	262	220	262	263	279	291	262	299	246	268	252	284	279	274	261	323	338	318	266	318	286	310	288	298	302	301	312	328	321	287	363	305	281	360	316	295	333	248	316	337	307	306	333	322
N06AA	22	24	15	19	26	29	24	28	33	29	27	37	20	34	33	31	23	38	27	40	30	46	24	32	37	24	29	35	25	31	35	24	33	33	41	27	31	41	37	31	33	31	33	26	30	37	40	33
N06AB	105	124	114	112	131	114	113	116	122	143	114	138	104	133	110	134	135	131	132	149	157	129	118	160	137	159	98	143	137	155	149	157	145	127	166	142	124	172	142	125	162	117	150	139	129	145	142	142
N06AG	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N06AX	95	130	99	119	104	76	125	109	124	119	111	124	122	101	109	118	121	104	91	134	149	143	113	126	111	127	142	120	140	115	128	147	143	127	146	136	126	137	137	139	138	100	132	172	148	123	151	147
Antipsychotics																																																
N05A	76	96	106	106	114	97	103	102	114	91	90	124	92	118	117	122	126	96	97	120	114	107	104	123	115	129	129	130	129	137	111	123	114	121	127	103	109	128	129	100	129	116	104	135	123	127	119	142
Benzodiazepines	206	242	238	247	241	236	211	202	271	240	229	260	226	236	248	269	243	219	214	272	284	208	246	276	238	286	236	265	251	282	231	302	299	260	282	265	258	331	242	262	260	242	245	292	239	261	232	211
N03AE	18	24	20	22	20	17	19	14	28	21	25	20	17	15	25	14	26	15	17	32	28	19	23	23	21	28	24	24	23	30	20	26	25	27	28	27	23	30	20	26	25	27	28	28	23	30	28	15
N05BA	156	173	183	187	186	178	158	153	191	172	160	198	166	181	181	211	182	177	168	195	216	150	188	220	180	221	182	202	200	207	172	229	234	188	194	210	197	259	180	198	202	178	192	223	173	187	161	156
N05CD	31	45	36	38	35	40	34	35	52	47	44	42	43	39	42	34	35	27	29	45	40	37	34	33	35	36	29	39	28	35	32	45	38	39	43	34	40	42	42	38	33	37	25	41	43	44	43	40
Z-drugs																																																
N05CF	44	65	42	55	71	52	54	67	64	58	73	74	60	60	66	61	59	72	66	81	82	47	58	67	65	45	44	50	63	65	54	62	68	64	78	79	71	69	79	67	61	81	80	67	76	56	75	60
Group 48-57																																																
Antidepressive	302	338	338	381	347	340	342	372	383	409	371	407	360	386	378	387	368	382	368	407	414	386	394	383	383	443	365	368	438	384	379	462	417	381	421	381	364	448	368	381	431	380	387	407	429	422	443	389
N06AA	28	45	39	46	46	31	37	53	52	57	36	37	36	37	47	42	56	47	44	39	56	38	54	53	32	51	45	40	48	47	48	54	65	59	58	58	46	62	42	56	51	40	49	49	57	65	48	50
N06AB	126	139	140	152	146	137	145	159	164	176	152	167	149	142	156	174	138	160	139	182	177	161	180	167	167	197	146	148	192	168	149	188	166	149	168	146	138	193	132	142	180	168	166	173	196	158	191	170
N06AG	1	0	0	0	0	0	2	0	0	0	2	0	0	0	0	2	0	1	1	1	1	0	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0
N06AX	147	155	157	163	155	172	158	160	167	176	181	203	165	187	175	179	165	174	174	185	180	186	160	163	163	195	164	171	199	169	182	209	186	172	194	187	180	191	183	183	200	182	182	185	176	199	204	179
Antipsychotics																																																
N05A	80	80	90	98	90	82	93	73	86	88	82	99	83	82	84	91	90	94	88	92	104	90	107	96	97	121	119	100	117	116	92	101	121	93	110	98	95	134	115	106	111	98	108	109	102	102	98	100
Benzodiazepines	320	368	323	364	321	291	311	311	413	320	320	367	328	292	331	384	288	311	316	340	387	317	338	346	316	367	325	325	366	345	334	363	364	374	361	311	340	364	348	364	345	344	329	345	381	362	347	318
N03AE	33	37	29	41	36	33	36	37	38	42	28	46	36	27	39	41	34	26	31	31	41	31	44	33	30	31	36	27	39	30	35	35	34	43	37	41	42	40	39	39	47	41	27	41	50	41	38	35
N05BA	212	342	236	237	227	204	216	216	277	207	219	236	203	199	211	260	194	216	214	240	264	216	221	235	223	254	209	217	240	240	227	252	249	255	234	211	239	239	261	258	218	244	239	234	245	256	254	217
N05CD	75	79	58	76	58	54	59	58	98	71	73	75	84	66	81	73	60	69	70	69	82	70	73	78	62	72	80	81	87	75	72	66	71	76	80	59	59	75	48	67	80	59	63	70	66	65	55	66
Z-drugs																																																
N05CF	97	106	81	91	94	87	95	88	128	96	109	120	108	102	113	108	123	91	113	114	116	119	106	116	123	108	109	95	130	106	110	114	118	109	127	117	95	126	103	91	115	105	119	133	110	98	124	96

Dataset **Gender: M**

	Pre-COVID																						COVID																								
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressiva	1361	1543	1384	1608	1551	1474	1580	1520	1861	1787	1682	1788	1596	1701	1893	1806	1668	1763	1847	1838	1968	1882	1710	1840	1748	2064	1728	1789	2034	1878	1824	2100	2027	1943	2061	1875	1784	2084	1906	1870	2088	1861	2000	2047	1945	2121	2161	1978
N06AA	164	185	184	206	194	187	204	187	241	237	197	220	183	212	221	214	226	208	208	216	223	265	221	248	215	249	223	220	232	250	220	231	271	265	265	251	219	266	237	244	270	227	229	247	252	267	243	258
N06AB	589	651	592	683	687	625	652	652	778	751	659	749	697	706	689	761	705	763	706	806	859	764	749	844	744	911	690	779	853	809	772	899	840	801	879	798	740	911	783	763	875	786	858	869	850	883	916	810
N06AG	4	2	3	3	4	2	2	3	2	4	3	2	1	2	3	3	0	5	4	6	3	1	3	2	3	0	0	2	0	0	0	2	2	2	2	1	1	0	2	1	0	3	0	0	0	3	0	0
N06AX	594	705	615	716	666	660	702	678	830	795	723	815	715	781	780	828	728	777	729	811	874	832	737	846	786	894	813	788	949	817	832	968	914	875	905	825	834	907	884	862	944	845	913	931	843	968	992	910
Antipsychotica																																																
N05A	390	455	441	507	498	434	460	478	514	488	476	556	440	533	501	513	528	526	474	517	547	522	526	552	520	625	606	579	629	625	581	592	633	633	635	588	587	689	673	556	665	540	588	651	563	611	667	646
Benzodiazepines	1888	1928	1788	1923	1886	1738	1868	1771	2124	2037	1741	2033	1808	1819	1987	1897	1805	1921	1888	1890	2129	1988	1872	2165	1888	2274	2060	2060	2148	2080	1938	2089	2184	2213	2035	2002	1868	2317	1864	2041	2112	2062	1868	2268	2037	2210	2181	1881
N03AE	122	147	139	151	150	134	148	127	156	173	134	156	135	139	163	160	157	136	142	165	168	173	153	180	140	161	151	154	169	177	162	180	174	199	179	159	175	199	176	169	185	188	160	202	192	207	202	165
N05BA	1113	1289	1203	1297	1274	1170	1227	1200	1389	1334	1140	1346	1163	1217	1290	1321	1195	1298	1247	1324	1441	1287	1232	1407	1279	1511	1352	1360	1420	1358	1278	1411	1460	1464	1337	1335	1339	1536	1320	1377	1379	1353	1300	1482	1335	1455	1406	1251
N05CD	434	492	444	475	442	435	484	444	579	530	467	531	508	463	514	516	453	487	497	501	520	538	487	568	479	602	557	536	557	545	498	508	560	550	519	508	474	582	458	495	548	511	499	572	510	548	553	555
Z-drugs																																															
N05CF	529	595	535	569	603	523	605	597	727	661	554	750	594	631	617	672	622	647	628	648	758	710	614	742	687	713	676	678	743	657	703	735	763	758	742	734	650	794	737	673	738	702	735	801	727	774	804	749
Group 58-67																																															
Antidepressiva	275	319	279	315	316	316	318	301	403	387	303	381	338	370	388	386	360	341	368	381	431	408	382	435	411	481	398	385	469	421	380	487	443	445	442	381	404	445	417	388	485	414	433	464	431	464	495	418
N06AA	47	48	49	42	47	46	54	40	52	57	50	50	46	52	50	54	51	44	54	42	55	72	57	54	48	72	50	55	61	52	51	49	52	71	50	57	52	55	59	52	84	50	54	62	61	57	61	72
N06AB	112	128	100	124	131	97	116	126	146	132	118	138	133	135	129	149	139	121	129	138	162	158	138	163	139	184	142	155	174	169	134	177	179	167	167	156	164	169	146	143	167	157	158	183	160	174	199	160
N06AG	0	1	0	1	0	0	0	2	0	1	1	0	0	0	2	0	0	1	0	2	0	0	0	1	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
N06AX	116	142	130	148	137	173	148	133	205	177	134	193	160	183	188	192	170	175	185	179	214	176	167	217	223	205	174	185	234	190	205	241	211	207	224	178	188	221	212	203	234	207	221	219	210	233	235	187
Antipsychotica																																															
N05A	55	81	67	90	80	59	68	85	73	84	77	81	75	80	75	81	103	89	75	70	76	81	92	82	83	105	92	105	107	99	87	99	105	110	106	112	96	122	112	102	119	80	109	111	91	106	119	96
Benzodiazepines	373	408	383	404	379	380	401	389	421	462	380	428	370	382	418	404	378	426	406	386	419	425	418	468	420	481	422	421	488	447	420	429	464	462	481	388	414	481	430	420	481	437	437	477	443	480	483	420
N03AE	26	25	35	24	34	38	39	27	26	36	25	34	24	30	38	38	34	30	21	32	28	41	34	37	34	34	33	35	37	48	36	36	44	37	47	29	40	37	36	34	38	42	42	47	46	46	54	34
N05BA	241	270	237	268	250	255	251	269	269	309	244	278	231	247	273	260	241	280	266	255	281	270	266	302	278	335	279	287	300	266	284	287	291	294	296	271	296	323	292	290	309	287	290	319	298	298	312	272
N05CD	106	111	91	112	95	97	111	93	126	107	111	116	115	115	105	106	103	115	118	98	110	114	116	120	108	122	110	99	129	133	100	106	119	121	118	88	88	121	102	96	114	108	105	111	99	116	127	114
Z-drugs																																															
N05CF	110	134	121	115	137	93	145	135	151	153	116	159	120	134	120	148	121	155	124	157	177	147	135	169	137	170	141	153	153	140	155	166	176	191	173	158	140	181	146	154	170	139	152	174	158	192	167	198
Group 68-77																																															
Antidepressiva	187	237	200	282	212	222	248	203	291	282	219	293	237	267	287	258	260	287	244	288	293	303	283	301	288	330	291	298	309	298	284	342	308	335	301	272	298	303	293	301	311	314	304	305	295	361	297	297
N06AA	36	36	34	50	30	38	44	20	44	52	33	39	40	42	43	39	43	30	43	44	42	55	41	52	48	40	48	43	44	54	45	47	53	55	46	50	36	46	49	54	48	47	37	52	50	47	38	45
N06AB	67	90	80	86	76	93	96	80	116	97	83	88	82	93	102	98	102	97	93	103	113	108	105	116	104	128	109	115	120	113	119	132	106	117	131	100	93	128	100	106	113	125	112	115	127	122	108	100
N06AG	0	0	0	1	2	1	0	0	1	0	0	2	0	1	0	0	0	1	1	0	1	0	1	0	0	0	0	1	0	0	0	1	1	1	0	1	0	0	0	0	1	0	0	0	0	1	0	0
N06AX	84	111	86	125	104	90	109	103	130	133	103	104	115	131	122	121	105	139	107	121	137	140	116	133	114	162	134	139	145	132	120	162	146	162	124	121	137	129	144	141	150	141	155	138	118	181	151	152
Antipsychotica																																															
N05A	41	48	43	42	47	44	57	53	51	55	51	51	47	66	49	44	53	63	52	55	60	58	45	58	66	74	67	61	75	69	62	74	72	82	65	65	63	78	63	51	74	52	68	75	63	68	83	77
Benzodiazepines	338	383	387	370	382	381	408	378	425	480	381	404	378	384	448	418	387	430	383	437	486	488	383	458	407	483	474	447	487	478	412	443	482	626	427	426	418	488	388	416	420	481	378	477	381	488	438	400
N03AE	19	34	21	24	31	19	23	19	31	27	27	22	21	34	30	34	30	26	31	33	31	39	22	39	20	33	33	27	33	38	30	34	34	38	33	36	29	43	35	28	22	35	24	46	38	36	36	33
N05BA	223	249	226	249	245	240	263	239	263	295	246	247	247	252	281	264	224	284	240	272	303	285	236	280	260	294	294	293	301	302	252	278	292	339	272	258	258	285	249	267	256	288	220	295	230	301	271	245
N05CD	94	110	120	97	116	102	122	118	131	138	108	135	111	98	135	120	113	120	122	132	131	145	125	140	127	166	147	127	133	136	130	131	156	148	122	132	129	140	104	120	142	138	132	136	123	129	131	122
Z-drugs																																															
N05CF	143	138	141	139	148	139	146	147	188	194	115	195	152	164	163	163	151	170	168	130	196	195	161	188	174	190	185	189	199	170	177	203	198	193	168	175	157	200	207	166	204	176	190	212	185	214	212	197
Group 78-87																																															
Antidepressiva	119	125	118	168	148	128	114	131	184	146	144	166	124	137	148	167	138	163	141	148	166	167	123	188	127	186	171	181	186	160	142	182	191	184	120	183	168	157	170	131	174	162	170	188	163	190	184	182
N06AA	10	15	23	25	16	17	21	26	24	20	21	20	17	17	19	24	24	23	24	26	18	21	19	25	18	20	27	18	25	28	16	24	26	21	26	25	22	22	19	18	25	24	21	21	25	28	22	28
N06AB	50	44	37	61	63	60	43	47	65	52	54	66	62	53	60	58	55	73	50	56	70	54	51	67	49	79	60	73	55	49	63	61	75	61	43	61	58	51	71	54	70	51	73	71	60	81	73	69
N06AG	3	1	2	1	1	0	0	1	1	2	0	0	1	1	1	0	0	0	1	3	1	1	2	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0
N06AX	56	65	54	69	68	49	50	57	74	71	69	69	44	66	69	75	57	57	66	63	66	81	51	74	59	96	84	69	85	73	63	77	90	82	51	77	78	84	79	59	79	76	76	74	68	81	89	95
Antipsychotica																																															
N05A	39	39	30	40	42	41	33	36	54	38	43	44	36	46	53	44	33	40	41	49	49	40	42	43	41	52	61	45	55	60	61	47	52	72	54	54	47	63	53	48	68	54	57	55	46	60	82	75
Benzodiazepines	214	282	241	273	273	266	288	264	338	291	245	307	291	297	288	297	272	286	308	299	314	308	272	318	298	368	330	341	327	295	300	301	327	331	290	345	284	382	281	333	347	328	330	369	330	388	378	361
N03AE	10	10	12	14	12	14	17	9	18	17	11	14	18	11	10	16	15	19	17	16	16	19	11	24	20	18	16	28	18	17	18	18	16	25	17	19	16	27	25	20	30	24	25	17	18	29	25	26
N05BA	116	158	130	145	168	132	156	148	188	156	129	171	159	174	150	152	159	152	174	169	174	174	157	170	180	199	186	181	180	162	159	170	184	187	164	199	160	211	146	186	189	177	175	193	188	218	209	187
N05CD	88	114	99	114	93	109	113	97	132	118	105	122	114	112	109	129	98	114	115	114	124	113	104	124	96	141	128	132	129	116	123	113	127	119	109	127	108	144	120	127	128	127	130	149	124	141	142	148
Z-drugs																																															
N05CF	84	103	99	117	92	96	107	92	114	100	90	121	97	103	102	119	94	96	103	100	119	127	105	134	113	119	118	119	129	108	125	107	118	135	110	120	108	133	119	109	115	119	120	130	132	120	139	113
Group 88_plus																																															
Antidepressiva	18	19	24	20	22	15	18	22	21	28	17	25	30	33	34	28	25	33	30	36	33	24	21	34	34	23	40	29	38	33	33	23	35	35	36	41	38	28	32	35	28	30	40	38	34	45	37	40
N06AA	0	2	4	2	2	3	2	1	0	3	2	4	3	3	3	2	3	2	4	6	5	1	1	4	2	5	5	4	4	3	2	4	5	6	4	7	5	3	6	8	5	4	7	5	4	10	4	6
N06AB	9	10	9	7	9	5	9	10	12	10	7	9	14	16	8	14	15	17	14	17	17	10	12	9	19	9	11	12	18	13	14	8	12	16	16	20	16	11	15	16	10	12	20	14	15	9	12	12
N06AG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N06AX	9	7	11	11	11	7	7	11	9	13	8	12	13	14	23	12	7	13	12	12	11	13	8	20	13	9	24	13	16	17	17	11	18	13	16	14	14	14	11	11	11	14	13	20	15	26	21	22
Antipsychotica																																															
N05A	5	10	8	10	14	6	9	11	11	5	10	9	13	18	14	18	9	17	23	15	13	22	14	19	14	14	25	20	15	18	23	12	24	20	15	20	36	15	22	18	13	18	18	21	23	16	26	28
Benzodiazepines	41	33	42	44	53	38	41	40	48	50	40	53	81	61	48	64	62	82	60	68	36	67	38	76	61	83	87	70	72	68	62	63	74	81	67	86	72	82	89	82	86	68	83	88	78	81	78	106
N03AE	0	2	2	3	2	0	1	3	2	2	2	2	3	4	2	2	5	2	4	3	1	4	1	4	4	3	4	2	3	4	2	2	4	2	2	1	4	4	2	2	2	0	2	6	1	4	5	5
N05BA	18	15	22	21	26	16	18	15	23	15	21	22	27	25	21	26	30	32	30	30	15	25	20	27	22	42	34	29	31	29	22	22	34	23	21	38	35	31	34	30	27	27	35	38	37	40	34	57
N05CD	23	16	18	20	25	22	22	22	21	33	17	29	31	22	26	36	27	28	26	23	19	38	18	44	35	38	49	39	38	33	28	29	36	36	34	46	33	47	33	30	36	29	26	42	38	37	39	44
Z-drugs																																															
N05CF	15	10	15	16	15	12	12	12	17	16	9	26	15	26	17	24	23	17	14	19	23	23	13	23	24	33	32	30	30	27	20	21	32	23	29	28	30	25	24	31	26	30	20	29	21	39	29	32

Total absolute prescriptions count per age group, Pre-COVID versus COVID

Age groups	18-27	28-37	38-47	48-57	58-67	68-77	78-87	88+
Antipsychotics precovid	967	1802	2555	2142	1879	1233	995	303
Antipsychotics postcovid	1064	2170	2929	2563	2473	1647	1362	474
Z-drugs precovid	255	821	1498	2521	3276	3834	2514	412
Z-drugs postcovid	194	1051	1579	2681	3884	4541	2878	665
Antidepressants precovid	2037	4312	6501	8882	8429	6015	3389	607
Antidepressants postcovid	2528	4930	7413	9651	10370	7270	3909	822
Benzo precovid	1163	3588	5749	7951	9680	9703	6785	1202
Benzo postcovid	1163	3493	6228	8267	10644	10595	7950	1717

Calculated differences in absolute prescriptions, Pre-COVID versus COVID

Som AD pre covid	40172	Percentage verschil	16,73%
Som AD post covid	46893		
Som AP pre covid	11876	Percentage verschil	23.63
Som AP post covid	14682		
Som benzo pre covid	45821	Percentage verschil	9.24%
Som benzo post covid	50057		
Som Z-drugs pre covid	15131	Percentage verschil	15.48
Som Z-drugs post covid	17473		

Supplementary table 8.4. Male prescription rates classified per medication type, time period and age groups. Calculate prescription rates per 1000 patients can be found at the bottom 4 lines of the table.

Dataset: **Gender:** **M**

	Pre-COVID																								COVID																								
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**	**46**	**47**	**48**
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	**0.961**	**1.097**	**0.991**	**1.144**	**1.103**	**1.048**	**1.110**	**1.081**	**1.316**	**1.271**	**1.125**	**1.084**	**0.968**	**1.032**	**1.027**	**1.096**	**1.007**	**1.064**	**0.999**	**1.116**	**1.189**	**1.130**	**1.038**	**1.070**	**0.964**	**1.133**	**0.952**	**0.987**	**1.122**	**1.035**	**1.006**	**1.158**	**1.118**	**1.072**	**1.131**	**1.020**	**0.976**	**1.134**	**1.037**	**1.017**	**1.138**	**1.012**	**1.088**	**1.113**	**1.058**	**1.154**	**1.170**	**12.931**
N06AA	0.117	0.132	0.131	0.147	0.138	0.133	0.145	0.133	0.171	0.169	0.140	0.133	0.111	0.129	0.134	0.130	0.137	0.126	0.126	0.131	0.135	0.161	0.134	0.137	0.119	0.137	0.123	0.121	0.128	0.138	0.121	0.127	0.149	0.146	0.146	0.137	0.119	0.145	0.129	0.133	0.147	0.123	0.125	0.134	0.137	0.145	0.132	1.687
N06AB	0.419	0.483	0.421	0.486	0.489	0.445	0.464	0.464	0.553	0.534	0.489	0.454	0.423	0.428	0.418	0.462	0.428	0.463	0.428	0.489	0.521	0.484	0.454	0.486	0.410	0.503	0.381	0.430	0.471	0.446	0.426	0.496	0.483	0.442	0.485	0.434	0.402	0.496	0.426	0.415	0.476	0.428	0.467	0.473	0.462	0.480	0.498	5.295
N06AG	0.003	0.001	0.002	0.002	0.003	0.001	0.001	0.002	0.001	0.003	0.002	0.001	0.001	0.001	0.002	0.002	0.000	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.000	0.002	0.000	0.000	0.000	0.000	0.002	0.000	0.000
N06AX	0.422	0.501	0.437	0.509	0.474	0.469	0.499	0.482	0.590	0.565	0.514	0.495	0.434	0.474	0.473	0.502	0.442	0.471	0.442	0.492	0.530	0.505	0.447	0.487	0.434	0.493	0.448	0.435	0.524	0.451	0.459	0.534	0.504	0.483	0.499	0.449	0.454	0.493	0.481	0.469	0.513	0.460	0.497	0.506	0.459	0.527	0.540	5.949
Antipsychotics	**0.277**	**0.324**	**0.314**	**0.361**	**0.354**	**0.309**	**0.327**	**0.340**	**0.366**	**0.347**	**0.339**	**0.337**	**0.267**	**0.323**	**0.304**	**0.311**	**0.320**	**0.319**	**0.288**	**0.314**	**0.332**	**0.317**	**0.319**	**0.305**	**0.287**	**0.345**	**0.334**	**0.319**	**0.347**	**0.345**	**0.321**	**0.327**	**0.349**	**0.349**	**0.350**	**0.320**	**0.319**	**0.375**	**0.366**	**0.302**	**0.362**	**0.294**	**0.320**	**0.354**	**0.306**	**0.332**	**0.363**	**4.223**
N05A	0.277	0.324	0.314	0.361	0.354	0.309	0.327	0.340	0.366	0.347	0.339	0.337	0.267	0.323	0.304	0.311	0.320	0.319	0.288	0.314	0.332	0.317	0.319	0.305	0.287	0.345	0.334	0.319	0.347	0.345	0.321	0.327	0.349	0.349	0.350	0.320	0.319	0.375	0.366	0.302	0.362	0.294	0.320	0.354	0.306	0.332	0.363	4.223
Benzodiazepines	**1.187**	**1.371**	**1.270**	**1.368**	**1.327**	**1.237**	**1.322**	**1.260**	**1.511**	**1.449**	**1.238**	**1.234**	**1.095**	**1.104**	**1.194**	**1.212**	**1.095**	**1.166**	**1.144**	**1.208**	**1.292**	**1.212**	**1.136**	**1.189**	**1.047**	**1.254**	**1.136**	**1.131**	**1.184**	**1.147**	**1.069**	**1.158**	**1.210**	**1.221**	**1.123**	**1.089**	**1.081**	**1.260**	**1.063**	**1.110**	**1.149**	**1.116**	**1.066**	**1.227**	**1.108**	**1.202**	**1.175**	**12.950**
N05AE	0.087	0.105	0.099	0.107	0.107	0.095	0.105	0.090	0.111	0.123	0.095	0.095	0.082	0.084	0.099	0.097	0.095	0.083	0.086	0.100	0.102	0.105	0.093	0.099	0.077	0.089	0.083	0.085	0.093	0.098	0.089	0.099	0.096	0.110	0.099	0.086	0.095	0.108	0.098	0.092	0.101	0.102	0.087	0.110	0.104	0.113	0.110	1.079
N05BA	0.792	0.917	0.856	0.922	0.906	0.832	0.873	0.853	0.988	0.949	0.811	0.817	0.706	0.738	0.783	0.802	0.725	0.788	0.757	0.803	0.874	0.781	0.748	0.776	0.706	0.834	0.746	0.750	0.783	0.749	0.705	0.778	0.805	0.808	0.738	0.726	0.728	0.835	0.718	0.749	0.750	0.736	0.707	0.806	0.726	0.791	0.765	8.243
N05CD	0.309	0.350	0.316	0.338	0.314	0.309	0.344	0.316	0.412	0.377	0.332	0.322	0.306	0.281	0.312	0.313	0.275	0.296	0.302	0.304	0.316	0.326	0.296	0.313	0.264	0.332	0.307	0.296	0.307	0.301	0.275	0.260	0.309	0.303	0.286	0.276	0.258	0.317	0.249	0.269	0.298	0.278	0.271	0.311	0.277	0.298	0.301	3.828
Z-drugs	**0.376**	**0.423**	**0.381**	**0.405**	**0.429**	**0.372**	**0.430**	**0.425**	**0.517**	**0.470**	**0.394**	**0.455**	**0.360**	**0.383**	**0.374**	**0.408**	**0.377**	**0.393**	**0.381**	**0.393**	**0.460**	**0.431**	**0.373**	**0.409**	**0.379**	**0.393**	**0.373**	**0.374**	**0.410**	**0.362**	**0.388**	**0.405**	**0.421**	**0.418**	**0.409**	**0.399**	**0.354**	**0.432**	**0.401**	**0.366**	**0.401**	**0.382**	**0.400**	**0.436**	**0.395**	**0.421**	**0.437**	**4.896**
N05CF	0.376	0.423	0.381	0.405	0.429	0.372	0.430	0.425	0.517	0.470	0.394	0.455	0.360	0.383	0.374	0.408	0.377	0.393	0.381	0.393	0.460	0.431	0.373	0.409	0.379	0.393	0.373	0.374	0.410	0.362	0.388	0.405	0.421	0.418	0.409	0.399	0.354	0.432	0.401	0.366	0.401	0.382	0.400	0.436	0.395	0.421	0.437	4.896
Group 18-27																																																	
Antidepressive	**0.046**	**0.053**	**0.043**	**0.060**	**0.043**	**0.049**	**0.070**	**0.053**	**0.073**	**0.070**	**0.063**	**0.063**	**0.057**	**0.050**	**0.041**	**0.053**	**0.053**	**0.056**	**0.050**	**0.049**	**0.055**	**0.052**	**0.058**	**0.063**	**0.040**	**0.050**	**0.049**	**0.045**	**0.062**	**0.055**	**0.057**	**0.063**	**0.068**	**0.051**	**0.074**	**0.052**	**0.058**	**0.055**	**0.056**	**0.065**	**0.061**	**0.054**	**0.061**	**0.061**	**0.059**	**0.057**	**0.067**	**0.752**
N06AA	0.003	0.002	0.005	0.003	0.005	0.004	0.006	0.001	0.008	0.004	0.007	0.007	0.004	0.007	0.002	0.002	0.004	0.003	0.002	0.002	0.004	0.006	0.005	0.007	0.005	0.005	0.003	0.006	0.004	0.003	0.004	0.004	0.008	0.004	0.008	0.004	0.003	0.006	0.005	0.003	0.007	0.007	0.007	0.005	0.003	0.004	0.007	0.052
N06AB	0.028	0.029	0.022	0.041	0.024	0.028	0.035	0.031	0.037	0.039	0.028	0.033	0.030	0.024	0.021	0.025	0.028	0.035	0.033	0.025	0.036	0.027	0.029	0.035	0.022	0.027	0.029	0.021	0.032	0.025	0.026	0.036	0.033	0.026	0.034	0.028	0.030	0.029	0.029	0.041	0.031	0.031	0.032	0.030	0.032	0.031	0.032	0.340
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000
N06AX	0.015	0.021	0.016	0.016	0.014	0.016	0.029	0.022	0.028	0.027	0.027	0.022	0.023	0.019	0.018	0.027	0.021	0.018	0.015	0.021	0.015	0.019	0.024	0.021	0.013	0.018	0.017	0.019	0.025	0.026	0.026	0.029	0.028	0.022	0.031	0.020	0.025	0.021	0.022	0.021	0.024	0.016	0.023	0.025	0.024	0.021	0.028	0.360
Antipsychotics																																																
N05A	0.018	0.030	0.021	0.026	0.029	0.030	0.023	0.029	0.032	0.034	0.026	0.034	0.025	0.026	0.023	0.026	0.022	0.030	0.021	0.022	0.031	0.027	0.025	0.018	0.019	0.020	0.022	0.022	0.026	0.025	0.027	0.028	0.030	0.027	0.028	0.026	0.024	0.028	0.022	0.025	0.026	0.023	0.016	0.029	0.023	0.020	0.023	0.268
Benzodiazepines	**0.026**	**0.043**	**0.034**	**0.040**	**0.038**	**0.025**	**0.030**	**0.036**	**0.034**	**0.042**	**0.033**	**0.031**	**0.024**	**0.025**	**0.028**	**0.030**	**0.032**	**0.029**	**0.028**	**0.028**	**0.035**	**0.036**	**0.030**	**0.023**	**0.019**	**0.029**	**0.023**	**0.022**	**0.022**	**0.022**	**0.030**	**0.028**	**0.029**	**0.030**	**0.027**	**0.026**	**0.029**	**0.028**	**0.021**	**0.023**	**0.030**	**0.023**	**0.022**	**0.032**	**0.034**	**0.032**	**0.032**	**0.275**
N05AE	0.002	0.002	0.004	0.005	0.001	0.002	0.004	0.003	0.000	0.005	0.004	0.001	0.003	0.004	0.002	0.002	0.005	0.001	0.002	0.003	0.004	0.004	0.003	0.001	0.002	0.002	0.001	0.002	0.001	0.002	0.002	0.004	0.003	0.001	0.002	0.001	0.002	0.002	0.001	0.001	0.003	0.002	0.002	0.002	0.002	0.005	0.001	0.020
N05BA	0.022	0.039	0.026	0.031	0.033	0.023	0.024	0.030	0.029	0.033	0.026	0.028	0.020	0.021	0.024	0.023	0.024	0.025	0.024	0.024	0.029	0.028	0.026	0.017	0.014	0.022	0.020	0.017	0.018	0.018	0.026	0.021	0.024	0.026	0.024	0.023	0.025	0.025	0.017	0.020	0.027	0.021	0.020	0.026	0.029	0.026	0.028	0.242
N05CD	0.002	0.002	0.003	0.004	0.003	0.000	0.002	0.003	0.005	0.004	0.003	0.002	0.001	0.001	0.002	0.005	0.003	0.002	0.002	0.001	0.003	0.004	0.001	0.005	0.003	0.006	0.002	0.003	0.003	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.002	0.004	0.002	0.003	0.013
Z-drugs																																																
N05CF	0.004	0.009	0.010	0.007	0.009	0.006	0.007	0.011	0.010	0.008	0.006	0.008	0.006	0.007	0.005	0.007	0.006	0.004	0.003	0.008	0.004	0.009	0.007	0.006	0.004	0.005	0.003	0.004	0.002	0.002	0.006	0.006	0.005	0.003	0.006	0.005	0.004	0.004	0.005	0.005	0.004	0.004	0.005	0.006	0.002	0.004	0.006	0.078
Group 28-37																																																
Antidepressive	**0.116**	**0.108**	**0.107**	**0.114**	**0.131**	**0.118**	**0.113**	**0.116**	**0.148**	**0.120**	**0.134**	**0.111**	**0.107**	**0.107**	**0.107**	**0.121**	**0.099**	**0.128**	**0.105**	**0.132**	**0.125**	**0.111**	**0.120**	**0.104**	**0.104**	**0.111**	**0.081**	**0.092**	**0.110**	**0.104**	**0.100**	**0.116**	**0.105**	**0.112**	**0.135**	**0.118**	**0.096**	**0.138**	**0.118**	**0.114**	**0.117**	**0.116**	**0.124**	**0.118**	**0.102**	**0.131**	**0.130**	**1.268**
N06AA	0.012	0.009	0.009	0.013	0.014	0.012	0.010	0.013	0.018	0.010	0.013	0.013	0.009	0.009	0.013	0.012	0.012	0.012	0.005	0.009	0.006	0.013	0.010	0.009	0.012	0.015	0.008	0.008	0.009	0.010	0.008	0.012	0.013	0.007	0.014	0.010	0.011	0.014	0.009	0.011	0.007	0.010	0.009	0.012	0.010	0.009	0.010	0.105
N06AB	0.057	0.053	0.058	0.059	0.069	0.056	0.058	0.050	0.072	0.061	0.065	0.054	0.063	0.057	0.054	0.056	0.046	0.065	0.058	0.073	0.063	0.060	0.059	0.054	0.049	0.058	0.040	0.052	0.055	0.053	0.053	0.061	0.054	0.065	0.070	0.066	0.049	0.073	0.067	0.055	0.063	0.054	0.065	0.064	0.057	0.075	0.072	0.886
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000
N06AX	0.047	0.046	0.040	0.042	0.048	0.050	0.046	0.053	0.058	0.048	0.056	0.044	0.035	0.041	0.039	0.053	0.041	0.052	0.042	0.050	0.056	0.038	0.050	0.041	0.044	0.038	0.033	0.031	0.046	0.041	0.039	0.044	0.039	0.040	0.051	0.041	0.035	0.051	0.042	0.048	0.048	0.052	0.050	0.042	0.035	0.047	0.048	0.477
Antipsychotics																																																
N05A	0.049	0.042	0.048	0.060	0.050	0.045	0.048	0.055	0.057	0.056	0.061	0.056	0.032	0.049	0.043	0.042	0.047	0.047	0.039	0.049	0.049	0.048	0.049	0.054	0.039	0.052	0.042	0.040	0.044	0.046	0.044	0.053	0.047	0.050	0.047	0.059	0.048	0.053	0.053	0.076	0.048	0.054	0.044	0.051	0.050	0.039	0.052	0.053	0.569
Benzodiazepines	**0.102**	**0.109**	**0.116**	**0.124**	**0.111**	**0.095**	**0.113**	**0.106**	**0.115**	**0.117**	**0.070**	**0.105**	**0.070**	**0.076**	**0.068**	**0.086**	**0.087**	**0.086**	**0.089**	**0.094**	**0.101**	**0.090**	**0.078**	**0.099**	**0.071**	**0.085**	**0.080**	**0.078**	**0.087**	**0.082**	**0.074**	**0.093**	**0.083**	**0.086**	**0.076**	**0.073**	**0.082**	**0.091**	**0.080**	**0.078**	**0.086**	**0.077**	**0.075**	**0.088**	**0.073**	**0.072**	**0.075**	**0.804**
N05AE	0.009	0.009	0.011	0.011	0.010	0.007	0.006	0.010	0.009	0.015	0.007	0.010	0.007	0.007	0.009	0.007	0.003	0.010	0.011	0.008	0.010	0.008	0.008	0.010	0.004	0.006	0.002	0.004	0.008	0.009	0.006	0.010	0.006	0.010	0.008	0.005	0.011	0.008	0.009	0.006	0.010	0.009	0.009	0.005	0.008	0.007	0.007	0.092
N05BA	0.083	0.090	0.092	0.104	0.090	0.080	0.093	0.084	0.097	0.095	0.060	0.090	0.059	0.064	0.061	0.073	0.076	0.070	0.070	0.075	0.086	0.073	0.061	0.078	0.061	0.070	0.072	0.067	0.075	0.066	0.063	0.074	0.073	0.072	0.062	0.056	0.064	0.077	0.069	0.061	0.070	0.062	0.061	0.070	0.060	0.059	0.061	0.588
N05CD	0.010	0.010	0.013	0.009	0.011	0.008	0.014	0.012	0.009	0.008	0.004	0.005	0.005	0.005	0.008	0.006	0.007	0.006	0.008	0.011	0.005	0.009	0.009	0.011	0.006	0.009	0.006	0.008	0.004	0.007	0.006	0.008	0.005	0.004	0.006	0.010	0.007	0.006	0.003	0.007	0.008	0.007	0.009	0.010	0.005	0.007	0.006	0.124
Z-drugs																																																
N05CF	0.022	0.018	0.016	0.018	0.023	0.026	0.026	0.029	0.036	0.023	0.023	0.025	0.019	0.019	0.017	0.022	0.025	0.024	0.021	0.021	0.024	0.022	0.015	0.019	0.024	0.022	0.023	0.019	0.019	0.020	0.026	0.026	0.024	0.021	0.026	0.026	0.023	0.029	0.027	0.025	0.022	0.024	0.024	0.024	0.022	0.026	0.026	0.288
Group 38-47																																																
Antidepressive	**0.158**	**0.198**	**0.163**	**0.178**	**0.186**	**0.156**	**0.186**	**0.180**	**0.198**	**0.207**	**0.179**	**0.181**	**0.149**	**0.163**	**0.153**	**0.172**	**0.169**	**0.166**	**0.152**	**0.196**	**0.204**	**0.193**	**0.155**	**0.175**	**0.157**	**0.171**	**0.148**	**0.164**	**0.167**	**0.166**	**0.172**	**0.181**	**0.177**	**0.158**	**0.195**	**0.166**	**0.153**	**0.190**	**0.172**	**0.160**	**0.181**	**0.135**	**0.171**	**0.183**	**0.167**	**0.166**	**0.181**	**2.105**
N06AA	0.016	0.017	0.011	0.014	0.018	0.021	0.017	0.020	0.023	0.021	0.019	0.022	0.012	0.021	0.020	0.019	0.014	0.023	0.016	0.024	0.018	0.028	0.015	0.018	0.020	0.013	0.016	0.019	0.014	0.017	0.019	0.013	0.018	0.018	0.023	0.015	0.017	0.022	0.020	0.017	0.018	0.017	0.018	0.014	0.016	0.020	0.022	0.216
N06AB	0.075	0.088	0.081	0.080	0.093	0.081	0.080	0.083	0.087	0.102	0.081	0.084	0.063	0.081	0.067	0.081	0.082	0.079	0.080	0.090	0.095	0.078	0.072	0.088	0.076	0.088	0.054	0.079	0.076	0.086	0.082	0.087	0.080	0.070	0.092	0.077	0.067	0.094	0.077	0.068	0.088	0.064	0.082	0.076	0.070	0.079	0.077	0.928
N06AG	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.068	0.092	0.070	0.085	0.074	0.054	0.089	0.078	0.088	0.085	0.079	0.075	0.074	0.061	0.066	0.072	0.073	0.063	0.055	0.081	0.090	0.087	0.069	0.070	0.061	0.070	0.078	0.066	0.077	0.063	0.071	0.081	0.079	0.070	0.061	0.074	0.069	0.075	0.075	0.076	0.075	0.054	0.072	0.064	0.060	0.067	0.082	0.961
Antipsychotics																																																
N05A	0.054	0.068	0.075	0.075	0.081	0.069	0.073	0.073	0.081	0.065	0.064	0.075	0.056	0.072	0.071	0.074	0.076	0.058	0.059	0.073	0.069	0.065	0.063	0.068	0.063	0.071	0.071	0.072	0.071	0.076	0.061	0.068	0.063	0.067	0.070	0.056	0.059	0.070	0.070	0.054	0.070	0.063	0.057	0.073	0.067	0.069	0.065	0.928
Benzodiazepines	**0.146**	**0.172**	**0.170**	**0.176**	**0.171**	**0.167**	**0.150**	**0.144**	**0.193**	**0.171**	**0.163**	**0.158**	**0.137**	**0.143**	**0.150**	**0.157**	**0.147**	**0.133**	**0.130**	**0.165**	**0.172**	**0.125**	**0.149**	**0.152**	**0.130**	**0.157**	**0.130**	**0.146**	**0.138**	**0.145**	**0.127**	**0.157**	**0.165**	**0.143**	**0.145**	**0.144**	**0.140**	**0.180**	**0.132**	**0.143**	**0.141**	**0.132**	**0.133**	**0.159**	**0.130**	**0.142**	**0.126**	**1.379**
N05AE	0.013	0.017	0.014	0.016	0.014	0.012	0.014	0.010	0.020	0.015	0.018	0.012	0.010	0.009	0.015	0.008	0.016	0.009	0.010	0.019	0.017	0.012	0.014	0.013	0.012	0.015	0.013	0.013	0.013	0.011	0.015	0.015	0.015	0.018	0.014	0.011	0.011	0.016	0.011	0.014	0.014	0.015	0.015	0.015	0.013	0.016	0.015	0.098
N05BA	0.111	0.123	0.130	0.133	0.132	0.127	0.112	0.109	0.136	0.122	0.114	0.120	0.101	0.110	0.110	0.128	0.110	0.107	0.102	0.118	0.131	0.091	0.114	0.121	0.099	0.122	0.100	0.111	0.110	0.114	0.095	0.129	0.129	0.104	0.107	0.114	0.107	0.141	0.098	0.108	0.110	0.097	0.104	0.121	0.094	0.102	0.088	1.020
N05CD	0.022	0.032	0.026	0.027	0.025	0.028	0.024	0.025	0.037	0.033	0.031	0.025	0.026	0.024	0.025	0.021	0.021	0.016	0.018	0.027	0.024	0.022	0.021	0.018	0.019	0.020	0.016	0.022	0.015	0.019	0.018	0.025	0.021	0.022	0.024	0.018	0.022	0.023	0.023	0.021	0.018	0.020	0.014	0.022	0.023	0.024	0.023	0.261
Z-drugs																																																
N05CF	0.031	0.046	0.030	0.039	0.050	0.037	0.038	0.048	0.046	0.041	0.052	0.045	0.036	0.036	0.040	0.037	0.036	0.044	0.040	0.049	0.050	0.029	0.035	0.037	0.036	0.025	0.024	0.028	0.035	0.036	0.030	0.034	0.038	0.035	0.043	0.043	0.039	0.038	0.043	0.036	0.033	0.044	0.044	0.036	0.041	0.030	0.041	0.392
Group 48-57																																																
Antidepressive	**0.215**	**0.241**	**0.239**	**0.257**	**0.247**	**0.242**	**0.243**	**0.265**	**0.272**	**0.291**	**0.264**	**0.247**	**0.212**	**0.222**	**0.229**	**0.241**	**0.218**	**0.232**	**0.217**	**0.247**	**0.251**	**0.234**	**0.239**	**0.211**	**0.200**	**0.244**	**0.196**	**0.198**	**0.242**	**0.212**	**0.209**	**0.249**	**0.230**	**0.210**	**0.232**	**0.213**	**0.198**	**0.243**	**0.195**	**0.207**	**0.234**	**0.212**	**0.216**	**0.221**	**0.233**	**0.230**	**0.241**	**2.608**
N06AA	0.020	0.032	0.028	0.033	0.033	0.022	0.026	0.038	0.037	0.041	0.026	0.022	0.022	0.022	0.029	0.025	0.034	0.029	0.027	0.024	0.034	0.023	0.033	0.029	0.018	0.028	0.025	0.022	0.026	0.026	0.026	0.026	0.030	0.036	0.033	0.032	0.025	0.034	0.023	0.030	0.028	0.022	0.027	0.027	0.031	0.035	0.026	0.327
N06AB	0.090	0.099	0.100	0.108	0.104	0.097	0.103	0.113	0.117	0.125	0.108	0.101	0.090	0.086	0.095	0.106	0.084	0.097	0.084	0.110	0.107	0.098	0.109	0.092	0.092	0.109	0.081	0.082	0.106	0.093	0.082	0.104	0.092	0.082	0.093	0.079	0.075	0.105	0.072	0.077	0.098	0.091	0.090	0.094	0.107	0.086	0.104	1.111
N06AG	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000

Dataset: **Gender:** **M**

	Pre-COVID																								COVID																								
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	**0.961**	**1.097**	**0.991**	**1.144**	**1.103**	**1.048**	**1.110**	**1.081**	**1.316**	**1.271**	**1.125**	**1.084**	**0.968**	**1.032**	**1.027**	**1.096**	**1.007**	**1.064**	**0.999**	**1.116**	**1.189**	**1.130**	**1.038**	**1.070**	**0.964**	**1.133**	**0.952**	**0.987**	**1.122**	**1.035**	**1.006**	**1.158**	**1.118**	**1.072**	**1.131**	**1.020**	**0.976**	**1.134**	**1.037**	**1.017**	**1.136**	**1.012**	**1.088**	**1.113**	**1.058**	**1.154**	**1.170**	**12.931**
N06AA	0.117	0.132	0.131	0.147	0.138	0.133	0.145	0.133	0.171	0.169	0.140	0.133	0.111	0.129	0.134	0.130	0.137	0.126	0.126	0.131	0.135	0.161	0.134	0.137	0.119	0.137	0.129	0.121	0.128	0.138	0.121	0.127	0.149	0.146	0.146	0.137	0.119	0.145	0.129	0.133	0.147	0.123	0.125	0.134	0.137	0.145	0.132	1.687
N06AB	0.419	0.463	0.421	0.486	0.469	0.445	0.464	0.464	0.553	0.534	0.469	0.454	0.423	0.428	0.418	0.462	0.428	0.463	0.428	0.469	0.521	0.464	0.454	0.466	0.410	0.503	0.381	0.430	0.471	0.446	0.426	0.496	0.463	0.442	0.465	0.434	0.402	0.496	0.426	0.415	0.476	0.428	0.467	0.473	0.462	0.480	0.498	5.295
N06AG	0.003	0.001	0.002	0.002	0.003	0.001	0.001	0.002	0.001	0.003	0.002	0.001	0.001	0.001	0.002	0.002	0.000	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.000	0.000	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.001	0.001	0.000	0.002	0.001	0.001	0.000	0.002	0.000	0.000	0.000	0.002	0.000	0.000
N06AX	0.422	0.501	0.437	0.509	0.474	0.469	0.499	0.482	0.590	0.565	0.514	0.495	0.434	0.474	0.473	0.502	0.442	0.471	0.442	0.492	0.530	0.505	0.447	0.467	0.434	0.493	0.448	0.435	0.524	0.451	0.459	0.534	0.504	0.483	0.499	0.449	0.454	0.493	0.481	0.469	0.513	0.460	0.497	0.506	0.459	0.527	0.540	5.949
Antipsychotics	**0.277**	**0.324**	**0.314**	**0.361**	**0.354**	**0.309**	**0.327**	**0.340**	**0.366**	**0.347**	**0.339**	**0.337**	**0.267**	**0.323**	**0.304**	**0.311**	**0.320**	**0.319**	**0.288**	**0.314**	**0.332**	**0.317**	**0.319**	**0.305**	**0.287**	**0.345**	**0.334**	**0.319**	**0.347**	**0.345**	**0.321**	**0.327**	**0.349**	**0.349**	**0.350**	**0.320**	**0.319**	**0.375**	**0.366**	**0.302**	**0.362**	**0.294**	**0.320**	**0.354**	**0.306**	**0.332**	**0.363**	**4.223**
N05A	0.277	0.324	0.314	0.361	0.354	0.309	0.327	0.340	0.366	0.347	0.339	0.337	0.267	0.323	0.304	0.311	0.320	0.319	0.288	0.314	0.332	0.317	0.319	0.305	0.287	0.345	0.334	0.319	0.347	0.345	0.321	0.327	0.349	0.349	0.350	0.320	0.319	0.375	0.366	0.302	0.362	0.294	0.320	0.354	0.306	0.332	0.363	4.223
Benzodiazepines	**1.187**	**1.371**	**1.270**	**1.368**	**1.327**	**1.237**	**1.322**	**1.260**	**1.511**	**1.449**	**1.238**	**1.234**	**1.096**	**1.104**	**1.194**	**1.212**	**1.095**	**1.166**	**1.144**	**1.208**	**1.292**	**1.212**	**1.136**	**1.189**	**1.047**	**1.254**	**1.136**	**1.131**	**1.184**	**1.147**	**1.069**	**1.158**	**1.210**	**1.221**	**1.123**	**1.089**	**1.081**	**1.260**	**1.063**	**1.110**	**1.149**	**1.116**	**1.066**	**1.227**	**1.108**	**1.202**	**1.175**	**12.950**
N03AE	0.087	0.105	0.099	0.107	0.107	0.095	0.105	0.090	0.111	0.123	0.095	0.095	0.082	0.084	0.099	0.097	0.095	0.083	0.086	0.100	0.102	0.105	0.093	0.099	0.077	0.089	0.083	0.085	0.093	0.098	0.089	0.099	0.096	0.110	0.099	0.086	0.095	0.108	0.096	0.092	0.101	0.102	0.087	0.110	0.104	0.113	0.110	1.079
N05BA	0.792	0.917	0.856	0.922	0.906	0.832	0.873	0.853	0.988	0.949	0.811	0.817	0.706	0.738	0.783	0.802	0.725	0.788	0.757	0.803	0.874	0.781	0.748	0.778	0.706	0.834	0.746	0.750	0.783	0.749	0.705	0.778	0.805	0.808	0.738	0.726	0.728	0.835	0.718	0.749	0.750	0.736	0.707	0.806	0.726	0.791	0.765	8.243
N05CD	0.309	0.350	0.316	0.338	0.314	0.309	0.344	0.316	0.412	0.377	0.332	0.322	0.308	0.281	0.312	0.313	0.275	0.296	0.302	0.304	0.316	0.326	0.296	0.313	0.264	0.332	0.307	0.296	0.307	0.301	0.275	0.280	0.309	0.303	0.286	0.276	0.258	0.317	0.249	0.269	0.298	0.278	0.271	0.311	0.277	0.298	0.301	3.826
Z-drugs	**0.376**	**0.423**	**0.381**	**0.405**	**0.429**	**0.372**	**0.430**	**0.425**	**0.517**	**0.470**	**0.394**	**0.455**	**0.360**	**0.383**	**0.374**	**0.408**	**0.377**	**0.393**	**0.381**	**0.393**	**0.460**	**0.431**	**0.373**	**0.409**	**0.379**	**0.393**	**0.373**	**0.374**	**0.410**	**0.362**	**0.388**	**0.405**	**0.421**	**0.418**	**0.409**	**0.399**	**0.354**	**0.432**	**0.401**	**0.366**	**0.401**	**0.382**	**0.400**	**0.436**	**0.395**	**0.421**	**0.437**	**4.896**
N05CF	0.376	0.423	0.381	0.405	0.429	0.372	0.430	0.425	0.517	0.470	0.394	0.455	0.360	0.383	0.374	0.408	0.377	0.393	0.381	0.393	0.460	0.431	0.373	0.409	0.379	0.393	0.373	0.374	0.410	0.362	0.388	0.405	0.421	0.418	0.409	0.399	0.354	0.432	0.401	0.366	0.401	0.382	0.400	0.436	0.395	0.421	0.437	4.896
N06AB	0.080	0.091	0.071	0.088	0.093	0.069	0.083	0.090	0.104	0.094	0.084	0.084	0.081	0.082	0.078	0.090	0.084	0.073	0.078	0.084	0.098	0.096	0.084	0.090	0.077	0.102	0.078	0.086	0.096	0.093	0.074	0.098	0.099	0.092	0.092	0.085	0.089	0.092	0.079	0.078	0.091	0.085	0.086	0.100	0.087	0.095	0.108	1.046
N06AG	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.001	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.083	0.101	0.092	0.105	0.097	0.123	0.105	0.095	0.146	0.126	0.095	0.117	0.097	0.111	0.114	0.117	0.103	0.106	0.112	0.109	0.130	0.107	0.101	0.120	0.123	0.113	0.096	0.102	0.129	0.105	0.113	0.133	0.116	0.114	0.124	0.097	0.102	0.120	0.115	0.110	0.127	0.113	0.120	0.119	0.114	0.127	0.128	1.222
Antipsychotics																																																
N05A	0.039	0.058	0.048	0.064	0.057	0.042	0.048	0.060	0.052	0.060	0.055	0.049	0.048	0.049	0.046	0.049	0.063	0.054	0.046	0.042	0.046	0.049	0.056	0.045	0.046	0.058	0.051	0.058	0.059	0.055	0.048	0.055	0.058	0.061	0.058	0.061	0.052	0.066	0.061	0.055	0.065	0.044	0.059	0.060	0.049	0.058	0.065	0.629
Benzodiazepines	**0.265**	**0.289**	**0.258**	**0.287**	**0.270**	**0.277**	**0.285**	**0.277**	**0.299**	**0.321**	**0.270**	**0.260**	**0.225**	**0.238**	**0.252**	**0.245**	**0.229**	**0.258**	**0.246**	**0.234**	**0.254**	**0.258**	**0.252**	**0.253**	**0.232**	**0.271**	**0.233**	**0.232**	**0.257**	**0.247**	**0.232**	**0.237**	**0.250**	**0.249**	**0.254**	**0.211**	**0.225**	**0.262**	**0.234**	**0.228**	**0.251**	**0.238**	**0.238**	**0.259**	**0.241**	**0.250**	**0.288**	**2.746**
N03AE	0.018	0.018	0.025	0.017	0.024	0.027	0.028	0.019	0.018	0.026	0.018	0.021	0.015	0.018	0.023	0.023	0.021	0.018	0.013	0.019	0.017	0.025	0.021	0.020	0.019	0.019	0.018	0.019	0.020	0.026	0.020	0.020	0.024	0.020	0.026	0.016	0.022	0.020	0.020	0.018	0.021	0.023	0.023	0.026	0.025	0.025	0.029	0.222
N05BA	0.171	0.192	0.169	0.191	0.178	0.181	0.179	0.191	0.191	0.220	0.174	0.169	0.140	0.150	0.166	0.158	0.146	0.170	0.161	0.155	0.171	0.164	0.161	0.167	0.153	0.185	0.154	0.158	0.165	0.147	0.157	0.158	0.161	0.162	0.163	0.147	0.156	0.178	0.159	0.158	0.168	0.156	0.158	0.174	0.162	0.162	0.170	1.778
N05CD	0.075	0.079	0.065	0.080	0.068	0.069	0.079	0.066	0.090	0.076	0.079	0.070	0.070	0.070	0.064	0.064	0.063	0.070	0.072	0.059	0.067	0.069	0.070	0.066	0.060	0.067	0.061	0.055	0.071	0.073	0.055	0.058	0.066	0.067	0.065	0.048	0.048	0.066	0.055	0.052	0.062	0.059	0.057	0.060	0.054	0.063	0.069	0.745
Z-drugs																																																
N05CF	0.078	0.095	0.086	0.082	0.097	0.068	0.103	0.096	0.107	0.109	0.083	0.096	0.073	0.081	0.073	0.090	0.073	0.094	0.075	0.095	0.107	0.089	0.082	0.093	0.076	0.094	0.078	0.084	0.084	0.077	0.088	0.092	0.097	0.105	0.095	0.086	0.076	0.098	0.079	0.084	0.092	0.076	0.083	0.095	0.086	0.104	0.091	1.294
Group 55-77																																																
Antidepressive	**0.133**	**0.169**	**0.142**	**0.186**	**0.151**	**0.158**	**0.177**	**0.144**	**0.207**	**0.201**	**0.156**	**0.141**	**0.144**	**0.162**	**0.162**	**0.157**	**0.152**	**0.162**	**0.148**	**0.163**	**0.178**	**0.164**	**0.160**	**0.166**	**0.147**	**0.182**	**0.161**	**0.164**	**0.170**	**0.165**	**0.157**	**0.189**	**0.169**	**0.185**	**0.166**	**0.148**	**0.145**	**0.165**	**0.159**	**0.164**	**0.169**	**0.171**	**0.165**	**0.166**	**0.160**	**0.191**	**0.162**	**1.942**
N06AA	0.026	0.026	0.024	0.036	0.021	0.027	0.031	0.014	0.031	0.037	0.023	0.024	0.024	0.025	0.026	0.024	0.026	0.018	0.026	0.027	0.025	0.033	0.025	0.029	0.026	0.022	0.029	0.024	0.024	0.030	0.025	0.026	0.029	0.030	0.025	0.027	0.020	0.025	0.027	0.029	0.026	0.026	0.020	0.026	0.027	0.026	0.021	0.294
N06AB	0.048	0.064	0.057	0.061	0.054	0.066	0.068	0.057	0.083	0.069	0.059	0.053	0.050	0.056	0.062	0.059	0.062	0.059	0.056	0.063	0.069	0.066	0.064	0.064	0.057	0.071	0.060	0.063	0.066	0.062	0.066	0.073	0.058	0.065	0.072	0.054	0.051	0.070	0.054	0.058	0.061	0.068	0.061	0.063	0.069	0.066	0.059	0.654
N06AG	0.000	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.001	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.000
N06AX	0.060	0.079	0.061	0.089	0.074	0.064	0.078	0.073	0.092	0.095	0.073	0.063	0.070	0.079	0.074	0.073	0.064	0.084	0.065	0.073	0.083	0.085	0.070	0.073	0.063	0.089	0.074	0.077	0.080	0.073	0.066	0.089	0.081	0.089	0.068	0.066	0.075	0.070	0.078	0.077	0.082	0.077	0.084	0.075	0.064	0.098	0.082	0.994
Antipsychotics																																																
N05A	0.029	0.034	0.031	0.030	0.033	0.031	0.041	0.038	0.036	0.039	0.036	0.031	0.029	0.040	0.030	0.027	0.032	0.038	0.032	0.033	0.036	0.035	0.027	0.032	0.036	0.041	0.037	0.034	0.041	0.038	0.034	0.041	0.040	0.045	0.036	0.035	0.034	0.042	0.034	0.028	0.040	0.029	0.037	0.041	0.034	0.037	0.045	0.503
Benzodiazepines	**0.239**	**0.280**	**0.261**	**0.283**	**0.279**	**0.257**	**0.290**	**0.267**	**0.302**	**0.327**	**0.271**	**0.245**	**0.230**	**0.233**	**0.271**	**0.254**	**0.223**	**0.261**	**0.238**	**0.265**	**0.282**	**0.265**	**0.232**	**0.253**	**0.225**	**0.272**	**0.261**	**0.247**	**0.258**	**0.263**	**0.227**	**0.244**	**0.266**	**0.290**	**0.236**	**0.232**	**0.226**	**0.255**	**0.211**	**0.226**	**0.225**	**0.251**	**0.205**	**0.259**	**0.213**	**0.253**	**0.238**	**2.615**
N03AE	0.014	0.024	0.015	0.017	0.022	0.014	0.016	0.014	0.022	0.019	0.019	0.013	0.013	0.021	0.018	0.021	0.018	0.016	0.019	0.020	0.019	0.024	0.013	0.022	0.011	0.018	0.018	0.015	0.018	0.021	0.017	0.019	0.019	0.021	0.018	0.020	0.016	0.023	0.019	0.015	0.012	0.019	0.013	0.025	0.021	0.020	0.020	0.216
N05BA	0.159	0.177	0.161	0.177	0.174	0.171	0.187	0.170	0.187	0.210	0.175	0.150	0.150	0.153	0.171	0.160	0.136	0.172	0.146	0.165	0.184	0.173	0.143	0.154	0.143	0.162	0.162	0.162	0.166	0.167	0.139	0.153	0.161	0.167	0.150	0.140	0.140	0.155	0.135	0.145	0.139	0.157	0.120	0.160	0.125	0.164	0.147	1.602
N05CD	0.067	0.078	0.085	0.069	0.083	0.073	0.087	0.084	0.093	0.098	0.077	0.082	0.067	0.059	0.082	0.073	0.069	0.073	0.074	0.080	0.079	0.088	0.076	0.077	0.070	0.092	0.081	0.070	0.073	0.075	0.072	0.072	0.086	0.082	0.067	0.072	0.070	0.078	0.057	0.065	0.077	0.075	0.072	0.074	0.067	0.070	0.071	0.798
Z-drugs																																																
N05CF	0.102	0.098	0.100	0.099	0.105	0.099	0.104	0.105	0.134	0.138	0.082	0.118	0.092	0.100	0.099	0.099	0.092	0.103	0.102	0.079	0.119	0.118	0.098	0.104	0.096	0.105	0.102	0.104	0.110	0.094	0.098	0.112	0.109	0.106	0.093	0.095	0.085	0.109	0.113	0.090	0.111	0.096	0.103	0.115	0.101	0.116	0.115	1.288
Group 78-87																																																
Antidepressive	**0.085**	**0.089**	**0.083**	**0.111**	**0.105**	**0.090**	**0.081**	**0.093**	**0.117**	**0.103**	**0.102**	**0.094**	**0.075**	**0.083**	**0.090**	**0.095**	**0.083**	**0.093**	**0.086**	**0.090**	**0.094**	**0.095**	**0.075**	**0.092**	**0.070**	**0.108**	**0.094**	**0.089**	**0.091**	**0.083**	**0.078**	**0.089**	**0.105**	**0.090**	**0.066**	**0.089**	**0.086**	**0.085**	**0.092**	**0.071**	**0.095**	**0.083**	**0.092**	**0.090**	**0.083**	**0.103**	**0.100**	**1.255**
N06AA	0.007	0.011	0.016	0.018	0.011	0.012	0.015	0.018	0.017	0.014	0.015	0.012	0.010	0.010	0.012	0.015	0.015	0.014	0.015	0.016	0.011	0.013	0.012	0.014	0.010	0.011	0.015	0.010	0.014	0.015	0.009	0.013	0.014	0.012	0.014	0.014	0.012	0.012	0.010	0.010	0.014	0.013	0.011	0.011	0.014	0.015	0.012	0.183
N06AB	0.036	0.031	0.026	0.043	0.045	0.043	0.031	0.033	0.048	0.037	0.038	0.040	0.038	0.032	0.036	0.035	0.033	0.044	0.030	0.034	0.042	0.033	0.031	0.037	0.027	0.044	0.033	0.040	0.030	0.027	0.035	0.034	0.041	0.034	0.024	0.033	0.032	0.028	0.039	0.029	0.038	0.028	0.040	0.039	0.033	0.044	0.040	0.451
N06AG	0.002	0.001	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.002	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.040	0.046	0.038	0.049	0.048	0.035	0.036	0.041	0.053	0.050	0.049	0.042	0.027	0.040	0.042	0.048	0.035	0.035	0.040	0.038	0.040	0.049	0.031	0.041	0.033	0.053	0.048	0.038	0.047	0.040	0.035	0.042	0.050	0.045	0.028	0.042	0.042	0.048	0.043	0.032	0.043	0.041	0.041	0.040	0.037	0.044	0.048	0.621
Antipsychotics																																																
N05A	0.028	0.028	0.021	0.028	0.030	0.029	0.023	0.026	0.038	0.027	0.031	0.027	0.022	0.028	0.032	0.027	0.020	0.024	0.025	0.030	0.030	0.024	0.025	0.024	0.023	0.029	0.034	0.025	0.030	0.033	0.034	0.026	0.029	0.040	0.030	0.029	0.026	0.034	0.029	0.026	0.037	0.029	0.031	0.030	0.025	0.033	0.045	0.490
Benzodiazepines	**0.152**	**0.201**	**0.171**	**0.194**	**0.194**	**0.181**	**0.203**	**0.181**	**0.240**	**0.207**	**0.174**	**0.186**	**0.177**	**0.180**	**0.163**	**0.180**	**0.165**	**0.173**	**0.186**	**0.181**	**0.191**	**0.186**	**0.165**	**0.175**	**0.163**	**0.197**	**0.152**	**0.188**	**0.180**	**0.163**	**0.165**	**0.166**	**0.180**	**0.183**	**0.160**	**0.188**	**0.154**	**0.208**	**0.158**	**0.181**	**0.189**	**0.178**	**0.179**	**0.179**	**0.211**	**0.205**	**2.360**
N03AE	0.007	0.007	0.009	0.010	0.009	0.010	0.012	0.008	0.013	0.012	0.008	0.008	0.011	0.007	0.008	0.010	0.009	0.012	0.010	0.010	0.010	0.012	0.007	0.013	0.011	0.010	0.009	0.015	0.010	0.009	0.010	0.010	0.009	0.014	0.009	0.010	0.009	0.015	0.014	0.011	0.016	0.013	0.014	0.009	0.010	0.016	0.014	0.170
N05BA	0.083	0.112	0.092	0.103	0.119	0.094	0.111	0.105	0.134	0.111	0.092	0.104	0.096	0.106	0.091	0.092	0.096	0.092	0.106	0.103	0.106	0.106	0.095	0.094	0.099	0.110	0.103	0.100	0.099	0.089	0.088	0.094	0.102	0.103	0.090	0.108	0.087	0.115	0.079	0.101	0.103	0.096	0.095	0.105	0.102	0.119	0.114	1.222
N05CD	0.063	0.081	0.070	0.081	0.066	0.078	0.080	0.069	0.094	0.084	0.075	0.074	0.069	0.068	0.066	0.078	0.059	0.069	0.070	0.069	0.075	0.069	0.063	0.068	0.053	0.078	0.071	0.073	0.071	0.064	0.068	0.062	0.070	0.066	0.060	0.069	0.059	0.078	0.065	0.069	0.070	0.069	0.071	0.081	0.067	0.077	0.077	0.966
Z-drugs																																																
N05CF	0.060	0.073	0.070	0.083	0.065	0.068	0.076	0.065	0.081	0.071	0.064	0.073	0.059	0.063	0.062	0.072	0.057	0.058	0.063	0.061	0.072	0.077	0.064	0.074	0.062	0.066	0.065	0.066	0.071	0.060	0.069	0.059	0.065	0.074	0.061	0.065	0.059	0.072	0.065	0.059	0.063	0.065	0.065	0.071	0.072	0.065	0.076	0.739
Group 88_plus																																																
Antidepressive	**0.013**	**0.014**	**0.017**	**0.014**	**0.016**	**0.011**	**0.013**	**0.016**	**0.015**	**0.018**	**0.012**	**0.015**	**0.018**	**0.020**	**0.021**	**0.017**	**0.015**	**0.020**	**0.018**	**0.021**	**0.020**	**0.015**	**0.013**	**0.019**	**0.019**	**0.013**	**0.022**	**0.016**	**0.021**	**0.018**	**0.018**	**0.013**	**0.019**	**0.019**	**0.020**	**0.022**	**0.020**	**0.015**	**0.017**	**0.019**	**0.014**	**0.016**	**0.022**	**0.021**	**0.018**	**0.024**	**0.020**	**0.261**
N06AA	0.000	0.001	0.003	0.001	0.001	0.002	0.001	0.001	0.000	0.002	0.001	0.002	0.002	0.002	0.002	0.001	0.002	0.001	0.002	0.004	0.003	0.001	0.001	0.002	0.001	0.003	0.003	0.002	0.002	0.002	0.001	0.002	0.003	0.003	0.002	0.004	0.003	0.002	0.004	0.003	0.002	0.004	0.003	0.002	0.005	0.002	0.005	0.039
N06AB	0.006	0.007	0.006	0.005	0.006	0.004	0.006	0.007	0.009	0.007	0.005	0.005	0.008	0.010	0.005	0.008	0.009	0.010	0.008	0.010	0.010	0.006	0.007	0.005	0.010	0.005	0.006	0.007	0.010	0.007	0.008	0.004	0.007	0.009	0.009	0.011	0.009	0.006	0.008	0.009	0.005	0.007	0.011	0.008	0.008	0.005	0.007	0.078
N06AG	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N06AX	0.006	0.005	0.008	0.008	0.008	0.005	0.005	0.008	0.006	0.009	0.006	0.007	0.008	0.008	0.014	0.007	0.004	0.008	0.007	0.007	0.007	0.008	0.005	0.011	0.007	0.005	0.013	0.007	0.009	0.009	0.009	0.006	0.010	0.007	0.009	0.008	0.008	0.008	0.006	0.006	0.006	0.008	0.007	0.011	0.008	0.014	0.011	0.144
Antipsychotics																																																
N05A	0.004	0.007	0.006	0.007	0.010	0.004	0.006	0.008	0.008	0.004	0.007	0.005	0.008	0.011	0.008	0.011	0.005	0.010	0.014	0.009	0.008	0.013	0.008	0.010	0.008	0.008	0.014	0.011	0.008	0.010	0.013	0.007	0.013	0.011	0.008	0.011	0.020	0.008	0.012	0.010	0.007	0.010	0.010	0.011	0.013	0.009	0.014	0.183
Benzodiazepines	**0.029**	**0.023**	**0.030**	**0.

Dataset: **Gender:** **M**

	Pre-COVID																								COVID																							
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
All	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Antidepressive	**0.961**	**1.097**	**0.991**	**1.144**	**1.103**	**1.046**	**1.110**	**1.061**	**1.316**	**1.271**	**1.125**	**1.084**	**0.968**	**1.032**	**1.027**	**1.096**	**1.007**	**1.064**	**0.999**	**1.116**	**1.189**	**1.130**	**1.038**	**1.070**	**0.964**	**1.133**	**0.952**	**0.987**	**1.122**	**1.035**	**1.006**	**1.158**	**1.118**	**1.072**	**1.131**	**1.020**	**0.976**	**1.134**	**1.037**	**1.017**	**1.136**	**1.012**	**1.088**	**1.113**	**1.058**	**1.154**	**1.170**	**12.931**
N06AA	0.117	0.132	0.131	0.147	0.138	0.133	0.145	0.133	0.171	0.169	0.140	0.133	0.111	0.129	0.134	0.130	0.137	0.126	0.126	0.131	0.135	0.161	0.134	0.137	0.119	0.137	0.123	0.121	0.128	0.138	0.121	0.127	0.149	0.146	0.146	0.137	0.119	0.145	0.129	0.133	0.147	0.123	0.125	0.134	0.137	0.145	0.132	1.667
N06AB	0.419	0.483	0.421	0.486	0.489	0.445	0.464	0.464	0.553	0.534	0.469	0.454	0.423	0.428	0.418	0.482	0.428	0.463	0.428	0.489	0.521	0.464	0.454	0.466	0.410	0.503	0.381	0.430	0.471	0.446	0.426	0.496	0.483	0.442	0.485	0.434	0.402	0.496	0.426	0.415	0.476	0.428	0.467	0.473	0.482	0.480	0.498	5.295
N06AG	0.003	0.001	0.002	0.002	0.003	0.001	0.001	0.002	0.001	0.003	0.002	0.001	0.001	0.001	0.002	0.002	0.000	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.002	0.000	0.000	0.000	0.002	0.000	0.000
N06AX	0.422	0.501	0.437	0.509	0.474	0.469	0.499	0.482	0.590	0.565	0.514	0.495	0.434	0.474	0.473	0.502	0.442	0.471	0.442	0.492	0.530	0.505	0.447	0.467	0.434	0.493	0.448	0.435	0.524	0.451	0.459	0.534	0.504	0.483	0.499	0.449	0.454	0.493	0.481	0.469	0.513	0.480	0.497	0.506	0.459	0.527	0.540	5.949
Antipsychotics	**0.277**	**0.324**	**0.314**	**0.361**	**0.354**	**0.309**	**0.327**	**0.340**	**0.366**	**0.347**	**0.339**	**0.337**	**0.267**	**0.323**	**0.304**	**0.311**	**0.320**	**0.319**	**0.288**	**0.314**	**0.332**	**0.317**	**0.319**	**0.305**	**0.287**	**0.345**	**0.334**	**0.319**	**0.347**	**0.345**	**0.321**	**0.327**	**0.349**	**0.349**	**0.350**	**0.320**	**0.319**	**0.375**	**0.366**	**0.302**	**0.362**	**0.294**	**0.320**	**0.354**	**0.306**	**0.332**	**0.363**	**4.223**
N05A	0.277	0.324	0.314	0.361	0.354	0.309	0.327	0.340	0.366	0.347	0.339	0.337	0.267	0.323	0.304	0.311	0.320	0.319	0.288	0.314	0.332	0.317	0.319	0.305	0.287	0.345	0.334	0.319	0.347	0.345	0.321	0.327	0.349	0.349	0.350	0.320	0.319	0.375	0.366	0.302	0.362	0.294	0.320	0.354	0.306	0.332	0.363	4.223
Benzodiazepines	**1.187**	**1.371**	**1.270**	**1.368**	**1.327**	**1.237**	**1.322**	**1.260**	**1.511**	**1.449**	**1.238**	**1.234**	**1.096**	**1.104**	**1.194**	**1.212**	**1.095**	**1.166**	**1.144**	**1.208**	**1.202**	**1.212**	**1.136**	**1.189**	**1.047**	**1.254**	**1.136**	**1.131**	**1.184**	**1.147**	**1.069**	**1.158**	**1.210**	**1.221**	**1.123**	**1.089**	**1.081**	**1.260**	**1.063**	**1.110**	**1.149**	**1.116**	**1.066**	**1.227**	**1.108**	**1.202**	**1.175**	**12.950**
N03AE	0.087	0.105	0.099	0.107	0.107	0.095	0.105	0.090	0.111	0.123	0.095	0.095	0.082	0.084	0.099	0.097	0.095	0.083	0.086	0.100	0.102	0.105	0.093	0.099	0.077	0.089	0.083	0.085	0.093	0.098	0.089	0.099	0.096	0.110	0.099	0.086	0.095	0.108	0.096	0.092	0.101	0.102	0.087	0.110	0.104	0.113	0.110	1.079
N05BA	0.792	0.917	0.856	0.922	0.906	0.832	0.873	0.853	0.988	0.949	0.811	0.817	0.706	0.738	0.783	0.802	0.725	0.788	0.757	0.803	0.874	0.781	0.748	0.776	0.706	0.834	0.746	0.750	0.783	0.749	0.705	0.778	0.805	0.808	0.738	0.726	0.728	0.835	0.718	0.749	0.750	0.736	0.707	0.806	0.726	0.791	0.765	8.243
N05CD	0.309	0.350	0.316	0.338	0.314	0.309	0.344	0.316	0.412	0.377	0.332	0.322	0.308	0.281	0.312	0.313	0.275	0.296	0.302	0.304	0.316	0.326	0.296	0.313	0.264	0.332	0.307	0.296	0.307	0.301	0.275	0.280	0.309	0.303	0.286	0.276	0.258	0.317	0.249	0.269	0.298	0.278	0.271	0.311	0.277	0.298	0.301	3.628
Z-drugs	**0.376**	**0.423**	**0.381**	**0.405**	**0.429**	**0.372**	**0.430**	**0.425**	**0.517**	**0.470**	**0.394**	**0.455**	**0.360**	**0.383**	**0.374**	**0.408**	**0.377**	**0.393**	**0.381**	**0.393**	**0.460**	**0.431**	**0.373**	**0.409**	**0.379**	**0.393**	**0.373**	**0.374**	**0.410**	**0.362**	**0.388**	**0.405**	**0.421**	**0.418**	**0.409**	**0.399**	**0.354**	**0.432**	**0.401**	**0.366**	**0.401**	**0.382**	**0.400**	**0.436**	**0.395**	**0.421**	**0.437**	**4.896**
N05CF	0.376	0.423	0.381	0.405	0.429	0.372	0.430	0.425	0.517	0.470	0.394	0.455	0.360	0.383	0.374	0.408	0.377	0.393	0.381	0.393	0.460	0.431	0.373	0.409	0.379	0.393	0.373	0.374	0.410	0.362	0.388	0.405	0.421	0.418	0.409	0.399	0.354	0.432	0.401	0.366	0.401	0.382	0.400	0.436	0.395	0.421	0.437	4.896
Z-drugs	**3.760**	**4.230**	**3.810**	**4.050**	**4.290**	**3.720**	**4.300**	**4.250**	**5.170**	**4.700**	**3.940**	**4.550**	**3.600**	**3.830**	**3.740**	**4.080**	**3.770**	**3.930**	**3.810**	**3.930**	**4.600**	**4.310**	**3.730**	**4.090**	**3.790**	**3.930**	**3.730**	**3.740**	**4.100**	**3.620**	**3.880**	**4.050**	**4.210**	**4.180**	**4.090**	**3.990**	**3.540**	**4.320**	**4.010**	**3.660**	**4.010**	**3.820**	**4.000**	**4.360**	**3.950**	**4.210**	**4.370**	**48.960**
Antidepressive	**9.610**	**10.970**	**9.910**	**11.440**	**11.030**	**10.460**	**11.100**	**10.610**	**13.160**	**12.710**	**11.250**	**10.840**	**9.680**	**10.320**	**10.270**	**10.960**	**10.070**	**10.640**	**9.990**	**11.160**	**11.890**	**11.300**	**10.380**	**10.700**	**9.640**	**11.330**	**9.520**	**9.870**	**11.220**	**10.350**	**10.060**	**11.580**	**11.180**	**10.720**	**11.310**	**10.200**	**9.760**	**11.340**	**10.370**	**10.170**	**11.360**	**10.120**	**10.880**	**11.130**	**10.580**	**11.540**	**11.700**	**129.31**
Antipsychotics	**2.770**	**3.240**	**3.140**	**3.610**	**3.540**	**3.090**	**3.270**	**3.400**	**3.660**	**3.470**	**3.390**	**3.370**	**2.670**	**3.230**	**3.040**	**3.110**	**3.200**	**3.190**	**2.880**	**3.140**	**3.320**	**3.170**	**3.190**	**3.050**	**2.870**	**3.450**	**3.340**	**3.190**	**3.470**	**3.450**	**3.210**	**3.270**	**3.490**	**3.490**	**3.500**	**3.200**	**3.190**	**3.750**	**3.660**	**3.020**	**3.820**	**2.940**	**3.200**	**3.540**	**3.060**	**3.320**	**3.630**	**42.230**
Benzodiazepines	**11.870**	**13.710**	**12.700**	**13.680**	**13.270**	**12.370**	**13.220**	**12.600**	**15.110**	**14.490**	**12.380**	**12.340**	**10.960**	**11.040**	**11.940**	**12.120**	**10.950**	**11.660**	**11.440**	**12.080**	**12.920**	**12.120**	**11.360**	**11.890**	**10.470**	**12.540**	**11.360**	**11.310**	**11.840**	**11.470**	**10.890**	**11.580**	**12.100**	**12.210**	**11.230**	**10.890**	**10.810**	**12.600**	**10.630**	**11.100**	**11.490**	**11.160**	**10.660**	**12.270**	**11.080**	**12.020**	**11.750**	**129.50**

Supplementary table 9.

COVID-19 Wave	Date	Interwave period
1	From 01-03-2020 until 22-06-2020	Yes
Lockdown 1	Started 18-03-2020, gradually decrease from 04-05-2020 and onwards.	
2	Started 31-08-2020	No
Lockdown 2	Started 02-11-2020	
3	From 15-02-2021 until 27-06-2021	Yes
4	Started 04-10-2021	No
Lockdown 3	Started 26-10-2021	
5	Started 27-12-2021	No

Supplementary table 9. COVID-19 infectious waves and lockdown periods in Belgium. Source: https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_FAQ_ENG_final.pdf and *www.info-coronavirus.be*.

15. PROTOCOL

Applicants:
Ben Verbeke
Eric Vleeshouwers

Promotor:
Prof. Dr. Bert Vaes

Title:
The effect of the Covid-19 pandemic on the use of psychoactive substances.

Type of study:
Epidemiological study, combined with a brief literature review.

Study objectives:
The primary aim of this paper is to identify if there is a correlation between the Covid-19 pandemic and increased prescription rates of psychoactive substances. More specifically, we will focus on antidepressants and benzodiazepines. In order to achieve this, we will perform an epidemiological study in the Intego database. Complementary to our study, we will execute a literature study prior to the database review to see what knowledge already exists on this matter.
Since Covid-19 is a relatively new infectious disease, we don't expect to find many articles on our subject.
Therefore, the secondary aim of this paper is to compare the prescription rates during the Covid-19 pandemic to other disasters or critical events. Examples of these events are the economic crisis of 2008, terrorism, including the Afghanistan war triggered by 9/11 and natural disasters. We will look

specifically for events that happened on a global scale as these events need to have an effect on the prescription rates in Belgium.

Literature study

Primary PICO:

P – Adult population 18 years and older.

I – Use of psychoactive medication with focus on benzodiazpines and antidepressants, starting 01/01/2020 till 31/12/2021(during Covid-19 pandemic).

C – Use of psychoactive medication with focus on benzodiazpines and antidepressants, starting 01/01/2018 till 31/12/2019(before Covid-19 pandemic).

O – Amount of psychoactive medication prescriptions.

Secondary PICO:

P – Adult population 18 years and older.

I – Use of psychoactive medication with focus on benzodiazpines and antidepressants, starting 01/01/2020 till 31/12/2021(during Covid-19 pandemic).

C – Use of psychoactive medication with focus on benzodiazpines and antidepressants, during critical events. More specific: Financial crisis from 01/09/2008 till 31/08/2010 and Afghanistan war triggered by 9/11 from 01/09/2001 till 31/08/2003.

O – Amount of psychoactive medication prescriptions.

Search strategy:

We will consult Pubmed, Embase and Cochrane.

Our primary search terms are:

1. Covid-19: "COVID-19", "SARS-CoV-2", “coronavirus disease”, “2019 novel coronavirus”, “sars coronavirus”, “wuhan coronavirus”, “wuhan seafood market pneumonie virus”, “coronavirus”
2. Psychoactive drugs: "psychotropic drugs", "benzodiazepines", “antidepressive agents", “psychopharmaceutical”, “psychotropic agents”, “antidepressants”, “prescriptions”

Our secondary search terms are:

“Economic crisis”, “economic recession”, “terrorism”, “pandemics”, “disasters”, “anxiety”, “mental health”

Selection criteria:

For our primary question, we will look for articles that were published since the beginning of 2020. We will look specifically for articles that report on prescription rates of psychoactive drugs. Article that are not related to this subject will be excluded.

To answer our secondary question, we will look for articles which have published data consisting the given timelines of the financial crisis and Afghanistan war. Articles not related to the subject will be excluded.

Other exclusion criteria are: articles where the full text is not available, articles that report in any other language than English and Dutch, articles with a population age below 18 years of age**.**

Any articles eligible for selection will be read by the two applicants of this paper. Agreement will result in inclusion of the article. Disagreement will be settled by an objective third party.

Epidemiological study

The Intego database will be used to research a quantifiable difference in prescription rate. In order to do so, we will compare the period of covid pandemic to a time period before the pandemic. This time period will be set from 01/01/2018 till 31/12/2019. The covid pandemic period will be set from 01/01/2020 till 31/12/2021**.** We will be carefully to examine the time period before the covid pandemic to make sure this period is free of any other disasters or critical events to prevent any bias. This is necessary as this is our base line for comparison.
If possible, we would like to compare the timelines mentioned above to the time periods of critical events. To answer our secondary research question on critical events, we will also compare the timelines mentioned above to the following time periods of critical events:

- Financial crisis: from 01/09/2008 until 31/08/2010.
- Afghanistan war triggered by 9/11: from 01/09/2001 until 31/08/2003.
- …..

SEARCH:

(((((((("COVID-19"[Mesh] OR "SARS-CoV-2"[Mesh]) OR "Economic Recession"[Mesh]) OR "Disasters"[Mesh]) OR "Terrorism"[Mesh]) OR "Pandemics"[Mesh]) OR "Anxiety"[Mesh]) OR "Mental Health"[Mesh]) AND "Psychotropic Drugs"[Mesh]) OR "Benzodiazepines"[Mesh]) OR "Antidepressive Agents"[Mesh]

➔ 131.231 results

(((((("COVID-19"[Mesh] OR "SARS-CoV-2"[Mesh] OR "Economic Recession"[Mesh] OR "Disasters"[Mesh] OR "Terrorism"[Mesh] OR "Pandemics"[Mesh] OR "Anxiety"[Mesh] OR "Mental Health"[Mesh]) AND ("Psychotropic Drugs"[Mesh] OR "Benzodiazepines"[Mesh]) OR "Antidepressive Agents"[Mesh])

➔ 69.172

("COVID-19"[Mesh] OR "SARS-CoV-2"[Mesh] OR "Economic Recession"[Mesh] OR "Disasters"[Mesh] OR "Pandemics"[Mesh] OR "Terrorism"[Mesh] OR "Mental Health"[Mesh] OR "Anxiety"[Mesh]) AND ("Psychotropic Drugs"[Mesh] OR "Antidepressive Agents"[Mesh] OR "Benzodiazepines"[Mesh])

➔ 8.921 results

("COVID-19"[Mesh] OR "SARS-CoV-2"[Mesh]) AND ("Psychotropic Drugs"[Mesh] OR "Antidepressive Agents"[Mesh] OR "Benzodiazepines"[Mesh])

➔ 268 results

(((((((("Economic Recession"[Mesh]) OR "Disasters"[Mesh]) OR "Anxiety"[Mesh]) OR "Mental Health"[Mesh]) OR "Pandemics"[Mesh]) OR "Terrorism"[Mesh]) AND "Psychotropic Drugs"[Mesh]) OR "Antidepressive Agents"[Mesh]) OR "Benzodiazepines"[Mesh]

➔ 131.150 results

("Economic Recession"[Mesh] OR "Disasters"[Mesh] OR "Anxiety"[Mesh] OR "Mental Health"[Mesh] OR "Pandemics"[Mesh] OR "Terrorism"[Mesh]) AND ("Psychotropic Drugs"[Mesh] OR "Antidepressive Agents"[Mesh] OR "Benzodiazepines"[Mesh])

➔ 8.783 results

16. ETHICAL AGREEMENT

The effect of the Covid-19 pandemic on the use of psychoactive substances.

Dossiernr.:	MP018632
Masterproef:	Masterproef I HAIO, 2020 – 2023
Faculteit/opleiding:	Faculteit Geneeskunde - Master in de huisartsgeneeskunde
Studiefase:	eerste fase
Academiejaar:	2021-2022
Korte omschrijving / abstract:	During our internship over the last year, we observed high rates of anxiety and stress in patients. In the light of the recent covid-19 outbreak, we were wondering whether there could be a correlation between covid-19 and increased prescription rates of psychoactive substances. Therefore, we will perform an epidemiological study on this subject. More specifically, we will focus on antidepressants and benzodiazepines. Our primary focus will be the Intego database. A literature study will also be performed. Depending on the course of our research, there is a possibility to expand our epidemiological study.
Toegepaste technieken:	Epidemiologisch onderzoek met een aanvullende literatuurstudie.
Gewenste taal van communicatie:	nl
Promotor:	Professor Bert Vaes (u0087897)
Organisatie:	KU Leuven
Dienst:	Academisch Centrum voor Huisartsgeneeskunde
Discipline:	Masterproef
Extra groepsleden:	Eric Vleeshouwers eric.vleeshouwers@student.kuleuven.be s0216933 Ben Verbeke ben.verbeke@student.kuleuven.be s0216729

De verstrekte informatie toont aan dat het onderzoek in het kader van de masterproef integraal deel uitmaakt van een studie die reeds werd goedgekeurd door een erkend ethisch comité.

U hoeft bijgevolg geen nieuw dossier in te dienen in het kader van uw masterproef. Wel dient u het UZ/KU Leuven toe te voegen als nieuw deelnemend centrum aan het huidige dossier indien dit nog niet het geval was. Gelieve u bij het betreffende comité te informeren en u te conformeren aan de daar geldende procedures en hun adviezen te volgen.

Onder voorbehoud van de volledigheid en correctheid van de door u verstrekte gegevens, krijgt u hierbij de goedkeuring om het onderzoek in het kader van de masterproef te starten.

Wij willen u erop attent maken dat u zelf verantwoordelijk blijft voor uw onderzoek. Bovendien doet elke wijziging aan de door u verstrekte gegevens omtrent de onderzoeksopzet elke eerdere goedkeuring vervallen. U dient in dat geval een amendement te maken aan uw huidig dossier bij het comité dat eerder uw dossier goedkeurde.