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Impact of the early COVID-19 pandemic on adult mental health-related dispensed medications, hospitalizations and specialist outpatient visits in Norway and Sweden: Interrupted time series analysis

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Aims: Norway and Sweden had different early pandemic responses that may have impacted mental health management. The aim was to assess the impact of the early COVID-19 pandemic on mental health-related care.

Methods: We used national registries in Norway and Sweden (1 January 2018–31 December 2020) to define 2 cohorts: (i) general adult population; and (ii) mental health adult population. Interrupted times series regression analyses evaluated step and slope changes compared to prepandemic levels for monthly rates of medications (antidepressants, antipsychotics, anxiolytics, hypnotics/sedatives, lithium, opioid analgesics, psychostimulants), hospitalizations (for anxiety, bipolar, depressive/mood, eating and schizophrenia/delusional disorders) and specialist outpatient visits.

Results: In Norway, immediate reductions occurred in the general population for medications (−12% antidepressants to −7% hypnotics/sedatives) except for antipsychotics; and hospitalizations (−33% anxiety disorders to −17% bipolar disorders). Increasing slope change occurred for all medications except psychostimulants (+1.1%/month hypnotics/sedatives to +1.7%/month antidepressants); and hospitalization for anxiety disorders (+5.5%/month), depressive/mood disorders (+1.7%/month) and schizophrenia/delusional disorders (+2%/month). In Sweden, immediate

David Moreno-Martos and Jing Zhao are joint first author. Hedvig Nordeng and Daniel R. Morales are joint last author.

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reductions occurred for antidepressants (−7%) and opioids (−10%) and depressive/mood disorder hospitalizations (−11%) only with increasing slope change in psychostimulant prescribing of (0.9%/month). In contrast to Norway, increasing slope changes occurred in specialist outpatient visits for depressive/mood disorders, eating disorders and schizophrenia/delusional disorders (+1.5, +1.9 and +2.3%/month, respectively). Similar changes occurred in the pre-existing mental health cohorts.

Conclusion: Differences in early COVID-19 policy response may have contributed to differences in adult mental healthcare provision in Norway and Sweden.

KEYWORDS

COVID-19, healthcare delivery, mental health, Norway, pandemic, Sweden

1 | INTRODUCTION

Mental health disorders are a leading cause of health-related burden globally, with depressive and anxiety disorders ranked among the top conditions, and their management represents a significant burden to healthcare systems.¹ The Coronavirus Disease 2019 (COVID-19) pandemic has represented a crucial challenge to public health worldwide. The association between COVID-19 severity and physical health has been well documented, whilst less is known about the association between COVID-19 and mental health and its management.² In a systematic review of 19 studies, Xiong *et al.*³ reported a prevalence of 15–48% for depressive symptoms and 6–51% for anxiety symptoms in the general population during the COVID-19 pandemic. Persons with pre-existing mood disorders were reported to have more severe COVID-19 outcomes, with a 1.3-fold increased risk of COVID-19 hospitalization and 1.5-fold increased risk of COVID-19-related death, based on a meta-analysis of studies early in the pandemic.⁴ Persons with mental health disorders are also potentially at increased risk for the development of post-COVID complications, with a prior history of depression and anxiety associated with a 1.3- to 1.5-fold increased risk of self-reported long COVID-19 symptoms.⁵ Several studies have found that the pandemic affected mental health and its management in the general population reporting that adverse psychological outcomes may occur more commonly at the start of the pandemic due to mandatory quarantine, unemployment and uncertainty associated with the disease.^{3,6–8} COVID-19 pandemic responses have varied between countries, with some countries implementing stricter measures aimed at infection control than others that may lead to different effects on adverse psychological outcomes and the delivery of mental health services. Similarly, population interventions may have variably impacted on the management of mental health conditions in terms of dispensed medications and hospital contacts, which may also act as surrogates for mental health and/or its management by health systems.

Several studies have reported changes in dispensed medications in general during the pandemic, with fewer studies focusing on medications related to mental health. Of those that have, some studies have shown an increased antidepressant use, whilst others have

What is already known about this subject

- The COVID-19 pandemic disrupted routine healthcare services.
- Norway and Sweden had differences in early COVID-19 pandemic response.
- It was uncertain how this impacted mental health care provision in Norway and Sweden.

What this study adds

- The onset of the COVID-19 pandemic was associated with short-term changes in prescribing and hospitalization for some mental health conditions
- Differences in early COVID-19 policy response may have contributed to the extent of changes.

shown a more complex pattern, especially when evaluating antidepressants alongside anxiolytics and sedatives.^{9–11} However, there is still limited information on medication used for other mental health conditions, such as in persons with schizophrenia. It may also be instructive to examine healthcare utilization due to mental health disorders in the 2 countries Norway and Sweden, given their differences in COVID-19 pandemic response, but relatively similar healthcare and social systems. This includes whether indirect pandemic effects on mental health or its management may have been immediate, transient or persistent. In March 2020, Norway announced a mandatory national lockdown in response to the COVID-19 pandemic, in contrast to Sweden, which had fewer restrictions and more voluntary recommendations. The aim of the study was therefore to examine patterns of dispensed psychotropic medications and healthcare utilization related to mental health conditions in the general population and among pre-existing mental health populations in Norway and Sweden during the early COVID-19 pandemic.

2 | METHODS

2.1 | Data sources

Data consisted of national registries in Norway and Sweden linked at a person level in each country, covering together over 15 million persons (Table S1). In Norway, data sources included the Norwegian Prescription Database covering all medications dispensed to patients, the National Patient Register (NPR) covering secondary care, the Norwegian Cause of Death Registry covering death data, and Statistics Norway covering age and sex.^{12,13} In brief, the Norwegian Prescription Database includes information on all prescribed medication irrespective of reimbursement dispensed to individuals in ambulatory care. It includes detailed information on medications dispensed and date of dispensing. Medications are classified according to the Anatomic Therapeutic Chemical (ATC) classification system. NPR covers all hospitals and outpatient clinics, and all private health clinics that receive governmental reimbursement. The data include date of admission, and discharge, primary and secondary diagnosis. Diagnostic codes in the NPR follow the World Health Organization's International Classification of Diseases, version 10 (ICD-10). The Norwegian Cause of Death Registry includes the official cause of death statistics. The data is based on death certificates filled out by physicians. Since 1996, ICD-10 codes have been used. Detailed information about cause of death is provided.^{12,13} From Sweden, registered data of very similar type included the Swedish National Prescribed Drug Register containing detailed data on all prescribed drugs dispensed at pharmacies in Sweden. Medications are classified according to the ATC classification system. The Swedish NPR collects data for specialist outpatient visits and hospitalizations. The Swedish NPR includes date on admission date, discharge date, primary and underlying diagnosis. ICD-10 codes are used to classify diagnostic codes. The Swedish Cause of Death Register collects data on the date of death, location of death and cause of death using ICD-10 codes to classify the causes. Finally, Statistics Sweden contains information on age and sex. All Swedish registries mentioned above are held by the National Board of Health and Welfare.^{14–16}

2.2 | Study period and study population

The study period ranged from 1 January 2018 until 31 December 2020, based on data availability. Two study cohorts were evaluated in each country. The first cohort consisted of all adults in the general population aged 18 years or older on 1 January 2018. The second cohort consisted of patients with pre-existing mental health diagnosis, which was defined as an open cohort with index date being the date of the first ICD-10 revision diagnosis of a mental health condition (Table S2) recorded in secondary care during the study period, or on 1 January 2018 if they had a diagnosis within 3 years before that date. Those diagnosed for the first time during the study period (incident mental health diagnoses) were only included and followed up from the date of their diagnosis. In both cohorts the cohort exit date was the earliest of date of death or end of the study period.

2.3 | Outcomes

Trends in the rate of 3 broad outcomes during each period were analysed, namely counts of medication dispensation, hospitalizations, and specialist outpatient visits. ATC codes were used to define class groupings of dispensed medications, which included antidepressants, antipsychotics, anxiolytics hypnotics and sedatives, **lithium**, opioid analgesics, and psychostimulants (Table S3). ICD-10 codes were used to identify hospital admissions (analysed separately) for anxiety disorders, bipolar disorders, depressive and mood disorders, eating disorders and schizophrenia, and delusional disorders. Hospital admissions were registered at the date of admission (Table S3). The same conditions were included for specialist outpatient visits but also with the inclusion of attention deficit hyperactivity disorder.

2.4 | Statistical analysis

We report basic descriptives of each cohort population. We performed interrupted time-series (ITS) regression analyses in each country, modelling the rate of all events per 100 persons per month.¹⁷ Classes of medication dispensations, hospitalizations and specialist outpatient visits were analysed separately. The study period (1 January 2018 to 31 December 2020) was subdivided into 36 monthly time periods: 26 before and 9 after the interrupting point, which was set as March 2020, being the 36th month and the start of the pandemic. The denominator was the total number of persons observable in the general population (or pre-existing mental health cohort) at the start of each calendar month. The numerator was the number of dispensed medications, hospital admissions, or specialist outpatient visit of interest during each calendar month. Individuals were allowed to contribute more than once to an outcome event of interest during each time period. The ITS models evaluated the immediate effect of the intervention (step change) and the change in trend after the intervention (slope change), accounting for baseline trend. Models were fitted using either Quasi-Poisson or Poisson regression to estimate the relative risk (RR), depending on if the data were overdispersed or not.¹⁷ Autocorrelation was assessed by inspecting autocorrelation and partial autocorrelation function plots to detect nonzero autocorrelations.¹⁸ Seasonality was accounted for by introducing lagged terms into the model based on the largest nonzero autocorrelation observed,¹⁹ typically requiring a 12-month lag after inspection of the autocorrelation plots. For dispensed medications, we ran the primary ITS model accounting for medication stockpiling (saving up on medications) by including a pulse function (a peak at the interruption point) to account for observed short-term increases in dispensed medications counts immediately before the interruption point, whilst a secondary modelling without accounting for stockpiling may provide supporting information related to net effects. Analyses were performed using R (version 4.1.2). We used the function `glm()` from the stats package.²⁰ To check for overdispersion we used the function `dispersiontest()` from the AER package.²¹ To assess autocorrelation we used the function `acf()` from the stats package.

2.5 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in <http://www.guidetopharmacology.org>.

3 | RESULTS

On 1 March 2020, the general adult population cohort consisted of 4 232 459 persons in Norway and 8 180 542 persons in Sweden. On 1 March 2020, the general adult populations were similar in terms of sex and age distribution (Table 1). In the general adult population from both countries, the most common mental health conditions identified from hospital admissions and specialist outpatient visits data were anxiety disorder and depressive/mood disorders (5.3 and 3.5% in Norway respectively, and 3.9 and 2.3% in Sweden respectively).

On 1 March 2020, the pre-existing adult mental health population consisted of 367 868 persons in Norway and 590 729 persons in Sweden. On 1 March 2020, the pre-existing adult mental health population included more women than men, and more persons from younger age categories (Table S4).

3.1 | Dispensed medications

Antidepressant, lithium and psychostimulant dispensing were higher in the general population in Sweden compared to Norway, whilst opioid dispensing was lower (Figure 1, Table 2). When stockpiling was modelled, immediate reductions in all dispensed medications in the general population in Norway were observed, except for antipsychotics. This ranged from -12% for antidepressants (RR 0.88, 95% confidence interval [CI] 0.83–0.94) to -7% for hypnotics and sedatives (RR 0.93, 95% CI 0.87–0.99). There was an increasing slope change for all dispensed medications ranging from 1.1% per month for hypnotics and sedatives to 1.7% per month for antidepressants, apart for psychostimulants. Significant immediate step reductions in Sweden were observed only for antidepressants (RR 0.93, 95% CI 0.88–0.99) and opioid analgesics (RR 0.90, 95% CI 0.85–0.96), with a significant increasing slope change in psychostimulant dispensing only of 0.9% per month. When stockpiling was not modelled, the start of the COVID-19 pandemic was not associated with a significant immediate step change in dispensed medications in Norway or Sweden (Figure S1, Table S5), but with an increasing trend change observed for opioids in Norway only of 0.9% per month.

A similar pattern was observed for the pre-existing mental health population when stockpiling was accounted for as in the general adult population but immediate step reductions in anxiolytics and for hypnotics and sedatives in Norway were not significant, nor with antidepressants in Sweden (Figure S2, Table S6). When stockpiling was not modelled, a similar pattern was observed for dispensed medication in the pre-existing mental health population as in the general adult population (Figure S3, Table S7).

TABLE 1 Demographics for the general adult population for Norway and Sweden at the beginning of the COVID-19 pandemic on 1 March 2020.

	General adult population, n (%)	
	Norway N = 4 232 459	Sweden N = 8 180 542
Sex		
Female	2 104 047 (49.7)	4 084 462 (49.9)
Male	2 128 412 (50.3)	4 096 080 (50.1)
Age group (years)		
18–24	348 443 (8.2)	602 801 (7.4)
25–34	783 678 (18.5)	1 556 253 (19.0)
35–44	730 378 (17.3)	1 366 145 (16.7)
45–54	757 559 (17.9)	1 368 204 (16.7)
55–64	653 577 (15.4)	1 225 390 (15.0)
65–74	540 500 (12.8)	1 088 786 (13.3)
>74	418 324 (9.9)	972 963 (11.9)
Conditions		
Anxiety disorders	222 235 (5.3)	317 653 (3.9)
Bipolar disease	17 957 (0.4)	39 335 (0.5)
Depressive and mood disorders	147 569 (3.5)	187 299 (2.3)
Eating disorders	10 160 (0.3)	13 486 (0.2)
Schizophrenia and delusional disorders	14 207 (0.3)	23 504 (0.3)

Note: Measurements were taken from each cohort as of 1 March 2020. Conditions were defined using codes from hospital admissions and specialist outpatient visits.

3.2 | Hospitalizations

Hospitalizations for the included conditions were higher in the general population in Norway than in Sweden. In the general population in Norway, the start of the pandemic was associated with immediate step reductions in hospitalization for all conditions, ranging from -33% for anxiety disorders (RR 0.67, 95% CI 0.57–0.79) to -17% for bipolar disorders (RR 0.83, 95% CI 0.71–0.98; Figure 2, Table 3). In Norway, there was an increasing slope change in hospitalization for: anxiety disorders (5.5% per month); depressive and mood disorders (1.7% per month); and schizophrenia and delusional disorders (2% per month). An immediate step reduction occurred in the general population in Sweden for depressive and mood disorders only (RR 0.89, 95% CI 0.81–0.98). In Sweden, there were no significant slope changes in hospitalization for any condition. A similar pattern was observed for hospitalization in the pre-existing mental health population (Figure S4, Table S8).

3.3 | Specialist outpatient visits

Changes in specialist outpatient visits occurred in the general population in Sweden only, where the start of the pandemic was associated

Medications (General population)

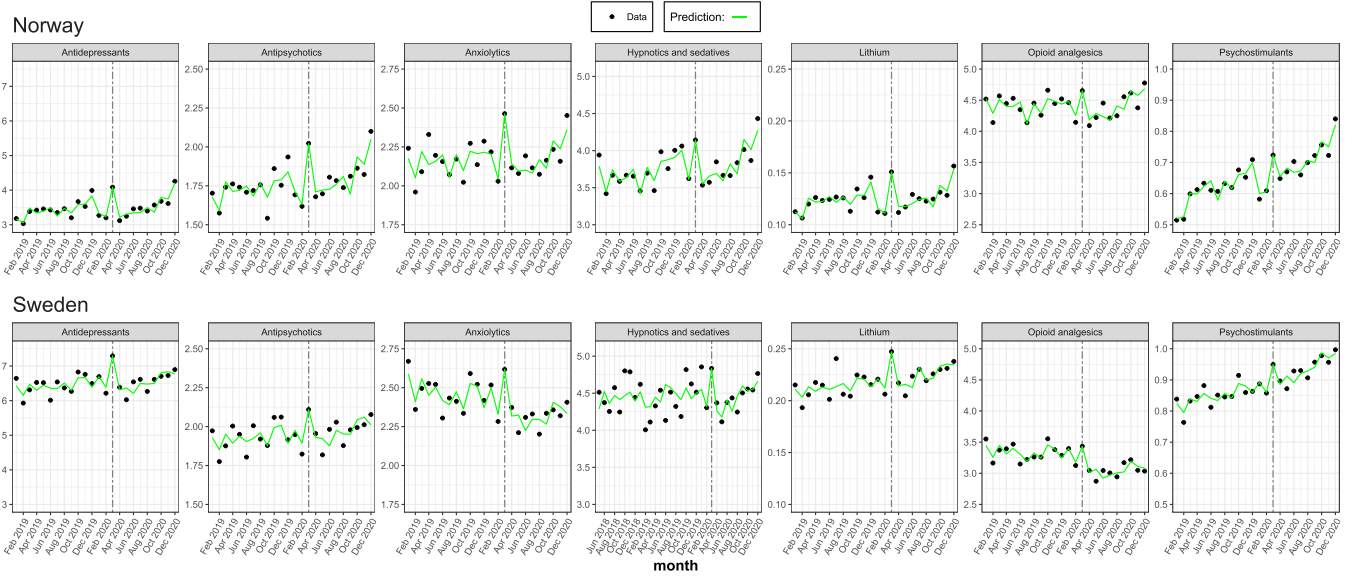


FIGURE 1 Impact of the COVID-19 pandemic on dispensed medications for the general adult population in Norway and Sweden, accounting for stockpiling. The dots correspond to the 36 monthly data points (rate per 100 person per month = total number of dispensed prescriptions / number of individuals in the general population × 100). In green is the prediction of the model adjusted for seasonality (as detected). The vertical dashed line indicates the interrupting point (March 2020). Four-month seasonality was present in hypnotics and sedatives in Sweden and 12-month seasonality in the rest.

TABLE 2 Impact of the COVID-19 pandemic onset in March 2020 on dispensed medications for the general adult population in Norway and Sweden during 2018–2020, accounting for medication stockpiling.

	Intercept Number of dispensed medications per 100 individuals	Baseline trend RR (95% CI)	Immediate step change after March 2020 RR (95% CI)	Trend change after March 2020 RR (95% CI)
Norway				
Antidepressants	3.168	1.002 (0.998–1.007)	0.882 (0.827–0.941)	1.017 (1.007–1.026)
Antipsychotics	1.676	0.999 (0.994–1.005)	0.951 (0.881–1.026)	1.016 (1.005–1.027)
Anxiolytics	2.176	1.001 (0.996–1.006)	0.923 (0.856–0.996)	1.013 (1.002–1.025)
Hypnotics and sedatives	3.790	1.002 (0.998–1.006)	0.928 (0.87–0.989)	1.011 (1.002–1.020)
Lithium	0.112	1.000 (0.994–1.006)	0.896 (0.828–0.971)	1.018 (1.006–1.029)
Opioid analgesics	4.523	0.999 (0.995–1.002)	0.92 (0.871–0.973)	1.015 (1.007–1.023)
Psychostimulants	0.519	1.007 (1.003–1.011)	0.925 (0.876–0.976)	1.006 (0.997–1.014)
Sweden				
Antidepressants	6.431	1.002 (0.997–1.006)	0.932 (0.876–0.993)	1.008 (0.999–1.017)
Antipsychotics	1.930	1.001 (0.996–1.006)	0.955 (0.887–1.029)	1.007 (0.996–1.018)
Anxiolytics	2.588	0.998 (0.994–1.002)	0.952 (0.897–1.011)	1.006 (0.997–1.015)
Hypnotics and sedatives	4.289	1.000 (0.997–1.003)	0.946 (0.864–1.037)	1.008 (0.996–1.021)
Lithium	0.211	1.002 (0.997–1.008)	0.94 (0.864–1.023)	1.010 (0.998–1.022)
Opioid analgesics	3.446	0.998 (0.994–1.002)	0.903 (0.851–0.959)	1.008 (0.999–1.017)
Psychostimulants	0.824	1.004 (1.000–1.007)	0.962 (0.915–1.011)	1.009 (1.002–1.016)

Note: Baseline trend = change in relative risk (RR) of dispensed medications per month during the baseline period. Changes in step = the immediate change in RR of dispensed medications in the month following the start of the pandemic (1 March 2020). Slope change = change in RR of dispensed medications per month in the post-intervention period.

Hospitalizations (General population)



FIGURE 2 Impact of the COVID-19 pandemic on hospitalizations for the general adult population in Norway and Sweden. The dots correspond to the data points (rate per 100 person per month = total number of hospital admissions / number of individuals in the general population \times 100). In green is the prediction of the model adjusted for seasonality (as detected). The vertical dashed line indicates the interrupting point (March 2020). Twelve-month seasonality was present in anxiety disorders, depressive and mood disorders in Norway and depressive and mood disorders in Sweden; 8-month seasonality present in bipolar diseases and schizophrenia and delusional disorders in Norway; 6-month seasonality present in eating disorders in Sweden and no seasonality detected in the rest.

TABLE 3 Impact of the COVID-19 pandemic onset in March 2020 on hospitalization for the general adult population in Norway and Sweden during 2018–2020.

	Intercept Number of hospitalizations per 100 individuals	Baseline trend RR (95% CI)	Immediate step change after March 2020 RR (95% CI)	Trend change after March 2020 RR (95% CI)
Norway				
Anxiety disorders	0.031	0.983 (0.971–0.994)	0.669 (0.566–0.791)	1.055 (1.028–1.083)
Bipolar diseases	0.012	0.997 (0.989–1.006)	0.833 (0.710–0.977)	1.017 (0.994–1.041)
Depressive and mood disorders	0.026	1.002 (0.992–1.012)	0.693 (0.601–0.799)	1.035 (1.014–1.057)
Eating disorders	0.004	0.988 (0.982–0.994)	0.775 (0.615–0.977)	1.003 (0.969–1.039)
Schizophrenia and delusional disorders	0.031	0.994 (0.988–1.000)	0.700 (0.622–0.788)	1.020 (1.002–1.039)
Sweden				
Anxiety disorders	0.013	1.001 (0.998–1.005)	0.904 (0.814–1.004)	0.995 (0.980–1.010)
Bipolar diseases	0.006	0.996 (0.993–1.000)	0.943 (0.843–1.055)	1.010 (0.994–1.026)
Depressive and mood disorders	0.011	0.999 (0.992–1.007)	0.890 (0.807–0.981)	1.005 (0.990–1.020)
Eating disorders	0.001	1.007 (0.997–1.017)	0.892 (0.721–1.103)	1.010 (0.980–1.042)
Schizophrenia and delusional disorders	0.005	1.004 (1.002–1.006)	0.944 (0.878–1.014)	0.993 (0.983–1.004)

Note: Baseline trend = change in relative risk (RR) of hospitalizations per month during the baseline period. Changes in step = the immediate change in RR of hospitalizations in the month following the start of the pandemic (1 March 2020). Slope change = change in RR of hospitalizations per month in the post-intervention period.

Abbreviations: CI, confidence interval.

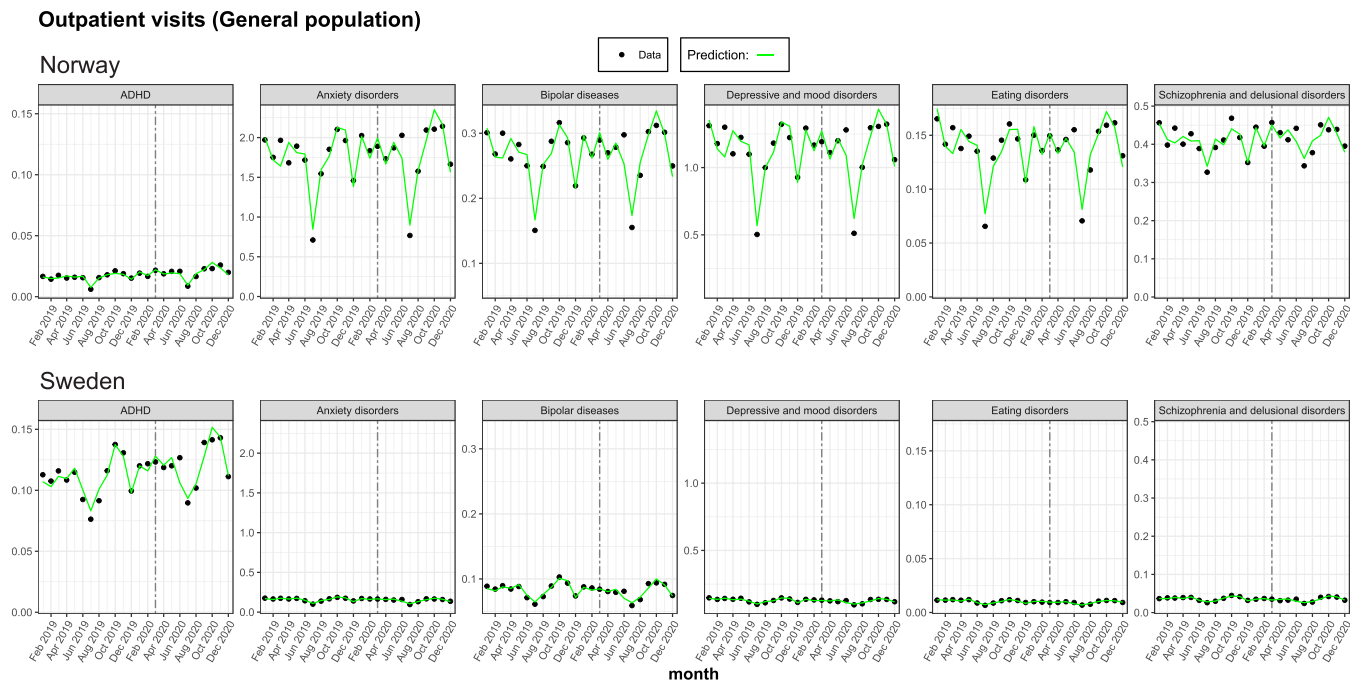


FIGURE 3 Impact of the COVID-19 pandemic on specialist outpatient visits for the general adult population in Norway and Sweden. The dots correspond to the data points (rate per 100 person per month = total number of specialist outpatient visits / number of individuals in the general population \times 100). In green, we present the prediction of the model adjusted for seasonality. The vertical dashed line indicates the interrupting point (1 March 2020). Twelve-month seasonality was present in all conditions. ADHD = attention deficit hyperreactivity disorder.

with a -12% immediate step reduction in visits for eating disorders (RR 0.88, 95% CI 0.80–0.97; Figure 3, Table S9). In Sweden, there was an increasing slope change in specialist outpatient visits for depressive and mood disorders (1.5% per month), eating disorders (1.9% per month), and schizophrenia and delusional disorders (2.3% per month). A similar pattern was observed for outpatient visits in the pre-existing the mental health population in Sweden (Figure S5, Table S10).

4 | DISCUSSION

In the general adult population cohort from Norway, the early COVID-19 pandemic was associated with stockpiling followed by immediate reductions in dispensed medications followed by an increasing trend in medication dispensing. Similarly, immediate significant reductions in hospitalizations were also observed, except for eating disorders and bipolar disorders, followed by an increasing trend in hospitalizations. In Sweden, the COVID-19 pandemic was associated with smaller immediate reductions in medication dispensation, being significant only for antidepressant and opioid dispensing. Similarly, the immediate impact on hospitalizations was smaller, being significant for depressive and mood disorders only with no change in longer-term hospitalization trend. Specialist outpatient visits in Norway did not appear to be impacted by the pandemic. In contrast, a significant immediate reduction in specialist outpatient visits was observed for eating disorders in Sweden, and an increasing longer-term trend of

specialist outpatient visits for depressive and mood disorders, eating disorders and schizophrenia and delusional disorders. Broadly, similar effects were observed in the pre-existing mental health cohort. When potential stockpiling of dispensed medications was not included in the model, the pandemic had no significant observed impact on dispensed medications in either country. This suggests that although changes in the exact timing of dispensing behaviour occurred, there is no strong evidence to suggest a net increase or decrease in medications received overall. The exception to this was the small increasing trend in opioid analgesic dispensing in Norway and psychostimulant dispensing in Sweden.

A 2021 Global Burden of Disease update concluded that the pandemic directly or indirectly was associated with increased rates of major depression and anxiety disorders.¹ Whilst we did not directly measure rates of new diagnoses, we did not observe a net increase in the occurrence of antidepressant prescribing or hospitalizations for these conditions, except for a small increasing trend of specialist outpatient visits for depressive and mood disorders and schizophrenia and delusional disorders in Sweden, where, by contrast, no significant immediate reductions were seen.

Although several studies have found increased symptom severity of depression and anxiety during the pandemic, this does not imply that there is a higher occurrence of clinical diagnoses in the population due to the pandemic that may require therapeutic management. A Norwegian cross-sectional study used psychiatric interviews to assess mental disorders before and after the onset of the pandemic,

observing stable rates of clinically assessed psychiatric diagnoses.²² Also, a recent systematic review and meta-analysis of 134 cohorts comparing mental health symptoms before and during the COVID-19 pandemic concluded that there was little change in general mental health, anxiety, or depression symptoms.²³ However, it was similarly noted that many studies included in the systematic review were deemed to be at high risk of bias.

Having a history of mental illness may be an important risk factor for increased healthcare resource use during the pandemic. Several studies have found that having a pre-existing mental health condition was associated with worsened anxiety and depression symptom levels during the pandemic.^{3,8,24} However, we observed a similar impact for persons with pre-existing mental health conditions as in the general adult population, except for the impact on medication dispensing that was modestly attenuated in persons with a prior mental health disorder. In terms of other illnesses, it has been reported elsewhere that the COVID-19 pandemic has exacerbated the severity of symptoms and burden of eating disorders with increases in specialist outpatient and inpatient care being reported in several countries.²⁵⁻²⁷

Although our focus was on relative changes in the trend of mental health-related medications, outpatient visits and hospitalizations over time, we observed differences in the absolute rate of hospitalizations and outpatient visits that were lower in Sweden compared to Norway. This is in keeping with Sweden having a lower number of hospital beds per capita and lower rate of outpatient visits compared to Norway.²⁸⁻³⁰

Strengths of this study include the use of 2 national linked data sets to evaluate the impact of the start of the pandemic on different aspects of mental health. We used a standard analysis run across both databases to reduce heterogeneity. Whilst we have used a robust design to evaluate effects of sudden policy changes at the population level, ITS models evaluate associations that may be subject to other time-varying confounders. We evaluated a wide range of mental health-related outcomes. However, we did not differentiate between new or incident disease from pre-existing health outcomes, but instead focused on the overall population's mental health burden. It is also possible that changes in the trend of outcomes may have occurred in specific subpopulations that were not included (for example in children and adolescents).

The impact of mental health diagnoses within primary care has not been evaluated, although medication dispensing is likely to correlate. Therefore, the proportion of persons identified with each condition in the pre-existing mental health cohort should not be considered a comprehensive estimate of prevalence for the condition among the population. Whilst we have evaluated dispensed medications at the population level, we do not have information on the exact indication for those medications and only capture prescriptions dispensed to outpatients. Nor do we know whether the patient took the medication, as medications dispensed may not always reflect actual use. Also, we are uncertain whether significant changes in the quantity of medication contained within dispensed prescriptions occurred during this time, although we still saw evidence of stockpiling. We measured trends in outcomes until the end of 2020 only and could consequently not capture longer-term changes for example

associated with later pandemic waves. Access to specialist outpatient care is dependent upon capacity to deliver services. Detecting an increasing trend in specialist outpatient visits is dependent on the health system having capacity to meet an increased demand. If additional capacity is limited, it is possible that symptom burden (e.g. depression or anxiety) may still have increased but would not be observed using the outcomes we defined if there are difficulties in accessing specialist care.

The national lockdown in Norway resulted in the rapid mandatory closure of offices and institutions, social distancing, and restriction of public gatherings. These restrictions commenced on 12 March 2020, which helped control SARS-CoV-2 infection rates in the population.³¹ In contrast, Sweden had fewer mandatory restrictions, relying more on recommendations regarding distancing and restrictions in public gatherings that were gradually tightened, and had higher infection rates and a greater number of hospitalization and deaths during this period.

The start of the COVID-19 pandemic was associated with a stronger observed impact on the immediate and longer-term management of mental health in Norway compared to Sweden. This is possibly related to changes in healthcare provision in response to mandatory national restrictions in Norway vs. voluntary but strong national recommendations in Sweden. However, there is limited evidence of a net increase in disease burden based on the outcomes studied. These changes may therefore represent a backlog in the health system attempting to catch up with patient need that would normally have occurred earlier or, in the case of stockpiling, gradual normalization over time of immediate changes due to acute stockpiling at pandemic start. However, we cannot exclude the possibility that higher untreated disease burden not captured by our outcomes may have occurred, either through direct or indirect effects of infection, such as in the development of post-COVID complications.⁵ Further evaluation over time is therefore warranted.

5 | CONCLUSION

The start of the COVID-19 pandemic was associated with a greater impact on dispensed medications and healthcare provision for mental health conditions in Norway as compared to Sweden, both in the general population and similarly in those with pre-existing mental health conditions. However, observed changes are more likely to be associated with differences in healthcare provision in relation to the COVID-19 policy response rather than an overall net increase in disease burden.

AUTHOR CONTRIBUTIONS

Ludvig Daae Bjørndal, Angela Lupattelli and Hedvig Nordeng drafted the initial study protocol. Daniel R. Morales and David Moreno-Martos revised the initial study protocol. All authors reviewed and approved the final study protocol. David Moreno-Martos conducted the analyses in Norway with the support of Daniel R. Morales and Jing Zhao. Huiqi Li ran the study package in Sweden. Daniel R. Morales

and David Moreno-Martos wrote the first draft of the manuscript. All authors contributed to the interpretation of the results and commented on all previous versions of the manuscript. All authors have read and approved the final manuscript. Hedvig Nordeng was responsible for data acquisition and ethical approvals in Norway and Fredrik Nyberg in Sweden.

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CONFLICT OF INTEREST STATEMENT

F.N. and A.L. declare having some AstraZeneca shares. The other authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Restrictions apply to the availability of these data, which were used under licence for the EU-COVID-19 and SCIFI-PEARL study as part of the Nordic COHERENCE project. Data are available with the permission of registry custodians in Norway and Sweden.

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REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204–1222. doi:[10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9)
2. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020; 584(7821):430–436. doi:[10.1038/s41586-020-2521-4](https://doi.org/10.1038/s41586-020-2521-4)
3. Xiong J, Lipsitz O, Nasri F, et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. *J Affect Disord*. 2020;277:55–64. doi:[10.1016/j.jad.2020.08.001](https://doi.org/10.1016/j.jad.2020.08.001)
4. Ceban F, Nogo D, Carvalho IP, et al. Association between mood disorders and risk of COVID-19 infection, hospitalization, and death: a systematic review and meta-analysis. *JAMA Psychiatry*. 2021;78(10): 1079–1091. doi:[10.1001/jamapsychiatry.2021.1818](https://doi.org/10.1001/jamapsychiatry.2021.1818)
5. Wang S, Quan L, Chavarro JE, et al. Associations of depression, anxiety, worry, perceived stress, and loneliness prior to infection with risk of post-COVID-19 conditions. *JAMA Psychiatry*. 2022;79(11): 1081–1091. doi:[10.1001/jamapsychiatry.2022.2640](https://doi.org/10.1001/jamapsychiatry.2022.2640)
6. Li Y, Wang A, Wu Y, Han N, Huang H. Impact of the COVID-19 pandemic on the mental health of college students: a systematic review and meta-analysis. *Front Psychol*. 2021;12:669119. doi:[10.3389/fpsyg.2021.669119](https://doi.org/10.3389/fpsyg.2021.669119)
7. De Kock JH, Latham HA, Leslie SJ, et al. A rapid review of the impact of COVID-19 on the mental health of healthcare workers: implications for supporting psychological well-being. *BMC Public Health*. 2021;21(1):104. doi:[10.1186/s12889-020-10070-3](https://doi.org/10.1186/s12889-020-10070-3)
8. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav Immun*. 2020;89:531–542. doi:[10.1016/j.bbi.2020.05.048](https://doi.org/10.1016/j.bbi.2020.05.048)
9. Rabeea SA, Merchant HA, Khan MU, Kow CS, Hasan SS. Surging trends in prescriptions and costs of antidepressants in England amid COVID-19. *Daru*. 2021;29(1):217–221. doi:[10.1007/s40199-021-00390-z](https://doi.org/10.1007/s40199-021-00390-z)
10. Frangou S, Travis-Lumer Y, Kodesh A, et al. Increased incident rates of antidepressant use during the COVID-19 pandemic: interrupted time-series analysis of a nationally representative sample. *Psychol Med*. 2022;10:1–9.
11. Estrela M, Silva TM, Gomes ER, et al. Prescription of anxiolytics, sedatives, hypnotics and antidepressants in outpatient, universal care during the COVID-19 pandemic in Portugal: a nationwide, interrupted time-series approach. *J Epidemiol Community Health*. 2022;76(4):335–340. doi:[10.1136/jech-2021-216732](https://doi.org/10.1136/jech-2021-216732)
12. Furu K, Wettermark B, Andersen M, Martikainen JE, Almarsdottir AB, Sørensen HT. The Nordic countries as a cohort for pharmacoepidemiological research. *Basic Clin Pharmacol Toxicol*. 2010;106(2):86–94. doi:[10.1111/j.1742-7843.2009.00494.x](https://doi.org/10.1111/j.1742-7843.2009.00494.x)
13. Furu K. Establishment of the nationwide Norwegian Prescription Database (NorPD)—new opportunities for research in pharmacoepidemiology in Norway. *Norsk Epidemiologi*. 2008;18:129–136.
14. Nyberg F, Franzén S, Lindh M, et al. Swedish Covid-19 investigation for future insights—a population epidemiology approach using register linkage (SCIFI-PEARL). *Clin Epidemiol*. 2021;13:649–659. doi:[10.2147/CLEP.S312742](https://doi.org/10.2147/CLEP.S312742)
15. Ludvigsson JF, Andersson E, Ekblom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011;11(1):450. doi:[10.1186/1471-2458-11-450](https://doi.org/10.1186/1471-2458-11-450)
16. Brooke HL, Talbäck M, Hörnblad J, et al. The Swedish cause of death register. *Eur J Epidemiol*. 2017;32(9):765–773. doi:[10.1007/s10654-017-0316-1](https://doi.org/10.1007/s10654-017-0316-1)
17. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. 2017;46(1):348–355. doi:[10.1093/ije/dyw098](https://doi.org/10.1093/ije/dyw098)
18. Box GEP, Jenkins GM, Reinsel GC, Ljung GM. *Time Series Analysis: Forecasting and Control*. Prentice Hall; 1994.
19. Zanobetti A, Schwartz J, Samoli E, et al. The temporal pattern of respiratory and heart disease mortality in response to air pollution. *Environ Health Perspect*. 2003;111(9):1188–1193. doi:[10.1289/ehp.5712](https://doi.org/10.1289/ehp.5712)
20. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2020. Accessed January 20, 2024. <https://www.R-project.org/>
21. Kleibler C, Zeileis A. *Applied Econometrics with R*. Springer-Verlag; 2008. ISBN 978-0-387-77316-2. <https://CRAN.R-project.org/package=AER>
22. Knudsen AKS, Stene-Larsen K, Gustavson K, et al. Prevalence of mental disorders, suicidal ideation and suicides in the general population before and during the COVID-19 pandemic in Norway: a population-based repeated cross-sectional analysis. *Lancet Reg Health Eur*. 2021; 4:100071. doi:[10.1016/j.lanepe.2021.100071](https://doi.org/10.1016/j.lanepe.2021.100071)
23. Sun Y, Wu Y, Fan S, et al. Comparison of mental health symptoms before and during the COVID-19 pandemic: evidence from a systematic review and meta-analysis of 134 cohorts. *BMJ*. 2023;380:e074224.
24. Hao F, Tan W, Jiang L, et al. Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry. *Brain Behav Immun*. 2020;87:100–106. doi:[10.1016/j.bbi.2020.04.069](https://doi.org/10.1016/j.bbi.2020.04.069)

25. Lin JA, Hartman-Munick SM, Kells MR, et al. The impact of the COVID-19 pandemic on the number of adolescents/young adults seeking eating disorder-related care. *J Adolesc Health*. 2021;69(4):660-663. doi:10.1016/j.jadohealth.2021.05.019
26. Hartman-Munick SM, Lin JA, Milliren CE, et al. Association of the COVID-19 pandemic with adolescent and young adult eating disorder care volume. *JAMA Pediatr*. 2022;176(12):1225-1232. doi:10.1001/jamapediatrics.2022.4346
27. Raventós B, Abellan A, Pistillo A, Reyes C, Burn E, Duarte-Salles T. Impact of the COVID-19 pandemic on eating disorders diagnoses among adolescents and young adults in Catalonia: a population-based cohort study. *Int J Eat Disord*. 2023;56(1):225-234. doi:10.1002/eat.23848
28. The Global Economy. Sweden: hospital beds per 1000 people; 2000. Accessed December 19, 2023. https://www.theglobaleconomy.com/Sweden/hospital_beds_per_1000_people/
29. The Global Economy. Norway: hospital beds per 1000 people; 2020. Accessed December 19, 2023. https://www.theglobaleconomy.com/Norway/hospital_beds_per_1000_people/
30. Statista. Number of outpatient visits in Sweden in 2021, by type; 2023. Accessed December 19, 2023. <https://www.statista.com/statistics/953535/number-of-doctors-visits-in-sweden-by-type/>
31. Korseberg L, Saunes SI. Norway country snapshot: the role of public health agencies and services in the response to COVID-19; 2022. Accessed January 20, 2024. <https://eurohealthobservatory.who.int/news-room/articles/norway-country-snapshot-the-role-of-public-health-agencies-and-services-in-the-response-to-covid-19>

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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