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Staying strong, but for how long? Mental health during COVID-19 in Italy

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ABSTRACT

A recent literature investigating mental health consequences of social distancing measures, has found a substantial increase in self-reported sleep and anxiety disorders and depressive symptoms during lockdown periods. These evidence are in contrast with the results we obtain using data on monthly purchases of psychiatric drugs by the universe of Italian pharmacies over the period of interest. We argue that this discrepancy has three potential causes: *i)* use of non-pharmaceutical therapies and non-medical solutions during lockdown periods; *ii)* unmet needs due to both demand- and supply-side shortages in healthcare services and *iii)* the subjectivity of self-assessed psychological health in survey studies, capturing also mild mental distress which might not evolve into mental disorder needing pharmacological treatment. This last point seems to be confirmed by lack of statistical significance of any measure of mobility change and reason of mobility (which we proxy with mobile phone data) on antidepressants and anxiolytics purchases during the entire 2020 period.

The COVID-19 epidemic, caused by the novel coronavirus SARS-COV-2, originated in Wuhan, China at the end of 2019 and spread rapidly worldwide in the following months. In the absence of effective treatment and vaccination, to prevent the contagion, countries have implemented diverse Non-Pharmaceutical Interventions (NPIs). School closures, travel restrictions, national lockdowns and various social distancing measures affected people's lives from different perspectives.

Italy was the first Western country to experience a major and immediate outbreak of the virus, with the first infected patient isolated on February 18th 2020. As early as of March 9th 2020, Italy declared a complete national lockdown which lasted until May 18th 2020 (the so-called "phase 1"), with other severe mobility restrictions that continued until June 3rd ("phase 2"). In parallel, the World Health Organization declared COVID-19 a global pandemic on March 11th 2020, followed by large-scale NPIs introduced in many other countries. The events of the following months caused a widespread and dramatic disruption in daily lives, with an emotional, social and economic burden that still remains to be understood[1].

According to the OECD[2], the prevalence of mental health problems was on a stable path until the outbreak of COVID-19 in 2020, when rates of depressive and anxiety disorders increased in several countries. In particular, according to several surveys, self-reported prevalence has more than doubled in Belgium, France, Italy, Mexico, New Zealand, the United Kingdom and the United States in the case of anxiety; and in Australia, Belgium, Canada, France, the Czech Republic, Mexico, Sweden, the United Kingdom and the United States in the case of depression. Despite limited scope for representativeness and cross-country comparability of these surveys due to different designs and sampling techniques, the evidence clearly points to a significant increase in prevalence of subjective anxiety and depressive disorders.

A recent WHO report[3] provides a comprehensive overview of the mental health effects of COVID-19 pandemic, based on the Global Burden of Disease data[1] and other research including an umbrella of systematic reviews and meta-analyses[4–6]. According to the GBD[1], the COVID-19 pandemic has led to a 27.6% increase in major depressive disorder (MDD) cases and a 25.6% increase in anxiety disorders (AD) cases worldwide in 2020. Overall, the pandemic is estimated to have caused 137.1 additional disability-adjusted life years (DALYs) per 100,000 population for MDD and 116.1 for AD. The report suggests that the surge in mental health disorders has disproportionately affected the young, females and patients with pre-existing health conditions.

The results of both the OECD and the WHO reviews are far from conclusive. On the one hand, longitudinal studies are necessary to assess how sustained these new trends are. On the other hand, as the WHO highlights, "most of the eligible meta-analyses reviewed were rated as low quality and with a high risk of bias,..., which makes rates across studies difficult to interpret." This is partly due to the types of survey design used, which in most cases were non-representative and frequently conducted on online social media platforms, imposing several forms of statistical and methodological bias. Finally, most of the studies are purely descriptive, and do not allow to identify and measure the real effects and the mechanisms at play.

As a matter of fact, when longitudinal data are gathered and trajectories of mental health are analyzed, results lead to more optimistic conclusions: Fancourt et al. (2021)[7] and Saunders et al. (2021)[8] use the results of a survey administered on a weekly basis in the UK and find, after a sharp increase at the beginning of the lockdown, a common declining trajectory of depression and anxiety symptoms in the weeks after the beginning of mobility restrictions. They also highlight how individuals with previous diagnoses of mental health conditions, although reporting higher anxiety and depression in the early phases of the lockdown compared to the rest of the sample, did not show greater levels of emotional reactivity, possibly because already experienced in coping strategies in stressful situations.

Overall, despite the huge proliferation of studies that relate COVID-19 to population mental health, the evidence do not yield convergent nor robust results on the phenomenon. To the best of our knowledge, to date there is a limited number of studies worldwide based on objective data.[9–12]

For what concerns the Italian case, the studies documenting mental health effects of COVID-19 are mostly, if not entirely, based on online surveys and self-reported mental health contidion and several of those suffer from limited representativeness of the data and/or small sample sizes.[13–15] Gualano et al (2021)[16] mention that several studies reported a greater prevalence of depressive and anxiety symptoms in the Italian population during the lockdown, despite a reduction in voluntary admissions in the 40 days after the beginning of COVID-19 epidemic in Italy a non-significant increase in outpatient pharmaceutical consumption in March of antidepressants and a significant one of anxiolytics. They stress the urge for stronger indicators of mental health conditions and mental well-being of the general population.

Overall, such studies find a consistent reduction of the mental health conditions of Italians[15,17,18], in particular for females, the young and patients with pre-existing conditions and worse socio-economic status.[19,20] The prevalences of (self-reported) anxiety and depressive symptoms observed in the cited studies, which range between 17.6% to 41.5% for the first and between 12.4% and 33.2%, are strikingly above the prevalence of depressive symptoms reported by the Italian National Health Institute (ISS) for the pre-pandemic period (6% for the period 2016-2019).

Interestingly, the Italian Observatory of Drug Consumption (OSMED) led by the Italian Medicines Agency (AIFA)[21] document a significant increase in the use of anxiolytics and sedatives over the last years due to a recent surge in stress disorders. In particular, in Italy the consumption of Benzodiazepine raised from 47.4 DDD/1000 inhabitants-die in 2014 to 55.0 in 2020, while that of antidepressants from 39.2 in 2014 to 43.6 in 2020. According to AIFA, this rise is symptomatic of a consolidated habit of resorting easily to pharmaceutical therapies, urging for more controlled prescribing practices. Additionally, the same report also mentions an increase in prevalence of depression in the latest years, with a consequent increase in GPs' attention and management skills, with only 1 out of 3 patients with depressive symptoms who have been pharmacologically treated. Overall, the report does not find an excessive surge in consumption in these drug categories out of the historical trends.

A recurrent weakness of the literature presented above, is inherent in sample selection bias and, as consequence, lack of representativeness. Individuals who readily take surveys on the internet are likely to represent a non generalizable sample of the population. The intercorrelations between mental health measures and sample selection criteria might result in inflated or deflated results. Additionally, studying single cross-sections of these mental health measures without pinning down the baseline conditions is of limited scope, where instead longitudinal studies which monitor the evolution of mental health due to the pandemic would be more informative. In fact, cross-sectional observations may document short-term fluctuations in the mental health responses to COVID-19 pandemic. This is also exacerbated by the subjective nature of the evaluations. Self-administration of the survey might be temporarily affected by social isolation, intolerance to uncertainty or loneliness, influencing individuals' well-being during the outbreak, without a persistent effect on mental health. For example, subjective wellbeing has been analyzed through social media data, such as Twitter[22,23].Furthermore, a significant reduction in wellbeing is found in Japan and Italy (-8.3% and -11.7%, respectively) in the first nine months of 2020[22], resulting from prolonged mobility restrictions, flu and COVID-like symptoms, economic uncertainty, social distancing and news about the pandemic. Furthermore, in Italy researchers found that an increase in daily deaths and daily new cases due to COVID-19 provoked negative emotions and somatosensory words, often linked to traumatic events and PTSD symptoms[23].

Our aim in this context is to offer a clinician-based objective reading of what the mental health consequences of COVID-19 were in Italy in the first year of the pandemic. To avoid the issue of limited generalizability pervading other studies, we employ detailed data on the universe of purchases of anxiolytics and antidepressants (measured at three level ATC codes) during COVID-19 pandemic and quantify the, eventual, increase in the consumption of anxiolytics and antidepressants sold in Italy in 2020 with respect to 2019. One of the main advantages of the data is the absence of selection bias, as they are equivalent to administrative data. Importantly, in order to tease out the channels through which COVID-19 pandemic might affect mental health in Italy, we combine the drug purchases with granular mobile phone data on mobility within and across Italian provinces. Subsequently, by adopting a multivariate regression approach, we test whether there is an interplay between consumption of drugs for mental health disorders and COVID-19 pandemic, controlling for heterogeneous local mobility restrictions, COVID contagion threat and mortality effect. Interestingly, we measure two different mobility flows, namely the one between home and workplace versus the one occurring between home and other locations. By limiting our analysis to the first year of the COVID-19 pandemic, we avoid potential confounding effects of long-covid on mental health, given that "severe acute COVID-19 illness – indicated by extended time bedridden – is associated with long-term mental morbidity among recovering individuals in the general population."[24]

We find that purchases of mental health-related drugs have increased with respect to 2019, but the excess volumes do not match the massive increase in anxiety and depressive disorders found in survey-based studies. Furthermore, while we find incremental effects on anxiolytics consumption in the months corresponding to the national lockdown introduction, we do not observe any further significant effect of mobility restrictions. We interpret the divergence of our results with respect to findings based on self-administered survey studies according to three main hypotheses. First, the mismatch is likely to be inherent in a milder nature of self-reported psychological distress with respect to conditions that require pharmaceutical interventions. Importantly, as we observe an increase in anxiolytics and antidepressants consumption in the last part of 2020, we conclude that an important share of mental health disorder cases might have been overlooked during the first year of the pandemic, possibly leading to the onset of more severe conditions in a longer-term. An alternative reading is that individuals affected by the pandemic distress might have exhibited differential mental health responses due to their differential (optimal) investments in defensive expenditures, coping mechanisms or compensatory behaviors, such as mild non specific drugs, support groups or specialist psychotherapy. Our estimates of the marginal effect of COVID pandemic on mental health is thus likely to measure the net effect, whose welfare and policy design implications highlight an important role for economic incentives determining such defensive spending.

Results

Our analysis is based on monthly purchases of psychiatric drugs of the universe of Italian pharmacies from January 1st 2019 to December 31st 2020, which are then aggregated at administrative level in 107 provinces belonging to 20 regions. The type of psychiatric drugs considered are anxiolytic and antidepressant therapies (Anatomical Therapeutic Chemical (ATC) codes N05B and N06A, respectively), with pharmaceutical purchases measured in standard units (i.e., Defined Daily Dose, DDD).

In Italy the market for antidepressants is almost double compared to the anxiolytic one (see Table A.1 in Appendix). In terms of dispensing, anxiolytics are mostly sold without physician prescription (92.73% in 2019 and 93.01% in 2020), while antidepressants are mainly dispensed with prescription (85.65% in 2019 and 85.49% in 2020). Given these different dispensing practices, in the analysis we focus on overall volumes of drugstores' purchases of anxiolytics and antidepressant separately, rather than considering the single channels of dispensing. We will discuss more about this aspect in the Discussion section.

In order to describe how COVID-19 mobility restrictions affected mental health of individuals over time and space, we focus on monthly mobility patterns in Italy in 2020. We exploit anonymous mobile phone data by Teralytics, which collects information on more than 30% of all Italian cell phone users. We first measure the overall mobility (including all the reasons for movement such as home to work, home to other, work to home, work to other, other to home, other to work and others), and subsequently we distinguish two subcategories, home-to-work and home-to-other mobility. For the three mobility types, we compute the difference between mobility in each day of 2020 compared to the average mobility of the same day of the week in all weeks of January 2020. We aggregate the data at the month and province level, matching the drug consumption data (see Methods for a detailed description of our mobility algorithm).

Figure 1a and Figure 1b trace the evolution of anxiolytics and antidepressants purchases, respectively, together with the most salient moments of the COVID-19 pandemic in Italy. The vertical lines mark the most stringent containment measures, i.e., the national lockdown (from March 9th to May 18th) and the institution of 'zones' with differentiated mobility restrictions on November 6th. The background of the two Figures shows additionally the evolution of both the monthly excess mortality (yellow area) and the change in mobility (purple area) in 2020. Most importantly, the figures picture monthly drugstore purchases for 2019 (dashed blue line) and 2020 (solid green line).

We detect clear seasonality patterns for both anxiolytics (Figure 1b) and antidepressants (Figure 1b). The differences in each month-of-year purchases are not very large, although with the exception of April and March, the volumes in 2020 supersede the ones in 2019. In March 2020, the onset of the national lockdown, we observe a pronounced spike in the purchases of both classes of drugs (ATC codes), followed by a substantial drop in the subsequent two months. In fact, in May 2020, at the end of the national lockdown, the purchases are significantly lower compared to 2019. During the summer months, the differentials in purchases shrink and start to widen again only in November for antidepressants and in December 2020 for anxiolytics. This pattern might indicate the lag in the onset of mental health effects of the first wave of the pandemic, or new short-term effects of the second wave of COVID-19 contagion spread and the subsequent localized lockdown measures.

Figures A.1 and A.1b in Appendix show the evolution of the percentage change in both drugstore purchases and reimbursable prescriptions in 2020, with respect to 2019. Indeed, in the case of antidepressants, drugstore purchases mirror customer purchases dispensed upon reimbursable prescription, confirming that the share of antidepressants sold without prescription is negligible. Conversely, there seems to be a systematic proportion of anxiolytics dispensed without medical prescription. Table A.2 in Appendix shows that the the 2020 *vs*. 2019 differences in monthly purchases are all statistically significant in the case of anxiolytics (Panel *A*) and almost ever significant in the case of antidepressants (Panel *B*).

In order to uncover the interplay between mental health and COVID-19 pandemic, we employ a fixed effects regression analysis. In particular, we quantify monthly excess purchases of psychiatric drugs as percent variations between volumes purchased in 2020 and in 2019. We thus analyze how the excess volumes of anxiolytics and antidepressants, respectively, were related to specific effects of the COVID-19 pandemic, over and above region-specific time trends in purchases observed in 2020 and national time fixed effects. In particular we identify the effect of contagion (proxied by the number of contagions over the previous month per 1,000 inhabitants), the threat of mortality (proxied by excess mortality over the previous month per 1,000 inhabitants) and changes in mobility (both overall and purpose-specific).

Table 1. Anxiolytics, percent variation

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
March-Dec	0.0002					
	(0.0101)					
Mar		0.0822***	0.0715***	0.0656	0.0717***	0.0762***
		(0.0100)	(0.0125)	(0.0371)	(0.0116)	(0.0148)
Apr		-0.0441***	-0.0624***	0.0107	-0.0654***	-0.0247
		(0.0121)	(0.0147)	(0.0870)	(0.0153)	(0.0352)
May		-0.1457***	-0.1528***	-0.1338***	-0.1519***	-0.1592***
		(0.0096)	(0.0115)	(0.0233)	(0.0112)	(0.0140)
Jun		0.0511***	0.0498***	0.0416***	0.0469***	0.0409**
		(0.0108)	(0.0111)	(0.0115)	(0.0118)	(0.0152)
Jul		0.0124	0.0121	0.0062	0.0070	0.0064
		(0.0108)	(0.0108)	(0.0109)	(0.0110)	(0.0137)
Aug		-0.0282*	-0.0222	-0.0290*	-0.0331**	-0.0421*
		(0.0109)	(0.0117)	(0.0121)	(0.0124)	(0.0173)
Sep		0.0247*	0.0232	0.0208	0.0186	0.0195
		(0.0120)	(0.0121)	(0.0133)	(0.0123)	(0.0158)
Oct		-0.0064	-0.0098	-0.0134	-0.0105	-0.0141
		(0.0121)	(0.0125)	(0.0142)	(0.0124)	(0.0152)
Nov		0.0024	-0.0061	0.0082	-0.0063	-0.0040
		(0.0115)	(0.0126)	(0.0194)	(0.0121)	(0.0167)
Dec		0.0933***	0.0834***	0.1134***	0.0802***	0.0855**
		(0.0195)	(0.0199)	(0.0280)	(0.0209)	(0.0260)
Mobility			-0.0225	0.0160		
			(0.0134)	(0.0302)		
Mobility					-0.0352	-0.0931
(home to work)					(0.0244)	(0.0525)
Mobility					-0.0003	0.0698
(Home to other)					(0.0225)	(0.0506)
Excess mortality	-0.0611***	-0.0050	-0.0035	-0.0020	-0.0033	-0.0025
× 1k inhab, last month	(0.0139)	(0.0066)	(0.0065)	(0.0066)	(0.0065)	(0.0067)
Contagions	0.0002***	-0.0000	-0.0000	-0.0000	-0.0000	-0.0000
× 1k inhab, last month	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)
Region specific time trend	Yes	Yes	Yes	Yes	Yes	Yes
Mobility × months	No	No	No	Yes	No	Yes
N. Obs	1177	1177	1144	1144	1144	1144

Notes: Robust standard errors in parentheses, * for p<.05, ** for p<.01, and *** for p<.001. The dependent variable is the percent variation with respect to 2019 of the monthly DDD of anxiolytics purchased by Italian pharmacies at the Province level. February is the reference category. Coefficients for monthly dummies are increase or decrease with respect to the percent variation of purchases in February.

Table 1 and 2 report regression results for 6 different model specifications for anxiolytics and antidepressants purchases, respectively. The most parsimonious specification (Model 1) identifies a homogeneous effect of the pandemic period (March - December 2020) as well as the intensity of contagion and excess mortality. The coefficient estimates on the local excess mortality is negative, while the one on contagion is positive, both being statistically significant. On the one hand, psychiatric drugs consumption represent concomitant therapies in neuro-degenerative disorder treatments, and given that COVID-19 excess mortality was disproportionately higher among the elderly, the latter is likely to drive a decrease in the consumption. On the other hand, higher contagion rates are likely to promote suffering and distress, which net of lockdown measures, is likely to promote a surge in anxiety disorders.

In order to account for the heterogeneity in the impact of pandemic across time, we introduce month specific time dummies (Model 2), which wipe out the effects of both excess mortality and contagions. The sign and magnitude of the coefficients of the month dummies are consistent with the patterns observed in Figure 1a: a positive and significant increase in the early stages of the lockdown, followed by a reduction in the subsequent months and a sharp increase in December. While the time dummies effectively capture the evolution of the pandemic at the national level, one might argue that they do not explain the heterogeneities in the differentials of how single territories were affected by lockdowns. For this reason we further enrich our specification with the aggregate indicator of monthly changes in mobility (Model 3). However, mobility fluctuations do not seem to affect purchases of anxiolytics. Nor do we find any effect of mobility in Model 4, when it is interacted with month specific dummies, or when, in model 5 and 6, we distinguish home-to-work from home-to-other mobility type (the interaction coefficients are never statistically significant and are not reported in the tables, but are available upon request). The multitude of model specifications that we adopt show that net of scattered spikes in purchases in March, June and December, differential local mobility patterns play no role in determining the utilization of psychiatric drugs patterns.

The results for antidepressants are very similar: mobility, number of contagions and excess mortality do not seem to play any role, while the time dummies show larger magnitudes which are all strongly significant, with the exception of the month of December.

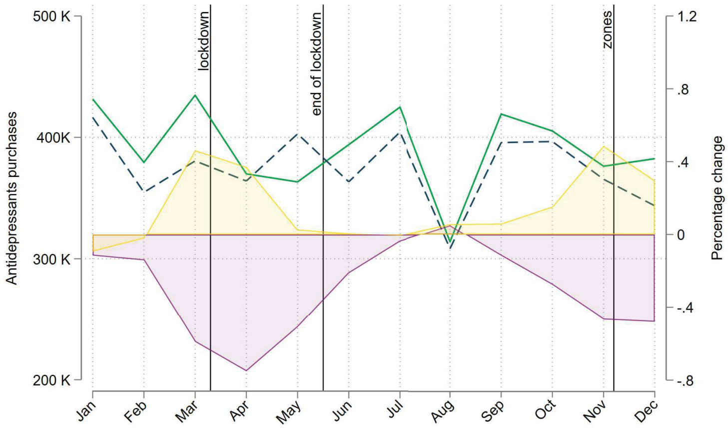
Table 2. Antidepressants, percent variation

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
March-Dec	-0.0175**					
	(0.0067)					
Mar		0.1234***	0.1229***	0.1075***	0.1218***	0.1100***
		(0.0068)	(0.0081)	(0.0298)	(0.0077)	(0.0121)
Apr		-0.0902***	-0.0956***	-0.0213	-0.0981***	-0.0832***
		(0.0070)	(0.0094)	(0.0579)	(0.0092)	(0.0193)
May		-0.2320***	-0.2326***	-0.2352***	-0.2332***	-0.2426***
		(0.0072)	(0.0081)	(0.0158)	(0.0077)	(0.0102)
Jun		-0.0339***	-0.0346***	-0.0436***	-0.0355***	-0.0441***
		(0.0077)	(0.0079)	(0.0080)	(0.0083)	(0.0098)
Jul		-0.0464***	-0.0466***	-0.0487***	-0.0478***	-0.0502***
		(0.0078)	(0.0079)	(0.0079)	(0.0085)	(0.0108)
Aug		-0.0975***	-0.0946***	-0.0966***	-0.0972***	-0.0972***
		(0.0095)	(0.0096)	(0.0095)	(0.0104)	(0.0135)
Sep		-0.0270*	-0.0275**	-0.0310**	-0.0287**	-0.0384**
		(0.0103)	(0.0103)	(0.0101)	(0.0107)	(0.0126)
Oct		-0.0732***	-0.0737***	-0.0729***	-0.0742***	-0.0745***
		(0.0117)	(0.0118)	(0.0123)	(0.0118)	(0.0131)
Nov		-0.0615***	-0.0630***	-0.0847***	-0.0638***	-0.0663***
		(0.0125)	(0.0130)	(0.0148)	(0.0129)	(0.0146)
Dec		0.0050	0.0013	0.0098	-0.0004	-0.0013
		(0.0169)	(0.0171)	(0.0214)	(0.0171)	(0.0185)
Mobility			-0.0043	0.0194		
			(0.0087)	(0.0186)		
Mobility					-0.0100	-0.0342
(home to work)					(0.0160)	(0.0297)
Mobility					-0.0007	0.0464
(home to other)					(0.0170)	(0.0343)
Excess mortality	-0.0768***	-0.0034	-0.0024	-0.0010	-0.0022	-0.0019
× 1k inhab, last month	(0.0168)	(0.0043)	(0.0043)	(0.0044)	(0.0044)	(0.0045)
Contagions	0.0002***	0.0000	0.0000	0.0000	0.0000	0.0000
× 1k inhab, last month	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)	(0.0000)
Region specific time trend	Yes	Yes	Yes	Yes	Yes	Yes
Mobility × months	No	No	No	Yes	No	Yes
N. Obs	1177	1177	1144	1144	1144	1144

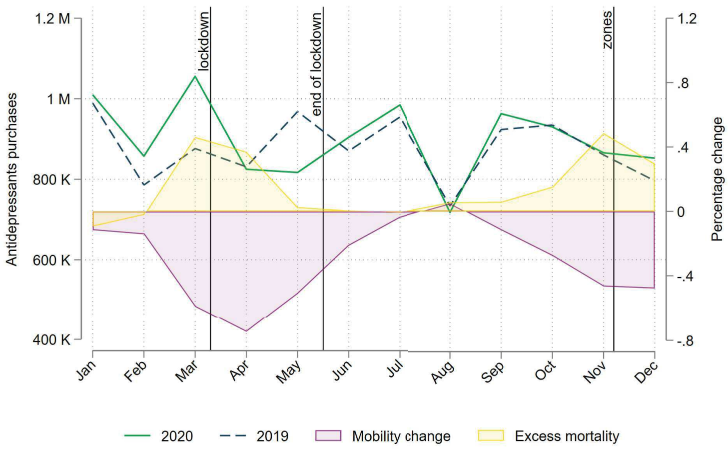
Notes: Robust standard errors in parentheses, * for p<.05, ** for p<.01, and *** for p<.001. The dependent variable is the percent variation with respect to 2019 of the monthly DDD of antidepressants purchased by Italian pharmacies at the Province level. February is the reference category. Coefficients for monthly dummies are increase or decrease with respect to the percent variation of purchases in February.

Figure 1. Monthly purchases of anxiolytics in standard units for 2020 and 2019

(a) Anxiolytics



(b) Antidepressants



Note: Average municipality-level drugstores' purchases in DDD per month, for 2020 (green solid line) and 2019 (blue dashed line) of anxiolytics (panel 1a, ATC code N05B) and antidepressants (panel 1b, ATC code N06A). The yellow shaded area reports monthly excess death in percentage change for 2020 with respect to the average number of deaths in the period 2015-2019, while the purple shaded area reports the average change in mobility with respect to mobility patterns in January 2020 (see Methods section for a detailed description of the mobility algorithm used). Vertical lines indicates the beginning and ending of the national lockdown and the creation of zones with differentiated mobility restrictions.
Source: Our calculation on IQVIA, Teralytics and ISTAT data.

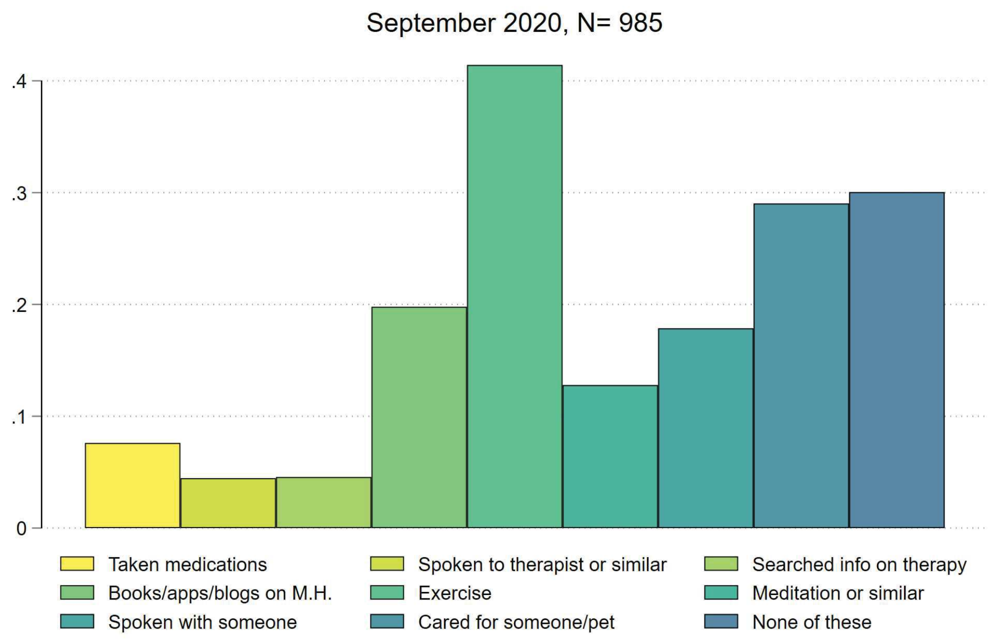
Discussion

The increase in purchases of anxiolytics and antidepressants during 2020 was only moderate compared to 2019 and mostly concentrated during the very early months of the pandemics (February and March). Furthermore, we show that, net of the national lockdown effect, region-specific trends in purchases in 2020, and the evolution of the virus spread in terms of contagion and mortality, there is no association between psychiatric drugs volumes and changes in mobility.

If mobility patterns effectively capture the heterogeneities in effective confinement and social distancing measures, the evidence of our analysis diverges from the prevailing findings in the literature pointing to a pronounced surge in the prevalence of anxiety and depression disorders[25]. This apparent mismatch may however be due to a number of concomitant practices and behaviors, whose final result is to lead to a downward bias in the marginal effect of COVID-19 restrictions on mental health. Below, we present and discuss these phenomena:

- *Stockpiling*. The trends in purchases we observe are in line with the stockpiling practices already documented by other studies during 2020, with consequences at different levels. On the one hand, if stockpiling behavior is adopted by healthcare providers, as was the case with U.S. hospitals in the early phases of the pandemic, it may lead to short-run shortages[26]. On the other hand, if adopted by consumers, stockpiling or "panic buying" with the scope of preventive consumption smoothing, is likely to cause uneven purchase patterns over time, as evidenced during the first COVID-19 wave in several product categories, including medicines[27], and antidepressants in particular[28]. This last practice seems to be more in line with what we document in March 2020, when we observe a pronounced peak of purchases, followed by a proportional reduction in April and May. This implies that a large portion of the increase in the *stocked* quantity did not reflect an equivalent real increase in the *demanded* quantity. As a matter of fact, purchased quantities in summer 2020 and during the second wave exceed only slightly those of 2019.
- *Compensatory behavior and defensive expenditure*. Adopting compensatory behaviors before engaging in psychiatric therapies might also be a reason for the mismatch between the perceived disruption in mental health condition and drug consumption. A number of these practices have become easily accessible online, with recent studies documenting mental health benefits accruing from access to mindfulness meditation apps[29], and increasing proportion of psychotherapy sessions delivered online during the lockdowns[30]. Support to the hypothesis of resorting to compensatory behaviors during 2020 can be found looking at the results of a study of the Imperial College London[31] on the adoption of a broad set of solutions to reduce stress and to improve mental health and mental wellbeing. Limiting the analysis to the Italian sample, Figure 2 shows that Italians frequently adopted self-care practices (e.g., physical exercise and meditation) and social connections, while resorting less frequently to medications, and even less to mental health professionals. Interestingly, the results for Italy are in line the rest of Europe (Figure A.2 in Appendix plots the respective evidence for other European countries studied). It is then clear that these behaviors play a role when we estimate the effect of COVID-19 mobility restrictions on mental health, by imposing an under-estimation of the true effect. At the same time, from a policy perspective, we should be able to account for both the benefits (lower drug costs) and the costs (of non pharmaceutical drug therapies) of compensatory behaviors, especially from the point of view of welfare implications. Under the assumption of defensive investments, there may be an important scope for economic incentives promoting such behavior.
- *Unexpressed and unmet needs*. Unexpressed needs originate from the demand side and are usually defined as unexpressed demand due to either a cultural reluctance in resorting to mental health professionals or very mild conditions that do not require pharmaceutical and medical therapies. On the contrary, unmet needs signal supply side problems. For example, it is possible that during the lockdown period patients may have either lost access to adequate mental health care (if already on therapy) or had difficulties in accessing it (if new patients)[32]. While we do not have clear evidence in favor or against the first hypothesis, for the second hypothesis we can find support in the results reported in the two graphs in Figure A.1 in Appendix, where we show the year-over-year monthly percentage change between 2019 and 2020 of both overall drugstore purchases and purchases of reimbursed prescription only drugs for anxiolytics and antidepressant. In particular, in graph A.1a we observe that the percentage change of reimbursable prescriptions for anxiolytics have been, except for March, below their 2019 levels. This stylized fact seems to point to a difficulty in the access to (reimbursable) prescriptions, which need a GP or specialist intermediation. In fact, drugstores' overall purchases have been consistently above their 2019 levels, pointing to the fact that patients may have partially resolved the problem using anxiolytics that do not require a prescription and thus a GP or a specialist visit (and may also signal mild mental health conditions). At the same time, we can safely rule out any stockpiling effect on the pharmacy side as they strongly rely on just-in-time management strategies for their purchases. This behavior is coherent also with the stockpiling hypothesis discussed above with the "panic buying" pattern observed in March followed by a sharp decrease in the following months, which is also observed in quantities sold via prescriptions.

Figure 2. Self-reported solutions for stress, mental health and mental wellbeing (Italian representative sample)



Note: Answers to the question: "In the past week have you done any of the following [to improve your stress, mental health or mental wellbeing]? Please tick all that apply."
Source: Our elaboration of data provided by Imperial College London YouGov COVID-19 Behaviour Tracker Data Hub[31]

A further proof of this hypothesis comes from the inspection of the antidepressants data (see Figure A.1b). In this case we see that the year-over-year monthly percentage change between 2019 and 2020 of both drugstores overall purchases and reimbursable prescription only drugs had very similar patterns, without showing a relevant mismatch. By comparing the rate of changes in both markets and given the different prescription rules governing anxiolytics and antidepressant we can infer that patients with already diagnosed chronic conditions (i.e. depression), might have encountered less obstacles in obtaining a prescription with a smooth continuation of their therapy, while new incident patients with non-chronic or episodic disorders (such as anxiety) may have either experienced more difficulties to access adequate mental healthcare services or not considered it at all (see point on Compensatory behavior), which should confirm the unmet need hypothesis. Clearly, if the first interpretation is correct, it is well possible that numerous new cases of depression have been overlooked and not yet targeted by formal care, as suggested by the sharp increase in December 2020 with respect to 2019, with patients resorting to non-pharmaceutical or non-medical interventions.

Methods

Data

Drugs. Data on anxiolytics and antidepressants are provided by IQVIA[1] and consist in anonymized data on the number of Defined Daily Doses (DDDs) purchased monthly by Italian drugstores at municipality level by ATC code (3 digit) and the amount sold via reimbursable prescriptions. For the purposes of this paper, we focus on drugs belonging to ATC codes N05B (anxiolytics) and N06A (antidepressants) sold from January 1^{st} 2019 to December 31^{st} 2020. The DDDs not sold via Reimbursable Prescriptions (R-Rx) is either sold via Non-Reimbursable Prescriptions (NR-Rx), over the counter, or kept as pharmacies' stock. However, given that for DDDs not sold via R-Rx we cannot observe the specific selling channel, we focus our analysis mainly on overall drugstore purchases. Additional details concerning the volume of DDD sold via reimbursable prescriptions are provided in the Appendix.

[1] https://www.iqvia.com

Mobility. We use mobility data collected by Teralytics[2], which gathers individual anonymized data from mobile phones for the providers Wind and 3 (approximately 30% of the Italian population). Teralytics provides the daily number of trips aggregated at the sub-Province level (between LAU1, i.e. NUTS3, and LAU2) in a dyadic form, from January 1^{st} to December 31^{st} 2020. Our data distinguishes trips according to the mean of transportation (road, train, plane and not classified) and to the reason for movement. In particular, we can identify the individual's place of residence as the place where (s)he regularly spends the night and subsequently labels trips according to their purpose, *home-to-work, home-to-other,...*.[3]

Let us define the number of trips from location l, $l = (1,...,L)$, on day of week d, $d = (1,...,7)$, and with purpose of trip p, $p \in${*home-to-work, home-to-other, work-to-home, work-to-other, other-to-home, other-to-work, others*}, as $V_{l,d,p}$. We then define the baseline $B_{l,d,p}$ as the average of $V_{l,d,p}$ in all weeks of January 2020 (e.g. the average number of home-to-work trips from the province of Milan to any other Province in all Mondays of January). The change in purpose-specific mobility with respect to the baseline is then defined as

$$V'_{l,d,p} = \frac{V_{l,d,p} - B_{l,d,p}}{B_{l,d,p}},$$

while we compute the 'Overall' mobility change as

$$V'_{l,d} = \frac{\sum_p V_{l,d,p} - \sum_p B_{l,d,p}}{\sum_p B_{l,d,p}}.$$

In order to have a common aggregation level across pharmaceutical and mobility data, we average daily mobility changes $V'_{l,d,p}$ and $V'_{l,d}$ at the month and Province (NUTS3) level.

Additional controls. Data on daily all-causes deaths and municipalities' population are provided by the Italian National Statistical Institute (ISTAT). We construct an indicator of excess mortality as the percent variation of the number of monthly excess deaths in each month of 2020 with respect to the average monthly number of deaths for the period 2015-2019. Data on daily COVID-19 cases are provided by the Italian Government, Department of Civil Protection and are used to compute a measure of per capita infections at month and province level.

Regression analysis

The outcome studied is the monthly percent variation of purchased DDDs of anxiolytics and antidepressant with respect to the same month in 2019 at province level. In order to investigate the relationship between these outcomes and the mobility variation compared to a pre-pandemic situation we used the following province level two-way fixed-effects model:

$$y_{it} = \beta m_{it} + \gamma_t m_{it} d_{it} + \mathbf{z}_{it-1}\theta + \mu_j d_j t + c_i + \tau_t + \varepsilon_{it} \qquad t = 3,\ldots,12 \tag{1}$$

where m_{it} is our mobility indicator for province i and month t, d_{it} dummy for the t-th month of 2020 (base category February), $\mathbf{z}_{it-1} =$ include both the one-period lagged excess mortality and COVID-19 cases per capita, $d_j t =$ is linear time trend for region j, with d_j being dummy for the j-th region, c_i is the province specific fixed-effect, τ_t is the month fixed-effect and ε_{it} is the usual idiosyncratic error term.

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[3] Data for the Friuli-Venezia Giulia region are provided at the sub-regional level and the unique Province for which data are identifiable is Trieste, the Regional County Seat. Therefore, mobility data are missing for the Provinces of Udine, Gorizia and Pordenone.

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Appendix

Table A.1. Drugstores' purchases of anxiolytics and antidepressant in Italy in 2019 and 2020 in DDD

	Drugstore's purchases	Reimbursable prescriptions	% not reimbursed	Pct Var purchases
		Anxiolytics (N05B)		
2019	481,098,516	36,687,947	92.37%	-
2020	502,369,453	35,099,829	93.01%	4.42%
		Antidepressants (N06A)		
2019	1,126,019,226	964,474,493	14.35%	-
2020	1,153,648,647	986,233,682	14.51%	2.45%

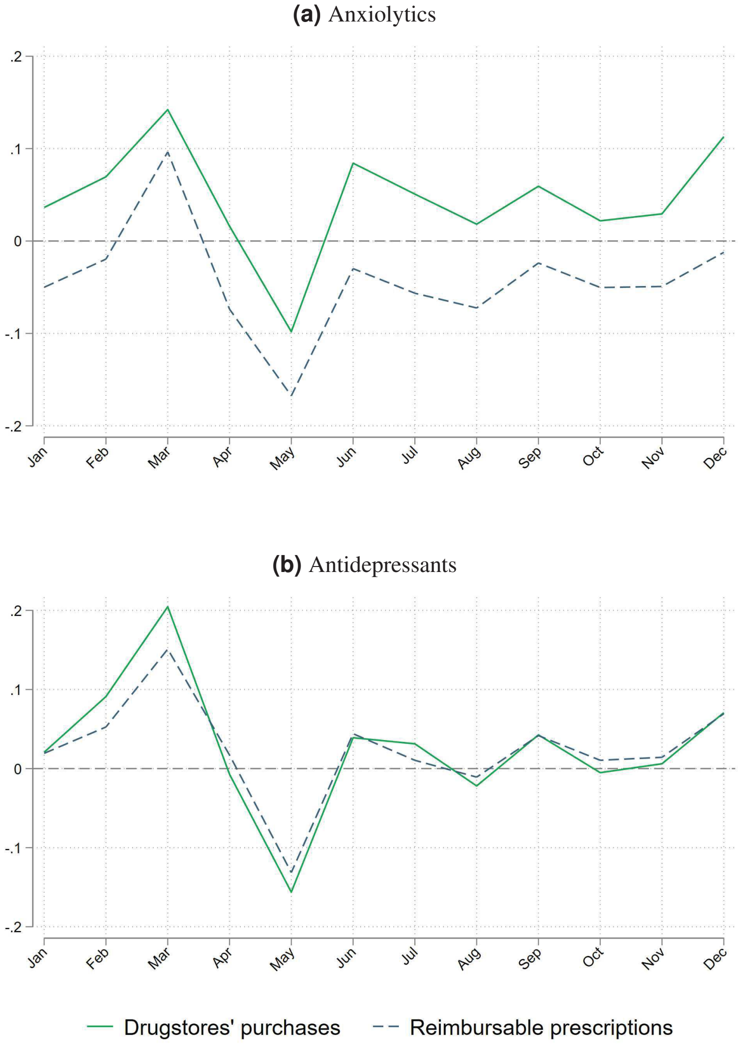
Notes: the amount not reimbursed is either sold via Non Reimbursable prescriptions (NR-Rx), over the counter or kept as pharmacies' stock. The percent variation between 2020 and 2019 is computed as $\frac{2020-2019}{2019} \cdot 100$, for drugstores' purchases only.

Table A.2. Differences in the average monthly purchases between 2020 and 2019

		A: Anxiolytics		
	2020	2019	δ	Pct Var
Jan	431,524.70	416,397.58	15,127.12***	3.85%
Feb	379,457.84	354,783.93	24,673.91***	6.51%
Mar	434,725.57	380,593.90	54,131.67***	14.38%
Apr	369,953.39	364,083.32	5,870.07*	1.13%
May	363,331.40	402,864.36	-39,532.96***	-9.50%
Jun	394,027.48	363,391.28	30,636.20***	9.91%
Jul	424,975.44	404,425.66	20,549.78***	5.74%
Aug	313,957.28	308,332.87	5,624.41**	1.36%
Sep	419,192.29	395,721.37	23,470.92***	6.30%
Oct	405,240.57	396,553.90	8,686.67***	2.84%
Nov	376,233.58	365,480.13	10,753.45***	3.12%
Dec	382,422.07	343,619.50	38,802.57***	10.58%
		B: Antidepressants		
	2020	2019	δ	Pct Var
Jan	1,009,613.67	989,128.88	20,484.79***	2.17%
Feb	857,378.65	785,791.0	71,587.57***	8.88%
Mar	1,055,734.24	876,379.77	179,354.48***	20.98%
Apr	824,951.24	830,934.79	-5,983.55	-0.73%
May	816,883.63	968,074.50	-151,190.87***	-15.00%
Jun	904,362.65	870,376.60	33,986.05***	4.75%
Jul	984,656.70	954,744.46	29,912.24***	3.30%
Aug	717,513.26	733,559.52	-16,046.26***	-2.02%
Sep	962,778.30	923,405.21	39,373.08***	4.81%
Oct	929,833.88	934,629.80	-4,795.93	0.00%
Nov	865,664.37	860,387.33	5,277.04	1.02%
Dec	852,392.45	796,132.21	56,260.24***	7.77%

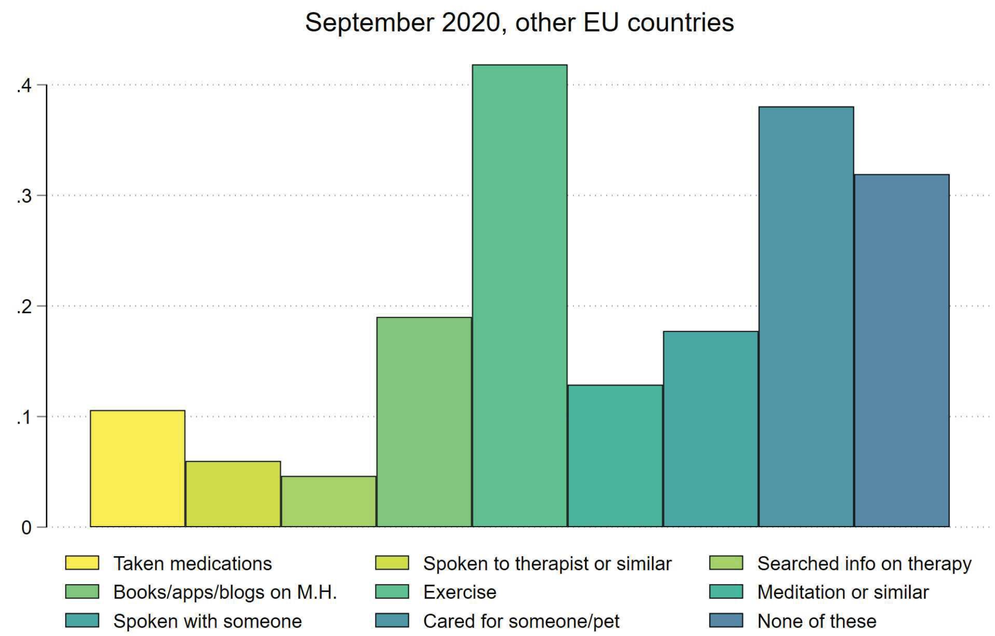
Notes: p-values from paired tests run on average drugs purchased at the Province level ,* for p<.05, ** for p<.01, and *** for p<.001.

Figure A.1. Monthly drugstores' purchases and reimbursable prescriptions of anxiolytics and antidepressants, percentage change between 2020 and 2019



Note: Monthly percentage change of drugstores' purchases (green solid line) and reimbursable prescriptions (blue dashed line) of 2020 with respect to the same month in 2019. Anxiolytics (panel A.1a) refers to ATC code N05B and Antidepressants (panel A.1b) to ATC code N06A.
Source: our elaboration of IQVIA data.

Figure A.2. Self-reported solutions for stress, mental health and mental wellbeing (other European countries)



Note: Answers to the question: “In the past week have you done any of the following [to improve your stress, mental health or mental wellbeing]? Please tick all that apply.” The sample includes all the European countries available, except Italy, i.e. Denmark, Finland, France, Germany, Netherlands, Norway, Spain, Sweden and United Kingdom ($N = 8,328$).
Source: Our elaboration of data provided by Imperial College London YouGov COVID-19 Behaviour Tracker Data Hub[31]

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